Review Article

How masticatory function and periodontal disease relate to senile dementia

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Summary This study reviews the research of dementia, a pathology for which numerous studies have found associations with masticatory function in the elderly. These issues are presently major problems in geriatric medical and welfare settings, and we discuss the prospects for future research into mastication. Dementia and masticatory function have been examined in a range of epidemiological and neuroscientific studies, and associations between the two have been reported. However, a causal relationship has not been satisfactorily established. Biochemical studies have also clarified the basis of the association between dementia and periodontal disease, but have not yet yielded sufficient evidence. Studies offering a high level of evidence, such as intervention studies and meta-analyses, are expected to be undertaken in this area in the future. Maintenance and recovery of masticatory function is of great importance with respect to achieving healthy longevity. Dental science will have considerable obligations and will have to take on an important role in this regard. For dental treatment to take on such important roles in the fields of health, medicine and welfare, it is necessary to provide information that will be understood not just by other medical and healthcare professionals, but also by the general public.

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1. Introduction

Japan has become a super-aged society, reaching this situation before any other country [1]. The 2012 Survey of Dental Diseases found that the proportion of elderly individuals with at least 20 of their own teeth at 80 years of age was 38.3% [2]. At the same time, an increase has been seen in the number of elderly people who have many of their own teeth but have decreased masticatory function [3]. Masticatory function may therefore be conjectured to be affected not only by reductions in the number of teeth, but also by increasing age [4].

Mastication, in which food is crushed and mixed with saliva to form a bolus for swallowing, is a complex process involving the repeated opening and closing of the jaw, the secretion and mixing of food with the tongue. Mastication is a rhythmic, automatic movement similar to breathing or walking, and is a characteristic movement that can intentionally be made faster, slower or even stopped [5]. In addition, mastication and swallowing of solid food differs from command swallowing of fluid or semi-solid food. With solid food, the masticated bolus is transported to the oropharynx (stage II transport) before the swallowing reflex begins, and bolus formation within the mouth continues. This transport to the oropharynx is not gravity-dependent, but takes place as a result of active movement of the tongue during mastication. The bolus sent to the pharynx is swallowed while the next bolus is masticated in the mouth and then is sent to the pharynx. Swallowing also occurs sequentially while food that has not been fully masticated remains in the mouth [6]. For this reason, humans are able to efficiently form, divide and swallow boluses of food while masticating and tasting them, even when large amounts of food are placed in the mouth, and can thus ingest abundant nutrition within a short period. This complex feeding and swallowing function is essential for humans to be able to ingest nutrients of the quality and in the quantity necessary for an intellectually and physically active life [7].

The neural circuits for mastication, together with those for the regulation of breathing, walking, posture and blood circulation, exist within the lower brainstem. The rhythmic movement of the jaw and tongue is regulated by the lower brainstem, mainly as a mechanism of rhythm formation based on information generated during mastication from sensory receptors in the oral cavity and masseter muscles [5]. In addition, control is achieved via regulatory mechanisms in areas of the upper brain, including the cerebral cortex, amygdala, basal ganglia, midbrain reticular formation, hypothalamus and cerebellum, which are involved in arousal, higher mental activity, emotion, instinct, homeostasis, taste, motivation to eat, food discrimination, saliva secretion, elicitation of swallowing and movement [8]. Moreover, there are many integrative effects, including health maintenance by the stimulation of saliva secretion, promotion of digestion and appetite regulation by stimulation of digestive juices and hormonal secretion, elicitation of a sense of safety and euphoria via the secretion of pleasure-related substances in the brain by the jaw and oral cavity sensation during mastication, brain activation, and promotion of faciocranial growth and development [8]. In other words, mastication is not only directly involved in digestive function in the oral cavity, but also plays very important and broad-ranging roles in maintaining vital functions.

One important factor inhibiting masticatory function in elderly people is periodontal disease, and numerous reports in recent years have examined relationships between the sustained chronic inflammation in periodontal disease and pathologies such as dementia, diabetes, cardiovascular disease, cancer, premature birth and low birth weight [9]. Associations of periodontal disease with these conditions are supported by a large body of epidemiological data [10], but no causal relationships have been adequately established [11]. This review summarizes the findings on dementia [12–15], which numerous recent studies have reported to be associated with masticatory function in the elderly. This issue is presently a major problem in geriatric medical and care-giving settings, and we consider the prospects for future research into mastication.

2. Relationship between masticatory function and dementia in the elderly

According to results published by a study group of the Japanese Ministry of Health, Labor and Welfare, an estimated 4.62 million people with dementia lived in Japan in 2012. A further 4.0 million people had mild cognitive impairment (MCI), which has a high probability of developing into dementia [16]. Altogether, one in four people ≥65 years old in Japan has or is at risk of dementia [17]. The prevalence of dementia increases with age, so the number of individuals with dementia is expected to continue rising.
Dementia and its associated problem behaviors lead to the need for more intensive levels of care and are major factors preventing independent living [18]. Consequently, prevention of dementia and protection against aggravation of the condition are enormously important. This review examines the relationship between masticatory function and dementia in the elderly.

2.1. Studies of masticatory function and dementia

Activity levels are higher in elderly individuals with good chewing ability compared to those without, and in particular, marked differences in items related to cognitive ability have been demonstrated. Kondo et al. reported that the loss of teeth, which can markedly impair masticatory function, is a significant risk factor for Alzheimer’s disease (AD) [19]. Moreover, the risk of developing AD increases as the number of intact teeth decreases. Kusaga et al. observed a relationship between chewing score and dementia level, and stated that the number of remaining teeth, molar occlusion, and chewing habits may exert influences on dementia [20]. Moreover, chewing scores decreased rapidly from the mild dementia group to the moderate dementia group. Chewing scores thus did not gradually decrease with dementia progression, but rather decreased rapidly with loss of teeth after mild dementia started, suggesting some degree of influence on cerebral function. Encouraging the prevention of tooth loss and adjustment of dentures is of course important when subjects are healthy, but is particularly essential in individuals with mild dementia.

In a separate study, in addition to blood pressure measurements, blood testing and electrocardiography, magnetic resonance imaging (MRI) was performed on volunteers to comprehensively evaluate overall function, including cognitive function, motor function and mental status. The relationship between intraoral status, masticatory function and number of remaining teeth was examined. Elderly individuals who underwent testing were divided into three groups: a “healthy group” (n = 652, 55.8%), an “age-associated cognitive decline group” (n = 460, 39.4%) and a “suspected dementia group” (n = 55, 4.7%). The healthy elderly group had a mean of 14.9 teeth remaining, whereas the 55 elderly individuals with suspected dementia had a significantly lower mean of 9.4 teeth. This suggested a relationship between the number of teeth and dementia. In addition, a total of 195 individuals in the healthy and age-associated cognitive decline groups underwent MRI of the brain to clarify the relationships between both the number of remaining teeth and number of occlusions with the volume of gray matter in the brain. In individuals with a smaller number of teeth, the volume near the hippocampus was decreased. The volume of the frontal lobes, associated with higher brain functions such as volition and thought, was also decreased [21]. Similarly, in a study of 155 people who had undergone MRI, the prevalence of lacunar infarction from asymptomatic cerebrovascular disease and leukoaraiosis, which represent high risk factors for dementia onset, increased with the decreasing number of remaining teeth [22].

A study of 218 elderly individuals in Brazil found that edentulous participants who did not use any dental prostheses scored significantly lower on the Mini-Mental State Examination [23]. People hospitalized with dementia also showed a significantly increased risk of AD as the number of lost teeth increased [24]. Numerous other reports have found associations between tooth loss and decreased cognitive function [25, 26].

Animal experiments have reported significant effects on learning and significant extension in memory time as a result of eating hard food [27, 28]. Studies using aged animals have shown that hard food delays the decline in learning effectiveness brought on by old age when compared to soft food, which suggests that hard food may curtail senile deterioration [29]. Also, the results of an experiment in which masticatory function disorder was caused by tooth extraction in senescence-accelerated mice suggested an association between masticatory function disorder and declines in cognitive function [30]. Studies using animal models of AD show that soft food causes declines in memory and learning ability compared to hard food, suggesting that the hardness of food affects cognitive function [31]. Studies using animal models of cerebral infarction have also reported that hard food is associated with significantly greater recovery from learning and memory defects than soft food [32].

2.2. Studies of periodontal disease and dementia

The greatest cause of impaired masticatory function among elderly individuals is periodontal disease. In one study of periodontal disease and dementia, the relationship between a serological marker for periodontal disease (Porphyromonas gingivalis serum immunoglobulin G antibody titer) and cognitive function was investigated in 2355 individuals ≥60 years old as part of the National Health and Nutrition Examination Survey III in the United States. That study reported impairments of recent memory and calculation ability as associated with detection of a serological marker for periodontal disease [33, 34]. A separate study looking at AD also found that AD patients show high levels of inflammatory mediators such as tumor necrosis factor (TNF)-α and antibodies to bacteria related to periodontal disease in their sera, suggesting a statistically independent association between periodontal disease and AD [35].

A number of reviews of the literature [36–38] concerning AD and bacterial infections found significant correlations between AD and the presence of P. gingivalis. In a brain analysis study of patients with AD, bacteria of the genus Treponema, one type of bacteria related to periodontal disease, were observed in ≥90% of the cases [39]. In vitro experiments have also suggested an association between neurospirochetosis and AD. A research group in the UK recently carried out an analytic study of brain samples from 10 AD patients and found traces of P. gingivalis in four of them. However, bacteria were not detected in brain samples from 10 people of the same age range who did not display symptoms of dementia [40]. In a recent study, we examined AD model mice (J20 mice) with periodontal disease caused by oral inoculation of P. gingivalis. Compared to mice not inoculated with the bacteria, the mice with periodontal disease showed lower maintenance of cognitive function, increased deposition of senile plaques in the hippocampus.
and cortex of the brain tissue, and increased levels of interleukin 1β and TNF-α in the brain tissue [41]. These findings suggest the possibility that persistent infection in a localized area of the host, such as periodontal tissue, and the resulting inflammatory response may spill over to the whole body, including the brain, and may be involved in systemic inflammation and the development of AD [42]. Lexomboon et al. reported that persons with multiple tooth loss and/or difficulty of chewing hard food had significantly higher odds of cognitive impairment, in a cross-sectional survey of 557 people who were nationally representative of the Swedish population aged 77 or older [43]. When adjusted for sex, age and education, the odds of cognitive impairment were not significantly different between persons with natural teeth and with those multiple tooth loss, but the odds of impairment remained significantly higher for persons with chewing difficulty even when adjusted for sex, age, education, depression and mental illness.

In response to that report, Savikko et al. sent a response letter stating that people with dementia differed from those without dementia in several characteristics although dementia was not related to dentition status or chewing difficulty in a cross-sectional survey that included 3164 people living in long-term care facilities (nursing homes and service housing) in Helsinki [44]. Individuals with dementia were more likely to have malnutrition than those without. It may be that in this frail, highly selected older population residing in long-term institutional care, lifetime risk factors, such as cardiovascular disease, depression, inflammation, use of alcohol or tobacco, and nutrition, have had more of an effect on the prevalence of dementia than dentition or chewing ability at this late point in life. It may also be that these risk factors have had their effect on cognitive impairment and chewing abilities. Savikko et al. further commented that these results may imply that chewing difficulties alone do not lead to cognitive decline, but may be a marker of comorbidities and nutritional status partly responsible for initiating processes that lead to the development of dementia. As yet, insufficient data has accumulated to verify a causal relationship [45], but the nature of the relationship will doubtless become clearer as the mechanisms involved are clarified and intervention studies are carried out in the future.

2.3. Neuroscientific studies of mastication

As discussed in the preceding section, a number of biochemical studies have reported factors linking periodontal disease and dementia. However, factors linking masticatory function and dementia are unclear. In light of studies showing that reduced masticatory function affects cognitive function, we reviewed the current neuroscientific findings on masticatory function and examined factors that link masticatory function and dementia.

Increases in cerebral cortical activity with mastication have been studied using various devices measure brain function, and have been shown by increased blood flow and increased metabolic and nervous activity in various regions of the brain [46]. Cerebral blood flow (CBF) decreases with aging, and the brain atrophy index (BAI) increases when regional CBF decreases [47]. In elderly individuals, a positive correlation has been observed between carotid artery blood flow and intellectual and mental functions [48]. In addition, decreased CBF is a factor associated with cerebrovascular dementia [49].

Mastication causes an autonomous nervous system response that results in increased metabolic activity. This activity also stimulates oral tissues, resulting in increased blood flow not only to oral tissues, but also to the brain. Increases in regional CBF, by chewing sensory information sent to the brain via a sensory input subsystem from an effector subsystem of the masticatory system, and by a rise in carbon dioxide partial pressure produced by an increase in metabolic activity of feedback cortical sensorimotor neurons, are elicited as a result of the capillary lumens being dilated [50]. Based on these findings, sensory stimuli from the periodontal membrane and masseter muscle spindles are thought to reach cerebral blood vessels during chewing movements via trigeminal afferent pathways, leading to blood vessel dilation, and increasing CBF by an increase in heart rate [51]. A recent study using near-infrared spectroscopy (NIRS) evaluated differences in CBF during clenching in edentulous subjects and in those with implant prostheses. CBF was significantly increased with the implant prostheses [52].

With measurement of brain function using functional MRI (fMRI), increased CBF in motor areas, sensory areas, supplementary motor areas, insula, thalamus and the cerebellum have been observed when chewing gum [53]. Moreover, gum chewing on both sides of the mouth has been reported to significantly increase CBF in the primary sensory area, motor area and prefrontal cortex on both sides, while gum chewing on only one side of the mouth preferentially increases CBF on one side [54–58]. Prefrontal cortical activation as a result of mastication was observed in a study using NIRS, and this increased activity was particularly marked in the elderly, suggesting that mastication may be useful in maintaining cognitive function [59].

Fibroblast growth factors released into the brain as a result of mastication regulate appetite and promote growth, and also are believed to promote brain cell repair and learning and memory formation [60–62].

In an electroencephalographic study, attention to language and processing speed were both increased by chewing, and effects on long-term memory were also suggested [63]. A study by Hirano et al. measured brain activity by fMRI when performing working memory tasks, and the effects of gum chewing were examined [64]. When gum was chewed before performing memory tasks, CBF was increased in the prefrontal area (Brodmann’s areas 9 and 46). Furthermore, increased CBF was observed in the right premotor area, precuneus, thalamus, hippocampus and inferior parietal lobe. These findings suggest that chewing can stimulate arousal and may also accelerate the working memory process. Another study on working memory using magnetoencephalography was also conducted [65]. In that study, the magnetic field was measured when gum was chewed, when gum was not chewed and when the hands were opened and closed before performing the visual Sternberg task (working memory task). Under all conditions, in the occipital lobe during memory and in the calcarine and parieto-occipital sulci during memory maintenance, α
waves were observed. After no gum chewing and after hand opening and closing, as compared to after gum chewing but before performing the tasks, the correct response rate decreased and α waves increased. This was attributed to decreases in concentration ability. The conclusion of that study was that chewing exerted effects on maintaining concentration and working memory acquisition. Neuroscientific studies have thus shown that mastication promotes CBF and cerebral metabolic and nervous activities, thus affecting cognitive function.

3. Prospects for research into mastication and dementia among the elderly

The above findings indicate a certain level of consensus that mastication affects dementia through the promotion of CBF and cerebral metabolic and nervous activities. However, very few studies have been carried out to verify the effects on dementia of the recovery of masticatory function in the elderly, and there is a need for intervention studies and large-scale prospective cohort studies in this area.

Dementia includes core symptoms of memory defects, disorientation, deterioration of judgment, aphasia, apraxia, agnosia, and behavioral and psychological symptoms of delirium, depression, agitation, wandering and delusions [66]. These symptoms can cause impaired eating and swallowing functions or impairments related to eating behaviors, such as refusing food, overeating, allotriophagy or interrupted meals. When severe, such impairments can lead directly to malnutrition, impacting the prognosis and increasing the burden on caregivers [67, 68]. Also, factors such as declines in awareness and behaviors related to oral hygiene, difficulty in carrying out oral care and eating soft food due to declines in eating and swallowing functions clearly increase the risk of periodontal disease [69] (shown schematically in Fig. 1). Mice in which periodontal disease was induced experimentally, as mentioned earlier, showed reduced cognitive function and increased deposition of amyloid β-protein in the hippocampus and cerebral cortex [41]. Such findings suggest that the oral function and oral hygiene condition of elderly individuals may affect the status of dementia. However, clarification of causal relationships between dementia and oral function or oral hygiene will require comprehensive survey analysis not only of factors such as the knock-on effect of oral infection or chronic inflammation, but also factors strongly influenced by masticatory function, such as the effectiveness of periodontal disease treatment, nutrient intake, motor function, sphere of activity and intellectual activity. The emergence of clear causal relationships will mean that dental treatment can contribute in a substantial way to the prevention of dementia and the control of its progress. We hope that large-scale studies carried out not just by dental professionals, but also with the input of personnel from various different occupational categories will clarify the relationship between mastication and dementia.

4. Conclusion

Looking to the future of health, medicine and welfare, society will be confronted by the issue of how a healthy longevity that encompasses the quality of life and the purpose in life can be achieved. In this respect, the maintenance and recovery of masticatory function is of great importance, as shown by the various effects of mastication on the whole body. Dental science will therefore have considerable obligations and will have important roles to play in this respect [70]. For dental treatment to take on these challenging problems in the fields of health, medicine and welfare, an understanding will be crucial not just by other medical or healthcare professionals, but also by the general public. For this reason, it is important to promote research into the relationship between mastication and health with cooperation between oral biology and clinical dentistry, and with the collaboration of fields such as medicine, nutritional science, and science and engineering to disseminate necessary and accurate information to the general public.

Conflict of interest statement

The authors have no conflict of interest to declare.

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