MINI-REVIEW

Contribution of umami taste substances in human salivation during meal

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Abstract : The oral gustatory perception during a meal has very important physiological roles such as inducing appetite, smoothing mastication and swallowing, promoting digestion and each nutrient availability. One hundred years ago, L-glutamate was discovered as a new taste substance in Japan. Since then, Japanese taste physiologists have lead the research to establish L-glutamate as the prototype molecule for the fifth basic taste (umami taste), in addition to saltiness, sweetness, bitterness and sourness. Meanwhile, various lines of evidence demonstrated that taste perception is linked to taste stimuli-oral/pharyngeal reflexes. In this review, we focus on the efficacy of L-glutamate for human salivation and discuss the possible application of umami taste simulation to the nutritional management for the elderly due to amelioration of their quality of life (QOL). J. Med. Invest. 56 Suppl. : 197-204, December, 2009

Keywords **:** *dietary L-glutamate, umami taste, human salivation, elderly nutrition.*

INTRODUCTION

The Oral gustatory perception during a meal fulfills very important physiological roles in food selection, subsequently oral functions such as salivation, which essential for mastication, and swallowing, and nutrient availability through pre-ingestive responses as a cephalic phase. From time immemorial, human beings have used their sense of taste to identify which foods are good to eat in order to ensure survival. Each taste portray a different meaning for the selection of food. Therefore, in the field of taste physiology research, each sensation of the five basic tastes (saltiness, sweetness, sourness, bitterness and umami taste) are thought to have a physiological meaning to ingest and maintain each nutrient homeostasis. A sweet taste indicates that a foodstuff contains carbohydrates. Sourness tells us whether a fruit or a vegetable is ripe. Bitterness warns us of the presence of poisonous substances, and saltiness helps us to choose foods that contain sufficient minerals, particularly sodium ion. Umami taste indicates the presence of amino acids, *i.e.* proteins. We can distinguish a slight change in each nutrient composition among daily meals by perception for soluble taste materials of foods. Purified carbohydrates or proteins are generally tasteless due to their high molecular sizes.

Cephalic-phase responses triggered by sensory properties of food shape the coordinated response of an incoming nutrient load and enhance food digestion, nutrient absorption and utilization (1). Particular attention has focused on the cephalic-phase of exocrine (gastric and pancreatic juices) and endocrine (insulin) secretions because of their crucial roles in regulating food digestion and limiting postabsorptive hyperglycemia (2). Umami as well as sweet taste stimulation evokes an increase of gastric juice section (pepsinogen and gastric acid) and pancreatic juice secretion in animals (3, 4).

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One hundred years ago, the new taste molecule, umami taste substance (L-glutamate), was discovered in Japan from the extract of dried sea tangle. Since then, Japanese taste physiologists have lead the research that establish L-glutamate as the fifth basic taste (umami) (5). Meanwhile, many lines of evidence demonstrated that there is a taste stimuli-oral/pharyngeal reflex with taste perception. Now we just began to apply the effect of taste stimulation to improve oral functions, such as salivation, mastication and swallowing. In this paper, we would like to review recent clinical advancements on between umami taste sensation and human salivation. We will discuss the importance of taste stimulation during a meal to maintain nutrient homeostasis due to our health, and propose the possible applications of umami taste substances, particularly L-glutamate for the nutritional management in the elderly.

UMAMI TASTE SUBSTANCES IN FOODS

Extracts of seaweed (*konbu*) have been used as a soup stock for over a thousand years in Japan. In 1908, moved by the desire to improve the nutritional status of Japanese, Dr. Kikunae Ikeda at the Tokyo imperial university discovered that salts of the amino acid L-glutamic acid were the taste-active components of the *konbu* stock, and named this taste the umami taste (6). He also invented the production process for the monosodium salt of L-glutamic acid (monosodium glutamate : MSG), which consisted on the hydrolysis of wheat gluten with HCl. Aftter his discovery and invention, MSG became commercially available as an umami seasoning for the first time in the world. In recent, it was appreciated that the molecular discovery of umami receptors in the taste buds established umami taste as one of the five basic tastes, distinct from the other basic tastes such as saltiness, bitterness, sourness and sweetness. Even though it was only recently recognized, many foods and seasonings popular throughout history have appeared to be naturally high in umami taste materials. One such flavoring agent used in ancient Greece and Rome was a pickled fish sauce called *Garum*. This condiment dates back 2500 years, making it the oldest recorded umami seasoning. Various traditional seasonings around the world, such as soy and oyster sauce, tomato ketchup, nam plaa and others as well as food ingredients such as tomatoes and cheese have been found to be rich sources of free glutamate, and L-glutamate in amino acid form contributes to the deliciousness of foods (7, 8).

In 1913, Shintaro Kodama, a colleague of Kikunae Ikeda, examined the components of *katsuo-bushi* (dried bonito) and reported that 5'-inosinate was also involved in umami taste (9). Many years later, during a study of ribonucleotide production through biochemical degradation of yeast RNA, Dr. Akira Kuninaka, another Japanese scientist, identified 5'-guanylate to be one more important umami substance (10). This nucleotide is naturally present in a soup stock "*dashi*" stuff and comes from dried Japanese black mushroom, *shiitake*. Now, these L-glutamate and 5'-ribonucleotides are considered typical umami taste substances (Fig. 1).

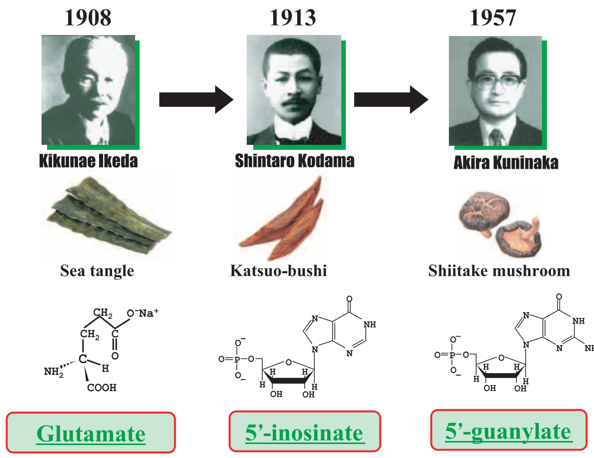

Fig. 1 Discovery of major three umami taste substances
The amino acid L-glutamate is the major umami taste component in Konbu (Japanese sea kelp). 5'-nucloeotides, 5'-inosinate and 5'-guanylate, are major umami taste substance in Katsuo-bushi (dried bonito) and shiitake (dried Japanese mushroom), respectively. Those three umami substances are commercially available as monosodium L-glutamate (MSG), 5'-inosine monophosphate (IMP) and 5'-guanosine monophosphate (GMP). Figure was quoted from Uneyma & Yamada (11).

The Ministry of Health and Welfare in Japan (the Ministry of Health, Labor and Welfare) reported a daily free L-glutamate intake for people over 20 years of over 1.6 g (12). We wanted to know the real content of free glutamate to evaluate the practical free glutamate intake through daily meals. We measured free amino acid contents in a typical Japanese lunch box as shown in figure 2. Interestingly, the concentration of total free amino acids in this lunch was about 1,500 mg from which only 450 mg was free glutamate. Obviously, the total daily ingestion of free L-glutamate has to be divided into three meals through breakfast, lunch and dinner.

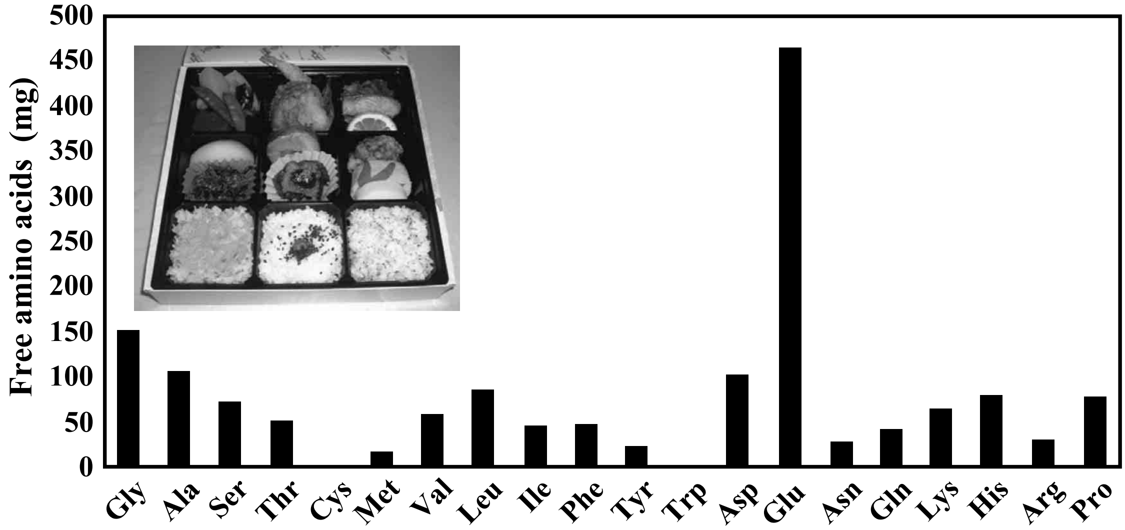

Fig. 2. Amino acid contents in a typical Japanese lunch box.
Amino acids were measured by an amino acid analyzer in hot-water soluble components. Data were quoted from Uneyama (13).

SENSORY PERCEPTION OF UMAMI TASTE IN THE ELDERLY

The nutritional management of the elderly, due to the maintenance of their appetite, mastication, swallowing, food digestion and each nutrient absorption, is very important to regulate their body nutritional status during their daily meals. Taste is a fundamental sensory system because it regulates food selection, the hedonic and sensory experience of food, and related metabolism efficiency. At the end of all meals, these factors help to preserve a good quality of life in people, especially the elderly. Taste also regulates fundamental physiological functions through cephalic phase reflex, such as exocrine (saliva, gastric and pancreatic juices) and endocrine (gut hormones) activities during meals. Neck cancer patients treated with radiation therapy show sometimes taste dysfunction including umami taste loss and umami insensitivity. Among the five basic tastes, perception of umami taste dysfunctions in patients is the one presents the strongest co-relationship with appetite loss (14), suggesting that umami taste is an important taste quality for appetite in humans. Thinking together, umami taste stimulation is also expected to normalize oral and gut functions, when some retardation occurs.

There are several reports describing the taste threshold of MSG in the old people of the Western world (15, 16), whereas there is little knowledge rather than them in Eastern one. Thus, we examined that relationship between umami taste sensitivity and preference in the Japanese elderly (Fig. 3).

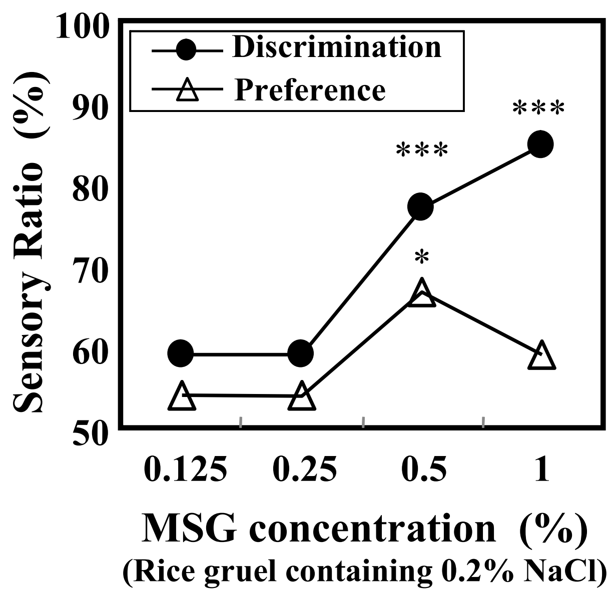

Fig. 3. Umami taste sensitivity and preference of Japanese elderly
Two-alternative forced choice test was performed using 0.2% NaCl containing rice gruel as medium in old women (n=39, 84±6.1 year-old). The ratio of correct answer (filled circle) means the ratio of subjects who correctly chose the gruel with MSG as the stronger taste comparing gruels with and without MSG. For the calculation of the preference ratio (open triangle), the preference in subjects that gave the wrong answer in the sensitivity test was ignored. Asterisks show statistical significance by binomial test (* : $p < 0.05$, *** : $p < 0.001$). Data were modified from Hayakawa *et al.* (17).

In this study, we used rice gruel as taste medium, because it is a familiar ingredient for Japanese elderly who are used to combine gruel with traditional savory pickles. As a result, the taste threshold for MSG in these old subjects was 0.5% (39 women, 84.3±6.1 year-old), higher than those for the middle-aged adults (40 women, 49.6±5.6 year-old) in which was less than 0,063%. Accordingly, the optimal preferred concentration of MSG in old Japanese was around 0.5 % showing a bell-shaped concentration-preference curve (17). Thus, as observed in other gustatory perceptions, the amount of ingested L-glutamate seems to be self-limiting by the intensity of umami taste in food.

UMAMI TASTE STIMULATION IMPROVES SALIVA SECRETION IN THE ELDERLY

Saliva has many essential functions as shown in the figure 4. It is the first digestive juice in the alimentary canal and is secreted in response to food assisting mastication, swallowing and initiation of the oral digestion of starch and lipids (18). During this process, saliva acts as a solvent of taste substances allowing the sensation of taste substances in variety of foods. Clinically, the most important role of saliva is the formation of the food bolus and maintenance of oral health, including the protection of teeth and mucosa from infections, maintenance of the milieu of taste receptors and communication through speech.

Beyond oral health, considerable evidence now demonstrates that saliva and its components have multiple functions in the esophageal and gastric mucosa. Saliva aids the formation of the bolus ; it lubricates, protects and cleanses the pharyngeal and esophageal mucosa. Salivary bicarbonate buffers esophageal acid in common reflux. Salivary epidermal growth factor (EGF) stimulates gastrointestinal (GI) mucosal proliferation *via* a direct lumenal effect in the esophagus and stomach (20). Normal salivary flow decreases the duration of acid contact with esophageal mucosa, an important factor in the development of gastro-esophageal reflex disease (GERD). For instance, the esophageal mucosal barrier is significantly enhanced by the quantity and the quality of salivary organic components such as salivary mucin, nonmucin protein, salivary EGF and salivary prostaglandin E_2 (21). If salivary flow is depressed or if the esophago-salivary reflex is lost, a patient may be predisposed to develop GERD.

Ingestion of palatable foods yields the greatest pleasures in life in general. In the elderly it is most important to satisfy their appetite and maintain their dignity and quality of life (QOL). Since the normal physiological functions in the elderly are compromised and often take various drugs, their taste sensitivity, salivary secretion, chewing and swallowing,

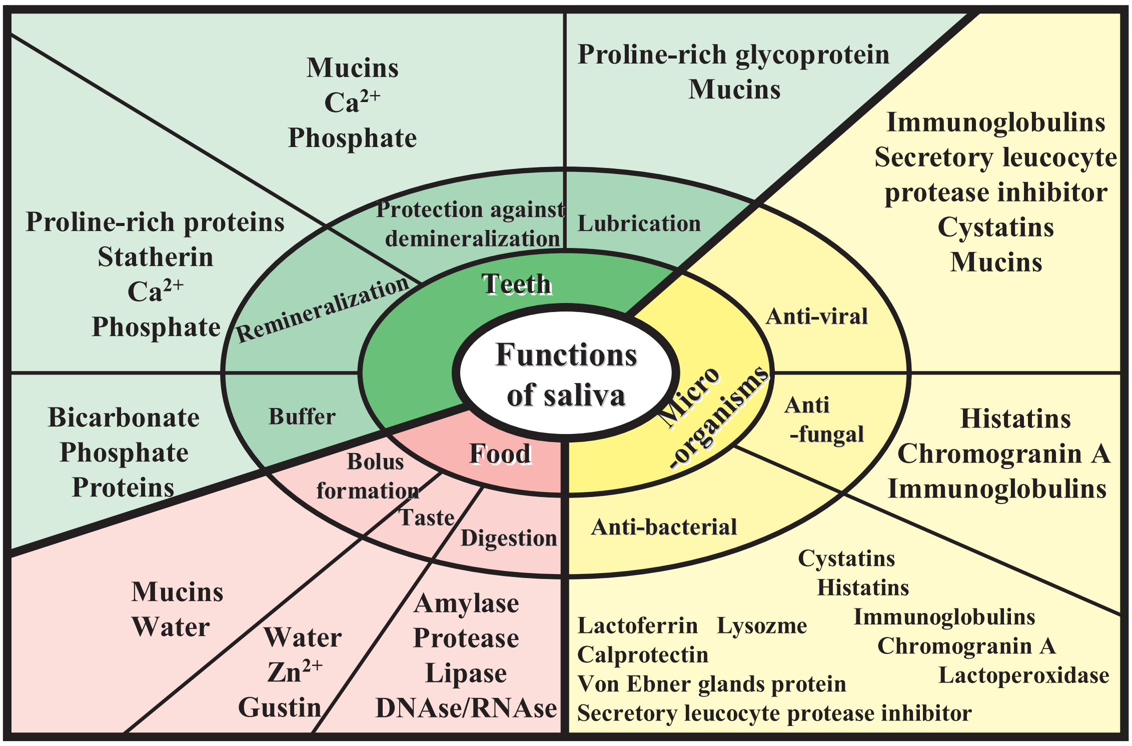

Fig. 4. Physiological functions of saliva
Saliva has many essential functions regulating appetite, mastication, swallowing, digestion, and maintenance of the gastrointestinal mucosa. The figure was modified from ref. 19. See the text for details.

as well as the sanitary condition of the oral cavity, are often prone to deterioration. The effectiveness of umami taste se sensation for salivation in humans was first reported by Dr. Kawamura and colleagues from Osaka university, Japan (22). Recently, it has been re-confirmed that a typical umami taste material (MSG) at most preferable concentration (0.5%) induces salivary secretion in the healthy adults (23). We investigated the temporal pattern of MSG-induced salivation in the healthy adults (Fig. 5). The time-course of salivation after the gustatory stimulation with umami taste (MSG) was compared with the effect of sour taste (citric acid) at the same intensity. The reason why we used sourness as a control taste stimuli is that sourness is often used for promotion of salivary secretion in hospital for the oral care. Interestingly, sour taste was a strong salivary inducer but during a short period of time (within 2 min after taste stimulation in our condition). In contrast, umami taste sensation induced a long-lasting salivary secretion (more than 10 min). Therefore, the total amount of saliva induced by umami taste (MSG) stimulation became significantly larger than the case of sour taste stimulation (24). As considering the function of saliva in mastication, swallowing and cleanness of the oral cavity, this feature of umami taste seems to be important for normal digestion. The use of umami taste materials in oral care might be helpful to maintain the oral mucosal integrity in patients with dry mouth. Indeed, an effective salivation with umami taste stimulation was observed in the elderly with otherwise hyposalivation (25). Shiffman reported previously that the supplementation of foods with MSG improved salivary flow and increased the total amount of secreted IgA in the elderly (25) (Fig. 6). As

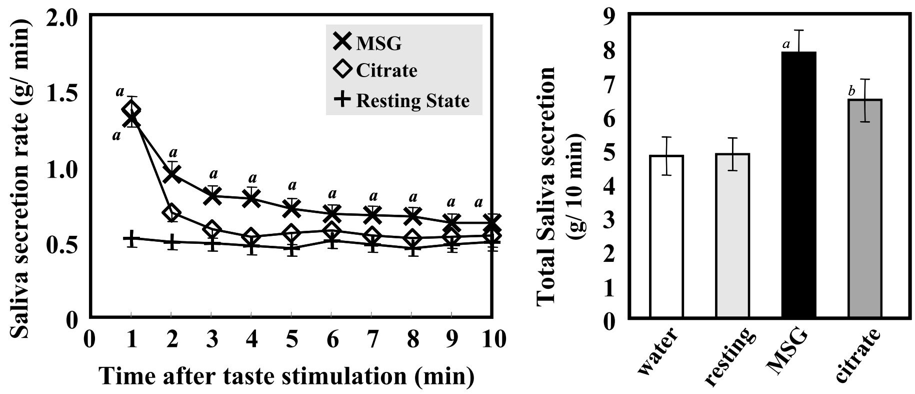

Fig. 5. Effects of umami taste stimulation on human salivation.
After subjects tasted 3 ml of each stimulus solution for 30 sec, then they spat content in their mouth at every 30 sec for 10 min (n=24). The weight of the content except stimulus solution was regarded as the weight of secreted saliva. Salivary flow per min (left) and total saliva for 10 min (right) were presented with mean± s.e.m.. In the graph for salivary flow, same symbol in each time means that there is no significant difference. Data was modified from Hayakawa *et al.* (24).

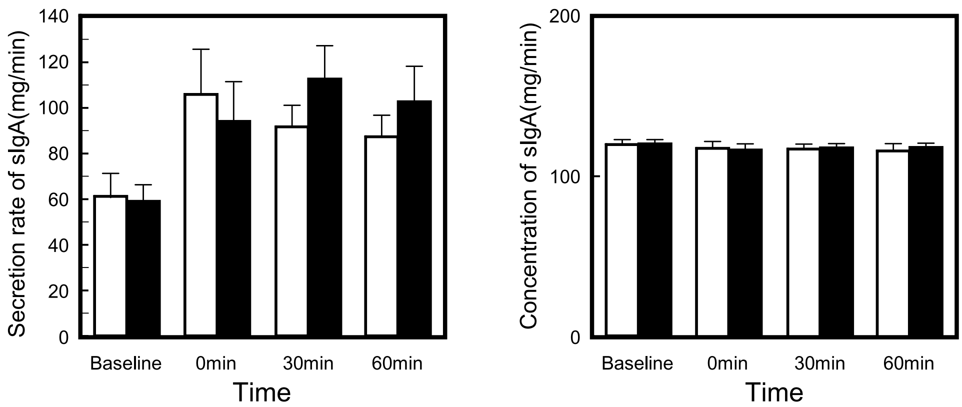

Fig. 6. Effects of umami taste stimulation on the salivary IgA in the elderly.
Secretion rate of sIgA (left), and concentration of sIgA (right) of collected saliva secreted were shown after taking chicken soup with (black bar) and without (white bar) MSG. Each column and vertical bar indicates mean± s.e.m., respectively. Data were quoted from Schiffman *et al.* (25).

mentioned before, IgA is one of key molecules to maintain the mucosal environment as a barrier system against bacterial contamination in the oral cavity. Thus, umami-fortified meals might contribute to the oral care management in the elderly.

POSSIBLE CONTRIBUTION OF UMAMI TASTE SUBSTANCES IN THE ELDERLY QOL

Recent animal evidence using L-glutamate indicate that dietary free L-glutamate is sensed by the alimentary tract and helps gastric digestion, nutrient absorption and utilization *via* visceral glutamate information through vagal afferent pathways (26-29). Altogether, umami taste substance, especially MSG, might be used for its properties in gustatory and visceral perception to improve the management of nutritional stasus (Fig. 7). We ingest certain amount of free L-glutamate, which is a residue of peptides and proteins, every day through our daily meals because a great variety of foods (vegetables, meats and traditional seasonings) contain free L-glutamate. During ingestion, free glutamate is sensed by the umami taste receptors on the tongue and the umami sensation to be yielded, which is thought to indicate protein intake. The specific appetite for proteins allows maintaining the body protein (L-amino acid) homeostasis. At the same time, the sensation of umami taste induces taste reflexes such as salivary secretion that is required for mastication and swallowing of meals, and the cephalic phase responses to prepare the gastrointestinal tract for protein digestion. At the same time, saliva keeps the oral hygiene after each meal. After swallowing the food bolus, the free glutamate in the bolus is sensed again by the visceral afferents that innervate the gastrointestinal tract. Glutamate-mediated visceral nutrient information might increase the efficiency of protein digestion, absorption and utility within the body, by stimulating the gut function. Free glutamate itself is consumed in the mucosa as energy during protein digestion. The visceral sensation through post-ingestive process is expected to control the appetite for protein intake and the visceral afferent inputs to the brain stem can contribute to the maintenance of the basal brain activity. The input of peripheral sensory stimuli plays very important role for the activation of brain circuits. Old people has special difficulties to maintain a proper oral and gut function, which reduces their QOL with diseases such as anorexia, aphasia, diarrhea, constipation and memory dysfunction. Umami taste substances have the potential to improve these conditions in the elderly with some disorders of GI functions. After MSG fortification trials in hospitalized elderly, some of the expected outcomes were reconfirmed (improve the redox status of plasma albumin, immunity and consciousness) (30-32).

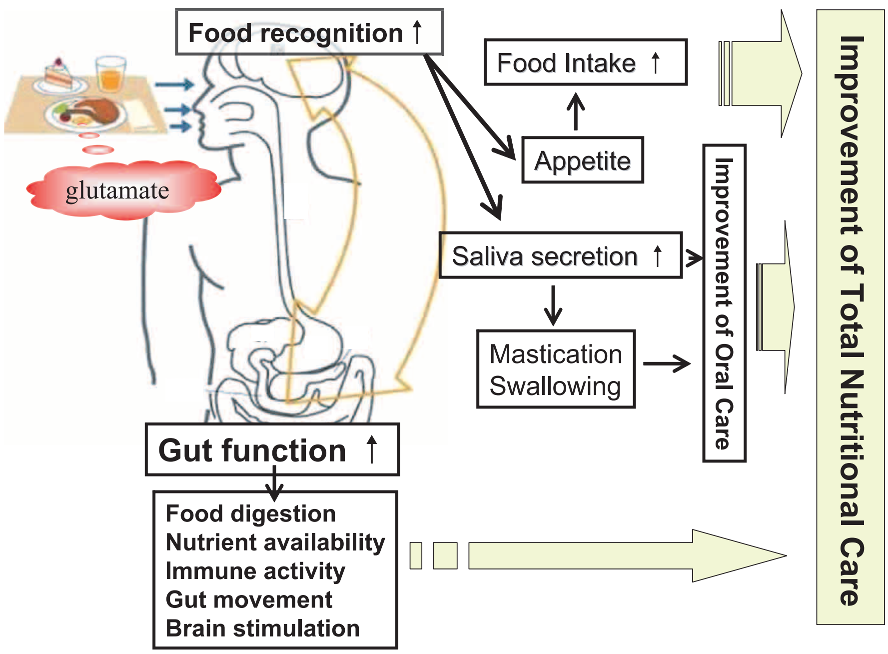

Fig. 7. A new hypothesis based on the scientific evidence for the umami taste substance glutamate in nutritional management. Scientific evidence for contributing the nutritional management for the elderly was summarized. See text for details.

CONCLUSIONS

The elderly usually suffers from hyposalivation due to a reduction of sensory perception such as taste and smell. Compared to other taste stimuli such as sourness, umami taste induces long-lasting salivation in humans. Recently, Sato-Kuriwada and colleagues reported that oral stimulation with MSG increased salivary flow in minor salivary glands (33). It is essential to encourage the ingestion of food in bedridden old people. With the proper nutritional management the appetite, mastication, and swallowing can improve in this elderly subjects. A better understanding of the umami taste physiology especially in taste reflex will help develop new methods or new treatments for eating-related disorders such as disgeusia, dysphagia, dry mouth, and anorexia.

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