Monitoring illicit psychostimulants and related health issues

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Chapter 5

Impact of a transient instability of the ecstasy market on health concerns and drug use patterns in The Netherlands

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Abstract

Background: Recently, a profound decline in MDMA-like substances in ecstasy tablets has been reported for a number of countries within the European Union. This study aims to describe this instability of the ecstasy market in The Netherlands during 2008 and 2009 and investigates whether this had any impact on health concerns and drug use patterns of drug users. Methods: The effect of the ecstasy market instability on the health concerns of drug users handing in drug samples at drug testing facilities was measured using intervention time-series analysis. In addition, ecstasy users handing in tablets were asked about changes in their drug use pattern. Results: Nationwide, the instable situation on the ecstasy market showed an impact on the number of users handing in ecstasy tablets for the reason of health concerns. This impact was substance specific, since there was no impact the number of users handing in cocaine or gamma hydroxybutyrate (GHB). Despite increased health concerns, respondents reported no major changes in their drug use due to the shortage of MDMA-like substances. Conclusions: These findings provide further insight in drug policy based on both harm reduction and use reduction. In the event of reduced ecstasy quality, ecstasy users in The Netherlands increasingly utilized drug testing as a potential harm reduction tool, but there was no change in their drug use pattern. This might indicate that a transient reduction of drug quality does not serve as a good drug use reduction strategy for ecstasy users.

Introduction

One of the foremost clandestine manufactured synthetic drugs that has gained worldwide popularity in the party scene is ecstasy (3,4-methylenedioxymethamphetamine or MDMA) (EMCDDA, 2010; UNODC, 2010). The ecstasy market in The Netherlands during the last decade has been described to be relatively stable in terms of MDMA content (Vogels et al., 2009). The percentage of tablets containing an MDMA-like substance (MDMA and its structural analogues 3,4-methylene-dioxyamphetamine
(MDA), 3,4-methylene-dioxyethylampheta mine (MDEA) and N-methyl-a-
(1,3-benzodioxol-5-yl)-2-butamine (MBDB)) varied between 80% to more
than 95% from 1999 to 2008. However, during 2008, the percentage of
ecstasy tablets containing MDMA-like substances (MLS) declined rapidly,
resulting in a situation in the first six months of 2009 with only 40% of the
tablets containing MLS (Brunt et al., 2010). A decline in MLS has also been
described for other countries within the European Union (EU) during the
same time period (EMCDDA, 2010; UNODC, 2010).

Various reasons have been suggested underlying the decline of MLS in the
EU: redirected export and import, law enforcement measures to curtail
manufacture, and increased efforts to prevent diversion of precursors to
manufacture MLS, such as piperonyl methyl ketone (PMK) (UNODC,
2010). Whatever the background, this shortage of MLS in The Netherlands
provided a unique natural experiment to study the impact of declining
ecstasy quality on the behaviour of drug users. Shortages on the drug or
alcohol consumer market have been conceptualized before as natural
experiments to provide insights into environmental, sociological or physical
phenomena (Smithson et al., 2004; Cunningham & Liu, 2003, 2005;
Gilmour et al., 2006; Asbridge & Weerasinghe, 2008; Callaghan et al.,
2009). However, these studies were restricted to drugs with a high
addictive potential (e.g. heroin, methamphetamine) and very little research
has been devoted to relatively less addictive drugs of abuse, such as
ecstasy.

The aim of this study is to establish the impact of the shortage of MLS on
health-related behaviour of ecstasy users. More specifically, a convenience
sample of drug users that submit ecstasy tablets to the drug testing
facilities of the Drug Information and Monitoring System (DIMS) in The
Netherlands is investigated. Drug users can hand in their drug samples at
the DIMS and provide additional information, such as their main reason for
having drugs analyzed. After toxico-chemical analysis, they receive
information about the content of the tablets or powders they handed in
(Spruit, 2001; Vogels et al., 2009). It has been established in previous
research that one of the main reasons why drug users utilized the drug
testing system was health concerns (Benschop et al., 2002). In the current
study, data of the collected drug samples at the DIMS are analysed prospectively, i.e. comparing the number of users handing in drug samples preceding, during and after the event of shortage of MLS by intervention time-series analysis. This analysis method has been frequently used by others to study the impact of a natural event on regularly collected surveillance data on different health outcomes of interest (Cunningham & Liu, 2003, 2005; Gilmour et al., 2006; Koski et al., 2007; Asbridge & Weerasinghe, 2008; Callaghan et al., 2009; Hertua et al., 2009). Shortage of MLS might also have led to a change in drug use, since many ecstasy users are in fact polydrug users (Gouzoulis-Mayfrank & Daumann, 2006; Medina & Shear, 2007; Wu et al., 2009). Previous studies describing reductions in drug availability also addressed the issue of drug consumers switching to other, better available, drugs or quitting drugs altogether (Topp et al., 2003; Weatherburn et al., 2003). Alternatively, drug users might compensate lower quality by increasing the number of ecstasy tablets they ingest to obtain the desired effect (Tanner-Smith, 2006). Therefore, the current study examines whether the decline of MLS led to subsequent changes in drug use patterns among a convenience sample of ecstasy users.

This is the first study investigating the impact of a real world reduction in the quality of ecstasy on the drug users’ behaviour. The outcomes will be discussed in the context of drug policy and drug-related use or harm reduction strategies.

**Methods**

**Drug data**

All drug samples were collected at the DIMS according to the methods described previously by Vogels et al. (2009). The DIMS covers all provinces and major cities in The Netherlands. Briefly, drug users handed in their drugs voluntarily and free of charge at a DIMS testing facility, in order to find out the chemical contents of the specific drugs they purchased and whether there were unexpected health risks associated with those purchases. The prevention professionals at the testing facilities
communicated the analysis outcomes to the users. The drugs were analysed by gas spectrometry coupled to mass spectrometry. For this study, all tablets containing at least a trace of any of the MLS were specified as percentage tablets containing MLS.

Within the DIMS, drug samples are tested on a weekly basis. This allows for a very detailed monitoring of the situation on the street drug market and DIMS data can be considered as the best possible up-to-date indicator of the illicit drug market in The Netherlands. DIMS data are used annually by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), which in turn supplies information to the United Nations Office on Drugs and Crime (UNODC) (EMCDDA, 2010; UNODC, 2010). Comparison of the DIMS data with those of 'seized samples' by the police from various cafés, clubs and dance venues in The Netherlands has shown that DIMS data are representative for the Dutch drug market (Vogels et al., 2009).

**Measuring impact on drug users**

One of the routine questions asked at the drug testing facilities is why the drug user wants to have a particular drug tested; one the foremost reasons given for testing drugs was “health concerns” (Benschop et al., 2002). The possible impact of the shortage of MLS on the number of users utilizing drug testing facilities for various reasons, and especially “health concerns”, was investigated with monthly time series of users handing in ecstasy tablets. Control series of users handing in other drugs at DIMS for the reason of health concerns were included in the analysis to check for further specificity of the impact of the intervention (i.e. MLS shortage) and to exclude possible confounders affecting supply of drug samples to the DIMS system. Possible confounders include increased popularity or accessibility of the testing facilities in general or some other underlying cause. Similar shifts in the use of the test services for cocaine and GHB as for ecstasy would be suggestive of another explanation than the specific shortage of MLS. Cocaine and GHB were used because these drug markets were reported to be stable in terms of purity throughout the studied period (Van Laar et al., 2010). In addition, these drugs are often
reported to be used by the same groups in the club circuit that also use ecstasy (Grov et al, 2009; Van Laar et al., 2010).

*Time series analysis*

Because the exact time of onset of shortage of MLS (the intervention event) was not reported by the available official sources, it was inferred in an exploratory fashion, as previously described by others (Smithson et al., 2005; Gilmour et al., 2006; Wood et al., 2006). It was possible to infer the time of onset using the chemo-analytical monitoring data on ecstasy tablets as an objective and reliable source for timing the event of the shortage of MLS. To obtain a more rigorous set of validity criteria, two different parameters of MLS shortage were used simultaneously and findings were cross-referenced: percentage of tablets containing MLS and average dose of MDMA per tablet (in mg), on the assumption that these two measures are defining parameters of a shortage of MLS. Both timelines were analyzed using a change-point analysis method (for more details, see Taylor, 2000). Change points with probabilities of >99% were identified and the cross-referencing of both timelines revealed common change points. Average dose of MDMA was taken as an indicator of the ecstasy quality, because the presence of other MLS on the Dutch market was very low during the entire studied period, and because other MLS are not dosage-equivalent.

Autoregressive Integrated Moving Average (ARIMA) intervention time-series analysis was used to investigate the impact of the shortage of MLS on the number of users handing in drugs at the drug testing facilities. For all time series, the model fitting and noise component was estimated using pre-intervention time series (Box & Jenkins, 1975; Box & Tiao, 1976). Except for the intervention, the ARIMA model was fitted directly to the series, the intervention was then modelled and the nature of the time series after the intervention was estimated by applying transfer functions. In order to describe the relationship between the intervention and its effect, the best candidate model was determined according to the following criteria: smallest Akaike Information Criterion (AIC), autocorrelation function (ACF) and partial autocorrelation function (PACF). ARIMA models were fitted to
the time series, adjusting for outliers, serial dependence, autocorrelation and adjusting for seasonal effects. SPSS version 15.0 was used for all ARIMA statistics.

Drug use patterns

Possible changes in drug use patterns during the MLS shortage were investigated by self-reports of ecstasy users at the DIMS testing facilities. Participants were asked whether they were frequent users (i.e. at least monthly use of ecstasy) and whether they were aware of the shortage of MLS (the main inclusion criteria). 914 users handing in tablets sold as ecstasy completed questionnaires and 761 were eventually included. The others were excluded, because post hoc inclusion criteria revealed no frequent ecstasy use or no ecstasy use altogether. In compliance with basic DIMS guidelines, the participants were treated anonymously. Therefore, no additional information was asked. Questionnaires were collected from May 1st 2009 until October 1st 2009.

Results

Shortage of MLS

Three change points were identified (> 99% confidence) on the timeline of percentage of tablets containing MLS, and five change-points (> 99% confidence) on the timeline of average dose MDMA/tablet (Figure 1). Of these, two common change-points were identified (November 2008 and December 2009), whereas the other change points showed no overlap. The first change point (November 2008) was taken as time of onset of MLS shortage, the second as time of offset. The period in between was considered the intervention interval.
Figure 1. Graphical display of the timelines of percentage of tablets containing MLS and average content of MDMA per tablet in mg with arrows denoting change points detected by change point analysis; black arrows, change points not showing overlap between timelines; white arrows, change points showing overlap between timelines.
Drugs handed in at DIMS

A total of 22,280 users handed in ecstasy tablets during the period January 2004 - September 2010 motivated by various reasons. 13,445 users specifically indicated “health concerns” as reason for having their ecstasy tablet analyzed. A seasonal effect seemed to be present, with relatively more users handing in tablets during summertime (Fig. 2). The number of users indicating “health concerns” in the pre-intervention period (until November 2008) ranged from 90 to 169 per month. A sharp increase in the slope of the time series was visible in the beginning of 2009, indicating that many more users were handing in tablets because of health concern by this time. The increase resulted in a maximum of 395 users in July 2009, then steeply declined during the second half of 2009 and towards the beginning of 2010 and then stabilized at a level that was still relatively high compared to the period before 2008. No shifts of this magnitude in the patterns of any of the control time series (ecstasy other reasons, cocaine health concerns, GHB health concerns) were detectable upon visual inspection (Fig. 2).
Figure 2. Number of drug users handing in ecstasy tablets, cocaine samples and GHB samples from January 2004 - September 2010, intervention interval indicated by dotted lines.
**Intervention analysis**

Based on the pre-intervention time series the best fitting ARIMA models were determined and shown in Table 1. The study of the ACF and PACF suggested a \((1,0,0)(0,1,1)_12\) model for the time series of users handing in ecstasy because of health concern, with differencing required for removing the seasonal trend. Then, the nature of the transfer function was tested on the time series of health concern and the hypothesis of a gradual, temporary intervention effect was rejected (according to McCleary & Hay, 1980). Subsequently, the intervention effect was modelled as a step function. ARIMA intervention analysis was done, with time points coding 1 for the intervention interval and 0 for the remaining time points as the intervention dummy variable. Box-Ljung Q statistics revealed that residuals of all analyses were consistent with white noise for the first 24 lags (Table 1, last row). The impact of the intervention interval (i.e. shortage of MLS) on the number of users handing in drugs was expressed by the estimated coefficient for the intervention dummy variable. The estimated number of users handing in tablets because of “health concern” increased after the intervention with 62 users per month (Table 1). Intervention analysis revealed no significant impact of the shortage of MLS for each of the control series.

**Changes in drug use pattern**

Out of 761 ecstasy users that completed the questionnaires, 555 (72.9%) indicated that they had not changed their drug use pattern after they knew about the shortage of MLS (Fig. 3). The others reported that they had decreased their ecstasy use (8.2%), increased their ecstasy use (4.8%), switched to other substances (12.7%) or stopped using drugs altogether (1.4%). The 12.7% ecstasy users that reported a switch mainly indicated using cocaine instead of ecstasy, often in combination with alcohol (Fig. 4). Of the 72.9% users reporting no change in their drug use, about 25% indicated in the free space for comments to be more cautious about the
source of their ecstasy and more alert on testing before using future ecstasy purchases.

**Figure 3.** Drug use patterns of ecstasy users, following the shortage of MLS.

**Figure 4.** Frequencies of the different drugs used by ecstasy users that switched to other drugs than ecstasy.
Table 1. Impact of shortage of mdma-like substances on the number of users handing in drug samples; ARIMA model parameter estimates.

<table>
<thead>
<tr>
<th>Dependent variables</th>
<th>Ecstasy health concern $(1,0,0)(0,1,1)_{12}$</th>
<th>Ecstasy other reasons $(0,0,1)(0,0,1)_{12}$</th>
<th>Cocaine $(0,1,1)$</th>
<th>GHB $(1,0,1)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARIMA-intervention parameters</td>
<td>Estimate</td>
<td>SE</td>
<td>t</td>
<td>Estimate</td>
</tr>
<tr>
<td>Intervention</td>
<td>61.70**</td>
<td>19.46</td>
<td>3.17</td>
<td>6.92</td>
</tr>
<tr>
<td>AR(1)</td>
<td>0.90**</td>
<td>0.05</td>
<td>9.98</td>
<td>-</td>
</tr>
<tr>
<td>MA(1)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.95**</td>
</tr>
<tr>
<td>SMA(1)</td>
<td>0.60*</td>
<td>0.18</td>
<td>3.11</td>
<td>-0.96</td>
</tr>
<tr>
<td>Box-Ljung test (24 lags)</td>
<td>Q = 16.55 ($p = 0.42$)</td>
<td>Q = 21.77 ($p = 0.15$)</td>
<td>Q = 10.26 ($p = 0.89$)</td>
<td>Q = 19.01 ($p = 0.33$)</td>
</tr>
</tbody>
</table>

AR: autoregressive term; MA: moving-average term; SMA: seasonal moving-average term; *$P < 0.01$; **$P < 0.001$. 

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Discussion

The present results suggest that the recent shortage of MLS was accompanied by an increase in health concern among Dutch ecstasy users who visited drug testing facilities. Apparent efforts made by more users to visit these testing facilities for health concerns largely reflected the need for reassurance. The increase in the number of ecstasy users with approximately 62 per month after the shortage of MLS might also indicate a rapid increase in awareness about the situation of the ecstasy market among users throughout The Netherlands. This was confirmed by personal communication with the testing facilities, which revealed many first time visitors during 2009 and more awareness than usual through their own experiences, friends or internet about the shortage of MLS. Alternative hypotheses for the increase in ecstasy testing, such as increased population prevalence of ecstasy use, were not supported by any national figures (Van Laar et al., 2010).

It is important to note that, in general, there were no immediate reasons for major health concern during the period of shortage of MLS from a public health perspective: e.g. no new substances were found in tablets sold as ecstasy that were known to cause acute toxicity. Nevertheless, there might have been grounds for concern among ecstasy users. A host of alternative substances were sold as ecstasy during the shortage of MLS to meet the market demand: 2C-B, amphetamine, methamphetamine, 4-fluoroamphetamine, ketamine, n-formylamphetamine, 1-(4-fluorophenyl)piperazine and most notably mCPP (in >30% of the ecstasy tablets) and mephedrone (in approximately 10% of the ecstasy tablets) (Brunt et al., 2010). Some of these substances may have been introduced by producers in an attempt to market them through an already successful vehicle product like ecstasy tablets (Parrott, 2004). None of these substances mimic the effects of MDMA very closely and some actually exert distinct unpleasant effects, especially if one is expecting an MDMA-like experience (Bossong et al., 2010; Brunt et al., 2010). Additionally, scientific facts or even commonplace knowledge about the effects of many of these substances is
lacking. This may well explain the increased health concerns and the level of uncertainty expressed by many ecstasy users.

There have been a number of reasons proposed that might be the cause of the transient shortage of MLS in the EU: increased demand in other parts of the world for PMK intended for MDMA manufacture, effective law enforcement to curtail manufacture and prevention of illegal imports or diversions of precursor chemicals from countries of origin (UNODC, 2010). The rapid resurgence in 2010 of ecstasy tablets containing MLS again seen in this study could suggest retooling ecstasy manufacture in Europe. It has been suggested that other countries have taken over the role of China as supplier of PMK and also that other precursors are now being used to synthesize MLS (Milhazes et al., 2007; UNODC, 2010). This latter hypothesis could be tested by tracing the origin of the MDMA present in tablets using synthetic drug profiling (Europol, 2007; Milliet et al., 2009).

Because many ecstasy users are polydrug users, they might have changed their drug use, following the unavailability of good quality ecstasy (Parrott et al., 2001; Parrott, 2004). Some studies have predicted hypothetical lower consumption of ecstasy by drug consumers if ecstasy quality was considered to be poor (Sumnall et al., 2004; Goudie et al., 2007; Cole et al., 2008). However, this was never investigated in a real world market situation. The present findings suggest that the majority of ecstasy users, despite awareness of the market situation, did not change their ecstasy use during the peak of the shortage of MLS. Apparently, ecstasy use is less elastic in response to quality fluctuations than would be predicted beforehand (given the relatively low addiction potential; van Amsterdam et al., 2010; Nutt et al., 2007, 2010).

The finding that most ecstasy users did not change their ecstasy use is confusing, but might be explained by one or more of the following reasons: (1) confidence about their own networks of ecstasy supply, (2) peer pressure or drug dependence preventing a change in drug use, (3) users being oblivious to the risks involved in using drugs sold as ecstasy or (4) test results and communication about these test results not being alarming enough. Reasons 3 and 4 are less likely to play an important role since the current study seems to indicate increased health concerns during the
shortage period and because the DIMS emphasized the unknown risks when ingesting new substances with unknown psychopharmacological effects and in fact stated that users were experimenting on themselves. Actually, it has been described previously that ecstasy users were depending on their network of peers to eventually obtain safe good quality tablets (Korf et al., 2003).

There are some studies on real world examples of illicit drug shortages that reported switching to other, better available, drugs or drug users leaving the drug market altogether (Topp et al., 2003; Weatherburn et al., 2003; Roxburgh et al., 2004; Cunningham et al., 2008). For example, the heroin shortage in Australia between 2000 and 2001 was associated with heroin users temporarily switching to cocaine and methamphetamine. However, these examples of drug substitution involved highly addictive drugs associated with a marginalized and problematic group of users, in contrast to the generally well-integrated ecstasy users who tend to use in a recreational, not depended, fashion (Van Laar et al., 2010). Dependent users may be more driven to look for substitutes when their preferred drug is no longer available.

Whereas this study tries to describe drug user’s behaviour in response to a changing drug market, it has to be stressed that a convenience sample was used, i.e. drug users that had access to ecstasy tablets and had the opportunity to test them. Therefore, generalization of results to the whole population of potential ecstasy users is hampered. Notwithstanding this limitation, the situation on the ecstasy market seemed to have drawn more ecstasy users than usual to the testing facilities. With regard to the time-series analysis, there are also some limitations of this study that have to be mentioned. ARIMA intervention time-series analysis is one of the most powerful methods to infer causality in time-dependent phenomena (Edwards, 2001; Shadish et al., 2002), but other influences can not entirely be excluded. With a time-series analysis design with only one intervention event there is a slight possibility of another event that co-occurred and influenced the effect. Secondly, the time points of the intervention event (shortage of MLS) in this study were not known a priori, as is the case with well documented dates like law or policy regulations (Koski et al., 2007;
Herttua et al., 2008; Callaghan et al., 2009). However, some studies have successfully coped with poorly identified time points of the intervention, like the heroin shortage in Australia (Smithson et al., 2005; Gilmour et al., 2006). In the present study, there is confidence about the timing of the MLS shortage intervention event in the current study, because of the exact nature of the month-by-month chemo-analytical monitoring data of a large and representative number of Dutch ecstasy tablets from the streets, which might even be considered a more precise measurement of the shortage of MLS, without using the presumption that law or policy regulations actually resonated to the level of the street drug market.

Shortages of MLS do not occur frequently and there has been only one previous period reported in The Netherlands in the mid-nineties (Spruit, 2001; Vogels et al., 2009). However, the DIMS did not cover the whole country in those days and the database was not as informative as it is today. Therefore, the present data provided an unprecedented challenge to measure the impact of a shortage of MLS on drug user behaviour and this may be a valuable contribution to previous insights gained from other drug markets (Weatherburn et al., 2003; Wood et al., 2004; Callaghan et al., 2009). Secondly, it may provide further insight into drug policy based on both harm reduction and use reduction (Caulkins & Reuter, 1997; Weatherburn, 2009). When alerted about a drastic change on the ecstasy market, more ecstasy users in The Netherlands utilized the DIMS as a potential harm reduction tool for their own safety and probably for reassurance. As a behavioural intervention however, the shortage of MLS did not prove to be effective in reducing ecstasy use in this specific population. The unavailability of good quality ecstasy did not lead ecstasy users to suddenly reduce or change their use, in contrast to what has described with more dependent drug users. Their behaviour could be of a rather pragmatic nature: awaiting the endurance of the shortage of MLS and having their drugs tested in the meantime for health reassurance. The increased motivation to have their drugs tested in this study showed that many users were at least unwilling to take too many health risks.