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Multi-modal exercise training and protein-pacing enhances physical performance adaptations independent of growth hormone and BDNF but may be dependent on IGF-1 in exercise-trained men☆

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ABSTRACT

Objective: Protein-pacing (P; 5–6 meals/day @ 2.0 g/kg BW/day) and multi-mode exercise (RISE; resistance, interval, stretching, endurance) training (PRISE) improves muscular endurance, strength, power and arterial health in exercise-trained women. The current study extends these findings by examining PRISE on fitness, growth hormone (GH), insulin-like growth factor-1 (IGF-1), and brain-derived neurotrophic factor (BDNF) response, cardiometabolic health, and body composition in exercise-trained men.

Design: Twenty active males (>4 days exercise/week) completed either: PRISE ($n = 11$) or RISE (5–6 meals/day @ 1.0 g/kg BW/day; $n = 9$) for 12 weeks. Muscular strength (1-repetition maximum bench and leg press, 1-RM BP, and 1-RM LP), endurance (sit-ups, SU; push-ups, PU), power (squat jump, SJ, and bench throw, BT), flexibility (sit-and-reach, SR), aerobic performance (5 km cycling time-trial, TT), GH, IGF-1, BDNF, augmentation index, (AIx), and body composition, were assessed at weeks 0 (pre) and 13 (post).

Results: At baseline, no differences existed between groups except for GH (RISE, 230 ± 13 vs. PRISE, 382 ± 59 pg/ml, $p < 0.05$). The exercise intervention improved 1-RM, SJ, BT, PU, SU, SR, 5 km-TT, GH, AIx, BP, and body composition in both groups (time, $p < 0.05$). However, PRISE elicited greater improvements in 1-RM BP (21 vs. 10 Δlbs), SJ (171 vs. 13 ΔW), 5 km-TT (−37 vs. −11 Δs), and sit-and-reach (5.3 vs. 1.2 Δcm) over RISE alone ($p < 0.05$) including increased IGF-1 (12%, $p < 0.05$).

Conclusions: Exercise-trained men consuming a P diet combined with multi-component exercise training (PRISE) enhance muscular power, strength, aerobic performance, and flexibility which are not likely related to GH or BDNF but possibly to IGF-1 response.

1. Introduction

The use of protein supplementation is commonly used to enhance muscle recovery and/or improve satiety. Recently, we demonstrated that a protein-pacing diet alone (P; 5–6 meals/day @ >1.4 g/kg body weight (BW) protein/day) [1] and when combined with a multi-mode (RISE; resistance, interval, stretching, endurance) exercise intervention (PRISE) results in greater reductions in total and regional (abdominal/visceral) fat mass, greater gains in lean mass, and enhanced cardiometabolic health compared to a combined protein-pacing and traditional resistance training intervention in obese/overweight women [2]. Following on this work, we recruited healthy, normal weight, exercise-trained women who were randomized to either a control (1.0 g/kg BW protein/day) or protein-pacing group (2.0 g/kg BW protein/day), and both groups completed 12 weeks of RISE exercise training [3]. Women consuming the protein-pacing diet (PRISE, 2.0 g/kg BW protein/day) exhibited significantly greater gains in muscular strength, endurance, power, and improvements in markers of cardiovascular health [3] compared to the RISE only (1.0 g/kg BW protein/day) intervention. Thus, in exercise-trained healthy, normal weight women, protein-pacing improves the adaptations to multi-modal exercise training.

Indeed, the majority of studies investigating the potential physical or performance benefit of protein supplementation have focused on men, specifically in acute and/or mono-modal exercise paradigms (e.g. resistance training or running), which have shown protein ingestion improves muscle recovery [4,5], enhances improvements in muscle mass [6] and/or exercise performance [7–9]. However, the most recent recommendations by the American College of Sports Medicine, suggest a comprehensive approach to exercise training, by including not only endurance exercise, but also resistance, flexibility, and neuro-motor

☆ This study was registered with ClinicalTrials.gov Identifier: NCT02593656.

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training [10]. Taken together with the progression of the fitness field towards a more multi-modal paradigm, understanding the potential benefit of elevated protein intake in this context is paramount. Additionally, while protein-pacing has been demonstrated to increase muscle protein synthesis [11,12], the purported mechanisms responsible for the enhanced response to multi-modal training with elevated protein intake, such as enhanced anabolic hormonal milieu (i.e. growth factors), remain relatively unexplored.

It is well recognized that growth factors such as growth hormone (GH), insulin-like growth factor-1 (IGF-1), and brain derived neurotrophic factor (BDNF) and their receptors are key regulators of neuromuscular development [13]. Indeed, recent work has found that both acute and chronic exercise increases anterior pituitary activity and GH release, suggestive of a prominent role of the endocrine system in muscular adaptations [14]. However, recent work has suggested that circulating levels of growth factors might not reflect functional changes in muscle (i.e. strength) [15], perhaps depending more upon neurological development [16] or the biological compartment being explored [17]. As much of the previous work has focused on the response to monomodal resistance exercise training, coupled with mounting controversy over whether circulating hormones reflect functional changes (i.e. strength, power, etc.), further work is needed to determine if circulating anabolic factors might explain the adaptations to training.

Accordingly, the primary aim of the present study was to compare the response to the multi-modal RISE training in healthy active men consuming either a normal protein (RISE, control group) intake versus a higher protein intake (PRISE) on fitness-related performance, cardiovascular, metabolic, and hunger/satiety outcomes, as well as blood levels of GH, IGF-1, and BDNF. We hypothesized that 1.) RISE would improve fitness, cardiovascular health, metabolic markers, and hunger/satiety, and 2.) Such improvements would be enhanced in the protein supplemented (PRISE) group, perhaps mediated by greater anabolic signaling, as measured by GH, IGF-1, and BDNF.

2. Methods

2.1. Participants

A total of 63 men from the Saratoga Springs, NY area, responded to emails, flyers and local newspapers to advertisements and were initially screened, of which 30 were eligible for participation (Fig. 1). Participants were nonsmoking, healthy, physically active men with no known cardiovascular or metabolic diseases as assessed by a medical history and a comprehensive medical examination. Specifically, all participants were highly active (minimum of >30 min, 4 day/week of structured physical activity), normal weight (BMI < 25 kg/m^2; % body fat ≤ 30%), middle aged (25–55 years), and weight stable (±2 kg) for at least 6 months prior to the beginning of the study. All participants provided informed written consent prior to participation, and the study was approved by the Institutional Review Board of Skidmore College (IRB#: 1401-382). All experimental procedures were performed in accordance with the Federal Wide Assurance and related New York State regulations, which are consistent with the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and in agreement with the Helsinki Declaration as revised in 1983. This study was registered with ClinicalTrials.gov Identifier: NCT02593656.

2.2. Experimental design

2.2.1. Study timeline

Participants were randomly assigned to one of two groups: (1) protein pacing and multi-mode exercise training (PRISE; n = 12; 5–6 meals/day @ 2.0 g/kg BW/day) or (2) normal protein and multi-mode exercise training (RISE; n = 14; 5–6 meals/day @ 1.0 g/kg BW/day). All participants performed the same RISE exercise training program consisting of 4 days/week of closely supervised and monitored progressive exercise training for 12 weeks (see previous references [2,3]). All testing procedures (see below) were administered pre-intervention (week 0) and post intervention (week 13) unless noted otherwise. Upon arrival at the laboratory, anthropometric and body composition measurements and blood sampling for subsequent analysis were performed.

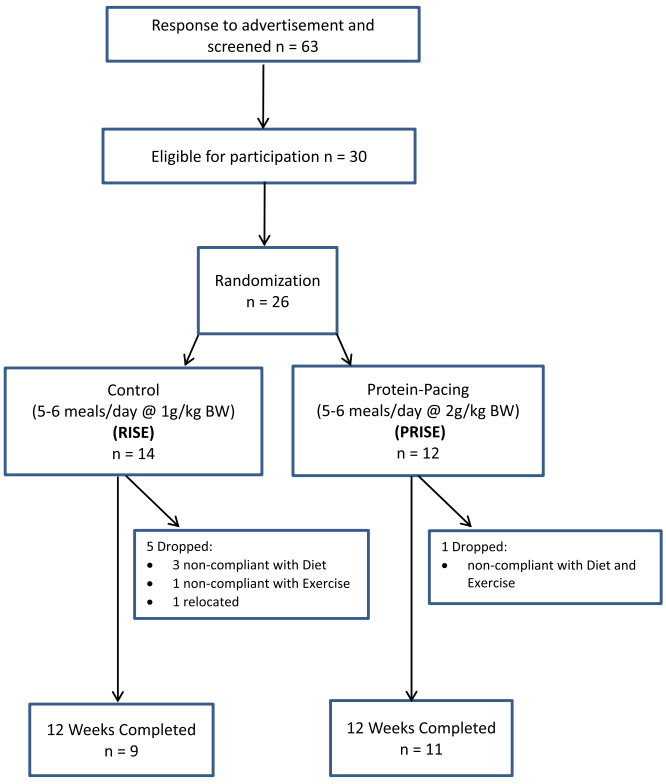

Fig. 1. Subject recruitment, enrollment, and assignment procedures.

2.3. Nutrition intervention

Meal plans were identically matched in terms of total kcals, meal frequency and timing and dietary support. By design, the only differences between the two groups was the amount of protein (1.0 vs. 2.0 g/kg BW per day). Additional supplementation (daily multi-vitamin/minerals, and caffeine and electrolytes on workout days) was also provided to participants and differed only by the type of product manufacturer. Participants in both groups were provided detailed meal plans designed by a registered dietitian and instructed to follow the meal plans throughout the 12-week intervention (Table A1). The registered dietitian met with participants weekly for the first two weeks and thereafter on an "as needed" basis. In addition, investigators met with participants a minimum of 4 day/week to answer questions and reinforce compliance to meal plans. To facilitate adherence to the meal plans, food was provided to both groups. It's important to note that the protein dosing was equivalent to >0.25 g/kg BW per meal which has been shown to be the optimal intake for muscle protein synthesis [18]. By study design, the only macronutrient that was intentionally different between groups was the protein per kg BW. Participants in both groups were given a 1-week. supply of the supplements and asked to return empty packets before they received the next week's supply as a means of assessing their compliance. Both groups were provided equivalent nutritional support and similar caloric intakes throughout the 12 week intervention.

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