Oral microbiota and periodontal health: the oral–brain axis in cognitive ageing

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Cognitive decline is a persistent and disabling global challenge, with the number of people living with dementia projected to reach 82 million by 2030 and 152 million by 2050.[1] Alongside ageing populations, the incidence of Parkinson's disease–associated cognitive impairment is also rising.[2] While vascular and metabolic disorders are well-established contributors to cognitive impairment, other factors—including advanced age, daytime dysfunction, sex, anaemia, physical inactivity, and social isolation—have also been implicated.[3] Chronic peripheral inflammation has emerged as a potentially modifiable driver of cognitive deterioration. Identifying such modifiable risk factors is essential for developing preventive strategies and discovering early biomarkers of neurodegeneration.

Oral infections and inflammation are among the most prevalent chronic diseases worldwide. Periodontitis, dental caries, and endodontic infections—conditions affecting more than 80% of adults—result from the interplay between microbial activity and host susceptibility. Although preventable, these diseases impose substantial health and economic burdens and diminish quality of life across the lifespan. Beyond discomfort, pain, and tooth loss that impair mastication and daily functioning, oral diseases incur high costs for individuals and healthcare systems. Global treatment expenditures for oral diseases exceed USD 350 billion annually, representing nearly 5% of worldwide health spending.[4] Emerging evidence also links oral diseases with systemic conditions such as cardiovascular disease, diabetes, and stroke.[5] Oral health is increasingly recognised as a lifestyle-related factor relevant to neurological disorders, including Alzheimer's disease.

Periodontitis, a chronic inflammatory disease driven by dysbiotic polymicrobial communities, exemplifies this connection. As the microbial balance shifts from health-associated commensals to pathogenic pathobionts, microbial functions also change, promoting sustained inflammation and tissue destruction. Oral dysbiosis may contribute to systemic infectious and inflammatory burdens through microbial translocation and immune activation. These processes can influence neurological health via the oral–brain axis, a framework linking oral microbial ecosystems to neuroinflammatory pathways involved in cognitive decline. However, population-level evidence connecting the oral microbiome, periodontal health, and cognitive ageing remains limited.

In a recent issue of *eBioMedicine*, Li and colleagues offered valuable insights into these relationships through a community-based study of 1157 older adults.[6] Using high-throughput oral microbiome profiling and detailed clinical assessments, they demonstrated that periodontal health is associated with cognitive performance. Measures such as clinical attachment loss, deep periodontal pockets, and overall periodontitis severity were significantly linked to cognitive function, supporting previous epidemiological findings connecting periodontal deterioration with cognitive impairment.[7]

Differential abundance analyses revealed 70 oral taxa differing across cognitive groups, with 63 genera associated with periodontal status. Microbial enrichment displayed a graded pattern across disease severity: health-associated taxa such as *Haemophilus*, *Rothia*, and *Schaalia* in no or mild periodontitis; intermediate genera including *Streptococcus*, *Granulicatella*, and *Slackia* in moderate disease; and established periodontopathogens such as *Treponema*, *Porphyromonas*, and *Fusobacterium* in severe disease. Functional profiling identified 70 pathways linked to periodontal health, with enrichment of bacterial colonisation, motility, and immune-activation pathways, and depletion of pathways supporting systemic homoeostasis.

Ten genera were significantly associated with cognitive function: *Rothia* and *Haemophilus* were positively associated, while *Abiotrophia* showed negative associations. Twenty-one functional pathways were linked to cognition, including those involved in lipid and energy metabolism, immune responses, and infection-related mechanisms. Co-abundance analyses identified 17 species-level microbial modules, nine of which were associated with periodontal health, and two with cognition. Modules enriched in early colonisers and nitrate-reducing commensals (e.g., *Actinomyces*, *Neisseria*, *Haemophilus*) showed positive associations, whereas those dominated by inflammatory periodontopathogens (e.g., *Treponema*, *Tannerella*, *Filifactor*) were negatively associated. Mediation analysis revealed that oral microbiome features partially mediated the relationship between periodontal health and cognitive

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function. Eleven microbial and functional features contributed to 24 significant mediation pathways, with *TM7x*, ribosome biogenesis pathways, *Haemophilus*, and *Treponema* being identified as key mediators.

These results highlight oral microbial dysbiosis and periodontal health as influential components of the complex microbial and functional networks that may shape cognitive ageing. Methodological considerations remain: the use of 16S rRNA sequencing limits species-level resolution and functional insight compared with shotgun metagenomics, which can more comprehensively characterise multi-kingdom microbial communities and functional potential.[8] Clinical periodontal examinations relied on half-mouth assessments and did not include other common oral diseases, such as caries, endodontic infections, or mucosal conditions.

Clinically, once established, oral dysbiosis is largely irreversible, underscoring the importance of preventing caries, periodontitis, and other microbial imbalances throughout life. Evidence suggests that oral disease burden in childhood may contribute to later cardiovascular and systemic pathology, potentially extending to neurodegenerative outcomes.[9,10] Therefore, maintaining good oral hygiene, attending regular dental visits, following a healthy diet, engaging in physical activity, and avoiding tobacco use are critical preventive behaviours from early life onwards.

Future research should aim to elucidate the underlying mechanisms through biological validation, replicate findings across diverse populations, integrate multi-omics and inter-kingdom microbial analyses, and employ longitudinal designs to determine whether modulating the oral microbiome may offer viable strategies for preventing cognitive decline and dementia.

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Declaration of interests

The authors declare no conflict of interest.

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