# Chapter 7
# Umami and Healthy Aging

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## 7.1 Introduction

The World Health Organization has declared 2021–2030 as the Decade of Healthy Ageing, calling for coordinated actions by governments, civil society, international agencies, professionals, academia, media, and the private sector over the next decade to attain sustainable development goals (World Health Organization. UN Decade of Healthy Ageing, 2020). This includes ensuring that the people, families, and communities age healthily as the world's population ages at an accelerating rate. In Japan, the average life expectancy and healthy life expectancy are among the highest in the world (World Health Organization. World Health Statistics, 2021), and this is considered to be due to the high level of medical care and improvement in the healthcare system relative to the past. However, it has also been suggested that the Japanese dietary patterns play a role in reducing the mortality risk (Matsuyama et al., 2021). The typical Japanese diet is a well-balanced diet with a wide variety of ingredients that leads to the intake of many beneficial nutrients. The Japanese people have a great interest in food, and Japan has many of the world's most advanced technologies and ideas. Therefore, the contribution of the food industry to health is likely to be significant. We believe that efforts in various areas are necessary for healthy longevity, and diet is one of the most important areas.

Humans acquire nutrients predominantly by consuming food, which helps maintain homeostasis in the body. In other words, daily diet plays an important role in maintaining good health throughout one's life. Especially in older adults, it is important to maintain good nutritional status by consuming sufficient nutrients from the diet, not only to prevent diseases but also to delay the functional decline associated with aging. However, older people are more likely to suffer from

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malnutrition due to a variety of factors, including decreased food intake, changes in eating and swallowing functions (oral functions), and changes in taste, which may occur with aging (Ahmed & Haboubi, 2010; Pilgrim et al., 2015; Landi et al., 2016; Minakuchi et al., 2018; Iwasaki et al., 2021). They may also suffer from disorders that result in impaired nutrient absorption and abnormal loss of nutrients from the body. Malnutrition leads to a decrease in activities of daily living, increased risk of infectious diseases, prolonged hospitalization, and increased mortality (Lonterman-Monasch et al., 2013; Marshall et al., 2016; Katona & Katona-Apte, 2008; Hao et al., 2019; Cederholm et al., 1995). This can have a serious impact not only on the person but also on the society, because of the possible medical and nursing care costs.

Among the several approaches for improving nutrition in older adults, this chapter focuses on umami taste. L-Glutamic acid and its salt, a type of amino acid, were discovered in Japan as flavors and flavor enhancers, and its sodium salt, monosodium L-glutamate (MSG), is used as umami seasoning (see also Chap. 1). Umami taste is accepted as the fifth basic taste, in addition to salty, sweet, sour, and bitter, and the potential of umami ingredients for enhancing the taste and appetite among vulnerable individuals has gained attention. Umami for seniors can be discussed from two points of view: its relationship with appetite, salivation, and taste in older adults and the effects on nutritional status, quality of life (QOL), and cognitive function from continuous MSG intake. However, few studies have investigated umami with older adults as the target group or interventions with MSG in particular. Therefore, in this chapter, we discuss how umami can be used to improve the health of older adults by introducing studies that have been conducted not only on older people but also on the general adult population.

## 7.2 Umami in Older Adults for Nutritional Health

Undernutrition results from an imbalance between the intake (or absorption) of specific nutrients and their required amounts, in addition to necessary energy and protein, and is followed by sequential changes in metabolic function and body composition. Factors that have been correlated with lower food intake and malnutrition in older adults and are associated with aging are impairment of chewing and swallowing, compromised digestion and absorption rates, and decline of physical activity. These factors are also associated with depression, dementia, loneliness, and isolation (Robinson et al., 2018; Nieuwenhuizen et al., 2010). As a result, health problems may rise from malnutrition, or malnutrition may cause health problems.

Older people often suffer from some form of disease that may deteriorate their nutritional status. On the other hand, age-related changes may also lead to problems with nutrient intake, such as compromised digestion and absorption. This section considers the following age-related changes: oral function, digestion and absorption function, dietary intake, and sensory function. Although umami taste alone is not a "one-size-fits-all" solution for malnutrition, interventions utilizing umami have reported improved salivary secretion, a factor that causes dysphagia, which affects the promotion of digestion, meal enjoyment, and taste sensation, which in turn relate to appetite and dietary intake. Treating taste disorders may lead to higher interest in the diet and solve nutritional problems by enabling the sensation of various tastes, including umami.

### *7.2.1 Umami for Food Enjoyment and Appetite Enhancement Among Older Adults*

Improving the enjoyment of eating and appetite is important to prevent malnutrition and health problems. MSG is a seasoning agent that improves the flavor and palatability of foods. For example, one study investigated whether enhancing flavor increases appetite (Mathey et al., 2001). One of four flavors, chicken, beef bouillon, turkey, and lemon butter (fish), was added (1 ± 0.2 g) into the main dish using a spice shaker to enhance flavor. Each 100 g of added flavor contained about 60 g sugars/starch and 30 g MSG, as well as protein, fat, salt, and so on. Thus, the added flavor had a high MSG content. After a 16-week intervention targeting people older than 65 years living in a nursing home, the body weight of the flavor-enhanced group increased (mean ± standard deviation: 1.1 ± 1.3 kg) compared with that of the control group (−0.3 ± 1.6 kg). Daily dietary intake was significantly decreased in the control group, whereas no significant change was observed in the flavor-enhanced group, which remained relatively stable. In the flavor-enhanced group, the consumption of flavor-enhanced cooked meals significantly increased, degree of daily hunger increased, and the subjective sense of smell improved. Since the sense of smell plays an important role in meal enjoyment, it is possible that providing the participants with a meal with a good aroma enhanced their enjoyment of the meal, which in turn led to increased food intake and weight gain, thereby improving nutritional status. The results suggest a favorable effect of MSG-containing seasonings on flavor enhancement.

Several studies have examined the effects of adding only MSG. A study that investigated changes in food palatability, perceived saltiness, and food intake among young people (18–39 years old) with MSG supplementation in the diet (Bellisle et al., 1989) found that, depending on the type of meal, the addition of 0.6% MSG was preferred in spinach mousse, and 0.6% or 1.2% MSG was preferred in beef jelly. However, as the concentration of MSG increased, the degree of perceived saltiness also tended to increase, as expected. The addition of 1.2% MSG led to an increase in dietary intake on the first week of testing, whereas the addition of 0.6% MSG to the diet increased dietary intake over successive weeks. Thus, high levels of stimulation may exert rapid effects, but moderate levels may be better for lasting effects.

Another study, in which 0.6% MSG was added to two lunch menus of older people to evaluate dietary and nutrient intake in each menu (Bellisle et al., 1991), found that intake of some but not all enhanced foods increased. This is considered to result from expecting an appetite-stimulating effect by adding MSG, but there was no increase in intake of MSG-containing soups with different menus, suggesting MSG may be compatible only with specific foods. Moreover, the influence of food choices in the diet could also have an effect, as the results were different for two lunch menus, and intake of calcium and magnesium increased in one of the menus, and intake of sodium and fats increased in the other. Sodium in MSG is about one-third that in sodium chloride (NaCl) (Bellisle, 1999), and if the amount of NaCl is reduced and an appropriate amount of MSG is added, the palatability is maintained (Morita et al., 2021; Hayabuchi et al., 2020) (see also Chap. 4 Dunteman and Lee); therefore, the effective use of MSG to reduce salt intake may help prevent hypertension and even reduce the risk of cardiovascular disease, and from a health perspective, enhancing flavor and taste with MSG is beneficial. Taken together, these studies suggest that the use of an appropriate amount of MSG is expected to increase palatability and appetite, resulting in enhanced enjoyment of eating.

The mechanism of appetite enhancement by MSG may also involve its effect of promoting the digestion of food. Glutamate is thought to regulate digestive function not only through receptors in the oral cavity but also through activation of the vagal afferent fibers from the gastric branch via glutamate receptors in the stomach (Uneyama et al., 2006; Yamamoto et al., 2009; Toyomasu et al., 2010). A study conducted in healthy men 27–45 years of age showed that adding 0.5% MSG to protein-rich liquid meals enhanced gastric emptying compared with the absence of MSG (Zai et al., 2009), suggesting it is involved in protein digestion. In another study, targeting healthy individuals 30–50 years of age, MSG or NaCl was added to lunch and dinner for 7 consecutive days, and then pre- and post-meal assessment was conducted on day 7. Results showed that MSG supplementation at nutritional doses elicits elevation of several plasma amino acid concentrations in healthy humans (Boutry et al., 2011), suggesting that adding MSG may affect uptake of amino acids in addition to digestion of protein. Adding MSG to the diet may thus increase dietary intake by promoting digestion and may also improve nutritional status due to increased nutrient uptake.

### *7.2.2 Effect of Umami Stimulation on Salivary Secretion in Older Adults*

*Dry mouth* has been used as a comprehensive term to refer both to xerostomia (the subjective sensation of dry mouth) and to salivary gland hypofunction (objective findings of dry mouth), such as hyposalivation or altered salivary components (Nakagawa, 2016; Thomson, 2015; Han et al., 2015). Decreased salivary secretion may cause complaints of xerostomia; however, xerostomia may or may not be accompanied by decreased salivary secretion due to salivary gland hypofunction (Hopcraft & Tan, 2010; Napeñas et al., 2009). Reduced salivary secretion negatively affects oral health, and xerostomia affects QOL.

The proportion of patients with xerostomia and salivary gland hypofunction increases with age, and factors include high prevalence of systemic diseases and side effects of regular medications (Villa & Abati, 2011; Smidt et al., 2010; Johanson et al., 2015). Although age-related changes in the structure of salivary gland tissue have been shown (Moreira et al., 2006), many believe that aging itself does not affect salivary secretion (Hopcraft & Tan, 2010; Smidt et al., 2010). Dry mouth causes problems related to food intake, such as inability to chew food thoroughly, inability to form a bolus, and inability to swallow; therefore, this condition has a strong relation to nutritional disorders. There is a report that treating xerostomia in the context of systemic diseases enabled and improved the sensation of umami taste, improved appetite and body weight, promoted the enjoyment of eating, and improved health conditions (Satoh-Kuriwada et al., 2012a). Treatment of dry mouth is crucial considering its role in nutrition in older adults.

Saliva is secreted by the major (parotid, submandibular, and sublingual) and minor salivary glands. Most saliva secreted into the oral cavity originates from the major salivary glands. However, in some cases, xerostomia may not be accompanied by a decrease in salivary secretion, suggesting the involvement of a minor salivary gland in xerostomia. Previous studies have suggested an association between complaints of xerostomia and decreased labial minor salivary gland secretion rate, even in the presence of normal or reduced salivary output throughout the oral cavity (Eliasson et al., 2009). It has also been reported that people with xerostomia had a more remarkable decrease in lower labial minor salivary gland secretion than in chewing-stimulated whole salivary secretion and that lower labial minor salivary gland secretion measurement had superior sensitivity, negative predictive value, and diagnostic accuracy for discriminating xerostomia compared to chewing-stimulated whole salivary secretion measurement (Satoh-Kuriwada et al., 2012b).

In an attempt to treat dry mouth, a study examined the change in the amount of salivary secretion of major salivary glands and minor salivary glands by taste stimulation (Hodson & Linden, 2006). Eight healthy subjects 18–55 years of age were tested to determine whether stimulation with the basic five tastes (sweet, salty, sour, bitter, umami) increased parotid salivary flow. The relative efficacy for eliciting salivation was sour > umami > salty > sweet ≥ bitter. Another study verified the amount of stimulation by the basic 5 tastes on minor salivary glands using an iodine-starch filter paper method, in 11 healthy subjects with an average age of 31 years (Sasano et al., 2014, 2015). The order from the highest to the lowest amount of salivation by stimulation was umami > sour > salty = sweet = bitter. The salivary reaction evoked by umami stimulation lasted longer than that of other stimuli. Regarding sour stimulation, which is commonly associated with salivary secretion, a salivary secretion equivalent to the umami taste stimulation was induced immediately after the stimulation, but the amount decreased following stimulation; therefore, the effect was not sustained. Furthermore, the increase in total salivary secretion from the major and minor salivary glands was transient with sour stimulation but persisted longer with umami stimulation when 24 healthy volunteers were stimulated with sour or umami (Sasano et al., 2010).

Another study was conducted with ten older adults with a mean age of 69.5 years where saliva was collected three times at intervals of 30 min after the ingestion of food (at 0, 30, and 60 min) (Schiffman & Miletic, 1999). Test foods were chicken broth, onion soup, corn, and carrots, with and without 2.0%, 1.5%, 3.5%, and 2.0% MSG, respectively. After 30 and 60 min, the secretion rates of secretory immunoglobulin A (μg/min) after ingesting food containing MSG were high, due to increased salivary flow, because no significant differences in absolute concentration were found. Thus, repeated taste stimulation may affect immune function through increased salivary flow.

A method using kelp stock containing MSG has also been reported as a treatment for dry mouth using umami (Satoh-Kuriwada & Sasano, 2015). Twenty women with an average age of 61.9 years who complained of dry mouth were asked to drink or to gargle kelp stock five to six times a day when they felt dry mouth. Around 80% of respondents answered that their dry mouth had improved, and 67% said they felt the effect after 1 month of use. In addition to improvement of dry mouth, respondents also said that the method "improved roughness in the mouth," "prevented food clogging which made it easier to swallow," and so on. Improvement of various symptoms related to dry mouth was observed; thus, this may be a practical method to enhance salivation.

To summarize, based on available data, umami stimulation appears to promote salivary secretion and improve xerostomia in both the major and minor salivary glands, suggesting that umami stimulation can be used to improve dry mouth. However, since there are a relatively few studies in older adults, and many of these include only small numbers of subjects, further examination is needed.

### *7.2.3 Perception of Umami Taste in Older Adults*

It is generally believed that as we age we begin to prefer stronger flavors (the combination of taste, smell, and irritant properties of foods). Indeed, a study comparing the strength of flavor and palatability of four food items (bouillon, tomato soup, chocolate custard, and orange lemonade) found that older adults tended to have a preference for higher flavor concentrations than did younger individuals (de Graaf et al., 1996). One of the reasons that older people prefer stronger flavors is a change in taste function. To date, many studies have been conducted on the relationship between taste thresholds and aging (Liu et al., 2016; Boesveldt et al., 2011; Mojet et al., 2001; Yoshinaka et al., 2016; Yamauchi et al., 2002; Methven et al., 2012; Welge-Lüssen et al., 2011). Most researchers have thus come to the conclusion that taste function decreases with age; however, which taste sensitivities are reduced differs across studies. For example, on one study, recognition thresholds for sweet, salty, sour, and bitter tastes were in the normal range, but recognition thresholds for umami were elevated (Satoh-Kuriwada et al., 2012a). Thus, age-related deterioration in taste function can be understood to vary, because sensitivity for all tastes is not lost; rather, the detection and recognition ability for specific taste qualities may be impaired.

Low salivary volume, low serum zinc, the effect of comorbidities, and prescribed medications have been pointed out as underlying factors for decreased taste function in older adults (Sasano et al., 2014; Ikeda et al., 2008; Kinugasa et al., 2020), with a variety of factors having secondary effects. It may also result from decreased signaling mechanisms for taste in the brain. Previous studies have shown that people with Alzheimer's disease dementia (ADD), which is more likely to develop at an older ages, may exhibit a decline of taste sensitivities (Ogawa et al., 2017; Kouzuki et al., 2020). The cause of the decline is thought to be due not to impaired transmission from peripheral receptors but to a decrease in taste-perception cognitive ability that accompanies brain atrophy and neurodegeneration. In our study (Kouzuki et al., 2020), many participants, not only those with ADD but also nondementia controls (NDCs), could not recognize umami. With respect to umami, the cumulative distribution curves for detection and recognition thresholds, for the percentage of correct answers for each taste solution, differed from those of other taste solutions, especially with respect to recognition: a concentration higher than that of other taste solutions was required (Fig. 7.1). However, 21.4% of NDCs were not able to recognize of umami taste even at the highest concentration, and its recognition became worse with age.

Studies in humans do not necessarily achieve consistent results, due to differences in the background factors and living environments of the subjects, differences in the concentrations of taste solutions between studies, and the fact that some

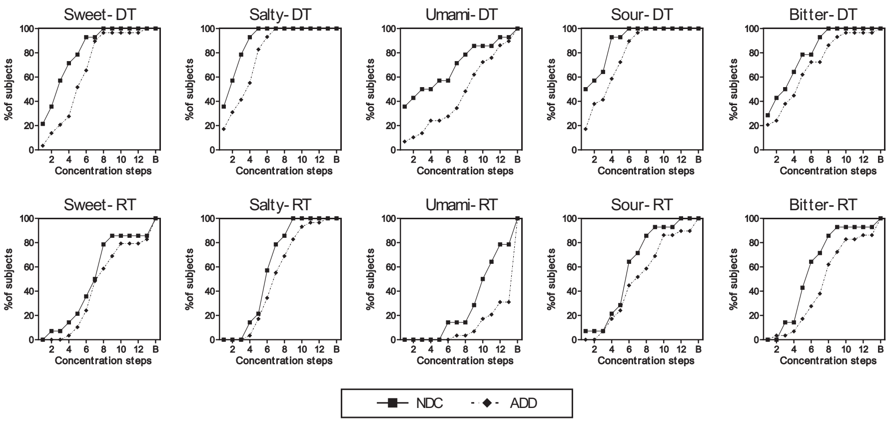


**Fig. 7.1** Cumulative curves for detection thresholds (DT, top row) and recognition thresholds (RT, bottom row) in patients with Alzheimer's disease dementia (ADD) and in nondementia controls (NDCs). The taste functions of patients with ADD and of NDCs were evaluated in detail by the whole-mouth gustatory test using taste solutions for sweet, salty, sour, bitter, and umami, each diluted to 13 levels. If the participants could not detect or recognize a taste, even at the highest concentration, those results are indicated as "burst" (B) on the x-axis. (Modified from reference Kouzuki et al. (2020), licensed under a Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/))

studies evaluate only detection or recognition thresholds. However, these thresholds do not usually decrease, at least in older adults. Because elevated thresholds imply the need for more intense taste stimuli for taste detection, it can be understood that older adults prefer a stronger-tasting diet due to a lower perception of taste.

Reports on improvements to taste function indicate that taking the zinc agent polaprezinc at 150 mg/day (administered as 75 mg twice daily; 75 mg of polaprezinc contains approximately 17 mg of zinc) resulted in improvements in the mean recognition thresholds for sweet, salty, and sour tastes in 74% of older adults with taste disorders (Ikeda et al., 2008). Regarding umami, seven cases 62–78 years of age with reduced umami sensitivity were treated for xerostomia in addition to systemic disease and improved their recognition threshold for umami, as assessed by a filter paper disk test (Satoh-Kuriwada et al., 2012a). In another study, in 28 patients 45–78 years of age, with complaints of taste impairment, clinical examinations (blood tests, salivary tests, an oral candida culture test, and oral hygiene tests) and investigation of systemic diseases and drug prescriptions were carried out, and appropriate treatment was performed based on these results. After treatment, all patients showed lower recognition thresholds of umami than before treatment, indicating that loss of umami taste sensitivity can be improved with appropriate treatment (Satoh-Kuriwada et al., 2014). Evaluation of taste function and treatment for taste disorders are important because decreased interest in meals due to reduced taste function may reduce appetite and adversely affect nutritional status.

## 7.3 Clinical Trials for Continued Ingestion of MSG in Old Age

Here, we introduce the effects of long-term ingestion of MSG in older adults. MSG transmits gustatory signals to the brain via oral and gastric receptors, affecting digestive functions by increasing the secretion of saliva (Hodson & Linden, 2006; Sasano et al., 2014; Sasano et al., 2015) and gastric juices (Zolotarev et al., 2009) and promoting digestion (Zai et al., 2009; Boutry et al., 2011). There have also been reports that the neural organization of the primary gustatory cortex receives inputs from glutamate receptors on the tongue (Schoenfeld et al., 2004) and that umami-stimulated activation of the primary gustatory cortex (insular and opercular regions) and orbitofrontal cortex were observed in functional MRI (de Araujo et al., 2003), suggesting that ingestion of MSG may affect the brain. Although very few interventional studies have involved MSG consumption for a long time by older adults, this section introduces studies that attempted to improve the nutritional status and QOL of older adults by MSG intake (Toyama et al., 2008; Tomoe et al., 2009), as well as those that examined the effects of continuous transduction of taste signals to the brain by MSG intake on cognitive function (Kouzuki et al., 2019).

### *7.3.1 Umami and Improved Behaviors and Nutritional Status in Old Age*

Here, we present a study evaluating the improvement of nutritional status and QOL of older people by long-term consumption of MSG (Toyama et al., 2008; Tomoe et al., 2009) and provide our opinion on the subject. Older individuals with malnutrition are more likely to have reduced QOL, while interventions that improve nutritional status lead to significant improvements in physical and mental aspects of QOL (Rasheed & Woods, 2013), and nutritional status of older people is a modifiable factor associated with QOL.

A study of 11 inpatients (mean age ± standard deviation: 85.8 ± 8.2 years) who consumed 0.5% (w/w) MSG added to their staple rice gruel three times daily for 2 months reported no change in body weight before and after the intervention and no change in serum total protein or albumin, an indicator of the nutritional status (Toyama et al., 2008). However, the number of lymphocytes in blood increased significantly during the intervention period and then decreased significantly 1 month after the intervention period. Low lymphocyte count is an indicator of loss of immune defenses caused by malnutrition (Ignacio de Ulíbarri et al., 2005) and is affected by increases or decreases in nutritional status. This parameter is perhaps connected with protecting the body from infection by enhancing immune function, indicating that glutamate may activate biological defense systems. Moreover, in the evaluation of daily performance by the nursing staff, "clear speech," "cheery facial expression," and "eye opening" showed more remarkable improvement, which correlated with improvements in QOL. In addition, the revised Hasegawa's Dementia Scale (HDS-R), a screening test for cognitive function, showed that five patients improved, three deteriorated, and three showed no change. These results support the hypothesis regarding positive effects of MSG intake on cognitive function.

These conclusions were subsequently supported using a similar intervention in a 3-month placebo-controlled, double-blind study (Tomoe et al., 2009). In this investigation, the group that consumed MSG (MSG group) comprised 14 inpatients (mean age ± standard deviation: 83.0 ± 8.9 years), and the control group comprised 15 inpatients (84.3 ± 9.6 years). Blood tests revealed no increase in albumin, as in the previously described study (Toyama et al., 2008), but the ratio of reduced-form albumin to total albumin, considered an indicator of redox status or quality and quantity of dietary protein ingestion in the body (Kuwahata et al., 2017; Tabata et al., 2021; Wada et al., 2020), was increased only in the MSG group, suggesting an improvement in protein nutritional status. Evaluation of daily performance by nurses without knowledge of the presence or absence of the intervention indicated improvement in the MSG group after the intervention, with results comparable to those of the earlier study (Toyama et al., 2008). On the other hand, no significant changes were observed in HDS-R scores. However, HDS-R as a screening test for dementia may have inadequate detection power to assess effects of the intervention.

In addition, to evaluate behavior of patients during the actual diet, the researchers recorded behavior during meals before and at the end of the intervention and had both videos evaluated by 13 university students. In the MSG group, activity level, eye opening (e.g., eating awake), swallowing (e.g., timing of swallowing), cheery expression, motion of arms and hands (e.g., handling of cutleries), and position holding showed improvement; overall dietary behavior was improved, and there was a tendency to try to consume independently.

In summary, these results suggest that continuous intake of MSG in the older adults may improve the immune system and nutritional status, as evidenced by improvement in some biochemical markers, and may also contribute to improvement of QOL based on behavioral changes.

### *7.3.2 Umami and Slower Cognitive Decline in Old Age with Dementia*

Studies to verify brain activation by MSG stimulation have been reported (Schoenfeld et al., 2004; de Araujo et al., 2003). In addition, as mentioned above, HDS-R scores improved in 45.5% of patients when MSG was added at 0.5% (w/w) to rice gruel in each meal given three times a day for 2 months (Toyama et al., 2008), suggesting MSG may have a beneficial effect on the brain. Therefore, we investigated the impact of continued MSG consumption on cognitive function and interest in food in older people with dementia (Kouzuki et al., 2019). The subjects of this study were 159 dementia older persons living in hospitals or nursing homes (e.g., geriatric health service facilities, special nursing homes for the aged, and group homes). The subjects were divided into two groups: one with MSG added to their daily diet (MSG group) and the other with NaCl added as a placebo (control group); the dietary intervention was performed for 12 weeks. MSG (0.9 g/dose) or NaCl (0.26 g/dose, equivalent to the amount of sodium contained in the molecular content of MSG) was added to three meals daily: breakfast, lunch, and dinner. When applicable, MSG or NaCl was added to rice porridge, miso soup, or other soup; otherwise, these additives were mixed in the main dish. After completion of the intervention, a follow-up period without dietary intervention was provided for an additional 4 weeks, and examinations of dementia symptomatology, blood tests, daily performance, and preference for diet were conducted pre- and post-intervention and post-follow-up.

Cognitive function was tested using the Touch Panel-type Dementia Assessment Scale (TDAS) (Nihon Kohden Corporation, Tokyo, Japan) (Inoue et al., 2011) as a subjective method to assess subjects' cognitive functions. TDAS is a cognitive function test introduced to touch-panel computers by partially modifying the Alzheimer's Disease Assessment Scale, which is considered the most reliable decision-making method for progress of ADD and treatment effectiveness. TDAS scores did not differ significantly between the baseline, post-intervention, and post-follow-up groups

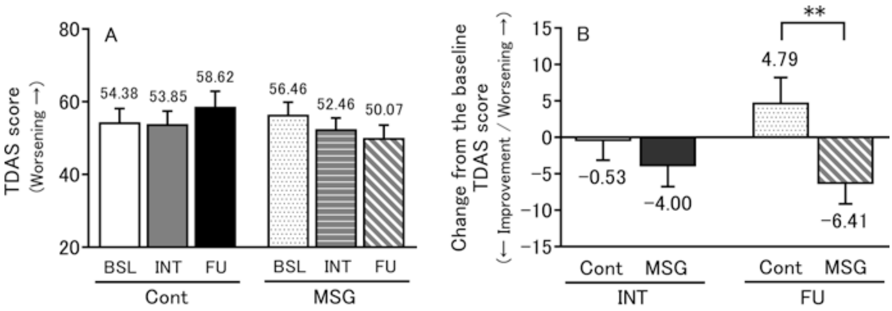


**Fig. 7.2** The Touch Panel-type Dementia Assessment Scale (TDAS) score: overall (**a**) and mean change from the baseline (**b**). *BSL* = baseline, *INT* = intervention, *FU* = follow-up, *Cont* = control, *MSG* = monosodium L-glutamate. All data represent mean ± standard error; the numbers above the error bars are the mean values. **$p$ < 0.01. (Modified from reference Kouzuki et al. (2019), licensed under a Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/))

in either the MSG or the control group (Fig. 7.2a); however, comparisons of scores between the two groups from baseline showed significant improvement in the MSG group after follow-up (Fig. 7.2b). Thus, it is possible that improved cognitive function was observed in a test performed at 4 weeks after the intake was discontinued, thereby indicating the necessity of further investigation. In addition, when examining the correlation between changes in baseline and post-intervention TDAS scores and a food palatability survey, we found a significant association between the total TDAS score and the enjoyment of the meal in the MSG group and a trend toward a correlation between the total TDAS score and the deliciousness of the meal. In other words, the greater the improvement in food quality, the greater the improvement in cognitive function.

Although MSG enhances umami taste, we considered the effect of MSG ingestion on taste function. It has previously been reported that the percentage of people with low serum zinc levels rises with age (Ikeda et al., 2008; Kogirima et al., 2007); this tendency was also observed in subjects in this study (Kouzuki et al., 2019), with baseline mean serum zinc levels as low as 61.8 μg/dL in the MSG group and 63.5 μg/dL in the control group (reference value in the study, 64–111 μg/dL). Zinc plays an important role in taste bud homoeostasis, and patients with taste disorders have exhibited significant improvements in taste sensitivity after treatment with a zinc-containing compound (Ikeda et al., 2008; Sakagami et al., 2009). The variation in serum zinc levels before the intervention did not significantly differ between the two groups compared to variation after the intervention and at follow-up, but the MSG group showed increased serum zinc levels in the post-intervention test. Zinc is absorbed from the intestine, and the ingestion of MSG increased the secretion of gastric juice and upper gut motility via vagus nerve stimulation (Toyomasu et al., 2010; Zai et al., 2009; Boutry et al., 2011; Zolotarev et al., 2009) and enhanced digestive absorption, which may have led to a better absorption of zinc. In rats, the average life span of a taste bud cell is about 250 ± 50 h (Beidler & Smallman, 1965).

It was suggested that zinc deficiency induces delayed proliferation of taste bud cells (Hamano et al., 2006). Although we cannot make a clear conclusion, taste bud regeneration in response to increased zinc absorption during the MSG intake period might have appeared as a sustained effect even after MSG discontinuation. These results suggest that elevation of serum zinc caused the regeneration of taste buds, and the effect of MSG on the umami receptors T1R1 + T1R3, mGluR1, and mGluR4 in taste cells (Yasumatsu et al., 2015) led to a greater perception of the taste of cooked meals and affected cognitive function by enhancing the taste signaling to the brain via glutamate receptors in the oral cavity, as well as via the vagus nerve from the stomach (Tsurugizawa et al., 2008; Tsurugizawa et al., 2009).

## 7.4 Conclusions

Life expectancy is increasing worldwide; however, it is important for healthy life expectancy to increase concomitantly. Preventive measures to avoid becoming ill are important to maintain health, and this chapter focuses on nutrition as one of the factors associated with disease. Although age-related changes may lead to a decrease in nutritional status, a variety of methods have been shown to potentially prevent or improve malnutrition. Adding substances that elicit umami taste, such as MSG, has been proposed as a way to address malnutrition. It may also be possible to promote nutrient intake from meals by increasing interest in meals by enhancing appetite and by promoting digestion via the addition of MSG, thereby increasing the amount of salivation by the stimulatory action of MSG and improving the ability to recognize umami through appropriate treatment targeting decreased taste function. Long-term consumption of MSG by older adults is also expected to improve nutritional status, QOL, and cognitive function. One's daily diet is important for living healthily even in old age, and we believe that the approach using umami taste has many possibilities for preventing or improving various health disorders by enhancing the palatability of the diet.

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