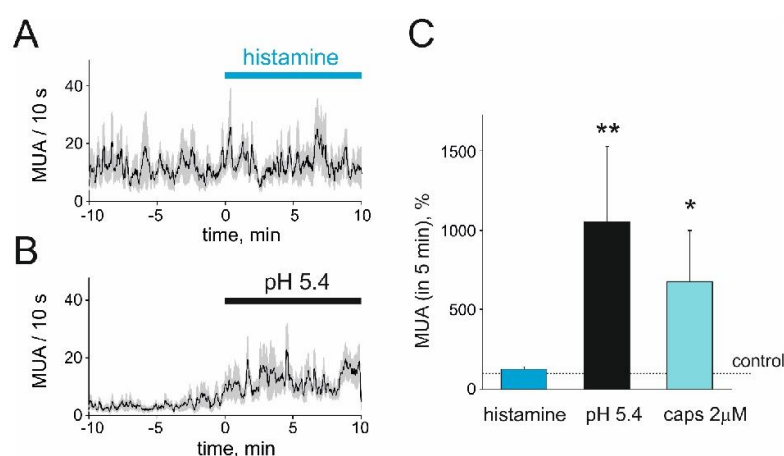


# Serotonergic mechanisms of trigeminal meningeal nociception: Implications for migraine pain

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## Supplementary Figure 1

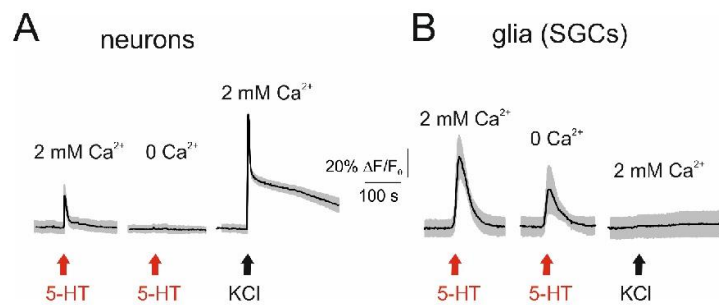


(A) Effect of 100 µM histamine on multiunit activity density in the nervus spinosus.

(B) Effect of pH 5.4 on nervus spinosus multiunit activity density.

(C) Histograms showing the effects on spike frequency of 100 µM histamine (126±17%, p=0.16, n=6), pH 5.4 (1053±474%, p=0.0039, n=9) and capsaicin 2 µM (637±323%, p=0.0313, n=7). Notice strong facilitation of firing by acid pH. \*, p<0.05, \*\*, p<0.001.

## Supplementary Figure 2



**(A)** From 43 trigeminal neurons, 11 responded to 20  $\mu$ M 5-HT (26 %) by Ca<sup>2+</sup> transients (average of 5 traces  $\pm$  SEM) in the normal basic solution. However, none of these neurons responded to 5-HT 5 min later when Ca<sup>2+</sup> was omitted from basic solution indicating that the 5-HT responses were mediated by Ca<sup>2+</sup> flux from the extracellular space. This is consistent with the role of ligand-gated 5-HT<sub>3</sub> receptors expressed in trigeminal neurons.

**(B)** In contrast to neurons, in trigeminal satellite glial cells (SGC), not only the first (average of 5 traces  $\pm$  SEM) test pulse of 20  $\mu$ M 5-HT in normal basic solution but also the second application 5-HT in nominally Ca<sup>2+</sup> free solution still induced responses with amplitude 50.4  $\pm$  7.0 % (n=of the first one suggesting that the major part of response was mediated by Ca<sup>2+</sup> release from the intracellular stores.