Association of experimental periodontitis and aging with cognitive decline in C57BL/6 mice.

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Abstract

Periodontal disease and aging are known to be a risk factor for dementia. It has been reported that inflammatory cytokines produced with *P. gingivalis* (*P. g*) infection and onset of periodontitis may activate microglia in the brain and cause neuroinflammation. However, the association between aging, periodontal disease and *P. g* infection in cognitive decline has not been fully understood.

We induced experimental periodontitis by *P. g* infection in the oral cavity of young and old C57BL/6 mice and compared cognitive functions using Y-maze behavioral tests, pathological observations, and RNA-Sequence to elucidate effects of aging and periodontitis on the onset and progression of dementia in those mice.

The results of the Y-maze behavioral test showed a significant decrease in learning and memory ability in the old + *P. g* group compared to the other groups. Alveolar bone resorption was significantly larger in the old group compared with the young and young + *P. g* groups, and significantly larger in the old + *P. g* group compared with the other groups. Aβ42 concentrations in the cerebral cortex measured using ELISA were significantly higher in the old + *P. g* group compared with the young + *P. g* group. The genetic distribution in the hippocampus of the old + *P. g* group was clearly separated from that of the young + *P. g* group based on RNA-Seq, Heatmap and PCA. Among differentially expressed genes (DEGs), 762 genes showed a greater than twofold increase and 622 genes showed a greater than twofold decrease, in the old + *P. g* group compared with the old group. Gene Ontology (GO) analysis revealed increased expression of GO pathways associated with dendrite formation. RNA-Seq and GO analysis showed an increased expression of *NSMF* and decreased expression of *SCRN1*. q-PCR results showed that gene expression of *NSMF* and *SCRN1* were significantly up-regulated in the old + *P. g* group compared to the old group in the hippocampus.

These findings indicated that administration of *P. g* in old age were associated with increased alveolar bone resorption, cognitive decline, enhanced Aß42 accumulation in the cerebral cortex and decreased numbers of cone cells in hippocampus. It is also suggested that *P. g* infection in older age may affect on the synaptic signaling and increased expression of *NSMF* associated with neurodegeneration.