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Early-onset drug use and risk for drug dependence problems

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Abstract

There is substantial evidence that alcohol, tobacco, and cannabis dependence problems surface more quickly when use of these drugs starts before adulthood, but the evidence based on other internationally regulated drugs (e.g., cocaine) is meager. With focus on an interval of up to 24 months following first drug use, we examine drug-specific and age-specific variation in profiles of early-emerging clinical features associated with drug dependence. Based upon the United States National Surveys on Drug Use and Health (NSDUH) conducted in 2000–2002, the risk of experiencing drug dependence problems was robustly greater for adolescent recent-onset users of cocaine, psychostimulant drugs other than cocaine, analgesics, anxiolytic medicines, inhalants drugs, and cannabis, as compared to adult recent-onset users (odds ratio=1.5~4.3, $p<0.05$). This was not the case for the NSDUH hallucinogens group (e.g., LSD). The adolescent onset associated excess risk was not constant across all clinical features. Our evidence suggests promoting earlier detection and interventions, as well as greater parent and peer awareness of drug dependence clinical features that may develop early among young people who have just started using drugs.

Keywords

Early-onset; drug dependence syndrome; clinical features; adolescents; adolescence; development

1. Introduction

There is substantial evidence that drug problems surface more quickly when use starts before adulthood, even when length or duration biases are taken into account (Anthony & Petronis, 1995; Grant & Dawson, 1998; Janson, 1999; Chen, O'Brien, & Anthony, 2005). Some observers even express a view that preventing or delaying onset of drug use (until adulthood) might be sufficient to prevent occurrence of drug dependence syndromes. King and Chassin (2007) take a more sobering perspective; their evidence supports the idea that early-onset alcohol use is simply a marker and not a cause of later alcohol problems.

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Our literature review indicates that no more than a handful of human studies have investigated early-onset issues with respect to drugs other than alcohol, tobacco and cannabis (Anthony, Chen, & Storr, 2005). In addition, most studies in this area are based upon self-reports made during cumulative ("lifetime history") assessments, and do not control for the confounding influence of a statistical problem known as a "length" or "duration" bias, as discussed by Anthony & Petronis (1995) in a re-examination of evidence from the Epidemiologic Catchment Area Program. Here, with a broad view across multiple psychoactive drug compounds and with control over length biases, this research project seeks new evidence on whether adolescent-onset users have excess risk for all measured clinical features of the drug dependence syndromes. The analyses clarify specific problems that emerge most rapidly within a 24 month interval after onset of use among adolescent-onset and adult-onset users.

2. Methods

2.1 Subjects and Measures

This project's data are from public use datasets released after the 2000 to 2002 United States National Surveys on Drug Use and Health (US, NSDUH), which were designed to produce estimates for prevalence and correlates of drug use in annual federal reports (Substance Abuse and Mental Health Services Administration [SAMHSA], 2003). These public use datasets are made available so that investigators can design and complete their own novel analyses with respect to research questions not planned in advance. During the NSDUH computer-assisted interviews, each participant was asked a series of standardized survey items about extra-medical drug self-administration (e.g., to get high, or in amounts greater than was prescribed). These items made it possible for the NSDUH team to create variables that can be used to identify 'recent-onset' users (i.e., those assessed within 24 months after onset of first extra-medical use, as described in detail elsewhere, as in Anthony et al., 2005; Chen et al., 2005; Storr et al., 2004), including 5,547 recent-onset users of: cannabis, including 4,049 adolescents (age<17) and 1,498 adults (age 18+)(n=5,547, 27% onset ≥ age 18); analgesic drugs (n=3,739, 42% adult), the "hallucinogens group" (n=3,138, 44% adult), inhalants (n=2,213, 24% adult), cocaine (n=1,887, 58% adult), anxiolytic medicines (n=1,691, 52% adult), and psychostimulants other than cocaine, such as amphetamines (n=1,567, 39% adult). For all recent-onset users who had used one of the drug compounds on at least one occasion in the 12 months prior to assessment, 9–11 clinical features associated with the drug dependence syndromes were assessed, also with standardized item, though for cannabis, the threshold was 6+ days of use (SAMHSA, 2003).

2.2 Data Analysis

Mindful of strong interdependencies linking clinical features to one another within drug categories, the study estimates are based upon a generalized linear model, generalized estimating equations (GLM/GEE), multivariate response profile analysis of the clinical feature binary variables, with the logit link function (Liang, Zeger, & Qaqish, 1992; Anthony et al., 2005). Under a 'common slope' specification for this GLM/GEE model, information is borrowed across all available clinical features to yield a single estimate of the degree to which adolescent-onset users might be at excess (or reduced) risk of experiencing clinical features, as compared to adult-onset users, among the pool of recent-onset users for each drug compound or group. During estimation of this 'common slope' RR estimate, additional covariates are added to the model to hold constant potentially confounding characteristics such as sex, race-ethnicity, yielding a covariate-adjusted estimate of the relative risk (aRR). Next, a drug- and feature-specific slope model probes for a possibility that some clinical features have emerged more rapidly than others among the adolescent-onset as compared to the adult-onset users. All estimates involved an application of the NSDUH analysis weights with Taylor series linearization to accommodate the multi-stage nested cluster sampling plan.

3. Results

According to 'common slope' models without covariates (Table 1), adolescent-onset cannabis users were an estimated 2–4 times more likely to experience clinical features within 24 months after first use as compared to their adult-onset counterparts (estimated crude relative risk, RR=3.0, p<0.001). An association of similar magnitude was observed for recent-onset users of inhalant drugs (RR=3.2, p<0.001). With the 'hallucinogens' group as the sole exception, all corresponding unadjusted RR estimates for other drugs also were statistically significant at p<0.05, but adolescent excess risk was slightly smaller: cocaine (including crack), RR=1.6; psychostimulants other than cocaine, RR=1.7; analgesic compounds, RR=1.7; anxiolytic medicines, RR=2.2 (Table 1). Estimates were essentially unchanged with covariate adjustment for sex and race/ethnicity.

For cannabis, adolescent-onset users more rapidly developed virtually all of the clinical features under study, as shown in Table 2. With respect to cocaine, especially prominent excess risk was seen among adolescent-onset users for 'emotional problems' (see G in Table 2: aRR=2.4; p=0.005) and 'reduced activities' (B: aRR=1.9; p=0.01). Five clinical features occurred more often among adolescent-onset users of analgesics as compared with their adult-onset counterparts: the excess risk was strongest in magnitude and most statistically robust for 'getting over the effects' (B: aRR=7.3; p=0.001). Among recent-onset extra-medical users of anxiolytic medicines, the excess risk for adolescents was most substantial for 'unable to keep to limits' (see C in Table 2: aRR=13.3) and was statistically robust (p=0.001).

4. Discussion

In summary, based upon these US data about experiences of a nationally representative sample of recent-onset drug users during 2000–2, we confirm an excess risk of developing clinical features associated with drug dependence when extra-medical drug use starts before age 18 versus during adulthood, for all drug groups under study except for hallucinogens. we observed statistically robust excess risk of clinical features of drug dependence (and associated problems) among adolescent recent onset users (age 11–17 years old), as compared to adult recent-onset users (age 18+) for all drugs studied except the NSDUH hallucinogens group. As shown in Table 2, adolescent excess risk was most pronounced in relation to the drug 'hangover' (e.g., how much time was spent 'getting over' the drug effects) and tolerance with a behavioral or neuroadaptational substrate (e.g., needing more drug to achieve the same effect; using the same amount but getting less effect).

Whereas it might be argued that these observations might be traced back to differential item functioning (e.g., item-level biases found by Chen & Anthony, 2003), or to the possibility of age-related differences in routes of administration or dosage formulations (e.g., powder cocaine versus crack; glue or gases versus 'poppers')), some investigators speculate that age of first drug use might be a manifestation of underlying vulnerability to become drug dependence (e.g., inherited or acquired early) – i.e., a marker of the type noted by King & Chassin (2007), and discussed by others (e.g., McGue et al., 2001; Fergusson et al., 2003; Tarter et al., 2003). Alternately, in co-twin research, escalation of later drug problems is not always completely explained by genetic or shared environmental influences (Lynskey et al., 2003). Instead, early-onset drug use may reflect exposure to non-shared environmental or contextual factors that increase or reinforce a progression toward more advanced stages of drug involvement, which might include differences in micro- and macro-social environments, such as family drug-taking habits or socioeconomic status, and drug availability in the larger community or local neighborhood. In some prospective research, earlier drug availability (but not lower socioeconomic status) is predictive of cannabis smoking initiation and frequency of smoking; lower SES is more of an influence on development of cannabis dependence problems once

smoking starts (Hofler et al., 1999; von Sydow et al., 2002). Applying a developmental psychopathology perspective, one might look for explanations of the observed adolescence-associated excess risk in a drug-induced disruption of processes of adolescent brain development or possibly a higher threshold for reinforcement in neurochemical reward systems (Chambers et al., 2003; Laviola et al., 1999; Spear, 2000).

Several limitations merit special attention, including reliance upon self-reports, although the NSDUH research seeks optimal response validity (e.g., private computer-administered assessment; protection of a federal Certificate of Confidentiality). The nationally representative survey sampling frame and recruitment plan is of high quality, but excludes children under age 12, meaning that age 10–11 is an implicit lower age boundary for recent-onset and newly incident drug-taking. Prompted by an anonymous reviewer, we note that drug-related emotional problems are implicit in the 'distress' and 'clinical significance' facets of the drug dependence syndrome, but are not listed within the explicit diagnostic criteria for drug dependence.

It will be a relatively easy matter to conduct new epidemiological research in an effort to replicate these results, now that NSDUH has released more recent national survey data. More intensive clinical and pre-clinical experiments may be required to probe deeply into the underlying mechanisms (e.g., disrupted adolescent brain development). The work of Chen & Anthony (2003) illustrates how differential item functioning and other forms of test item bias can be ruled in or out. Nonetheless, based upon the epidemiological evidence available to date, and possibly for all but one of the drug categories under study (i.e., the NSDUH 'hallucinogens' group), adolescent-onset drug users seem to be experiencing an excess risk of clinical features associated with drug dependence soon after onset of drug use, relative to their adult-onset counterparts. If adolescent-onset is no more than a marker of excess risk, then randomized trials to evaluate drug prevention programs seeking delayed onset of drug use should make no difference in population-level estimates for incidence of drug dependence problems. This is evidence that can be secured via extended longitudinal followup assessment plans once randomized trials show that a promising drug prevention program actually has prevented or delayed the onset of adolescent drug use, years and even decades before the mechanisms of program action or excess risk are known thoroughly (e.g., see Wynder, 1994).

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Table 1

Estimated associations linking onset adolescent onset drug use (age 11–17) with subsequent risk of clinical features within 24 months after first use, based upon a common slope model.[a] Data from the 2000–2002 United States National Survey on Drug Use and Health.

	Crude RR (95% CI)	p value	Adjusted[b] RR (95% CI)	p value
Cannabis[c]	3.0 (2.3–3.8)	<0.001	3.0 (2.3–3.8)	<0.001
Cocaine/Crack[d]	1.6 (1.1–2.2)	0.006	1.5 (1.1–2.1)	0.02
Hallucinogens[e]	1.2 (1.0–1.6)	0.12	1.2 (1.0–1.6)	0.12
Inhalants[f]	3.2 (1.9–5.3)	<0.001	3.0 (1.8–5.2)	<0.001
Analgesic drugs[gj]	1.7 (1.2–2.2)	0.001	1.6 (1.2–2.2)	0.001
Anxiolytic drugs[hj]	2.2 (1.4–3.5)	<0.001	2.3 (1.5–3.5)	<0.001
Stimulants[ij]	1.7 (1.0–2.8)	0.03	1.7 (1.1–2.6)	0.009

[a] Estimated RR based on odds ratio from Generalized Linear Models with General Estimation Equations (GLM/GEE) to estimate 95% confidence intervals (CI). Reference group: adults (age 18 and above).

[b] Adjusted for sex and race/ethnicity

[c] Cannabis category includes: Marijuna and hashish (e.g., smoked in joints, blunts, or in a pipe), and hash oil.

[d] Cocaine category includes: Cocaine hydrochloride powder, crack, free base, and coca paste

[e] The ‘Hallucinogens Group’ includes hallucinogenic compounds (i.e., LSD, peyote, mescaline, and psilocybin), as well as mixed stimulant-hallucinogens (e.g., Ecstasy, MDMA), and phencyclidine.

[f] Inhalant category includes: amyl nitrite, correction fluid, gasoline fluid, glue, paint solvents, lighter gases, nitrous oxide, spray paints or other psychoactive aerosol sprays.

[g] Analgesic drugs include: prescription type pain relievers (e,g., codeine, hydrocodone, methadone, and morphine).

[h] Anxiolytic medicines include: diazepam and meprobamate, as well as newer benzodiazepine compounds.

[i] Stimulants include methamphetamine, amphetamine, methylphenidate, and dextroamphetamine, or stimulants other than cocaine.

[j] Use defined as “Extra-medical use”: use of a drug or medicine to get high, more than prescribed, for indications other than those intended by the prescribers, or for other experiences, sensations, or effects beyond the boundaries of approved prescribing procedures or indications.

Table 2

Estimated associations linking adolescent onset drug use (age 11–17) with subsequent risk of clinical features within 24 months after first use using feature-specific slope model.[a] Data from the 2000–2002 United States National Survey on Drugs Use and Health

	Cannabis[b]		**Cocaine/Crack[c]**		**Hallucinogens[d]**	
	aRR (95%CI)	**p value**	**aRR (95%CI)**	**p value**	**aRR (95%CI)**	**p value**
A. More time getting drugs	2.8 (2.1–3.8)	<0.001	1.5 (1.0–2.4)	0.08	1.3 (0.9–1.9)	0.16
B. Getting over the effects	4.8 (1.7–13.7)	0.004	1.8 (1.0–3.3)	0.06	1.8 (1.0–3.3)	0.07
C. Unable to keep to limits	2.1 (1.0–4.4)	0.07	1.0 (0.5–1.8)	0.95	1.0 (0.5–2.2)	1.00
D. More drugs same effect	3.3 (2.3–4.6)	<0.001	1.2 (0.8–1.8)	0.30	1.0 (0.7–1.5)	0.92
E. Same amount less effect	3.1 (1.8–5.2)	<0.001	1.8 (1.0–3.3)	0.06	1.7 (1.0–3.0)	0.05
F. Unable to cut down	5.2 (2.7–10.0)	<0.001	0.8 (0.4–1.7)	0.63	1.5 (0.6–4.1)	0.38
G. Emotional problems	2.4 (1.5–4.0)	<0.001	2.4 (1.3–4.4)	0.005	1.0 (0.6–1.7)	0.93
H. Physical problems	7.0 (1.5–31.7)	0.01	1.3 (0.4–4.5)	0.64	2.0 (0.4–9.6)	0.38
I. Reduced activities	3.6 (2.3–5.7)	<0.001	1.9 (1.1–3.1)	0.01	1.2 (0.7–1.9)	0.48
J. Withdrawal symptoms	NA		1.6 (0.9–2.8)	0.11	NA	
K. Feeling blue while cutting down	NA		1.5 (1.0–2.4)	0.06	NA	

	Analgesic drugs[e,h]		Anxiolytic medicines[f,h]		Stimulants[g,h]	
	aRR (95%CI)	p value	aRR (95%CI)	p value	aRR (95%CI)	p value
A. More time getting drugs	1.3 (0.8–2.0)	0.29	1.9 (0.9–4.0)	0.09	1.1 (0.6–2.0)	0.86
B. Getting over the effects	7.3 (2.5–21.8)	0.001	4.8 (1.3–17.9)	0.02	3.8 (1.3–11.4)	0.02
C. Unable to keep to limits	0.9 (0.4–2.0)	0.79	13.3 (3.1–57.6)	0.001	2.0 (0.6–6.3)	0.24
D. More drugs same effect	1.6 (1.1–2.5)	0.03	3.7 (2.1–6.6)	< 0.001	2.8 (1.5–5.3)	0.002
E. Same amount less effect	1.9 (1.0–4.0)	0.07	1.4 (0.6–3.3)	0.47	2.0 (1.0–4.2)	0.06
F. Unable to cut down	1.7 (0.8–3.7)	0.20	1.7 (0.5–6.3)	0.40	5.7 (1.5–20.8)	0.009
G. Emotional problems	2.9 (1.3–6.5)	0.008	6.0 (1.7–21.9)	0.006	2.1 (1.0–4.4)	0.04
H. Physical problems	0.7 (0.2–3.4)	0.69	3.3 (0.3–31.9)	0.29	0.5 (0.1–3.1)	0.50
I. Reduced activities	1.8 (1.0–3.0)	0.04	1.5 (0.7–3.4)	0.34	2.3 (1.0–5.2)	0.04
J. Withdrawal symptoms	2.2 (1.1–4.5)	0.03	NA		1.5 (0.8–3.0)	0.21
K. Feeling blue while cutting down	NA		NA		1.5 (0.8–3.0)	0.19

[a] Estimated RR based on odds ratio from Generalized Linear Models with General Estimation Equations (GLM/GEE) to estimate 95% confidence intervals (CI) adjusted for sex and race/ethnicity. Reference group: adults (age 18 and above).

[b] Cannabis category includes: Marijuna and hashish (e.g., smoked in joints, blunts, or in a pipe), and hash oil.

[c] Cocaine category includes: Cocaine hydrochloride powder, crack, free base, and coca paste.

[d] Hallucinogen category includes: Hallucinogenic compounds (e.g., LSD, peyote, mescaline, and psilocybin), mixed stimulant-hallucinogens (e.g., Ecstasy, MDMA); and phencyclidine.

[e] Analgesic drugs include: prescription type pain relievers (e,g., codeine, hydrocodone, methadone, and morphine).

[f] Anxiolytic medicines include: diazepam and meprobamate, as well as newer benzodiazepine compounds.

[g] Stimulants include methamphetamine, amphetamine, methylphenidate, and dextroamphetamine, or stimulants other than cocaine.

[h] Use defined as “Extra-medical use”: use of a drug or medicine to get high, more than prescribed, for indications other than those intended by the prescribers, or for other experiences, sensations, or effects beyond the boundaries of approved prescribing procedures or indications.

NA, clinical feature not assessed for particular drug. We were unable to obtain the feature specific estimates for inhalants due to a non positive definite matrix in the model.