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Université de Lausanne Faculté de biologie et de médecine

Concurrent and simultaneous polydrug use among young Swiss males: use

patterns and associations of number of substances used with health issues

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Abstract

Background. Simultaneous polydrug use (SPU) may represent a greater incremental risk factor for human health than concurrent polydrug use (CPU). However, few studies have examined these patterns of use in relation to health issues, particularly with regard to the number of drugs used.

Methods. In the present study, we have analyzed data from a representative sample of 5,734 young Swiss males from the Cohort Study on Substance Use Risk Factors. Exposure to drugs (i.e., alcohol, tobacco, cannabis, and 15 other illicit drugs) as well as mental, social, and physical factors were studied through regression analysis.

Results. We found that individuals engaging in CPU and SPU followed the known stages of drug use, involving initial experiences with licit drugs (e.g., alcohol and tobacco) followed by use of cannabis and then other illicit drugs. In this regard, two classes of illicit drugs were identified, including first uppers, hallucinogens and sniffed drugs; and then 'harder' drugs (ketamine, heroin, and crystal meth), which were only consumed by polydrug users who were already taking numerous drugs. Also, we observed an association between the number of drugs used simultaneously and social issues (i.e., social consequences and aggressiveness). In fact, the more often the participants simultaneously used substances, the more likely they were to experience social problems. In contrast, we did not find any relationship between SPU and depression, anxiety, health consequences, or health.

Conclusions. Here, we have identified some associations with SPU that are independent of CPU. Also, we found that the number of concurrently used drugs can be a strong factor associated with mental and physical health, and that their simultaneous use may not significantly contribute to this association. Furthermore, the negative effects related to the use of one substance might be counteracted by the use of an additional substance.

Keywords: concurrent polydrug use; drug use pattern; mental and physical health; number of drugs used; simultaneous polydrug use.

1. Introduction

Substance use disorder represents the most prevalent form of psychopathology in young adults [1, 2]. Although it is well known that single drug use is rare [3-7], there have been few studies investigating polydrug use (i.e., the ingestion of more than one drug [3]). Indeed, polydrug use is associated with a unique set of consequences [8], including psychological morbidity/pathology [9-11], health risk behaviors [12] (e.g., HIV risk-taking [5]), difficulties engaging in drug-abuse therapy [13], and worse outcomes following drug-abuse treatment [14]. Moreover, some studies have indicated that the abuse of a higher number of substances is associated with more severe health outcomes [15-18].

Two forms of polydrug use have been described: concurrent and simultaneous [19]. Concurrent polydrug use (CPU) is the use of two or more substances within a given time period. On the other hand, simultaneous polydrug use (SPU) is the use of two or more substances at the same time, on a single occasion [20]. SPU is known to be a subset of CPU [21]. Furthermore, SPU is considered to be a key characteristic of the substance use patterns associated with many drug users, especially teenagers and young adults [1, 22-24], and studies have demonstrated that SPU poses a greater health risk than CPU [21]. For example, simultaneous polydrug users reported more drug use-related problems than concurrent polydrug users [21]. Also, those engaging in SPU displayed more social problems/consequences, psychosocial distress (e.g., depression) [19, 20], anxiety [19], and health problems [19, 20, 25]. In addition, the risk of injury, poisoning, overdose [26] or suicide [25] was higher during SPU. Similarly, SPU led to an increased likelihood for later substance-related problems among teenagers [27].

The present investigation addresses some of the limitations of earlier studies within this field. First of all, few studies have compared CPU and SPU [21, 25]. Second, studies have not thoroughly investigated the impact of the number of drugs simultaneously used, a variable that has already been suggested to reflect the level of severity of drug use in studies of CPU [15]. Notably, it has even been reported that the number of drugs used may be more important than the type of drugs used for the prediction of first suicide attempts [17]. However, there may be a methodological problem when studying SPU since it can be confounded with CPU (i.e., the more drugs people use simultaneously, the more drugs they must use concurrently). For this reason, some studies comparing SPU and CPU [21, 25] have not assessed the associations of SPU with variables while controlling for CPU. Another limitation of past studies is that they have focused on select substances, such as alcohol, tobacco, cannabis, and specific illicit drugs. Therefore, no previous study has investigated polydrug use patterns while considering a comprehensive list of drugs.

The aims of this study were to examine the patterns of CPU and SPU in relation to a wide variety of drugs (18 drugs) and to determine the additional associations of SPU with health (i.e., relevant outcomes identified in previous studies on polydrug use: mental/physical health, social problems and consequences) following adjustment for CPU. Although this cross-sectional study did not allow us to define causality, regression models were used to test associations between health and SPU after adjusting for several factors, including CPU.

2. Materials and methods

2.1 Subjects

The data for this study were obtained from the Cohort Study on Substance Use Risk Factors (C-SURF). C-SURF is an ongoing, longitudinal study designed to assess substance use patterns and related consequences in young Swiss men. Enrollment took place between August 23, 2010 and November 15, 2011 in three of the six army recruitment centers located in Lausanne (French-speaking), and Windisch and Mels (German-speaking). These three centers cover 21 of 26 cantons in Switzerland, including all French-speaking cantons. In Switzerland, army service is compulsory, so all young men ~20 years of age were eligible for inclusion in the study. Thus, our cohort is highly representative of young Swiss men. Moreover, this study was approved by the Ethics Committee for Clinical Research of the Lausanne University Medical School and followed the Helsinki declaration.

Of the 13,245 conscripts informed about the study, 7,563 gave written consent to participate, and 5,990 filled in the baseline questionnaire. This, analysis was performed on baseline data only. The study focused on the 5,636 participants who had used at least one drug during the past 12 months, including alcohol (94.1% of the sample). Subjects with missing values related to outcome variables were not considered in the analysis. Thus, the final study cohort included 5,319 participants (94.4% of the sample). More information about sampling and non-response can be found in Studer et al. [28]. Early respondents (responses obtained without extra effort) were compared to late respondents (responses acquired through increased efforts [i.e., encouraging telephone calls]) and non-respondents (who answered a five-minute questionnaire on substance use during the enrollment phase of the C-SURF). Early respondents were less likely to be either substance users or heavy users in comparison to late respondents, and non-

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respondents showed generally higher patterns of substance use than late respondents (excluding alcohol use). Therefore, using late respondents greatly reduced the magnitude of the non-response bias, even if it was insufficient to free survey estimates from the risk of non-response bias. However, differences between respondents and non-respondents were small and might be significant only because of the large sample size (N = 11,819).

2.2 Measures

2.2.1 CPU

CPU. Concurrent polydrug use was assessed by asking participants whether they had used specific drugs during the past 12 months. Each drug was coded as "used" or "non-used". The drugs included: 1) alcohol; 2) tobacco; 3) cannabis; 4) hallucinogens, magic mushrooms, psilocybin, peyote, or mescaline; 5) other hallucinogens (LSD, PCP/angeldust, 2-CB, or 2-CI); 6) salvia divinorum; 7) speed; 8) amphetamine, methamphetamine, or amphetaminsulfate (e.g., Dexedrine, Benzedrine); 9) crystal meth (Ice); 10) poppers (amyl nitrite, butyl nitrite); 11) solvent sniffing (e.g., glue, solvent, or gas [benzin, ether, toulol, trichloroethylene, nitrous oxide, etc.]); 12) ecstasy, MDMA; 13) cocaine, crack, or freebase; 14) heroin; 15) ketamine (Special K) or DXM; 16) GHB/GBL/I-4 Butanediol (BDB); 17) research chemicals (e.g., mephedrone, butylone, or methedrone); and 18) spice or similar substances.

Total CPU score. The global CPU score was determined by summing all of the drug categories used during the past 12 months (licit and illicit drugs combined, total score from 1 to 18, each positive category counted as "1" in the total score).

2.2.2 SPU

SPU. The co-use of drugs was assessed by questioning participants about the drugs that they had combined during the past 12 months. Specifically, individuals were asked to divulge the usual number of drugs that they used on a usual occasion ("usual SPU") and the maximum number of drugs that they had combined ("maximum SPU"). The drug categories used for this assessment were the same as those used for CPU scoring.

Total SPU score. Two global SPU scores were determined (i.e., "usual SPU" and "maximum SPU") by summing the total drugs used (licit and illicit drugs combined, total score from 0 to 18, each category counted as "1" for the total scores).

2.2.3 Mental, social, and physical factors

Anxiety and aggressiveness. In order to assess anxiety and aggressiveness, two subscales from the Zuckerman–Kuhlmann Personality Questionnaire (ZKPQ-50-cc) [29] were used: neuroticism/anxiety and aggression/hostility. The participants agreed or disagreed with each statement. A mean score was computed for each subscale (anxiety: $\alpha = .73$; aggressiveness: $\alpha = .56$).

Depression. Depression level was determined by using the Major Depressive Inventory (MDI) from the International Statistical Classification of Diseases and Related Health Problems (ICD-10) by the World Health Organization (WHO) [30, 31]. This is a 10-item questionnaire that screens answers on a 6-point scale from "never" (0) to "all the time" (5). A mean score was computed ($\alpha = 0.91$). A continuous scale (ranging from 0 to 50) was used instead of a cutoff value in order to better capture variability across the range of depression symptoms.

Mental and physical health. The Short Form Health Survey (SF-12) was used to assess mental and physical health [32] based on two subscales: mental/social health and physical health. The

subscale scores were computed according to the standard system, yielding two composite scores, which ranged from 0 (health problem) to 100 (no health problem). SF-12 primarily covered sadness, nervousness, and depression.

Consequences. A total of 15 consequences were selected from standard instruments [33-36]. However, these items were not explicitly substance related, which has been shown to result in different associations compared to consequences that can be causally attributed to substances. Included items were related to social, personal, and health consequences. Each consequence was coded "0" if it had not occurred in the past 12 months and "1" if it had taken place at least once during the past 12 months. Two mean scores of consequences were computed. The first score was related to social consequences, which included physical fights, problems with family/ friends, poor performance at school/work, theft, trouble with the police, regretted sexual intercourse, or damage to property. The second score was related to health consequences, including accident/injury, admittance to an emergency department, attempted suicide, need for medical treatment, overnight stay in a hospital, outpatient surgery, and treatment of an accident/injury in an emergency department.

2.3 Analyses

To examine CPU and SPU patterns, descriptive cross tables were created for each kind of polydrug use (CPU, usual SPU, and maximum SPU). The association of SPU with health factors was subsequently tested using linear regression analyses. However, although linear regression analyses were performed, a causal relationship between SPU and health factors was not assessed. The aim of this study was to investigate their actual relationship. First of all, two models were created to test the association of SPU alone (usual SPU and maximum SPU) with the seven

factors considered as dependent variables (unadjusted models). We then took into account the effect of CPU (adjusted models). As SPU is part of CPU, we initially conducted linear regression analyses with CPU as the predictor and SPU (usual SPU and maximum SPU) as the dependent variable, recording the residual factors for each model. The residual factors were then used as independent variables when analyzing each of the seven health-related variables. This allowed us to extract the unique variance of SPU and to test the 'pure' association of SPU with health. Holm–Bonferroni correction [37] was used, and statistical significance was set at .05. All analyses were conducted using SPSS software (version 20). Also, standardized regression slopes (β) were presented instead of raw slopes to allow comparison between unadjusted and adjusted SPU with a scale free estimation [38].

3. Results

3.1 Descriptive analysis

Prevalence rates and descriptive statistics are shown in Tables 1 and 2. On average, the participants used 2.07 drugs for CPU (SD = 1.48), 1.46 drugs for usual SPU (SD = 1.03), and 1.84 drugs for maximum SPU (SD = 1.27). The most commonly used drugs were: alcohol (the most widely used substance, with 97.8% of participants drinking at least once during the past 12 months, 81.0% drinking at least once simultaneously on a usual occasion, and 84.6% drinking at least once simultaneously on occasions where they combined a maximum of various drugs), tobacco (49.8% CPU, 44.0–56.5% SPU), and cannabis (32.1% CPU, 15.4–29.2% SPU). Crystal meth, heroin, ketamine, GHB/GBL, research chemicals, and spice were the least commonly used drugs (0.3–0.5% CPU, 0.0–0.2% SPU).

10

[Please insert Tables 1 & 2 about here]

3.2 CPU and SPU patterns

Cross tables displaying the calculated CPU and maximum SPU values for each drug are presented. Cross tables are not presented for usual SPU because of the small sample size obtained for some drugs. Table 3 shows the results for CPU. Participants using only one drug, predominantly consumed alcohol (97.4%). When two drugs were used, it was most commonly alcohol (98.6%) and tobacco (78.3%). When three drugs were used, cannabis was added to alcohol and tobacco (94.3%). When 4–7 drugs were used as CPU, hallucinogens (magic mushrooms, others hallucinogens, salvia divinorum), uppers (ecstasy, cocaine, speed amphetamines/methamphetamines), and sniffed drugs (poppers and solvents) were incorporated. Finally, when eight or more drugs were used, spice, crystal meth, heroin, GHB/GBL, research chemicals, and ketamine were the choice substances to be added. Commonly, these 'later stage' drugs (i.e., spice, crystal meth, heroin, GHB/GBL, research chemicals, and ketamine) were added without replacing "early stage" drugs.

[Please insert Table 3 about here]

The results for maximum SPU were similar to CPU (Table 4). The first association was alcohol and tobacco (among the participants who reported the use of two drugs simultaneously, 98.7% used alcohol and 89.9% used tobacco), which were combined with cannabis when three drugs were used at the same time. When 4–5 drugs were used simultaneously, hallucinogens (magic mushrooms, others hallucinogens, salvia divinorum), uppers (ecstasy, cocaine, speed

amphetamines/methamphetamines), and sniffed drugs (poppers and solvents) were added to those drugs already being used. Spice, crystal meth, heroin, GHB/GBL, research chemicals, and ketamine were incorporated when six or more drugs were used. As with CPU, if additional drugs were simultaneously used, then participants commonly added them without replacing other drugs that were already in use.

[Please insert Table 4 about here]

3.3 Associations of SPU with mental, social, and physical factors

The results for the models of usual and maximum SPU associations, with and without taking CPU into account, are shown in Table 5. In the unadjusted model, usual SPU was associated with all seven dependent variables, whereas maximum SPU was associated with six out of the seven dependent variables. When participants used more substances simultaneously, they also felt more depressed ($\beta = .124-.136$, p < .001), anxious ($\beta = .053-.064$, p < .001), and aggressive ($\beta = .147-.182$, p < .001). In addition, they had a poorer state of mental health ($\beta = -.113$ to – .098, p < .001), and reported more negative social ($\beta = .290-.304$, p < .001) and health ($\beta = .088-.109$, p < .001) consequences. There was also a negative association between physical health and usual SPU ($\beta = -.052$, p < .001). In the adjusted models, SPU also had an additive association with aggressiveness ($\beta = .058-.115$, p < .001) and negative social consequences ($\beta = .098-.110$, p < .001). However, SPU was no longer negatively associated with depression, anxiety, health consequences, or mental/physical health. The remaining associations were not as strong as those of the unadjusted models (e.g., aggressiveness: $\beta = .147$ for maximum SPU and $\beta = .058$ for residuals of maximum SPU).

[Please insert Table 5 about here]

4. Discussion

4.1 Patterns of CPU and SPU

This study investigated the patterns of CPU and SPU by examining separate cross tables for CPU and maximum SPU with each drug. The results indicated that drugs were commonly added for both CPU and maximum SPU. We found that when participants increased the number of drugs they using, they usually did not replace one drug with another. Instead, they added more drugs to those that were already in use. The order in which drugs were added resembled the sequential drug use patterns described in previous studies, with licit drugs (alcohol and tobacco) used initially, followed by cannabis and then other illicit drugs [39-42]. Apart from cannabis, the use of two distinct classes of illicit drugs was identified. The drugs that we found to be used first included: hallucinogens (magic mushrooms); other hallucinogens (LSD or salvia divinorum); uppers (speed, ecstasy, cocaine, amphetamines, or methamphetamines); and sniffed drugs (poppers or solvents). The use of these substances was followed by use of other 'hard' drugs, such as ketamine, heroin, GHB/GBL, research chemicals, crystal meth, and spice. In fact, it appeared that there was an escalation in the types of illicit drugs being used. In other words, the number of drugs used can be considered as an indicator of the severity of polydrug use. This result supports the use of "total number of drugs" as a relevant variable, as an increasing number of drugs added information (i.e., additional drugs to those already used), but was not something qualitatively different (e.g., other drugs instead of those already used).

4.2 Associations of SPU with mental, social, and physical factors

Regression analyses showed that CPU was a confounding variable for SPU. When the models were not adjusted for CPU, SPU showed an association with all factors related to mental, social, and physical consequences (except physical health with SPU maximum). When the variance between CPU and SPU was taken into account, the only remaining associations were aggressiveness and negative social consequences (for both usual and maximum SPU). In other words, the number of drugs used concurrently had an important association with health factors, which is in line with previous studies [15-18]. It is well known that aggressiveness and social consequences are interrelated. Therefore, this finding might suggest that SPU will only display this independent association among a subgroup of individuals prone to these types of behavioral disorders. There was no significant association between SPU and depression, anxiety, or mental/physical health consequences when CPU was taken into account. These results were interesting as they may indicate that users understood the pharmacology of the drugs they used, combining them intentionally to reduce undesired effects [20, 43, 44]. Indeed, some associations are well known (e.g., alcohol reduces the discomfort of coming down from cocaine [26, 45], and cocaine attenuates the negative effects of alcohol) [26]. In addition, heroin can be used when coming down from cocaine to attenuate its anxiogenic effects, whereas cocaine can be used to temper the depressive effects of heroin [46]. Thus, the absence of association between SPU and depression, anxiety, or mental health may be explained by a users' intention to combine drugs in order to avoid particular detrimental effects, such as depression and anxiety. Another explanation could be that the number of drugs used accounts for associations with health/consequences and that combined simultaneous use does not add more to this association. This would mean that measuring the solely number of drugs used, and not necessarily their simultaneous use, may be

sufficient in substance use surveys. Further investigations will be needed to test these two hypotheses.

4.3 Limitations

The main limitation of this study was its cross-sectional design. This design did not allow a conclusion to be made on whether polydrug use was a cause or a consequence of health, mental, and social problems, as is often the case in these types of studies [47, 48]. However, C-SURF is a longitudinal study, and future analyses will focus on studying the effect of past drug use on current psychological distress. Another limitation of our study was that it did not include female participants. Associations between polydrug use and health factors should be studied in a sample of women in order to assess the potential differences between men and women with regard to these findings. A third limitation involved the use of a personality scale to assess anxiety and aggressiveness. Although this scale can be employed to examine the level of anxiety or aggressiveness at a given time point, further studies using questions more closely related to psychological health or distress are needed.

5. Conclusion

Here, we have demonstrated that the pattern of CPU and SPU within a sample of young adult men followed previously described stages of drug use, involving the sequential use of alcohol, tobacco, cannabis, and then other illicit drugs. In addition, two distinct classes of illicit drugs were identified. The first class included uppers, hallucinogens, and sniffed drugs, whereas the second class included ketamine, heroin, GHB/GBL, research chemicals, crystal meth, and spice. As the users progressed along this sequence of drug use, they did not stop taking any of the drugs that they were already using. For this reason, the number of drugs used can be seen as a proxy of the severity of polydrug use.

The additive effect of SPU on CPU was also assessed in this study. Previous reports have indicated that SPU can be distinguished from CPU. Thus, even though these two concepts are linked, they remain discriminable constructs [19]. Consistent with this idea, we have found that SPU is independently associated with social factors, including aggressiveness and negative social consequences among young men. However, we did not observe any relevant associations with some specific outcomes related to mental health, such as depression or anxiety.

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	% of users					
	CPU	Usual SPU	Maximum SPU			
Alcohol	97.8	81.0	84.6			
Tobacco	49.8	44.0	56.5			
Cannabis	32.1	15.4	29.2			
Hallucinogens/magic mushrooms	2.7	0.3	1.1			
Other hallucinogens	2.3	0.5	1.3			
Salvia divinorum	2.1	0.2	0.8			
Speed	2.7	0.7	1.6			
Amphetamine/methamphetamines	1.9	0.5	0.9			
Crystal meth	0.3	0.1	0.1			
Poppers	2.6	0.3	0.8			
Inhalants	2.2	0.2	0.6			
Ecstasy	3.8	1.1	2.6			
Cocaine	3.3	0.9	2.4			
Heroin	0.3	0.1	0.1			
Ketamine	0.5	0.0	0.2			
GHB/GBL	0.4	0.1	0.2			
Research chemicals	0.3	0.0	0.1			
Spice	0.5	0.0	0.1			

Table 1. Prevalence rates for each drug for CPU, usual SPU, and maximum SPU

For example, 97.8% of the participants used alcohol concurrently during the past 12 months, whereas only 0.5% used spice concurrently during the past 12 months. On a usual occasion, 81.0% of the participants drank alcohol simultaneously with another substance, and only 0.1% of them used heroin simultaneously with another substance.

	Mean	SD
CPU (1-18)	2.07	1.48
SPU usual (0-18)	1.46	1.03
SPU maximum (0-18)	1.84	1.27
Social consequences (0-1)	0.22	0.21
Health consequences (0-1)	0.17	0.19
Depression (0-5)	0.69	0.70
Aggressiveness (0-1)	0.42	0.21
Anxiety (0-1)	0.20	0.20
Mental health $(0-100)^1$	47.36	9.01
Physical health (0-100) ¹	53.11	6.26

Table 2. Descriptive statistics for polydrug use and outcomes

Remarks: Ranges are given in brackets. SD: standard deviation.

¹ A higher score indicated better health, in contrast to the other variables in the table. The value 50 is the standardized mean.

	CPU – number of drugs used								
	1	2	3	4	5	6	7	8	9 and more
	N=	N=	N=	N=	N=	N=	N=	N=	N=
	2341	1459	1077	199	72	58	39	22	52
Alcohol	97.4	98.6	99.9	98.5	100	100	100	100	94.2
Tobacco	2.2	78.3	96.5	98.0	97.2	96.6	97.4	100	90.4
Cannabis	0.3	19.5	94.3	91.5	98.6	94.8	92.3	100	86.5
Poppers	0.0	1.3	1.8	19.6	20.8	22.4	17.9	13.6	42.3
Hallucinogens/magic mushrooms	0.0	0.3	0.8	17.1	23.6	34.5	43.6	40.9	69.2
Salvia divinorum	0.0	0.2	0.5	17.1	19.4	13.8	30.8	31.8	61.5
Ecstasy	0.0	0.1	0.9	14.1	33.3	63.8	74.4	100	96.2
Cocaine	0.0	0.1	1.1	12.1	33.3	55.2	59.0	59.1	90.4
Solvent sniffing	0.0	1.4	2.4	11.6	20.8	17.2	12.8	9.1	28.8
Speed	0.0	0.0	0.8	6.5	16.7	36.2	61.5	68.2	94.2
Other hallucinogens	0.0	0.1	0.3	3.5	15.3	37.9	46.2	77.3	82.7
Amphetamine/methamphetamines	0.0	0.0	0.2	5.5	13.9	13.8	41.0	54.5	84.6
Spice	0.0	0.1	0.1	1.5	2.8	6.9	7.7	4.5	19.2
Chrystal meth	0.0	0.1	0.1	0.0	1.4	0.0	2.6	13.6	19.2
Heroin	0.0	0.0	0.0	0.5	1.4	0.0	0.0	4.5	25.0
GHB/GBL	0.0	0.0	0.2	1.0	0.0	1.7	0.0	13.6	28.8
Research chemicals	0.0	0.0	0.1	1.0	0.0	3.4	5.1	4.5	19.2
Ketamine	0.0	0.0	0.0	1.0	1.4	1.7	7.7	4.5	34.6

Table 3. Percentages of each drug use according to the number of CPU

For example, among the participants who used 1 drug concurrently (n= 2,341), 97.4% drink alcohol, 2.2% smoke tobacco, 0.3% use cannabis, and 0.1% use solvent

	Maximum SPU – number of drugs used					
	2	3	4	5	6	7 and more
	N=	N=	N=	N=	N=	N=
	1734	1159	153	47	40	36
Alcohol	98.7	99.1	98.7	97.9	97.5	94.4
Tobacco	89.9	98.4	98.0	95.7	97.5	94.4
Cannabis	10.5	95.7	90.8	100	97.5	100
Ecstasy	0.1	1.3	22.2	53.2	75.0	94.4
Cocaine	0.2	1.4	19.6	53.2	60.0	77.8
Hallucinogens/magic mushrooms	0.1	0.5	14.4	10.6	17.5	44.4
Others hallucinogens	0.1	0.5	12.4	14.9	27.5	61.1
Salvia divinorum	0.0	0.3	13.1	12.8	10.0	25.0
Poppers	0.2	0.7	12.4	10.6	10.0	13.9
Speed	0.1	0.7	5.9	25.5	67.5	72.2
Solvent sniffing	0.1	1.1	5.2	4.3	7.5	13.9
Amphetamine/methamphetamines	0.1	0.1	2.6	14.9	22.5	69.4
GHB/GBL	0.0	0.0	0.7	0.0	5.0	22.2
Research chemicals	0.0	0.1	1.3	0.0	2.5	8.3
Ketamine	0.0	0.1	2.0	2.1	2.5	13.9
Spice	0.1	0.1	0.7	2.1	0.0	11.1
Crystal meth	0.1	0.0	0.0	0.0	0.0	5.6
Heroin	0.0	0.0	0.0	2.1	0.0	16.7

Table 4. Column percentages of each drug use according to the number of maximum SPU drug

use

For example, among the participants who used 2 drugs simultaneously (n=1,734), 98.7% drink alcohol, 89.9% smoke tobacco, 10.5% use cannabis, 0.2% use cocaine, 0.2% use poppers, and 0.1% use ecstasy, hallucinogens such as magic mushrooms, others hallucinogens, speed, solvent, amphetamines/methamphetamines, spice and crystal meth.

	SPU (ui	nadjusted)	Residuals from CPU models (adjusted)			
	usual	maximum	usual	maximum		
Outcomes	β (SE)	β (SE)	β (SE)	β (SE)		
Social consequences	.290 (0.003)***	.304 (0.002)***	.110 (0.004)***	.098 (0.003)***		
Health consequences	.088 (0.014)***	.109 (0.14)***	.011 (0.013)	.025 (0.014)		
Aggressiveness	.182 (0.014)***	.147 (0.014)***	.115 (0.014)***	.058 (0.014)***		
Anxiety	.064 (0.014)***	.053 (0.014)***	.021 (0.014)	004 (0.013)		
Physical health	052 (0.014)***	034 (0.014)	020 (0.014)	.012 (0.013)		
Mental health	098 (0.014)***	113 (0.014)***	011 (0.014)	013 (0.014)		
Depression	.124 (0.014)***	.136 (0.014)***	.021 (0.014)	.014 (0.013)		

Table 5. Standardized slopes (β) of regression analyses for unadjusted and adjusted models of health issues on SPU.

Remarks: Standardized standard errors (SE) are given in parentheses.

 $r_{CPU,\ usual\ SPU} = 0.645^{***};\ r_{CPU,\ maximum\ SPU} = 0.748^{***}$

 * p < .05, ** p < .01, *** p < .001. p-values with a Holm–Bonferroni correction are given.