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Adverse Oral Health and Cognitive Decline: The Health, Aging and Body Composition Study

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Abstract

Background/Objectives—Periodontal disease has been associated with poorer cross-sectional cognitive function and is correlated with adverse vascular outcomes, but has received little prospective investigation in relation to cognitive decline.

Design—Analysis of a prospective cohort study.

Setting—The Health, Aging and Body Composition (Health ABC) Study

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Author contributions: The study was conceived by Robert Stewart, Robert Weyant and Anne Newman with input from all authors. The data were analysed by Robert Stewart under the supervision of Robert Weyant and Anne Newman. The first draft of the paper was prepared by Robert Stewart and all authors commented on this and provided critical input. All authors have seen and approved the final version of the manuscript.

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Participants and measurements—We examined the prospective association between a range of oral health parameters and cognitive function using data on 1053 participants who were administered the Modified Mini-Mental State Examination (3MS) at year 1 (baseline) and year 3, and had participated in a comprehensive periodontal examination at year 2. We investigated 3MS decline from year 3 to 5 in 947 (89.9%) participants. Covariates included age, sex, education, race, cardiovascular disease/risk and depressive symptoms.

Results—Most indicators of adverse oral health at year 2 were associated with cognitive impairment based on averaged 3MS scores <80 for years 1 and 3, but these associations were substantially confounded by education and race. Higher gingival index, a measure of gingival inflammation, at year 2 remained independently associated with this definition of cognitive impairment and, in fully adjusted analyses, was also an independent predictor of a 5+ point cognitive decline from years 3 to 5.

Conclusion—Periodontitis may be a risk factor for cognitive decline. Gingivitis is reversible and periodontitis to some degree is preventable and controllable when manifest. Therefore, further research is needed to clarify potential underlying mechanisms and oral health interventions that potentially might ameliorate cognitive decline.

Keywords

cognitive decline; cognitive impairment; periodontitis; periodontal diseases; gingivitis

INTRODUCTION

Periodontitis is among the most common sources of chronic infection and inflammation in old age, with exposure to periodontal pathogens nearly universal in older people.[1] Antibodies to common periodontal pathogens are associated with an increased risk of stroke and atherosclerosis,[2–4] and the profile of inflammatory markers accompanying periodontitis,[5;6] is similar to that accompanying vascular risk factors such as diabetes, obesity and smoking.[7;8]

There is growing interest in the role of inflammatory processes in the etiology of cognitive decline and dementia. Elevated levels of inflammatory markers such as interleukin-6 have been associated with cognitive impairment and cognitive decline.[9;10] Higher levels of mid-life C-reactive protein are associated with an elevated risk of late-life dementia,[11] and pro-inflammatory cytokines have been associated with dementia particularly in the presence of cardiovascular disease.[12] Despite the potential importance of periodontitis as a common, chronic pro-inflammatory condition, there has been relatively little investigation into its associations with cognition. Some studies have found cross-sectional relationships between fewer teeth, other periodontal disease markers and dementia or cognitive impairment.[13–16] However, the direction of causation cannot be inferred and there has been some suggestion that tooth loss is confined to advanced dementia,[17] potentially because of reduced salivatiton.[18] Prospective relationships have been suggested between dementia and more general measures of oral health: with edentulism 12 years previously,[19] between cognitive impairment and fewer teeth 6 years previously,[20] and between cognitive impairment and previous decline in oral health over a 30 year period.[21] To our knowledge, the relationship between periodontal disease and decline in cognition has not been previously reported in a community sample.

In order to clarify this relationship we investigated the prospective association between oral health status and cognitive decline in the Health, Aging and Body Composition (Health ABC) study, a large community cohort study which included measures of both these factors. We hypothesized that worse oral health status would be associated with both cross-sectional

cognitive impairment and subsequent cognitive decline, and that these associations would be in part accounted for by raised levels of inflammatory markers.

METHODS

The study population

The Health ABC study is a longitudinal cohort study consisting, at baseline, of 3075 well-functioning black and white men and women aged 70–79 years. Participants were identified from a random sample of white Medicare beneficiaries and all black community residents living in designated ZIP code areas around Memphis and Pittsburgh. Inclusion criteria at baseline included reporting no difficulty walking one quarter of a mile, climbing up 10 steps without resting, and performing basic activities of daily living. Exclusion criteria at baseline included active treatment for cancer within the previous 3 years, plans to move out of the study area within the following 3 years, and current participation in a lifestyle intervention trial. Baseline examinations were carried out between April 1997 and June 1998 with subsequent annual follow-up interviews and examinations. Relevant to this analysis, global cognitive function – the primary outcome – was measured at baseline (year 1), and years 3 and 5 while examinations of oral health were carried out at year 2. Ethics approval was granted for Health ABC and subsequent data analyses from institutional review boards at University of Pittsburgh, University of Tennessee – Memphis, UCSF and NIH.

Measurements

Cognitive function—The Modified Mini-Mental State Examination (3MS), a brief assessment of global function with components for orientation, concentration, language, praxis, and immediate and delayed memory,[22] was administered at years 1 (baseline), 3 and 5. Consistent with other work,[23;24] cognitive impairment was defined *a priori* as a score of less than 80 on this scale and cognitive decline as a fall of 5 or more points between two examination points. Because there had been no cognitive assessment at the time of the oral health assessment (year 2), 'contemporaneous' cognitive impairment for primary analyses was defined from the average of the year 1 and year 3 3MS scores. The following other cognitive assessments had been administered on different occasions and were used to derive secondary outcome variables in order to supplement the primary focus of the study on global cognitive function: 1) the Digit Symbol Substitution Test (DSST) was administered at year 1 and year 5, measuring attention, psychomotor speed and executive function;[25] 2) a clock drawing test had been administered at year 3 to measure executive function;[26] 3) the EXIT-25 assessment was carried out at year 3, investigating further executive function impairments such as inhibition of automatic responses, word and design fluency, and sequencing tasks.[27] Impairments on each of these tests at first administration were defined applying cut-offs to categorise as impaired the same proportion (i.e. 10%) as the 3MS <80 definition. In order to generate a comparable binary measure of DSST change from years 1 to 5, the same proportion (i.e. most declining 20%) were categorized as having cognitive decline as that defined for the 3MS fall of 5 points or more.

Oral health—Of the 3075 participants in the original Health ABC cohort, a subset of 1843 had been approached at year 2 to participate in the study of periodontal disease and oral health. The oral health examinations have been described in detail previously.[28] A subset was used because examinations could only be carried out on certain days of the week. Number of teeth was counted by visual inspection in this group and further detailed periodontal assessments were offered. Within this group of 1843, 38 declined to participate, 193 were excluded because of edentulism, and 441 were ineligible because they would have required antibiotic prophylaxis before periodontal probing. Periodontal clinical assessment was therefore completed in 1171 participants. Examinations took place in a dental chair

using a dental examination light and consisted of an entire mouth examination (i.e. data collected from all teeth as sites). The following measures were used for this analysis, applied to all teeth: number of teeth, number of occluding pairs of teeth, probing depth (mean value and proportion with ≥3mm depth), loss of attachment (≥3mm; defined as the mean number of sites affected and the proportion of sites examined that were affected), mean gingival index (rating gingival inflammation for each tooth on a scale of 0 to 3),[29] mean plaque score (measured on the buccal surface of each tooth),[29] and number of sites with bleeding on probing. For comparison between independent variables, because of non-normal distributions for some variables and in order to identify non-monotonic associations, if present, all measures were categorized into quartiles for analysis.

Covariates—The following variables were selected as covariates for primary analyses: age, sex, level of education (3 groups), race (white/non-white), year 1 cardiovascular disease/risk (coronary heart disease, cerebrovascular disease, diabetes, hypertension and smoking status), and year 1 depressive symptoms (Center for Epidemiologic Studies Depression scale, CES-D).[30] Coronary heart disease was defined by self-report of a physician diagnosis of myocardial infarction or angina, confirmed by use of heart disease medication or self-report of coronary or other artery bypass or angioplasty. Cerebrovascular disease was defined by self-report of a physician diagnosis of stroke or transient ischemic attack. Diabetes was defined from self-report or use of insulin or oral hypoglycemic medication, and hypertension was defined from self-report and use of antihypertensive medication. Further exploratory adjustments were made for systolic and diastolic blood pressure and fasting glucose levels taken at the same examination. Smoking status was categorised from self-reported information into never, former and current status. To investigate the potential role of systemic inflammation which has been previously found to be associated with worse periodontal health in this cohort,[5] further separate adjustments were made for levels of C-reactive protein and interleukin-6 which had been measured at year 1. To investigate the role of weight loss, previously found to be associated with both poor oral health and worse cognition,[28;31] exploratory adjustments were carried out for body mass index (BMI) at year 3, and for change in BMI from year 1 to 3. Finally, from the medication inventory taken at year 2, the prescription of any agent with anticholinergic properties was extracted as a binary covariate. Associations of interest were stratified by presence or absence of the apolipoprotein E (APOE) ε4 allele, and by year 1 interleukin-6 levels (above and below median).

Statistical analysis

As stated above, cognitive impairment and cognitive decline were modelled as binary dependent variables with quartiled oral health measures as primary independent variables, the latter entered into logistic regression models as ordinal variables on one degree of freedom. Covariates were entered as listed with successive adjustment for age, sex, education, race, cardiovascular risk and depressive symptoms in initial logistic regression models, followed by further exploratory separate adjustments for inflammatory markers, BMI, BMI change, and anticholinergic medication use. For analysis of 3MS decline between year 3 and 5, adjustments were also made for year 1 3MS and for 3MS change from year 1 to 3.

Stratification was used to investigate effect modification by APOE genotype. Finally, adjusted associations were re-assessed for the secondary definitions of cognitive impairment and decline. Stata 10 software was used for all analyses.

RESULTS

Of the 1171 participants with full data from the periodontal examinations at year 2, 1053 (89.9%) had cognitive data recorded at both year 1 and year 3, forming the minimum sample for analyses with respect to contemporaneous cognitive function. Of these, 947 (89.9%) also had year 5 cognitive data and formed the minimum sample for analyses with respect to cognitive decline. The sample for cross-sectional analyses is compared to the remainder of the Health ABC cohort in Table 1 and was similar with respect to age and sex, but had higher education levels, fewer non-white participants and a healthier profile on all other measures.

Associations between oral health measures and contemporaneous cognitive impairment are displayed in Table 2. Worse oral health on all measures apart from bleeding on probing was associated with cognitive impairment. These associations were investigated further in logistic regression analyses (Table 3), selecting the strongest associations where two variables were alternative measures of a similar construct (e.g. probing depth). In these analyses, education and race emerged as powerful confounding factors reducing the strength of association substantially for all independent variables, so that only mean gingival index and mean plaque score remained significant. In comparison, adjustments for other covariates had little effect on the associations of interest. For gingival inflammation, further separate adjustments for the two inflammatory markers, BMI, BMI change and anticholinergic medication made little difference to the odds ratio of interest (data not shown). The adjusted odds ratio (including covariates specified in Table 3, Model 4) between gingival index quartiles and cognitive impairment was 1.38 (0.97–1.97) in participants without the APOE ε4 allele and 2.44 (1.23–4.84) for those in whom this was present. Both gingival index and plaque score were significantly associated with equivalent levels of impairment on the Exit 25 score, and gingival index was also associated with DSST impairment, but neither were significantly associated with impairment on the clock drawing test.

Associations between oral health measures at year 2 and cognitive decline between years 3 to 5 are summarised in Table 4. When analysed by ascending quartiles, none of the measures were associated with subsequent cognitive decline, although that for gingival inflammation came close to statistical significance. Furthermore, the likelihood of decline on the 3MS was significantly increased for participants with gingival inflammation (i.e. highest quartile gingival index score; odds ratio for this group compared to the remainder 1.62, 1.09–2.42) and it was therefore felt reasonable (in view of this and the previously identified associations for this measure with baseline cognitive impairment) to analyse this further, investigating potential confounding factors. In logistic regression models (Table 5), this remained robust to adjustment and was actually strengthened considerably when adjusted for year 1 to 3 3MS change. It also persisted if participants with previous cognitive decline were excluded. On stratification by APOE genotype, the opposite pattern was found to that observed for the cross-sectional association with impairment in that the association with cognitive decline was, if anything, stronger in those without the ε4 allele. Contrary to our hypothesis, adjustment for inflammatory markers did not meaningfully alter the association of interest.

In additional secondary analyses relating to those findings displayed in Table 5, further individual adjustment of Model 4 for year 1 systolic blood pressure, diastolic blood pressure and fasting blood glucose resulted in stronger rather than weaker associations (adjusted odds ratios 1.58, 1.64 and 1.62 respectively). Similarly strong associations were found for gingival inflammation and 3MS decline measured from year 1 to 3 or from year 1 to 5, but no association was found with DSST decline from year 1 to 5.

DISCUSSION

In a large prospective cohort study of people aged 70–79 years at baseline, we investigated the association between oral health measures and both cognitive impairment and cognitive decline. Although worse scores on almost all oral health measures were associated with cognitive impairment, these associations were to a large extent accounted for by previous education and race. Furthermore, most were not associated with later cognitive decline. One exception was gingival inflammation which was both the factor most strongly associated with impairment and the only factor predicting cognitive decline – an association which was robust to adjustment for a large number of potential confounding factors.

As stated earlier, there has been relatively little research into adverse oral health as a risk factor for cognitive decline or dementia despite the fact that it is a commonly occurring chronic infection with an accompanying systemic inflammatory response. Atherosclerosis and stroke have, both been implicated as risk factors themselves for cognitive decline,[32;33] and there is evidence to suggest that periodontal disease is associated with cardiovascular disease independent of obvious potential confounders; however, a recent consensus report highlighted the methodological deficiencies of research in this area and concluded that there was insufficient evidence to date for a causal association,[34] although equally there has been insufficient evidence to rule it out and the question requires further research.[35] Several studies have found that people with severe cognitive impairment or dementia are more likely to have fewer teeth.[14;15;36;37] These include a study of recent onset dementia,[14] where the recognised effects of severe cognitive impairment on oral health[13;18] are less likely to have exerted an influence. However, number of teeth is a relatively crude measure of oral health (particularly if chronic infection and inflammation are considered to be part of the causal pathway) since it is influenced by a variety of factors besides oral health itself, such as dental extraction policies and practice. Furthermore, cross-sectional associations with worse cognitive function may fail to take into account earlier confounding factors such as education and social class. Of interest, associations between worse oral health and worse cognitive function were found in a large survey sample to a similar extent in both younger and older age groups,[16] suggesting that oral health might well be a marker of cognitive reserve in older people rather than a risk factor for cognitive decline. Consistent with this, associations with most oral health measures in this analysis were stronger with contemporaneous cognitive impairment than with later cognitive decline, and the former associations were largely accounted for by education and race. Although we were principally interested in the effect of oral health as an exposure on cognitive decline as an outcome, it is also possible that cognitive impairment itself contributes to poor dental self-care and worse oral health (i.e. a bi-directional association).

Gingival inflammation (highest 25% gingival index) emerged as a significant predictor of cognitive decline. Although this finding should be treated with caution as one of a number of independent variables investigated, it is noteworthy that it was robust to adjustment and that it was also the factor most strongly associated with contemporaneous cognitive impairment. In addition, gingivitis implies current active inflammation, the process of greatest interest in this analysis. Several studies have found associations between elevated circulating cytokines and both cognitive impairment,[38] and cognitive decline.[9;10;39] What is less clear is whether these represent risk factors for cognitive outcomes or biomarkers of underlying neurodegenerative processes.[40] One approach is to investigate common conditions like periodontal disease, known to be associated with a systemic inflammatory response, and the extent to which they predict decline. The precise nature of the association between periodontitis and cardiovascular disease remains controversial, as described above, although one suggested mechanism is a direct effect of periodontitis on endothelial cell function which might be reversed with intensive therapy.[41] If further research were to

confirm this, there might be wider benefits to improving oral health than cardiovascular outcomes, since cognitive decline and dementia are known to have a substantial vascular aetiology. In our study, we found no attenuation of the association of interest after adjustment for inflammatory markers (Table 5); however, it should be borne in mind that levels on a single occasion may not fully reflect those over a longer period. An anomaly in our findings was that bleeding on probing, another measure of gingivitis, was not associated with cognitive decline to the same extent. One possible explanation might be that a long duration of cardiovascular disease and the relatively advanced age of the sample might have been associated with microvascular disease which reduced gingival bleeding propensity. However, further research would be required to clarify this.

Other causal pathways may also link adverse oral health with cognitive decline. Poor dentition is known to be an important determinant of nutrition in late life,[20] with a substantial influence on food selection.[14;42] Adverse effects of oral health on nutritional status and consequent effects of nutritional changes on cognition could link the two processes. The fact that periodontitis was more strongly associated with cognitive impairment than number of teeth both in this and other studies,[16] and the lack of association of BMI or BMI change as covariates diminish the plausibility of this pathway. However, more specific nutritional deficiency syndromes cannot be ruled out. Investigation of effect modification by APOE genotype gave rise to inconsistent findings: namely that the association between gingival inflammation and cognitive *impairment* was stronger in e4 allele carriers while that with cognitive *decline* was weaker in this group. One possible explanation is that people with the e4 allele had longstanding lower cognitive function and the stronger association between gingival inflammation and cognitive impairment arose because these participants had already been closer to the cut-off defining impairment before the influence of gingival inflammation. Weaker associations between gingival inflammation and cognitive decline in e4 carriers might, on the other hand, be accounted for by differential loss to follow-up if the combination of gingival inflammation and cognitive decline were more strongly associated with mortality in e4 carriers compared to non-carriers.

The Health ABC study is one of the very few longitudinal investigations in which oral health was specifically examined and cognitive function was measured prospectively, making it well-suited to the objectives of this analysis. Although the sample was relatively healthy and high-functioning at baseline, and the sub-sample used in this analysis healthier still, follow-up rates were high indicating good internal validity. One drawback was that the oral health exposures and cognitive outcomes were limited in scope: e.g. only the relatively brief 3MS measure had been repeated on sufficient occasions for primary analyses and analyses focused on binary outcomes of impairment and decline rather than continuously distributed parameters. We used the derived variables for periodontal disease in the existing dataset instead of applying more recent case definitions for periodontitis [43–45] because these variables were sufficient for the purpose of this paper and actual periodontal disease prevalence was not the focus of this report. It is also possible that associations with specific domains of impairment or decline may have been missed. A second limitation was that the timing of measurements was not optimal – in particular, cognitive function was not measured contemporaneously with oral health. Furthermore, the covariates were principally measured one year before the periodontal examination – a particular drawback for the two inflammatory markers which are unlikely to reflect levels at the time of the periodontal examination, so that their lack of effect on the associations of interest should be interpreted with caution. Finally, given the lack of previous research for the outcome of interest, the approach taken was exploratory in nature with respect to independent variables. Although the association of gingival inflammation as a potentially important risk factor for impairment was to some extent replicated or confirmed by the association with decline, other independent investigations are required to verify this.

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Table 1

Characteristics of the study population with respect to the Health Aging and Body Composition Study at Baseline

Baseline status	Minimum study population[a] (n=1053)	Remainder of the baseline sample (n=2022)
Age: mean (SD)	73.5 (2.8)	73.7 (2.9)
Female (%)	50.2	52.2
Non-white (%)	34.2	45.6
Education (%)		
Less than High School	17.6	29.3
High School graduate	33.1	32.3
Post-secondary	49.3	38.4
Smoking status (%)		
Never	47.4	42.1
Previous	44.8	46.2
Current	7.8	11.7
Coronary heart disease (%)	15.9	23.4
Cerebrovascular disease (%)	6.5	9.0
Diabetes (%)	11.7	17.2
Hypertension (%)	44.8	54.7
Depressive symptoms[b]: mean (SD)	4.2 (4.9)	5.0 (5.6)

[a] Sample with full dental examination and cognitive assessment at years 1 and 3

[b] Centre for Epidemiologic Studies Depression scale score

Abbreviations: SD = standard deviation

Table 2

Cross-Sectional Associations between Baseline Oral Health and Cognitive Impairment

Oral health exposure at year 2	Number of subjects	% with cognitive impairment[a] by quartiles of oral health parameters[b]				Odds ratio (95% CI) for cognitive impairment per quartile increase
		Q1	Q2	Q3	Q4	
Number of teeth	1,817	14.5	10.2	6.0	2.5	**0.56 (0.48–0.67)**
Number of occluding pairs	1,700	13.3	10.2	5.5	2.6	**0.58 (0.49–0.70)**
Mean probing depth	1,053	4.6	4.0	2.3	12.3	**1.50 (1.17–1.92)**
Proportion with probing depth >=3mm	1,053	4.8	4.1	2.6	11.7	**1.42 (1.12–1.82)**
Mean loss of attachment	1,051	4.1	3.8	6.5	8.5	**1.35 (1.06–1.72)**
Proportion with loss of attachment	1,051	3.7	4.6	7.3	7.4	**1.30 (1.02–1.65)**
Mean gingival index score	1,110	2.0	3.9	6.1	15.5	**2.10 (1.66–2.67)**
Mean plaque score	1,524	3.0	2.4	6.0	15.4	**2.07 (1.67–2.57)**
Number of sites with bleeding on probing	1,046	4.8	6.3	5.2	6.9	1.09 (0.87–1.38)

[a] Cognitive impairment defined as 3MS score<80 (based on the average 3MS score for years 1 and 3)

[b] Quartiles arranged in ascending order for each parameter (e.g. cognitive impairment was present in 14.5% of the 25% participants with fewest teeth and 2.5% of the 25% of participants with the most teeth; 4.6% of participants with lowest mean probing depth and 12.3% of participants with highest mean probing depth)

Abbreviations: 95% CI = 95% confidence intervals

Table 3

Logistic Regression Analyses of the Associations between Oral Health Exposures and Contemporaneous Cognitive Impairment

	Association between quartile increment of oral health measure at year 2 and year 1–3 cognitive impairment[a] (odds ratio, 95% confidence interval)				
	Number of teeth (fewer)[b]	**Mean probing depth**	**Mean loss of attachment**	**Mean gingival index score**	**Mean plaque score**
Associations with 3MS impairment					
Unadjusted	**1.77 (1.50–2.10)**	**1.50 (1.17–1.92)**	**1.35 (1.06–1.72)**	**2.10 (1.66–2.67)**	**2.07 (1.67–2.57)**
1. Adj. age and gender	**1.77 (1.50–2.10)**	**1.51 (1.18–1.94)**	**1.34 (1.04–1.71)**	**2.09 (1.64–2.65)**	**2.01 (1.62–2.50)**
2. Model 1 plus education and race	1.20 (0.98–1.47)	0.93 (0.71–1.22)	0.81 (0.61–1.08)	**1.49 (1.14–1.94)**	**1.33 (1.05–1.69)**
3. Model 2 plus cardiovascular risk[c]	1.17 (0.95–1.44)	0.91 (0.69–1.21)	0.79 (0.59–1.07)	**1.56 (1.18–2.07)**	**1.32 (1.04–1.69)**
4. Model 3 plus depressive symptoms[d]	1.18 (0.95–1.45)	0.90 (0.67–1.20)	0.83 (0.61–1.12)	**1.55 (1.17–2.06)**	**1.34 (1.05–1.72)**
Model 4 for other impairment outcomes[e]					
Digit symbol test score at year 1	1.07 (0.88–1.29)	0.99 (0.77–1.28)	1.10 (0.84–1.44)	**1.51 (1.18–1.94)**	1.05 (0.84–1.30)
Clock drawing score at year 3	1.10 (0.94–1.27)	0.98 (0.80–1.20)	1.08 (0.89–1.32)	1.06 (0.88–1.27)	1.10 (0.94–1.29)
Exit25 at year 3	1.02 (0.83–1.25)	0.90 (0.68–1.19)	0.83 (0.62–1.12)	**1.63 (1.25–2.14)**	**1.29 (1.02–1.63)**

[a] Cognitive impairment defined as 3MS score<80 (based on the average 3MS score for years 1 and 3)

[b] Odds ratios displayed per quartile decrease for number of teeth and per quartile increase for the other variables

[c] Baseline (3 group) smoking status, coronary heart disease, cerebrovascular disease, diabetes, hypertension

[d] Centre for Epidemiologic Studies Depression scale score

[e] Defined so that impairment proportions were the same as the 3MS<80 proportion (i.e. defining as close as possible to the lowest 10% of the distribution)

Table 4

Associations between Quartiles of Oral Health Parameters at Year 2 and Incident Cognitive Decline between Years 3–5

Oral health exposure at year 2	Number in analysis	% with cognitive decline[a] by quartiles of oral health parameters[b]				Odds ratio (95% CI) for cognitive decline per quartile increase
		Q1	Q2	Q3	Q4	
Number of teeth	1603	15.6	14.6	13.7	10.8	0.88 (0.77–1.00)
Number of occluding pairs	1508	15.2	13.4	15.6	10.1	0.90 (0.79–1.03)
Mean probing depth	954	8.9	14.5	14.9	13.1	1.12 (0.95–1.34)
Proportion with probing depth >=3mm	954	9.3	15.2	12.8	14.6	1.12 (0.95–1.34)
Mean loss of attachment	952	12.0	15.1	12.7	11.8	0.97 (0.82–1.16)
Proportion with loss of attachment	952	11.2	14.3	15.5	10.6	1.00 (0.84–1.18)
Mean gingival index score	1000	12.0	11.4	11.6	17.7	1.17 (0.99–1.38)
Mean plaque score	1358	11.8	13.5	15.9	13.1	1.06 (0.92–1.22)
Number of sites with bleeding on probing	947	13.2	12.8	13.1	12.8	0.99 (0.84–1.17)

[a] Cognitive decline defined as a drop in 3MS score of 5 or more points from years 3–5

[b] Quartiles arranged in ascending order for each parameter (e.g. cognitive decline occurred in 15.6% of the 25% participants with fewest teeth and 10.8% of the 25% of participants with the most teeth; 8.9% of participants with lowest mean probing depth and 13.1% of participants with highest mean probing depth)

Abbreviations: 95% CI = 95% confidence intervals

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Table 5

Logistic Regression Analyses of the Associations between Gingival Inflammation and Subsequent Cognitive Decline

	Odd ratio (95% CI) for the association between highest quartile gingival index score at year 2 and cognitive decline[a]
Associations with 3MS decline from years 3–5	
Unadjusted (n=1000)	1.62 (1.09–2.42)
1. Adj. age and gender (n=1000)	1.70 (1.14–2.55)
2. Model 1 plus education and race (n=995)	1.47 (0.97–2.25)
3. Model 2 plus cardiovascular risk[b] (n=964)	1.52 (0.98–2.36)
4. Model 3 plus depressive symptoms[c] (n=961)	1.57 (1.01–2.45)
Further individual adjustments to Model 4	
Year 1 3MS score	1.49 (0.94–2.34)
3MS score change between years 1–3	2.01 (1.26–3.18)
Year 1 C-reactive protein level	1.61 (1.03–2.51)
Year 1 Interleukin-6 level	1.66 (1.06–2.61)
Year 3 body mass index	1.57 (1.01–2.45)
Body mass index change from years 1–3	1.57 (1.01–2.45)
Year 2 anticholinergic agent use	1.54 (0.98–2.41)
Further exploratory stratification (Model 4)	
APOE e4 negative (n=690)	1.60 (0.93–2.75)
APOE e4 present (n=224)	1.08 (0.43–2.70)
Excluding previous cognitive decline (years 1–3)	1.64 (1.00–2.67)
Other decline outcomes	
3MS decline (5+ points) over years 1–5	2.34 (1.66–3.29) unadjusted
	2.54 (1.75–3.70) fully adjusted (Model 4)
3MS decline (5+ points) over years 1–3	2.60 (1.88–3.59) unadjusted
	2.28 (1.60–3.25) fully adjusted (Model 4)
Digit symbol decline[d] over years 1–5	1.17 (0.82–1.67) unadjusted
	1.19 (0.82–1.75) fully adjusted (Model 4)

[a] Defined as a decline of 5 or more points on the 3MS between years 3–5 unless stated otherwise

[b] Baseline (3 group) smoking status, coronary heart disease, cerebrovascular disease, diabetes, hypertension

[c] Centre for Epidemiologic Studies Depression scale score

[d] Defined to obtain the same proportion (lowest 20%) as observed for 3MS decline (years 1–5)