1. **No.**

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2. **Title**

   Confounding Effects of Smoking and Dietary Fat Intake on Hypothalamic Dysfunction in Obesity

3. **Period**

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4. **Summary**

   Obese smokers are high risk subjects who need intensive medical intervention because of the co-existence of two independent cardiovasucular morbidity and mortality. However, hypothalamic pathophysiology characterizing obese smokers have not been thoroughtly addressed.

   Here we have demonstrated that 1) Nicotine potently suppress food intake and body weight in high fat-induced obesity in mice along with suppression of NPY, an important orexigenic neuropeptide within the arcuate nucleus of the hypothalamus and that 2) Gene expression changes provoked in high fat diet-induced obesity is largely reversed by acute treatment with nicotine by transcriptome-based analysis. 3) We identified that the expression of CB1R endocannabinoid receptor is increased by high fat diet and nicotine in combination, suggesting a potential crosstalk between obesity and exposure to nicotine. When we inhibited CB1R by an administration of rimonabant, a selective inhibitor, nicotine-induced suppression of body weight in obese mice was further augmented, suggesting that the latent activation of central endocannabinoid system in obese smokers may serve as an inhibitor of weight loss by antagonizing the weight-reducing effect of nicotine.

   Taken together, our study has contributed to the understanding of molecular pathophysiology of obesity and the effect of nicotine on energy metabolism and may potentially lead to the future therapeutic strategy for the treatment of obese smokers.