

*Current Perspective***Sensory Stimulation to Improve Swallowing Reflex and Prevent Aspiration Pneumonia in Elderly Dysphagic People**Satoru Ebihara^{1,*}, Masahiro Kohzuki¹, Yasunori Sumi², and Takae Ebihara³¹*Department of Internal Medicine and Rehabilitation Science, Tohoku University Graduate School of Medicine, Seiryomachi 1-1, Aoba-ku, Sendai 980-8574, Japan*²*Division of Oral and Dental Surgery, Department of Advanced Medicine, National Center for Geriatrics and Gerontology, 36-3, Gengo, Morioka, Obu 474-8511, Japan*³*Department of Geriatrics and Gerontology, Institute of Development, Aging and Cancer, Tohoku University, Seiryomachi 4-1, Aoba-ku, Sendai 980-8575, Japan**Received September 1, 2010; Accepted December 14, 2010*

Abstract. Morbidity and mortality from aspiration pneumonia continues to be a major health problem in the elderly. A swallowing disorder, such as a delayed triggering of the swallowing reflex, exists in patients with aspiration pneumonia. We found that the swallowing reflex in elderly people was temperature-sensitive. The swallowing reflex was delayed when the temperature of the food was close to body temperature. The actual swallowing time shortened when the temperature difference increases. The improvement of swallowing reflex by temperature stimuli could be mediated by the temperature-sensitive transient receptor potential (TRP) channel. The administration of a pastille with capsaicin as an agonist stimulus of TRPV1, a warm-temperature receptor, decreased the delay in swallowing reflex. Food with menthol, an agonist of TRPM8, a cold-temperature receptor, also decreased the delay in swallowing reflex. Olfactory stimulation such as black pepper was useful to improve the swallowing reflex for people with low activity of daily living (ADL) levels or with decreased consciousness. Oral care also shortened the latent time of swallowing reflex presumably due to stimulating the nociception of the oral cavity. A combination of these sensory stimuli may improve the swallowing disorders and prevent aspiration pneumonia.

Keywords: elderly, olfactory stimulation, swallowing reflex, drug delivery system, aspiration pneumonia

1. Introduction

The demographic trend in both developed and developing countries is moving towards a society with an increasing percentage of people above 65 years of age (1). More significant will be the shift in composition of the elderly population over the 4 decades towards more people above 80 years of age, attributed to increased life expectancy and the baby-boomer generation passing the age of 65 years. Therefore, it is important to draw special attention to this generation in terms of their specific health and management (2). Medicines and medication management are much more complex and challenging in

the elderly than younger adults due to the age-associated change of homeostatic mechanisms, the co-morbidity, and the increasing number of the drugs for the treatment of different conditions. Medication of the elderly will not only be judged by their efficacy to treat disease conditions, but also should be judged on their ability to manage the disease by reducing morbidity and mortality (3). Moreover, in addition to the scientific aspect of the elderly, research on the social aspects such as needs of the elderly and health care system for the elderly are warranted (4).

Pneumonia is a major medical problem in the elderly. The mean age of hospitalized patients with community-acquired pneumonia is usually around 65 years, an age that is considered the onset of old age (5). Consequently, about 50% of admitted patients with pneumonia can be defined as elderly. Moreover, about 20% are older than

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75–80 years and have been deemed very elderly patients. In patients with dementia and in very old people, aspiration was the commonest cause of pneumonia (6, 7). In a multicenter prospective study, the incidence of aspiration pneumonia was 80.1% (306/382) among hospitalized Japanese patients aged ≥ 70 years (8). Therefore, it is proposed that most pneumonia in the very old is aspiration pneumonia. Aspiration pneumonia results from the aspiration of colonized oropharyngeal or gastric contents, leading to an infectious process. The high rate of aspiration in the elderly presumably is related to an increased incidence of dysphagia due to strokes and other degenerative neurologic diseases (9).

2. Bacteriology of aspiration pneumonia — normal flora pneumoniae

Data about microbiological diagnosis of aspiration pneumonia are disparate for the following three reasons: First, several studies enrolled patients relatively late, when complications such as necrotizing pneumonia, lung abscess, or empyema had already occurred; and in these patients, anaerobic organisms were found to be the predominant pathogens isolated alone or with aerobes (10, 11), whereas most common pathogens isolated in relatively early enrolled patients with aspiration pneumonia are *Streptococcus pneumoniae*, gram-negative bacilli, anaerobes, and *Staphylococcus aureus* (12). Second, in many cases, it is impossible to isolate the responsible pathogens. Mier et al. (13) studied the bacteriology of early aspiration pneumonia with the use of protected brushing. Positive results were obtained for only 9 of 42 patients (47%). In another study, the cultures were positive in 60% of patients (14). Notably, significant isolation of anaerobic bacteria in patients suffering from lower respiratory tract infection is difficult because it requires specific sampling techniques, adequate transport conditions, and specific growth media. Third, and this might be most crucial, the diagnosis of aspiration pneumonia is not really certain in many studies.

Although, to date, there are several studies describing the microbiology of aspiration pneumonia (12, 14), in these studies, the criteria for dysphagia is not really clear. Recently, aspiration pneumonia was defined by the Japanese Study Group on Aspiration Pulmonary Disease as pneumonia in a patient with predisposition to aspiration because of dysphagia or swallowing disorders (8). We diagnosed one aspect of dysphagia by evaluating swallowing reflex sensitivity. This type of dysphagia is known to be closely related to silent aspiration. Here, the swallowing dysfunction was assessed by evaluating the latent time of the swallowing reflex, induced by an injection of a 1 ml solution into the pharynx (15), and the

etiology of aspiration pneumonia was investigated (16). We found that most of the cases in this study with aspiration pneumonia could not show obvious respiratory pathogens. When we highlighted bacteria representing more than 10^6 cfu/ml, which are more likely to be a pathogen, 31 patients did not show more than 10^6 cfu/ml bacteria. Among the bacteria that represent more than 10^6 cfu/ml, the normal flora is still dominant bacteria with a detected ratio reaching 48.4% (16). Figure 1 shows the detected ratio of bacteria that represent more than 10^6 cfu/ml. It ought to be noted that even normal flora should not present in tracheal fluid. Therefore, the pathogen of aspiration pneumonia could be oral and/or pharyngeal normal flora, suggesting that a large portion of aspiration pneumonia is normal flora pneumonia. Therefore, in the treatment of aspiration pneumonia, management of aspiration may be of importance rather than choice of antibiotics (17).

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3. Management of food for aspiration

The management of elderly patients with dysphagia requires an interdisciplinary team approach coordinated by a number of health professionals, including the patients' primary care physician, pulmonologist, speech and language therapist, clinical dietitian, occupational therapist, physiotherapist, nurse, and dentist, as well as caregivers (9). The management should be directed towards not only maintaining adequate nutrition and hydration but also to enhancing the quality of life by optimizing the safety, efficiency, and effectiveness of oropharyngeal swallowing. The management plan is developed according to the clinical and instrumental assessment results.

However, the evidence available on the effectiveness of many preventive strategies is limited. Although there

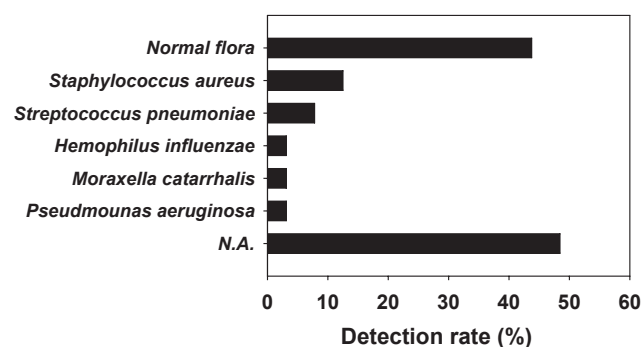


Fig. 1. Detected ratio of bacteria representing more than 10^6 cfu/ml. NA: Not applicable. The graph was constructed from the data of reference 16.

are several medicines that modulate swallowing and cough reflexes in the elderly (18–20), manipulation of diet is one of the most common strategies facilitating swallowing in dysphagic people. Patients vary in their ability to swallow thin and thick liquids, semi-solids, and solids. The consistency of patients' food should be individualized according to the findings from clinical testing. Heretofore, dietary modification to help swallowing has focused only on texture matters such as inconsistency and thickness. We found several elements of meals that should be individualized for elderly people with dysphagia. The swallowing reflex was delayed the most around body temperature (30°C–40°C) and the delay shortened as the difference from body temperature became greater (21). The results of this research suggest that the food should be prepared immediately prior to consumption for dysphagic people. Based on the above finding concerning the temperature sensitivity of the swallowing reflex in the dysphagic elderly, we also found spices play important roles in improvement of swallowing in dysphagic patients. The improvement of the swallowing reflex by temperature stimuli could be mediated by the temperature-sensitive transient receptor potential (TRP) channel. The administration of a pastille with capsaicin as an agonist stimulus of TRPV1, a warm-temperature receptor, decreased the delay in swallowing reflex (22–24). Food with menthol, an agonist of TRPM8, a cold-temperature receptor, also decreased the delay in swallowing reflex (15).

4. Improvement of swallowing reflex by temperature stimulation

Peripheral sensory fibers such as vagal c-fibers are known to have TRPV1 and/or TRPM8. Direct stimulation of these TRP channels on peripheral neurons activates the neurons by opening the large-cation channels (25).

The mechanism for how chronic stimulation of TRP channels improves swallowing even without direct applications of those agonists is speculative. By using a single photon emission study, we found significant cerebral blood flow reduction in the bilateral anterior insular cortex compared with the group without a history of pneumonia, suggesting the involvement of dysfunction of the bilateral insular cortex in impaired cough reflex sensitivity (26). Afferent neuronal pathways provide for discriminative sensation and for homeostatic control of body temperature. In discriminative sensation, the lamina-I neurons carry temperature signals to the final insular cortex with one or two relays (27). Since we found that the function of the insular cortex is impaired in patients with aspiration pneumonia, we speculate that repeated

TRP channel thermoreceptor stimulation may restore the function of the insular cortex, resulting in restoration of the functions of the swallowing reflex.

Therefore, we speculate that TRP channel thermoreceptor agonists such as capsaicin and menthol have dual effects on the neural circuit of swallowing reflex (Fig. 2). One is the direct (acute) effects on peripheral sensory neurons and the other is indirect (chronic) effects by repetitive thermal sensory stimuli to the insular cortex. Based on the elucidation of the neural circuit of the swallowing reflex, we also found that smell should be modified for the elderly with difficulty in swallowing.

5. Swallowing improvement by olfactory stimulation using black pepper oil

Medicine for oral intake or food to improve dysphagia patients is not applicable for individuals at risk of aspiration with very low activity or decreased consciousness. Therefore, olfactory stimulation is proposed to improve feeding and aspiration of elderly people who cannot orally consume food. The effectiveness of olfactory stimulation known as aromatherapy is yet to be scientifically proven, but some evidence exists that essential oils may have therapeutic potential (28). When we investigated the effect of black pepper essential oil inhalation on nursing residents, we found that black pepper oil improved the swallowing reflex and serum substance P concentration, suggesting that olfactory stimulation using black pepper is an effective method to treat feeding and swallowing disorders and to prevent aspiration pneumonia (29). This beneficial effect of black pepper aromatherapy is confirmed not only in the elderly but also in children (30). The single photon emission tomography study showed that olfactory stimulation with black pep-

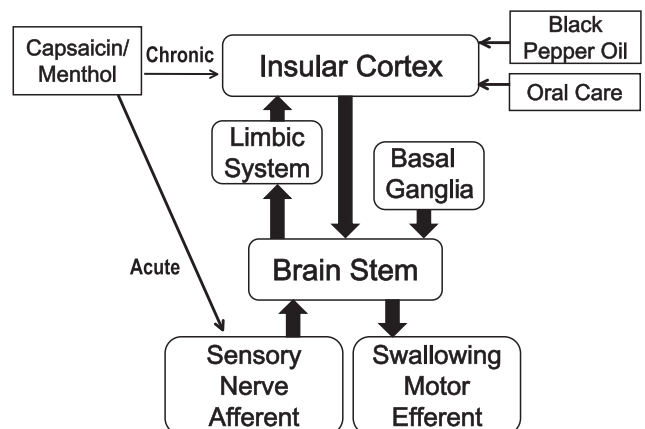


Fig. 2. Neural circuit involved in the swallowing reflex. The sites of action of capsaicin/menthol, black pepper oil olfactory stimulation, and oral care painful stimuli are indicated by thin arrows.

per oil increased cerebral blood flow in the right anterior cingulate cortex and the left insular cortex (29), which is impaired in patients with aspiration pneumonia (26).

Since olfactory stimulation using essential oil is inconvenient for the caregiver and conducting daily aromatherapy is a large caregiver burden, we developed an easier method to conduct black pepper aromatherapy using a new drug gas delivery system (DGDS) (31). DGDS is a novel drug delivery system of transdermal absorption, which takes a volatile bioactive component into the body in a gaseous condition safely and steadily. It was developed as a technology that can safely administer a volatile component (terpenoid) of a plant secondary metabolite. The aroma component of black pepper is continuously transported to the target for 24 h by a DGDS used for black pepper essential oil (Fig. 3). This sheet easily and stably provides olfactory stimulation using the aroma component of black pepper oil by changing the aroma patch sheet daily (31). It is almost equally as effective as direct black pepper oil stimulation. We experienced many cases of refractory pneumonia in the elderly treated with many antibiotics, whose swallowing reflexes were restored by the application of black pepper oil DGDS (black pepper aroma patch sheet) (Fig. 4).

6. Oral care and cough and swallowing reflex

Oral care has been recognized as helping to keep the bacteria in the mouth, thereby preventing aspiration

pneumonia. Yoneyama et al. (32, 33) showed significant results in reducing aspiration-induced pneumonia when professional dental hygienists came to nursing facilities on a regular basis. We investigated the effects of oral care on airway protective reflexes and found that one-month daily oral care significantly improved both swallowing and cough reflexes in the elderly nursing home patients (34). Our data suggest that oral care may reduce the risk of pneumonia by improving the swallowing reflexes and by improving overall functional status. Tooth brushing, pain stimuli to gingiva, is known to activate the insular cortex in a functional MRI study (35). Since the insular cortex function is impaired in patients with aspi-

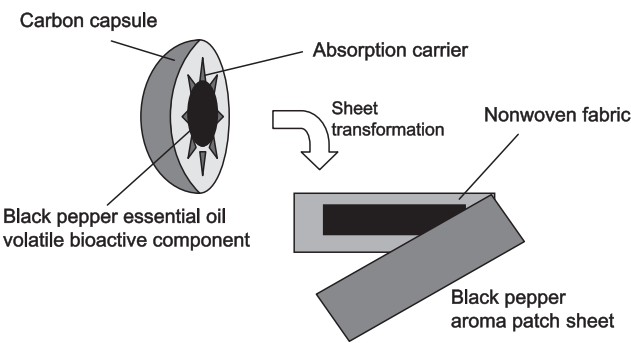


Fig. 3. Development of new drug gas delivery system (DGDS) (Aroma Patch) to provide olfactory stimulation using black pepper with less burden to the caregiver.

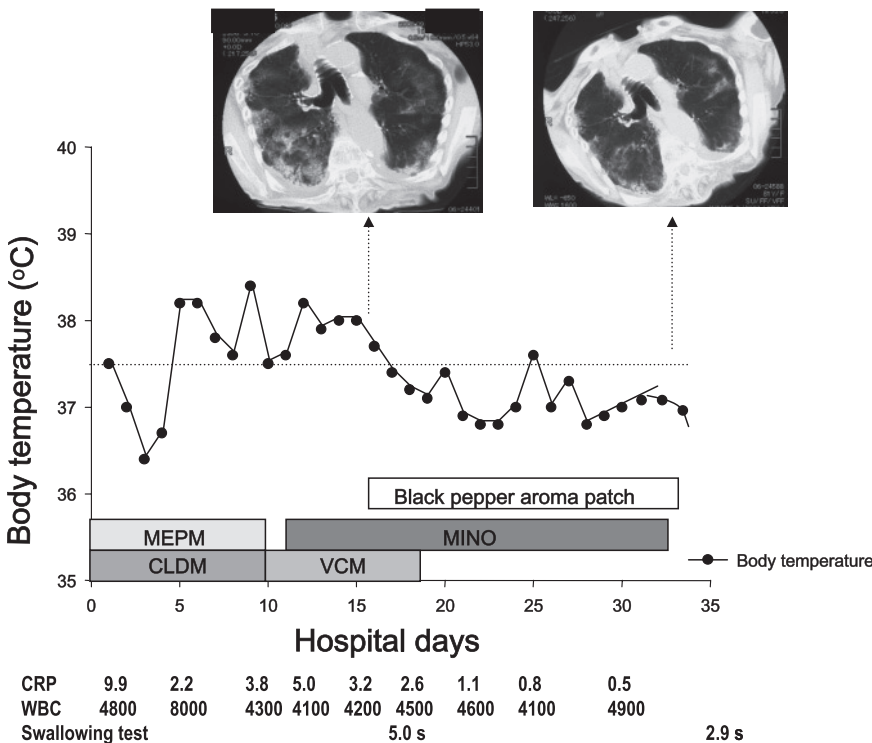


Fig. 4. A case of a black pepper aroma patch sheet use for the elderly with intractable pneumonia due to aspiration. MEM: Mero-penem, CLDM: Clindamycin, VCM: Vanco-mycin, MINO: Minomycin.

ration pneumonia and severe dysphagia (26), we speculate that repeated oral nociceptive sensory stimulation may restore the function of insular cortex, resulting in restoration of the functions of the swallowing reflex.

7. Future perspectives

In addition to TRPV1 and TRPM8 agonists, there might be other food components with the ability to improve swallowing function. For example, we found that red wine polyphenol improve the swallowing reflex by modulating the TRPV1 response (36). The study by Watando et al. (21) suggests that TRPA1 agonists such as allyl-isothiocyanate (wasabi) and cinnamaldehyde (cinnamon) may be beneficial for the swallowing reflex; Further research is needed to uncover the effects of these agonists. Oral care and swallowing rehabilitation are also known to improve the swallowing function and prevent aspiration pneumonia in the elderly (34). Since the aspiration pneumonia in the elderly is often very refractory (37), we should put all these remedies together in the treatment and prevention of aspiration pneumonia. Patients with severe aspiration pneumonia are usually given nothing to eat at the time of admission to the hospital. The most important and challenging step in aspiration pneumonia treatment is restarting eating after recovery using antibiotic treatment. We developed a protocol to restart eating in patients with feeding and swallowing disorders by a combination of aromatherapy, spices, oral care, and swallowing rehabilitation (31). Implementation of this protocol helped avoid re-aspiration as well as gastrostomy in many elderly people.

The shift in demographic composition is supposed to raise the costs of nursing home care service. Prescription drug spending for the elderly is increasing. Research on how to manage the frail elderly is crucial not only for medical but also for economic reasons.

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References

- 1 Stegemann S, Ecker F, Maio M, Kraahs P, Wohlfart R, Breikreutz J, et al. Geriatric drug therapy: Neglecting the inevitable majority. *Ageing Res Rev.* 2010;9:384–398.
- 2 Ebihara S, Arai H. Prospects for health-systems research. *Lancet.* 2008;371:1914.
- 3 Kanda A, Ebihara S, Okazaki T, Yasuda H, Sasaki H. Loxoprofen sodium and survival in older people with advanced non-small cell lung cancer. *J Am Geriatr Soc.* 2004;52:471–472.
- 4 Ebihara S, Takahashi H, Ebihara T, Satoh E, Sasaki H. Japanese nursing system. *Lancet.* 2001;357:1451.
- 5 Diaz A, Barria P, Niederman M, Restrepo MI, Dreyse J, Fuentes G, et al. Etiology of community-acquired pneumonia in hospitalized patients in Chile: the increasing prevalence of respiratory viruses among classic pathogens. *Chest.* 2007;131:779–787.
- 6 Mitchell SL, Teno JM, Kiely DK, Shaffer ML, Jones RN, Prigerson HG, et al. The clinical course of advanced dementia. *N Engl J Med.* 2009;361:1529–1538.
- 7 Janssens JP, Krause KH. Pneumonia in the very old. *Lancet Infect Dis.* 2004;4:112–124.
- 8 Teramoto S, Fukuchi Y, Sasaki H, Sato K, Sekizawa K, Matsuse T; Japanese Study Group on Aspiration Pulmonary Disease. High incidence of aspiration pneumonia in community- and hospital-acquired pneumonia in hospitalized patients: a multicenter, prospective study in Japan. *J Am Geriatr Soc.* 2008;56:577–579.
- 9 Marik PE, Kaplan D. Aspiration pneumonia and dysphagia in the elderly. *Chest.* 2003;124:328–336.
- 10 Lorber B, Swenson RM. Bacteriology of aspiration pneumonia. A prospective study of community- and hospital-acquired cases. *Ann Intern Med.* 1974;81:329–331.
- 11 Cesar L, Gonzalez C, Calia FM. Bacteriologic flora of aspiration-induced pulmonary infections. *Arch Intern Med.* 1975;135:711–714.
- 12 El-Solh AA, Pietrantonio C, Bhat A, Aquilina AT, Okada M, Grover V, et al. Microbiology of severe aspiration pneumonia in institutionalized elderly. *Am J Respir Crit Care Med.* 2003;167:1650–1654.
- 13 Mier L, Dreyfuss D, Darchy B, Lanore JJ, Djedaini K, Weber P, et al. Is penicillin G an adequate initial treatment for aspiration pneumonia? A prospective evaluation using a protected specimen brush and quantitative cultures. *Intensive Care Med.* 1993;19:279–284.
- 14 Bartlett JG, Gorbach SL, Fiegold SM. The bacteriology of aspiration pneumonia. *Am J Med.* 1974;56:202–207.
- 15 Ebihara T, Ebihara S, Watando A, Okazaki T, Asada M, Ohnri T, et al. Effects of menthol on the triggering of the swallowing reflex in elderly patients with dysphagia. *Br J Clin Pharmacol.* 2006;62:369–371.
- 16 Yamada S, Ebihara S, Ebihara T, Yamasaki M, Arai H, Kohzaki M. Bacteriology of aspiration pneumonia due to delayed triggering of the swallowing reflex in elderly patients. *J Hosp Infect.* 2010;74:399–401.
- 17 Kanda A, Ebihara S, Yasuda H, Takashi O, Sasaki T, Sasaki H. A combinatorial therapy for pneumonia in elderly people. *J Am Geriatr Soc.* 2004;52:846–847.
- 18 Kubo H, Nakayama K, Ebihara S, Sasaki H. Medical treatments and cares for geriatric syndrome: new strategies learned from frail elderly. *Tohoku J Exp Med.* 2005;205:205–214.
- 19 Ebihara T, Ebihara S, Okazaki T, Takahashi H, Wantando A, Yasuda H, et al. Theophylline-improved swallowing reflex in elderly nursing home patients. *J Am Geriatr Soc.* 2004;52:1787–1788.
- 20 Ebihara S, Ebihara T, Yamada S, Asada M, Arai H. Angiotensin-converting enzyme inhibitors and smoking cessation. *Respiration.* 2007;74:478.
- 21 Watando A, Ebihara S, Ebihara T, Okazaki T, Takahashi H, Asada

- M, et al. Effect of temperature on swallowing reflex in elderly patients with aspiration pneumonia. *J Am Geriatr Soc.* 2004;52: 2143–2144.
- 22 Ebihara T, Sekizawa K, Nakazawa H, Sasaki H. Capsaicin and swallowing reflex. *Lancet.* 1993;341:432.
- 23 Ebihara T, Takahashi H, Ebihara S, Okazaki T, Sasaki T, Watando A, et al. Capsaicin troche for swallowing dysfunction in older people. *J Am Geriatr Soc.* 2005;53:824–828.
- 24 Yamasaki M, Ebihara S, Ebihara T, Yamanda S, Arai H, Kohzuki M. Effects of capsiate on the triggering of the swallowing reflex in elderly patients with aspiration pneumonia. *Geriatr Gerontol Int.* 2010;10:107–109.
- 25 Dhaka A, Viswanath V, Patapoutian A. TRP ion channels and temperature sensation. *Annu Rev Neurosci.* 2006;29:135–161.
- 26 Okamura N, Maruyama M, Ebihara T, Matsui T, Nemoto M, Arai H, et al. Aspiration pneumonia and insular hypoperfusion in patients with cerebrovascular disease. *J Am Geriatr Soc.* 2004;52: 645–646.
- 27 Romanovsky AA. Thermoregulation: some concepts have changed. *Functional architecture of the thermoregulatory system.* *Am J Physiol Regul Integr Comp Physiol.* 2007;292:R37–R46.
- 28 Edris AE. Pharmaceutical and therapeutic potentials of essential oils and their individual volatile constituents: a review. *Phytother Res.* 2007;21:308–323.
- 29 Ebihara T, Ebihara S, Maruyama M, Kobayashi M, Itou A, Arai H, et al. A randomized trial of olfactory stimulation using black pepper oil in older people with swallowing dysfunction. *J Am Geriatr Soc.* 2006;54:1401–1406.
- 30 Munakata M, Kobayashi K, Niisato-Nezu J, Tanaka S, Kakisaka Y, Ebihara T, et al. Olfactory stimulation using black pepper oil facilitates oral feeding in pediatric patients receiving long-term enteral nutrition. *Tohoku J Exp Med.* 2008;214:327–332.
- 31 Ebihara T, Ebihara S, Yamazaki M, Asada M, Yamanda S, Arai H. Intensive stepwise method for oral intake using a combination of transient receptor potential stimulation and olfactory stimulation inhibits the incidence of pneumonia in dysphagic older adults. *J Am Geriatr Soc.* 2010;58:196–198.
- 32 Yoneyama T, Yoshida M, Matsui T, Sasaki H. Oral care and pneumonia. Oral Care Working Group. *Lancet.* 1999;354:515.
- 33 Yoneyama T, Yoshida M, Ohnishi T, Mukaiyama H, Okamoto H, Hoshioka K, et al; Oral Care Working Group. Oral care reduces pneumonia in older patients in nursing homes. *J Am Geriatr Soc.* 2002;50:430–433.
- 34 Yoshino A, Ebihara T, Ebihara S, Fuji H, Sasaki H. Daily oral care and risk factors for pneumonia among elderly nursing home patients. *JAMA.* 2001;286:2235–2236.
- 35 Weigelt A, Terekhin P, Kemppainen P, Dörfler A, Forster C. The representation of experimental tooth pain from upper and lower jaws in the human trigeminal pathway. *Pain.* 2010;149:529–538.
- 36 Ebihara S, Maruyama Y, Ebihara T, Ohshiro T, Kohzuki M. Red wine polyphenols and swallowing reflex in dysphagia. *Geriatr Gerontol Int.* 2010;10:329–330.
- 37 Tsubouchi T, Tsujimoto S, Sugimoto S, Katsura Y, Mino T, Seki T. Swallowing disorder and inhibition of cough reflex induced by atropine sulfate in conscious dogs. *J Pharmacol Sci.* 2008;106: 452–459.