1. No.
   2022Y005

2. Title
   Study of the Effects of Smoking on Cellular Senescence in the Human Brain Tissue

3. Period
   2022-2024

4. Summary
   [Background] Cigarette smoking is reported to accelerate the aging process of various organs, including the brain. The hippocampus is a brain structure important in cognition and mood regulation, and the hippocampal dentate granule cells play a critical role in learning and memory. However, associations between cigarette smoking and cellular senescence in human dentate granule cells are poorly understood.
   [Methods] Human hippocampal tissues of 10 never-smokers (5 men and 5 women) and 10 ever smokers (5 men and 5 women) were retrieved from autopsy files. Immunohistochemical expressions of p16 and p21, representative biomarkers of cellular senescence, were investigated. We also examined telomere lengths of the hippocampal dentate granule cells, using the quantitative fluorescence in situ hybridization, and compared the telomere lengths between never-smokers and ever smokers by gender. This study included 27 never-smokers (13 men and 14 women) and 31 ever smokers (21 men and 10 women).
   [Results] Almost all neural cells in hippocampal tissues, including the dentate granule cells, were p16 and p21 negative in both never-smokers and ever smokers. In men, the telomere lengths in dentate gyrus granule cells of the hippocampus did not differ between never-smokers and ever smokers ($P = 0.9717$). However, in women, the telomere lengths in these cells were shorter in ever smokers than in never-smokers ($P = 0.0017$). The mean pack-year of the male and female smokers was 53.1 (range 10.75-140) and 46.5 (range 10-90), respectively. The mean number of years of smoking of the male and female smokers was 49.57 years (range, 30-64 years) and 42.5 years (range, 20-60 years), respectively.
   [Conclusions] Our results suggest that the impact of long-term high‐intensity cigarette smoking on aging process in the dentate granule cells is greater in women compared with men. Additionally, there were no significant differences in p16 and p21 expressions in human hippocampal tissues between never-smokers and ever smokers.