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What are the high risk periods for incident substance use and transitions to abuse and dependence? Implications for early intervention and prevention

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Abstract

Background: *For a better understanding of the evolution of addictive disorders and the timely initiation of early intervention and prevention, we have to learn when and how quickly the critical transitions from first substance use (SU) to regular use and from first SU and regular SU to abuse and dependence occur. Little data are currently available on the transitions to substance use disorders (SUDs) across the spectrum of legal and illegal drugs taking into account gender differences. It is the aim of this paper to describe the high density incidence and transition periods of SU and SUD for alcohol, nicotine, cannabis and other illicit drugs for young males and females.*

Methods: *A sample of (N = 3021) community subjects aged 14–24 at baseline were followed-up prospectively over 10-years. SU and SUD were assessed using the DSM-IV/M-CIDI. Results: Ages 10–16 are the high risk period for first alcohol and nicotine use (up to 38% of subjects start before age 14). Onset of illegal SU occurs later. Substantial proportions of transitions to regular SU and SUD occur in the first three years after SU onset. Only few gender differences were found for time patterns of SU/SUD incidence and transition.*

Conclusion: *Except for alcohol the time windows for targeted intervention to prevent progression to malignant patterns in adolescence are critically small, leaving little time for targeted intervention to prevent transition. The fast transitions to abuse and dependence in adolescence may be indicative for the increased vulnerability to substance effects in this time period. Basic research on the determinants of transitions should thus target this period in adolescence.* Copyright © 2008 *John Wiley & Sons, Ltd.*

Key words: substance use, age, onset, epidemiology

Introduction

First use of alcohol and nicotine is almost a normative experience in adolescence in Western countries (Bonomo et al., 2004; Everett et al., 1999; Nelson and Wittchen, 1998a, 1998b; Poelen et al., 2005). Also, cannabis use (CU) is a frequent phenomenon in adolescence (Boden et al., 2006; Monshouwer et al., 2005; Wittchen et al., 2007). Rates for illicit SU of other type are lower but still considerable (Boden et al., 2006; Wittchen et al., 2007).

Epidemiological research over the past two decades has shown that even in adolescence and early adulthood substance use disorders (SUDs; abuse and dependence) according to DSM-IV criteria are more frequent than previously thought. Prevalence estimates for dependence on alcohol, cannabis or other illicit drugs were considerable, in some studies up to 10% and above (Boden et al., 2006; Compton et al., 2004; Harford et al., 2005; Nelson and Wittchen, 1998a, 1998b). In a German community sample the cumulative incidence for any SUD up to age 27 was 45.9% (Wittchen et al., 2007). These high rates were in contrast to older clinical observations that rarely saw substance dependent patients in institutional settings. It was also inconsistent with traditional addiction models that assumed that addiction predominantly develops only after many years of substance use (SU) (Feuerlein, 1989). Thus, it has become important to re-examine the issue of the temporal evolution of SU, regular SU and SUDs. Earlier observations in this respect were largely based on retrospective cross-sectional evidence. This paper will now re-examine the issue with prospective-longitudinal data from the EDSP (Early Developmental Stages of Psychopathology) study.

Despite evidence for substantial gender differences in the prevalence of SU and SUD (Bonomo et al., 2004; Wagner and Anthony, 2007), it is not as clear, whether there are gender differences in transition patterns. Wagner and Anthony (2007) could show that the higher risk of cannabis dependence in males emerged at about 2–5 years after first CU, while the greater risk of alcohol dependence already showed during the first year after first alcohol use. In a high-risk sample, for alcohol, nicotine and cannabis, no significant difference in speed of transition from first to regular SU and dependence emerged (Ridenour et al., 2006). Males were more likely to initiate smoking at under 13 years (Everett et al., 1999). In contrast, no gender differences were found for incidence patterns of CU and cannabis use disorder (CUD) (Perkonigg et al., 1999).

To summarize, possibly as a result of differences in assessment instrument, study design, region and culture, it remains difficult to draw a coherent pattern of the incidence and transition patterns of SU and SUD in Germany across the whole spectrum of substances and gender differences. Such information though, is of high relevance for planning interventions and prevention in the core risk period for incident SU and SUD in adolescence and young adulthood.

Aims

Using data from a large prospective-longitudinal community survey in adolescents and young adults followed up to age 34, and taking into account gender differences, we aim to identify:

(1) the core periods of incidence of SU, regular SU and SUD for alcohol, nicotine, cannabis and other illicit drugs;
(2) the proportion of transitions to more problematic SU and the periods of transition from initial use to regular use, abuse and dependence;
(3) the periods of transition from first regular use to abuse and dependence.

Methods

Sample and overall design

Data were derived from the EDSP study, a prospective-longitudinal study designed to investigate the course and risk-factors for SU and SUD and other mental disorders. The study sample is a stratified community sample aged 14–24 at baseline ($N = 3021$). The baseline sample was drawn from metropolitan Munich, Germany government registries in 1994 and followed-up over a 10 year period with up to three follow-up assessments. Because the study emphasizes early developmental stages of psychopathology, individuals aged 14–15 at baseline were sampled at twice the probability of those aged 16–21. Individuals aged 22–24 were sampled at half the probability of those aged 16–21. The baseline examination was conducted in 1995 (T_0, $N = 3021$); the follow-up waves took place approximately 1.6 years (T_1, median interval since baseline, only for the younger cohort of $N = 1228$ subjects aged 14–17 at baseline), 3.5 years (T_2) and 8.2 years (T_3) after T_0. Response rates were 71% at T_0 ($N = 3021$), 84.3% ($N = 2548$) at T_2 and 73.2% ($N = 2210$) at T_3. The age ranged at T_3 was 21–34 years. Further descriptions of the sample, the study design and objective have been presented elsewhere (Lieb et al., 2000; Wittchen et al., 1998b).

Diagnostic assessment

At each assessment, participants were assessed with the baseline or follow-up computer-assisted versions of the Munich-Composite International Diagnostic Interview (DIA-X/M-CIDI) (Wittchen et al., 1998a; Wittchen and Pfister, 1997), an updated version of the World Health Organization (WHO) CIDI (Wittchen and

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Semmler, 1990). The DIA-X/M-CIDI is a fully standardized diagnostic interview (Wittchen et al., 1998a) with which it is possible to assess symptoms, syndromes and diagnosis of 48 mental disorders along with information about impairment, course, and severity. The diagnoses presented in this article are based on the computerized M-CIDI/DSM-IV algorithms. The validity and test–retest reliability of DIA-X/M-CIDI diagnoses have been established and reported elsewhere (Lachner et al., 1998; Reed et al., 1998; Wittchen, 1994; Wittchen et al., 1998a). The intra-class-coefficients (ICC) for age of onset information were good for first use of nicotine (ICC = 0.83), alcohol (ICC = 0.96), and other illicit drugs (ICC = 1.00) (Lachner et al., 1998). All interviews were conducted by trained clinical interviewers.

Assessment of SU and SUD

SU and SUD were assessed with the three DIA-X/M-CIDI-sections for alcohol, nicotine, and medication and illicit drugs. These sections have been described elsewhere (Perkonigg et al., 2008). SUD criteria were assessed if a participant reported minimal SU of the respective substance. Thresholds were (a) daily tobacco use over one month, (b) at least regular alcohol consumption (at least three times a week or more than three standard drinks per day in subjects who had drunk on more than 12 occasions in at least one year of their lives; applied for alcohol dependence; alcohol use on at least 13 occasions in at least one year of their lives; applied for alcohol abuse), (c) CU and other illicit SU more than four times. For this paper, four classes of substances were considered: alcohol, nicotine, cannabis and other illicit drugs. The following use levels were used for each substance: no use, any use, regular use, abuse, and dependence (DSM-V-diagnoses of abuse and dependence were non-hierarchical). Regular use was defined as: (a) at least weekly alcohol consumption, (b) at least daily nicotine use over at least four weeks, (c) CU and other illicit SU on at least five occasions.

Statistical analysis

To account for different sampling probabilities at baseline according to age, and response rates at baseline varying over age, gender, and geographic region, data were weighted. The Stata Software package 10.0 (StataCorp., 2007) was used for calculations and to compute robust variances, confidence intervals, and *p*-values (by applying the Huber–White sandwich matrix) which is required for analyses with weighted data (Royall, 1986). When generating cumulative lifetime incidences, the LOCF (Last Observation Carried Forward) method (i.e. the information obtained until the last available assessment was taken into account) was applied. To estimate the age-dependent cumulative lifetime incidence of SU and SUD the Kaplan–Meier estimator was used (Therneau and Grambsch, 2000). In addition, the Nelson–Aalen estimator was used. Over the waves, age of onset information was aggregated by using the minimum reported age of onset. When comparing this approach to the use of the age of onset reported first, ICCs were very high (between rho = 0.96 and rho = 1.00) for SU and SUD. Logistic regressions were applied to assess group differences. Cox regressions were applied to assess overall differences in the risk of developing SU and SUD over time between males and females. We allowed for different curves according to age ['stratified Cox regression', (Therneau and Grambsch, 2000)]. To assess whether group differences varied over age, the proportional hazard assumption was tested using Schoenfeld residuals (Therneau and Grambsch, 2000). In case the assumption was violated, the interaction term covariate* age was added to the model in order to improve the model fit and to assess how strongly the hazard ratios depended on age. Here, the model-based age-dependent hazard ratio equals HR (main effect of covariate) * HR (interaction effect of covariate)^{age}. In a next step, the proportional hazard assumption was tested again. If the model-fit was still poor, we identified time intervals between which the hazard ratios showed the highest differences in an exploratory way.

The analysis was conducted for each substance separately, i.e. for the transition from alcohol use to alcohol abuse. Only few subjects had not provided information on age of onset. Data from these subjects could not be used in the survival analyses. For the analyses on transitions, information on age of onset of SU and SUD was necessary. In some cases such information was missing but case numbers were low [between $N = 1$ and $N = 24$; with the exception of onset of other illicit drug use ($N = 198$)]. Also, a number of cases had reported onset of regular SU or SUD as prior to onset of SU (between $N = 3$ and $N = 21$, with the exception of $N = 84$ for regular CU and $N = 210$ for regular other illicit SU). Some cases had reported onset of SUD as before onset of regular use (between $N = 2$ and $N = 100$; detailed information available upon request). These cases had to be excluded from the analyses requiring

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the respective age of onset information but were included in the reports on prevalence.

The time scale used to assess transitions to SUD was the number of years since the onset of SU. Cases with onset of SU and SUD onset within the same 12-months period (i.e. length of transition = 0 years) are automatically excluded from the Cox-regression analysis. To prevent this and to include all cases in the Cox-regression, we shifted the time scale one year upwards, replacing zero years by one year, one year by two years, and so on. This approach was not used for the curves.

Results

Baseline prevalence and cumulative incidence of use, regular use, abuse and dependence

The lifetime prevalence for any SU among males aged 14–24 was 93.8% for alcohol, 79.9% for nicotine, 39.6% for cannabis and 12.0% for other illicit drugs (among females: 95.2% for alcohol, 72.6% for nicotine, 28.8% for cannabis and 10.5% for other illicit drugs). For regular use, rates were 50.8% for alcohol, 36.5% for nicotine, 19.4% for cannabis and 5.6% for other illicit drugs (among females: 30.4% for alcohol, 35.2% for nicotine, 12.6% for cannabis and 4.2% for other illicit drugs). For abuse, rates were 21.4% for alcohol, 5.2% for cannabis and 1.7% for other illicit drugs (among females: 6.2% for alcohol, 2.2% for cannabis and 0.7% for other illicit drug abuse). 10.0 percent reported alcohol dependence, 19.1% nicotine dependence, 2.1% cannabis dependence and 0.9% other illicit drug dependence (among females: 2.5% reported alcohol dependence, 18.5% nicotine dependence, 0.9% cannabis and 0.7% other illicit drug dependence).

At T_3 (see Table 1), having used alcohol and nicotine at least once was almost a normative experience and at least one-time use of cannabis and other illicit drugs was widespread for both genders. SUD rates

Table 1. Cumulative incidence up to age 34 of use, regular use, abuse and dependence by substance and gender

	Total		Males		Females	
	N	Percentage[1]	*N*	Percentage[1]	*N*	Percentage[1]
Alcohol						
Alcohol use	2929	97.69	1481	97.47	1448	97.90
Regular alcohol use	2063	70.59	1167	79.20	896	62.17
Alcohol abuse	741	24.72	560	37.60	181	12.13
Alcohol dependence	327	10.98	250	17.46	77	4.65
Nicotine						
Nicotine use	2354	79.21	1247	82.91	1107	75.60
Regular nicotine use	1596	51.55	829	52.87	767	50.25
Nicotine dependence	847	28.50	440	29.47	407	27.55
Cannabis						
Cannabis use	1485	50.69	862	58.15	623	43.34
Regular cannabis use	933	31.00	585	38.81	348	23.31
Cannabis abuse	304	9.27	235	14.43	69	4.19
Cannabis dependence	102	3.14	72	4.54	30	1.76
Other illicit drugs						
Other illicit drug use	692	24.47	374	26.26	318	22.71
Regular other illicit drug use	377	13.58	207	15.07	170	1.11
Other illicit drug abuse	87	3.19	53	4.22	34	2.18
Other illicit drug dependence	44	1.67	23	1.87	21	1.47

[1] Weighted percentages.

Note: These percentages are incidence measures and indicate that the person has met the respective pattern at some point in the observation period up to age 34. The rates do not indicate current prevalences!

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were considerable, with 28.5% for nicotine and 11.0% for alcohol dependence. Females had lower rates of alcohol and cannabis regular use, abuse and dependence.

Transitions from SU to regular SU, abuse, and dependence

As shown in Table 2, the proportion of transition from first to regular SU was considerable for all substances

Table 2. Proportion of subjects making the transition from use to disorders by gender, type of substance and mean duration of time of transition[1]

Type of transition by substance	Gender	Proportion (%)[1,2]	Time lapse, mean years[2]	Standard deviation[2]
Alcohol				
First use to regular use	males	81.16	4.31	3.01
	females	63.50	4.39	2.99
First use to abuse	males	38.58	3.92	2.94
	females	12.39	4.38	3.19
First use to dependence	males	17.92	4.23	3.06
	females	4.75	4.78	5.08
First regular use to abuse	males	44.29	1.14	1.73
	females	16.86	1.53	2.10
First regular use to dependence	males	21.17	1.43	2.35
	females	7.13	2.46	3.21
Nicotine				
First use to regular use	males	63.77	2.38	2.66
	females	66.47	2.35	2.44
First use to dependence	males	35.54	3.49	2.99
	females	36.44	3.49	3.02
First regular use to dependence	males	55.74	1.47	1.96
	females	54.82	1.57	2.25
Cannabis				
First use to regular use	males	66.75	0.20	0.70
	females	53.77	0.26	1.18
First use to abuse	males	24.81	2.12	2.21
	females	9.67	2.46	3.39
First use to dependence	males	7.81	2.02	1.94
	females	4.06	1.54	1.41
First regular use to abuse	males	36.75	2.18	2.32
	females	17.99	2.26	3.34
First regular use to dependence	males	11.70	2.05	1.94
	females	7.54	1.48	1.14
Other illicit drugs				
First use to regular use	males	57.38	0.52	1.77
	females	53.33	0.12	0.63
First use to abuse	males	16.07	2.44	2.87
	females	9.59	3.45	4.59
First use to dependence	males	7.13	1.07	1.68
	females	6.46	1.71	1.65
First regular use to abuse	males	26.86	4.44	3.09
	females	16.78	5.12	4.18
First regular use to dependence	males	12.43	3.91	2.26
	females	12.12	3.46	2.24

[1] Proportion making the transition.
[2] Weighted.

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and both genders, ranging between 53.3% and 81.2%. The proportion of transitions to abuse and dependence lay between 9.6% and 38.6% (abuse) and 4.1% and 36.4% (dependence), varying with substance and gender.

Males had a higher risk of transition from alcohol use to regular alcohol use [Odds ratio (OR) = 0.38, p = 0.000, 95% confidence interval (CI) = 0.3–0.5; males as comparison group], alcohol abuse (OR = 0.22, p = 0.000, 95% CI = 0.1–0.3), and dependence (OR = 0.22, 95% CI = 0.1–0.3, p = 0.000). Males had a higher risk of transition from CU to regular CU (OR = 0.57, p = 0.000, 95% CI = 0.4–0.7), cannabis abuse (OR = 0.32, p = 0.000, 95% CI = 0.2–0.4), and dependence (OR = 0.49, p = 0.007, 95% CI = 0.3–0.8) as well as from other illicit SU to other illicit drug abuse (OR = 0.55, p = 0.025, 95% CI = 0.3–0.9).

Transitions from regular SU to abuse and dependence

Males made the transition from regular alcohol use to alcohol abuse and dependence more frequently than females (abuse: OR = 0.25, 95% CI = 0.2–0.3, p = 0.000; dependence: OR = 0.28, 95% CI = 0.2–0.4, p = 0.000). They also had a higher risk of transition to cannabis abuse (OR = 0.36, 95% CI = 0.2–0.5, p = 0.000) and abuse of other illicit substances (OR = 0.55, 95% CI = 0.3–0.9, p = 0.039).

Age of onset of SU, regular SU and SUD

Survival analyses were run in order to describe the distribution of onset of SU, regular SU, abuse and dependence in males and females (see Figures 1–4). Table 3 provides an overview over the results on age of onset. First alcohol and nicotine use mainly took place between ages 10 and 17. Incidence of cannabis and other illicit drug use mainly occurred between ages 14 and 20. The proportion of subjects with onset of SU prior to age 14 is remarkably high for nicotine (up to 32.2%) and alcohol (up to 38.5%) but low for cannabis and other illicit drugs (1.6–3.5%) in both genders (Table 3). Regular alcohol and nicotine use mainly started between ages 13 and 21; regular use of illicit drugs between ages 14 and 19. For SUD, the high density incidence phases were clearly in the second decade of life.

We assessed, whether gender was associated with an earlier onset of SU and SUD. With three exceptions, all results were non-significant and the proportional

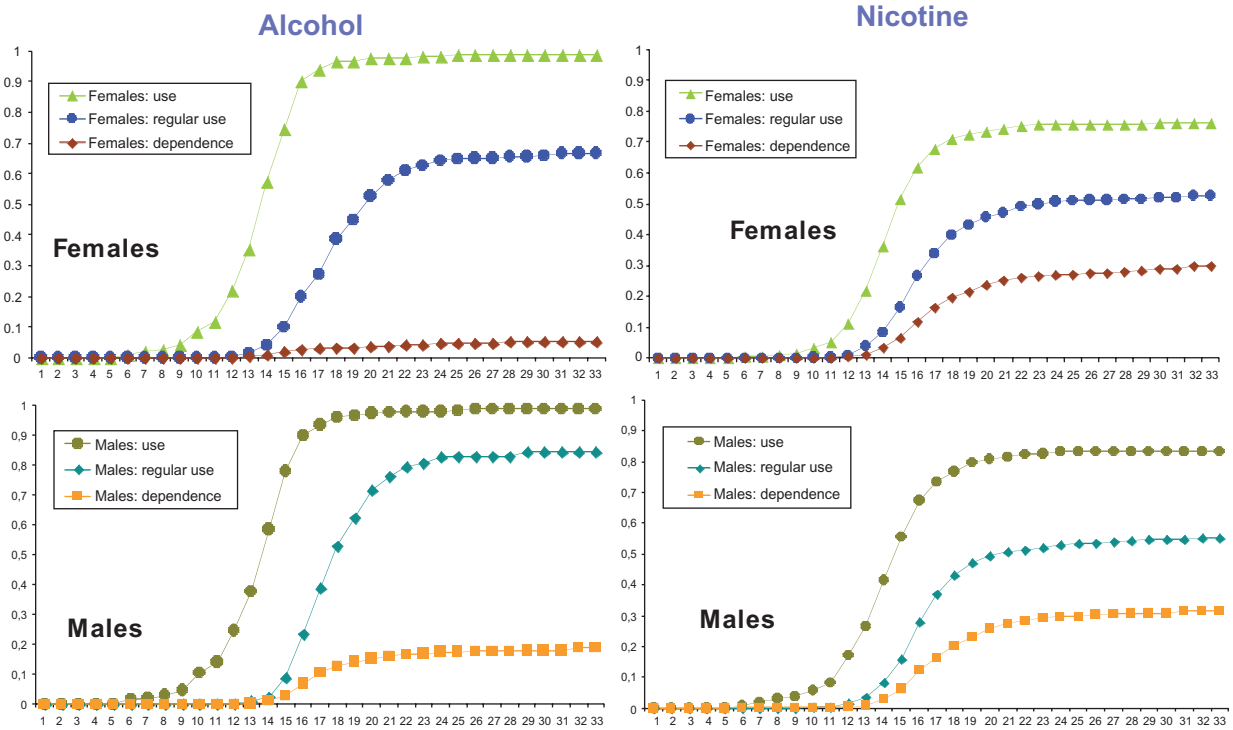

Figure 1. Cumulative probability of first use, regular use, and dependence by gender: alcohol and nicotine.

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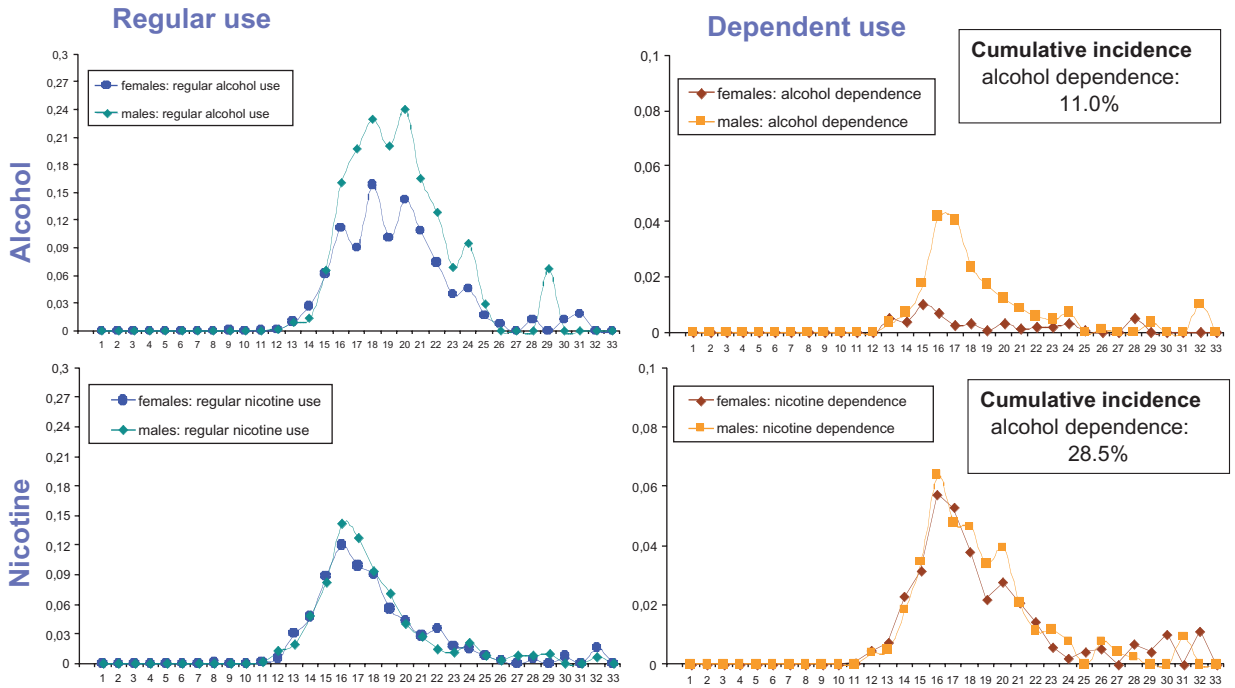

Figure 2. Hazard rates of alcohol and nicotine regular use and dependence in females and males.

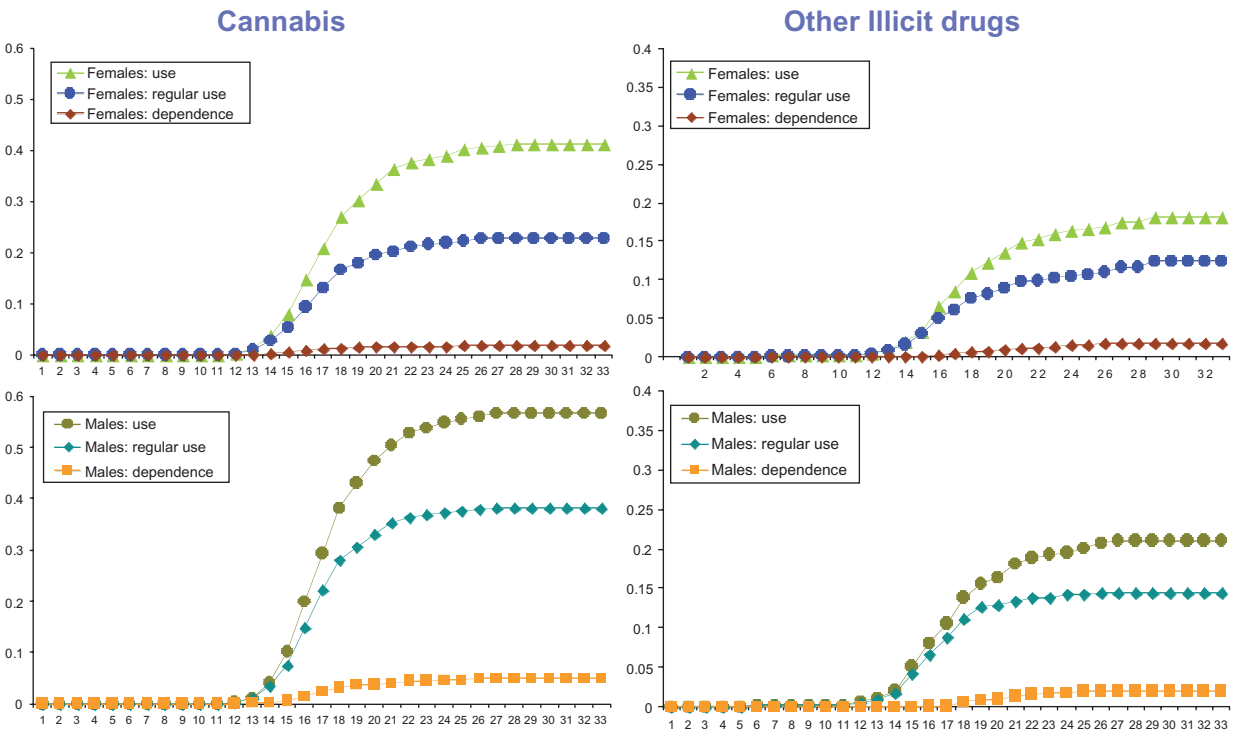

Figure 3. Cumulative probability of first use, regular use, and dependence by gender: cannabis and other illicit drugs.

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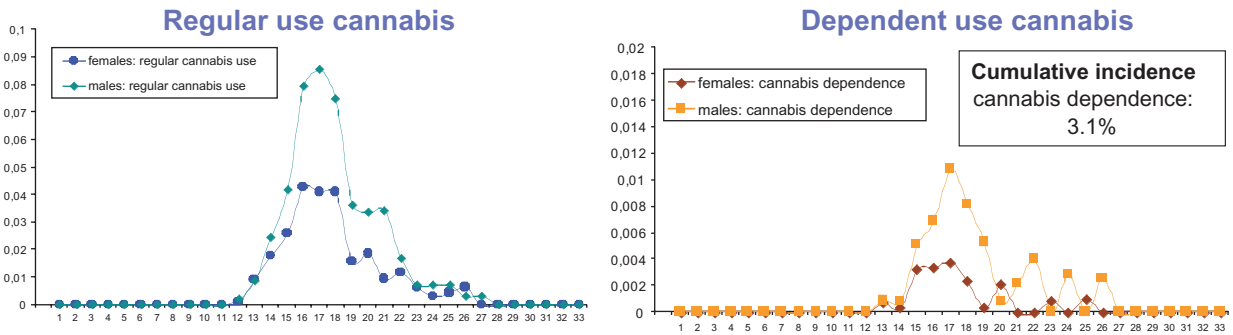

Figure 4. Hazard rates of cannabis regular use and dependence in females and males.

Table 3. Onset of SU and SUD

	Gender	N	Main incidence phase (years)	Mean age of onset[1]	Standard deviation[1]	Proportion (%) with incident SU/SUD under age 14[1]
Alcohol use	males	1479	10–16	13.75	2.54	38.53
	females	1442	10–15	13.93	2.43	35.88
Nicotine use	males	1210	11–17	14.44	2.87	32.23
	females	1084	11–17	14.66	2.60	29.33
Cannabis use	males	788	14–20	17.77	2.61	1.62
	females	555	14–19	17.76	2.83	3.34
Other illicit drug use	males	266	14–20	19.19	3.69	3.22
	females	228	14–20	19.09	3.95	3.54
Regular alcohol use	males	1167	14–21	17.91	2.34	1.43
	females	896	14–21	18.07	2.71	2.07
Regular nicotine use	males	828	13–19	16.79	2.75	6.67
	females	767	13–19	16.85	2.83	7.66
Regular cannabis use	males	571	14–18	17.32	2.46	2.96
	females	338	14–18	17.30	2.71	4.71
Regular other illicit drug use	males	199	14–18	16.75	2.96	6.80
	females	161	14–19	17.70	4.17	7.64
Alcohol abuse	males	556	14–18	17.11	2.56	3.28
	females	179	14–18	17.85	3.15	3.60
Cannabis abuse	males	234	15–20	18.25	2.72	1.26
	females	69	15–18	18.11	3.46	4.20
Other illicit drug abuse	males	52	16–21	20.80	3.72	0.00
	females	34	15–21	19.47	4.13	4.84
Alcohol dependence	males	245	15–18	17.59	2.80	2.11
	females	75	14–16	17.63	4.09	10.80
Nicotine dependence	males	436	14–20	17.57	3.08	3.43
	females	402	14–19	17.53	3.25	4.47
Cannabis dependence	males	72	15–18	18.03	2.84	2.11
	females	30	16–18	17.30	2.67	4.01
Other illicit drug dependence	males	23	18–21	20.15	2.50	0.00
	females	21	17–20	19.27	4.56	7.19

[1] Weighted.

hazard assumption was not violated. Results suggested an earlier onset of regular alcohol use in females (HR main effect 1.58, HR interaction effect 0.94, 95% CI = 0.91–0.98). However, the Cox-proportional hazard assumption was still violated. We assessed different time periods of risk in an exploratory way and found that for onset at or before age 14, the difference in risk of regular alcohol use was non-significant (HR = 1.12, 95% CI = 0.9–1.4, $p = 0.267$). After age 14, males had a higher risk of regular alcohol use (HR = 0.60, 95% CI = 0.5–0.7, $p = 0.000$). For onset of regular other illicit drug use, the risk in females was lower until age 16 (HR = 0.68, 95% CI = 0.5–0.9, $p = 0.007$) and differences in risk were non-significant between ages 17 and 19. For other illicit abuse, differences were non-significant until age 16. Thereafter, males had a higher risk (HR = 0.40, 95% CI = 0.2–0.7, $p = 0.001$).

Speed of transitions from first use to regular use, abuse and dependence

Table 2 informs about the average time lapse between first use and regular use and SUD.

Alcohol

Of all transitions to regular use, abuse and dependence, about 10% occurred during the first year after first use. Of transitions to regular use and abuse, 20–30% had taken place at two and about 40% at three years after first use. For dependence, at two years after first use, about 30% had made the transition. At three years, 50% of female and 40% of male transitions had occurred. We also assessed the risk of transition for different time periods after onset of alcohol use for the first years after onset of use using Cox-regressions. We tested the time periods (a) in the first year and (b) in the second and third year after onset of use. For transitions to regular alcohol use, alcohol abuse and dependence, females had a lower risk during the first year and in the second and third year after first use (table available upon request).

Nicotine

Of all transitions to regular use, 30% took place in the first year, 50–60% had taken place at two years and 70% at three years after first use. For nicotine dependence, almost 20% of transitions had occurred at one year, 30–40% at two years and over 50% at three years after initial use. The tests of gender differences in the first years after initial use were non-significant.

Cannabis

Of all transitions to regular CU, 20–30% occurred during the first year after first use and almost 40% had occurred at two years. For transitions to abuse, almost 30% had occurred at one year after first use, over 50% (females: over 40%) at two years and 70% (females: over 60%) at three years. For cannabis dependence, over 30% of female transitions (males: over 20%) had occurred at one year, 70% (males: over 50%) at two years and 80% (males: 70%) at three years after first use.

Males had a higher risk of transition to regular CU in the first year after CU onset, but not in the second and third year. Males had a higher risk of transition to cannabis abuse in the first three years after onset of use. Males had no higher risk of transition to cannabis dependence during the first three years after first CU. The higher risk of transition to cannabis dependence in males emerged after this period (HR = 0.26, 95% CI = 0.0–0.9, $p = 0.041$).

Other illicit drugs

Of all transitions to regular illicit SU, about 5% had occurred during the first, about 10% at two and about 20% at three years after first use. Of transitions to abuse in males, 30% (females: 20%) had occurred at one year, over 40% (females: over 30%) at two years and over 50% (females: 40%) at three years. Of transitions to dependence in males, 40% (females: 5%) had taken place at one year, over 50% (females: 50%) at two years and 70% (females: 70%) at three years after first use. However, for other illicit dependence, case numbers were low. In the first year after first use, females had a higher risk of transition to regular other illicit SU (1.45, 95% CI = 1.0–2.0, $p = 0.022$). This was not found in the second and third year after initial use. For the first three years after onset of illicit SU, we found no differences in the risk of transition to abuse. For dependence, case numbers were too small to conduct the analysis.

Speed of transitions from regular use to abuse and dependence

Alcohol

Of transitions from regular alcohol use to alcohol abuse in females, over 20% had occurred at one year (males: over 10%), 30% at two (males: 30%) and over 50% at four years (males: between 30 and 40%). An inward pattern was found for alcohol dependence: over 20% of

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male transitions had taken place at one year (females: over 10%), 30% (females: 20%) at two and over 40% (females: 30%) at four years. During the first three years after initial regular use females had a lower risk of transition to abuse and dependence.

Nicotine

Of transitions to nicotine dependence, 40% had occurred at one year, 50–60% at two and 70% at three years after first regular use. Gender differences in risk were non-significant in the first three years (see Figure 5).

Cannabis

Of all transitions from regular CU to cannabis abuse, about 30% had occurred at one year, over 50% had occurred at two and 70% at three years. Of transitions to cannabis dependence, over 30% of female transitions (males: 20%) had taken place at one year after onset of regular use, over 70% (males: almost 50%) at two and over 90% (males: 70%) at three years. The risk of transition to cannabis abuse was greater in males during the first three years after onset of regular CU, while differences in risk of transition to dependence were non-significant in this time period. After this period, a higher risk of dependence in males emerged (HR = 0.10, 95% CI = 0.0–0.7, $p = 0.029$).

Other illicit drugs

The analysis could not be conducted because of low case numbers.

Discussion

This paper provides a description of incidence patterns of legal and illicit SU, regular SU, abuse and dependence derived from a community study of adolescents and young adults. We identified substance-specific gender differences in the probability of transition to more severe SU stages. Our analyses show that transitions from SU to SUDs may occur within very few years during adolescence. Thus, the time window for targeted intervention is critically small. Further core findings are:

(1) The high density incidence periods for alcohol and nicotine use are ages 10–17 with some indications that alcohol exposure takes place slightly earlier than nicotine exposure. The proportion of 30 to almost 40% of adolescents initiating alcohol and/or nicotine use before age of 14 is noteworthy, especially since early use of these substances has been linked to an elevated risk of SUD (Breslau et al., 1993; Nelson and Wittchen, 1998a). However, early onset of use may be part of a cohort trend (Monshouwer et al., 2005; Nelson and Wittchen, 1998b) and considerable variation in subsequent risk may exist in early onset users (Toumbourou et al., 2007).

(2) The proportion of adolescents with initiation of cannabis and other illicit drug use before the age of 14 is substantially lower than for licit substances

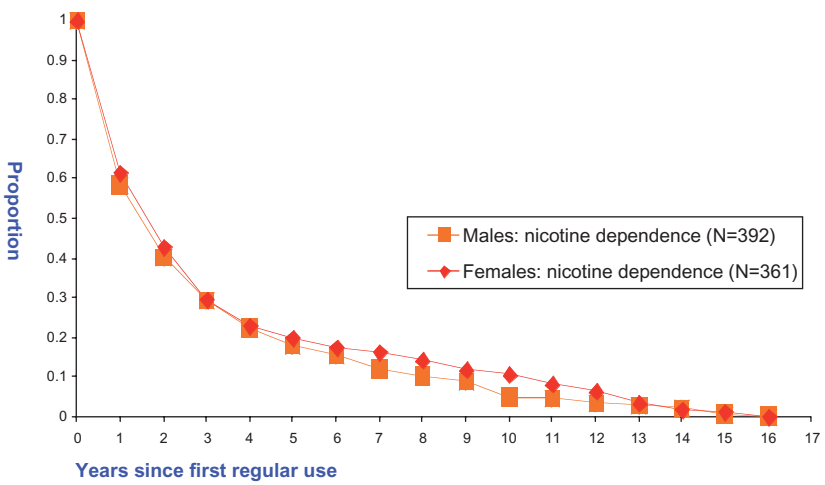

Figure 5. Transition (1 – incidence) from regular nicotine use to nicotine dependence in subjects with nicotine dependence.

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(1.6–3.5%). However, onset of CU before late adolescence is associated with an elevated risk of cannabis and dependence (Chen et al., 2005) as well as CU stability (Perkonigg et al., 2008). This indicates that it is of importance to take into account the actual high-risk period of SU incidence for a specific substance when defining early onset of SU.

(3) The considerable overlap in high density incidence periods for SU and SUD of different substances, the relative similarity of mean ages of onset (e.g. mean age of onset of regular nicotine use and nicotine dependence) as well as the proportion of onset before the age of 14 for use, regular use and partially for abuse/dependence indicates that the transitions to higher use frequency and problematic use typically occurs fast for almost all substances. This overlap may provide indirect evidence for existence of a substantial subgroup of subjects that are particularly vulnerable for substance abuse and dependence. However, the majority of those with even regular use do not progress to abuse and dependence. Certain factors as early onset of SU may contribute to a higher vulnerability for transitions to SUD within a relatively short time period (Chen et al., 2005) in those who make the transition. It is interesting, that our results on main incidence phases of alcohol, nicotine, and CU are relatively comparable to those from large surveys in the US (Chen et al., 2005; Everett et al., 1999; Vega et al., 2002).

(4) Most gender differences in risk concern alcohol and cannabis. Gender differences are predominantly related to the more severe stages of SU and SUD. Comparable results have been found in surveys in the US where adolescent males were at greater risk of alcohol dependence and cannabis dependence (Bonomo et al., 2004; Wagner and Anthony, 2007) while this difference was not found for nicotine use (Everett et al., 1999).

(5) The incidence phases for SU and SUD did not differ by gender. The same was found, with few exceptions, for the periods of transitions to regular SU, abuse and dependence. Similarities between genders in the early course of SU and SUD have also been reported from other studies (Costello and Erkanli, 1999). This may be due to shared environmental factors as availability. However, the timing of first SU may play a different role for boys and girls, but so far, results have been inconsistent (Costello and Erkanli, 1999; Nelson and Wittchen, 1998a). A substantial proportion of transitions occur during the first three years after first use and during the first two years after onset of regular use. It is noteworthy that transitions to regular alcohol use and disorders occurred more slowly. Wagner and Anthony (2002) reported comparable results for transitions to alcohol dependence and pointed out that the risk of this transition may be stable over a longer period. The finding that the higher risk of cannabis dependence in males emerges at three years after onset of use is comparable to results reported by Wagner and Anthony (2007) as is the finding that the higher risk of alcohol dependence in males can be found during the first years after onset of alcohol use. In addition, we could show that the core period for the higher risk of transition to regular CU in males was in the first year after first CU.

Limitations

The analysis does not take into account risk factors for onset and the risk and speed of transitions as for example mental disorders, social factors or particular early onset of SU (Breslau et al., 1993; Chen et al., 2005; Wittchen et al., 2007). Thus, any causal interpretations are cautioned. We only considered incidence but not persistence or complete remission that does not occur infrequently (Perkonigg et al., 2008; Perkonigg et al., 1999). No interactions between substances were considered. We did not consider the symptom level of SU and SUD development while this may be a subject of interest (Chen and Anthony, 2003; Harford et al., 2005; Saha et al., 2006). We did not consider typologies of subgroups of users of a specific substance. Our results may not be generalizable to other countries because of economical and cultural differences (Vega and Gil, 2005). Our data should be seen as representative for the adolescents and young adults born between years 1971 and 1981 living in Munich, Germany. It should be noted, that rates for CU in Germany have recently been decreasing (Pfeiffer-Gerschel et al., 2007). It should be noted that the age range of the sample restricts the analysis; SUDs may occur later in life. We cannot exclude the possibility of recall bias in age of onset information. For SUD-related questions, the DIA-X/M-CIDI thresholds for minimal SU were applied. In consequence, we could not investigate the occurrence of SUD after minimal SU in adolescence.

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Implications

With these limitations in mind, our findings may have several implications. (1) Firstly, since most transitions to malignant outcomes occur in a small time window basic research on the putative moderators and mediators for addiction should target this time period in adolescence (Bühringer, 2006; Bühringer et al., 2008). This time period seems to be the core period during which the given or acquired prior vulnerabilities of a subject interact with more proximal factors and the effects and the context of substance use. (2) Preventive methods aiming at reducing the initiation of SU should start before the age of 14 for smoking and alcohol. Preventive approaches aimed at reducing or delaying first SU have been effective (Toumbourou et al., 2007). This is also of importance with regard to the prevention of progression to disorders related to other drugs. For example, nicotine use in early and mid-adolescence has been linked to an elevated risk of cannabis and other illicit drug disorders in late adolescence (Vega and Gil, 2005). (3) Intervention aiming at preventing the progression from regular use to abuse and dependence should occur as early as possible after first regular use, because the window of progression is quite limited. For this stage of SU involvement, motivational brief intervention and drug education provided at school have been successfully applied to reduce SU and harmful consequences (Marlatt et al., 1998; Mcbride et al., 2003). There is evidence that harm reduction can even be achieved in adolescents with early alcohol use (Mcbride et al., 2003). This is noteworthy because of the large proportion of subjects with first alcohol and nicotine use at under age 14 in our sample. However, mental disorders other than SUD co-occur frequently with adolescent (early onset) SU and SUD (Armstrong and Costello, 2002), predict onset of CU and CUD (Wittchen et al., 2007) and are associated with greater severity of SUD symptoms and poorer treatment outcome (Rowe et al., 2004), indicating that comorbidity deserves attention in the planning of interventions. Also, interventions must not lead to stigmatization of the adolescent (Lubman et al., 2007).

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Declaration of interest statement

Silke Behrendt, Dr. Perkonigg, Dr. Bühringer and Dr. Höfler state, that they do not have a conflict of interest. Dr. Beesdo has a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation. She receives or has in the past three years received Speaking Honoraria from: Pfizer. Dr. Wittchen has a financial interest/arrangement or affiliation with one ore more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation. He receives or has in the past three years received Research Support from: Eli Lilly and Company; Novartis; Pfizer; Schering-Plough. He is currently or in the past three years has been a Consult for: Eli Lilly; GlaxoSmithKline Pharmaceuticals; Hoffmann-La Roche Pharmaceuticals; Novartis; Pfizer; Wyeth. He receives or has in the past three years received Speaking Honoraria from: Novartis; Schering-Plough; Pfizer; Wyeth. Dr. Lieb has a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

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