

## Simultaneous use of Alcohol, Tobacco and Cannabis in Relation to Severity of Substance Dependence: A Study among Young Swiss Men

Stéphanie Baggio<sup>1\*</sup>, Joseph Studer<sup>1</sup>, Stéphane Deline<sup>1</sup>, Alexandra N'Goran<sup>1</sup>, Meichun Mohler-Kuo<sup>2</sup>, Jean-Bernard Daepfen<sup>1</sup> and Gerhard Gmel<sup>1,3-5</sup>

<sup>1</sup>Alcohol Treatment Centre, Lausanne University Hospital CHUV, Av. Beaumont 21 bis, Pavillon 2, CH-1011 Lausanne, Switzerland

<sup>2</sup>Institute of Social- and Preventive Medicine, University of Zurich, Hirschengraben 84, CH-8001 Zurich, Switzerland

<sup>3</sup>Addiction Switzerland, Case postale 870, CH-1001 Lausanne, Switzerland

<sup>4</sup>Centre for Addiction and Mental Health, 250 College St, Toronto, Ontario, M5T 1R8, Canada

<sup>5</sup>University of the West of England, Frenchay Campus, Coldharbour Lane, Bristol BS16 1QY, United Kingdom

\*Corresponding author: Baggio S, Alcohol Treatment Centre, Lausanne University Hospital CHUV, Av. Beaumont 21 bis, Pavillon 2, CH-1011 Lausanne, Switzerland, Tel: +41 21 3143951; Fax: +41 21 3140562; E-mail: [Stephanie.Baggio@chuv.ch](mailto:Stephanie.Baggio@chuv.ch)

Received date: December 17, 2013; Accepted date: April 28, 2014; Published date: April 30, 2014

Copyright: © 2014 Baggio S, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### Abstract

**Objective:** This study investigated patterns of the simultaneous use of alcohol, tobacco and cannabis among young polydrug users, and whether use of one substance might be a cue for use of another and associations with the severity of substance dependence.

**Methods:** The study focused on 3 subsamples from the ongoing Swiss Cohort Study on Substance Use Risk Factors (C-SURF, N=5,990). It used 12 months of data on alcohol/tobacco co-users, alcohol/cannabis co-users and tobacco/cannabis co-users (N=2,660, 1,755 and 1,460 respectively). Simultaneous use, numbers of symptoms of substance dependence, and hazardous use of alcohol, tobacco and cannabis were assessed. The effect of simultaneous polydrug use (SPU) on the numbers of symptoms of substance dependence was tested using analysis of variance.

**Results:** Polydrug use was most common as SPU, and less common as non/occasional SPU. Moreover, when participants started to use one substance while using another, the severity of substance dependence was more strongly associated with the triggered substance than with cue.

**Conclusions:** This study highlights the necessity to take SPU into account. First, SPU rather than separate drug use was the most common pattern for polydrug users. Second, frequent SPU was associated with increased numbers of symptoms of substance dependence compared to non/occasional SPU. Furthermore, SPU may reveal the severity of substance use dependence, when substance use is triggered by a cue substance. For these reasons, SPU should be a serious cause for concern for prevention and intervention purposes.

**Keywords:** Alcohol; Cannabis; Cue reactivity; Simultaneous polydrug use; Symptoms of substance dependence; Tobacco

### Introduction

Use of a single drug is very rare among drug users [1-4]. A common form of polydrug use (i.e. the use of more than one drug) is simultaneous polydrug use (SPU), which refers to the use of two or more substances at the same time, on a single occasion [5]. SPU remains an understudied topic, despite it being a widespread substance use pattern [6-8] which carries more health, social and mental-related consequences than other forms of non-simultaneous polydrug use [9]. Indeed, studies often focus on use of single drugs even though these drugs are often used together. More research is needed about related risks and consequences of SPU [10], even for the most common substances (alcohol, tobacco and cannabis). Furthermore, little is also known about the potential for substance use dependence of SPU in comparison with non-SPU, especially among young adults. This study investigated this topic.

Some studies have reported increased consequences and adverse effects of simultaneous alcohol and cannabis use [10-12], such as later substance-related problems (relational, academic, health) and dependence [13-15]. Others studies have shown that simultaneous use of tobacco and cannabis increased the risk of cannabis abuse and dependence [16,17]. Studies dealing with alcohol and tobacco co-use have shown that current smoking status predicts alcohol dependence [18,19], but these studies did not focus specifically on simultaneous use of alcohol and tobacco. Moreover, to our knowledge, no study has investigated different kinds of SPU. For example, one can smoke while drinking (i.e. alcohol use triggers tobacco use: start to smoke while drinking) or drink while smoking (i.e. tobacco use triggers alcohol use: start to drink while smoking). Substance users can show a pattern of use including either one of these simultaneous uses (e.g. smoking while drinking, but not drinking while smoking), or both. These aspects of substance use can be understood using the cue-reactivity model [20]. In this conditioning model of addiction, people with a substance dependence are highly susceptible reactive to cues from earlier use (e.g. environmental cues, such as a place, or physical cues, such as smell or sight). The ingestion of another psychoactive

substance may also be a cue for the alternate substance [21]. Drobos [22] showed that alcohol cues promote cravings to smoke and that smoking cues trigger cravings to drink alcohol. However, this is true for drinkers who were alcoholic smokers, but not for nonalcoholic smokers, for whom smoking cues did not promote cravings to drink alcohol. Thus, encouragement to use a substance because another acts as a cue may reveal dependence to triggered substance. Nevertheless, to our knowledge, no studies have investigated how or whether people are more dependent to substances when their use has been triggered by a cue substance. Moreover, neither cannabis use as a cue for the use of other substances, nor cannabis use triggered by a cue substance has yet been studied.

The present study looked at the 3 most commonly used substances – alcohol, tobacco and cannabis and its aims were thus twofold. We investigated the patterns of SPU and the relationships between the severity of alcohol, tobacco and cannabis dependence and different kinds of SPU. We hypothesized that: a) the severity of substance dependence is most common with SPU, and less common with non/occasional SPU, and b) that the severity of substance dependence is more strongly associated with the substance that is triggered by the cue substance.

## Methods

### Sample

The data are part of the Cohort Study on Substance Use Risk Factors (C-SURF), a longitudinal study designed to assess substance use patterns and related consequences in young Swiss men. Enrolment took place in three out of six national army recruitment centers, located in Lausanne (French-speaking), Windisch and Mels (German-speaking). These three centers cover 21 of 26 cantons in Switzerland, including all French-speaking cantons. There is no pre-selection for this conscription, and all young men around 20 years-old are evaluated to determine their eligibility for military, civil or no service because army recruitment is obligatory in Switzerland. Thus, all young Swiss men around 20 years-old were eligible for study inclusion. The recruitment centers were only used to enroll participants. Assessment was carried out outside the army environment and independently of eligibility for military service. Participants who gave a written consent to participate in recruitment centers were invited two weeks later by mail or email to fill in a paper and pen or an online questionnaire, according to the favorite way they indicated in the written consent. The study received approval from Lausanne University Medical School's Ethics Committee for Clinical Research, and conformed to the Helsinki declaration.

A total of 5,990 participants filled in the questionnaire (mean age: 20 years old) between September 2010 and March 2012. This study focuses on 3 subsamples of polydrug users: participants who had used both alcohol and tobacco during the previous 12 months (N=2,760); those who used both alcohol and cannabis during the previous 12 months (N=1,807); and those who used both tobacco and cannabis during the previous 12 months (N=1,506). Single substance users were excluded from the following subsamples. Missing values were listwise deleted, which left a final sample size of 2,540, 1,730 and 1,429 participants for each subsample (92.0%, 95.7% and 94.9% of the participants who indicated their simultaneous or concurrent use of each polydrug use pairing). More information about sampling and non-response can be found in Studer et al. [23]. Briefly, non-respondents were more likely to be substance users, but differences

between respondents and non-respondents and non-response bias were small.

## Measures

### Alcohol use

The Diagnostic and Statistical Manual of Mental Disorders' (DSM IV) 7 criteria of alcohol dependence were examined as in Knight et al. [24]. We used a continuous numbered scale of criteria (from 0 "no symptom of dependence" to 7 "high number of symptoms of dependence") instead of a cut-off of 3 or more criteria. This was because current literature assumes a more continuous dimensional construct to alcohol dependence rather than a categorical model [25], and because alcohol dependence may not yet have been diagnosed in such young populations. The level of alcohol use was measured by drinking volume (usual quantity multiplied by frequency of alcohol use) and frequency of risky single-occasion drinking (RSOD, i.e. 6 drinks or more on a single occasion); it was defined as either "hazardous" (more than 20 drinks per week or one RSOD episode per month or more) or "not hazardous" (20 drinks or less per week, and less than one RSOD episode per month). Heavy drinking volume without RSOD is rare in this age group.

### Tobacco use

Nicotine dependence levels were assessed using the Fagerström Test for Nicotine Dependence [26], with a continuous scale total score ranging between 0 "no symptom of dependence" and 10 "high number of symptoms of dependence". The level of tobacco use was measured with frequency of tobacco use and defined as "hazardous" (daily smoking) and "not hazardous" (less than daily smoking).

### Cannabis use

Cannabis use disorder was assessed using the Cannabis Use Disorder Identification Test [CUDIT, 27], with a total score between 0 "no symptom of dependence" and 40 "high number of symptoms of dependence". The level of cannabis use was measured by the frequency of its use and defined as either "hazardous" (cannabis used twice per week or more) and "not hazardous" (cannabis used less than twice per week).

### Simultaneous polydrug use

Participants were asked whether they had used any combination of alcohol, tobacco and cannabis simultaneously during the previous 12 months. Participants were asked if, while drinking, they simultaneously consumed tobacco or cannabis (e.g. "How often did you take the following substances along with alcohol (i.e. simultaneously) in the past 12 months?"). They were asked how often, while smoking, they used alcohol, or cannabis, at the same time. They were also asked whether they consumed alcohol and tobacco while using cannabis. The answers were collected using a 6-level scale ("all the time", "most of the time (more than half of the time)", "half of the time", "seldom (less than half of the time)", "hardly ever", "never"). Participants who answered "half, more, or all of the time" were recorded as frequent simultaneous drug users for the pair of substances considered, whereas participants who answered "seldom, hardly, or never" were recorded as non/occasional simultaneous drug users. Frequent versus non/occasional simultaneous use was assessed instead of absence versus presence of simultaneous use because non-

simultaneous use was rare among the participants. Groups of users were then defined according to their types of simultaneous use. The subsample of alcohol/tobacco users was separated into 4 groups: a) non/occasional simultaneous users (who never or occasionally used alcohol and tobacco at the same time); b) cross-simultaneous users (who used alcohol at least half of the time while smoking and tobacco at least half of the time while drinking); c) partial simultaneous users, smokers while drinking (alcohol was a cue triggering tobacco use; they smoked at least half of the time while they were drinking, but never or occasionally drank while they were smoking; and d) partial simultaneous users, drinkers while smoking (smoking was a cue triggering alcohol use; they drank at least half of the time while they were smoking, but never or occasionally smoked while they were drinking). The same kinds of groups were created for the sample of alcohol/cannabis users and tobacco/cannabis users.

use pairing. Multiple analyses of variance (ANOVA type III for unbalanced data) with pairwise post-hoc comparisons (Tukey's honest significant difference test) were then performed to assess the differences between the 4 groups in each polydrug use pairing on the number of symptoms of substance dependence. Six models were tested in total. In each of the 3 subsamples, one model was tested for each of the related symptoms of dependence (e.g. alcohol and nicotine dependence for the subsample of alcohol/tobacco users). We performed multiple ANOVA because we adjusted results for hazardous use, as level of use may affect substance dependence. A Bonferroni correction was performed in post-hoc comparisons to keep the type I error rate at 5%. All analyses were performed using SPSS 21 software.

**Analyses**

Descriptive statistics were first computed to examine the patterns of non/occasional, partial and cross-simultaneous use for each polydrug

		Subsample/polydrug use pairing			
		Alcohol/tobacco users	Alcohol/cannabis users	Tobacco/cannabis users	
Frequent SPU	Cross-SPU		One substance triggers the other and vice versa		
	Partial SPU	Alcohol cue	Alcohol triggers tobacco use	Alcohol triggers cannabis use	
		Smoking cue	Smoking triggers alcohol use		Smoking triggers cannabis use
		Cannabis cue		Cannabis triggers alcohol use	Cannabis triggers tobacco use
Non/rare SPU		Substances are rarely or never used at the same time			

**Table 1:** The different kinds of simultaneous polydrug use measured

**Results**

Table 2 summarizes the descriptive statistics. Combining alcohol/tobacco was more common than combining alcohol/cannabis, or combining tobacco/cannabis (respectively 42.4%, 28.9% and 23.9% of the whole sample). Non/occasional SPU was quite uncommon (11.6% for alcohol/tobacco users; 32.4% for alcohol/cannabis users; 28.1% for tobacco/cannabis users). Cross-simultaneous use was more frequent for alcohol/tobacco (49.4%), whereas drinking while using cannabis or smoking was more frequent for alcohol/cannabis users (35.7%) and tobacco/cannabis users (38.8%). Using cannabis while drinking or smoking was the least common pattern (12.8% of the alcohol/cannabis users, and 6.0% of the tobacco/cannabis users).

The number of symptoms of dependence and disorder were low for all the 3 SPU subsamples. However, all 3 subsamples revealed hazardous use at non negligible prevalence rates, especially for alcohol use (range across the 3 subsamples: alcohol: 63.1%–69.5%; tobacco: 45.5%–49.8%; cannabis: 31.3%–35.1%).

**Number of symptoms of substance dependence according to the SPU pairing**

The results of the 6 models tested are presented in Table 3 (means for numbers of symptoms of substance dependence) and Table 4 (post-hoc comparisons). Cross-SPU was always associated with more symptoms of substance dependence than non/occasional SPU. Cross-SPU was also related to a higher number of symptoms of substance

dependence than partial forms of SPU (i.e. when one substance is a cue for the other, but not vice versa), except for 4 comparisons. Respondents who used cannabis while smoking (smoking cue triggered cannabis use) showed a number of symptoms of cannabis use disorder comparable to cross-SPU users, and those who drank at least half of the time while using cannabis (cannabis cue triggered alcohol use) showed a number of symptoms of alcohol dependence comparable to cross-SPU users. On the other hand, respondents who used tobacco while drinking alcohol (alcohol cue triggered tobacco use) showed a higher number of symptoms of nicotine dependence than cross-SPU users, and those who used cannabis while using drinking alcohol (alcohol cue triggered cannabis use) showed a higher number of symptoms of cannabis use disorder than cross-SPU users.

Furthermore, there were differences according to the kind of partial SPU. Users showed a higher number of symptoms of dependence for the substance triggered by cue. For example, users who smoked at least half of the time while they were drinking (alcohol cue triggered tobacco use) had more symptoms of nicotine dependence ( $t=22.11, p<.001$ ) than users who drank at least half of the time while smoking (smoking cue triggered alcohol use). This result was the same for most of the cases of partial SPU: users who smoked at least half of the time while using cannabis (cannabis cue triggered tobacco use) had more symptoms of nicotine dependence than those who used cannabis at least half of the time while smoking (smoking cue triggered cannabis use) ( $t=-3.90, p<.01$ ); users who used cannabis at least half of the time while drinking (alcohol cue triggered cannabis use) showed a higher

number of symptoms of cannabis use disorder than users who drank at least half of the time while using cannabis (cannabis cue triggered alcohol use) ( $t=32.00, p<.001$ ); users who used cannabis at least half of the time while smoking (smoking cue triggered cannabis use) showed a higher number of symptoms of cannabis use disorder than users who smoked at least half of the time while using cannabis (cannabis cue triggered tobacco use) ( $t=12.60, p<.001$ ); and users who drank at least half of the time while using cannabis (cannabis cue for alcohol use) had more symptoms of alcohol dependence than users who used cannabis at least half of the time while drinking (alcohol cue triggered cannabis use) ( $t=-4.09, p<.05$ ). One result did not show the same pattern was the use of alcohol at least half of the time while smoking (smoking cue triggered alcohol use), which had a comparable number of symptoms of alcohol dependence to the use of tobacco at least half

of the time while drinking (alcohol cue triggered tobacco use) (non-significant t-test:  $t=-2.20$ ). Moreover, the substance triggered by the cue showed a higher number of symptoms of substance dependence than in non/occasional SPU (e.g. number of symptoms of nicotine dependence was higher when users started to smoke while using cannabis (cannabis cue triggered tobacco use) than when they used the 2 substances in non/occasional SPU, ( $t=-8.55, p<.001$ ). The results were consistent over the 6 models tested. On the other hand, the cue substance did not show a higher number of symptoms of substance dependence than in non/occasional SPU (e.g. number of symptoms of alcohol dependence was comparable for non/occasional SPU of alcohol and tobacco and for users who started to smoke at least half of the time while drinking (alcohol cue for tobacco use), ( $t=-3.58$ ). These results were also consistent across the 6 models tested.

		Sample/polydrug use pairing (Total N=5,990)		
		Alcohol/tobacco N = 2,540 (42.4%)	Alcohol/cannabis N = 1,730 (28.9%)	Tobacco/cannabis N = 1,429 (23.9%)
Frequent SPU	Cross-SPU1	49.4% (N = 1,255)	19.1% (N = 331)	27.1% (N = 387)
	Alcohol cue1	23.2% (N = 589)	12.8% (N = 221)	-
	Smoking cue1	15.8% (N = 402)	-	6.0% (N = 86)
	Cannabis cue1	-	35.7% (N = 617)	38.8% (N = 554)
Non/occasional SPU1		11.6% (N = 294)	32.4% (N = 561)	28.1% (N = 402)
Hazardous use	Hazardous alcohol use1	63.1% (N = 1,602)	69.5% (N = 1,202)	-
	Hazardous tobacco use1	45.5% (N = 1,156)	-	49.8% (N = 712)
	Hazardous cannabis use1	-	31.3 (N = 542)	35.1% (N = 502)
Number of symptoms of substance dependence	Alcohol2 (0–7)	0.16 (0.19)	0.18 (0.20)	-
	Tobacco2 (0–10)	1.84 (2.10)	-	2.01 (2.17)
	Problematic cannabis use2 (0–40)	-	6.66 (6.95)	7.28 (7.14)

**Table 2:** Descriptive statistics and patterns of use for alcohol, tobacco and cannabis use, <sup>1</sup>Percentages are given; <sup>2</sup>Means and standard errors under brackets are given

		Non/occasional SPU	Alcohol cue	Smoking cue	Cannabis cue	Cross-SPU
Subsample alcohol/tobacco N = 2,540	N	294	589	402	-	1,255
	No. of symptoms alcohol dep.	0.08 (0.01)	0.12 (0.01)	0.13 (0.01)	-	0.17 (0.01)
	No. of symptoms nicotine dep.	1.83 (0.12)	2.13 (0.08)	1.90 (0.18)	-	2.02 (0.04)
Subsample alcohol/cannabis N = 1,730	N	561	221	-	617	331
	No. of symptoms alcohol dep.	0.13 (0.01)	0.13 (0.01)	-	0.17 (0.01)	0.19 (0.02)
	No. of symptoms probl. cannabis use	7.28 (0.28)	10.29 (0.42)	-	6.77 (0.38)	10.30 (0.27)
Subsample tobacco/cannabis N = 1,429	N	402	-	86	554	387
	No. of symptoms nicotine dep.	1.77 (0.09)	-	1.84 (0.18)	2.00 (0.07)	2.32 (0.09)

	No. of symptoms probl. cannabis use	7.17 (0.33)	-	9.82 (0.52)	8.40 (0.25)	10.33 (0.27)
--	-------------------------------------	-------------	---	-------------	-------------	--------------

**Table 3:** Means for the number of symptoms of alcohol, tobacco and cannabis dependence according to groups of simultaneous users.

			Alcohol cue	Smoking cue	Cannabis cue	Cross-SPU
Subsample alcohol/ tobacco N = 2,540	No. of symptoms of alcohol dependence	Non/occasional SPU	-3.58	-5.18***	-	-10.10***
		Alcohol cue	-	-2.2	-	-7.99***
		Smoking cue	-	-	-	-4.49**
	No. of symptoms of nicotine dependence	Non/occasional SPU	-16.63***	3.17	-	-11.23***
		Alcohol cue	-	22.11***	-	9.20***
		Smoking cue	-	-	-	-16.95***
Subsample alcohol/ cannabis N = 1,730	No. of symptoms of alcohol dependence	Non/occasional SPU	0.48	-	-4.84***	-6.87***
		Alcohol cue	-	-	-4.09*	-5.92***
		Cannabis cue	-	-	-	-2.85
	No. of symptoms of problematic cannabis use	Non/occasional SPU	-29.84***	-	2.38	-28.73***
		Alcohol cue	-	-	32.00***	4.36**
		Cannabis cue	-	-	-	-31.26***
Subsample tobacco/ cannabis N = 1,429	No. of symptoms of nicotine dependence	Non/occasional SPU	-	-0.92	-8.55***	-12.63***
		Smoking cue	-	-	-3.90**	-6.63***
		Cannabis cue	-	-	-	-5.12***
	No. of symptoms of problematic cannabis use	Non/occasional SPU	-	-14.44***	-3.92	-28.04***
		Smoking cue	-	-	12.60***	-2.36
		Cannabis cue	-	-	-	-26.26***

**Table 4:** Post-hoc comparisons of ANOVA for the number of symptoms of alcohol, tobacco and cannabis dependence according to groups of simultaneous user's t-tests with corrected p-value are given (Bonferroni corrections). Example: post-hoc comparison of non/occasional SPU users versus complete SPU users for the number of symptoms of alcohol dependence:  $t = -3.58$ . Means are given in Table 3. Adjusted results for hazardous use of alcohol, tobacco and cannabis are given. \*\*\* $p < .001$ ; \*\* $p < .01$ ; \* $p < .05$ .

## Discussion

This study investigated the SPU of 3 pairings of widely used substances: alcohol, tobacco and cannabis. It aimed to explore SPU patterns and the relationships between different kinds of SPU and severity of substance dependence.

First of all, SPU seems to be a usual drug use pattern among young adults, especially for combinations of alcohol with another substance. Cross-SPU and partial forms of SPU were more frequent than non/occasional SPU for all 3 combinations of substance pairings. As reported in previous studies, frequent SPU seemed to be the most common pattern of polydrug use [6-8]. Furthermore, different kinds of SPU were distinguished with regard to each subsample pairing. Alcohol and tobacco were often cues triggering cannabis use (35.7% and 38.8%), whereas alcohol and tobacco accompany each other (cross-SPU) for almost half of the alcohol and tobacco users. Cannabis as a cue triggering alcohol or tobacco use was a less common pattern (12.8% and 6.0% of participants, respectively). This result seemed

consistent with the pathway that goes from licit drugs (alcohol, tobacco) to cannabis use [28-32].

The polydrug pairing users showed different numbers of symptoms of substance dependence according to their patterns of simultaneous use. First, cross-SPU participants showed a higher number of symptoms of substance dependence than other forms (non/occasional SPU or partial SPU), except in 4 cases out of 18. That is, participants who frequently used substances simultaneously were more dependent on them than participants who reported other forms of SPU, and this was independent of the level of use of each substance, as we adjusted for hazardous use. This result was consistent with our first hypothesis, a), which supposed that the severity of polydrug dependence is most common with SPU rather than with non/occasional SPU. This result replicated those reported for alcohol and cannabis co-use [13-15], tobacco and cannabis co-use [16,17], and alcohol and tobacco co-use [18,19], even these results did not specifically focused on SPU.

However, frequent SPU was not necessarily synonymous with an increased number of symptoms of substance dependence compared to

more occasional SPU. When the participants started to use one substance while using another (partial forms of SPU), the number of symptoms of substance dependence was higher for the substance that was triggered by the cue, as reported in the cue-reactivity model [20]. For example, the number of symptoms of nicotine dependence was higher among users who started to smoke while drinking (alcohol cue triggered tobacco use), than for users who never or occasionally used these 2 substances at the same time, but the number of symptoms of alcohol dependence in this group did not differ from the number of symptoms of occasional/non SPU users. Thus, severity of substance dependence was not only related to the frequent versus non/occasional SPU, but also to the kind of SPU. People who light a cigarette while drinking (alcohol cue triggered tobacco use) may be more addicted to nicotine than people who poured themselves a drink while smoking (smoking cue triggered alcohol use). When the use of one substance was triggered by the use of a first one, the need to start using the second one seemed related to the severity of dependence to this substance. It is possible that the more participants were dependent on a substance, the more they felt the craving to start using it while using a cue substance. These results were highlighted among alcoholic smokers (i.e. alcohol-dependent users), for whom smoking cues trigger cravings to drink alcohol [22]. Data are scarce for the other substances. Previous studies did not focus on substance dependence and substance use as a cue, but on craving and other cues such as visual ones (e.g. pictures of glasses of beer or cigarette packs). For example, for alcohol cue and cravings to smoke, Carpenter et al. [33] showed that daily smokers reported a higher response to alcohol visual cue rather than occasional smokers. Polydrug use has been well studied for alcohol and tobacco use [34], and we know that cigarette smoking increases during alcohol self-administration and vice versa [35]. For cannabis and alcohol, a study reported higher craving to use cannabis among cannabis users when they were presented a visual stimulus related to alcohol (not controlling for baseline craving) [36]. For cannabis use as a cue for nicotine dependence, we only know that cannabis use is a predictor of nicotine dependence, according to the reverse gateway theory [37]. Indeed, studies with cannabis cue are very rare [38]. This study filled in the gap for substance use as a cue for polydrug dependence for the couple of substance alcohol/cannabis and tobacco/cannabis. Therefore, the specific type of partial SPU may be an indicator of severity of substance dependence, and further investigations will be necessary to explore this assumption. This result was consistent for all 3 polydrug use pairings and was related to the severity of dependence, except for the number of symptoms of alcohol dependence: When alcohol/tobacco users drank while smoking (smoking cue triggered alcohol use), they did not have more symptoms of alcohol dependence than users who smoked while drinking (alcohol cue triggered tobacco use). However, they did have more symptoms of alcohol dependence than non/occasional simultaneous users. These results were consistent with our second hypothesis, b), which suggested that the severity of substance dependence is more strongly associated with the triggered substance than by the cue substance.

This study has some limitations. The first was that we assessed frequent SPU versus non/occasional SPU instead of presence of SPU versus absence of SPU. Indeed, it was difficult to assess presence versus absence, because SPU was the most common pattern among polydrug users (67.6%–88.4% of frequent SPU) and total absence of SPU was rare. Thus, this assessment was not able to show the “pure” effect of presence of SPU versus absence of SPU. The second limitation was the study’s cross-sectional design. It was impossible to show whether more

frequent SPU leads to an increased severity of substance dependence, or whether more frequent SPU was a consequence of the severity of substance dependence. Further longitudinal studies are needed to verify the hypothesis of SPU’s harmful effects (i.e. SPU worsened substance dependence). A third limitation was that no women could be included. This study is largely representative of men, but further investigations will be needed to know if women show the same patterns of SPU and substance dependence. Indeed, previous studies showed that polydrug use was higher among men than women (see for example Font-Mayolas et al. [39]). It is also the case for SPU [40]. Concerning cue reactivity, results are inconsistent. Some studies reported that women seemed more sensible to cues [33], others reported that men were [41], whereas others did not find any difference [42]. More investigations are needed on this topic. Finally, a last shortcoming was that at age 20, the participants were more likely to still engage in experimental substance use rather than dependent substance use. For example, withdrawal seems rare among youth. On the opposite, young people are likely to experiment tolerance and hazardous use [43]. To avoid misinterpretations and use of an inaccurate diagnose [44], we used the whole continuum of severity instead of a threshold. Indeed, studies reported that the total information provided by the dependence criteria was comparable among younger and older adults [45].

This study provided insight into the patterns of simultaneous polydrug use. Two results highlighted the necessity of taking SPU into account. First, frequent SPU was the most common pattern for young polydrug users and few of them never or occasionally used substance pairings at the same time. Second, a frequent SPU was associated with increased severity of substance dependence compared to non/occasional SPU. For both these reasons, SPU should be a serious concern for drug use prevention and intervention purposes. Moreover, the kind of partial SPU (i.e. one substance is a trigger for a second one) should be considered, as the level of use of a substance, triggered by a cue, reveals the severity of dependence to that substance.

## Implications and Contribution

SPU is a common pattern of drug use among young polydrug users. A frequent SPU was associated with increased severity of substance dependence compared to non/occasional SPU. When a substance is a trigger for a second one, it reveals the severity of dependence to that second substance.

## Funding

Swiss National Science Foundation FN 33CS30\_139467.

## References

1. Darke S, Hall W (1995) Levels and correlates of polydrug use among heroin users and regular amphetamine users. *Drug Alcohol Depend* 39: 231-235.
2. Ball JC, Ross A (2012) The effectiveness of methadone maintenance treatment: Patients, programs, services, and outcome. Springer-Verlag Publishing, New York
3. Hubbard RL, Gail S, Flynn PM, Anderson J, Etheridge RM (1997) Overview of 1-year follow-up outcomes in the Drug Abuse Treatment Outcome Study (DATOS). *Psychol Addict Behav* 11: 261-278.
4. Hammersley R, Forsyth A, Lavelle T (1990) The criminality of new drug users in Glasgow. *Br J Addict* 85: 1583-1594.
5. Earleywine M, Newcomb MD (1997) Concurrent versus simultaneous polydrug use: prevalence, correlates, discriminant validity, and

- prospective effects on health outcomes. *Exp Clin Psychopharmacol* 5: 353-364.
6. Barrett SP, Darredeau C, Pihl RO (2006) Patterns of simultaneous polysubstance use in drug using university students. *Hum Psychopharmacol* 21: 255-263.
  7. Barrett SP, Gross SR, Garand I, Pihl RO (2005) Patterns of simultaneous polysubstance use in Canadian rave attendees. *Subst Use Misuse* 40: 1525-1537.
  8. Olthuis JV, Darredeau C, Barrett SP (2013) Substance use initiation: the role of simultaneous polysubstance use. *Drug Alcohol Rev* 32: 67-71.
  9. McCabe SE, Cranford JA, Morales M, Young A (2006) Simultaneous and concurrent polydrug use of alcohol and prescription drugs: prevalence, correlates, and consequences. *J Stud Alcohol* 67: 529-537.
  10. Brière FN, Fallu JS, Descheneaux A, Janosz M (2011) Predictors and consequences of simultaneous alcohol and cannabis use in adolescents. *Addict Behav* 36: 785-788.
  11. Ramaekers JG, Robbe HW, O'Hanlon JF (2000) Marijuana, alcohol and actual driving performance. *Hum Psychopharmacol* 15: 551-558.
  12. Kelly E, Darke S, Ross J (2004) A review of drug use and driving: epidemiology, impairment, risk factors and risk perceptions. *Drug Alcohol Rev* 23: 319-344.
  13. Midanik LT, Tam TW, Weisner C (2007) Concurrent and simultaneous drug and alcohol use: results of the 2000 National Alcohol Survey. *Drug Alcohol Depend* 90: 72-80.
  14. Smucker Barnwell SV, Earleywine M, Gordis EB (2006) Confirming alcohol-moderated links between cannabis use and dependence in a national sample. *Addict Behav* 31: 1695-1699.
  15. Smucker Barnwell S, Earleywine M, Gordis EB (2005) Alcohol consumption moderates the link between cannabis use and cannabis dependence in an internet survey. *Psychol Addict Behav* 19: 212-216.
  16. Agrawal A, Lynskey MT (2009) Tobacco and cannabis co-occurrence: does route of administration matter? *Drug Alcohol Depend* 99: 240-247.
  17. Ream GL, Benoit E, Johnson BD, Dunlap E (2008) Smoking tobacco along with marijuana increases symptoms of cannabis dependence. *Drug Alcohol Depend* 95: 199-208.
  18. McKee SA, Falba T, O'Malley SS, Sindelar J, O'Connor PG (2007) Smoking status as a clinical indicator for alcohol misuse in US adults. *Arch Intern Med* 167: 716-721.
  19. John U, Meyer C, Rumpf HJ, Hapke U (2003) Probabilities of alcohol high-risk drinking, abuse or dependence estimated on grounds of tobacco smoking and nicotine dependence. *Addiction* 98: 805-814.
  20. Carter BL, Tiffany ST (1999) Meta-analysis of cue-reactivity in addiction research. *Addiction* 94: 327-340.
  21. Rohsenow DJ, Niaura RS, Childress AR, Abrams DB, Monti PM (1990) Cue reactivity in addictive behaviors: theoretical and treatment implications. *Int J Addict* 25: 957-993.
  22. Drobles DJ (2002) Cue reactivity in alcohol and tobacco dependence. *Alcohol Clin Exp Res* 26: 1928-1929.
  23. Studer J, Baggio S, Mohler-Kuo M, Dermota P, Gaume J, et al. (2013) Examining non-response bias in substance use research-are late respondents proxies for non-respondents? *Drug Alcohol Depend* 132: 316-323.
  24. Knight JR, Wechsler H, Kuo M, Seibring M, Weitzman ER, et al. (2002) Alcohol abuse and dependence among U.S. college students. *J Stud Alcohol* 63: 263-270.
  25. Kerridge BT, Saha TD, Gmel G, Rehm J (2013) Taxometric analysis of DSM-IV and DSM-5 alcohol use disorders. *Drug Alcohol Depend* 129: 60-69.
  26. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO (1991) The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict* 86: 1119-1127.
  27. Adamson SJ, Sellman JD (2003) A prototype screening instrument for cannabis use disorder: the Cannabis Use Disorders Identification Test (CUDIT) in an alcohol-dependent clinical sample. *Drug Alcohol Rev* 22: 309-315.
  28. Kandel D (1975) Stages in adolescent involvement in drug use. *Science* 190: 912-914.
  29. Kandel DB, Yamaguchi K (2002) Stages of involvement in the U.S. population. In Kandel DB (Ed.) *Stages and pathways of drug involvement: Examining the gateway hypothesis*. Cambridge University Press, Cambridge, pp. 65-89
  30. Kandel DB, Yamaguchi K, Klein LC (2006) Testing the Gateway Hypothesis. *Addiction* 101: 470-472.
  31. Scholey AB, Parrott AC, Buchanan T, Heffernan TM, Ling J, et al. (2004) Increased intensity of Ecstasy and polydrug usage in the more experienced recreational Ecstasy/MDMA users: a WWW study. *Addict Behav* 29: 743-752.
  32. Hamburg BA, Kraemer HC, Jahnke W (1975) A hierarchy of drug use in adolescence: behavioral and attitudinal correlates of substantial drug use. *Am J Psychiatry* 132: 1155-1163.
  33. Carpenter MJ, Saladin ME, Larowe SD, McClure EA, Simonian S, et al. (2014) Craving, cue reactivity, and stimulus control among early-stage young smokers: effects of smoking intensity and gender. *Nicotine Tob Res* 16: 208-215.
  34. Bien TH, Burge R (1990) Smoking and drinking: a review of the literature. *Int J Addict* 25: 1429-1454.
  35. Witkiewitz K, Desai SA, Steckler G, Jackson KM, Bowen S, et al. (2012) Concurrent drinking and smoking among college students: An event-level analysis. *Psychol Addict Behav* 26: 649-654.
  36. Wölfling K, Flor H, Grüsser SM (2008) Psychophysiological responses to drug-associated stimuli in chronic heavy cannabis use. *Eur J Neurosci* 27: 976-983.
  37. Patton GC, Coffey C, Carlin JB, Sawyer SM, Lynskey M (2005) Reverse gateways? Frequent cannabis use as a predictor of tobacco initiation and nicotine dependence. *Addiction* 100: 1518-1525.
  38. Henry EA, Kaye JT, Bryan AD, Hutchison KE, Ito TA (2014) Cannabis cue reactivity and craving among never, infrequent and heavy cannabis users. *Neuropsychopharmacology* 39: 1214-1221.
  39. Font-Mayolas S, Gras ME, Cebrián N, Salamó A, Planes M, et al. (2013) Types of polydrug use among Spanish adolescents. *Addict Behav* 38: 1605-1609.
  40. Whitehorn-Smith P, Simich L, Strike C, Brands B, Giesbrecht N, Khenti A (2012) Gender differences in simultaneous polydrug use among undergraduate students of one university, Kingston - Jamaica. *Texto & Contexto - Enfermagem*, 21: 74-78.
  41. Petit G, Kornreich C, Verbanck P, Campanella S (2013) Gender differences in reactivity to alcohol cues in binge drinkers: a preliminary assessment of event-related potentials. *Psychiatry Res* 209: 494-503.
  42. Saladin ME, Gray KM, Carpenter MJ, LaRowe SD, DeSantis SM, et al. (2012) Gender differences in craving and cue reactivity to smoking and negative affect/stress cues. *Am J Addict* 21: 210-220.
  43. Pabst A, Kraus L, Piontek D, Baumeister SE (2012) Age differences in diagnostic criteria of DSM-IV alcohol dependence among adults with similar drinking behaviour. *Addiction* 107: 331-338.
  44. Mewton L (2011) *The classification of substance use disorders in young adults*. University of New South Wales: Sydney.
  45. Mewton L, Teesson M, Slade T, Cottler L (2011) Psychometric performance of DSM-IV alcohol use disorders in young adulthood: evidence from an Australian general population sample. *J Stud Alcohol Drugs* 72: 811-822.

This article was originally published in a special issue, entitled: "**Addictions with Co-occurring Problems**", Edited by Dr. Marie-Josée Fleury and Dr. Serge Brochu, Montreal Addiction Rehabilitation Centre-University Institut, Canada