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## Pathways between Ecstasy Initiation and Other Drug Use

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### Abstract

This study aims to shed light on drug use pathways associated with ecstasy use initiation. Data from 54,573 respondents aged 12–21 years old from the 2002–2003 National Survey on Drug Use and Health (NSDUH) public use data files were analyzed via Cox proportional hazards models with time-dependent covariates. Our findings showed that marijuana, cocaine, and heroin were significant independent predictors of subsequent ecstasy use. Earlier ecstasy initiation was significantly associated with subsequent other illegal drug initiation (marijuana, cocaine and heroin). The strength of the association was greater for the pathway from earlier marijuana initiation to subsequent ecstasy initiation as compared to the pathway in the opposite direction. The pathway from earlier ecstasy initiation to subsequent cocaine and heroin initiation was also stronger as compared to pathways in the opposite directions. Pathways between ecstasy initiation and marijuana, cocaine and heroin initiation seem to be independent of the association between drug use and psychiatric symptoms/deviant behaviors. Ecstasy initiation seems to play a role in the subsequent initiation of cocaine and heroin.

### Keywords

Ecstasy initiation; drug use pathways; marijuana; cocaine; heroin

## 1. Introduction

Recent research (Martins Mazzotti & Chilcoat, 2005; Wu, Schlenger & Galvin, 2006) has established strong links between ecstasy (3–4, methylenedioxymethamphetamine, MDMA) and other drug use, but little is known about ecstasy initiation in relation to the initiation of other drugs, or if ecstasy initiation might play a role in subsequent other drug initiation. To date, only one study has used survival analysis to explore pathways associated with ecstasy initiation (Zimmerman et al., 2005), and it focused solely in the relationship of prior marijuana use and subsequent ecstasy initiation. On one hand, there might be a causal pathway between ecstasy initiation and prior initiation of other drugs (e.g. marijuana). On the other hand it is possible that ecstasy initiation might occur after other drug initiation simply due to the fact that

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there are common vulnerability factors that lead to the initiation of other drug use as well as to ecstasy use.

Ecstasy use has been associated with deviant behaviors and with psychiatric symptoms (Lieb Schuetz, Pfister, von Sydow & Wittchen, 2002; Martins, Mazzotti & Chilcoat, 2006); both might influence the initiation of ecstasy use and the progression from ecstasy to other drug use. Also, temporal pathways between ecstasy and other drug initiation might exist independently of the associations between ecstasy and psychiatric comorbidity/deviant behaviors.

The goal of this study is to shed light onto our understanding of drug use pathways associated with ecstasy use initiation. More specifically, its aims are to: 1) test whether previous marijuana, cocaine and heroin use increase the risk of subsequent ecstasy use, adjusting for demographics, deviant behaviors/psychiatric comorbidity, and previous marijuana initiation (in the case of cocaine and heroin), 2) explore whether previous ecstasy use increases the risk of subsequent marijuana, cocaine and ecstasy use, adjusting for the above covariates, 3) assess whether there is a bi-directional pathway (or not) between ecstasy initiation and marijuana, cocaine and heroin initiation, respectively, and, 4) investigate whether pathways between ecstasy initiation and marijuana, cocaine and heroin initiation exist independent of deviant behaviors/psychiatric comorbidity.

## 2. Methods

### 2.1. Sample and measures

We analyzed data from subjects aged 12-21 year old of the 2002 (n=26,865) and 2003 (n=27,708) National Survey on Drug Use and Health (NSDUH) public use data files with an aggregate sample size of 54,573. Detailed information about the sampling and survey methodology in the NSDUH are found elsewhere (SAMHSA, 2003, 2004). Our report was restricted to subjects aged 12-21 years old because ecstasy use is highly prevalent among adolescents and young adults and also because the NSDUH only provides respondents actual age of respondents aged 12 to 21 years old, due to confidentiality issues. Demographic variables selected for this study were age, sex, race/ethnicity, and annual family income. Drug classes selected for this study were: ecstasy, marijuana, cocaine and heroin. The NSDUH assessed drug use and age of onset of drug use. To assess deviant behaviors we used the NSDUH questions that asked whether adolescents and young adults attacked someone, carried a handgun, sold illegal drugs, and stolen or tried to steal anything worth more than US\$50 in the past year. Based on the dichotomous response variables we generated a new dichotomous 'past year deviant behavior variable', where: 0- did not engage in any deviant behavior in the past year, 1- engaged in any deviant behavior at least once within the past year. Past-year psychiatric symptoms questions (depressive symptoms and panic attack symptoms) were only asked for respondents aged 18 years and older.

### 2.2. Statistical analysis

Statistical analysis was performed using STATA 8.0 software (StataCorp, 2003). STATA 8.0 survey commands were used to account for sample weighting and complex survey design. Demographic characteristics of the selected sample were analyzed through cross-tabulations and chi-square tests. Then, to investigate potential pathways between ecstasy initiation and other drug initiation (marijuana, cocaine and heroin) using retrospective reports of age of onset of drug use, we used Cox proportional hazards models with time-dependent covariates (Cox, 1974). By using time-dependent covariates we can take into account the change in the respondent's status. Chronological age was used as the indicator of time, and data from respondents not experiencing the specified outcome by the time of the final interview were censored. In cases in which the outcome and time-dependent covariate occurred during the

same year, it was impossible to determine which came first. To avoid imposing a temporal sequence based on a priori assumptions, observations with tied onset times were censored just before the year in which the tie occurred.

Different sets of Cox proportional hazards models with time-dependent covariates were used to address the study's aims. Different covariates were added in each model (see Tables 2 and 3). To estimate the relative hazard of ecstasy initiation in relation to previous cocaine and heroin initiation (Table 2, models 4-6), and to estimate the relative hazards of cocaine and heroin initiation in relation to previous ecstasy initiation (Table 3, models 4-6) we also added marijuana initiation as a covariate, because marijuana is usually typically the first illegal drug individuals use and most ecstasy users are marijuana users. All analyses were repeated stratifying by age groups (12-17 year olds and 18-21 year olds). Then, we then compared the findings from the models in Table 2 to the models in Table 3 to assess whether there is a bi-directional pathway (or not) between ecstasy initiation and marijuana, cocaine and heroin initiation, respectively.

### 3. Results

Lifetime ecstasy users represented 7.5% of the total population of 12-21 year olds in the 2002-2003-NSDUH. Demographics are shown in Table 1.

#### 3.1. Hazard of ecstasy initiation after marijuana, cocaine and heroin initiation

Previous marijuana, cocaine and heroin initiation, respectively, were significantly associated with an increased likelihood of subsequent ecstasy initiation, adjusted for race and sex (Table 2, model 1). With the addition of past-year deviant behaviors and of past-year psychiatric symptoms (the latter only in the 18-21 year-old models), the associations remained statistically significant and were still of large magnitude. Adjustment for previous marijuana initiation (in the previous cocaine and heroin models) did not change the results (Table 2, models 4-6).

#### 3.2. Hazard of initiating marijuana, cocaine and heroin use after initiating ecstasy use

Previous ecstasy initiation was significantly associated with an increased likelihood of subsequent marijuana, cocaine and heroin initiation, adjusted for race and sex (Table 3, model 1). After adjustment for past-year deviant behaviors however, the associations slightly weakened but remained statistically significant (Table 3, model 2). No significant changes were observed upon controlling for psychiatric symptoms in the 18-21 year-old sub-sample. Even when adjusted for previous marijuana initiation, previous ecstasy initiation was significantly associated with an increased risk of subsequent cocaine and heroin initiation, respectively (Table 3, models 4-6).

#### 3.3. Comparison of drug use pathways

The hazard ratios for previous marijuana use to predict future ecstasy initiation (overall HR, 36.7; 95%CI, 32.0-42.0) were much higher than the hazard ratios for previous ecstasy use to predict future marijuana initiation (overall HR, 3.9; 95%CI, 3.2-4.7). The hazard ratios for initiating cocaine and heroin use after having already initiated ecstasy use were higher than the hazards ratios in the opposite direction. Results were similar when stratified by age groups.

### 4. Discussion

The main findings of this study can be summarized as follows: 1) the strength of the association was stronger for the pathway from earlier marijuana initiation to subsequent ecstasy initiation as compared to the pathway in the opposite direction, 2) the strength of the associations were stronger for the pathways from earlier ecstasy initiation to subsequent cocaine and heroin

initiation as compared to the pathways in the opposite directions, 3) pathways between ecstasy initiation and marijuana, cocaine and heroin initiation seem to be independent of the association between drug use and psychiatric symptoms/deviant behaviors.

Our results are concordant with those of Zimmerman et al.'s (2005) that showed that marijuana use predicts subsequent ecstasy initiation among adolescent and young adults in Germany. However, they did not test for pathways between ecstasy and other drug use such as cocaine and heroin. Our findings also are consistent with studies that show that marijuana initiation typically precedes the initiation of other illegal drugs (Kandel, 2003; Lynskey et al., 2003). In our sample 96% of the ecstasy users were also marijuana users and 83% of the ecstasy users initiated marijuana use at a younger age than initiating ecstasy use.

The strength of the associations was stronger for the pathways from earlier ecstasy initiation to subsequent cocaine and heroin initiation as compared to the pathways in the opposite directions. Parallel to the marijuana gateway effect (Kandel, 2003), ecstasy might play a role in the future initiation of cocaine and heroin use although causal linkages remain to be demonstrated. Ecstasy has a role in the brain reward system by increasing dopamine release in the nucleus accumbens, and previous ecstasy use might increase the reinforcing effects of other drugs, particularly cocaine and amphetamines (Colado, O'Shea & Green, 2004). More animal and human studies are needed to better understand the role of ecstasy physiologic effects and future other drug use.

The addition of psychiatric symptoms and deviant behaviors to the bi-directional pathways between ecstasy initiation and other drug initiation only diminished slightly the strength of the associations. Thus, our findings suggest that these drug initiation pathways exist independent of the association between drug use and psychiatric symptoms/deviant behaviors. Longitudinal studies are needed to better investigate this matter.

Some limitations of our study include: 1) analyses were restricted to respondents aged 12-21 years old because the NSDUH does not provide current age of subjects older than 21 years old; 2) the NSDUH does not have data on frequency of ecstasy use; 3) the analyses relied on lifetime reports of ecstasy and other drug use, which is based on subject recall, 4) the NSDUH provides only cross-sectional data, 5) the NSDUH has limited measures of psychiatric comorbidity. Despite these limitations we believe that our study is a first step in examining pathways related to ecstasy initiation in the U.S.

In conclusion, our study shows that marijuana initiation precedes ecstasy use and that the latter precedes the initiation of cocaine and heroin use, even after controlling for previous marijuana initiation and deviant behaviors and psychiatric problems. This study is one of the few of its nature that sheds light on the strength and quite importantly the direction of the association; however, by no means does it tackle the mechanisms involved or the reasons behind such findings. The specific role of ecstasy initiation in the initiation of other illegal drugs needs to be further explored in future longitudinal studies.

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**Table 1**

Lifetime Ecstasy use by selected demographic characteristics in 12-21 year old respondents, 2002-3 NSDUH.

	All persons		Lifetime Ecstasy Users	
	n	n	row % wgt	OR (95%CI)
Total	54,573	3,690	7.5%	
<b>Sex</b>				
Male	27,460	1,770	7.3%	1.0
Female	27,113	1,920	7.7%	1.0 (1.0-1.1)
<b>Age</b>				
12-17	35,913	1,036	2.8%	1.0
18-21	18,660	2,654	14.6%	5.8 (5.3-6.4)
<b>Race/ethnicity</b>				
White	35,316	2,784	9.1%	1.0
African-American	7,480	169	2.3%	0.2 (0.2-0.3)
Hispanic	7,846	469	6.0%	0.6 (0.6-0.7)
Other <sup>1</sup>	3,931	268	7.7%	0.8 (0.7-1.0)
<b>Family income</b>				
0 to \$19,999	13,647	1,156	9.0%	1.0
\$20,000 to \$49,000	19,491	1,303	7.2%	0.8 (0.7-0.9)
\$50,000 to 74,999	9,654	562	7.1%	0.8 (0.7-0.8)
\$75,000+	11,781	669	6.7%	0.7 (0.7-0.8)

<sup>1</sup> Includes Native-Americans, Native Hawaiians, Pacific Islanders and Asians.

The relative hazards of initiating ecstasy use after first initiating marijuana, cocaine and heroin use, respectively (12-21 year olds). Results from separate Cox proportional hazards models with time-dependent covariates, NSDUH 2002-3.

Table 2

Drug Initiation	Model 1 Hazard ratio <sup>1</sup> (95%CI)	Model 2 Hazard ratio <sup>2</sup> (95%CI)	Model 3 Hazard ratio <sup>3</sup> (95%CI)	Model 4 Hazard ratio <sup>4</sup> (95%CI)	Model 5 Hazard ratio <sup>5</sup> (95%CI)	Model 6 Hazard ratio <sup>6</sup> (95%CI)
<b>Marijuana Use</b>						
Yes	36.7 (32.0-42.0)	29.2 (25.5-33.5)	---	---	---	---
No	1.0	1.0				
<b>Cocaine Use</b>						
Yes	8.9 (8.1-9.8)	5.9 (5.3-6.5)	---	9.2 (8.4-10.1)	6.0 (5.4-6.6)	---
No	1.0	1.0				
<b>Heroin Use</b>						
Yes	8.8 (6.9-11.2)	5.1 (4.0-6.5)	---	8.0 (6.1-10.4)	4.7 (3.6-6.1)	---
No	1.0	1.0				
<b>12-17 year olds only</b>						
<b>Marijuana Use</b>						
Yes	36.0 (29.4-44.2)	23.8 (19.3-29.4)	---	---	---	---
No	1.0	1.0				
<b>Cocaine Use</b>						
Yes	13.9 (11.3-17.2)	6.2 (5.0-7.7)	---	14.1 (11.3-17.5)	6.1 (4.9-7.7)	---
No	1.0	1.0				
<b>Heroin Use</b>						
Yes	16.3 (10.7-24.3)	6.8 (4.5-10.4)	---	12.8 (7.6-21.4)	5.5 (3.4-9.0)	---
No	1.0	1.0				
<b>18-21 year olds only</b>						
<b>Marijuana Use</b>						
Yes	36.9 (30.7-44.3)	31.7 (26.3-38.1)	31.3 (26.1-37.7)	---	---	---
No	1.0	1.0	1.0			
<b>Cocaine Use</b>						
Yes	8.1 (7.3-8.9)	6.0 (5.4-6.7)	5.9 (5.3-6.5)	8.4 (7.5-9.3)	6.1 (5.5-6.8)	6.0 (5.4-6.7)
No	1.0	1.0	1.0			
<b>Heroin Use</b>						
Yes	7.0 (5.2-9.5)	4.6 (3.4-6.3)	4.5 (3.3-6.1)	7.0 (5.1-9.6)	4.7 (3.4-6.4)	4.5 (3.3-6.2)
No	1.0	1.0	1.0			

<sup>1</sup> adjusted for race and sex.

<sup>2</sup> adjusted for race, sex and deviant behaviors.

<sup>3</sup> adjusted for race, sex, deviant behaviors, and depressive and panic symptoms (mental healthy symptoms only available for those 18 and older).

<sup>4</sup> adjusted for race, sex and marijuana initiation.

<sup>5</sup> adjusted for race, sex, marijuana initiation and deviant behaviors.

<sup>6</sup> adjusted for race, sex, marijuana initiation, deviant behaviors, and depressive and panic symptoms (mental healthy symptoms only available for those 18 and older).

The relative hazards of initiating marijuana, cocaine and heroin use, respectively, after initiating ecstasy use (12-21 year olds). Results from separate Cox proportional hazards models with time-dependent covariates, NSDUH 2002-3.

Table 3

Drug Initiation	Model 1 Hazard ratio (95%CI) <sup>1</sup>	Model 2 Hazard ratio (95%CI) <sup>2</sup>	Model 3 Hazard ratio (95%CI) <sup>3</sup>	Model 4 Hazard ratio (95%CI) <sup>4</sup>	Model 5 Hazard ratio (95%CI) <sup>5</sup>	Model 6 Hazard ratio (95%CI) <sup>6</sup>
<b>Ecstasy before Marijuana</b>						
Yes	3.9 (3.2-4.7)	2.9 (2.4-3.5)	---	---	---	---
No	1.0	1.0				
<b>Ecstasy before Cocaine Use</b>						
Yes	12.3 (11.2-13.6)	8.0 (7.3-8.9)	---	13.1 (11.8-14.4)	8.4 (7.6-9.3)	---
No	1.0	1.0				
<b>Ecstasy before Heroin Use</b>						
Yes	33.0 (24.7-44.0)	18.3 (13.5-24.6)	---	33.3 (24.8-44.7)	18.2 (13.4-24.6)	---
No	1.0	1.0				
<b>12-17 year olds only Ecstasy before Marijuana</b>						
Yes	4.2 (3.0-5.7)	2.6 (1.9-3.6)	---	---	---	---
No	1.0	1.0				
<b>Ecstasy before Cocaine Use</b>						
Yes	18.6 (15.2-22.7)	8.5 (6.9-10.4)	---	20.4 (16.6-25.1)	9.0 (7.3-11.1)	---
No	1.0	1.0				
<b>Ecstasy before Heroin Use</b>						
Yes	43.0 (25.9-71.5)	16.0 (9.5-27.0)	---	44.0 (25.9-74.8)	16.0 (9.3-27.4)	---
No	1.0	1.0				
<b>18-21 year olds only Ecstasy before Marijuana</b>						
Yes	4.0 (3.1-5.2)	3.4 (2.6-4.4)	3.3 (2.5-4.2)	---	---	---
No	1.0	1.0	1.0			
<b>Ecstasy before Cocaine Use</b>						
Yes	11.2 (10.0-12.6)	8.3 (7.4-9.3)	8.1 (7.2-9.1)	11.8 (10.5-13.2)	8.6 (7.7-9.7)	11.3 (10.1-12.7)
No	1.0	1.0	1.0			
<b>Ecstasy before Heroin Use</b>						
Yes	30.3 (21.4-43.1)	21.1 (14.7-31.5)	20.5 (14.2-29.6)	30.6 (21.5-43.6)	21.1 (14.6-30.6)	20.6 (14.2-29.7)
No	1.0	1.0	1.0			

<sup>1</sup> adjusted for race and sex.

<sup>2</sup> adjusted for race, sex and deviant behaviors.

<sup>3</sup> adjusted for race, sex, deviant behaviors, and depressive and panic symptoms (mental healthy symptoms only available for those 18 and older).

<sup>4</sup> adjusted for race, sex and marijuana initiation.

<sup>5</sup> adjusted for race, sex, marijuana initiation and deviant behaviors.



<sup>6</sup> adjusted for race, sex, marijuana initiation, deviant behaviors, and depressive and panic symptoms (mental healthy symptoms only available for those 18 and older).