



## Relationships between substance initiation sequence and further substance use: A French nationwide retrospective study



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### HIGHLIGHTS

- We explored relationships between initiation sequence and further substance use.
- Further use likelihood increased with the number of substances previously initiated.
- Order of sequence was not related with further use.
- Polysubstance initiation appears as a better predictor of further use than sequence.

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### ABSTRACT

The Gateway theory (GT) proposes that tobacco or alcohol use lead to cannabis use, which can itself be followed by other illicit drugs (OID) onset. Aim of this study was to evaluate if the order of initiation sequence could influence further substance use. Data from a 2010 population-based survey were used (22,774 subjects aged 15–64). Using reported ages at initiations, 7 sequences were identified: initiation of tobacco only (T), cannabis or OID only, tobacco followed by cannabis (T–C), cannabis followed by tobacco (C–T), alternative 2-substance sequences, gateway sequence (T–C–OID) and 3-substance alternative sequences. Logistics regressions were performed to study the impact of sequence on further use (tobacco, alcohol, cannabis and OID), and substance use disorders (SUD) (tobacco, alcohol and cannabis). The most observed sequences were T (45.5%), T–C (20.5%), C–T (5.1%) and T–C–OID (3.5%). Further use and SUD likelihoods, whatever the substance considered, increased with the number of substances previously initiated. However, for a same number of substances initiated, current use and SUD likelihoods did not significantly vary according to sequence. Polysubstance initiation appears as a better predictor of further use and SUD than the initiation sequence, questioning the GT and being more in line with a common liability to substance use.

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### 1. Introduction

Psychoactive substance use is widely observed in Europe, and particularly in France (European monitoring centre for drugs and drug addiction, 2015). According to the European monitoring centre for drugs and drug addiction, between 10% and 36% of 18–64 year-old reported a cannabis lifetime use (33% in France) and between 1.7% to 7.0% a past-month use (4% in France) (Beck, Guignard, Richard, Tovar, & Spilka, 2011a; European monitoring centre for drugs and drug addiction,

2014a). The most commonly used other illicit drugs (OID) are stimulants like cocaine (3% mean lifetime use prevalence in Europe and 4% in France), amphetamines and ecstasy (respective lifetime use prevalences around 2% in Europe and in France) (European monitoring centre for drugs and drug addiction, 2014a). These behaviors are mainly observed among adolescents and young adults, who frequently report polysubstance use. According to the European school survey on alcohol and other drugs (ESPAD), around 7% of students report lifetime use of more than one illicit drug. ESPAD also reports that those who had used cannabis were also more likely to be regular users of alcohol and tobacco (European monitoring centre for drugs and drug addiction, 2014b). Another study observed that 8% of the French population used regularly (at least 10 use occasions during the past month) some

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combination of alcohol, tobacco and cannabis, and suggested a strong association between cannabis regular use and OID lifetime use, particularly among the 15–34 year-old (Beck, Legleye, & Spilka, 2008).

If several substances are initiated during the life, these initiations are likely to follow a sequence. According to the gateway theory (GT), cannabis use typically follows licit drug use such as tobacco and/or alcohol use, whereas OID use follows cannabis use (Kandel, 1975). The GT is based on a temporal sequence in the initiation of different substances (Guxens, Nebot, & Ariza, 2007a) and on the statistical association between patterns of use, whereby substance experiment at the beginning of the sequence increases the risk of subsequent use of another substance at the end of the sequence (Lessem et al., 2006; Guxens, Nebot, Ariza, & Ochoa, 2007b; Korhonen et al., 2010). However, some studies observed that use sequences do not always follow the gateway pattern. Golub and Johnson (1994) found that a majority of illicit drug users in the general population were experimental users, few subjects becoming regular OID users. Another study among heavy drug users found that only 33% followed a sequence leading from alcohol to cannabis and then OID (Mackesy-Amity, Fendrich, & Goldstein, 1997).

The route of administration model (RAM) was proposed to explain the reverse sequences leading from cannabis to tobacco, suggesting that the shared inhaled route of both substances may explain why tobacco and cannabis use commonly coexists (Agrawal & Lynskey, 2009).

The impact of GT in terms of public health could also be questioned if considering the low prevalences of OID use compared with tobacco, alcohol and cannabis, suggesting that most of substance users do not follow the sequence as a whole. Moreover, if the use of OID, such as cocaine and heroin, is frequently preceded by cannabis use (Mayet, Legleye, Falissard, & Chau, 2011), the impact of the association between marijuana and OID appears negligible when taking account of cannabis use prevalence (Earleywine, 2002).

It should also be noted that the GT applies only to the use patterns between different substances rather than different levels or extent of drug involvement (from use to dependence) and does not extend to substance use disorders (SUD) development (Kandel & Jessor, 2002; Vanyukov et al., 2012). Some research even suggests no significant association between substance initiation sequence and SUD: Tarter et al. (2012) suggested that cannabis use disorders resulted from a transmissible risk measured at childhood, this relationship being mediated by non-normative socialization, without effect of order of initiations. Palmer et al. (2009) found that progression toward a SUD for tobacco, alcohol or cannabis in young adulthood was increased with prior involvement with any of the three substances during adolescence, suggesting a generalized risk that could explain early onset and subsequent development of SUD for all substances. This concept was also described as the common liability model (CLM). In contrast to the

GT, which only addresses the order of drug-use initiation, the CLM proposes that using both licit and illicit drugs could be attributable to the influence of a common liability (Morral, Mc Caffrey, & Paddock, 2002; Vanyukov et al., 2012). This liability could include a genetic and individual vulnerability, such as proneness to deviancy and familial liability to addiction (Agrawal, Neale, Prescott, & Kendler, 2004; Kendler, Myers, & Prescott, 2007; Hicks, Iacono, & McGue, 2012).

The aim of the present study was to explore the relationships between initiation sequence and current substance use and SUD in the French population, in order to evaluate if the number and the order of substances initiated during the life could have further clinical impact.

## 2. Methods

### 2.1. Sample

This study was based on the data from 2010 'Health Barometer', a French nationwide telephonic survey on health perceptions, knowledge, attitudes and behaviors among population aged 15–85 years, using a two-stage sampling frame (household/individual) (Beck, Gautier, Guignard, & Richard, 2011b). The study protocol included a request to participate, explaining the aims of the study, and a telephone interview conducted by a trained investigator using Computer-Assisted Telephone Interview (CATI) software. All collected data were anonymous and self-reported. Data were weighted by taking into account the inclusion probability (depending on the number of telephone lines and the number of eligible persons in each household). They were also adjusted to the latest distributions in the French population (available from the National Institute of Statistics and Economic Studies) according to gender, age, educational level, geographical region and urbanization level. This protocol was approved by the French Commission on Individual Data Protection and Public Liberties (CNIL). The initial sample included 27,653 people. The present study focused on the subjects who were asked about substance use (22,774 aged 18–65).

### 2.2. Measures

Current substance use status was approached with self-reported past 12-month use for tobacco, alcohol, cannabis and OID. OID use was defined as the use of at least one substance among three categories: hallucinogens (mushrooms, LSD, ecstasy, GHB, ketamine), stimulants (amphetamines, cocaine, crack) and depressants (Opiates, methadone, buprenorphine). Three validated instruments were used to explore SUD. Tobacco dependence was screened with the heavy smoking index (HSI) that combines two items of the Fagerström test: the number of cigarettes smoked per day and the time-lapse between waking and first cigarette smoked (Fagerström, 1978; Heatherton, Kozlowski, Frecker, Rickert, & Robinson, 1989). The thresholds were 2 for average dependence and 4 for high dependence. Alcohol use disorders were identified using the Alcohol use disorders identification test (AUDIT), a score ranging between 7 and 11 for men (6–11 for women) defining hazardous use and a score from 13 defining a risk for dependence for both genders (Bush, Kivlahan, McDonell, Fihn, & Bradley, 1998). The cannabis abuse screening test (CAST) was used to define low and high cannabis dependence risks with thresholds at 3 and 7, respectively (Legleye, Kraus, Piontek, Phan, & Jouanne, 2012).

The reported ages at tobacco, cannabis and OID initiation were used to define 7 initiation sequences: initiation of tobacco only (T), initiation of cannabis or OID only (Other1), tobacco followed by cannabis (T-C), cannabis followed by tobacco (C-T), sequences involving both cannabis and OID without tobacco (Other2), tobacco followed by cannabis followed itself by OID (T-C-OID), and other sequences involving 3 substances (Other3). Subjects who reported the initiation of several substances the same year were reclassified in the closest sequence according to current substance use prevalences.

**Table 1**  
Socio-demographic characteristics of the sample (12,427 women and 10,347 men).

Variables		Women		Men		p*
		N	%	N	%	
Age (years)	50–64	4246	57.6	3125	42.4	10 <sup>-3</sup>
	35–49	4100	53.4	3576	46.6	
	15–34	4080	52.8	3646	47.2	
Education level	Tertiary education	4229	24.6	3318	22.8	10 <sup>-4</sup>
	Upper secondary education	2458	19.6	1870	17.1	
	Low secondary education	4638	38.0	4292	42.9	
	No diploma	1082	17.8	867	17.1	
Household income (€)	>1800	3345	24.4	3367	29.7	10 <sup>-4</sup>
	1100–1800	4435	35.7	3757	36.5	
	<1100	3798	40.0	2612	33.9	
Poverty index	Well-to-do	6790	53.8	6176	57.6	10 <sup>-4</sup>
	Average	2640	20.8	2169	21.3	
	Insecure	2959	25.5	1973	21.1	

\* Fisher's test.

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