# Decision making as a predictor of first ecstasy use: a prospective study

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**Abstract**

*Rationale* Ecstasy (±3,4-methylenedioxymethamphetamine) is a widely used recreational drug that may damage the serotonin system and may entail neuropsychological dysfunctions. Few studies investigated predictors for ecstasy use. Self-reported impulsivity does not predict the initiation of ecstasy use; the question is if neuropsychological indicators of impulsivity can predict first ecstasy use.

*Objective* This study tested the hypothesis that a neuropsychological indicator of impulsivity predicts initiation of ecstasy use.

*Materials and methods* Decision-making strategy and decision-making reaction times were examined with the Iowa Gambling Task in 149 ecstasy-naive subjects. The performance of 59 subjects who initiated ecstasy use during a mean follow-up period of 18 months (range, 11–26) was compared with the performance of 90 subjects that remained ecstasy-naive.

*Results* Significant differences in decision-making strategy between female future ecstasy users and female persistent ecstasy-naive subjects were found. In addition, the gap between decision-making reaction time after advantageous choices and reaction time after disadvantageous choices was smaller in future ecstasy users than in persistent ecstasy-naives.

*Conclusion* Decision-making strategy on a gambling task was predictive for future use of ecstasy in female subjects. Differences in decision-making time between future ecstasy users and persistent ecstasy-naives may point to lower punishment sensitivity or higher impulsivity in future ecstasy users. Because differences were small, the clinical relevance is questionable.

**Keywords** Ecstasy · MDMA · Decision-making · Iowa Gambling Task · Neuropsychology

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## Introduction

Ecstasy or ±3,4-methylenedioxymethamphetamine (MDMA) is a popular recreational drug that is used by many teenagers, adolescents, and young adults (Drugs Informatie en Monitoring Systeem 2006; El-Mallakh and Abraham 2007). Given the extensive scientific literature suggesting sustained harmful consequences of ecstasy use on the serotonin system in the brain (Reneman et al. 2006; Ricaurte et al. 2000) and its neuropsychological correlates such as memory impairment (Gouzoulis-Mayfrank and Daumann 2006; Schilt et al. 2007), it seems desirable to investigate factors that predict future ecstasy use.

A few studies focused on predictors for future ecstasy use, looking either at internalizing factors such as anxiety and depression or externalizing factors such as sensation seeking and impulsivity. One prospective, population-based study (Huizink et al. 2006) reported that symptoms of

anxiety and depression in childhood were related to use of ecstasy in adolescence and adulthood. These findings are in line with a retrospective study showing a strong association between past-year depressive and panic symptoms and recent-onset ecstasy use (Martins et al. 2006). In addition, Lieb et al. (2002) reported that mental disorders precede ecstasy use (Lieb et al. 2002). On the other hand, our own prospective cohort study indicated that depressive symptoms did not predict future ecstasy use (de Win et al. 2006).

In addition, our prospective study failed to show self-reported sensation seeking or impulsivity to predict future ecstasy use (de Win et al. 2006). However, impulsivity is a complex phenomenon which can be divided into different aspects (Evenden 1999). For example, Patton et al. (1995) distinguish motor impulsivity, cognitive impulsivity, and non-planning impulsivity (Patton et al. 1995), whereas Whiteside and Lynam (2001) describe aspects such as urgency, (lack of) premeditation, (lack of) perseverance, and sensation seeking (Whiteside and Lynam 2001). One may not expect this complexity to be totally expressed in self-report measures, and it is conceivable that other measures, such as neuropsychological indicators of impulsivity, are more predictive of future ecstasy use. For example, decision making or making choices may be considered as an executive function in which behavioral inhibition and impulsivity play a substantial role (Deakin et al. 2004; Monterosso and Ainslie 1999). It has been proposed that high impulsivity and risky decision making are factors that might lead to drug use (Bechara and Damasio 2002; Bechara et al. 2001; Bolla et al. 2003; Ernst et al. 2003; Verdejo-Garcia et al. 2008). Some developmental studies on risks for alcohol abuse indeed show that mild executive dysfunctions in children with familial risk for alcohol or substance dependence enhance the risk for later addictions (Giancola and Tarter 1999; Tarter et al. 2004).

To our knowledge, there are currently no prospective studies on decision-making strategies before first ecstasy use. There are some studies that examined decision making in ecstasy users after the use of ecstasy because the investigators reasoned that altered decision making could be a sustained consequence of reduced serotonin availability (Vollenweider et al. 2005; Morgan et al. 2006; Quednow et al. 2007). Indeed, impaired decision making 90–120 min after MDMA administration was reported in one study (Vollenweider et al. 2005), but this was not replicated by another study (Ramaekers and Kuypers 2006). Two other studies showed impaired decision making in ecstasy users after a minimal abstention period of 3–5 days (Morgan et al. 2006; Quednow et al. 2007). However, no differences between ecstasy users and controls were found after a minimum abstention period of 2 weeks (Fox et al. 2002).

Instead of looking at the consequences of ecstasy use on decision making, the current study focused on decision-making strategy before the first use of ecstasy. A neuropsychological measure of risk taking, the Iowa Gambling Task, was used in a prospective cohort of at-risk young adults. It was hypothesized that future ecstasy users would show a more risky decision-making strategy on the gambling task than persistent ecstasy-naives, which should become visible in less advantageous choices and shorter reaction times after losses in future ecstasy users compared to persistent ecstasy-naives.

## Materials and methods

This study is part of the larger Netherlands XTC Toxicity Study investigating causality, course, and clinical relevance of ecstasy neurotoxicity (de Win et al. 2005).

### Participants and design

Between 2002 and 2004, 188 ecstasy-naive volunteers (18–35 years) who considered starting ecstasy use in the near future were recruited by targeted site sampling at colleges and dance events, paper and website advertisements, and through snowball sampling (Vervaeke et al. 2006). Exclusion criteria were ecstasy use in the past (at baseline session); a serious medical, neurological, or mental illness; use of medications that may influence cognition; pregnancy; and intravenous drug use. Subjects had to abstain from using psychoactive substances for at least 2 weeks and from alcohol for at least 1 week prior to examination. Drug use during the days before assessment was checked through urinalysis [enzyme-multiplied immunoassay for amphetamines, MDMA, opiates, benzoylecgonine (cocaine), benzodiazepines, 11-nor-$\Delta$9-THCCOOH, ethanol].

After inclusion, all subjects took part in neuropsychological assessment. Subjects had to complete validated substance use questionnaires at baseline and thereafter every 3 months during a mean follow-up period of 18 months (range, 11–26 months; Van de Wijngaart et al. 1997). Last-year use of alcohol (units/week), tobacco (cigarettes/week), cannabis (number of joints), and amphetamines and cocaine (occasions) were measured.

Verbal intelligence was estimated because correlations between IQ and performance on the Iowa Gambling Task have been reported (Monterosso et al. 2001). For this purpose, the Dutch version of the National Adult Reading Test (Nelson and O'Connell 1978), the Dutch Adult Reading Test (DART), was administered because it is relatively insensitive to cognitive impairment caused by neurological disorders (Schmand et al. 1991). As decision making might be affected by mood (Must et al. 2006; Taylor Tavares et al. 2007), also the Beck Depression Inventory (BDI) was used to compare future ecstasy users

and persistent ecstasy-naives on rate of depressive symptoms (Beck and Steer 1984; Beck et al. 1961). The BDI is a 21-item self-report rating inventory which measures characteristic attitudes and symptoms of depression in the week prior to assessment. Each item is scored 0 to 3, with higher scores indicating more depressive symptoms. The BDI showed high levels of reliability and validity (Beck and Steer 1984; Bouman et al. 1985). Total BDI scores were calculated. Scores higher than 13 are indicative for depression.

Subjects were paid for their participation (€100 or €150 per session depending on the number of assessments). Besides the tests described in this paper, subjects took part in more extensive neuropsychological testing and brain imaging, which are described elsewhere (e.g., de Win et al. 2007; Jager et al. 2008; Schilt et al. 2007). The study was approved by the local medical ethics committee. After complete description of the study, each subject gave written informed consent.

## Assessments

### Outcome variable: ecstasy use

Future first time ecstasy use was categorized in a binary variable (yes=1, no=0).

### Predictor variable: decision making

A computerized version of the Iowa Gambling Task was used (Bechara et al. 1994, 1999). Four decks of cards are displayed on a screen. Subjects have to choose a card from one of the decks by selecting keyboard numbers 1, 2, 3, or 4. Each choice results in winning or losing money. Two of the four decks give high rewards, but also high losses, and result in a net loss in the long run (disadvantageous decks 1 and 2). The two other decks result in low rewards, but also render lower losses, and result in a net gain in the long run (advantageous decks 3 and 4). The explicit goal of the test is to maximize profit on a loan of play money (Bechara et al. 2000). Standard test instructions were used (Bechara et al. 1999). Subjects were instructed to win as much money as possible, and they were told that some decks were worse than others but that they still could win if they avoided the worst decks. Reaction time was measured after each trial. Each deck consisted of 60 cards, and the task ended after 100 trials. The main measure for general performance was the number of cards picked from the advantageous decks (IGT performance). Because 14 subjects (9.4% of the total sample) finished all the cards in one deck in the last stage of the task, and would therefore bias the total IGT score, it was decided to exclude the last 20 responses of all subjects from the analyses. In addition, the mean difference in decision-making reaction time after net wins and losses was

analyzed (dRT: RTwin minus RTloss), indicating reflection following losses or negative feedback. Because the IGT involves a learning component, most of the participants learned to choose particular decks over time. Once subjects have decks of preference, they will be less affected by wins or losses, and therefore, reaction times after losses will decrease during the course of the task. Consequently, difference in reaction time (dRT) will change during the course of the task. In a repeated measures analysis of variance (ANOVA), with reaction time after losses as the dependent measure and stage (stage 1 through 4) as the within-subject factor, the effect of stage on reaction time was significant: $F_{2.04,301.47}=18.14$, $p<0.001$. For this reason, a more valid measurement for reward/loss sensitivity is dRT during the first three stages (0–60) of the task. The first 60 responses were included in the analysis.

## Statistical analyses

Unpaired $t$ tests were performed to examine differences between future ecstasy users and persistent ecstasy-naives in age, DART-IQ, and BDI total score. Group differences in gender were investigated using a chi-square test. In addition, we investigated whether the two groups were similar in the use of cannabis, alcohol, tobacco, cocaine, and amphetamine prior to the use of ecstasy with non-parametric Mann–Whitney tests. This is important because effects of substance abuse on decision making have been reported (Goudriaan et al. 2005, 2007; Grant et al. 2000; Rogers et al. 1999). We also investigated whether drug use at baseline was associated with IGT performance and dRT using Spearman's $r$.

A multivariate logistic regression analysis was performed with future ecstasy use (no=0, yes=1) as dependent variable and the cognitive measures IGT performance and dRT as predictor variables. Because some studies reported sex differences in IGT general performance (Bolla et al. 2004; Reavis and Overman 2001), we also added gender and the IGT performance by gender and dRT by gender interaction terms as covariates together with DART-IQ and substance use. Because of their skewed distribution, we used the logarithmic transformation for the cannabis, alcohol, and cigarette use variables. Since only a few subjects used cocaine (11%) and a normal distribution could not be reached after log transformation, this variable was dichotomized (no use=0, use=1). Only one participant used amphetamine. Therefore, separate analyses for the effects of amphetamine use on decision-making strategies were not performed. The subject was kept in the analyses; excluding this subject from the analyses did not change any of the results. In the multivariate logistic regression model, DART-IQ, gender, and substance use were entered first. After that, the cognitive measures were entered in order to estimate the additive predictive value of these variables on

future ecstasy use. Potential collinearity problems were tested using the tolerance factor (TF) and the variance inflation factor (VIF).

All analyses were performed using SPSS statistical software version 12.0.1 (SPSS, Chicago, IL, USA). Values of $p<0.025$ were considered statistically significant (Bonferroni correction).

## Results

Of the 188 recruited subjects, we acquired sufficient follow-up information on 149 volunteers (79%). Fifty-nine subjects started using ecstasy during the follow-up period, and 90 subjects remained ecstasy-naive. Reasons for not trying ecstasy include: fear of acute effects, knowledge about the harmfulness of the drug, and lack of opportunity. For a detailed description of this part of the study, the reader is referred to Vervaeke et al. (2008). Follow-up information of the other subjects was missing either because the volunteers did not want to participate in the follow-ups or because we could not reach them anymore. The group of subjects that dropped out had a significantly lower estimated DART-IQ (difference of five points between included subjects and dropouts). Age, sex distribution, and drug use did not differ significantly between dropouts and included subjects.

Demographics and substance use characteristics of the included subjects are shown in Table 1. The groups were similar in terms of gender distribution, age, DART-IQ, and BDI sum score. Drug use did not differ significantly between future ecstasy users and persistent ecstasy-naive subjects.

Iowa Gambling Task

A first exploration of Spearman's correlations between the use of substances other than ecstasy and IGT performance

and dRT, respectively, showed only a significant negative correlation between cocaine (number of times last year) and the number of advantageous deck choices (Spearman's $r=-0.28$, $p<0.001$): More cocaine use was associated with worse deck choices. However, cocaine use ever was not significantly associated with future ecstasy use [$\chi^2(1)=2.97$, $p=0.09$].

A logistic regression model with DART-IQ, gender, and substance use as independent variables did not significantly predict future ecstasy use [$\chi^2(6)=7.57$, $p=0.27$]. In the next step, the cognitive measures (IGT performance and the IGT performance by gender, dRT, and dRT by gender interaction terms) were added to the model. This improved the ability of the model to predict future ecstasy use significantly [$\chi^2(4,10)=16.27$, $p<0.01$] and added 13.3% (Nagelkerke $R^2$) to the explained variation of the model. Because the dRT by gender interaction term was not significant ($p>0.10$), this term was removed from the model (Hosmer and Lemeshow 2000). Repeated analysis showed that IGT performance, IGT performance × gender, and dRT still improved the predictive ability of the model significantly [$\chi^2(3,9)=15.28$, $p<0.01$] with 12.5% (Nagelkerke $R^2$). In our model, multi-collinearity was not an issue (TF 0.73–0.97, VIF 1.03–1.37). The regression coefficients of IGT performance or gender cannot be interpreted as main effects in a model with a significant IGT by gender interaction term. However, separate analysis without the interaction factor showed no significant effects of gender or IGT performance. For the significance of the predictors, we looked at IGT performance by gender interaction and dRT. The beta coefficients indicated that less advantageous deck choices in female participants and smaller differences in reaction times after wins and losses (in males and females) resulted in a higher likelihood of future ecstasy use (see Figs. 1 and 2 and Table 2).

Figure 2 shows that primarily, the reaction times after losses differed between the two groups, with persistent ecstasy-naives having longer reaction times after losses than

**Table 1** Characteristics of demographics and substance use ($N=149$)

|  | Future ecstasy users ($N=59$) | Persistent ecstasy-naives ($N=90$) | $p$ values |
|---|---|---|---|
| Gender (M/F%) | 25 M, 34 F (42/58%) | 38 M, 52 F (42/58%) | 0.99[a] |
| Age | 21.4±2.8 | 21.7±2.5 | 0.58[b] |
| DART-IQ | 104.1±9.2 | 105.2±9.5 | 0.47[b] |
| BDI | 3.9±3.8 | 3.2±3.3 | 0.21[b] |
| Alcohol (units/week) | 9.1±7.5 | 9.0±9.0 | 0.66[c] |
| Tobacco (cigarettes/week) | 34.1±49.2 | 26.7±52.0 | 0.07[c] |
| Cannabis (joints last year) | 36.8±64.8 | 19.4±37.6 | 0.09[c] |
| Amphetamine (times last year) | 0.0±0.0 | 0.6±5.5 | 0.42[c] |
| Cocaine (times last year) | 1.0±2.3 | 0.5±1.6 | 0.09[c] |

Values expressed as mean±SD

[a] Pearson chi-square

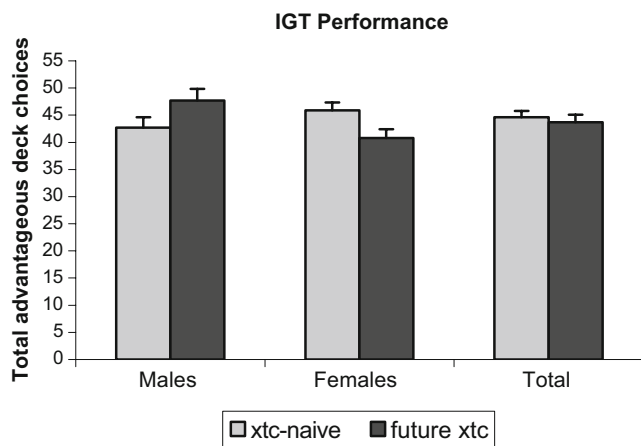[b] ANOVA

[c] Mann–Whitney

**IGT Performance**



**Fig. 1** Total advantageous deck choices of future ecstasy versus persistent ecstasy naives. Error bars depict standard errors of the mean

future ecstasy users. The overall classification accuracy of the whole model was 66.4%, with a negative predictive accuracy of 80% (persistent ecstasy-naives correctly classified in the ecstasy-naive group) and a positive predictive accuracy of 46% (future ecstasy users correctly classified in the future ecstasy use group).

## Discussion

The current study prospectively investigated the association between decision-making strategy and future first ecstasy use. We hypothesized that a risky decision-making strategy on a gambling task would predict future first ecstasy use. In our study population, only in female participants was a relationship found between decision-making strategy and future ecstasy use: Less advantageous deck choices on a gambling task resulted in a higher likelihood of future first ecstasy use. In addition, decision-making reaction time differed significantly between the total group of persistent ecstasy-naives and the total group of future ecstasy users: Future ecstasy users did not prolong their reaction times after punishments, whereas persistent ecstasy-naives did.

A possible explanation for the finding that decision-making strategy only was predictive for future ecstasy use in women and not in men might be sought in differences in working memory capacity. Some studies postulate a role for working memory in decision making (Bechara and Martin 2004; Pecchinenda et al. 2006), and therefore, it could be theorized that the disadvantageous responses in female subjects of our study sample are due to a decreased working memory. At first sight, there are indications that this is true because in our previous study in the same cohort, female future ecstasy users showed lower scores on working memory tasks than male future ecstasy users (Schilt et al. 2007). However, after correction for DART-IQ and sub-

stance use, differences turned out to be non-significant ($p>$ 0.17). Consequently, it seems unjustified to ascribe the differences in decision-making performance between male and female future ecstasy users to differences in working memory.

Possibly, initiation of ecstasy use in men is influenced by other factors than in women. In men, external factors like peer influence or availability of opportunities may play a greater role in the initiation of ecstasy use than in women (Van Etten et al. 1999), while in women, the start of using ecstasy might be regulated by more internal factors, like personality characteristics or decision-making strategies. In The Netherlands, the percentage of the population (age 15–64) that ever used ecstasy was higher in men than in women (3.7% versus 2.1% in 2001 and 6.6% versus 1.2% in 2005; Drugs Informatie en Monitoring Systeem 2006), suggesting that for men, ecstasy use is a less unusual thing to do than for women. Women might need to show more deviant behavior to take the first step to ecstasy use.

The finding that future ecstasy users did not prolong their reaction time after punishment may imply higher impulsivity and/or lower punishment sensitivity. Higher impulsivity was also put forward by Goudriaan et al. (2006) as a possible explanation for a lack of difference in reaction time after rewards or after punishments in alcohol-dependents (Goudriaan et al. 2006). However, in our study population, future ecstasy users did not report higher impulsivity on a self-report impulsiveness scale (de Win et al. 2006). This could be due to the lack of an association between self-reported impulsivity and decision-making scores (data not shown). Other studies also failed to find a significant relationship between self-report impulsivity scales and performance on the Iowa Gambling Task (Franken and Muris 2005; Goudriaan et al. 2007; Jollant et al. 2005, 2007). Three other studies, however, did find significant correlations between self-reported impulsivity and performance on the Iowa Gambling Task (Christodoulou et al. 2006; Franken et al. 2008; Zermatten et al. 2005), but in two
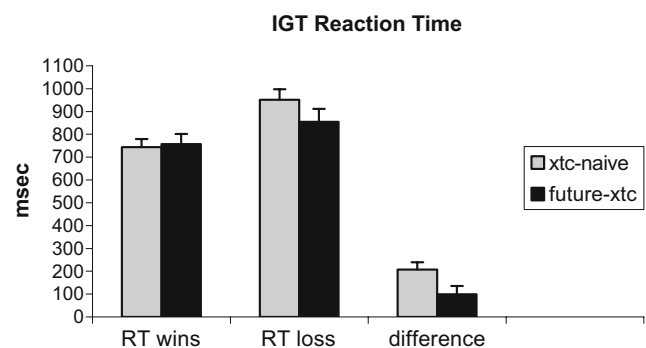
**IGT Reaction Time**



**Fig. 2** Mean reaction times (ms) after wins and after losses of future ecstasy versus persistent ecstasy-naives. Error bars represent standard errors of the mean

**Table 2** Prediction of IGT performance and difference in reaction time after IGT wins and losses (dRT) on future first ecstasy use

|  | B | SE | Wald statistics | p value | OR | 95% CI |
|---|---|---|---|---|---|---|
| DART-IQ | −0.01 | 0.02 | 0.14 | 0.71 | 0.99 | 0.95–1.03 |
| Sex | −5.19 | 1.70 | 9.35 | 0.00 | 0.01 | 0.00–0.16 |
| Cannabis (joints last year)[a] | 0.17 | 0.11 | 2.26 | 0.13 | 1.18 | 0.95–1.48 |
| Cocaine (use/no use last year) | 1.12 | 0.65 | 2.96 | 0.09 | 3.08 | 0.86–11.06 |
| Alcohol (units/week)[a] | −0.09 | 0.22 | 0.15 | 0.70 | 0.92 | 0.60–1.41 |
| Tobacco (cigarettes/week)[a] | 0.04 | 0.09 | 0.20 | 0.65 | 1.04 | 0.88–1.24 |
| IGT performance | −0.06 | 0.03 | 5.24 | 0.02 | 0.94 | 0.90–0.99 |
| IGT performance × sex | 0.11 | 0.04 | 9.19 | 0.00 | 1.11 | 1.04–1.20 |
| dRT | −0.00 | 0.00 | 5.59 | 0.02 | 0.99 | 0.99–1.00 |

*OR* odds ratio, *CI* confidence interval

[a] Log-transformed

of these studies, different self-report impulsivity scales were used other than the Barratt Impulsiveness Scale (BIS) used in our study. Possibly, the BIS does not capture the kind of impulsivity that is measured with the Iowa Gambling Task. As stated in "Introduction", impulsivity is a complex construct that consists of different dimensions (Evenden 1999). In the study of Zermatten (2005) for example, it appeared that only "premeditation" (thinking at forehand about a future action), as part of impulsivity, was related to decision making (Zermatten et al. 2005). Dawe and Loxton (2004) mentioned in their review an association between decision making and "rash unplanned impulsivity" rather than "reward sensitivity/drive" (Dawe and Loxton 2004). The fact that we did not find indications for self-reported impulsivity as an explanation for the shorter reaction times after losses in future ecstasy users does not mean that there is no connection between certain aspects of impulsivity and IGT performance. Instruments other than the self-report questionnaires used in the current study are needed to investigate this more thoroughly.

The results of this study possibly reflect lower punishment sensitivity in future ecstasy users. Individuals that start to use ecstasy may be less sensitive to the possible negative consequences of their choice. Although some studies did not find an association between substance misuse and sensitivity to punishment (Jorm et al. 1998; Leland and Paulus 2005), other studies showed that poor conditioning to signals for punishment is associated with an increased risk of alcohol abuse. This may be a reflection of a weak behavioral inhibition system (Finn et al. 1994; Loxton and Dawe 2001; Loxton et al. 2008). Subjects with low punishment sensitivity may be more prone to try ecstasy because they do not consider the potential negative consequences of drug use.

Some limitations of this study should be mentioned. An important limitation of this study is the selection of the participants. Subjects were selected on the basis of their self-reported wish to start using ecstasy in the near future.

Consequently, our study sample was not representative of the general population, which limits the generalizability of the results. This selection process could explain the small effect sizes and lack of associations between decision-making performance and self-report impulsivity questionnaires. Although the effect size for difference in IGT performance between female ecstasy-naives and female future ecstasy users was moderate (Cohen's $d=0.50$), the effect size for dRT between ecstasy-naives and future ecstasy users was rather small (Cohen's $d=0.37$). Another limitation is that we do not know if the persistent ecstasy-naive subjects would remain ecstasy-naive after the follow-up period of our study (11–26 months). Therefore, our results only provide information about prediction of ecstasy use in the near future, but not of ecstasy use ever. The current study provides only limited support for the use of neuropsychological decision-making tests in the prediction of initial ecstasy use. In contrast, neuropsychological measures of executive functioning and decision-making strategies appear to be stronger predictors for relapse in substance dependence or addictive behaviors (Bowden-Jones et al. 2005; Dallery and Raiff 2007; Goudriaan et al. 2008; Paulus et al. 2005). Moreover, neuropsychological tests other than the decision-making test used in our study might capture certain aspects of impulsivity better and subsequently could be superior predictors for future ecstasy use. Perhaps, other factors that we did not include in our study could better predict future ecstasy use. Some studies point at cannabis use as a risk factor for later ecstasy use (de Win et al. 2006; Martins et al. 2007; Pedersen and Skrondal 1999; Zimmermann et al. 2005). However, in the current study, cannabis and cocaine use did not significantly predict future ecstasy use. Possibly, the use of other drugs is especially predictive for frequent ecstasy use rather than for the first incidence of low-dose ecstasy use (mean ecstasy use at final evaluation was 6.3 pills, SD 12.1, median 2.0).

In summary, in this study, decision-making strategy was predictive for first incidental use of ecstasy in female

participants within the 11–26 months following baseline assessment. Furthermore, decision-making reaction time differed between future ecstasy users and persistent ecstasy-naives. However, the clinical relevance is limited because effect sizes were small to moderate only. It is conceivable that decision-making strategy is more important in the continuation of ecstasy use than in the initiation of first low-dose ecstasy use. Therefore, it is important to follow this study cohort and to compare decision-making strategy (before first ecstasy use) in the subjects that become frequent ecstasy users with persistent ecstasy-naives.

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