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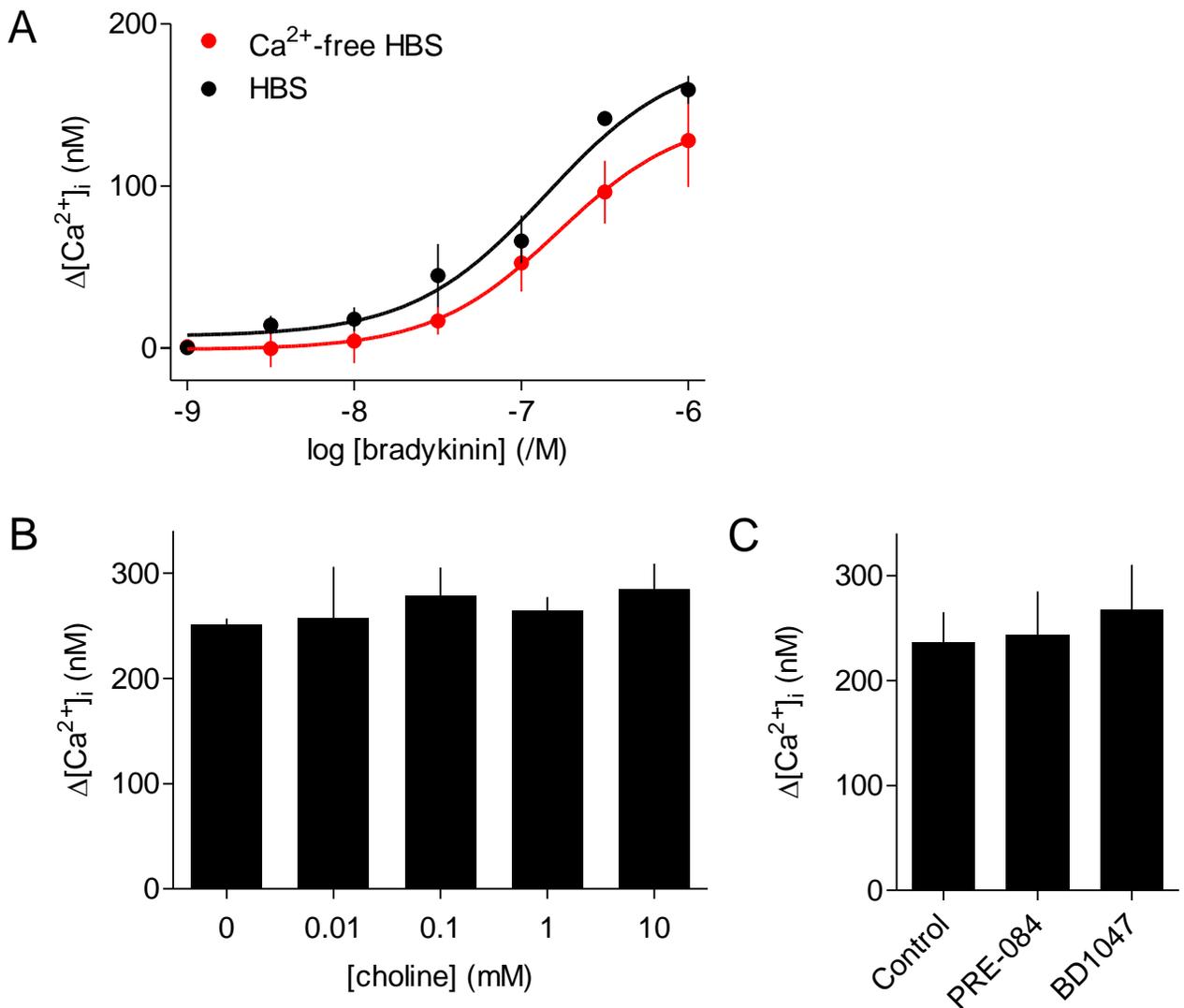
**Supplemental Information**

**Choline Is an Intracellular Messenger**

**Linking Extracellular Stimuli to IP<sub>3</sub>-Evoked**

**Ca<sup>2+</sup> Signals through Sigma-1 Receptors**

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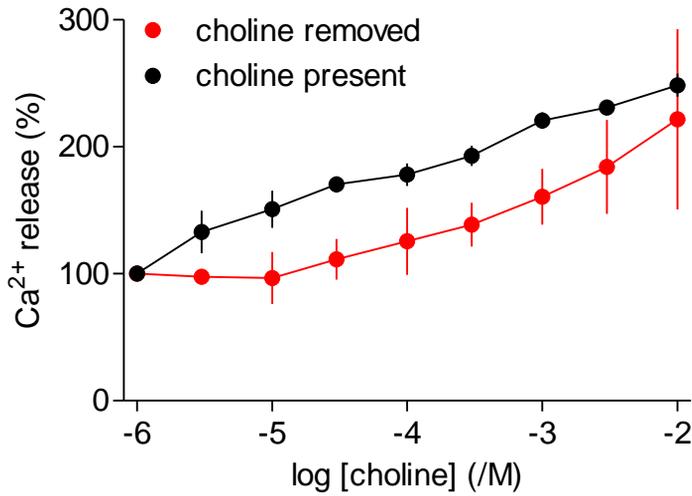


**Figure S1. Bradykinin Stimulates  $\text{Ca}^{2+}$  Release From the Intracellular Stores of NG108-15 Cells.**

**Related to Figures 1 and 2**

(A) NG108-15 cells were stimulated with the indicated concentrations of bradykinin in HBS or  $\text{Ca}^{2+}$ -free HBS. Results (means  $\pm$  SEM,  $n = 3$ , with duplicate determination) show  $\Delta[\text{Ca}^{2+}]_i$ .

(B,C) Intact cells were treated with the indicated concentrations of choline (1 h, 20°C) (B) or incubated (3 h, 37°C) with PRE-084 (25  $\mu\text{M}$ ) or BD1047 (25  $\mu\text{M}$ ) (C) before addition of ionomycin (5  $\mu\text{M}$ ) in  $\text{Ca}^{2+}$ -free HBS to assess the  $\text{Ca}^{2+}$  content of the intracellular stores. Results (mean  $\pm$  SEM,  $n = 3$ ) show  $\Delta[\text{Ca}^{2+}]_i$  evoked by ionomycin.



**Figure S2. Intracellular Choline Potentiates Bradykinin-Evoked Ca<sup>2+</sup> Signals. Related to Figure 4.**

NG108-15 cells were incubated (1 h) with the indicated concentrations of choline in HBS before recording the peak Ca<sup>2+</sup> signals evoked by bradykinin (1  $\mu$ M), which was added in either the continued presence of choline or immediately after its removal. Responses (mean  $\pm$  SEM,  $n = 3$  plates with duplicate determinations; several error bars are smaller than the symbols) are expressed as a percentage of the matched response to bradykinin without choline (100%).