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Tooth loss and periodontal disease predict poor cognitive function in older men

Elizabeth Krall Kaye, PhD[1,2], **Aileen Valencia, BS**[2], **Nivine Baba, MA**, **Avron Spiro III, PhD**[1,2,3], **Thomas Dietrich, DMD**[2,4], and **Raul I Garcia, DMD**[1,2]

[1]Veterans Affairs Boston Healthcare System, Boston MA

[2]Henry M. Goldman School of Dental Medicine, Boston University, Boston MA

[3]School of Public Health, Boston University, Boston MA

[4]The School of Dentistry, University of Birmingham, Birmingham, UK

Abstract

Objectives—To determine if rates of tooth loss, periodontal disease progression and caries incidence predict cognitive decline in men.

Design—Prospective study.

Setting—Community-dwelling men enrolled in the VA Dental Longitudinal Study.

Participants—Five hundred ninety-seven dentate men, aged 28–70 years at the study baseline, who have been followed up to 32 years.

Measurements—Oral examinations were conducted approximately every 3 years. Periodontal disease measures included probing pocket depth and radiographic alveolar bone height. Participants underwent cognitive testing beginning in 1993. Low cognitive statuses were defined as <25 points or <90% of the age and education-specific median on the MiniMental State Examination, and < 10 points on a Spatial Copying Task.

Results—Each tooth lost per decade since the baseline dental examination increased the risks of low MiniMental score (HR= 1.09, 95% CI=1.01, 1.18) and low spatial copying score (HR=1.12, CI= 1.05, 1.18). Risks were elevated per additional tooth with progression of alveolar bone loss (spatial copying: HR=1.03, CI= 1.01, 1.06), probing pocket depth (MiniMental: HR=1.04, CI= 1.01, 1.09; spatial copying: HR=1.04, CI= 1.01, 1.06) and caries (spatial copying: HR=1.05, CI= 1.01, 1.08). Risks were consistently higher among men who were older than 45.5 years at baseline than in younger men.

Conclusion—Risk of cognitive decline in older men increases as more teeth are lost. Periodontal disease and caries, major reasons for tooth loss, are also related to cognitive decline.

Corresponding Author: Elizabeth Krall Kaye, Goldman School of Dental Medicine, 560 Harrison Ave, Suite 301, Boston MA 02118, kralle@bu.edu, Ph: (617) 638-6386, Fax: (617) 638-6381. Alternate Corresponding Author: Raul I Garcia, rig@bu.edu.

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The authors declare that they have no conflicts of interest.

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Drs. Spiro and Garcia proposed the study. Drs. Garcia, Krall Kaye and Spiro acquired the data. Dr. Krall Kaye and Ms. Valencia conducted statistical analyses. Dr. Krall Kaye drafted the report and all authors contributed to its revision. Dr. Krall Kaye had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Keywords

Tooth loss; Periodontal Diseases; Dental Caries. MiniMental State Examination; Cognitive Impairment

INTRODUCTION

Emerging evidence suggests that a history of tooth loss may be associated with cognitive impairment in community-dwelling older adults. [1–7] Cross-sectional analyses of nationally representative data from several countries using a variety of cognitive function tests show increased odds of impaired and test performance or prevalence of dementia associated with a low number of teeth remaining. [1–5] In a case-control study of elderly identical twins discordant for dementias, loss of at least half of the teeth before age 35 was significantly related to risk of Alzheimer's disease and other dementias. [5] However, an examination of data from the US Health and Nutrition Examination Surveys (NHANES III, 1988–1994) found that poverty, cardiovascular risk factors and physical activity attenuated the positive associations between number of missing teeth and poor performance on three tests of cognitive function. [3] Findings from prospective studies are inconclusive. Elderly women with 9 or fewer teeth had a two-fold increase in risk of developing dementia relative to those with 10 or more teeth. [6] Edentulous persons age 70 and older scored lower on a battery of cognitive tests than those with teeth, but the difference did not persist after adjustment for age and IQ. [4]

One would expect a decline in cognitive function to disrupt normal activities of daily living such as oral hygiene and dental care, and this would explain the cross-sectional associations. The prospective findings by Sparks Stein et al [5] suggest that the reverse direction of events is also plausible, i.e., that tooth loss precedes and plays a causal role in cognitive decline. Several physiologic mechanisms have been proposed to explain a causal pathway. Low intakes of several B vitamins have been linked to cognitive decline [8], and loss of teeth negatively impacts the ability to consume recommended levels of many foods and nutrients. [2,9] Pro-inflammatory factors derived from the body's response to a chronic periodontal infection may travel by way of the systemic circulation to the brain where they exacerbate inflammatory processes and vascular pathologies. [10,11] This latter hypothesis is strengthened by reports that cognitive function is related to measures of periodontal disease as well as tooth loss. In the NHANES 1988–1994 and 2001–2002 surveys, poor performance on the Symbol Digit Substitution Test or Serial Digit Learning test was associated with clinical periodontal disease measures after adjusting for multiple confounding factors. [3,12] In further analyses, Noble et al [13] reported increased odds of difficulty recalling a three-word sequence or performing serial subtractions among older adults with the highest P. gingivalis exposure levels. However, only one study to date has prospectively examined periodontal disease and cognitive status. Women with moderate or severe alveolar bone loss tended to have an increased risk of developing dementia relative to women with less severe disease but the finding was not statistically significant. [6]

The purpose of this study was to determine if the rate of tooth loss predicts poor cognitive function in a cohort of community-dwelling men. In addition, we examined if periodontitis and caries, the primary causes of tooth loss, predict cognitive function.

METHODS

Study population

Participants were members of the US Department of Veterans Affairs Dental Longitudinal Study (DLS), a prospective observational study of oral health in men that began in 1968 as an ancillary to the Normative Aging Study. [14] The original DLS cohort numbered 1231 medically healthy men. This closed-panel longitudinal study cohort is a convenience sample of adult men, originally aged 24 to 84 and recruited from the Boston, Massachusetts metropolitan area. The men are not patients of Veterans Affairs hospitals; instead, they receive dental and medical care in the private sector and are fairly representative of the adult male population in the greater Boston area. The cohort has been well characterized with regard to health-related predictors of cognitive function. [8,15,16] Data from the dental examinations and cognitive testing were available for 597 dentate men.

Examination data

Comprehensive dental and physical examinations were conducted approximately every 3 years using commonly-available, standardized measurement techniques. At each dental examination, a calibrated periodontist assessed number of teeth remaining and scored levels of maximum probing pocket depth on each tooth following criteria used consistently over the course of the study. [17,18] Caries and restorations on each of 5 tooth surfaces were recorded. Alveolar bone loss (ABL), as percent of root length in 20% increments, was measured on the mesial and distal aspects of each tooth by superimposing a ruler onto periapical radiographs. [19] Participants completed questionnaires on oral hygiene practices, professional dental care, and smoking history. Dental examinations conducted between 1968 and 2002 are included in this report.

Beginning in 1993, the MiniMental State Examination (MMSE) and a spatial copying task were administered at each examination. The MMSE is widely used as a global test of cognitive function to screen for dementia and tests orientation, immediate memory, attention and calculation, short-term recall, and language. [20] Correlations between MMSE tests repeated at short intervals in cognitively healthy populations are generally 0.80 to 0.95. [21] Possible scores range from 0 to 30; mild impairment is indicated by scores between 21 and 24. MMSE scores were also converted to a percentage of the median for the participant's specific age and educational level [22], resulting in values that ranged from 54 to 116%. For the spatial copying task (SCT), a battery of figures derived from the Consortium to Establish a Registry for Alzheimer's Disease neuropsychological battery [23] and the Developmental Test of Visual-Motor Integration, [24] the participant is shown and asked to copy 9 geometric designs. The designs have an increasing level of difficulty, and test scores reflect the number of figures correctly drawn weighted by difficulty. [8] Two raters scored each participant's SCT figures and agreement was achieved between them. Possible SCT scores range from 0 to 26. Cognitive test results used in the analyses were obtained at between 1993 and 2001.

Other data

Data on alcohol and dietary intake were obtained from food frequency questionnaires administered at each exam since 1984. Diagnoses of co-morbidities (cardiovascular disease, coronary heart disease (CHD), cancer, diabetes) were obtained during examination by the study physician or from death certificates where applicable. Years of education, smoking, and frequency and amounts of all prescription and non-prescription medications were obtained by questionnaire at each examination. Weight (pounds) and height (inches) were measured on a beam balance and stadiometer, respectively and converted to metric units. Body mass index (BMI) was computed as weight divided by height squared. The protocols

were approved by the Institutional Review Board of the VA Boston Healthcare System. All participants gave informed consent on approved forms prior to each examination.

Statistical analysis

Tooth loss rate after baseline was computed as the number of teeth lost per decade of follow-up. Alveolar bone loss progression and probing pocket depth progression were defined, respectively, as numbers of teeth that showed decrease in bone height by at least 40% from baseline or were lost, and increase in pocket depth of 2 mm or more from baseline or were lost. Caries incidence was estimated by number of sound teeth at baseline that developed caries, were restored, or lost. Tooth loss was included in the periodontal disease and caries progression estimates in order to avoid underestimating disease due to missing values for absent teeth.

A low outcome on the MMSE was defined as follows: Among men in this cohort with scores of 21–24, the percentage of the age- and education-specific median ranged from 72 to 89%. Therefore, a low MMSE was defined as either <25 points, or <90% of the age- and education-specific median. By this criterion, 95 men had a low MMSE. A low SCT outcome was defined as a score more than 1 SD below the mean, yielding a cut-off of 10 points and 185 men with a score <10. We also examined several other cutoff points for each cognitive function test. The numbers of men who scored below 95 and 80% of the age and education specific median MMSE were 255 and 25 respectively, and the numbers who scored below 11 and 9 points on the spatial copying task were 211 and 124, respectively.

We examined potential confounding by age, years of education, smoking, BMI, regular medication use (aspirin, nonsteroidal anti-inflammatory drugs), development of coronary heart disease (CHD), stroke, hypertension, cardiovascular disease (CVD), cancer or diabetes during follow-up, and intakes of alcohol, coffee and tea, folate, vitamin B_6 and vitamin B_{12} using bivariate correlations and independent sample t-tests. Based on the results, variables were included as covariates in multivariable models if they were significant in bivariate analyses and remained in the multivariable models at $p<0{\cdot}15$.

Risks of developing low MMSE or spatial copying task scores in relation to tooth loss, progression of periodontal disease and progression of caries were estimated with adjusted hazard ratios (HR) and 95% confidence intervals (CI) obtained from Cox proportional hazards regression models stratified by median age (≤45.5 years or >45.5 years). Time to event, which varied from 20 to 32 years, was defined as the interval between the DLS baseline and year of the lowest cognitive test score. Analyses were performed using SAS, version 9.1 (SAS Institute, Inc., Cary, NC).

Between 1993 and 2001, 387 men had at least one repeat cognitive test. We estimated the attributable risk percent of cognitive test score deterioration that could be attributed to loss of any teeth. [25]

RESULTS

Of the 1,231 original enrollees, 659 dentate men participated in dental examinations between 1993 and 2001 at the time when cognitive tests were also administered. Of these men, 62 did not undergo any cognitive testing, leaving 597 men for our analyses. These 62 men without cognitive test results were older at the dental study baseline but otherwise were comparable with respect to prevalence of smoking and coronary heart disease and mean years of education, alcohol intake, tooth loss, and progression of periodontal disease and caries.

Men who developed low cognitive test status were older, had less education, were more likely to have CHD, lose more teeth, and develop more caries than men whose test scores remained normal (Table 1).

Men who were above the median age at baseline (45.5 years) were nearly 10 years older at the time of cognitive testing, 1.9 times more likely to have a low SCT score ($P<0.01$) and 1.7 times more likely to have a low MMSE ($p<0.02$) than men below the median age. On average, this older group had more teeth with ≥40% alveolar bone loss existing at baseline (1 vs. 0.5 in younger men) and experienced more tooth loss (5 teeth lost per decade vs. 3/decade in younger men) during follow-up, but rates of periodontal disease progression were similar.

Higher rates of tooth loss and periodontal disease progression independently increased the risks of low cognitive test scores during follow-up (Table 2). For each tooth lost per decade, the overall risk of a low MMSE score (<25 points or <90% of age and education-specific median) or low SCT score (<10 points) increased 9 to 12%. For each tooth that had progression of alveolar bone loss or probing pocket depth, the overall risks of low scores increased 2 to 5%. Development of new caries or restorations was associated with an increased risk of a low SCT score. When stratified by baseline age, the risks were consistently higher in the older men compared to younger. The results did not change when smoking, diabetes, additional co-morbidities, medication use, or dietary intakes were included in the models. The hazard ratio estimates were similar when the definitions of "low" scores were changed to <95 or <80% on the MMSE, and <11 or <9 on the spatial copying task.

Of the men who scored 26 points or higher on the initial MMSE, 23 (5%) later fell below this cut-off point, and of those who scored 10 points or higher on the initial spatial copying task, 59 (13%) later fell below this score. The attributable risk percentages for low scores on the MMSE and spatial copying task due to tooth loss were 46% and 9%, respectively. That is, among the men in our cohort who lost any teeth, 9–46% of those who scored low on a cognitive function test would not have done so had they kept all the teeth they had at baseline.

DISCUSSION

Our findings indicate that in older men, rates of tooth loss and periodontal disease progression during adulthood independently predicted performance on the MiniMental State Examination and Spatial Copying Task cognitive tests. Development of caries appeared to increase the risk of poor performance as well. The increased risks were most consistent among men who were older than 45.5 years at the dental baseline. This finding may reflect the higher prevalence of periodontal disease that existed in older men at baseline or some other unique characteristic of the older cohort.

Our results indicate that for each tooth lost per decade, the risk of a low cognitive test score increased 9 to 12%. Based on these estimates, if one lost 12 teeth per decade, the risk of impaired cognition would approach 100%. This prediction was borne out in our cohort. For example, nearly all (86%) of the participants whose tooth loss rate was 12/decade or more were classified as having a low SCT score. Such a rapid rate of loss in older adults is most likely a sign of severe periodontal disease.

A unique strength of our study is the prospective design with comprehensive data on tooth loss, periodontal disease, and caries recorded by trained dental examiners during a 32-year follow-up interval. Our measures of periodontal disease included radiographic alveolar bone loss which is an indicator of cumulative periodontitis history. In addition, there was

extensive information on important covariates obtained during serial physical examinations. We did not have cognitive tests at the dental baseline in 1968–1973 to rule out preexisting dementia. However, it is unlikely that these men were cognitively impaired at baseline since they continued to participate in examinations, mail surveys, and many other assessments for at least 20 years before cognition testing began. Other limitations of this study include the absence of data on women and ethnic minorities, and the fact the men in the analyses were younger than those who did not complete the cognitive tests. As a result, few of the men were moderately or severely impaired.

Our findings are consistent with previous literature that showed increased risk of impaired cognitive performance associated with various indicators of poor oral health. [1–7, 12,13] We also extend those findings by demonstrating that in our cohort the detrimental changes in oral health preceded rather than resulted from cognitive decline.

Dementia and cognitive impairment are growing worldwide health problems. By the year 2040, it is expected that dementia will affect more than 81 million people worldwide. [26] In the United States, Alzheimer's disease, the most common form of dementia, rose from being the 14th most common cause of death in 1995 to the rank of 7th just 10 years later. [27] Since there are no effective treatments for reversing dementia, it is important to identify modifiable risk factors in an attempt to intervene and reduce the incidence of disease. Attributable risk estimates from our cohort suggest that at least 14 cases of cognitive decline and perhaps as many as 37, detected by the SCT or MMSE tests respectively, would not have occurred if tooth loss had been prevented.

An inflammatory model has been invoked to explain degeneration of brain neuronal cells and increased risk of dementia [10] but a number of other mechanisms might also explain our findings. The similarities between risk factors for cardiovascular disease and Alzheimer's disease raise the possibility of a causal biologic pathway linking these two common disorders, while some investigators propose the two diseases are independent outcomes of the atherogenic process. [28] Poor nutritional status, especially in relation to the B vitamins [8,29], may also play a role in the progression of both diseases. Although our analyses evaluated these nutritional factors and controlled for the development of coronary heart disease and its common predictors, there may be other underlying but unmeasured risk factors that contribute to the associations we found. Another possibility is that a pro-inflammatory phenotype is the common factor linking periodontal disease, cardiovascular disease and cognitive decline. [30] Presence of the apo-E e4 genetic marker, a risk factor for Alzheimer's disease, attenuated the association between number of teeth present and prevalence of dementia. [6]

CONCLUSION

Our study of community-dwelling men showed that rates of tooth loss and periodontal disease progression predicted subsequent decline in cognitive function. These findings lend support to the hypothesis that oral health is an important modifiable determinant of cognitive function and suggests that peripheral inflammation contributes to the development of dementia and cognitive impairment.

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Table 1

Characteristics of Dental Study Participants who Completed Cognitive Testing (Mean±SD, or %).

	MMSE*		SCT†	
	Low	**Normal**	**Low**	**Normal**
N	**95**	**500**	**185**	**412**
At dental baseline (1968–1973):				
Age (yrs)	48±8	45±7	48±7	45±7
Years of education	13±3	15±3	14±3	15±3
% Ever smoked	41%	45	40%	46%
Number of teeth	24±6	24±5	24±5	24±5
Number of teeth with 1 or more decayed or filled surfaces	15±5	15±5	15±5	15±5
Number of teeth with probing pocket depth ≥4mm	4±4	4±4	4±5	4±4
Number of teeth with alveolar bone loss ≥40%	1±1	1±2	1±2	1±1
At time of first cognitive test (1993–2001):				
Age (yrs)	72±8	69±7	71±8	68±7
Time elapsed since baseline (yrs)	24±2	24±2	24±2	24±2
Mini Mental State Examination (MMSE) score	23.8±1.8	28.1±1.2	26.8±2.4	27.9±1.7
MMSE score as % of age and education-specific median	87±9	98±4	94±8	97±6
Weighted Spatial Copying Task (SCT) score	10.0±5.5	15.0±6.0	6.8±2.2	17.5±4.2
Alcohol intake (grams /day)	8±11	13±16	11±14	13±15
% With history of coronary heart disease (CHD)	24%	15%	22%	15%
% With any tooth loss	85%	74%	81%	73%
Number of teeth lost	6±6	4±5	5±6	4±5
Number of teeth with new caries and/or restorations	13±5	12±6	13±5	12±6
Number of teeth with probing pocket depth progression	16±7	15±8	15±8	15±8
Number of teeth with alveolar bone loss progression	12±8	11±9	12±9	11±9

*MiniMental State Examination. Range of scores=0 to 30. Low=<25 points or <90% of age and education-specific median.

†Spatial Copying Task. Range of scores=0 to 26. Low= <10 points.

Table 2

Risk of Low MiniMental State Examination (MMSE) and Spatial Copying Task (SCT) Scores in Relation to Prospective Tooth Loss, Periodontal Disease Progression, and Caries Incidence (Adjusted HR and 95% CI).

	Outcome					
	Low MMSE score *			Low SCT score †		
Age at dental baseline	**All**	**≤45.5 years**	**>45.5 years**	**All**	**≤45.5 years**	**>45.5 years**
N	**595**	**296**	**299**	**597**	**297**	**300**
Per additional tooth lost/decade	1.09 (1.01, 1.18)	1.08 (0.92, 1.26)	1.10 (1.01, 1.21)	1.12 (1.05, 1.18)	1.10 (1.01, 1.20)	1.13 (1.05, 1.21)
Per additional tooth with alveolar bone loss progression/decade	1.03 (1.00, 1.07)	1.00 (0.94, 1.07)	1.05 (1.01, 1.09)	1.03 (1.01, 1.06)	1.02 (0.97, 1.06)	1.04 (1.02, 1.07)
Per additional tooth with pocket depth progression/decade	1.04 (1.01, 1.09)	1.02 (0.95, 1.10)	1.05 (1.01, 1.10)	1.04 (1.01, 1.06)	1.02 (0.96, 1.07)	1.04 (1.01, 1.07)
Per additional tooth with new caries and/or restorations/decade	1.02 (0.97, 1.08)	1.01 (0.94, 1.09)	1.06 (0.96,1.16)	1.05 (1.01, 1.08)	1.02 (0.98, 1.06)	1.13 (1.07, 1.21)

* Range of scores=0 to 30. Low=<25 points or <90% of age and education-specific median. Adjusted for history of CHD and average alcohol intake (grams/day). Tooth loss also adjusted for number of teeth at baseline. Alveolar bone loss progression also adjusted for number teeth with <60% bone loss at baseline; Pocket depth progression also adjusted for number teeth with <3mm pocket depth at baseline; New caries also adjusted for number sound teeth at baseline.

† Range of scores=0 to 26. Low= score <10 points. Adjusted for age, years of education, history of CHD, and average alcohol intake (grams/day). Tooth loss also adjusted for number of teeth at baseline. Alveolar bone loss progression also adjusted for number teeth with <60% bone loss at baseline; Pocket depth progression also adjusted for number teeth with <3mm pocket depth at baseline; New caries also adjusted for number sound teeth at baseline.