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COMMENT ON HALPERN ET AL. (2011)

The study by Halpern and co-workers [1] published recently in this journal reports findings in which ecstasy users with modest use of other drugs did not exhibit deficits on the majority of measures that were administered. This paper may be criticized on a number of grounds, but our focus here will be on two main areas: the nature of the sample and the choice of measures that were administered.

First, as the authors acknowledge, the sample is not representative of typical ecstasy/polydrug users. While the stated rationale for this choice has its merits, clearly it limits the generalizability of any inferences that might be drawn. More specifically, relatively heavy users of ecstasy are not well represented in Halpern *et al.*'s sample. Furthermore, the absence of an ecstasy-related deficit on many of the measures does not give ecstasy a clean bill of health (as the authors acknowledge), as the restriction on the use of other drugs reduces the possibility of detecting cocktail effects in which ecstasy may interact with other drugs such as alcohol, producing both acute and more longer-lasting deficits [2].

The second criticism of Halpern *et al.*'s study involves the choice of measures that were used. First, as in many studies concerning illicit drug use the tests administered were not informed by current theoretical perspectives in cognitive psychology. Many of the measures that are commonly used were developed for use with clinical groups and often lack the sensitivity to detect the subtle deficits present in recreational drug users. Furthermore, it is not surprising that many of the measures administered by Halpern *et al.* failed to reveal ecstasy-related deficits because these measures have failed to do so in the past. For example, four of five studies utilizing the Trail-Making Test Part B (TMT-B) revealed no statistically significant differences (the remaining one yielding ambiguous results) [3]. Furthermore, a recent review of the literature [4] has demonstrated that, in relation to the Wisconsin Card Sorting Test (WCST) and the Stroop test, the majority of studies have failed to reveal ecstasy-related deficits; and only half of those studies using the F, A and S letter variant of the verbal fluency paradigm reported statistically significant ecstasy-related deficits. It is worthy of note that a more demanding task, Chicago word fluency, has been found to be associated with ecstasy-related deficits. The same review [4] has also shown that the majority of studies using simple spatial span or Corsi block tapping also failed to reveal ecstasy-related deficits.

Utilizing recent perspectives from cognitive psychology, in a number of studies [5,6] we have demonstrated that ecstasy/polydrug users are selectively impaired in executive pre-frontal tasks which require the updating of the contents of the working memory system. Other executive component processes which require the switching of attention (e.g. as assessed by the TMT-B and the WCST) or the inhibition of pre-potent responses (the Stroop) appear to be spared. Thus, in closing, we would argue that Halpern *et al.*'s results were not entirely unexpected. However, the implications of their findings are perhaps rather limited.

Declarations of interest

None.

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‘ECSTASY USE, BY ITSELF, DOES NOT RESULT IN RESIDUAL NEUROTOXICITY’ – A POWERFUL ARGUMENT?

We read with interest the paper published in this journal by Halpern and colleagues [1], which reported findings from a study examining cognitive function in ecstasy/3,4-methylenedioxymethamphetamine (MDMA) users. The authors conclude that they had failed to demonstrate ‘marked residual cognitive effects in ecstasy users’ and they suggest that their data may indicate that ecstasy use, by itself, does not result in ‘residual neurotoxicity’. The publication of this paper has resulted in significant press coverage in the United Kingdom, including a report in the *Guardian* newspaper which concludes that ‘There is no evidence that ecstasy causes “brain damage”’ [2]. Given the prevalence of ecstasy use, a well-designed and credible study that demonstrated no long-term sequelae would indeed be very welcome; however, we have significant concerns about the study, the conclusions drawn and the subsequent over/misinterpretation of the findings by the popular media, which may mislead the public into assuming that ecstasy can be used without risk.

A key objection to Halpern *et al.*’s conclusion concerns the statistical power of the study and the effect sizes expected for the impact of ecstasy use on cognitive function. Halpern *et al.* present the maximum effect size that their design could exclude for each measure tested (i.e. they could say confidently that if an effect of that magnitude existed then their design would find it). They report

that ‘we could exclude even a medium effect (Cohen’s $d \geq 0.5$) on many cognitive measures’ (p. 106). The problem here is that the typical effect sizes reported in previous research are lower than their threshold of likely detection. For example, Zakzanis *et al.* (2007) [3] conducted a meta-analysis of 35 empirical comparisons of the effects of ecstasy use on multiple domains of cognitive function. They present effect sizes (Cohen’s d adjusted for sampling bias) for each of these domains. For those cognitive domains where the effect size was significantly different to zero, the majority were below the magnitude $d \geq 0.5$ that Halpern *et al.* were confident of detecting (for learning and memory, $d = -0.55$; for verbal comprehension, $d = -0.36$; for processing speed, $d = -0.33$; for attention and concentration, $d = -0.27$; for executive function, $d = -0.26$; Zakzanis *et al.* 2007 [3], p. 431). Therefore, Halpern *et al.*’s design was not capable of detecting the effects found typically in similar research because their sample size was too small. The median value for the effect sizes Zakzanis *et al.* reported as significantly different from zero was -0.33 . The Halpern *et al.* study had two groups ($n = 59$ and $n = 52$). Using power analysis package G*Power 3 to determine *post-hoc* achieved power for the Halpern study, based on an independent-samples *t*-test comparing the groups’ achieved power was found to be only 0.405.

That is, if comparing the two groups directly with this (typical) magnitude of effect size and these numbers of participants, Halpern *et al.* had only a 40.5% chance of finding a significant difference between the groups should one actually exist. Their design simply does not have sufficient statistical power to detect effects of the magnitude found typically in comparisons of cognitive function between ecstasy users and non-users and is at significant risk of type II error.

It is also curious that having developed such an extensive test battery the authors downplay the significant differences that are detected between the groups on a variety of cognitive tasks, including memory, vocabulary and fine motor skills. The fact that the authors managed to detect significant differences on any measures despite very low statistical power indicates that these effects are real and important and should not be diminished.

It is also interesting to note that Halpern *et al.*’s paper makes no reference to the growing body of research into ecstasy-related memory deficits within a real-world context, such as prospective memory (PM) deficits. Given the expanding evidence base within this domain, including the observation that PM deficits persist after statistically controlling for other drug use [4], it would appear remiss of the authors to have excluded such research.

Research into the putative impact of ecstasy use is extensive, with many hundreds, if not thousands, of