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Title **The Harmful Health Effects of Recreational Ecstasy: A Systematic Review of Observational Evidence**

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Aim

To investigate the harmful health effects of taking ecstasy (3,4 methylenedioxymethamphetamine, MDMA) for recreational purposes.

Conclusions and results

A broad range of relatively low quality literature suggests that recreational use of ecstasy is associated with significant deficits in neurocognitive function (particularly immediate and delayed verbal memory) and increased psychopathological symptoms. The clinical significance of the exposure effect in individual cases will vary, but deficits are likely to be relatively small. Ecstasy is associated with acute harm, but appears to be a rare cause of death. Five Level I syntheses were identified. Small but significant deficits for ecstasy users compared to controls were reported, relating to attention, memory, psychomotor speed, executive systems functioning, and self-reported depressive symptoms. Data from Level II studies were directly pooled for 7 individual outcomes, suggesting that ecstasy users performed worse than controls on common measures of immediate and delayed verbal recall. No difference was seen in IQ. The 915 outcome measures identified in Level II studies were analyzed in broad domains. Ecstasy users performed significantly worse than polydrug controls in 13/16 domains and significantly worse than drug naïve controls in 7/12 domains for which sufficient data were available. The largest, most consistent exposure effects were seen in meta-analyses of memory (especially verbal and working memory. Former ecstasy users frequently showed deficits that matched or exceeded those seen among current users. At the aggregate level, the effects do not appear to be dose-related, but are variably confounded by other drug use, particularly alcohol. Of Level III evidence, in the 10 years to 2006, the np-SAD and the GMR recorded an average of around 50 drug-related deaths per year involving ecstasy; it was the sole drug implicated in around 10 cases per year. Retrospective case series, based on hospital emergency department records, reported a death rate up to 2% from emergency admissions related to ecstasy. Two major syndromes are most commonly reported as the immediate cause of death in fatal cases: hyperthermia and hyponatremia. For further details see Executive Summary link www.hta.ac.uk/project/1695.asp.

Recommendations

See Executive Summary link www.hta.ac.uk/project/1695.asp.

Methods

See Executive Summary link www.hta.ac.uk/project/1695.asp.

Further research/reviews required

Large, population-based, prospective studies need to examine the time relationship between ecstasy exposure and neurocognitive deficits and psychopathological symptoms. Further research synthesis of the social and other indirect health harms of ecstasy would provide a more complete picture. Similar synthesis of the health harms of amphetamines would provide a useful comparison. Cross-sectional studies will add to the evidence base only if they are large, as representative as possible of the ecstasy-using population, use well-validated outcome measures, measure outcomes as objectively as possible with researchers blind to the ecstasy-using status of their subjects, report on all outcomes used, and provide complete documentation of possible effect modifiers. Cohorts should be matched for baseline factors, eg, IQ and exposure to alcohol. The heterogeneity of outcome measures used by different investigators is unhelpful: consensus on the most appropriate instruments to use should be sought.

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