1. No.

   2019T005

2. Title

   Modulation of obesity-associated hypothalamic inflammation by nicotine exposure and withdrawal

3. Period

   2019-2023

4. Summary

In this five-year collaborative study project, our team have, through an analysis of hypothalamic inflammation/gliosis, a missing link between obesity and smoking/smoking cessation.

Firstly, we have undertaken a transverse epidemiologic study analyzing a potential difference of BMI and cardiovascular risk between never, current and past smokers among subjects of regular health check-ups. The data was clear in men showing significantly higher age-adjusted BMI and Hisayama cardiovascular score.

Secondly, human MRI study has shown a surprisingly tight positive correlation between BMI and MRI T2 relaxation time of the medio-basal hypothalamus, a marker of inflammation/gliosis.

Thirdly, bulk and single nucleus transcriptome analysis has shown a great diversity of cell populations in the arcuate nucleus of the hypothalamus, a gateway of peripheral energy cues. Withdrawal from nicotine in high fat diet-fed obese mice, a model of patients with obesity challenging tobacco cessation, swiftly provoked NPY expression in the hypothalamus with a rapid rise of body weight, but without an apparent increase of inflammatory gene expression, suggesting hypothalamic inflammation/gliosis-independent mechanisms underlying body weight gain following tobacco cessation.

Taken together, our study results provide human and animal evidence of the link between pathologic changes of the hypothalamic energy center in obesity and smoking/smoking cessation.