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**Increased sensitivity to visceral distension in
post-Nippostrongylus brasiliensis-infected rats:
involvement of mast cells and tachykinin receptors**

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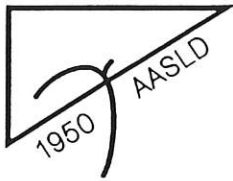
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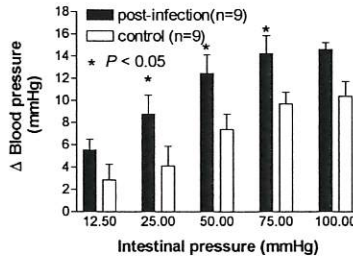
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INCREASED SENSITIVITY TO VISCERAL DISTENSION IN POST-NIPPOSTRONGYLUS BRASILIENSIS-INFECTED RATS: INVOLVEMENT OF MAST CELLS AND TACHYKININ NK₂ RECEPTORS.

P.G. McLean, C. Picard, R. Garcia-Villar, J. Ducos de Lahitte, J. Moré, J. Fioramonti, L. Buéno. Dept. Pharmacology, INRA, Toulouse, France.

The pathophysiology of the irritable bowel syndrome (IBS) has been suggested to involve an increase in the number of mast cells in the human gut (Weston *et al.*, 1993, *Dig. Dis. Sci.*, **38**, 1590-1595.). The present study investigated whether the long-term hypermastocytosis that occurs in the rat gut following *Nippostrongylus brasiliensis* infection affects visceral sensitivity. A model of visceral pain that utilises jejunal or colonic distension (JD or CD) as the noxious visceral stimulus was used in this investigation. JD or CD, in anaesthetised rats, elicits a marked cardiovascular depressor response. Hyeralgesia or antinociception is characterised by potentiation or inhibition, respectively of the response. The effect of a tachykinin NK₂ receptor antagonist on the depressor response was also investigated and compared in healthy (control) and infected rats.

Methods: Control or *N. brasiliensis*-infected (30-34 days post infection) male Wistar rats (300-400g) were anaesthetised with pentobarbitone sodium (60mg/kg). The distal colon or proximal jejunum was distended with a latex balloon via a polyethylene catheter.



Results: Histological analysis revealed hypermastocytosis in the jejunum but not in the colon at 30 days post-infection. No inflammation (myeloperoxidase activity and histological analysis) was detected in either region. JD or CD (12.5-75 mmHg, 25s every 5min) produced a stimulus-related decrease in blood pressure. The depressor responses to JD at 25, 50 and 75 mmHg

were significantly greater in post-infected rats (see figure, $P < 0.05$). However, the responses elicited by CD were not significantly affected following infection ($n=10$, $P > 0.05$). The i.p. administration of the tachykinin NK₂ receptor antagonist, SR48968 (0.1-10 mg kg⁻¹) produced a dose-dependent inhibition of the depressor response to JD (75 mmHg, 25s, every 5 min) giving rise to an ED₅₀ of 0.5±0.2 mg kg⁻¹ ($n=13$) in control rats. In infected rats SR48968 was 3.1-fold more potent against the JD-induced depressor response than in control rats (ED₅₀=0.15±0.1) mg kg⁻¹ ($n=13$).

Conclusions: This study has shown that the non-inflammatory, chronic changes which occur in rat jejunum post-infection with *N. brasiliensis*, such as hypermastocytosis and neural re-modelling cause increased visceral sensitivity. The data obtained with SR48968 indicate that tachykinin NK₂ receptors mediate nociception in response to noxious JD in anaesthetised rats and are possibly involved in the increased visceral sensitivity observed following intestinal infection.

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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