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Factors Affecting Plasma Glutamate Levels in Normal Adult Subjects

Lewis D. Stegink, L. J. Filer, Jr., G. L. Baker, S. M. Mueller, and M. Y-C. Wu-Rideout

Departments of Pediatrics, Biochemistry, and Neurology, The University of Iowa College of Medicine, Iowa City, Iowa 52242

The dicarboxylic amino acids, glutamate and aspartate, occupy unique positions in intermediary metabolism. Since they are important in energy production, movement of reducing equivalents into the mitochondrial matrix, urea synthesis, glutathione synthesis, and as neurotransmitters (52), it is not surprising that cells contain considerable quantities of free glutamate and aspartate. In particular, these amino acids are the major amino acids found in the mitochondria of the cell, where they may comprise 50 to 70% of the total free amino acids (21). Considerable quantities are normally found in human brain and liver (44,45,50).

Like all chemical compounds, glutamate and aspartate exert toxic effects when administered at high doses to susceptible animal species. In the case of glutamate salts, toxic effects in animals are associated with two factors: (a) high blood glutamate levels and (b) a species of animal susceptible to glutamate toxicity.

The neonatal rodent is acutely sensitive to large doses of glutamate administered either orally or intravenously. Administration of large quantities of glutamate to the newborn rodent produces a variety of neurotoxic effects (see review in ref. 52), the most marked of which is hypothalamic neuronal necrosis (22,34,35,38). The neurotoxic effects of glutamate in the neonatal primate, however, are highly controversial. The initial reports from the St. Louis group indicating that high glutamate doses cause hypothalamic lesions in the neonatal primate (39,40) have not been confirmed by four other independent laboratories (1,2,31,49,58,60). The latter research groups, however, had no difficulty in producing the rodent lesion. It has been suggested that the failure of research groups other than the St. Louis group to produce a lesion in the neonatal primate reflected a failure to elevate plasma glutamate levels (40). However, this is not the case, since our research group has studied animals in which plasma glutamate levels were grossly elevated without finding any evidence of hypothalamic neuronal necrosis (58).

Our data indicate that grossly elevated plasma glutamate levels are associated with neuronal necrosis in the neonatal mouse (59), but equivalent elevation of plasma glutamate in neonatal primates is not associated with neuronal necrosis (58). However, the continuing controversy over the advisability of glutamate ingestion by

man and the finding that glutamate neurotoxicity in sensitive animal species is always associated with grossly elevated plasma glutamate levels have led us to evaluate the factors that affect plasma glutamate levels in adult humans after ingestion of glutamate in either free or protein-bound form.

We will divide our discussion into three general areas: (a) normal biological variation in plasma glutamate levels, (b) the dose-response effect of glutamate ingested in water on plasma glutamate concentration, and (c) the dose-response effect of glutamate ingested with meals on these levels.

BIOLOGICAL VARIATION

Glutamate and aspartate account for 20 to 25% of the total amino acid composition of dietary proteins, including those found in human milk (23). In addition, human milk contains considerable quantities of these amino acids in free form (5,52,54). Thus, humans normally ingest a considerable portion of their protein-amino acid intake in the form of these amino acids.

In view of the large daily intake of glutamate in the diet, it is not surprising that glutamate and aspartate are rapidly metabolized by both the gut and the liver. Similarly, it is not surprising that individual differences in either absorption or metabolism of glutamate would affect plasma levels.

As shown in Fig. 1, glutamate and aspartate are absorbed from the intestinal lumen both as peptides and free amino acids (18,24). Protein-meal studies in man (32,33) strongly suggest that only the neutral amino acids and the dibasic amino acids are quantitatively taken in as free amino acids (18). The imino acids and glycine, as well as the dicarboxylic amino acids, all appear to enter the mucosal cells as constituents of small peptides, where specific intracellular peptidases hydrolyze them to component amino acids (24).

Despite the fact that most of the glutamate and aspartate peptides produced by

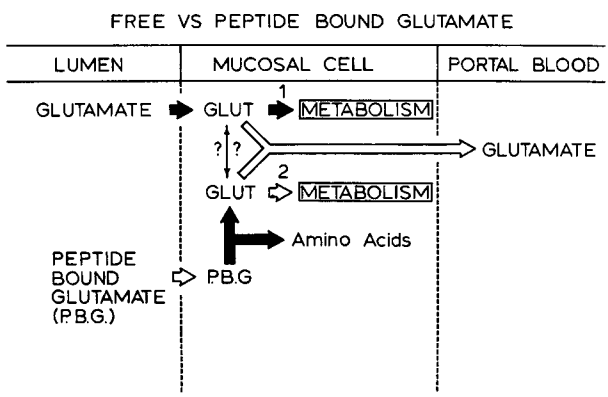

FIG. 1. Intestinal absorption of free vs peptide-bound glutamate.

pancreatic digestion of dietary protein are absorbed intact, the gut also has specific transport sites for free glutamate and aspartate, with maximal values for their transport noted in the terminal ileum (47,51).

A considerable fraction of glutamate is metabolized during the absorptive process for both free (25,29,30,41,43,48) and protein-bound (8,11,13,14,42,46,62) dicarboxylic amino acids. Much of the α-amino nitrogen initially present in these amino acids appears in the portal blood as alanine. As shown in Fig. 2, this alanine undoubtedly results from the transamination of pyruvate by the dicarboxylic amino acids, producing α-ketoglutarate or oxaloacetate as the other product. This process appreciably reduces the quantity of dicarboxylic amino acids released into the portal blood. Glutamate and aspartate escaping mucosal metabolism are carried by the portal vein to the liver, which controls the composition of the amino acid mixture released to the peripheral circulation. Our data in the neonatal pig and monkey (53,55,56,58) indicate a considerable conversion of glutamate and aspartate by the gut and liver into glucose and lactate, which then appear in the peripheral blood. One important question in considering sensitivity to glutamate is whether subgroups of the population metabolize glutamate less efficiently than the general population. Indeed, several children have been reported with apparent defects in glutamate metabolism and transport (26–28,63). Our data suggest that the neonatal rodent and nonhuman primate metabolize glutamate less readily than adult animals (57). The human infant has been shown to be able to metabolize protein-bound glutamate at the same rate as the human adult (17).

To evaluate the question of variable rates of glutamate absorption and metabolism, we reviewed our data to determine whether there was a population subset metabolizing glutamate poorly. In 1972, we reported apparent variations in the metabolism and absorption of glutamate during studies in lactating women

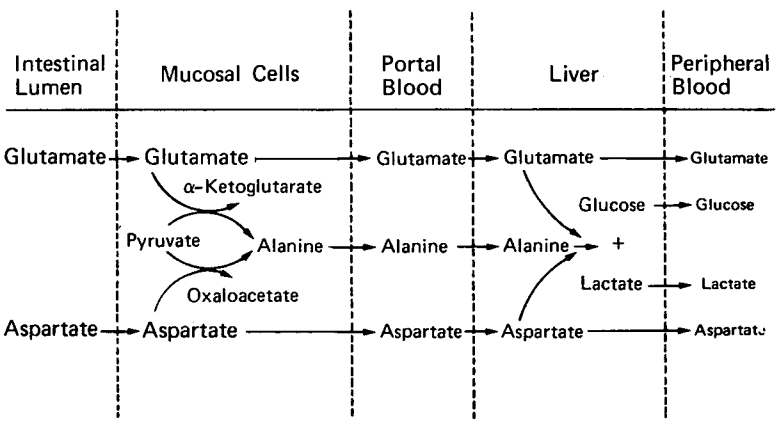

FIG. 2. Dicarboxylic amino acid absorption from the intestinal lumen, showing mucosal cell transamination to yield alanine and hepatic conversion of these amino acids to glucose and lactate as factors modulating peripheral plasma levels. (Reprinted with permission from Stegink, ref. 52.)

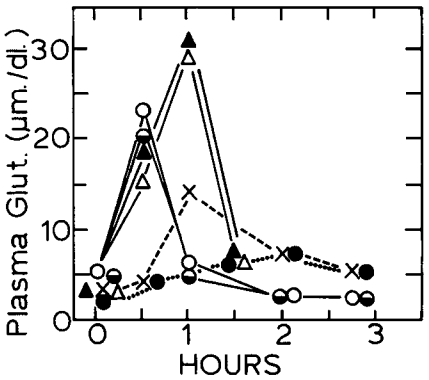

FIG. 3. Plasma glutamate levels in 8 subjects given 6-g loads of MSG in capsules with water. All symbols show values in individual subjects.

(5,54). In the original studies, four subjects were administered 6-g loads of monosodium glutamate (MSG) in capsules with water. We have since studied two additional nonlactating subjects under similar conditions. Figure 3 shows plasma levels in these subjects. Four of the subjects showed significant increases in plasma glutamate levels, with concomitant increases in plasma aspartate, whereas two subjects showed much smaller increases. These variations could have several causative factors: (a) biological variation in absorption and metabolism; (b) a differing rate of capsule dissolution in the gut; or (c) the possibility that two of the subjects had ingested a small amount of food prior to the study, contrary to instructions. Biological variation would be consistent with the earlier data of Himwich et al. (19), who noted considerable variation in plasma glutamate levels after MSG loading.

Recently, we have studied the variation in normal subjects given MSG dissolved in water. Six normal subjects (3 male, 3 female) drank a water solution (4.2 ml/kg) containing MSG at a level providing 100 mg/kg body weight. Peak plasma glutamate levels in these subjects are shown in Table 1. A substantial variation in peak plasma glutamate response was noted. However, all subjects showed substantial increases in plasma glutamate, in contrast to the study described earlier (54) where the equivalent load of MSG was given in capsule form. The variable rates of absorption and metabolism are consistent for each subject. Figure 4 shows plasma

TABLE 1. *Peak plasma glutamate levels in normal subjects given MSG in water at 100 mg/kg body weight*

Subject	Sex	Peak plasma glutamate levels (µmoles/dl)
1	F	87
2	F	56
3	F	30
4	M	61
5	M	62
6	M	51

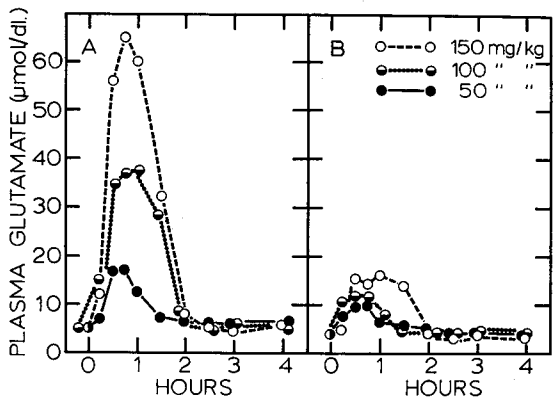

FIG. 4. Plasma glutamate levels in 2 adult subjects (**A** & **B**) administered MSG at 50, 100, and 150 mg/kg body weight dissolved in tomato juice.

glutamate levels in two subjects studied with varying doses of MSG administered in tomato juice. One subject metabolizes glutamate much more rapidly than the other, and this difference holds throughout the dose range studied. Moreover, the results are highly reproducible.

This variation in plasma glutamate response is not limited to subjects ingesting free glutamate dissolved in water. We have noted similar variation in normal adult subjects administered high protein meals where the major load comes from peptide-bound glutamate. Plasma glutamate levels were measured in six normal subjects (3 male, 3 female) ingesting a high protein meal consisting of an egg-milk custard (16). This meal, whose composition is shown in Table 2, was fed to the subjects at a level providing 1 g protein/kg body weight. As shown in Fig. 5, plasma glutamate levels in these subjects fall into three different patterns with two subjects in each group. Two subjects had essentially no change in plasma glutamate levels after ingestion of the meal. This result was reproducible. These same six subjects later participated in a meal study in which they were fed a high protein meal (1 g/kg)

TABLE 2. *Composition of custard meal*

Component	Weight (g)	Water (g)	Protein (g)	Fat (g)	CHO (g)
Egg	150	110	20	17	1
NFDM[a]	150	6	54	1	78
Fructose	30	0	—	—	30
Water	200	200	—	—	—
Total	530	316	74	18	109

Calculated protein content: 13.96 g protein/100 g custard. Actual protein content of each custard batch confirmed by analysis. Custard administered at a level providing 1 g protein/kg body weight.

[a] NFDM, nonfat dry milk.

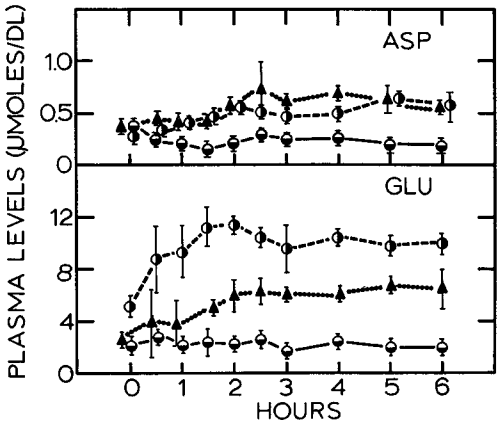

FIG. 5. Mean plasma glutamate (GLU) and aspartate (ASP) levels in 6 normal subjects administered a high protein meal (1 g protein/kg). The curves for these subjects appear to break down into three sets, with 2 subjects in each set. All symbols show values in the three sets of 2 subjects each.

consisting of a hamburger and a milk shake (4). Each subject showed a plasma glutamate response identical to that shown in the custard study. It was clear that the amino acids from the protein meal were absorbed by all subjects, since plasma levels of the branched-chain amino acids increased.

In summary, our data, like those of Himwich et al. (19), but in contrast to those of Bizzi et al. (7), indicate a considerable variation in the absorption and metabolism of both free and peptide-bound glutamate by normal adults.

PLASMA GLUTAMATE RESPONSE TO MSG ADMINISTERED IN WATER

Glutamate absorption and clearance following increasing doses of glutamate administered in water were studied in normal adult subjects. As expected, plasma glutamate levels in adult man increased sharply after ingestion of glutamate salts in water, with peak levels showing a high correlation to the administered dose.

Six normal adult subjects (3 male, 3 female) were studied after ingestion of MSG dissolved in water. The MSG was administered at levels of 100 and 150 mg/kg body weight. The 150 mg/kg body weight dose was chosen since it represents the Acceptable Daily Intake (ADI) for MSG as set by the WHO/FAO. The MSG was dissolved in water to provide either a 2.4 or 3.6% solution, and the subjects ingested these solutions at a level of 4.2 ml/kg body weight. Each subject was tested at both doses, with a 1-week interval between tests. Administration of doses was randomized.

Plasma glutamate levels in these subjects are shown in Table 3. Mean peak plasma glutamate levels were 50 μmoles/dl at a dose level of 100 mg/kg and 70 μmoles/dl at a dose level of 150 mg/kg. However, as noted previously (Table 1), considerable individual variation in peak plasma glutamate levels was observed. Subjects showing highest levels at the 100 mg/kg dose showed the highest values at the 150 mg/kg dose.

TABLE 3. *Plasma glutamate levels in normal adult subjects administered MSG at 100 and 150 mg/kg body weight dissolved in water*

Time (min)	Plasma levels (μmoles/dl)	
	100 mg/kg	150 mg/kg
0	2.69 ± 0.88	3.66 ± 1.00
15	14.4 ± 15.0	15.7 ± 11.8
30	47.1 ± 25.4	66.5 ± 50.0
45	50.1 ± 23.9	71.8 ± 35.7
60	24.9 ± 11.3	56.2 ± 29.8
90	8.19 ± 5.31	27.5 ± 13.4
120	4.28 ± 2.57	7.93 ± 3.72
150	3.72 ± 2.24	6.04 ± 4.18
180	4.19 ± 2.84	4.19 ± 1.39
240	3.05 ± 1.61	4.17 ± 2.28

Values listed as mean ± SD.

The magnitude of the observed plasma glutamate levels was surprising. Our previous studies with normal adult subjects given a load of MSG approximating 100 mg/kg in capsules had shown mean peak values of 16 μmoles/dl. Figure 6 compares plasma glutamate levels in the subjects given MSG at 100 mg/kg level dissolved in water, or given in capsules. The data suggest that administration of MSG in capsules affects plasma glutamate levels. However, it is also possible that these differences result from individual variations in the population groups studied.

The peak plasma glutamate levels observed after glutamate administration in water are consistent with those reported by other investigators in man. Figure 7 compares peak plasma glutamate levels obtained in our studies at 100 and 150 mg/kg body weight with values in other laboratories for human subjects adminis-

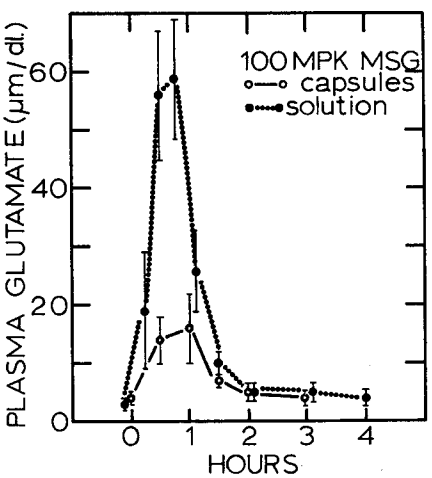

FIG. 6. Plasma glutamate levels in normal subjects after administration of 100 mg/kg loads either in capsules or in 4.2 ml water/kg body weight. Data are shown as the mean ± SEM.

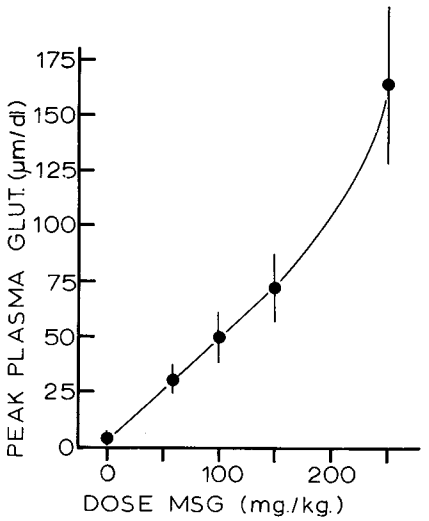

FIG. 7. Mean (± SEM) peak plasma glutamate levels in normal adults administered MSG in water. Data at 60 mg/kg from Bizzi et al. (7), data at 100 and 150 mg/kg from our studies, and data at 240 mg/kg from Himwich et al. (19).

tered glutamate at 60 (7) or 250 mg/kg body weight (19). These data indicate a high correlation of MSG dose to plasma glutamate levels in the 60 to 250 mg/kg body weight range when MSG is dissolved in water. The slope of this curve is significantly greater than that observed for adult mice and monkeys given equivalent doses (57).

Since tomato juice is often used as a vehicle for MSG administration during studies of Chinese restaurant syndrome, plasma glutamate levels were also measured in eight normal subjects administered MSG dissolved in tomato juice. Eight normal adult subjects (4 male, 4 female) were studied. The study was carried out double blind, with the subjects receiving either MSG (150 mg/kg) or NaCl (a dose equivalent to the sodium content of MSG) dissolved in unsalted tomato juice (Diet Delight, California Canners and Growers, San Francisco). The order in which the subjects received MSG or NaCl was randomized. The tomato juice was administered at a level of 4.2 ml/kg body weight, with sufficient MSG to give a 3.6% solution.

Plasma glutamate levels in these subjects are shown in Fig. 8. A marked elevation in plasma glutamate was noted after ingestion of MSG in tomato juice, whereas no change was seen after ingestion of the tomato juice containing NaCl. The free glutamate content of the unsalted tomato juice was 1 mg/4.2 ml of juice. Thus, subjects received approximately 1 mg MSG/kg body weight when ingesting tomato juice with NaCl. The data demonstrate a marked increase in plasma glutamate levels after ingestion of 150 mg MSG/kg body weight dissolved in tomato juice. Mean peak plasma levels were slightly lower than those noted in a different group of subjects ingesting the equivalent dose of MSG (150 mg/kg) in water (Table 3). It is not clear whether this difference reflects an effect of the other components of the tomato juice or a difference in the subject population studied.

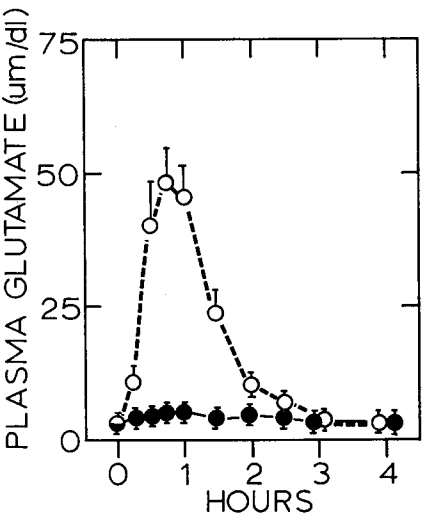

FIG. 8. Mean (± SEM) plasma glutamate levels in normal subjects administered glutamate (○) at 150 mg/kg body weight or NaCl (●) at a sodium content equal to that of the MSG dissolved in tomato juice.

EFFECT OF MSG INGESTION WITH MEALS ON PLASMA GLUTAMATE LEVELS

The critical questions about glutamate concern its use as a food additive. Thus, it is important to evaluate the effect of MSG addition to food systems on plasma amino acid levels. It is generally conceded that the large quantities of glutamate contained in dietary protein are readily metabolized. However, it has been suggested that the addition of free glutamate to a meal as MSG might produce a very rapid early increase in plasma glutamate and aspartate levels (36,37). It was suggested that the added free glutamate is metabolized less readily than the peptide-bound glutamate, producing a rapid early rise in plasma glutamate levels. We evaluated the plasma amino acid response in normal subjects ingesting MSG with a variety of meal systems to test the hypothesis that such an addition significantly affects plasma glutamate levels.

The data in Table 4 are taken from Appendix E of the Committee on GRAS List Survey—Phase III report (10). These data indicate a mean expected daily intake of 6.8 mg/kg body weight in the age group with the highest ingestion level. In this age group, a mean level of 30 mg/kg body weight represents the 90th percentile for the total expected *daily* ingestion of added MSG.

For our first study (4), a level of 34 mg MSG/kg body weight was chosen, slightly above the 90th percentile of daily ingestion. This dose was fed to normal adult volunteers in conjunction with a high protein meal. The meal chosen was a hamburger-milk shake system having the composition shown in Table 5. This meal was prepared with and without MSG. Normal adult volunteers were fed each meal in a quantity sufficient to provide a protein load of 1 g protein/kg body weight and a total glutamate load of 171 to 198 mg/kg body weight (Table 6). Figure 9 shows plasma glutamate and aspartate levels in these subjects. No significant

TABLE 4. *Expected daily intake of MSG based on person-days*

Age	Intakes (mg/kg/day)			
		Percentile		
	Mean	90th	99th	99.9th
0–5 months	0.3	0	11	25
6–11 months	1.9	1.9	36	46
12–23 months	6.8	30	43	61
2–5 years	5.5	23	37	56
6–17 years	2.7	10	25	40
18+ years	1.5	7	12	19

From Committee on GRAS List Survey—Phase III, ref. 10.

TABLE 5. *Composition of the hamburger—milk shake meal for a 70-kg adult*

Component	Quantity (g)	Protein (g)	Fat (g)	CHO (g)	Energy (kcal)
Hamburger	222	61	25.5	0	346
Bun	50	4.5	1.5	25.5	133
Milk	100	3.5	3.5	5	66
Ice cream	50	2	5	11	95
Total	422	71	35.5	72	640

For the 70-kg person, the meal supplies about 1 g/kg body weight as protein (=38% of total energy). Quantity of the hamburger in each meal was varied with each individual so as to provide protein at 1 g/kg body weight.

TABLE 6. *Estimated intake of protein, aspartic acid, and glutamic acid in meal studies*

Study	Protein (g/kg)	Total aspartate (g/kg)	Total glutamate (g/kg)
Hamburger-shake	1.0	90	171
Hamburger-shake with MSG	1.0	90	198[a]

[a] Corrected for the sodium content and water of hydration of MSG (78% of MSG is glutamate).

differences in plasma glutamate and aspartate levels were noted between groups. In particular, plasma glutamate and aspartate levels did not increase in the early part of the absorption-metabolism curve. A large number of blood samples were taken in the early postprandial state to detect such a rise if it did occur.

It has been suggested that under some circumstances, erythrocytes might carry amino acids to an extent greater than plasma (3,12–15). Accordingly, erythrocyte glutamate levels were also measured. As shown in Fig. 10, erythrocyte glutamate

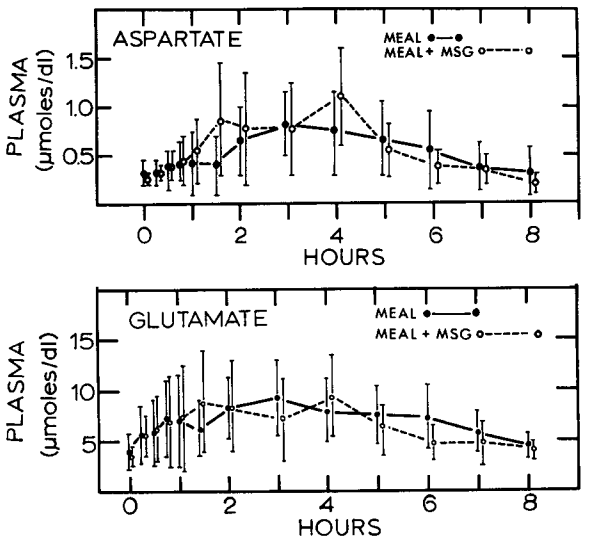

FIG. 9. Plasma glutamate and aspartate levels (mean ± SD) in normal adult subjects after ingestion of a high protein meal (1 g/kg) with and without added MSG (34 mg/kg body weight). (From Baker, Filer, Jr., and Stegink, ref. 4.)

and aspartate levels did not differ between the two groups. Thus, we concluded that the addition of MSG to a high-protein meal at a level of 34 mg/kg body weight had no significant effect on either plasma or erythrocyte glutamate and aspartate levels (4).

In view of the rapid metabolism of MSG when added to meals, additional studies

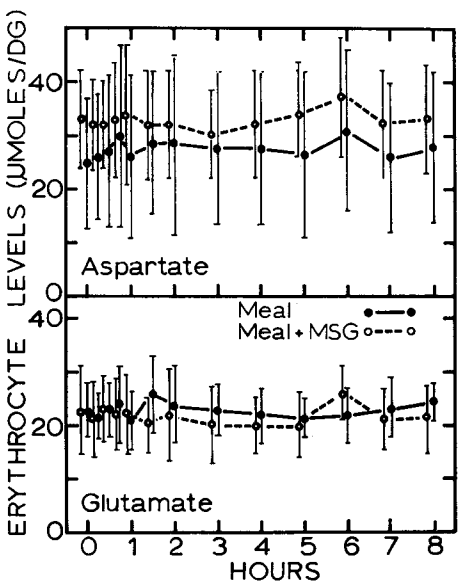

FIG. 10. Erythrocyte aspartate and glutamate levels (mean ± SD) in normal adults ingesting a high protein meal with and without added MSG (34 mg/kg). (From Baker, Filer, Jr., and Stegink, ref. 4.)

were carried out at higher doses. In these studies, glutamate was added to meals at levels of 0, 100, and 150 mg/kg body weight. The 150 mg/kg body weight load represents the ADI of MSG as published by the WHO/FAO.

The meal system used was Sustagen (composition shown in Table 7). Sustagen administered at 4.2 ml/kg provides 0.4 g protein, 1.12 g carbohydrate, and 6.61 kcal/kg. Six fasted adult humans (3 male, 3 female) were fed Sustagen meals with and without added MSG (6). Subjects were tested at 10-day intervals with the sequence randomized according to a Latin square design (9). Serial blood samples were obtained over a 6-hr period for determination of plasma concentrations of amino acids.

Table 8 shows the plasma glutamate levels in these subjects. Ingestion of Sustagen alone increased plasma glutamate levels from 4 μmoles/dl to approximately 6 to 7 μmoles/dl. The addition of MSG at 100 and 150 mg/kg increased plasma glutamate levels further, reaching mean values approximating 11 μmoles/dl. However, the levels noted at 150 mg/kg body weight in these studies are no higher

TABLE 7. *Composition of the Sustagen meal system fed was 4.2 ml/kg body weight*

Component	Quantity (gm/kg)	Energy (kcal/kg)
Protein	0.40	1.6
Fat	0.059	0.53
Carbohydrate	1.12	4.48
Water	4.2	0
Total	5.78	6.61

Sustagen (Mead-Johnson) also contains appropriate vitamins and minerals.

TABLE 8. *Plasma glutamate levels in normal subjects fed Sustagen with and without added MSG*

Time (min)	Plasma levels (μmoles/dl)		
	No MSG	100 mg MSG/kg	150 mg MSG/kg
0	4.21 ± 1.39	4.06 ± 0.63	4.59 ± 2.03
15	5.48 ± 2.03	6.90 ± 1.87	6.66 ± 2.62
30	6.43 ± 3.03	8.55 ± 3.30	8.89 ± 3.42
45	6.64 ± 1.99	11.2 ± 4.89	9.44 ± 2.58
60	6.37 ± 2.35	10.2 ± 4.38	10.7 ± 2.41
90	5.25 ± 1.67	8.61 ± 2.84	10.8 ± 3.10
120	5.78 ± 1.21	8.88 ± 2.49	9.27 ± 4.20
150	5.87 ± 2.15	7.78 ± 2.41	7.99 ± 2.46
180	6.68 ± 2.10	6.65 ± 2.99	6.59 ± 1.68
240	5.04 ± 1.24	5.11 ± 2.39	5.57 ± 0.48
300	4.21 ± 1.39	4.06 ± 0.63	4.59 ± 2.03
360	5.48 ± 2.03	6.90 ± 1.87	6.66 ± 2.62

Values listed as mean ± SD.

TABLE 9. *Correlation of plasma glutamate levels with glutamate ingested in a meal system*

Meal	Protein intake (g/kg)	MSG added (mg/kg)	Total glutamate (mg/kg)	Plasma glutamate levels (μm/dl)		
				Fasting[a]	Peak[a]	Range[b]
Custard (adults)	1.0	0	207	3.3 ± 1.6	6.3 ± 3.4	3–12
Hamburger—milk shake	1.0	0	171	4.1 ± 1.8	7.1 ± 3.9	4–15
Hamburger—milk shake + MSG	1.0	34	198	3.4 ± 1.0	8.8 ± 5.0	4–13
Sustagen	0.40	0	80	4.6 ± 1.6	7.6 ± 1.6	7–10
Sustagen + MSG	0.40	150	197	4.1 ± 1.2	10.5 ± 2.7	9–14

$N = 6$.
[a] Mean ± SD.
[b] Peak values.

than those noted postprandially in some normal adults ingesting a high protein meal alone (Table 9).

Our data indicate that MSG added to meals is metabolized much more rapidly than when ingested in water or tomato juice. Figure 11 summarizes the differences noted in plasma glutamate levels after ingestion of MSG (150 mg/kg) in either water or Sustagen. These data demonstrate a marked difference in the metabolism of glutamate depending on whether it is ingested in water or with a meal.

It is not clear how ingestion of the meal modulates the absorption of glutamate and its metabolism. A slower rate of absorption would permit greater catabolism of

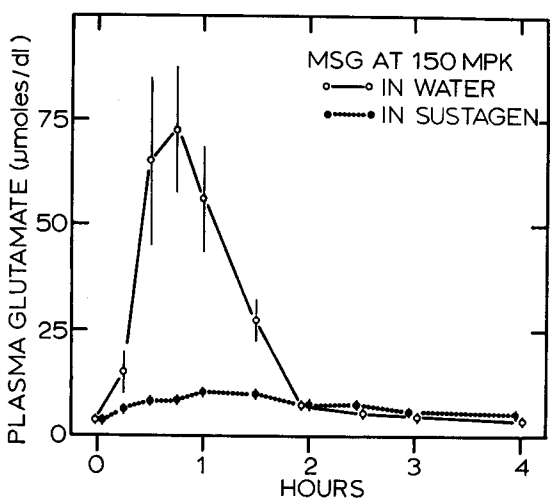

FIG. 11. Comparison of plasma glutamate levels (mean ± SEM) in normal adult subjects ingesting 150 mg MSG/kg body weight either dissolved in water or as part of a Sustagen meal.

glutamate by the intestinal mucosa, resulting in a decreased release of glutamate to portal blood. Alternatively, the carbohydrate present in Sustagen could serve as a source of pyruvate, facilitating the transamination of glutamate to α-ketoglutarate and its metabolism in the intestinal mucosa (Fig. 2). This would increase glutamate catabolism and decrease glutamate release to the peripheral circulation. The latter possibility was intriguing, since the Sustagen meal provided carbohydrate (as corn syrup solids) at 1.12 g/kg body weight.

To test this hypothesis, a normal subject was given 100 mg MSG/kg body weight, either dissolved in water or dissolved in water with sufficient carbohydrate to provide 1.12 g glucose/kg body weight. The carbohydrate was administered as Polycose (Ross Laboratories, Columbus, Ohio), a partially hydrolyzed corn starch preparation. The data in Fig. 12 compare glutamate and glucose levels in a typical individual after ingestion of 100 mg MSG/kg body weight in either water or Polycose. It is clear that the carbohydrate has a striking effect on the metabolism of glutamate. Changes in blood glucose and glutamate levels indicate that gastric emptying has occurred. It seems likely that the rapid metabolism of MSG noted after ingestion with meals reflects in part the carbohydrate content of the meal. Presumably, carbohydrate is absorbed into the intestinal mucosa and converted to glucose and pyruvate, ultimately facilitating the transamination and metabolism of glutamate by the mucosal cells (Fig. 13).

Studies of the Chinese restaurant syndrome described by Kenney (20) led us to examine the effect of the beverage mixture utilized in his studies on plasma glutamate levels. This study was prompted by the studies shown in Fig. 12 demonstrating the profound effect of added carbohydrate on the plasma glutamate levels after MSG loading. Since Kenney's beverage mixture contains 30 g sucrose, we wondered whether plasma glutamate levels would be depressed by this quantity of carbohydrate. Plasma glutamate levels were measured in one subject given MSG at 100 mg/kg body weight dissolved in water or the beverage mix. In both cases the

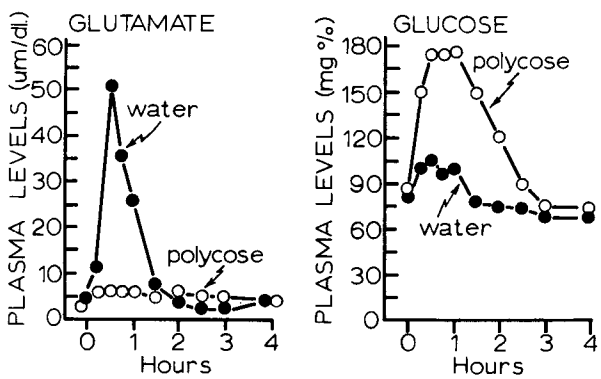

FIG. 12. Plasma glutamate and glucose levels in a normal adult subject administered MSG at 100 mg/kg body weight either in water or in a water solution containing 1.12 g Polycose/kg body weight.

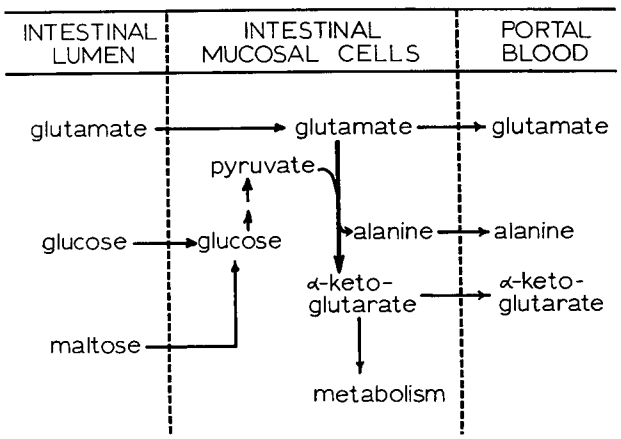

FIG. 13. Interrelationship between carbohydrate and glutamate metabolism in intestinal mucosal cells.

MSG concentration in the solution was 2.4%, and the mixture was administered at a level of 4.2 ml/kg body weight. In the first experiment, the subject ingested the MSG in water. In the second experiment, the basic beverage mixture described by Kenney was utilized, with the following exceptions: (a) additional MSG was added to bring the total dose to 100 mg/kg body weight and (b) the volume of the solution administered was increased so that the MSG concentration would be held constant at 2.4%. Figure 14 shows plasma glutamate and glucose levels in this study. The presence of sucrose (0.42 g/kg) had effected peak levels, but significant elevations of plasma glutamate occurred. This presumably reflects both the lower carbohydrate content of the beverage versus the Polycose feeding (0.42 versus 1.12 g/kg) and the

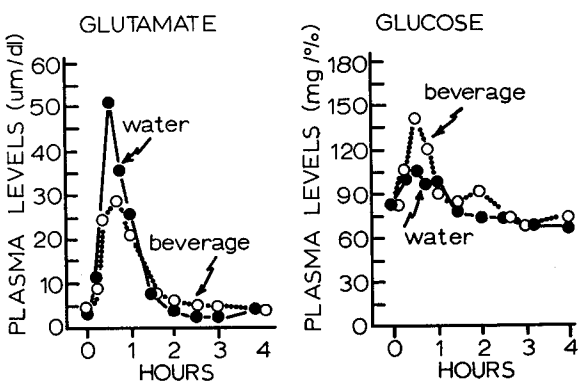

FIG. 14. Plasma glutamate and glucose levels in a single normal male subject administered MSG at 100 mg/kg body weight dissolved either in water or in a beverage mixture containing 30 g sucrose.

carbohydrate composition. Sucrose is composed of glucose and fructose. Fructose is not appreciably metabolized by the intestinal mucosa and probably does not exert a significant effect on mucosal metabolism of glutamate. Thus, the load of glucose available to the mucosal cells would be 0.21 g/kg. This suggestion is consistent with the data we have observed after ingestion of MSG with tomato juice (Fig. 8). The tomato juice used contained a significant quantity of carbohydrate (0.16 g/4.2 ml), largely as fructose (61). This level of carbohydrate had little effect on plasma glutamate levels.

SUMMARY

1. Our data indicate considerable variation in the absorption and metabolism of both free and peptide-bound glutamate by normal adults.

2. Plasma glutamate levels rapidly increase after MSG ingestion in water, with peak values showing a strong correlation with the dose administered.

3. Ingestion of MSG at 150 mg/kg with a single meal did not significantly elevate plasma glutamate levels above those noted after ingestion of a high protein meal alone (1 g protein/kg body weight). However, administration of this dose in water produced significant elevations of plasma glutamate levels.

4. The increased plasma glutamate levels noted after ingestion of MSG in water are markedly diminished by the presence of carbohydrates in the solution.

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