

047P THE EFFECT OF FLUOXETINE ON ELECTRICALLY-EVOKED CONTRACTIONS OF THE RAT SMALL INTESTINE

F.F. Mashhadi, F.A. Javid & R.J. Naylor, School of Pharmacy, University of Bradford, Bradford BD7 1DP.

The antidepressant action of fluoxetine, citalopram and related agents is attributed to a selective serotonin reuptake inhibition (SSRI). Recent studies suggest that the SSRIs might have other effects not related to inhibition of neuronal 5-HT reuptake (Pacher et al., 2001). The aim of the present study was to investigate the effect of fluoxetine on electrically-stimulated tissues taken from the rat small intestine.

Segments (two cm length) taken from the duodenum, jejunum, mid ileum and terminal ileum of male Lister Hooded rats (250-300 g) were mounted in 10 ml organ baths containing Krebs' solution (37°C, 95%O<sub>2</sub>, 5% CO<sub>2</sub>). The tissues were allowed to equilibrate for 45 min and washed every 20 min. The resting tension was maintained at 1 g and recorded isometrically. Electrical field stimulation (EFS; 0.4, 1, and 10 Hz, 30 V and 0.5 ms pulse width, double pulses with 75ms delay, with a 10 min interval of stimulation) was delivered by means of two platinum electrodes placed on either side of the tissue. Using a paired experimental design, the tissues were exposed to EFS (1 min) in the absence and presence of fluoxetine (10 nM, 0.1-10 µM). Tension changes were expressed as the mean ± s.e. mean of a control KCl (100µM) - induced contraction; n=6 and data were analysed using the paired student's t-test.

EFS induced a frequency dependent contraction in all segments examined. The contractile response to EFS at 1 Hz was significantly (p<0.05) increased by 10 nM fluoxetine only in the segments taken from the duodenum. The contractile response to EFS at 1 and 10 HZ were significantly (p<0.05,

0.001) attenuated by 1µM fluoxetine and abolished by 10 µM as compared to the control tissues; 0.1 µM fluoxetine had no effect.

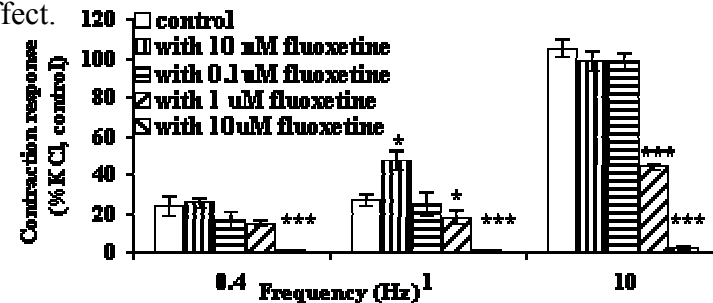


Figure 1-Representative data showing the contractile response induced by electrical field stimulation (30v, frequency 0.4,1 and 10 Hz, and 75 ms delay for 1 min) in the absence and presence of 10 nM, 0.1-10 µM) fluoxetine in the duodenal segments taken from the rat small intestine. \*p<0.05, \*\*p<0.01 and \*\*\*p<0.001 taken as significant differences compared to the control values.

The data suggest that fluoxetine at 10 nM may act as serotonin reuptake inhibitor to increase the level of serotonin (Velasco et al., 1997) leading to a greater size of contraction to EFS. However the ability of fluoxetine to attenuate or abolish the contractile response to EFS could be due to Ca<sup>2+</sup> channel blocking actions (Pacher et al, 2001) or antimuscarinic effect (Lucchelli et al., 1995). The latter effects of fluoxetine were achieved at concentrations approximately 100 times greater than required to block 5-HT reuptake sites. The significance of the effects of fluoxetine in the gut remains to be substantiated.

Pacher P. et. al.(2001) *Can. J. Physiol. Pharmacol.* 79, 580-584.  
Lucchelli A. et. al. (1995) *Br. J. Pharmacol.* 114, 1017-1025.  
Velasco A. et. al. (1997) *Gen. Pharmac.* 28, 4, 509-512.