Apart from methodological problems, this could mean that the decreased imipramine binding is due to the presence of an additional platelet binding site for imipramine, but not for paroxetine. The aim of the present study is to investigate this possibility.

Scatchard analyses with $^3$H-imipramine were performed with membranes preincubated with paroxetine in order to saturate the binding site on the 5HT-transporter. This results in a Bmax for $^3$H-imipramine of 200-300 fmol/mg protein.

Experiments with $^3$H-citalopram indicated that about 100 fmol/mg of these binding sites could be due to a small dissociation of the bound paroxetine. However, 100-200 fmol/mg of the $^3$H-imipramine binding may represent a 'new' binding site which is different from the imipramine binding site on the serotonin transporter. This 'new' imipramine binding site has been studied in platelets from depressed patients and control persons.

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## Neuroendocrine responses to intravenous flesinoxan as an index of serotonergic neurotransmission

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*Key words:* Flesinoxan; 5HT1A agonist; Neuroendocrine probe; Serotonin

Until now, no reliable serotonergic hormonal probe for i.v. use has been demonstrated. Flesinoxan is a highly potent 5-$HT_{1A}$ agonist ($K_i$ = 1.7), surpassing both buspirone, gepirone, and ipsapirone in receptor affinity, and affinity for other receptors by 80-fold (Olivier et al., 1990). In a double-blind placebo-controlled study, single doses of 0.5 mg and 1 mg were injected over 10 min to 12 healthy male volunteers at 1-week intervals and temperature and hormonal responses were measured over a 2-h period. Flesinoxan induced a significant and dose-dependent decrease in body temperature (mean $\delta$ = 0.03°C with placebo, 0.33°C with 0.5 mg and 0.81°C with 1 mg). Flesinoxan also induced a significant and dose-dependent increase in prolactin (mean $\delta$ peak = -38.3 mUI/l with placebo, 53.0 mUI/l with 0.5 mg and 431.3 mUI/l with 1 mg) ACTH (mean $\delta$ peak = -6.9 pg/ml with placebo, 21.5 pg/ml with 0.5 mg and 54.9 pg/ml with 1 mg), cortisol (mean $\delta$ peak = −10.2 µg/l with placebo, −3.2 µg/l with 0.5 mg and 50.2 µg/l with 1 mg) and GH (mean $\delta$ peak = 0.33 ng/ml with placebo, 0.77 ng/ml with 0.5 mg, and 3.58 ng/ml with 1 mg). The tolerance of flesinoxan was excellent and associated with a pleasant feeling of relaxation and slight drowsiness without any GI side-effect. Flesinoxan appears to fulfill all the criteria for an ideal serotonergic neuroendocrine probe and could represent a breakthrough in the neuroendocrine assessment of various psychopathological conditions.

### References

Olivier, B., Mos, J., Tulp, Mth.M., Van der Heyden, J.A.M., Ybema, C. and Slangen, J. (1990), Flesinoxan: A potent and selective 5-HT1A agonist. In Westenberg, H.G.M. (ed) Stress. Biological Rhythms and Psychiatric Disorders. Houten, Medical Didactic Systems, 1990.