

S1. The validation of subdiaphragmatic vagotomy (SDV)

(A) Schedule and (B) schematic diagram of the SDV surgery. A visual operative field for SDV surgeries. Microscopic photography of (C) the anterior vagus nerve (black arrowheads) and (D) the posterior vagus nerve (black arrowhead) at esophagus level (white arrowhead). (E) representative photography of the stomach size after Sham or SDV surgery. Verification of SDV by using retrograde labeling of the dorsal motor nucleus of the vagus nerve (right DMN, yellow arrowhead) beside right NTS: (F) SDV and (G) sham group. Scale bar represents 500  $\mu$ m and 20  $\mu$ m in the box; magnification 100× tiled scan and 200× in the box. Please note significant lack of FluoroGold labeled neurons in SDV-operated group compared to shame group.



S2. The patterns of c-Fos expression in the whole brain regions associated with homeostasis and pain modulation in formalin-treated SDV group

(A) Average number of c-Fos+ cell count in different group of sham, formalin-treated sham, SDV, and formalin-treated SDV group on acute inflammatory pain. (B) Schematic representation and representative photomicrographs of c-Fos observed in the aIC. (C) Schematic representation and representative photomicrographs of c-Fos observed in the ACC. (D) Schematic representation and representative photomicrographs of c-Fos observed in the mPFC. Scale bar represents 100  $\mu$ m; magnification 10×. Representative regions in coronal sections based on the atlas of Paxinos and Watson (2nd edition). Asterisk represents significant changes of c-Fos between sham and formalin-treated sham groups. Cross represents significant changes of c-Fos between formalin-treated sham and formalin-treated SDV group. Sharp represents

significant changes of c-Fos between SDV and formalin-treated SDV group. Data are presented as mean  $\pm$ SEM. \*p <0.05, \*\*p <0.01, \*\*\*p <0.001; +p <0.05, ++p <0.01, +++p <0.001; #p <0.05, ##p <0.01, ###p <0.001 (two-way ANOVA followed by Bonferroni test).





(A) aIC, (B) ACC, (C) mPFC. Scale bar represents 100  $\mu$ m; magnification 10×. Representative regions in coronal sections based on the atlas of Paxinos and Watson (2nd edition).