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## Sensory denervation with capsaicin decreases sensitization rate to milk proteins in guinea pigs

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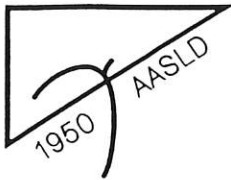
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SENSORY DENERVATION WITH CAPSAICIN DECREASES SENSITIZATION RATE TO MILK PROTEINS IN GUINEA PIGS. C. Leforestier, J. Gay, J. Fioramonti, R. Garcia-Villar, J. Moré L. Bueno. Dept. Pharmacology, INRA, Toulouse, France.

A close apposition between peptidergic fibers and mast cells has been described, and neuropeptides of sensory neurons such substance P are known to control activity of immunocytes, including mast cells. Sensitization to milk proteins is the most common food allergy, but its cause is poorly known and is multifactorial. The aim of our study was to determine whether capsaicin sensitive afferents play a role in oral sensitization to milk proteins in the guinea pig, a species considered as a clinically relevant model of food hypersensitivity.

**Methods:** Four groups of ten Dunkin-Hartley guinea pigs (250-300g) were used. Groups 1 and 2 were sensitized to milk proteins by drinking only pasteurized cow milk for four weeks. They returned to drinking water 4 days before experiments. Groups 3 and 4 were controls drinking tap water. Ten days before the period of sensitization, groups 2 and 4 were treated with capsaicin, injected subcutaneously on 4 consecutive days with increasing doses to reach a total dose of 55 mg/kg. IgG and IgE serum titers were evaluated by passive cutaneous anaphylaxis (PCA) test after cardiac puncture. Immune responsiveness was then assessed by measuring colonic fluid secretion triggered by antigen challenge ( $\beta$ -lactoglobulin, 100 mg) by perfusing a colonic loop with 14C polyethylene glycol 4000 in anesthetized animals. Before challenge, pieces of the proximal jejunum were fixed in Carnoy's solution and transverse sections were stained with Alcian Blue-Safranin O to count the number of mast cells.

**Results:** No positive response to the PCA test was observed in non-sensitized animals. IgG and IgE serum titers were significantly lower ( $P < 0.05$ ) in sensitized animals of group 2, treated by capsaicin, compared to group 1 ( $0.93 \pm 0.34$  vs  $1.45 \pm 0.22$ ). Anaphylaxis induced colonic fluid secretion observed in sensitized animals of group 1 ( $-35.5 \pm 15.4 \mu\text{l/cm/h}$ ) did not appear in sensitized animals treated with capsaicin where the net water flux ( $+15.2 \pm 8.6 \mu\text{l/cm/h}$ ) did not significantly differ ( $P > 0.05$ ) from control groups either treated or untreated with capsaicin ( $+20.2 \pm 9.8$  and  $22.1 \pm 10.6 \mu\text{l/cm/h}$ , respectively). The number of jejunal mast cells was significantly increased ( $P < 0.05$ ) in sensitized animals (group 1) in comparison with control group 3 ( $126.4 \pm 13.9$  vs  $86.5 \pm 17.1$  mast cells/mm<sup>2</sup>). In sensitized animals treated with capsaicin (group 2), the increase in mast cell number was not observed ( $87.4 \pm 22.9$  /mm<sup>2</sup>) and capsaicin treatment in non-sensitized animals did not modify the number of mast cells ( $76.9 \pm 17.6$  /mm<sup>2</sup>).

**Conclusion:** Capsaicin sensitive sensory neurons enhance sensitization rate to milk proteins, promote food allergy mastocytosis and, consequently, increase the mucosal immune response upon antigen challenge.

I affirm that this abstract meets all of the requirements stated in this booklet, and that the authors named are familiar with the presented data, and that Box C has been completed. On behalf of all of the authors, I hereby transfer copyright in the above abstract to American Gastroenterological Association.

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