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The influence of age and exercise modality on growth hormone bioactivity in women

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A B S T R A C T

Objective: Prior research has indicated that the loss of skeletal muscle mass and bone mineral density observed with aging is related to the prominent age-related decline in the concentration of serum growth hormone (GH). However, there is limited data on the effects of aging on GH responses to acute bouts of heavy resistance exercise (HRE) and aerobic exercise (AE).
Design: The present investigation examined the effects of a HRE protocol and an AE protocol on immunoreactive GH (IGH) and bioactive GH (BGH) in active young and old women.
Results: Older women had a diminished serum IGH response to both the HRE and AE protocols compared to the younger women, however a similar response was not observed in serum BGH. Additionally, the HRE protocol elicited a greater BGH response than the AE protocol exclusively in the younger group.
Conclusions: Regardless of exercise mode, aging induces an increase in growth hormone polymerization that specifically results in a loss of serum growth hormone immunoreactivity without a concurrent loss of serum growth hormone bioactivity. The greater BGH response to the HRE protocol found in the younger group can be attributed to an unknown serum factor of molecular weight between 30 and 55 kD that either potentiated growth hormone bioactivity in response to HRE or inhibited growth hormone bioactivity in response to AE.

1. Introduction

Human aging results in a profound, often clinically significant, loss of skeletal muscle mass and bone mineral density [1]. The prominent age-related decline in the concentration of serum growth hormone (GH), considered important for skeletal muscle and bone maintenance [2], may be a major factor in the loss of these two tissues throughout adulthood [3]. Experimental evidence from spaceflight, a commonly used model for aging, has demonstrated severe skeletal muscle and bone loss [4]. Exposure to microgravity also suppresses immunoreactive GH (IGH) secretion from rat pituitaries, a biological response thought to be similar in some respect to human aging [5]. The microgravity-induced reduction in IGH secretion from rat somatotrophs is accompanied by a correspondingly larger reduction in BGH secretion, particularly in those GH variants of high molecular weight [5]. Heterogeneity of GH variant families, particularly those of molecular weights greater than the 22 kD monomeric form of the hormone, have been postulated to explain at least part of the dichotomy between GH measurements made by immunoassay versus bioassay [5,6]. The numerous parallels in physiological outcomes documented between aging and spaceflight give rise to the possibility that non-immunoreactive high molecular weight forms of circulating GH may also be disproportionately reduced with age.

In contrast, physical exercise is one of the most potent of all natural stimuli known to release IGH from the pituitary [7]. Serum IGH has been shown to be dramatically elevated in response to an acute bout of heavy resistance exercise (HRE; high force/low repetitions) [8,9] as well as with an acute bout of aerobic exercise (AE; low force/high repetitions) [10]. Although the serum IGH response has been suggested to reflect one possible mechanism by which HRE training exerts its unique and potent anabolic effect on skeletal muscle and bone tissue [9], the fact that serum IGH concentrations are similar after HRE and AE undermines this in that AE training cannot compare to HRE training in magnitude of muscle and bone growth [11]. Since the physiological outcomes of HRE training directly contrast with both aging and spaceflight [11]; one

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potential mechanism that may play a key role in explaining the relatively greater increases in skeletal muscle mass, strength, and bone mineral density seen with HRE over AE could be a higher serum BGH response caused by selectively affecting high molecular weight GH variants.

Although the bioactivity of GH is generally considered to be of primary importance for the maintenance of bone and muscle tissue, serum BGH concentrations have not, to our knowledge, been compared in humans with respect to aging or exercise mode. Since the effect(s) of human aging on serum BGH concentrations remains largely uninvestigated, the primary purpose of this study was to test ideas a) that circulating BGH concentrations in older test subjects, relative to those of younger subjects, would be reduced; and b) that a regimen of HRE would result in a greater BGH response than AE.

2. Materials and methods

2.1. Subjects

Nine young and eight older healthy, active women participated in this investigation. Subjects' physical characteristics, together with peak aerobic capacity and strength measures, are presented in Table 1. This investigation was approved by the Institutional Review Board for the Use of Human Subjects at The Pennsylvania State University. All subjects were required to sign written informed consent documents prior to their participation. To ensure toleration of exercise protocols, subjects were required to have been actively participating in moderate physical activity (i.e. jogging, circuit resistance training) at least 2–3 times per week for a minimum of three months prior to the investigation. Additionally, as a rat tibial line bioassay was used in this study all procedures using animals for the bioassay were also approved by the Pennsylvania State University Institutional Animal Care and Use Committee.

All subjects were screened by a physician and found to be healthy and free of any orthopedic, metabolic, or endocrinological disorder. Menstrual status was assessed by a questionnaire and the possibility of pregnancy was further ruled out by measurement of resting serum immunoreactive human chorionic gonadotropin (hCG). Early follicular phase was verified by the determination of luteinizing hormone, estradiol, and progesterone concentration in pre-exercise blood samples. Since estrogen administration can falsely elevate serum IGH concentration in women [12], persons using hormonal supplements (i.e., birth control pills or estrogen replacement therapy) were not admitted to the study. Finally, subjects using tobacco products were also excluded from participation.

2.2. Experimental design

A randomized, counterbalanced experiment with crossover design was employed for this investigation. Subjects first underwent an initial medical screening visit which included assessment of peak aerobic capacity performance. After medical clearance and acceptance into the study, subjects attended a HRE protocol familiarization visit which included assessment of 1-repetition maximum (1RM) and an aerobic exercise (AE) familiarization visit. Familiarization visits were conducted in randomized order with a minimum of 72 h of rest in between. Following familiarization, each subject participated in two experimental sessions. These were done at exactly the same time of day (0830 h), but separated by one month (phased during the early follicular phase in the younger subjects). During each experimental session, subjects performed either an acute bout of aerobic exercise (AE) or heavy resistance exercise (HRE) both consisting of an 8-min warm-up period followed by a 45-min main workout. The AE and HRE protocols were designed to elicit significant blood IGH responses in both subject groups while avoiding the nausea that sometimes accompanies an HRE workout with short rest periods [8,9,13,14]. Since both AE and HRE training status can differentially affect the IGH response to acute exercise when comparing younger versus older men and women [13,15], no changes in subjects' frequency, volume, or intensity of physical activity patterns between experimental sessions were allowed.

Table 1
Physical characteristics, peak aerobic capacity, and one-repetition maximum (1RM) strength (mean ± 1 SEM) of the two experimental groups.

	Young	Old
Age (yrs)	23.7 ± 1.0	61.6 ± 1.3[a]
Height (cm)	164.7 ± 2.0	159.8 ± 2.9
Body mass (kg)	57.2 ± 2.7	59.6 ± 2.8
Peak aerobic capacity (ml/kg/min)	38.2 ± 1.8	24.1 ± 1.1[a]
Bench press 1RM (kg)	35.7 ± 1.8	24.4 ± 0.9[a]
Leg press 1RM (kg)	108.8 ± 7.3	75.3 ± 4.3[a]

[a] Significant ($p \leq 0.05$) effect of age for specified variable.

2.3. Aerobic exercise protocol

Subjects performed the AE experimental visit on a cycle ergometer (Monark Ergometer Model 818E, Monark AB, Varberg, Sweden) pedaling at 60 revolutions per min. The 8-min warm-up period consisted of two 4-min periods of pedaling at 30% and 50%, respectively, of the workload eliciting the subject's pre-determined peak aerobic capacity. At the end of the warm-up period, the intensity was immediately increased to 70% of the subject's peak aerobic capacity and the subject continued pedaling at this intensity for exactly 45 min. For determination of oxygen uptake, expired gases were measured throughout the exercise test via a metabolic cart (Applied Electrochemistry S-3A oxygen analyzer, Beckman LB-2 carbon dioxide analyzer, and Hans Rudolph pneumotach) with continuous on-line data reduction software capabilities (Physio-Dyne, Inc.). Peak aerobic capacity was assessed as the highest oxygen consumption values within any two consecutive 30-s sampling periods.

2.4. Heavy resistance exercise protocol

The HRE experimental session exercise protocol is shown in Table 2. Due to the large muscle mass involved, the leg press station was repeated in this sequence in an attempt to increase the metabolic stimulus and avoid a total lack of IGH response sometimes observed in older individuals in response to HRE [14]. 10-RM resistances were estimated for each exercise to be performed during the HRE experimental session protocol based on preliminary 1RM tests [16]. The resistance was lowered slightly from the 10-RM value if the subject was unable to complete 10 repetitions at that exercise during the previous circuit. Resistance exercises were performed on a Universal weight machine (Universal Equipment, Omaha, NE).

2.5. Experimental sessions

The timeline of both experimental sessions can be seen in Fig. 1. After arriving at the laboratory, seated subjects were cannulated with a 20-gauge Teflon cannula positioned in a superficial antecubital vein. Subjects sat quietly for 10 min before a pre-exercise (Pre-Ex) blood sample was drawn then proceeded directly into the warm-up period

Table 2
Overview of heavy resistance exercise (HRE) protocol.

Exercise	Circuit 1	Circuit 2	Circuits 3–5
Leg press	50% 1RM × 5	75% 1RM × 5	75% 1RM × 10
Bench press	50% 1RM × 5	75% 1RM × 5	75% 1RM × 10
High pull	50% 1RM × 5	75% 1RM × 5	75% 1RM × 10
Leg press	–	–	75% 1RM × 10
Shoulder press	50% 1RM × 5	75% 1RM × 5	75% 1RM × 10
Calf press	50% 1RM × 5	75% 1RM × 5	75% 1RM × 10

% 1RM, percentage of one repetition maximum; X #, Number of target repetitions.