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Review

Association between mastication and cognitive status: A systematic review

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ABSTRACT

Purpose: A substantial number of elderly people suffer from cognitive impairment and dementia, which are considered to have various risk factors, including masticatory dysfunction; however, the association between mastication and cognition is inconclusive. The objectives of this systematic review were to provide an overview of the literature on (1) the association between mastication and cognitive function and (2) the association between mastication and dementia incidence, in elderly people.
Materials and methods: Searches were conducted on five electronic databases (PubMed, EMBASE, CINHL, Cochrane Library, and Pro Quest) and publications were selected that met the following criteria: published between 2005 and 2015, written in English, and assessed associations between mastication and cognitive function, cognitive decline and dementia among population over 45 years old. The included publications were analyzed for study design, main conclusions, and strength of evidence by two reviewers who screened all abstracts and full-text articles, abstracted data and performed quality assessments by using a critical appraisal tool.
Results: A total of 33 articles (22 cross-sectional, and 11 prospective cohort studies) were evaluated. Poorer mastication was associated with lower cognitive function in 15 of the 17 cross-sectional studies and steeper decline in 5 of the 6 prospective studies. Poorer mastication was one of significant risk factors for having dementia or mild memory impairment (MMI) in 4 of 5 cross-sectional studies and for the incidence of dementia or MMI in 4 of 5 prospective studies.
Conclusions: Most studies point to a positive association between mastication and cognitive function, including dementia among elderly people.

Contents

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1. Introduction

As the world population ages, the proportion of elderly people with dementia and cognitive impairment is expected to increase. Cognitive impairment and dementia are serious public health problems that adversely affect the quality of life of elderly adults and increase health care costs (Alzheimer's Association, 2012). The wide range of risk factors for cognitive impairment and dementia includes demographic factors (e.g., increasing age and lower education levels) (Hugo & Ganguli, 2014; Qiu, De Ronchi, & Fratiglioni, 2007), genetic factors (e.g., APOE*4 allele) (Hugo & Ganguli, 2014; Tsuang et al., 2013), medical risk factors (e.g., cardiovascular disease and stroke) (Hugo & Ganguli, 2014; Justin, Turek, & Hakim, 2013; Qiu et al., 2007), psychiatric factors (Hugo & Ganguli, 2014; Dotson, Beydoun, & Zonderman, 2010), head injury (Hugo & Ganguli, 2014; Fleminger, Oliver, Lovestone, Rabe-Hesketh, & Giora, 2003), and lifestyle factors (smoking and heavy consumption of alcohol) (Hugo & Ganguli, 2014; Anstey, von Sanden, Salim, & O'Kearney, 2007; Anttila et al., 2004; Qiu et al., 2007). In the last decades, there has been a growing interest in elucidating the relationship between mastication and cognition. Epidemiological and clinical studies in populations have extensively been conducted to elucidate the association of mastication with cognitive function and on the incidence of dementia in many countries (Weijenberg, Scherder, & Lobbezoo, 2011). Consequently, a sizable body of knowledge has accumulated on this topic. However, no review article with a wide range of literature describing this association has been published. In addition, the studies addressing this topic have used a variety of age groups, subjects, settings, and methods to evaluate mastication and cognitive function and dementia; therefore, the review of the available data is of utmost importance in understanding the role of mastication in cognitive function and dementia. The present systematic review includes published studies that have examined the association between mastication, and cognitive function and dementia, and dementia with the view to further enhance the knowledge on these issues and critically evaluate the methods used in these studies. The objectives of this systematic review were to provide an overview of the literature on (1) the association between mastication and cognitive function and (2) the association between mastication and dementia incidence, in elderly people.

2. Methods

2.1. Literature search

Five electronic databases (PubMed, EMBASE, Cumulative Index to Nursing and Allied Health Literature [CINAHL], Cochrane Library, and Pro Quest) were searched using the following key words: ("mastication" OR "tooth number") AND ("cognitive" OR "dementia"); ("mastication" OR "tooth loss") AND ("cognitive" OR "dementia") and ("mastication" OR "edentulism") AND ("cognitive" OR "dementia"). Articles with the aforementioned combination of keywords anywhere in the paper were selected. The observational studies that investigated the association between oral health; cognitive function; and dementia in elderly people published between 2005 and 2015 were eligible for inclusion. Only studies published in English were included because most of the articles included in the searched databases were written in English. Two reviewers (AT and HM) independently screened each retrieved document for eligibility by examining the titles and abstracts; according to the inclusion and exclusion criteria shown in Table 1. After the literature search was completed; no additional publications were included. The reference list for each of the retrieved publications was also reviewed and any journal appearing in the reference list was added to a list of journals to be manually searched.

2.2. Quality assessments

A quality assessment was conducted using the Critical Appraisal Skills Programme (CASP) Cohort Studies Checklists (CASP, 2014). The checklist for cohort studies was modified for application to cross-sectional studies (e.g. Question 2, "Was the cohort recruited in an acceptable way?" was modified to "Was the sample recruited in an acceptable way?", and questions regarding follow-up of participants were excluded). For each study, the strength and

Table 1
Inclusion and exclusion criteria used in this review.

	Inclusion criteria	Exclusion criteria
Sample	Subjects aged 40 years or older, or population with a mean/median age > 45 years	Subjects who received oral and maxillofacial surgery or, radiotherapy Subjects who have systemic illness
Outcome	Cognitive functional test Diagnosis of dementia	Data on cognitive function is not obtained
Analysis	Any association between oral health and food and/or nutrient intake	Descriptive studies, review, or studies with no analyses investigating the association between oral health and cognitive function

Table 2
The results of the critical appraisal assessment.

(1) Cognitive function

a) Cross-sectional

	1	2	3	4	5a	5b	6	7	8	Quality assessment
Kimura et al. (2013)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Lexomboon et al. (2012)	✓	✓	X	✓	X	X	✓	✓	✓	Low
Scherder et al. (2008)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Nilsson et al. (2014)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Peres et al. (2014)	✓	✓	✓	✓	✓	✓	✓	✓	✓	High
Wang et al. (2014)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Park et al. (2013)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Saito et al. (2013)	✓	✓	✓	✓	✓	✓	✓	✓	✓	High
Grabe et al. (2009)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Bergdahl et al. (2007)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Del Brutto et al. (2014)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Hansson et al. (2013)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Weijenberg et al. (2015)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Listl (2014)	✓	✓	X	✓	X	X	✓	✓	✓	Low
Kamer et al. (2012)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Naorungroj et al. (2013a)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Stewart et al. (2008)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate

1 Did the study address a clearly focused issue?
2 Were the subjects recruited in an acceptable way?
3 Was the exposure accurately measured to minimise bias?
4 Was the outcome accurately measured to minimise bias?
5a Have the authors identified all important confounding factors?
5b Have they taken account of the confounding factors in the design and/or analysis?
6 Do you believe the results?
7 Can the results be applied to the local population?
8 Do the results of this study fit with other available evidence?

b) Cohort

	1	2	3	4	5a	5b	6a	6b	7	8	9	Quality assessmen
Reyes-Ortiz et al. (2013)	✓	✓	✓	✓	X	X	X	X	✓	✓	✓	Low
Kaye et al. (2010)	✓	✓	✓	✓	X	X	X	✓	✓	✓	✓	Moderate
Tsakos et al. (2015)	✓	✓	✓	✓	✓	✓	N	✓	✓	✓	✓	High
Naorungroj et al. (2015)	✓	✓	✓	✓	X	X	N	✓	✓	✓	✓	Moderate
Naorungroj et al. (2013b)	✓	✓	✓	✓	X	X	N	✓	✓	✓	✓	Moderate
Stein et al. (2010)	✓	X	✓	✓	X	X	N	X	✓	X	✓	Low

1 Did the study address a clearly focused issue?
2 Were the subjects recruited in an acceptable way?
3 Was the exposure accurately measured to minimise bias?
4 Was the outcome accurately measured to minimise bias?
5a Have the authors identified all important confounding factors?
5b Have they taken account of the confounding factors in the design and/or analysis?
6a Was the follow up of subjects complete enough?
6b Was the follow up of subjects long enough?
7 Do you believe the results?
8 Can the results be applied to the local population?
9 Do the results of this study fit with other available evidence?

(2) Incidence of dementia/MMI

a) Cross-sectional

	1	2	3	4	5a	5b	6	7	8	Quality assessment
Kim et al. (2007)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Okamoto et al. (2010)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Elsig et al. (2013)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate
Luo et al. (2015)	✓	✓	✓	✓	✓	✓	✓	✓	✓	High
Gil-Montoya et al. (2015)	✓	✓	✓	✓	X	X	✓	✓	✓	Moderate

1 Did the study address a clearly focused issue?
2 Were the subjects recruited in an acceptable way?
3 Was the exposure accurately measured to minimise bias?
4 Was the outcome accurately measured to minimise bias?
5a Have the authors identified all important confounding factors?
5b Have they taken account of the confounding factors in the design and/or analysis?
6 Do you believe the results?
7 Can the results be applied to the local population?
8 Do the results of this study fit with other available evidence?

b) Cohort

	1	2	3	4	5a	5b	6a	6b	7	8	9	Quality assessment
Stewart et al. (2015)	✓	✓	✓	✓	X	X	X	✓	✓	✓	✓	Moderate
Yamamoto et al. (2012)	✓	✓	✓	✓	X	X	✓	X	✓	✓	✓	Moderate

Table 2 (*Continued*)

b) Cohort

	1	2	3	4	5a	5b	6a	6b	7	8	9	Quality assessment
Paganini-Hill et al. (2012)	✓	✓	✓	✓	X	X	N	✓	✓	✓	✓	Moderate
Stein et al. (2007)	✓	X	✓	✓	X	X	N	X	✓	✓	✓	Low
Okamoto et al. (2015)	✓	✓	✓	✓	✓	✓	X	✓	✓	✓	✓	Moderate

1 Did the study address a clearly focused issue?
2 Were the subjects recruited in an acceptable way?
3 Was the exposure accurately measured to minimise bias?
4 Was the outcome accurately measured to minimise bias?
5a Have the authors identified all important confounding factors?
5b Have they taken account of the confounding factors in the design and/or analysis?
6a Was the follow up of subjects complete enough?
6b Was the follow up of subjects long enough?
7 Do you believe the results?
8 Can the results be applied to the local population?
9 Do the results of this study fit with other available evidence?

✓, satisfied; X, not satisfied; N, not applicable.

weakness of was calculated based on the relevant checklist items and a grade of "low", "moderate," or "high" was assigned with agreement of the two authors (AT and HM).

3. Results

3.1. Literature searches

A total of 803 publications were retrieved after the primary search of the four databases, and 728 of these were excluded in the first round of screening based on title and abstract. The full-text articles of the 75 potentially relevant references were reviewed, of which 42 did not fit the inclusion criteria and consequently were excluded. Finally, 33 publications (22 cross-sectional studies and 11 prospective cohort studies) were selected as the 'key articles', which would be subsequently scrutinized for study design.

3.2. Quality of studies

The results of the critical appraisal assessment are presented in Table 2. Recurrent strengths of the evidence included the following: 1) addressing a clearly focused issue (n = 33; 100%); 2) recruiting subjects in an acceptable manner (cognitive function, cross-sectional n = 17 [100%] and cohort n = 5 [83.3%]; dementia/minor memory impairment [MMI] incidence, cross-sectional n = 5 [100%] and cohort n = 4 [80%]); 3) measuring exposure to minimise bias (cognitive function, cross-sectional n = 16 [94.1%] and cohort n = 6 [100%]; dementia/MMI, cross-sectional n = 5 [100%] and cohort n = 5 [100%]); and 4) measuring outcome to minimise bias (n = 33 [100%]).

However, recurrent weakness of the evidence included adjusting for all potential confounding factors. Only four studies adequately adjusted their analyses for all potential confounders, such s socioeconomic factors, health habits, history of chronic diseases, and psychological variables (Saito et al., 2013; Peres et al., 2014; Luo et al., 2015; Tsakos, Watt, Rouxel, de Oliveira, & Demakakos, 2015). More than half of the prospective cohort studies have follow-up periods of 5 years or more (cognitive function n = 4 [66.7%]; dementia/MMI incidence, n = 4 [80%]).

The ratings were delegated as follows: 4 as "High" (2 cross-sectional studies for cognitive function, 1 prospective cohort study for cognitive function, and 1 cross-sectional study for dementia/MMI incidence); 24 as "Moderate" (13 cross-sectional studies for cognitive function, 3 prospective cohort studies for cognitive function, 4 cross-sectional studies for dementia/MMI incidence, and 4 prospective cohort studies for dementia/MMI incidence); and 5 as "Low" (2 cross-sectional studies for cognitive function, cross-sectional studies for cognitive function, 2 cross-sectional studies for dementia/MMI incidence, and 1 prospective cohort studies for dementia/MMI incidence).

3.3. Impact of mastication on cognitive function

The findings from the studies concerning cognitive function are described in Table 3.

3.3.1. Cross-sectional studies

Among the 17 cross-sectional studies evaluated, 10 were investigations of cognitive impairment using the Mini-Mental State Examination (MMSE) (Kimura et al., 2013; Lexomboon, Trulsson, Wårdh, & Parker, 2012; Scherder, Posthuma, Bakker, Vuijk, & Lobbezoo, 2008; Nilsson, Berglund, & Renvert, 2014; Peres et al., 2014; Wang, Chen, Liou, & Chou, 2014; Grabe et al., 2009; Park et al., 2013; Saito et al., 2013; Bergdahl, Habib, Bergdahl, Nyberg, & Nilsson, 2007). The findings from eight of these studies showed a significant association between mastication and cognitive impairment (Bergdahl et al., 2007; Grabe et al., 2009; Kimura et al., 2013; Lexomboon et al., 2012; Nilsson et al., 2014; Park et al., 2013; Peres et al., 2014; Saito et al., 2013). Higher cognitive impairment was observed in populations with lower chewing ability (Kimura et al., 2013; Lexomboon et al., 2012), fewer teeth remaining (Bergdahl et al., 2007; Grabe et al., 2009; Nilsson et al., 2014; Saito et al., 2013) and more tooth loss (Park et al., 2013; Peres et al., 2014). Nilsson et al. found a significant difference between subjects with ≥20 teeth and those who were edentulous, but not between subjects with ≥20 teeth and those with 1–19 teeth (2014). One study found a positive association among women only (Grabe et al., 2009). In the while, two studies did not find significant association between mastication and cognitive impairment (Scherder et al., 2008; Wang et al., 2014). In another study demonstrated that cognitive impairment by Montreal Cognitive Assessment (MoCA) had a significantly negative association with tooth number (Del Brutto et al., 2014).

The associations between various cognitive function tests and mastication have been previously assessed. Two studies used episodic memory as a measure of cognitive function (Hansson et al., 2013; Scherder et al., 2008). Episodic memory was predicted by the number of natural teeth (Hansson et al., 2013) and mastication performance (Scherder et al., 2008) by regression analyses. The association between verbal fluency and mastication performance was assessed in two studies in which a negative correlation between low mastication performance and verbal fluency was found (Weijenberg, Lobbezoo, Visscher, & Scherder, 2015; Listl, 2014). Three studies have investigated the relationship

Table 3
Summary of studies on the relationship between mastication and cognitive function.

(1) Cross-sectional study

Reference	Study sample	Mastication	Primary outcome	Key results
Kimura et al. (2013)	269 individuals (75 yrs and above, Japan)	Chewing ability evaluated by color-changeable chewing gum	Mini-Mental State Examination (MMSE), Hasegawa Dementia Scale Revised (HDS-R), Frontal Assessment Battery (FAB)	Association-chewing ability and cognitive status MMSE ($p = 0.022$), HDSR ($p = 0.017$) and FAB ($p = 0.002$)
Lexomboon et al. (2012)	557 Individuals (77–98 yrs, Sweden)	Self-assessed dental status and chewing difficulty	MMSE	Positive association-chewing difficulty and cognitive impairment (OR = 1.82 95%CI 1.13–2.94)
Scherder et al. (2008)	38 individuals (63–83 yrs, Netherland)	Masticatory performance (composed of mandibular excursions and bite force).	MMSE, Episodic memory, Executive functions	Positive association-masticatory performance and episodic memory ($p < 0.005$)
Nilsson et al. (2014)	1147 individuals (60–96 yrs, Sweden)	Number of teeth	MMSE, Clock-test.	Positive association-no teeth and cognitive impairment (OR = 3.2; 95% CI 1.9–53 for MMSE, OR = 1.9 95%CI 1.2–3.0 for Clock test)
Peres et al. (2014)	1705 individuals (60 yrs and above, Brazil)	Number of teeth (self-reported)	MMSE	Positive association- tooth loss and severe cognitive impairment (OR = 1.7 95%CI 1.1–2.4 for <10 teeth at lease one arch and edentulism)
Wang et al. (2014)	2286 subjects (65 yrs and above, Taiwan)	Number of teeth (self-reported)	MMSE	No association-<20 remaining teeth and cognitive impairment (OR = 1.302; 95% CI 0.934–1.811)
Park et al. (2013)	438 individuals (50 yrs and above, Korea)	Number of teeth and periodontitis	MMSE	Positive association-more than ten teeth lost and cognitive impairment (OR = 2.26; 95% CI 1.27–4.02)
Saito et al. (2013)	462 individuals (60 yrs and above, Japan).	Number of teeth	MMSE	Positive association-lower number of teeth (0–10) and cognitive impairment (OR = 20.21, 95% CI 2.20–185.47)
Bergdahl et al. (2007)	399 individuals (50 yrs and above, Sweden)	Number of teeth (self-reported)	MMSE	Positive association- natural dentition and cognitive test performance (Recall sentences, Recognition sentences, Recall of test session, Prospective memory $p < 0.05$)
Grabe et al. (2009)	1336 individuals (60–79 yrs, Germany)	Number of teeth	MMSE	Positive association – tooth number and cognitive impairment among women (coefficient = 0.052 $p = 0.002$) No association-tooth number and cognitive impairment among men (coefficient = 0.004, $p = 0.825$)
Del Brutto et al. (2014)	274 individuals (60 yrs and above, Ecuador)	Number of teeth	Montreal Cognitive Assessment (MoCA)	Negative association- number of teeth and cognitive impairment ($\beta = -1.06$. $p = 0.03$)
Weijenberg et al. (2015)	114 dementia individuals (mean age 85.3, Netherland)	Mastication (objective evaluation)	Neuropsychological test battery	Negative association-low masticatory performance and verbal fluency (b= −96.1, $p < 0.001$)
Listl (2014)	28,693 individuals (50 yrs and above, 14 European countries)	Chewing ability Use of dentures	Delayed word recall (DWR), Verbal fluency (WF), Numeracy	Negative associations-chewing ability and worse cognitive functioning (OR = 0.18 95%CI 0.13–0.22 for word record, OR = 0.43 95%CI 0.26–0.69 for verbal fluency, OR = 0.05 95%CI 0.03-0.07 for numeracy skills
Kamer et al. (2012)	152 individuals (70 yrs and above, Demark)	Number of teeth	Digit Symbol (DST), Block Design (BDT) tests	Negative associations- 11< missing teeth and cognitive functioning ($p < 0.001$)
Naorungroj et al. (2013a)	9874 individuals (45–64 yrs, US)	Number of teeth, Periodontitis	DWR digit-symbol substitution (DSS), WF	Negative association-edentulous and cognitive function (b = −0.16 for delayed word recall, b = −2.16 for DSS, and b = −1.87 for word fluency)
Hansson et al. (2013)	273 individuals (55–80 yrs, Sweden)	Number of teeth	Episodic memory, Semantic memory	Positive association-tooth number and cognitive function ($\beta = 0.20$ for episodic recall, $\beta = 0.24$ for episodic recognition, $\beta = 0.24$ for vocabulary)
Stewart et al. (2008)	1555 individuals (70 yrs and above, US)	Number of missing teeth, Gingival bleeding, Loss of periodontal attachment	Symbol Digit Substitution Test (SDST), Serial Digit Learning Test (SDLT), Story Recall test	No association-tooth loss and SDST cognitive function (coefficient = 0.02, 95%CI −0.001-0.003 for SDST, coefficient = 0.008, 95%CI −0.001-0.003 for SDLT, coefficient = 0.007, 95%CI −0.003-0.004 for Story recall test

(2) Cohort study

Reference	Study sample	Mastication	Primary outcome	Key results
Reyes-Ortiz et al. (2013)	1967 subjects (65 yrs and above at baseline, US)	Number of teeth (self-reported)	MMSE	Positive association- < 12 teeth and decline in total MMSE ($p < 0.01$)
Kaye et al. (2010)	597 individuals (median age of 45.5 yrs at baseline, US)	Number of missing teeth, Pocket depth, Alveolar bone height	MMSE	Positive association-Tooth loss and cognitive impairment (HR = 1.09 95% CI 1.01–1.18 for each tooth loss per decade)

Table 3 (*Continued*)

(2) Cohort study

Reference	Study sample	Mastication	Primary outcome	Key results
Tsakos et al. (2015)	3166 individuals (60 yrs and above at baseline, UK)	Number of teeth	10 word recall	Negative association- edentulous and continuous memory (B = −0.32, 95% CI 0.05–0.58)
Naorungroj et al. (2015)	911 individuals (mean age 64.7, US)	Number of teeth Periodontal disease (BGI)	DWR, DSS, WF	No association- Edentulous and cognitive decline (DWR b = −0.0053, p = 0.6109; DSS b = −0.0094, p = 0.8071; WF b = 0.035, p = 0.41)
Naorungroj et al. (2013b)	6676 individuals (45–64 yrs at baseline, US)	Number of teeth	DWR, DSS, WF	Positive association- Complete tooth loss and cognitive decline (DWR OR = 1.11, 95% CI 1.04–1.18; DSS OR = 1.08 95% CI 1.01–1.15; WF OR = 1.10 95%CI 1.03–1.18)
Stein et al. (2010)	144 Catholic sisters (75–98 yrs at baseline, US)	Number of teeth	DWR	Positive association- < 100 teeth and decline in DWR (β = −5.695, p < 0.0001), this association was strongest with one APOE ε4 allele and fewer teeth

between psychomotor performance and mastication (Kamer, Morse, Holm-Pedersen, Mortensen, & Avlund, 2012; Naorungroj et al., 2013a; Stewart, Sabbah, Tsakos, D'Aiuto, & Watt, 2008). Psychomotor performance was significantly lower among those with more missing teeth (Kamer et al., 2012) and being edentulous (Naorungroj et al., 2013a) compared to counterparts. On the contrary, Stewart found no significant association between tooth loss and Symbol Digit Substitution test scores (Stewart et al., 2008). The association between mastication and delayed word recall (DWR) was analyzed in two studies. Significantly poorer scores on the DWR were observed among persons who were edentulous (Naorungroj et al., 2013a) and with poor mastication performance (Listl, 2014).

3.3.2. Prospective cohort studies

Among prospective cohort studies, 2 studies analyzed the association between the number of teeth and tooth loss, and changes in cognitive impairment (Reyes-Ortiz, Luque, Eriksson, & Soto, 2013; Kaye et al., 2010). These studies showed a significantly greater decline in MMSE score in populations with fewer teeth. Kaye et al. (2010) reported that each tooth loss per decade increased the risks of a low MMSE score and low spatial copying. Other 4 evaluated the association of the number of teeth with tooth loss and with changes in cognitive function (Naorungroj et al., 2013b, 2015; Tsakos et al., 2015; Stein, Kryscio, Desrosiers, Donegan, & Gibbs, 2010). Naorungroj et al. found a significantly greater decline in cognitive function (DWR, digit-symbol substitution, and word fluency) during the study periods of 1990–1992 and 1996–1998 (2013b), but did not during 1996–1998 and 2004–2006 (2015) periods of the ARIC study. Stein et al. (2010) reported that DWR in individuals with the apolipoprotein E epsilon4 allele and with fewer teeth declined more quickly compared to those with neither of these risk factors or with either risk factor alone. Tsakos et al. (2015) showed that edentulous subjects had a significantly greater decline in continuous memory than dentate subjects.

3.4. Impact of mastication on dementia/MMI incidence

3.4.1. Cross-sectional studies

Four studies compared oral health between the patients and control groups. Individuals with a lower number of teeth had a significantly higher frequency of dementia (Kim et al., 2007) and MMI (Okamoto et al., 2015). Elsig et al. (2013), demonstrated that the chewing ability was significantly associated with incidence of dementia. Luo et al. (2015) found that tooth number was one of the significant risk factors associated with dementia. In the while, Gil-Montoya et al. (2015) showed no statistically significant difference in tooth loss between the control group and the case group (dementia and mild cognitive impairment).

3.4.2. Prospective studies

Four studies evaluated the association between the number of teeth, tooth loss, and dementia onset during the study period (Stewart et al., 2015; Yamamoto et al., 2012; Paganini-Hill, White, & Atchisonm, 2012; Stein, Desrosiers, Donegan, Yepes, & Kryscio, 2007). All but one showed that dementia incidence was higher in populations with a lower number of teeth than in their counterparts (Paganini-Hill et al., 2012; Stein et al., 2007; Yamamoto et al., 2012). Two studies found that having few teeth without denture had significantly higher dementia incidence, but few teeth with denture compared to having more teeth (Paganini-Hill et al., 2012; Yamamoto et al., 2012). Stewart et al. (2015) did not find a significantly association between dementia incidence and tooth number. Okamoto et al. (2010) demonstrated that edentulous was a significant factor for the incidence of MMI.

4. Discussion

In this review, we investigated the association between chewing status and cognitive status among elderly people by systematically summarizing the scientific evidence derived from the clinical studies conducted in this research area in the last decade. To locate as many relevant publications as possible, a database literature search with low specificity was conducted. PubMed, EMBASE, CINAHL, Cochrane Library, and Pro Quest were searched for clinical studies that focused on the association between mastication and cognitive status/dementia among elderly people (Table 4).

4.1. Quality assessment of the studies

One important finding of this review is the use of objective indicators for mastication in almost all studies. In this regard, subjective measurements yield very optimistic results than practitioner's measurements do (Slagter, Olthoff, Bosman, & Steen, 1992). Several studies used the number of present teeth or tooth loss based on self-report, which may attenuate the accuracy of the data (Bergdahl et al., 2007; Luo et al., 2015; Paganini-Hill et al., 2012; Peres et al., 2014; Reyes-Ortiz et al., 2013; Wang et al., 2014; Yamamoto et al., 2012). However, there are reports that indicated that self-reported number of teeth had high level of agreement with the ones collected from clinical examination data (Douglass, Berlin, & Tennstedt, 1991; Ando, Ikeda, & Yoshihara, 1997). It is unclear whether this high level of agreement is ubiquitous. The indices for cognitive impairment and cognitive function were also objectively evaluated using validated methods and these strategies guaranteed data reliability.

In most key articles, not all representative confounding factors were introduced in regression models. Health habits, history of

Table 4
Summary of studies on the relationship between mastication and dementia/MMI incidence.

(1) Cross-sectional

Reference	Study sample	Mastication	Primary outcome	Key results
Kim et al. (2007)	686 individuals (65 yrs and above, Korea)	Number of teeth, Use of dentures	Dementia,	Positive association- number of teeth (decreasing quintiles) and dementia (OR = 1.26 95%CI 1.00–1.59)
Okamoto et al. (2015)	2335 individuals (65 yrs and above, Japan)	Number of teeth	Mild memory impairment (MMI)	Positive association- having no teeth and MMI (OR = 2.39 95% CI 1.48–3.86) after 5 years
Elsig et al. (2013)	51 individuals (75 yrs and above, Switzerland)	Chewing efficiency evaluated with a two-color mixing test. Number of teeth	Dementia	Negative association- chewing efficiency and dementia ($p < 0.011$)
Luo et al. (2015)	3063 individuals (60 yrs and above, China)	Number of missing teeth (self-reported)	Dementia	Positive association- tooth loss > 16 and dementia (OR = 1.56 95%CI 1.12–2.18)
Gil-Montoya et al. (2015)[a]	409 individuals (50 yrs and above, Spain)	Number of teeth	Dementia, Mild Cognitive impairment	No association- tooth number with1 to 9 and cognitive impairment (OR = 1.25, 95% CI 0.67–2.36)

(2) Cohort

Reference	Study sample	Mastication	Primary outcome	Key results
Stewart et al. (2015)	697 women (70 yrs and older at baseline, Sweden)	Number of teeth	Incidence of dementia	No association- tooth number and incidence of dementia (OR = 1.81 95%CI 0.77–4.25)
Yamamoto et al. (2012)	4425 individuals (65 yrs and above at baseline, Japan)	Number of teeth (self-reported), Use of dentures	Incidence of dementia	Positive association- few teeth without dentures and incidence of dementia (HR = 1.85 95% CI 1.04–3.31)
Paganini-Hill et al. (2012)	5468 individuals (52–105 yrs at baseline, US)	Number of teeth (self-reported), Use of dentures	Incidence of dementia	Positive association- $\geq$10 upper teeth and $\geq$ 6 lower teeth and incidence of dementia (HR = 1.91 95% CI 1.13–3.21 for men HR = 1.22 95%CI 0.86–1.73 for women)
Stein et al. (2007)	144 Catholic sisters (75–98 yrs at baseline, US)	Number of teeth	Incidence of dementia	Positive association- tooth number $\leq$ 9 and incidence of dementia (HR = 2.2, 95% CI 1.1–4.5)
Okamoto et al. (2010)	3061 individuals (65 yrs and above at baseline, Japan)	Number of teeth	Incidence of MMI	Positive association- tooth number $\leq$ 10 and incidence of MMI (OR = 1.71 95% CI 1.05–2.78)

[a] As the data of this study was collected at one specific point in time, it was included in cross-sectional study.

chronic diseases, including cardiovascular disease, stroke, and diabetes, and psychological variables were controlled in less than half studies. It has been reported that progressing chronic periodontitis was seen more frequently in heavy smokers (Nociti et al., 2015; Osterberg & Mellström, 1986), patients with diabetes (Llambés, Arias-Herrera, & Caffesse, 2015), cardiovalcular disease (Cabrera et al., 2005; Beck, Garcia, Heiss, Vokonas, & Offenbacher, 1996), stroke (Elter, Offenbacher, Toole, & Beck, 2003) and depression (Araújo et al., 2016). Progressive choronic periodontitis has a strong link with decreased mastication. A lack of adjustment with these factors has a possibility of an overestimation of the relationship between mastication and cognitive status.

One third of cohort studies had follow-up periods of less than 5 years. A gradual progression of the degeneration of brain cells leads to a slow change in cognitive status and a prolonged latent period of dementia. Therefore, an insufficient follow-up period may fail to observe cognitive changes. However, it is also a concern that longer term follow-up may result in an increased dropout rate among elderly subjects, which decreases study quality.

4.2. Relationship between mastication and cognitive function

A significant association between chewing status and cognitive function was observed in most cross-sectional studies. These studies demonstrated that those having worse chewing status exhibited lower cognitive function and higher cognitive impairment. However, there is a general trend toward lower oral hygiene skills among those with cognitive impairment. Moreover, it has been reported that these individuals are often unable or unwilling to undergo restorative measures (Adam & Preston, 2006; Ellefsen et al., 2009). These circumstances highlight that poor oral hygiene and low skills of individuals with cognitive impairment may cause more tooth loss.

Evidence from prospective cohort studies have shown that those with a higher number of present teeth at baseline experienced a smaller decline of cognitive function than those with a lower tooth number. These findings support the hypothesis that a lower tooth number in early life is a risk indicator for cognitive decline in later life.

The articles reviewed have shown that mastication is significantly associated with various cognitive functions, including episodic memory, verbal fluency, psychomotor performance, and delayed word recall. These function are controlled in a distinct portion of the cerebral cortex and hippocampus. Mastication may influence a wide range of domains in the cerebral cortex and hippocampus. In studies using functional magnetic resonance imaging and position emission topography, mastication has been revealed to increase cortical blood flow (Momose et al., 1997) and activate the somatosensory area, supplementary motor area, insular cortex, striatum, thalamus, and cerebellum (Onozuka et al., 2002; Onozuka et al., 2003). Furthermore, an increase in the blood oxygen level in the prefrontal cortex and the hippocampus during the task was observed after mastication, which is essential for the learning and memory processes (Hirano et al., 2008; Onozuka et al., 2007). The activation of cerebral blood flow by mastication is considered to have a positive influence on a wide range of cognitive function.

4.3. Relationship between mastication and dementia incidence

A significant relationships between mastication and incidence of dementia has been shown in most of the cross-sectional studies

and prospective studies. These findings indicate that mastication may be associated with dementia. Evidence that those with a higher number of present teeth had a lower incidence of dementia suggests that decreased chewing ability may cause dementia. The articles reviewed in this study also suggested an association between cognitive impairment and mastication. Cognitive impairment can precede dementia. In the while, mastication has an association with incidence of MMI, which lacks cognitive impairment (Okamoto et al., 2010, 2015). It is considered that the influence of mastication on cognition is complicated.

The mechanisms by which decreased masticatory ability may cause dementia are considered as follows. First, decreased mastication in elderly people causes inadequate dietary habits, which are accompanied by the impaired intake of some nutrients (Tada & Miura, 2014). Subsequently, elderly people with an inadequate nutrient intake due to masticatory disorders may experience cognitive impairment. Some nutrients have been shown to have the potential to prevent or delay the incidence of dementia (Morris 2012; Swaminathan & Jicha, 2014). Several cohort studies demonstrated that lower nutrients induced more cognitive declination in elderly people (Miller et al., 2015; Taniguchi et al., 2014). Moreover, in analyses using experimental animals, reduced mastication, which was introduced by a loss of functionality of molar teeth or soft diet feeding, led to a deterioration in learning ability and memory (Kato et al., 1997; Terasawa et al., 2002; Yamamoto & Hirayama 2001). A different mechanism depends on the increase in cortical blood flow by mastication (Momose et al., 1997). Several cohort studies have shown that a lower cerebral blood flow is associated with faster progression of cognitive decline (Benedictus et al., 2016; Wolters, de Bruijn, Hofman, Koudstaal, & Ikram, 2016). These findings support the evidence found in epidemiological studies concerning the association between mastication and cognitive status.

4.4. Influence of periodontal disease on cognitive status

Two studies have investigated the association between periodontal status and cognitive status in elderly people in addition to the association between tooth number and cognitive status (Gil-Montoya et al., 2015; Kamer et al., 2012) and found positive association. In recent years, cross-sectional and longitudinal studies have suggested that periodontal disease is a risk factor for cognitive dysfunction and Alzheimer's disease (Kaye et al., 2010; Noble et al., 2009; Stewart et al., 2008). Severe periodontal disease exhibits as destruction of periodontal tissues, including alveolar bone and periodontal ligament, leading to the loosening and loss of teeth. The progression of periodontal disease has a considerable influence on mastication. Consequently, masticatory dysfunction from periodontal disease may cause cognitive impairment. Furthermore, periodonto-pathogenic microorganisms trigger inflammation. It is known that inflammation plays an important role in the ethiopathogeny of Alzheimer disease (Marchesi, 2011). The inflammation activated by periodontopathogens may explain the initial vascular damage and repercussions at the cerebral level (Noble, Scarmeas, & Papapanou, 2013). These findings suggest a possible effect of periodontal disease on the incidence of cognitive impairment and dementia. The evaluation of the association between oral health, as a comprehensive indicator with a combination of mastication and periodontal disease, and cognitive status may become necessary in the future.

4.5. Limitation

There are several limitations in this study. The primary limitation is that heterogeneity in research design and methodology may limit to draw broader conclusion about the relationship between mastication and cognitive status. Differences in research design and methodology may lead to different impacts in the effect of mastication on cognitive status. Second, the comparisons of data among the key articles are difficult because the number of teeth and MMSE in the key articles had distinct cut-off points. The cut-off values of the MMSE used in these studies were different, with 24/25 (Grabe et al., 2009; Nilsson et al., 2014; Wang et al., 2014), 23/24 (Okamoto et al., 2010; Park et al., 2013) and 22/23 (Saito et al., 2013). Similarly, the grouping of participants by the number of teeth differed among the studies, with <20 vs $20\leqq$ (Wang et al., 2014), 0 vs 20 (Nilsson et al., 2014), 6–10 vs $10<$ (Park et al., 2013), and 0–10 vs 22–32 (Saito et al., 2013). Differences in the cut-off values might have made different results in the associations between mastication and cognition in the same population. Third, the number of teeth as an indicator for mastication that was used in most key articles has some weaknesses to point out. Although a low number of natural teeth has been reported to be associated with a poor chewing performance (Ueno, Yanagisawa, Shinada, Ohara, & Kawaguchi, 2010; Tatematsu et al., 2004), it does not necessarily show a close relation with mastication. This can be explained by the fact that chewing efficiency differs depending on the portion of missing teeth among individuals with the same number of teeth. In addition, prosthetic treatment can compensate for a poor chewing ability, although it never increase the number of (natural) teeth. This problem poses an impediment to evaluating the association between chewing ability and cognitive status.

4.6. Future direction

The results of epidemiological studies that were available in this review support the hypothesis that mastication influence cognitive function. Nevertheless, wide ranging risk factors, including demographic factors, genetic factors, medical risk factors, psychiatric factors, head injury, and lifestyle factors are associated with cognitive function and dementia and it is difficult to exclude the influence of these factors in one study. Further understanding in addressing this association requires more data from intervention studies with a provision for new dentures. One study reported that prosthetic treatment showed a significantly greater improvement in cognitive state when compared to the pre-treatment state (Banu, Veeravalli, & Kumar, 2015). Further research with provision of new denture to edentulous patients with cognitive impairment is necessary.

The development of chewing evaluation method that evaluated color images of chewed gums by computer scanning, which has been used in key articles of this review, has made mastication assessment easy and made it possible to evaluate large-scale subjects in a short time (Elsig et al., 2013; Weijenberg et al., 2015). The reliability and validity of the color scale to evaluate the chewing ability have been reported previously (Hama, Kanazawa, Minakuchi, Uchida, & Sasaki, 2014). Since mastication is the process by which food is crushed and ground by teeth, it should be evaluated by functional parameters such as chewing efficiency rather than the count of anatomically present teeth. In the future, objective and direct evaluations will be used more frequently to evaluate chewing in large-scale studies to elucidate the impact of chewing efficiency on cognitive status.

5. Conclusions

Most cross-sectional studies show that poor mastication was associated with lower cognitive function and having dementia. Most prospective cohort studies demonstrated that poorer mastication is one of the risk factor of steeper cognitive decline

and increased incidence of dementia. These studies suggest that mastication may have close relationship with cognition. Further research, especially involving intervention studies are required to improve our current understanding of the relationship of mastication and cognitive function with dementia.

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Conflict of interest statement

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