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EFFECTS OF CHRONIC TREATMENT WITH ANTIDEPRESSANTS ON IN VITRO JEJUNAL CONTRACTILITY IN RATS.
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The involvement of psychotic disorders, mainly major depression, in the etiology of irritable bowel syndrome (IBS) is largely documented. Consequently, antidepressants and other psychiatric drugs are used, yet at low, non-psychiatric doses, for relief of IBS (40% of cases in the USA; 13% in France). The specific mechanism of the intestinal action of these agents, however, is unknown and most probably independent of mood improvement. Therefore, the present *in vitro* contractility study was aimed at assessing possible alterations of intestinal muscle sensitivity to cholinergic and serotonergic stimulation after one month of treatment with low doses of serotonin reuptake inhibitor antidepressants.

Methods: Four groups of 8 male Wistar rats (250-275 g) were treated (0.3 ml intraperitoneally, once per day for 28 days), with either an antidepressant (fluoxetine, 0.5 mg/d; amitriptyline, 2 mg/d; clomipramine, 2 mg/d) or NaCl 0.9% (controls). Longitudinal strips of jejunum (8 x 2 mm) were prepared and placed into an *in vitro* muscle superfusion system (Krebs, 2 ml/min, 37°C); isometric contractions were recorded and quantified. Concentration-response curves to carbachol and serotonin (5-HT) were constructed (1 nM to 10 mM) for the four groups. For both agents, maximal effects (Emax; mean±SEM) were expressed as the percentage of a 60 mM KCl-induced contraction in the same strip, and potency as EC50 (µM; mean±95%CI).

Results: Both 5-HT and carbachol concentration-dependently contracted the intestinal strips of the four groups studied. Nevertheless, although differences were not observed between groups for the responses to carbachol, significant differences (p<0.01) were measured for 5-HT, whose EC50s were reduced in two groups (Table 1):

Table 1: Parameters of concentration-response curves to 5-HT in the four groups.

	EC50 (µM)	Emax (%)
Controls	1.52 [0.68-3.40]	124.3 ± 23.6
Amitriptyline	0.12 [0.05-0.28]**	115.5 ± 17.3
Fluoxetine	0.10 [0.08-0.13]**	109.7 ± 9.7
Clomipramine	0.97 [0.35-2.70]	143.4 ± 11.0

** p<0.01; significantly different from controls; ANOVA and Bonferroni test

Conclusion: One month treatment with two serotonin reuptake inhibitor antidepressants, at non-psychiatric doses, lead to an enhancement of intestinal muscle sensitivity to 5-HT in rats. This finding may contribute to the understanding of the digestive effects of antidepressants which are used for relief of IBS.

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