Commentary on Morgan et al. (2010): Ketamine abuse: first medical evidence of harms we should confront

Ketamine is usually included in the ‘club’ drugs category that comprises psychotropic substances used in bars and clubs, at concerts and parties in combination with alcohol and cannabis. Ecstasy [3,4-methylenedioxymethamphetamine (MDMA)], gamma-hydroxybuturrate (GHB), flunitrazepam, methamphetamine, lysergic acid diethylamide (LSD) and ketamine are considered club drugs, although differences among countries may be found in terms of those misused more prevalently. One of the most popular drugs in this category in the past has been ecstasy. The synthesis of this compound is highly dependent upon the illicit import of some chemical synthetic precursors (e.g. MDP2P or its precursor isosafrole). In recent years ecstasy has been more difficult to find on the market [1]. While there are probably a number of contributory factors, the shortage of ecstasy on the market has meant that users have looked with more interest at other drugs, such as ketamine, speed (methamphetamine and amphetamine sulphate in Europe), ‘smart’ drugs and research chemicals [2].

Ketamine, an antagonist of the excitatory neurotransmitter glutamate at the N-methyl-D-aspartate (NMDA) receptors, is used in clinics for the induction and maintenance of general anaesthesia, sedation in intensive care, analgesia and treatment of bronchospasm. It is also a popular anaesthetic in veterinary medicine. Little attention has been paid to the misuse of this substance until recently, when a sizeable amount of young people began to abuse it. We do not know how many people use ketamine, and there is a need for research to identify trends in the population prevalence of these drugs. This could be achieved most easily by the inclusion of ketamine in household surveys that are currently collected routinely in a number of countries [3]. According to the Monitoring the Future (MTF) Survey in the United States (http://www.drugabuse.gov/InfoFacts/clubdrugs.html), in 2007 ketamine consumption was reported by 1.0% of 8th graders, 0.8% of 10th graders and 1.3% of 12th graders. Nevertheless, there is almost no mention of ketamine in the last United Nations Office on Drugs and Crime (UNODC) 2009 World Drug Report [4] or in the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2008 Annual Report [5]. Despite the lack of good studies concerning the consumption of ketamine among young people, there is a general consensus that it is increasing and that prices are falling.

Recreational use of ketamine has been associated with cognitive impairment and with a larger prevalence of psychopathology among users [6]. Scientific evidence of these dangers in the last 2 years has been provided mainly by Morgan and colleagues. In a cross-sectional study [7], frequent users of ketamine displayed impairments in working and episodic memory and executive functions and experienced reduced psychological wellbeing. In the current paper [8], the same population from the cross-sectional study was followed-up during 1 year. The same evaluation protocol was applied and cognitive deficits were confirmed mainly among frequent ketamine users. The picture is not substantially different from what we know from frequent ecstasy users; most probably the most distinctive aspects among ketamine users are alterations in psychological wellbeing, with a higher prevalence of dissociative symptoms and a dose–response effect on delusional symptoms (frequent users versus infrequent users versus abstinent users versus drug-free subjects).

The authors were able to recruit a population of frequent ketamine users who use relatively few other club drugs. Other drug use and any psychiatric diseases were controlled for adequately. We are waiting for further reports from this group describing psychiatric diagnoses prior to their inclusion in the study, as well as potentially new diagnoses (e.g. affective disorders, psychosis) during the follow-up among ketamine frequent users. It should not be forgotten that ketamine has been used in humans as a probe compound to model schizophrenia, as some of the effects induced by this drug mirror cognitive and perceptual alterations seen in this psychiatric disease [9,10].

Regardless of a good selection of subjects in this study, we should bear in mind that currently the vast majority of ketamine users are still polydrug users, and that clinical consequences attributable to a single compound are almost impossible to assess [11,12]. This would be the case concerning the transmission of infectious diseases and the status of the immune system among polydrug users [13]. Club drugs are used recreationally because they decrease social inhibitions; in this context they have been used to heighten sexual experience [14]. Consumption of club drugs increases sex risk behaviours among human immunodeficiency virus (HIV)-positive men who have sex with homosexual and bisexual men [15,16]. The increased risk of infectious disease transmission has to be combined with the fact that several club drugs such as ecstasy alone, or in combination with cannabis and alcohol, have already shown deleterious interactions with the immune system in humans in the mid- to long term, and that some users administer ketamine intravenously [17,18]. Ketamine is a well-known immune
modulator and, as for most club drugs, it behaves as an immunosuppressive drug [19]. The interaction of high non-therapeutic doses of non-pharmaceutical ketamine with the immune system among drug users awaits further studies confirming immune-induced alterations with clinical implications in the transmission of infectious diseases.

Morgan and co-workers provide the first evidence of the dangers we will confront among frequent ketamine users in the cognitive and psychological wellbeing domains. Now it is the time to disseminate these findings among young people and clinicians.

Declaration of interest
None.

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References