

A. C. Parrott · T. Buchanan · T. M. Heffernan ·
A. Scholey · J. Ling · J. Rodgers

Parkinson's disorder, psychomotor problems and dopaminergic neurotoxicity in recreational ecstasy/MDMA users

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In a recent article in *Science*, Ricaurte et al. (2002) reported dopaminergic neurotoxicity following closely spaced doses of MDMA in squirrel monkeys and baboons. They noted that its implications for human behaviour would need to be investigated, and raised the crucial question of why, if dopamine tracts are also being damaged in humans: "...more cases of MDMA-induced parkinsonism have not been reported". We would like to discuss the human implications of their article, and commence by quoting the following passage from Peroutka et al. (1988, p. 276), which was the very first empirical study of recreational MDMA users ever to be published:

"The major question that remains unanswered is whether MDMA produces neurotoxicity in human users of the drug. An analogy between MDMA and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) may be appropriate. MPTP is a selective neurotoxin to the substantia nigra that was sold as "synthetic heroin" to recreational drug users (Davis et al. 1979; Langston et al. 1983, 1984; Snyder 1984). Approximately 400 people in the San Jose, California, area are known to have been exposed to MPTP. Importantly, only seven of these patients currently

have clinical evidence of Parkinson's syndrome (Langston et al. 1983, 1984). However, positron emission tomography on four of the clinically normal patients has documented significant depletions of dopamine (Caine et al. 1985). These studies demonstrate that significant dopaminergic toxicity due to recreational MPTP use can exist in the absence of clinical deficits".

The above quotation illustrates that clinical manifestations may not always be apparent, even with a known dopaminergic neurotoxin. However, there is evidence for psychomotor problems in a minority of abstinent ecstasy/MDMA users. The acute side-effects described by recreational MDMA users include motor tics, twitches, muscular aches and pains (McCann et al. 1996; Kalant 2001). They tend to occur in the period immediately following drug use, although they can be more enduring. Thus one of our regular users complained that since first taking ecstasy, he now often made unconscious arm movements when drug-free: "I do not even realize that I am moving my arm until my friend tells me to stop...it may have caused some permanent damage or something" (Parrott and Lasky 1998, p. 267). Three of the 15 ecstasy users from Rodgers (2000) complained of making odd psychomotor movements when drug-free, including repetitive hand flicks "back and forth sometimes unconsciously", and spontaneous dance movements "like I have been programmed". In a recent study of 282 abstinent ecstasy users, we covered a number of potential problem areas (Parrott et al. 2002). Off-drug tremors or twitches attributed to ecstasy/MDMA, were reported by 14% of novice users (1–9 lifetime ecstasy occasions), 20% of moderate users (10–99 occasions), and 38% of experienced users (>100 lifetime occasions: dosage effect, $P<0.01$). Many other problems attributed to ecstasy were also reported, but generally at higher incidence rates. For instance, memory problems attributed to ecstasy were reported by 19% of novice users, 52% of moderate users, and 73% of heavy users ($P<0.001$); depression attributed to ecstasy was noted by 33% of novice users, 54% of moderate users, and 65% of heavy users ($P<0.001$). Thus while drug-attributed psychomotor problems were report-

A. C. Parrott (✉)
Department of Psychology,
University of East London,
London, UK
e-mail: a.c.parrott@uel.ac.uk

T. Buchanan
University of Westminster,
London, UK

T. M. Heffernan · A. Scholey
Northumbria University,
Newcastle-upon Tyne, UK

J. Ling
University of Teesside,
Middlesborough, UK

J. Rodgers
University of Newcastle,
Newcastle-upon-Tyne, UK

ed, they were only noted by a comparative minority of users (Parrott et al. 2002), which may help explain why they have not featured much in previous research.

In conclusion, we agree that the psychomotor functioning of drug-free ecstasy/MDMA users should be a key topic for future research. However, we would urge that broad approach towards assessment be taken, since the changes reported by ecstasy/MDMA users are rather idiosyncratic, and do not fit neatly with current diagnostic categories. It might be predicted that users with initial psychomotor signs, would be at greatest risk from developing Parkinson's disease later. Finally, the contributory role of other recreational dopaminergic drugs should also be monitored (e.g. amphetamine), since many regular ecstasy/MDMA users take a variety of CNS stimulants (Scholey et al. 2003).

References

- Caine DB, Langston JW, Martin WRW (1985) Positron emission tomography after MPTP: observations relating to the cause of Parkinson's disease. *Nature* 317:246–248
- Davis GC, Williams AC, Markey SP (1979) Chronic Parkinsonism secondary to intravenous injection of meperidine analogues. *Psychiat Res* 1:249–254
- Kalant H (2001) The pharmacology and toxicology of "ecstasy" (MDMA) and related drugs. *Can Med Assoc J* 165:917–928
- Langston JW, Ballard P, Tetrad JW, Irwin L (1983) Chronic Parkinsonism in humans due to a product of meperidine-analogue synthesis. *Science* 219:979–980
- Langston JW, Ballard P (1984) Parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP): implications for treatment and pathogenesis of Parkinson's disease. *Can J Neurol Sci* 11:160–165
- McCann UD, Slate SO, Ricaurte GA (1996) Adverse reactions with 3,4-methylenedioxymethamphetamine (MDMA; "Ecstasy"). *Drug Safety* 15:107–115
- Parrott AC, Lasky J (1998) Ecstasy (MDMA) effects upon mood and cognition; before, during, and after a Saturday night dance. *Psychopharmacology* 139:261–268
- Parrott AC, Buchanan T, Scholey AB, Heffernan TM, Ling J, Rodgers J (2002) Ecstasy/MDMA attributed problems reported by novice, moderate and heavy users. *Hum Psychopharmacol* 17:309–312
- Peroutka SJ, Newman H, Harris H (1988) Subjective effects of 3,4-methylenedioxymethamphetamine in recreational users. *Neuropsychopharmacology* 1:273–277
- Ricaurte GA, Yuan J, Hatzidimitriou G, Cord BJ, McCann UD (2002) Severe dopaminergic neurotoxicity in primates after a common recreational dose regimen of MDMA ("Ecstasy"). *Science* 297:2260–2263
- Rodgers J (2000) Cognitive performance amongst recreational users of "ecstasy". *Psychopharmacology* 151:19–24
- Scholey AB, Parrott AC, Buchanan T, Heffernan TM, Ling J, Rodgers J (2003) Increased intensity of ecstasy and polydrug use in the more experienced ecstasy users. *Addict Behav* (in press)
- Snyder SH (1984) Clues to aetiology from a toxin. *Nature* 311:514