

Response[☆]

In their letter (see pg. 333), McCann and Ricaurte (2001) raise objections to a Neuropsychopharmacology editorial (Lieberman and Aghajanian, 1999) pertaining to the article by Vollenweider et al. (1998) and a subsequent letter-to-the-editor by Gijnsman et al. (1999). Our editorial stated, “. . . the data do not support the view that single oral doses at 1.7 mg/kg of MDMA are likely to produce damage to serotonin terminals in humans” (Lieberman and Aghajanian, 1999). McCann and Ricaurte argue that if interspecies dose scaling is applied to the human dose that was used by Vollenweider et al. (1999) (i.e., 1.7 mg/kg), this would be within the range of the “known” single oral neurotoxic dose of MDMA in the monkey (5.0 mg/kg). It should be noted, however, that our editorial was aimed at the issue, of whether it had actually been demonstrated that a single 5.0 mg dose of MDMA was in fact neurotoxic in the monkey.

The salient passage from our editorial was as follows: “The key study that the authors [i.e., Gijnsman et al., 1999] cite to support their point is that of Ricaurte et al. 1988), who reported that a single 5 mg/kg dose of MDMA produced long-term damage (assessed at two weeks) to the serotonin system in non-human primates. An examination of these data, however, indicate that while multiple oral doses of 5 mg/kg MDMA produced a large depletion of serotonin in all regions examined, a single oral dose produced no change in the frontal cortex, hippocampus, putamen, or caudate, and only a small change in the thalamus and hypothalamus. The absence of depletion in the frontal cortex and caudate by a single dose is particularly important because these regions receive the type of fine fiber afferents from the dorsal raphe nucleus that have been shown to be most sensitive to MDMA neurotoxicity (O’Hearn et al. 1988; Wilson et al. 1989)”. Given these equivocal results, which were obtained with an “n” of three, it remains

unclear as to whether a single dose of 5 mg/kg of MDMA is in fact neurotoxic in the monkey. One would wish for more extensive dose-response data to determine the threshold for clear-cut neurotoxicity of single oral doses of MDMA in the monkey, especially in regions that are known to be vulnerable after chronic administration (e.g., frontal cortex and striatum). However, in the absence of such data, it would seem premature to conclude that a single oral dose of 1.7 mg/kg is likely to be neurotoxic in humans.

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