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Effects of aging and gastric lipolysis on gastric emptying of lipid in liquid meal

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Abstract: Lipid delays gastric emptying, and aging is associated with changes in gastric motor function and transit. However, little is known about the effect of lipid on gastric emptying time in the elderly. To determine the effect of aging on lipid gastric emptying, we used electrical impedance tomography (EIT) to study gastric emptying of liquid meals with or without lipid in five young (23.0 ± 0.6 years, mean ± SEM) and six elderly (73.3 ± 1.6 years) healthy male volunteers. These subjects drank 400 ml of non-lipid soup (triglycerides, 0 g) or lipid soup (triglycerides, 24.6 g) in liquid test meals. To study the effect of lipolysis in the stomach, a liquid test meal containing 240 mg of lipase in the lipid soup was also administered. Plasma cholecystokinin (CCK) concentration was measured by specific radioimmunoassay before and 30 min after the ingestion of a test meal. The gastric emptying time of the lipid soup was longer in the elderly than in the young subjects, and the time was significantly longer for lipid soup than for non-lipid soup ($P < 0.05$) in both the young and elderly subjects. Gastric emptying time for non-lipid soup was not significantly different between the elderly and young subjects. The administration of lipase shortened the gastric emptying time for lipid in both the elderly and the young subjects. Basal CCK concentration was significantly higher in the elderly than in the young subjects. However, there was no relationship between gastric emptying time and plasma CCK concentration after the ingestion of a test meal in the subjects overall. In conclusion, the delaying effect of lipid on gastric emptying is increased in the elderly, and the administration of lipase accelerates the emptying of lipid from the stomach.

Key words: gastric emptying, lipid, aging, lipase, cholecystokinin, electrical impedance tomography (EIT)

Introduction

Satiation occurs after the ingestion of fat-rich food, and an increase in this satiation is commonly experienced with aging. Dietary fat delays gastric emptying,[1] which is regulated by small-intestine nutrient-mediated feedback, such as by the duodenal receptor to the hydrolytic products of triglycerides[2] and release of cholecystokinin (CCK).[3] Aging is associated with changes in gastric motor[4] or neural function[5] that have effects on gastric emptying. Therefore, an aging effect on gastric emptying of lipid has been considered, but the relationship between them remains controversial.[3,6–8]

Lipase plays an important role in the digestion of fat. Recent studies have indicated the importance of gastric and pancreatic lipases in the regulation of gastric emptying.[9,10] In these studies, a lack of lipase accelerated gastric emptying in a pancreatic insufficiency model. Clinically, lipase is administered to improve satiation after the eating of fat-rich foods even in subjects without diseases; however, the effect of lipase administration on gastric emptying time in these subjects is unclear.

In this study, we used the non-invasive method of electrical impedance tomography (EIT) to measure gastric emptying of liquid meals with and without lipid in young and elderly healthy subjects to determine the age-associated effect of lipid on gastric emptying. Lipase was also administered to both age groups with the lipid meal to study the effect of lipolysis in the stomach.

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Patients and Methods

Subjects

We studied five young healthy men (mean age, 23.0 ± 0.6 years; range, 21–24 years; height, 175.0 ± 1.67 cm; weight, 64.6 ± 2.86 kg; body mass index (BMI), 21.1 ± 0.82 kg/m^2 [mean ± SEM]) and six elderly healthy men (mean age, 73.3 ± 1.6 years; range, 69–80 years; height, 162.5 ± 0.7 cm; weight, 58.5 ± 1.5 kg; BMI, 22.2 ± 0.6 kg/m^2); all subjects were volunteers. The young subjects were taller than the elderly subjects, but the weight and BMI in the two groups were not significantly different. None of the subjects had any history of major gastrointestinal disease, diabetes mellitus, or surgery, nor were any taking drugs that influence gastrointestinal motility. All subjects gave their fully informed consent for the studies, and the protocol was approved by the Ethical Committee of the Research Center of Health, Physical Fitness and Sports, Nagoya University.

Protocol

After the subjects fasted overnight, their gastric secretion was inhibited by the oral administration of 200 mg cimetidine (Tagamet; Smith Kline Beecham, Tokyo, Japan) 1 h before the test for EIT images. EIT images of gastric emptying were measured by applied potential tomography (APT; University of Sheffield, UK).[11] EIT images were collected over 15-s periods at 1-min intervals. The images were collected for 5 min before and 60 min after the ingestion of test meals. Subjects were asked to sit during the study. All subjects drank 400 ml of each of three kinds of liquid test meals with 0.65% NaCl: (1) non-lipid soup (triglycerides, 0 g; 13 kcal); (2) lipid soup (30 g of margarine mixed with non-lipid soup; triglycerides, 24.8 g; 237 kcal), and (3) lipid soup with lipase (240 mg of Lipase A12, donated by Amano Pharmaceutical, Nagoya, Japan, taken with lipid soup). The studies were performed in a double-blind manner, and the intervals between the three consecutive studies were more than 1 week.

Blood samples were drawn into ice-chilled tubes containing ethylenediamine-tetraacetic acid (EDTA) before and 30 min after the ingestion of the test meals, and were immediately centrifuged at 4°C at 3000 rpm for 15 min. The plasma samples were stored at −30°C until assay. Plasma CCK concentration was measured by radioimmunoassay (RIA), using OAL-656 antiserum (Otsuka Assay Laboratories, Tokushima, Japan),[12] after ethanol extraction of CCK from plasma. This CCK assay measures all forms of active human CCK.

Analysis of results

To obtain a profile of gastric emptying by EIT, the gastric region was outlined, using an integrated image of the first three frames obtained after ingestion, and the resistivity of this region was calculated by computer for all images. The percentage of the meal remaining in the stomach was calculated by expressing each value as a percentage of the minimum value after ingestion, and this was plotted against time. The times taken for a quarter ($T_{1/4}$) and for half the meal to empty ($T_{1/2}$) were calculated from the percentage plots.

Statistical analysis

Data values are expressed as means ± SEM. Comparison of gastric emptying time and plasma CCK concentration between the young and elderly groups was done with a Mann-Whitney *U*-test, and comparisons between the non-lipid soup test, lipid soup test, and lipid soup with lipase test were done with the paired *t*-test after adjusting for equal variance. Correlation between gastric emptying time and plasma CCK concentration was analyzed by Spearman rank correlation. The *P* values computed were two-tailed, and $P < 0.05$ was considered significant.

Results

There were no significant differences in the gastric emptying time of the non-lipid soup between the young and elderly subjects (5.3 ± 0.9 vs 5.8 ± 1.1 min for $T_{1/4}$, and 15.2 ± 2.9 vs 15.8 ± 6.3 min for $T_{1/2}$; Table 1). Gastric emptying time for the lipid soup was longer than that for the non-lipid soup in both the young and elderly subjects. In the elderly subjects, the percentage of remaining lipid soup was significantly greater from 10 to 22 min than that of non-lipid soup ($P < 0.05$; Fig. 1), and both $T_{1/4}$ (13.2 ± 3.5 min) and $T_{1/2}$ (28.0 ± 6.1 min) for lipid soup were significantly greater than the corresponding values for non-lipid soup ($P < 0.05$; Table 1). $T_{1/2}$ for lipid soup was longer in elderly subjects (28.0 ± 6.1 min) than in young subjects (19.1 ± 3.3 min), but the difference was not significant. The addition of lipase shortened the gastric emptying time for lipid soup in both young and elderly subjects (Table 1).

Basal (before ingestion of test meal) plasma CCK concentration was significantly higher in elderly subjects (10.9 ± 0.5 pg/ml) than in young subjects (8.5 ± 0.5 pg/ml; $P < 0.01$). However, there were no differences between young and elderly subjects in Δ plasma CCK concentration 30 min after ingestion for all test meals (Table 2).

There was no significant relationship between plasma CCK concentration 30 min after ingestion and gastric

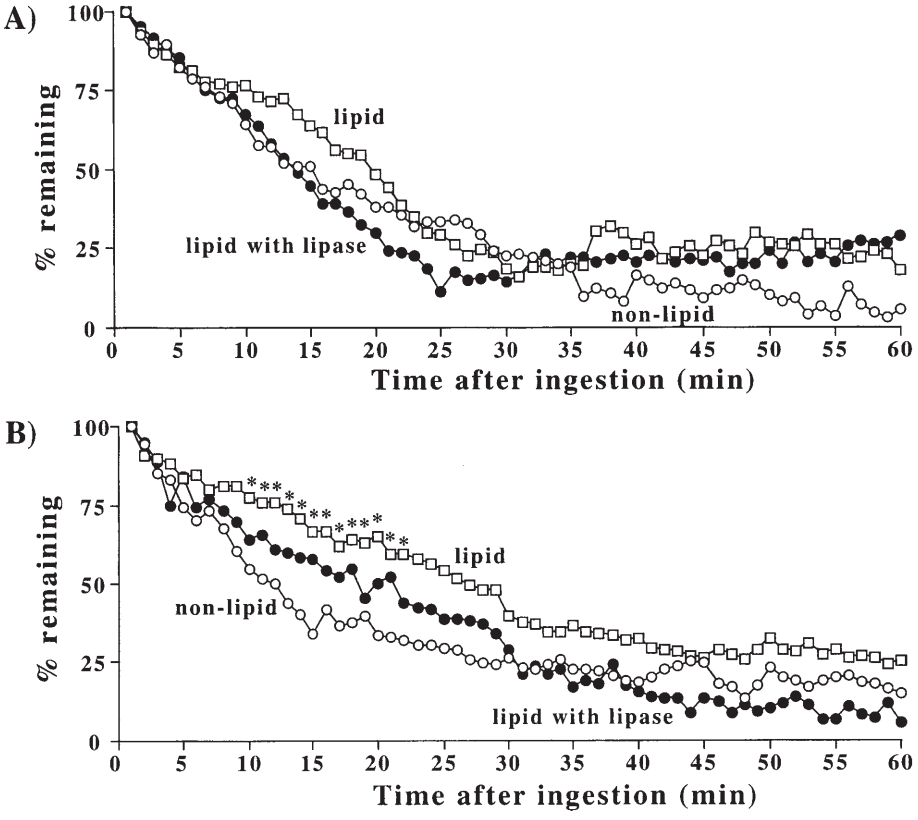

Fig. 1A,B. Percentage of liquid meal remaining in the stomach in **A** young subjects and **B** elderly subjects. *Open circles*, Non-lipid meal; *open squares*, lipid meal; *colsed circles*, lipid meal with lipase. $*P < 0.05$ non-lipid vs lipid meal

Table 1. Gastric emptying time of liquid meals

Test meal	Non-lipid	Lipid	Lipid with lipase
Quarter emptying time ($T_{1/4}$, min)			
Young subjects ($n = 5$)	5.3 ± 0.9	12.0 ± 3.4	6.5 ± 1.4
Elderly subjects ($n = 6$)	5.8 ± 1.1	13.2 ± 3.5*	9.8 ± 2.3
Half emptying time ($T_{1/2}$, min)			
Young subjects ($n \pm 5$)	15.2 ± 2.9	19.1 ± 3.3	11.5 ± 1.9
Elderly subjects ($n \pm 6$)	15.8 ± 6.3	28.0 ± 6.1*	18.4 ± 3.5

$*P < 0.05$ vs non-lipid meal
Values are means ± SEM

emptying time ($r = 0.247$ for $T_{1/4}$ and $r = 0.210$ for $T_{1/2}$) when the results of all subjects were analyzed together.

Discussion

This study showed that the effect of the lipid content in a liquid meal on gastric emptying was greater in elderly than in young subjects. Aging in normal subjects may be associated with retardation of gastric emptying.[4,6,7] However, Kasano et al.[8] demonstrated that gastric emptying of a semisolid meal with fat was almost constant in healthy subjects regardless of age. Moore et al.[4] and Kao et al.[13] demonstrated that the age effects on gastric emptying were shown in a liquid but not in a solid meal. Therefore, the effect of aging is related to the form of a test meal.

Age-related changes occur in gastric motility-related factors, such as gastric "pump" dysfunction[14] and abnormal sensory feedback from the small intestine.[15] Delay of gastric emptying in the elderly may reflect increased small-intestinal feedback, occurring as a result of "hypersensitivity" of small-intestinal receptors or increased exposure of small-intestinal receptors to nutrients.[14] CCK is released into the bloodstream from the small intestine in response to a nutrient meal, and it delays gastric emptying by relaxation of the fundus, inhibition of antral motility, and stimulation of pyloric contractions.[3] Since lipid is an important factor in the release of

Table 2. Plasma cholecystokinin (CCK) concentration

	Basal CCK (pg/ml)		ΔCCK (pg/ml) 30 min after ingestion of meal		
			Non-lipid	Lipid	Lipid with lipase
Young subjects ($n = 5$)	8.5 ± 0.5	**	−0.3 ± 0.2	1.3 ± 0.5	0.8 ± 0.4
Elderly subjects ($n = 6$)	10.9 ± 0.5		−0.6 ± 0.5	0.9 ± 0.7	1.2 ± 2.3

$^{**}P < 0.01$
Values are means ± SEM

CCK, this peptide is thought to be related to the greater delay of gastric emptying in elderly subjects. In the present study, basal plasma CCK concentration was higher in elderly subjects, and ΔCCK after ingestion of the lipid meal was similar in young and elderly subjects. Furthermore, there were no differences in gastric emptying time for a non-lipid meal between the young and elderly subjects regardless of the basal CCK concentration. Since gastric emptying of a liquid meal occurs by fundus contractions leading to a gastroduodenal pressure gradient, exposure to higher plasma CCK in elderly subjects may, in part, cause inhibition of emptying because of a greater than normal relaxation of the fundus. Cook et al.[16] reported that intraduodenal lipid infusion stimulated phasic pyloric pressure waves, and this response was greater in elderly subjects than in young subjects. This increased pressure may reflect a reduction in the activity of inhibitory neural pathways. Smits and Lefebvre[17] showed the relationship between gastric emptying of a liquid meal and the non-adrenergic noncholinergic neuron-stimulated relaxation of the gastric fundus with aging. Therefore, all the above factors are thought to be relevant to the delay of gastric emptying after the ingestion of a meal with lipid; however, we did not provide information about all the possible factors in this study.

Lipase is also related to the regulation of gastric emptying.[10] Lipase is secreted from gastric chief cells (gastric lipase) and pancreatic acinar cells (pancreatic lipase), and gastric lipase contributes to about 10% of triglycerides hydrolysis.[18] The lipolytic activity of lipase after the ingestion of a lipid meal plays an important role in gastric emptying because products of gastric lipolysis. such as diglycerides, monoglyceride, and free fatty acid, stimulate CCK secretion, leading to the inhibition of gastric emptying.[9,10] From the results of these studies, the administration of lipase with a lipid meal appears to cause further inhibition of gastric emptying with the elevation of plasma CCK, because large amounts of lipolysis products flow into the duodenum from the stomach. However, in our study, the addition of lipase to a lipid meal accelerated gastric emptying in both the elderly and young subjects. Furthermore, there was no difference in plasma CCK elevation after the ingestion of meals with and without lipase. The reasons for this difference in lipase effect are likely to be, in part, due to differences in methodology. Mayer et al. and Schwizer et al. used models that induced lack of lipase activity with a specific lipase inhibitor[9,10] or pancreatic fistula.[10] In our study, we observed the effect of adding lipase to a meal in subjects with normal gastric and pancreatic secretions. The administration of lipase may be expected to relieve satiation after a lipid meal.

In conclusion, the delaying effect of lipid on gastric emptying is accentuated in the elderly. The addition of lipase to lipid meals accelerates the emptying of lipid from the stomach.

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References

1. Hunt JN, Knox MT. Regulation of gastric emptying. In: Code CF, editor. Handbook of physiology—alimentary canal IV. Philadelphia: Williams and Wilkins; 1968. p. 1917–35.
2. Cortot A, Phillips SF, Malagelada JR. Parallel gastric emptying of nonhydrolyzable fat and water after solid-liquid meal in humans. Gastroenterology 1982;82:877–81.
3. Schwizer W, Borovicka J, Kunz P, Fraser R, Kreiss C, D'Amato M, et al. Role of cholecystokinin in the regulation of liquid gastric emptying and gastric motility in humans: studies with the CCK antagonist loxiglumide. Gut 1997;41:500–4.
4. Moore JG, Tweedy C, Christian PE, Datz FL. Effect of age on gastric emptying of liquid-solid meals in man. Dig Dis Sci 1983; 28:340–4.
5. Smits GJM, Lefebvre RA. Influence of age on the signal transduction pathway of nonadrenergic noncholinergic neurotransmitters in rat gastric fundus. Br J Pharmacol 1995;114:640–7.
6. Evans MA, Trigger EJ, Cheung M, Broe GA, Creasey H. Gastric emptying rate in the elderly: implications for drug therapy. J Am Geriatr Soc 1981;29:201–5.
7. Horowitz M, Maddern GJ, Chatterton BE, Collins PJ, Harding PE, Shearman DJ. Changes in gastric emptying rates with age. Clin Sci 1984;67:213–8.
8. Kasano T, Yoshida Y, Kihira K, Kimura K. Relationship between morphological and functional changes in the stomach with aging. Jpn J Geriatn 1991;28:606–10.

9. Mayer JH, Elashoff JD, Domeck M, Levy A, Jehn D, Hlinka M, et al. Control of canine gastric emptying of fat by lipolytic products. Am J Physiol 1994;266:G1017–35.
10. Schwizer W, Asal C, Kreiss C, Mettraux C, Borovicka J, Rémy B, et al. Role of lipase in the regulation of upper gastrointestinal function in humans. Am J Physiol 1997;273:G612–20.
11. Avill R, Mangnall YF, Bird NC, Brown BH, Barber DC, Seager AD, et al. Applied potential tomography. A new noninvasive technique for measuring gastric emptying. Gastroenterology 1987;92:1019–26.
12. Himeno S, Tarui S, Kanayama S, Kuroshima T, Shinomura Y, Hayashi C, et al. Plasma cholecystokinin responses after ingestion of liquid meal and intraduodenal infusion of fat, amino acids, or hydrochloric acid in man: analysis with region specific radioimmunoassay. Am J Gastroenterol 1983;78:703–7.
13. Kao CH, Lai TL, Wang SJ, Chen GH, Yeh SH. Influence of age on gastric emptying in healthy Chinese. Clin Nucl Med 1994;19: 401–4.
14. Clarkston WK, Pantano MM, Morley JE, Horowitz M, Littlefield JM, Burton FR. Evidence for the anorexia of aging: gastrointestinal transit and hunger in healthy elderly vs. young adults. Am J Physiol 1997;272:R243–8.
15. Horowitz M, Dent J. Disordered gastric emptying: mechanical basis, assessment and treatment. Bailliere's Clin Gastroenterol 1991;5:371–406.
16. Cook CG, Andrews JM, Jones KL, Wittert GA, Chapman IM, Morley JE, et al. Effects of small intestinal nutrient infusion on appetite and pyloric motility are modified by age. Am J Physiol 1997;273:R755–61.
17. Smits GJM, Lefebvre RA. Influence of aging on gastric emptying of liquids, small intestine transit, and fecal output in rats. Exp Gerontol 1996;31:589–96.
18. Carriere F, Barrowman JA, Verger R, Laugier R. Secretion and contribution to lipolysis of gastric and pancreatic lipases during a test meal in humans. Gastroenterology 1993;105:878–88.