Oral amino-acid provision does not affect muscle strength or size gains in older men

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ABSTRACT

GODARD, M. P., D. L. WILLIAMSON, and S. W. TRAPPE. Oral amino-acid provision does not affect muscle strength or size gains in older men. Med. Sci. Sports Exerc., Vol. 34, No. 7, pp. 1126–1131, 2002. Purpose: The intent of this investigation was to examine the effects of a daily oral provision consisting of amino acids (L-lysine, L-leucine, L-valine, L-phenylalanine, L-threonine, L-histidine, L-isoleucine, and L-methionine) in combination with carbohydrates (dextrose, sucrose, and fructose) on whole muscle strength and size characteristics during a 12-wk progressive knee extensor resistance training (PRT) program in older men (>65 yr). Methods: Seventeen older men were randomly assigned to either the experimental (EX) or control (CN) groups. The EX (N = 8) and CN (N = 9) groups had the following characteristics—EX: 70.8 ± 1.5 yr, 91.0 ± 4.9 kg, and 177.0 ± 3.9 cm; CN: 72.1 ± 1.9 yr, 75.4 ± 4.7 kg, and 176.1 ± 3.0. Pre and post PRT maximal unilateral isometric torque (N·m), isokinetic torque (1.05, 1.57, 2.09, 3.14, 4.19, and 5.24 rad·s−1), work capacity (30 consecutive reps at 3.14 rad·s−1) torque, one repetition maximum (1RM) bilateral isokinetic strength, and whole muscle cross-sectional area (CSA) of the mid-thigh were performed by computed tomography on each subject. Results: All variables showed and improvement with training (P < 0.05); however, there were no differences between the groups. Both groups increased in isometric strength by 21%, and isokinetic torque by 24% to 11% with the varying velocities (1.05–5.24 rad·s−1). Whole muscle 1RM strength and thigh CSA increased 50% and 6.5%, respectively. Additionally, voluntary torque/CSA increased 12% in both the EX and CN groups (P < 0.05). Conclusion: In conclusion, these data suggest that whole muscle strength and size are not enhanced with a postexercise daily provision of an oral amino-acid complex during 12 wk of PRT in older men. Key Words: AGING, COMPUTED TOMOGRAPHY, ISOMETRIC, ISOKINETIC, ISOTONIC

The effects of a knee extensor progressive resistance training (PRT) program on whole muscle strength and size in older men has been well established throughout the past two decades (13). It is known that there is an increase in both muscle protein synthesis (2,4,5,11,14,21) and breakdown (2,11) after exercise although the net muscle protein balance increases. The balance remains negative when the subjects are not fed (2). In older individuals (>60 yr old), there is a decrease in the myofibrillar and total muscle protein synthesis rate (17–19,21), which is thought to be a major contributor to sarcopenia, characteristic of aging adults.

Studies by Tipton et al. (15) and Rasmussen et al. (12) have found that orally ingested amino acids administered immediately after resistance exercise resulted in a net positive muscle protein balance. Due to lower protein synthesis rates in older adults and the negative muscle protein balance that is known to persist after exercise, oral provision of amino acids with carbohydrate administered immediately after resistance exercise (on the exercise days) may enhance muscle protein synthesis during resistance training due to hyperaminoacidemia and/or hyperinsulinemia. However, a recent investigation (16) found that carbohydrate administered with essential amino acids might result in diminished protein turnover by inhibiting protein breakdown and, as a result, suppress protein synthesis via amino acids.

A recent investigation (7) examined the timing (immediately postexercise and 2 h postexercise) of postexercise (resistance training) protein intake on muscle hypertrophy and strength in older men (74 ± 1 yr). The results of this study indicated that only the group that consumed the protein provision immediately postexercise demonstrated significant increases in muscle hypertrophy after 12 wk of progressive resistance training. A limitation of the this study (7) was the lack of a control group (i.e., a group that did not consume any oral protein provision postexercise); as a result, it is difficult to determine whether the differences that were observed in the timing of the postexercise protein intake were due to the provision or to some other unknown variable. The purpose of this current investigation was to examine the effects of the consumption of daily oral amino acids in combination with carbohydrates on whole muscle strength and size during a 12-wk knee extensor PRT program in older men (65–85 yr of age). We hypothesized the following: 1) both groups will demonstrate significant increases in whole muscle strength and size after PRT, and 2) the experimental group (consuming the daily solution immediately post resistance exercise on those days) will demonstrate greater whole muscle strength and size gains as compared with the control group.

It was our intent to determine whether a mixture of essential amino acids and carbohydrates (refer to methods) administered immediately post resistance exercise would augment muscle strength and size in older men with a PRT
program as was demonstrated in previous acute resistance training studies with younger adults (12,15). These hypotheses were proposed and initiated before the publication of Volpi et al. (16) and Esmarck et al. (7).

METHODS

Subjects

Seventeen older men between the ages of 65 and 80 participated in the study. The older men were randomly assigned to either the experimental (N = 8) or control (N = 9) group, refer to Table 1 for subject characteristics. Before any testing each subject was interviewed by a member of the investigation team to determine the subject’s eligibility based on the following criteria: 1) subjects were nonobese (BMI ≤ 28 kg·m−2), 2) normotensive, 3) with no formal weight training, 4) free of cardiovascular (a resting and exercise electrocardiograph was performed on all subjects) and musculoskeletal abnormalities and/or limitations due to previous injuries or conditions, and 5) nonsmokers. Before initiating the study, all volunteers were informed of all the procedures and risks associated with the study and signed an informed consent in accordance with the Ball State University and Ball Memorial Hospital Institutional Review Boards.

Drink Composition and Dietary Recall

The control group received no provision during the study, but completed all testing and training in the same order and fashion as the experimental group. The experimental group orally consumed an amino-acid drink everyday throughout the PRT program consisting of 12 g of essential amino acids and 72 g (total) of fructose and dextrose dissolved in 400 mL of water. Specifically, the essential amino acids consisted of L-lysine (1.86 g), L-leucine (2.24 g), L-valine (1.40 g), L-phenylalanine (1.86 g), L-threonine (0.38 g). On the days that the subjects reported to the laboratory for training (as described below), they were administrated the oral provision immediately after the training session and consumed the provision in the presence of a member of the investigative team. On the days that the subjects did not report to the laboratory for training, they consumed the oral provision independently at the same time each day.

A 3-d dietary analysis was performed on all subjects pre, mid, and post during the study. The subjects were asked to record everything in detail that they consumed (food and liquid) for 3 d (Sunday, Monday, and Tuesday). A nutritional software program (The Food Processor v. 7.0, Esha Research, Salem, OR) was used to assess and analyze the amount of daily calories, carbohydrate, protein, and fat from the dietary recall.

Training Regimen

A member of the investigative team supervised all training sessions (one on one). Subjects warmed-up at a low intensity (25–50 W) on a cycle ergometer for 5–10 min then performed bilateral isotonic knee extensions on a Cybex Eagle (Ronkonkoma, NY) device. The first two sets consisted of 10 repetitions, and the last set was performed to volitional exhaustion. All sets were performed at 80% of the one repetition maximum (1RM); this was reassessed every two weeks in an effort to maintain the intensity (80% of 1RM). The training was conducted 3 times a week for 12 wk with a minimum of 24 h off between training sessions.

Isometric and Isokinetic Measurements

Before any strength evaluations, the volunteers warmed up on a cycle ergometer for 5–10 min at low intensity (25–50 W). Unilateral maximal voluntary isometric (60° knee extension) and concentric strength of the right knee extensors was evaluated using a Cybex 340 Dynamometer. Subjects were evaluated for all parameters on the same day. While seated (85° hip flexion), they applied force to a cushioned lever arm positioned anteriorly on the ankle attached to the dynamometer. The axis of the dynamometer lever arm was aligned with the knee joint axis. Restraints were applied on the thigh, leg (proximal to the right lateral malleolus), pelvis, and shoulders. Range of motion was individually determined with full knee extension (~0°) and flexion (~110°). A gravity correction factor was calculated by the instrumentation to account for leg mass and weight of the lever arm. After physical screening, each subject participated in at least two orientation sessions to familiarize them with the dynamometer and all testing procedures. Measurement reliability of the strength parameters was determined on three subjects that were retested approximately 1 wk after their pretesting session. Coefficient of variation was determined at 2.2% for the test-retest reliability for both the isometric and isokinetic strength measures. Subjects were monitored and supervised during all testing sessions. The testing protocol was as follows.

Isometric. This step in the testing procedure involved applying a maximal torque in a stationary position. The knee angle was fixed at 60° (with neutral representing 90°). Subjects performed a two maximal voluntary contractions (MVC), with the subject applying as much torque as possible for 5 s at the test angle; two trials were performed for each maximal effort with the best effort for the maximal test being utilized for analysis.

Isokinetic. The isokinetic testing was employed at six different concentric velocities (1.05, 1.57, 2.09, 3.14, 4.19, and 5.24 rad·s−1). Three warm-up repetitions (~50% effort) were performed to allow the subject to regain familiarity with the test velocity. After a brief rest period (20 s), three maximal repetitions were performed with the peak torque of the three maximal contractions being utilized for analysis. Each velocity tested was separated with a 45-s rest period.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td>70.8 ± 1.5</td>
<td>91.0 ± 4.9</td>
<td>177.0 ± 3.9</td>
</tr>
<tr>
<td>Control</td>
<td>72.1 ± 1.9</td>
<td>75.4 ± 4.7</td>
<td>176.1 ± 3.0</td>
</tr>
</tbody>
</table>
To ensure that significant fatigue of the knee extensors was not occurring throughout the protocol, the isometric MVC was performed at the conclusion of the protocol and compared with the initial value that was achieved by the subject. A paired t-test revealed no significant differences before and after the test sessions for both pre to post PRT testing measurements.

**Work capacity.** Thirty consecutive maximal isokinetic muscle contractions were performed at 3.14 rad·s$^{-1}$ to assess the total work that the subjects could perform at this velocity. The subjects performed the 30 maximal repetitions with the total work from all of the maximal contractions being utilized for analysis.

**1-Repetition Maximum (1RM)**

Whole muscle strength was also assessed with a bilateral isotonic knee extensor device (Cybex Eagle). The resistance was increased in 2.6- to 5.2-kg increments until the subject was unable to lift the load to full knee extension. This evaluation was performed pre strength training, every 2 wk during the 12-wk progressive strength-training program and post strength training.

**Whole Muscle Cross-Sectional Area**

Whole muscle cross-sectional area (CSA) of the right thigh was determined with computed tomography (CT) (CTI helical scanner, General Electric, Milwaukee, WI). The circumference of the anatomical midpoint of the femur was used as the point of CT measurement. Subjects were supine with the legs in an anatomical position (feet were taped together) for 15 min before any scanning to minimize the influence of fluid shifts on the CSA measurement (9). An initial lower body scout scan of the right leg was taken to determine the length of the femur from the greater trochanter to the lateral epicondyle at an angle of 0°. Scan width was set at 5 mm with an exposure time of 3 s to enhance resolution quality. The image and its associated scale were then printed on a standard imaging transparency and were transferred to a computer using a flatbed scanner. CSA of the thigh minus the area of the bone and subcutaneous fat was determined using computerized planimetry (NIH Scion Image Program (Windows 98 version)). To ensure the accuracy of the CT measurement, bone area was analyzed and recorded for all subjects (pre and post scan). This allowed us to ascertain objectively the exactness of the scanning location on the right thigh in combination with the scanning software, which allowed for replication of the location pre to post scan. Our results indicated that there was less than 0.1% difference in the bone area between the two scans. This was under the assumption that there was no change in bone size and/or bone mineral density as reported by others (6,10). Furthermore, the CSA measurements were utilized in conjunction with the maximal unilateral voluntary isometric torque measurement (voluntary torque/CSA) to estimate a specific tension of the musculature involved.

**Statistics**

Analysis of variance (ANOVA) with repeated measures was applied to the isokinetic torque followed by post hoc tests for simple effects and interaction and simple contrasts as appropriate. Therefore, separate ANOVA with repeated measures were performed on each dependent variable. Paired t-tests were applied for bilateral isotonic 1RM and CSA to detect significant differences between pre and post PRT measurements. Additionally, fatigue of the testing protocol was examined with at the beginning and end of the testing session (pre and post PRT). Results were considered significant at $P < 0.05$. All data are presented as mean ± SE.

**RESULTS**

**Whole muscle strength.** Knee extensor isometric MVC increased from 178 ± 13 to 221 ± 15 N·m (24 ± 3% increase) and 172 ± 12 to 205 ± 15 N·m (19 ± 4% increase) as a result of the PRT program in the experimental and the control groups, respectively. These increases were significantly increased pre to post PRT ($P < 0.05$) but there were no differences between the groups. The isokinetic peak torques of the knee extensors increased ($P < 0.05$) for both the experimental and control groups on average 21 ± 6% and 17 ± 5%, respectively, for the velocities tested (Fig. 1), although there were no differences between the groups. One repetition maximum (1RM) increased approximately 30 kg ($P < 0.05$) in both the experimental and control groups with the PRT, no differences were observed between the groups, and the experimental and control groups had a 46 ± 7% and 53 ± 6% increase, respectively.

There were no differences between the two groups with respect to the knee extensor work capacity test (30 maximal contractions at 3.14 rad·s$^{-1}$) that was performed pre and post PRT.
examined muscle protein synthesis and breakdown after an acute bout of resistance exercise (1,2,11,12,15), and Welle and his colleagues (17) have examined the effects of 3 months of resistance training on protein synthesis in both young and old humans; however, there have been no studies to date that have investigated the whole muscle parameter effects of oral amino-acid provision in older men with 12-wk of PRT.

A recent investigation by Welle et al. (20) examined the effects of low (7%), normal (14%), and high (28%) protein meals on myofibrillar synthesis after acute resistance exercise in sedentary older men and women (62–75 yr). At rest, there were no differences in the myofibrillar synthesis between the three groups, and after the resistance exercise the synthesis was approximately 27% faster in all of the groups. These authors concluded that a high protein meal does not increase myofibrillar protein synthesis induced by resistance exercise. Although this study examined only the acute effects of resistance training on myofibrillar protein synthesis in older adults, the authors’ conclusions complement our findings that oral amino-acid provision with a 12-wk PRT program does not enhance whole muscle strength or size in older men. Welle et al. (20) administered 4.5, 9.0, and 18.0 g of protein per meal for the 6.5 h after the acute resistance-training bout (feedings every 30 min). The investigation by Welle et al. (20) and the current study are in disagreement with other acute resistance training studies (1,2,12,15) finding that amino-acid supplementation (oral or infused) enhances muscle protein synthesis.

The differences in the results of the current investigation and other studies are most likely related to methodological differences. In particular, differences in the study populations, the duration and frequency of the resistance exercise (12-wk training protocol compared with a single bout of resistance exercise), and the specific amino-acid mixture that was shown to be effective in these other studies (1,2,12,15) may have accounted for the discrepancies. Our study consisted of older men (average age 72 yr), whereas the subjects in the other studies (1,2,12,15) were young men and women (~27 yr). Recently, it was found that muscle protein anabolism is impaired in response to hyperamino-acidemia and endogenous hyperinsulinemia due to the unresponsiveness of protein synthesis in older adults (16). Thus, older adults may have alterations in their metabolic responses that impair certain responses to exercise.

Dietary protein intake has also been shown to influence skeletal muscle responses to resistance training. It has been demonstrated that older adults can increase their muscle strength and size consuming 1.1 g protein·kg⁻¹·d⁻¹ with no additional benefits observed if individuals consumed 1.6 g protein·kg⁻¹·d⁻¹ (3). In the present investigation, both the

**DISCUSSION**

The primary findings of this investigation were that a daily oral amino-acid provision in older men (70.8 ± 1.5 yr) provided no additional benefits to whole muscle strength and size compared with a control group (72.1 ± 1.9 yr) after a 12-wk knee extensor PRT program. Several studies have post PRT. The experimental group increased 24% and the control group increased 18%, both of which were significantly greater with the training ($P < 0.05$).

**Whole muscle CSA.** Computed tomography analysis of the muscle CSA increased ($P < 0.05$) after the 12-wk PRT in both the experimental (144.9 ± 6 to 155.0 ± 6 cm²) and control (134.0 ± 8 to 142.2 ± 8 cm²) groups (Fig. 2). This equates to a 7 ± 2% and 6 ± 1% increase in muscle size in the experimental and control groups, respectively. The increases between the groups were not significantly different from each other. The specific tension of the knee extensors was also examined with the use of the voluntary MVC and CSA data. The voluntary torque/CSA ratios increased from 1.22 ± 0.1 to 1.42 ± 0.1 (14 ± 0.1%) and from 1.28 ± 0.1 to 1.44 ± 0.1 (11 ± 0.1%) pre to post PRT ($P < 0.05$), in the experimental and control groups, respectively. Similarly to the CSA increases between the groups, there were no differences between the groups with respect to the specific tension analysis.

**Dietary analysis.** No differences were found in protein, carbohydrate, or fat at any of the three time points (pre, mid, and post PRT) between or within the groups (refer to Table 2).

**FIGURE 2**—Pre (□) and post (▲) PRT cross sectional area of the right thigh for the experimental ($N = 8$) and control ($N = 9$) groups. Data points represent means, and standard errors are expressed as error bars. There were statistically significant increases ($P < 0.05$) pre to post PRT within the groups but no differences between the groups.

![Cross-sectional area graph](image)

**TABLE 2.** Dietary analysis for both the experimental and control groups for pre (week 0), mid (week 6), and post (week 12) PRT; data are represented ± SE.

<table>
<thead>
<tr>
<th>Time</th>
<th>TC-EX (kcal)</th>
<th>TC-CN (kcal)</th>
<th>%CHO-EX</th>
<th>%PRO-EX</th>
<th>%FAT-EX</th>
<th>%CHO-CN</th>
<th>%PRO-CN</th>
<th>%FAT-CN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>2609 ± 86</td>
<td>2229 ± 32</td>
<td>54 ± 1</td>
<td>16 ± 1</td>
<td>30 ± 2</td>
<td>54 ± 2</td>
<td>16 ± 1</td>
<td>30 ± 1</td>
</tr>
<tr>
<td>Week 6</td>
<td>2237 ± 21</td>
<td>2270 ± 54</td>
<td>54 ± 2</td>
<td>18 ± 1</td>
<td>28 ± 2</td>
<td>52 ± 1</td>
<td>17 ± 1</td>
<td>31 ± 2</td>
</tr>
<tr>
<td>Week 12</td>
<td>2350 ± 29</td>
<td>2304 ± 72</td>
<td>53 ± 2</td>
<td>18 ± 2</td>
<td>29 ± 1</td>
<td>51 ± 1</td>
<td>18 ± 2</td>
<td>31 ± 1</td>
</tr>
</tbody>
</table>

TC, total calories; EX, experimental group; CN, control group; %, percentage; CHO, carbohydrate; PRO, protein.
experimental and control groups consumed at least 1.1 g protein-kg$^{-1}$-d$^{-1}$ during the 12-wk PRT program. Additionally, Fiatarone et al. (8) reported nutritional supplementation to be ineffective for augmenting muscle function in elderly individuals despite a 22% increase in total energy intake per day. This ineffectiveness was hypothesized to be a result of insufficient magnitude or duration and/or because the baseline nutritional status may have already been sufficient. Thus, adequate dietary intake may be all that is necessary from a nutritional perspective to maximize skeletal muscle responses to resistance training in older adults.

It has been demonstrated that acute (2 wk) muscle protein synthesis adaptations occur with knee extensor PRT in both young (24 yr) and older (63–66 yr) men and women without a concurrent increase in the rate of whole body protein breakdown (21). In addition, myofibrillar protein synthesis before and after 12-wk of PRT has is 33% slower in the older compared with young (17). These authors suggest that the decreased rate of myofibrillar synthesis does not appear to be related to physical inactivity (17). It appears that there may be an initial (2-wk) increase in the rate of myofibrillar protein synthesis with resistance training in older adults (21), but as the duration of the training progresses to 12 wk, the increase that was observed initially returns to baseline synthesis rates (17). A recent investigation by Esmarck and coworkers (7) showed that early provision (immediately postexercise) of a protein and carbohydrate provision was more effective than later provision (2 h postexercise). Specifically, these authors found that muscle hypertrophy resulted in the early-supplemented group (7%) but not in the later-supplemented group after a 12-wk PRT program. Our current study administered an immediate (within 5–10 min) postexercise provision and found no improvement in the degree of hypertrophy between our two groups. The major difference in the two studies is the lack of a control group (a no provision group) in the Esmarck investigation, which would have allowed for a more accurate interpretation of the results as they relate to the influence of the timing of postexercise protein intake. Additionally, it is interesting that the 2-h postexercise provision group did not demonstrate any appreciable increase in muscle size with 12-wk of PRT. This is in contrast to the numerous studies (13) that have demonstrated that hypertrophy normally occurs in older adults when exposed to an adequate resistance exercise stimulus. Esmarck and coworkers attributed this lack of hypertrophy in the 2-h group to the importance of the early timing of protein intake in recovery from resistance training.

The current investigation attempted to increase whole muscle strength and size in the exercising musculature by administering oral amino-acid provision to older men. Amino acids (L-lysine, L-leucine, L-valine, L-phenylalanine, L-threonine, L-histidine, L-isoleucine, and L-methionine) were orally administered daily to the experimental group. Also, based upon previous research (2), carbohydrate (sucrose, fructose, and dextrose) was added to the provision drink to increase insulin levels and possibly assist in promoting anabolism. Rasmussen et al. (12) demonstrated that the administration of oral essential amino acids in combination with carbohydrates (sucrose) positively increased muscle protein synthesis after an acute bout of resistance exercise in younger (34 yr old) adults when ingested 1 or 3 h after the exercise. However, as mentioned previously, a more recent study (16) found that in elderly humans muscle protein anabolism is impaired in response to hyperaminoacidemia and endogenous hyperinsulinemia due to the unresponsiveness of protein synthesis. Thus, in hind site, it appears that a potential limiting factor to muscle protein synthesis in the postexercise oral amino-acid group in the current the current study was the addition of carbohydrates to this drink.

Muscle strength and size increased significantly in both the experimental and control groups, with no differences between the groups. All results concerning whole muscle strength and size (cross-sectional area) are in conformity with previous PRT studies (13) conducted in older people (>65 yr old), and suggest that the anticipated effects of resistance training were attained. It is possible that the oral provision may have decreased muscle protein degradation and increase muscle protein synthesis rates, but that it was insufficient to result in an increased net muscle protein balance above that achieved by the control group or perhaps dietary protein intake was sufficient and the provisional amino acids had no effect and were simply oxidized, or stored as fat, whereas the excess nitrogen was excreted. The primary cause of the lack of an additional increased net muscle protein balance above that achieved by the control group is supported by several investigations (17–19) that have demonstrated a significantly slower muscle protein synthesis rate in older adults. These data suggest that, in the present study, provision of amino acid and carbohydrate with 12 wk of PRT was inadequate to elicit net anabolism.

In summary, this investigation demonstrated that whole muscle strength and size of older men can positively adapt to a high-intensity PRT program without further improvement with a daily oral acid provision administered immediately after resistance exercise. These data indicate that nutritional provisions (amino acids and carbohydrate) do not further improve skeletal muscle strength and size gains in response to resistance training in older men who have adequate daily protein intake (≥1.1 g protein-kg$^{-1}$-d$^{-1}$) (3).

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