ELSEVIER

RESPONSE

Response☆

We would like to thank Chalon and colleagues for their comments on the possibility that duloxetine blocks norepinephrine (NE) reuptake at doses used in clinical trials designed to assess its antidepressant properties. We agree that not all factors controlling the intravenous tyramine pressor response have been elucidated. We disagree, however, that concomitant serotonin (5-HT) reuptake inhibition may be a confounding factor when evaluating NE reuptake inhibition with an agent endowed with both properties. This is clearly indicated by the observation that the potent 5-HT/NE reuptake blocker clomipramine did produce a significant attenuation of the tyramine pressor response in the cited paper (Turcotte et al. 2001). Duration of drug treatment prior to challenge is probably not a confounding influence either, once steady state has been achieved. When the effects of clomipramine and of the NE reuptake blockers nortriptyline and reboxetine were studied after 7 days of treatment, as for duloxetine, a marked attenuation of the tyramine pressor response was observed with the former three drugs (Slater et al. 2000; Turcotte et al. 2001). A potential physiologic difference between normal and depressed patients is, however, very interesting. Indeed, after a 7-day treatment with venlafaxine, a significant attenuation of the tyramine pressor response was observed in depressed patients using 225 mg/day, but not using 300 mg/day in healthy volunteers. Plasma levels were in keeping with the doses of venlafaxine administered (Debonnel et al. 1998). Such results may in fact point to important differences between the properties of NE receptors and reuptake transporters in depression and normalcy.

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It should also be emphasized that in healthy volunteers desipramine, nortriptyline, maproptyline, amitriptyline, clomipramine, and reboxetine have produced significant attenuations of the tyramine pressor response, while paroxetine, sertraline and nefazodone have not (Ghose 1980; Hassan et al. 1985; Debonnel et al. 1998; Harvey et al. 2000; Slater et al. 2000; Turcotte et al. 2001). Therefore, before discarding the tyramine pressor test because duloxetine did not produce significant results in healthy volunteers, this drug should be tested in the population for which it is intended for (depressed patients), as was done with venlafaxine. Until a test is designed to evaluate NE reuptake in vivo in the human brain, its peripheral assessment using the intravenous tyramine pressor response still represents the most consistent paradigm available.

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