

Effects of Oral Ingestion of Amino Acids and Proteins on the Somatotropic Axis

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Context: GH is an important regulator of growth and body composition. It has been shown that GH release can be promoted by iv as well as oral administration of various amino acids (AAs), especially arginine (ARG) and lysine (LYS), which are amply present in soy protein. However, the effects of dietary protein on GH secretion are less well described.

Objective and Design: In an experiment, we compared the effects of oral ingestion of a mixture reflecting the AA composition of soy protein (AA), with oral ingestion of ARG + LYS, on GH secretion in eight healthy women (body mass index 19–25 kg/m²; age, 18–24 yr). In a second experiment, we compared oral ingestion of hydrolyzed soy protein and complete soy protein with the AA mixture on GH secretion in eight healthy women (body mass index 19–26 kg/m²; age, 19–36 yr). Both experiments were performed in a randomized, single-blind crossover design. GH, insulin, glucose, and plasma AA were determined every 20 min, during 3 h in the first experiment and during 5 h in the second experiment.

Results: Peak values of GH were higher after ingestion of the AA mixture compared with ingestion of ARG + LYS ($P < 0.05$). GH responses, as determined by area under the curve, did not significantly differ after ingestion of the complete soy protein, hydrolyzed soy protein, or AA mixture but were all higher than after placebo ($P < 0.05$). Insulin responses (area under the curve) were higher after ingestion of hydrolyzed soy protein, complete soy protein, and AA mixture, compared with placebo ($P < 0.05$). Glucose concentrations were unaffected.

Conclusion: Ingestion of soy protein, either hydrolyzed or intact, as well as AAs reflecting soy protein, stimulates GH release to a similar extent. (*J Clin Endocrinol Metab* 93: 584–590, 2008)

GH, a hormone originating from the anterior pituitary gland, is an important regulator of growth and body composition (1). GH exerts its growth promoting effect (typically of fat-free mass) through stimulation of the secretion of IGF-I from the target cells. Disorders such as obesity, sarcopenia, and growth retardation in children are characterized by low GH concentrations (1–4).

It has been shown by many authors (5, 6) that GH secretion can be promoted by iv administration of various amino acids (AAs), including arginine (ARG), methionine, phenylalanine, lysine (LYS), and histidine. Leucine and valine seem less potent, whereas isoleucine does not seem to affect plasma GH

concentrations. In particular, the stimulatory effect of iv ARG on GH is clinically used as a method to assess the responsiveness of the GH secretory system, e.g. when GH deficiency is suspected (7).

The stimulatory effect of AAs on GH secretion is also present when AAs are administered orally. Thus, ingestion of a dosage of 24 g of a mixture of essential AAs increased plasma GH concentrations 2.1-fold in comparison with basal values (8). It is not clear whether all AAs contribute equally to this phenomenon. Glutamine, ARG, glutamic acid, and ARG plus LYS have stimulated the GH response in several studies (5, 9). After oral ingestion of glutamine or ARG, plasma GH concentrations in-

0021-972X/08/\$15.00/0

Printed in U.S.A.

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doi: 10.1210/jc.2007-1784 Received August 9, 2007. Accepted November 13, 2007.

First Published Online November 20, 2007

Abbreviations: AA, Amino acid; ARG, arginine; AUC, area under the curve; BMI, body mass index; LYS, lysine; TTP, time to peak.

TABLE 1. Composition of the test drinks in experiments 1 and 2 based on a subject of 70 kg

	Study 1		Study 2			
	AA	ARG + LYS	Hydrolyzed soy protein	Complete soy protein	AA	Placebo
Volume (ml)	250	250	467	467	500	500
Cysteine (g)	0.22		0.46	0.46	0.44	
Methionine (g)	0.23		0.46	0.46	0.46	
Aspartic acid (g)	2.06		4.00	4.28	4.12	
Threonine (g)	0.67		1.30	1.40	1.36	
Serine (g)	0.91		1.76	1.93	1.82	
Glutamic acid (g)	3.38		6.34	7.04	6.76	
Proline (g)	0.89		1.76	1.89	1.79	
Glycine (g)	0.73		1.42	1.55	1.47	
Alanine (g)	0.75		1.46	1.60	1.51	
Valine (g)	0.88		1.72	1.84	1.76	
Isoleucine (g)	0.92		1.68	1.80	1.84	
Leucine (g)	1.49		2.81	3.02	2.98	
Tyrosine (g)	0.71		1.26	1.39	1.42	
Phenylalanine (g)	0.97		1.76	1.93	1.94	
Histidine (g)	0.49		0.88	0.96	0.98	
LYS (g)	1.13	1.13	2.14	2.34	2.27	
ARG (g)	1.43	1.43	2.60	2.81	2.86	
Tryptophan (g)	0.24		0.46	0.50	0.47	
Sugar-free syrup (ml)	20	20			40	40

creased 2- to 4.5-fold higher in comparison with time controls (9, 10), whereas a combination of ARG and LYS increased plasma GH concentration 3- to 8-fold (11, 12). In contrast, oral ingestion of aspartic acid or cysteine did not affect GH concentrations (5).

As mentioned previously, effects of AAs on GH secretion may suggest a role of dietary protein in the regulation of plasma GH concentrations. However, only a limited number of studies focused on the effects of dietary proteins and diet composition on GH secretion. It has been shown that in children, dairy, but not meat, consumption is positively associated with growth and plasma concentrations of IGF-I (13). In addition, the GH responses to an ARG stimulus were lower during a high carbohydrate diet than during a high-fat or a high-protein diet (14).

Because the effects of dietary protein on GH secretion are less well documented, this study aims to investigate the effects of dietary soy protein ingestion, containing approximately equal amounts of ARG and LYS, on plasma GH concentrations. AA mixtures are expected to be absorbed more rapidly than protein hydrolysates, which are expected to be absorbed more rapidly than intact proteins. This may result in different peak values of AAs in the plasma, which may affect GH release.

Subjects and Methods

Two series of experiments were performed to investigate the effects of dietary protein ingestion on plasma GH concentration. In the first experiment, the effects of ingestion of an AA mixture reflecting soy protein (AA) were compared with the effects of ARG and LYS (ARG + LYS). In the second series of experiments, the effects of oral ingestion of proteins (complete and hydrolyzed) were compared with the effects of the AA mixture on GH secretion.

Subjects

Subjects were recruited via advertisements at the university. In the first experiment as well as in the second experiment, eight healthy young females participated [experiment 1: age 21 ± 2.6 yr, body mass index (BMI) 22.5 ± 2.5 kg/m²; and experiment 2: age 24 ± 5.5 yr, BMI 22.7 ± 1.9 kg/m²]. Each subject participated once in this study. Subjects were in good health, nonsmokers, using contraceptives, free of any other medication, and spent no more than 3 h/wk on sport activities. Women came to the university in the same phase of their “menstrual cycle.” The Medical Ethics Committee of Maastricht University approved the study protocol, and all subjects gave their written informed consent before participating in the study.

Experimental design

A randomized crossover study design was applied in both series of experiments. In the first experiment, subjects reported to the laboratory for consumption of two different test drinks, and in the second experiment, for consumption of four different test drinks, all test drinks at separate test days. Each time, subjects arrived at the laboratory in a fasted state, in the morning. They were instructed to fast

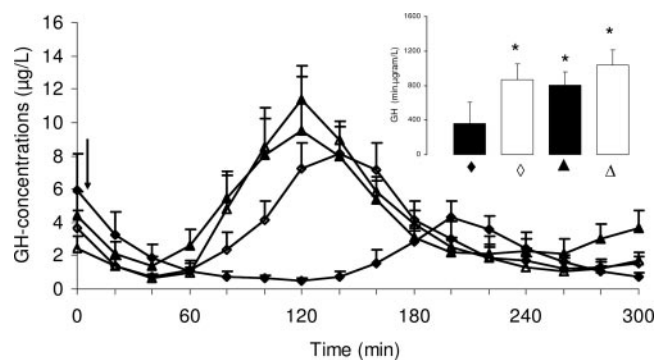


FIG. 1. GH concentrations after ingestion of placebo (◆), AA (◇), hydrolyzed soy protein (▲), and complete soy protein (△) test drinks ($n = 8$). Data are presented as means (\pm SEM). ↓, Ingestion of test drink. *, $P < 0.05$ compared with placebo.

TABLE 2. Blood parameters after ingestion of a placebo test drink, AA test drink, hydrolyzed soy protein test drink, and complete soy protein test drink (n = 8) expressed as AUC

	AUC			
	Placebo	AA mix	Hydrolyzed	Complete
GH (min·μg/liter)	357 ± 94	870 ± 176 ^a	804 ± 154 ^a	1035 ± 179 ^a
Insulin (min·mU/liter)	1985 ± 268	4452 ± 649 ^a	5988 ± 822 ^a	5087 ± 605 ^a
Glucose (min·mmol/liter)	874 ± 68	1044 ± 35	996 ± 39	998 ± 35
Urea (min·mmol/liter)	62 ± 42	307 ± 60 ^a	426 ± 78 ^a	366 ± 53 ^a
Total AA (min·mol/liter)	−23.0 ± 16.4	27.3 ± 4.7 ^a	43.0 ± 29.0 ^{a,b}	40.8 ± 22.9 ^{a,b}
Glutamine	−3.9 ± 1.6	11.4 ± 4.0 ^a	13.7 ± 1.5 ^a	12.4 ± 2.1 ^a
Aspartic acid	−1.3 ± 0.8	2.7 ± 0.4	22.4 ± 1.6 ^{a,b}	22.5 ± 1.0 ^{a,b}
Serine	−0.1 ± 0.9	13.7 ± 3.0 ^a	18.2 ± 2.5 ^a	19.3 ± 1.1 ^a
Glutamic acid	−2.8 ± 3.2	8.8 ± 3.5	18.3 ± 3.5 ^a	20.7 ± 3.2 ^a
Histidine	−0.2 ± 1.0	9.7 ± 2.8 ^a	9.8 ± 2.0 ^a	11.3 ± 1.3 ^a
Glycine	−0.2 ± 2.6	14.2 ± 2.5 ^a	9.5 ± 2.5 ^a	11.7 ± 1.7 ^a
Threonine	−2.9 ± 1.8	23.5 ± 2.5 ^a	23.2 ± 2.6 ^a	20.8 ± 2.3 ^a
Citrulline	−0.4 ± 0.2	1.6 ± 0.5 ^a	4.3 ± 0.5 ^{a,b}	4.1 ± 0.4 ^{a,b}
ARG	0.6 ± 0.9	19.5 ± 2.5 ^a	27.9 ± 3.2 ^{a,b}	26.7 ± 3.4 ^a
Alanine	−16.6 ± 5.1	19.6 ± 3.4 ^a	20.0 ± 6.4 ^a	20.7 ± 3.4 ^a
Taurine	0.2 ± 0.2	1.3 ± 0.4	0.6 ± 0.2	1.2 ± 0.3
aAB	0.9 ± 0.2	2.5 ± 0.3 ^a	2.7 ± 0.4 ^a	2.7 ± 0.3 ^a
Tyrosine	−1.3 ± 0.8	8.1 ± 1.5 ^a	21.5 ± 1.5 ^{a,b}	18.6 ± 1.1 ^{a,b}
Valine	0.4 ± 0.9	55.4 ± 3.9 ^a	58.5 ± 2.4 ^a	48.2 ± 6.9 ^a
Methionine	−0.6 ± 0.1	1.8 ± 0.7 ^a	3.4 ± 0.4 ^{a,b}	3.1 ± 0.2 ^a
Isoleucine	1.6 ± 0.6	19.9 ± 7.6 ^a	40.6 ± 0.2 ^{a,b}	35.2 ± 1.9 ^{a,b}
Phenylalanine	0.0 ± 0.4	13.9 ± 3.0 ^a	16.5 ± 1.4 ^a	14.1 ± 1.0 ^a
Tryptophan	−1.3 ± 0.8	5.3 ± 1.6 ^a	7.6 ± 1.0 ^a	6.6 ± 0.6 ^a
Leucine	3.6 ± 1.1	46.1 ± 3.3 ^a	57.1 ± 3.1 ^{a,b}	49.7 ± 2.7 ^{a,b}
Ornithine	−6.5 ± 6.6	10.0 ± 1.9	28.0 ± 17.8	10.9 ± 0.9
LYS	−2.4 ± 3.9	33.2 ± 2.7 ^a	42.1 ± 4.1 ^a	42.4 ± 3.3 ^a

Data are presented as means ± SEM.

^a *P* < 0.05 compared with the placebo test drink (repeated measures ANOVA).

^b *P* < 0.05 compared with the AA test drink (repeated measures ANOVA).

from 2200 h the night before the test day. A permanent cannula was inserted into a dorsal vein of the hand, which was placed in a thermoregulated (60 C) box for arterialized venous blood sampling (15). Blood sampling began 60 min after placement of the cannula. Blood was sampled every 20 min for the next 3 h in the first experiment and for the next 5 h in the second experiment. During blood sampling, subjects remained awake and fasted, and were allowed to drink water *ad libitum*. Immediately after obtaining the first blood sample, subjects received a test drink. The test drinks are described in Table 1. In the first experiment, subjects received the AA test drink and the ARG + LYS test drink. In the second experiment, subjects received a drink containing a complete soy protein, hydrolyzed soy protein, AA (reflecting soy protein), and a placebo test drink. The AAs in the AA test drinks were obtained from Bufa BV (Uitgeest, The Netherlands). The sugar-free syrup (Diaran, Cereal, Breda, The Netherlands) added to the AA drinks contained no proteins and fat, and a negligible amount of carbohydrates. The syrup was added to improve the taste of the test drink. The protein test drinks were produced by NIZO (Nederlands Instituut Zuivel Onderzoek, Ede, The Netherlands).

Blood analysis

In both experiments, arterialized venous blood was collected in cloth tubes (Becton Dickinson Vacutainer system; Becton Dickinson, Franklin Lakes, NJ), and in the second experiment, arterialized venous blood was also divided into cloth tubes and heparinized tubes (Becton Dickinson Vacutainer system). Blood in the cloth tube (containing “Silica Clot Activator”) was allowed to clot for 30 min and was centrifuged at 3000 × *g*, 4 C for 10 min to obtain serum. Serum in the first experiment was collected for determination of GH, and in the second experiment for determination of GH, insulin, glucose, and

urea concentrations. Blood in heparinized tubes was kept on ice to minimize enzymatic reactions. AA analyses were performed in plasma, which was obtained by centrifugation at 4 C for 10 min at 3000 × *g*. Subsequently, 250 μl plasma was deproteinized with 20 mg dry sulfosalicylic acid for analysis of plasma AA concentrations and enrichment. Each aliquot of serum and plasma was frozen immediately in liquid nitrogen and stored at −80 C, until analysis. All samples from one subject were run in the same assay.

The human GH concentrations were measured using an ultrasensitive human GH chemiluminescence immunoassay (Beckman Coulter, Inc., Fullerton, CA). The intraassay and interassay coefficients of variation were 1.4–2.1 and 6.8–8.6%, respectively, at GH concentrations of 3.7–14.2 and 3.1–7.3 μg/liter, respectively.

Insulin concentrations were measured by an electrochemiluminescence immunoassay (Roche Diagnostica, Hoffmann-La Roche, Basel, Switzerland). Glucose concentrations were measured using enzymatic assay (G6-PDH) (Roche Diagnostica, Hoffmann-La Roche). AA concentrations were measured using a HPLC system (Pharmacia, Woerden, The Netherlands). Urea concentrations were measured spectrophotometrically on a COBAS Mira S (Roche Diagnostica, Hoffmann-La Roche).

Statistics

All data are expressed as mean ± SEM. Statistical significance was set at *P* < 0.05. Statview SE + Graphics (1988; Abacus Concepts, Berkeley, CA) was used for the analysis. In the first experiment, GH responses were calculated as peak values. In the second experiment, GH, insulin, glucose, urea, and AA responses were calculated as area under the curve (AUC), peak values, and time to peak (TTP) values. Statistical analyses of the data were performed using repeated measures ANOVA, correcting

TABLE 3. Blood parameters after ingestion of a placebo test drink, AA test drink, hydrolyzed soy protein test drink, and complete soy protein test drink (n = 8) expressed as peak values

	Peak			
	Placebo	AA mix	Hydrolyzed	Complete
GH ($\mu\text{g/liter}$)	4 \pm 3	12 \pm 5 ^a	9 \pm 3 ^a	13 \pm 4 ^a
Insulin (mU/liter)		40 \pm 7	47 \pm 7	44 \pm 5
Glucose (mmol/liter)				
Urea (mmol/liter)				
Total AA ($\mu\text{mol/liter}$)		4592 \pm 229	4865 \pm 200	4782 \pm 221
Glutamine		171 \pm 24	232 \pm 19 ^b	230 \pm 18 ^b
Aspartic acid		58 \pm 4	182 \pm 9 ^b	203 \pm 11 ^b
Serine		247 \pm 26	255 \pm 11	251 \pm 13
Glutamic acid		540 \pm 17	597 \pm 32	577 \pm 27
Histidine		190 \pm 21	161 \pm 8	160 \pm 9
Glycine		338 \pm 21	292 \pm 16	289 \pm 16
Threonine		357 \pm 29	294 \pm 13	313 \pm 22
Citrulline		66 \pm 21	49 \pm 3	48 \pm 3
ARG		234 \pm 22	244 \pm 35	237 \pm 32
Alanine		455 \pm 29	469 \pm 23	471 \pm 20
Taurine		51 \pm 48	38 \pm 2	44 \pm 2
aAB		27 \pm 9	31 \pm 3	26 \pm 3
Tyrosine		96 \pm 2	160 \pm 10 ^b	147 \pm 6 ^b
Valine		563 \pm 28	451 \pm 17 ^b	418 \pm 13 ^b
Methionine		50 \pm 4	49 \pm 4	46 \pm 2
Isoleucine		277 \pm 30	276 \pm 14	258 \pm 11
Phenylalanine		153 \pm 12	139 \pm 8	127 \pm 5 ^b
Tryptophan		114 \pm 26	98 \pm 4	97 \pm 4
Leucine		445 \pm 23	407 \pm 20	384 \pm 16 ^b
Ornithine		138 \pm 34	109 \pm 8	97 \pm 8
LYS		459 \pm 35	437 \pm 27	442 \pm 40

Data are presented as means \pm SEM.

^a $P < 0.05$ compared with the placebo test drink (repeated measures ANOVA).

^b $P < 0.05$ compared with the AA test drink (repeated measures ANOVA).

for multiple analyses. *Post hoc*, the Scheffé F test was used to locate possible significant differences.

Results

In the first series of experiments, GH responses reached higher peak values after ingestion of the AA mixture (4.9 \pm 1.2 $\mu\text{g/liter}$) than after ingestion of the ARG + LYS test drink (2.2 \pm 0.7 $\mu\text{g/liter}$) ($P < 0.05$). In the second series of experiments, GH responses, as determined by AUC and peak values, were higher after ingestion of hydrolyzed soy protein, complete soy protein, and the AA mixture, compared with ingestion of the placebo test drink ($P < 0.05$). No differences between GH responses (AUC and peak values) were found after ingestion of hydrolyzed soy protein, complete soy protein, and the AA mixture (Fig. 1 and Tables 2–4).

The insulin concentrations, as determined by AUC and peak values, were higher after ingestion of hydrolyzed soy protein, complete soy protein, and the AA mixture, compared with ingestion of the placebo ($P < 0.05$). Ingestion of complete soy protein, hydrolyzed soy protein, or the AA mixture did not differently affect insulin responses (AUC and peak values) (Tables 2–4 and Fig. 2). The glucose response (AUC) did not differ between each of the test drinks (Tables 2–4).

The ARG concentration was higher after ingestion of the AA mixture, compared with the ARG + LYS test drink ($P < 0.05$) (Fig. 3).

No differences were found in total AA peak concentrations after ingestion of the protein and AA test drinks. However, glutamic acid, aspartic acid, and tyrosine showed a higher peak after ingestion of the hydrolyzed and complete soy protein test drinks compared with the concentrations obtained after ingestion of the AA test drink ($P < 0.05$). Valine, phenylalanine, and leucine peaks were lower after ingestion of the hydrolyzed and complete soy protein test drinks in comparison with the AA test drink ($P < 0.05$). In contrast with the total AA peak, total AAs (AUC) in response to the different test drinks were higher after ingestion of the hydrolyzed and complete soy protein test drink, compared with the AA test drink ($P < 0.05$). The difference in total AA concentrations (AUC) between the hydrolyzed and complete soy protein test drink in comparison with the AA test drink was also reflected in aspartic acid, glutamic acid, citrulline, ARG, tyrosine, methionine, isoleucine, and leucine responses ($P < 0.05$). Total AAs (AUC) and each separate AA (except for taurine and ornithine) were higher after ingestion of the hydrolyzed soy protein, complete soy protein, and AA test drinks in comparison with the placebo test drink ($P < 0.05$). TTP was later after

TABLE 4. Blood parameters after ingestion of a placebo test drink, AA test drink, hydrolyzed soy protein test drink, and complete soy protein test drink (n = 8) expressed as TTP

	TTP			
	Placebo	AA mix	Hydrolyzed	Complete
GH (min)	195 ± 8	120 ± 18 ^a	130 ± 9 ^a	113 ± 7 ^a
Insulin (min)		33 ± 7	40 ± 6	45 ± 7
Glucose (min)				
Urea (min)				
Total AA (min)		45 ± 4	88 ± 10 ^b	83 ± 8 ^b
Glutamine		75 ± 9	83 ± 11	70 ± 11
Aspartic acid		63 ± 37	75 ± 5	88 ± 11
Serine		45 ± 4	78 ± 6 ^b	78 ± 9 ^b
Glutamic acid		55 ± 7	70 ± 6	68 ± 6
Histidine		55 ± 5	95 ± 14 ^b	88 ± 7 ^b
Glycine		58 ± 5	75 ± 7	75 ± 7
Threonine		63 ± 9	198 ± 11	85 ± 9
Citrulline		100 ± 7	135 ± 7 ^b	125 ± 7
ARG		55 ± 5	63 ± 9	78 ± 9
Alanine		65 ± 4	80 ± 7	70 ± 6
Taurine		65 ± 11	48 ± 6	60 ± 7
aAB		83 ± 20	135 ± 13	110 ± 17
Tyrosine		53 ± 7	105 ± 8 ^b	95 ± 8 ^b
Valine		55 ± 10	115 ± 8 ^b	103 ± 6 ^b
Methionine		33 ± 6	78 ± 13 ^b	58 ± 8
Isoleucine		40 ± 4	98 ± 9 ^b	88 ± 8 ^b
Phenylalanine		40 ± 4	110 ± 7 ^b	90 ± 11 ^b
Tryptophan		48 ± 6	85 ± 10 ^b	88 ± 7 ^b
Leucine		43 ± 5	100 ± 8 ^b	93 ± 11 ^b
Ornithine		48 ± 4	80 ± 13	78 ± 12
LYS		53 ± 8	85 ± 13	83 ± 13

Data are presented as means (± SEM).

^a $P < 0.05$ compared with the placebo test drink (repeated measures ANOVA).

^b $P < 0.05$ compared with the AA test drink (repeated measures ANOVA).

ingestion of hydrolyzed and complete soy protein test drink (85 min) than after ingestion of the AA test drink (45 min) ($P < 0.05$). This difference in TTP was also reflected by the TTP in serine, histidine, citrulline, tyrosine, valine, methionine, isoleucine, phenylalanine, tryptophan, and leucine ($P < 0.05$). Tables 2–4 show an overview of the differences in AA concentration as measured by AUC, peak values, and TTP among the protein, AA, and placebo test drinks. Figure 4 shows each separate AA over time after ingestion of the test drinks.

As determined by AUC, urea concentrations did not differ among ingestion of hydrolyzed soy protein, complete soy pro-

tein, or the AA mixture but were higher than after ingestion of placebo ($P < 0.05$) (Tables 2–4).

Discussion

Oral administration of soy protein appeared to stimulate GH secretion. This effect was preserved when soy protein was ingested as either hydrolyzed soy protein or free AAs. These results suggested that the potency to stimulate GH secretion was not influenced by the rate of AA absorption.

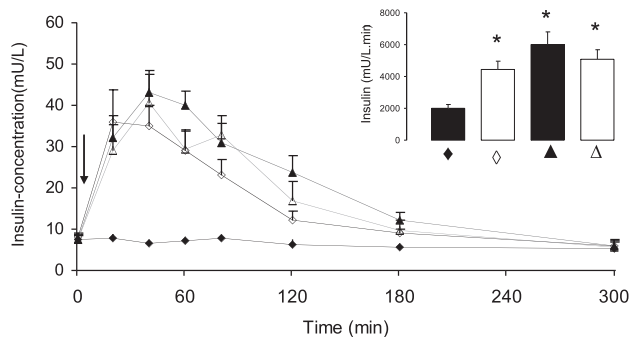


FIG. 2. Insulin concentrations after ingestion of placebo (◆), AA (◇), hydrolyzed soy protein (▲), and complete soy protein (△) test drinks (n = 8). Data are presented as means (± SEM). ↓, Ingestion of test drink. *, $P < 0.05$ compared with placebo.

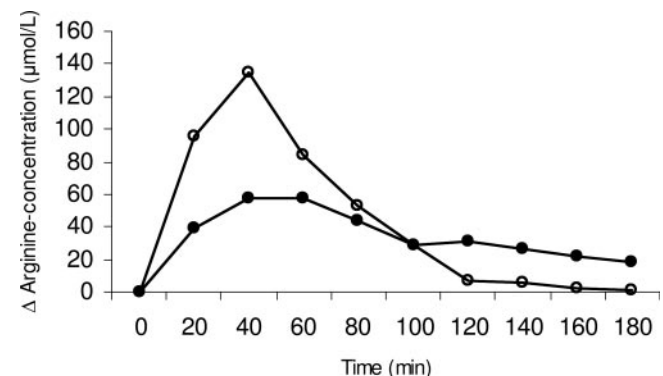


FIG. 3. ARG concentrations after ingestion of the ARG + LYS (●) and AA (○) test drinks, and placebo (n = 8).

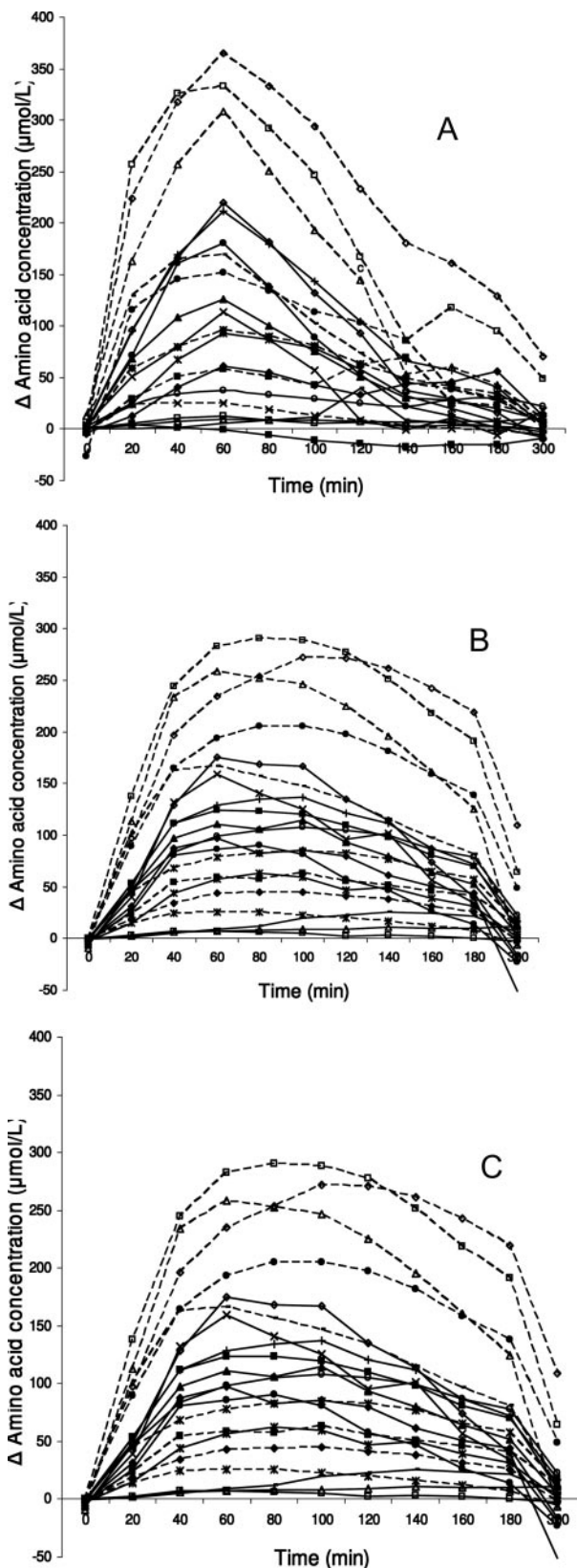


FIG. 4. AA concentrations after ingestion of the AA (A), hydrolyzed soy protein (B), and complete soy protein (C) test drinks (n = 8). —◆, Glutamine; —■, aspartic acid; —▲, serine; —×, glutamic acid; —*, histidine; —●, glycine; —|, threonine; ——, citruline; —◇, alanine; —□, taurine; —△, aAB; —○, tyrosine; —×, methionine; —*, phenylalanine; —◆, tryptophan; —■, ornithine; —▲, arginine; —●, isoleucine; —◇, valine; —□, leucine; —△, lysine.

A 2.3-fold increase in GH concentrations was found after oral ingestion of a test drink with approximately 1.2 g ARG and 1.2 g LYS in comparison with basal values. This finding confirms previous studies by Isidori *et al.* (11) and Suminski *et al.* (12), which showed that oral ingestion of 1.2 to 1.5 g ARG and 1.2- to 1.5 g LYS increased GH release 3- to 8-fold in comparison with placebo. In addition, we found that the AA mixture, reflecting soy protein (17 g AA), with equal amounts of ARG and LYS as in the ARG + LYS test drink, increased GH concentrations 2.2-peak fold more than ARG and LYS alone. We concluded that in addition to ARG and LYS, other AAs are involved in the observed stimulation of GH release, directly or indirectly via conversion to another AA. The somatotrophic effects of the AAs reflecting soy protein composition were unaffected whether these AAs were orally administered as either intact or as partially hydrolyzed soy protein.

To the best of our knowledge, this is the only human study performed analyzing the effects of variable chain length of proteins on GH secretion. Only one other animal study, performed in rats in which casein is used as a protein source in a meal or as free AAs, also showed no different results in GH concentrations after intake of a meal with dietary (casein) AAs in free form or as complete casein proteins (16).

The similar GH responses after ingestion of the AA mixture and soy protein are associated with comparable peak values of AA concentrations (Fig. 3). Absorption of the AAs was slower after ingestion of the (intact or hydrolyzed) proteins than after ingestion of the AA mixture, as indicated by the lower AUC and the lower TTP of the plasma AA responses. However, this was not associated with differences in GH responses, indicating that the absorption rate of the AAs after oral ingestion was not of pivotal value for the GH responses. Therefore, the underlying mechanism of the increased GH release after protein ingestion may be related to GH-secreting properties of insulin (7, 17, 18) because increased insulin responses to protein or AA ingestion may play a role in the observed GH responses (19, 20). This effect is independent of plasma glucose responses, which were unaffected by protein or AA ingestion.

We showed a clear effect of intact soy protein on GH secretion; the next step should be to assess the effects of soy protein as part of a meal. Previous studies on the effects of meals on plasma GH have produced controversial results. Some studies showed an increase of GH concentrations after normal and high protein meals in humans (6, 21–23), whereas other studies showed decreased or unaffected GH secretion after normal and high protein meals (14, 23–25).

The clinical and physiological relevance of the results of this study remains to be investigated. These results show that in normal healthy women, GH responses increase after oral ingestion of proteins. It is not known whether this effect also occurs in a GH-deficient population, such as in obese subjects, and if so, whether this has any physiological effects.

In conclusion, ingestion of soy protein, either hydrolyzed or intact, as well as AAs reflecting soy protein, stimulates GH release to a similar extent. Increased serum levels of insulin as well as peak AA concentration, but not the absorption rate of AA, may be responsible for the somatotrophic effects. Further inves-

tigations are necessary to elucidate the role of dietary protein in the regulation of plasma GH levels after meal ingestion.

Acknowledgments

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Disclosure Statement: The authors have nothing to declare.

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