2'-enyl)-barbituric acid (3M2B, which differs from amylobarbitone only in having a terminal double bond in the 5-C substitution) and picrotoxin (a convulsant antagonist of GABA at the receptor ionophore complex, Johnston et al., 1984).

The results are heterogeneous and paradoxical, with picrotoxin the only drug to give a uniform result (analgesia). They are summarised in the Table.

Test	Pain ratio #	Test	Pain ratio #
1. Pentobarbitone		3. Amylobarbitone	
footflick	0.82	footflick	1.57 *
tailflick	1.28 *	tailflick	1.39 *
formalin	1.04	formalin	0.77 *
constriction	1.59 *	constriction	4.90 *
2. Picrotoxin		4. 3M2B	
footflick	0.59 *	footflick	0.75
tailflick	0.65 *	tailflick	0.66 *
formalin	0.16 *	formalin	0.73 *
constriction	0.22 *	constriction	0.13 *

The ratio is of the index of pain sensitivity in saline treated animals/drug treated animals. A ratio of 1.0 indicates that nociception is unchanged by the treatment. A value greater than 1.0 indicates (after the band of statistical error has been taken into account) *hyper*algesia, while a value significantly less than 1.0 indicates analgesia.
* indicates a difference from 1.0 with a significance level of at least $P < 0.05$.

There is no obvious pattern in these results, either with a particular drug or in the acute *cf* the chronic tests. These disparities imply that different pathways must subserve the different nociceptive tests, while some but not all involve classic $GABA_A$ receptors.

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Evaluation of the analgesic effect of fluvoxamine on experimental acute and chronic pain

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Considerable evidence exits to implicate a role for the neurotransmitter serotonin (5HT) in the modulation of the nociceptive transmission (MESSING and LYTLE, 1977). Activation of the descending serotoninergic bulbospinal system produces inhibition of behavioral and dorsal horn neuronal response to noxious stimuli. For instance, increasing postsynaptic 5HT receptor activity by administration of selective 5HT inhibitors may induce antinociception in mice, rats and humans. However, variable effects of 5 HT uptake inhibitors have been reported. Antinociception as well as no effect in the hot plate and tail flick tests have been demonstrated in mice and rats. Moreover, in mice, some selective 5HT uptake inhibitors produced hyperalgesia in the formal in test. Antidepressants with 5HT inhibiting properties have been used in the treatment of chronic pain (WALSH 1983). On the other hand, sex differences in the sensitivity of mice to serotonin agonists have been reported, females are more susceptible than males (CARLSSON and CARLSSON 1988). The following experiments were undertaken to characterize the effects of

fluvoxamine (FVX) a selective inhibitor of 5 HT uptake, on several pain tests in male and female mice and rats.

Mice of the OF1 strain and Wistar rats provided by the Central Service ground of the University of Cádiz were used. The tests used were hot plate, acetic acid, tail flick and formalin test for the acute experiences and for chronic experiences we have used the deafferentation model in rats by sciatic nerve section. The right sciatic nerve was sectioned in the mid thight, and 5 to 10 mm of the distal stump was removed in order to avoid spontaneus reinervation. The autotomy degree was observed during 30 days and a tail flick test was carried out the day before surgical operation, 12 and 24 hours and 3, 8, 14, 22 and 30 days postsurgery. All experiences were conducted within the guide lines established by the International Association for the Study of Pain for research experiments in chronic animals models of pain. FVX (provided by Duphar) was injected i.p. at the doses of 0.3; 0.6; 1.25; 2.5; 5; 10; 20 and 40 mg/kg for acute experiences and at 10 twice daily for chronic experiences.

In chronic experiences it was observed that the start of autotomy behaviour did not show differences between both groups (saline 2.37 ± 0.18; FVX 2.28 ± 0.18; Mann-Whitney, $U = 25.5$, n.s.). The course of autotomy degree during the global period (30 days) showed a sensible but not significant differences as measured by AUC (Simpson's rule), (saline 63.08; FVX 48.42; $U = 21$, n.s.). The tail flick test carried out during different days of the same period showed a hyperalgesic response in control group, (Kruskal-Wallis, $H = 23.5$; $p < 0.05$), that was not present in FVX treated rats, ($H = 7.12$; n.s.).

In acute experiences FVX showed an analgesic effect in the hot plate test from the dose of 2.5 mg/kg ($U = 20$, $p < 0.05$) in female mice, while in male mice this effect was not evident until the dose of 20 mg/kg ($U = 16$, $p < 0.05$). In acetic acid method, FVX also exerted analgesic effect at lower doses in female mice (2.5 mg/kg $U = 0$, $p < 0.01$) than in males (5 mg/kg $U = 2$, $p < 0.01$). In tail flick test FVX did not exert analgesic effect in males at the doses used, however female mice showed analgesia when we used FVX from 20 mg/kg ($U = 17$, $p < 0.01$). In formal in test, the analgesic effect was slightly more evident in female mice (2.5 mg/kg $U = 18$. $p < 0.01$) than in males (2.5 mg/kg $U = 21$, $p < 0.01$).

In conclussion, FVX like other antidepressants elicits test dependent analgesic properties, besides this effect is more evident in female animals than in males.

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Central, naloxone-reversible antinociception by diclofenac in the rat

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The antinociceptive effect of diclofenac administered subcutaneously (s.c.), intracerebroventricularly (i.c.v.) and intrathecally (i.t.) was studied in a series of experiments employing the tail-flick (0,01-10 mg/kg body weight i.p.), hot-plate (0,01-50 mg/kg body weight i.p., 1-50 μg i.c.v., 1-10 μg i.t.) and writhing tests. Diclofenac produced no antinociceptive effects in the tail-flick or hot-plate models.

In the writhing test, diclofenac induced a dose-dependent inhibition of the number of writhings after s.c. administration (0,001-10 mg/kg body weight). A similar dose-dependent action of diclofenac was seen after i.c.v. (0,1-200 μg) or i.t.(0,1-100 μg) administration with an ED_{50} of 3 μg and 3 μg, respectively. The antinociceptive effect of diclofenac was reversed by naloxone, 1 mg/kg body weight, injected s.c. 5 minutes prior to the s.c., i.c.v. or i.t. administration of diclofenac.

In the colorectal distension model, the i.c.v. administration of diclofenac 1-200 μg attenuated the cardiovascular response to colorectal distension. The pressor response to a 20 seconds, 80 mm Hg colorectal distension was inhibited