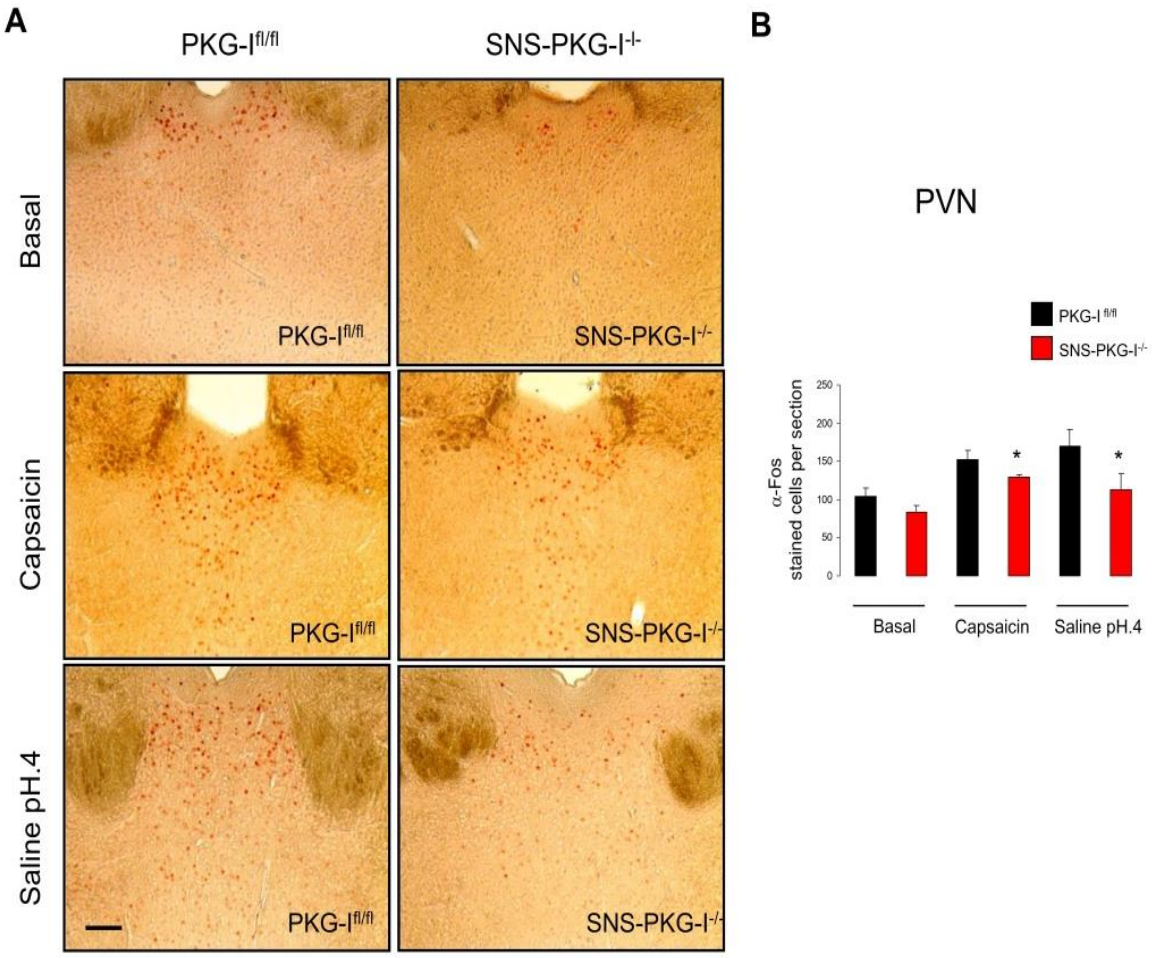
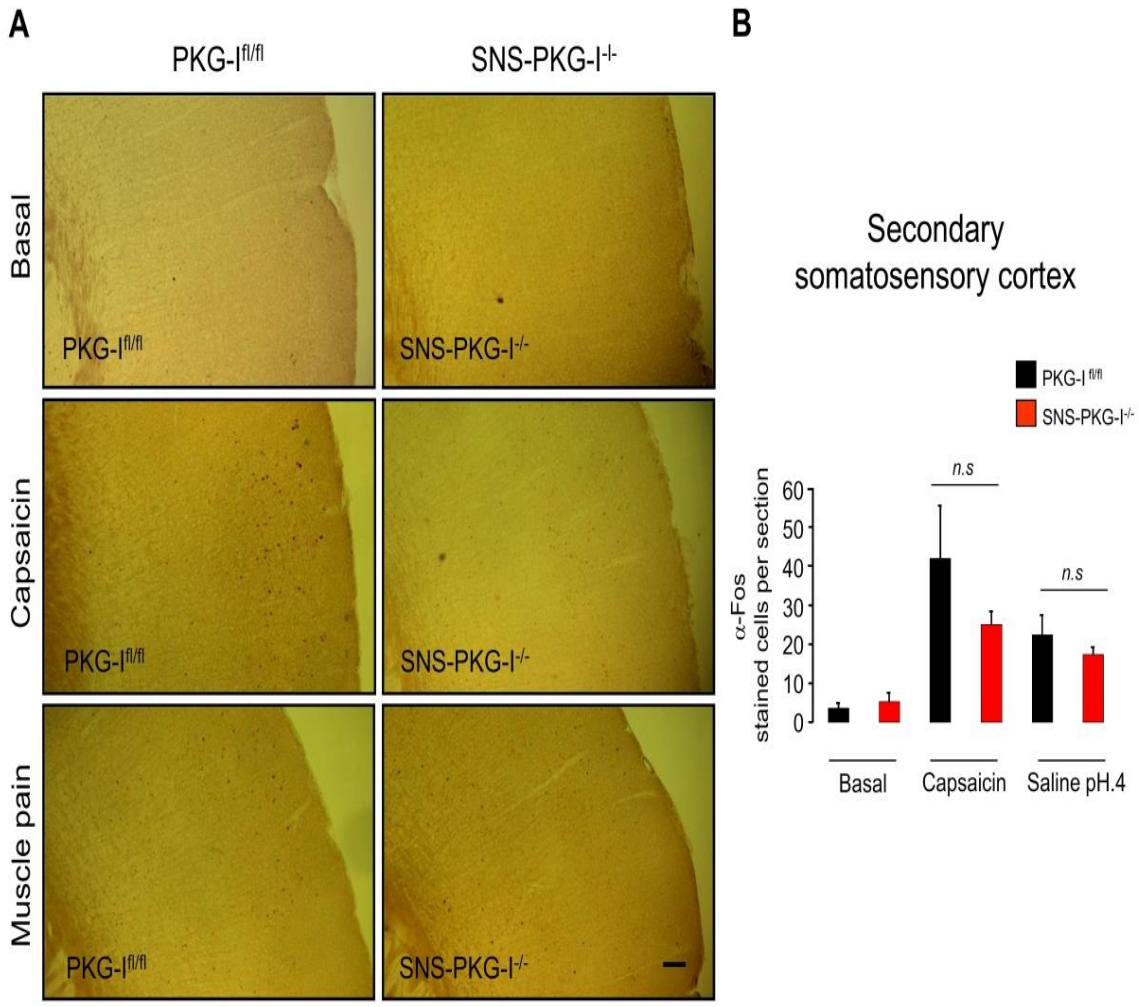
Supplementary figure 1



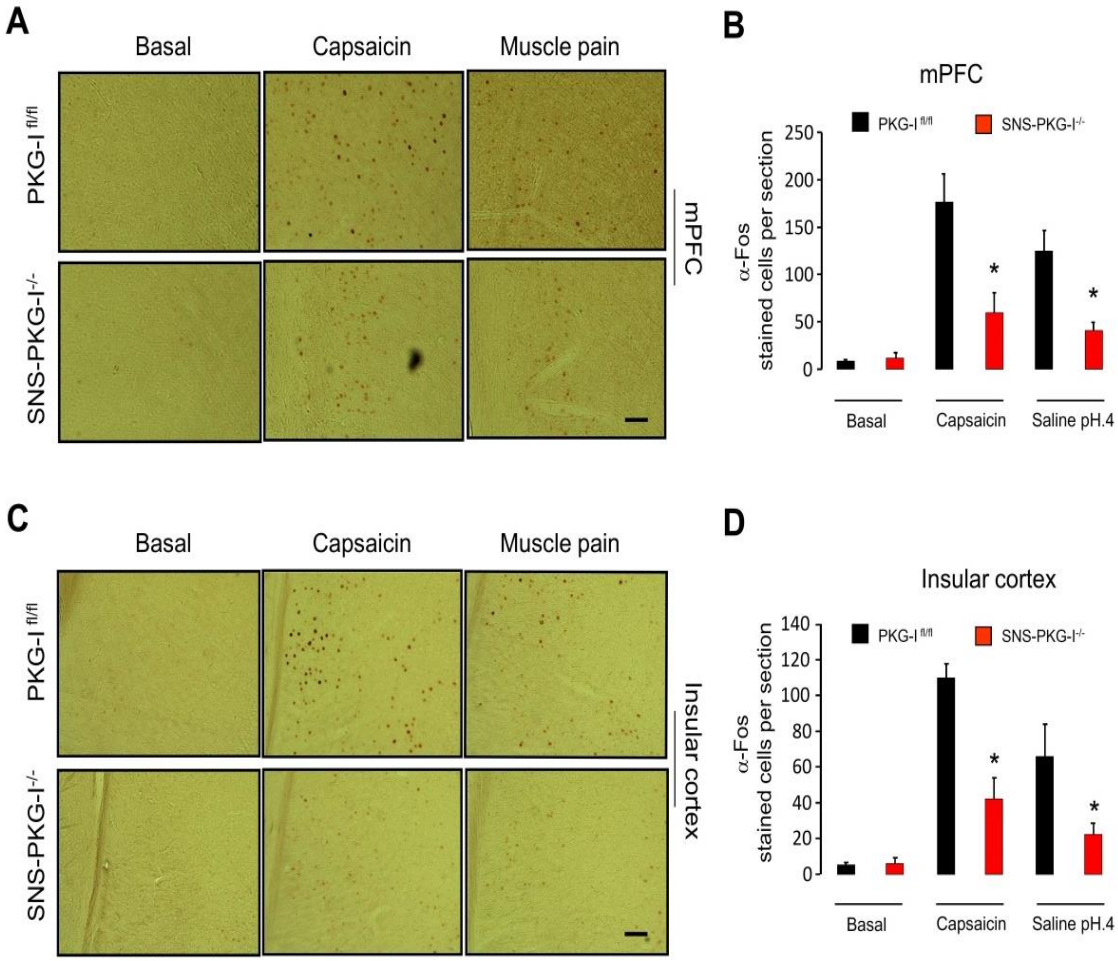
Supplementary Fig 1 (A) Induction of c-Fos in the paraventricular nucleus (PVN) following capsaicin and acidic saline injection, respectively, in PKG-I$^{fl/fl}$ mice and SNS-PKG-I$^{-/-}$ mice. (B) Quantification of the number of Fos-positive cells revealed that Fos immunoreactivity in both capsaicin and muscle pain model was significantly reduced in the PVN in SNS-PKG-I$^{-/-}$ mice, as compared to PKG-I$^{fl/fl}$ mice. ∗indicates statistically significant differences (P <0.05) between PKG-I$^{fl/fl}$ mice and SNS-PKG-I$^{-/-}$ mice (ANOVA, post hoc Fisher's test, n = 4 mice per genotype). Scale bars represent 300 μm.

Supplementary figure 2



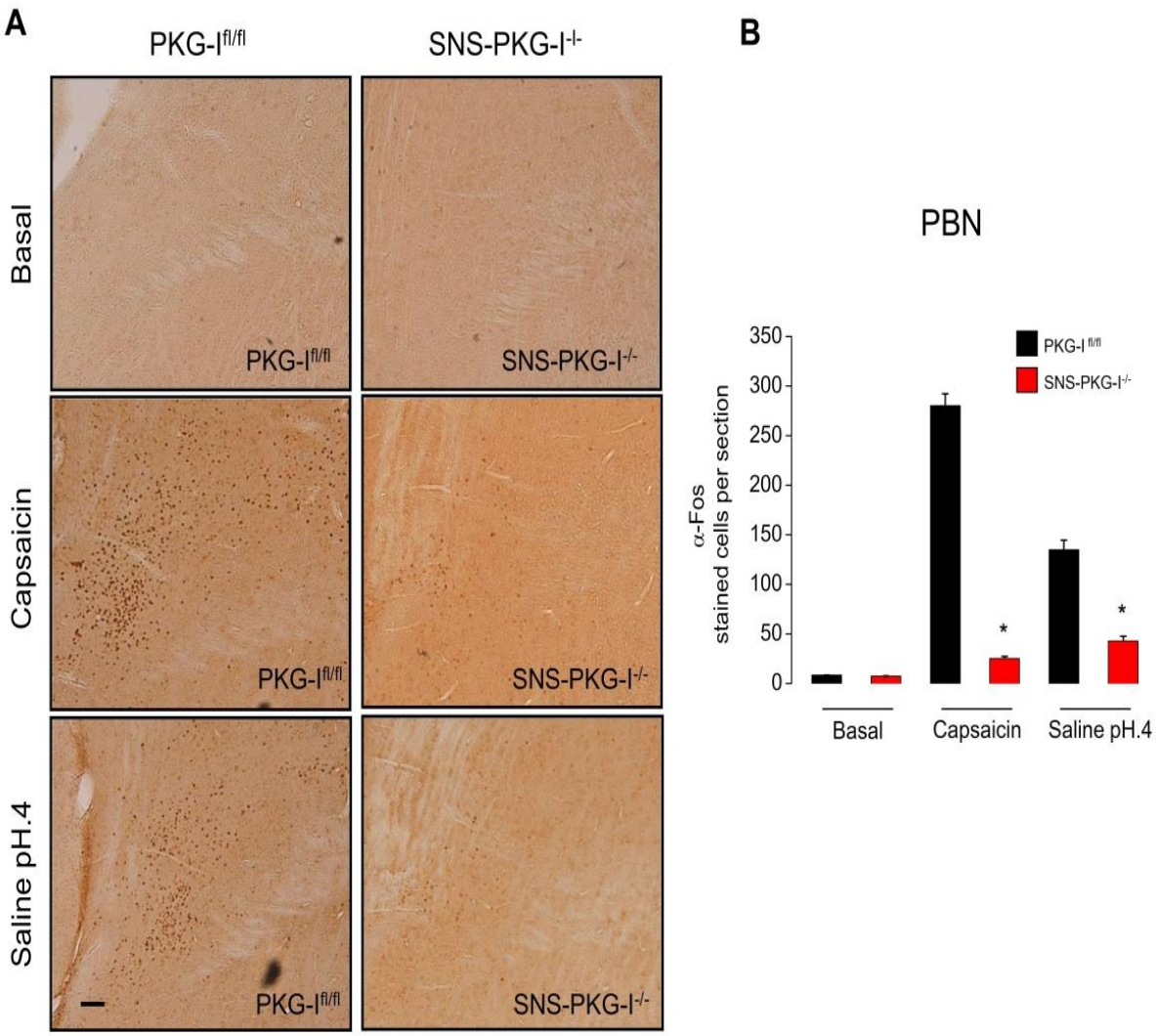
Supplementary Fig 2 (A) Induction of c-Fos in the secondary somatosensory cortex (SII) following capsaicin and acidic saline injection, respectively, in PKG-I$^{fl/fl}$ mice and SNS-PKG-I$^{-/-}$ mice. (B) Quantification of the number of Fos-positive cells revealed that Fos immunoreactivity in both capsaicin and muscle pain model was not significantly different in the SII between PKG-I$^{fl/fl}$ and SNS-PKG-I$^{-/-}$ mice. n.s indicates no statistic differences ($P > 0.05$) between PKG-I$^{fl/fl}$ mice and SNS-PKG-I$^{-/-}$ mice (ANOVA, post hoc Fisher's test, n = 4 mice per genotype). Scale bars represent 600 μm.

Supplementary figure 3



Supplementary Fig 3 (A, C) Induction of c-Fos in the medial prefrontal cortex (mPFC) (A) and insular cortex (C) following capsaicin and acidic saline injection, respectively, in PKG-$I^{fl/fl}$ mice and SNS-PKG-$I^{-/-}$ mice. (B, D) Quantification of the number of Fos-positive cells revealed that Fos immunoreactivity in both capsaicin and muscle pain model was significantly reduced in the mPFC (B) and insular cortex (D) in SNS-PKG-$I^{-/-}$ mice, as compared to PKG-$I^{fl/fl}$ mice. ∗indicates statistically significant differences ($P < 0.05$) between PKG-$I^{fl/fl}$ mice and SNS-PKG-$I^{-/-}$ mice (ANOVA, post hoc Fisher's test, n = 4 mice per genotype). Scale bars represent 300 μm.

Supplementary figure 4



Supplementary Fig 4 (A) Induction of c-Fos in the parabrachial nucleus (PBN) following hindlimb capsaicin and acidic saline injection, respectively, in PKG-$I^{fl/fl}$ mice and SNS-PKG-$I^{-/-}$ mice. (B) Quantification of the number of Fos-positive cells revealed that Fos immunoreactivity in both capsaicin and muscle pain model was significantly reduced in the PBN in SNS-PKG-$I^{-/-}$ mice, as compared to PKG-$I^{fl/fl}$ mice. ∗indicates statistically significant differences ($P < 0.05$) between PKG-$I^{fl/fl}$ mice and SNS-PKG-$I^{-/-}$ mice (ANOVA, post hoc Fisher's test, n = 4 mice per genotype). Scale bars represent 500 μm.