Male–female differences in the risk of progression from first use to dependence upon cannabis, cocaine, and alcohol

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Abstract

Introduction: We extend prior reports about the risk of dependence on specific drugs by providing developmental-specific risk estimates for progression from first use to meeting criteria for DSM-III-R dependence upon cannabis, cocaine, or alcohol, as well as male–female differences.
Methods: The data are from the National Comorbidity Survey, with a national probability sample of persons 15–44 years old in the United States, which included many respondents who used cannabis, cocaine and alcohol on at least one occasion ($n = 3558$, 1337, and 6149, for cannabis, cocaine, and alcohol, respectively). Survival analysis procedures provided cumulative risk estimates of progression from first use to dependence upon each drug.
Results: The estimated risk of cannabis dependence among male cannabis users was 1% in the first year after first use, and reached a peak at 4% per year 2 years later, before declining. In contrast, the estimated risk of cannabis dependence among female cannabis users remained at 1% per year for 3 years, without the peak. For both male and female cocaine users, the estimated risk for developing cocaine dependence was 5 to 6% within the first year after first use. Thereafter, the estimated risk declined from the peak value, with a somewhat faster decline for females in the next 3 years after first use. For alcohol, the estimated risk period extended for many years after the first drink, with female drinkers becoming alcohol dependent at a rate of about 1% per year; with somewhat higher risk for male drinkers. For both male and female drinkers, the period of risk for developing alcohol dependence extended for a span of more than 20 years since first use; for cannabis and cocaine, the estimated period of risk was much shorter.
Comment: There are male–female differences in the risk of becoming cannabis dependent during the first several years after initiation of cannabis use, less pronounced male–female differences for alcohol, and relatively smaller male–female differences for cocaine. These results should interest scientists whose focus is upon the origins of male–female differences in the occurrence of drug dependence.
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1. Introduction

Epidemiologists commonly report male–female differences in the prevalence of drug use and dependence (e.g., see Anthony et al., 1994; Vega et al., 2002; SAMHSA, 2003). It has been suggested that there may be male–female differences in the incidence (or 'risk') of becoming dependent, or in persistence of dependence once the syndrome develops. However, to date, analyses focused upon male–female differences in prevalence of drug dependence have tended to ignore this distinction between 'risk' and persistence. This paper focuses on the first issue—namely, that male–female differences can be seen in the instantaneous risk or hazard of becoming dependent once drug use starts.

Males tend to be more likely than females to have developed dependence upon alcohol and other controlled substances and inhalants; this does not appear to be the case for tobacco (Anthony et al., 1994; Warner et al., 1995). In lifetime (retrospective) analyses restricted to users of cannabis and alcohol, males were more likely than females to have developed dependence upon these two drugs. Nonetheless, minimal differences were observed between male and female cocaine users with respect to the cumulative occurrence of developing cocaine dependence between first use and date of dependence assessment (i.e., "cumulative" to that date without regard to elapsed time; Anthony et al., 1994).

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In a recent report of epidemiological evidence from the United States (US), our research group estimated both cumulative occurrence and instantaneous risk of first drug use and first progression to dependence upon cannabis, cocaine, and alcohol, with an age-specific approach that considers age of first use and the time course to development of dependence upon these drugs (Wagner and Anthony, 2002a). There, we reported that estimated peak values for becoming dependent upon alcohol and cannabis were found at age 17–18, while peak values for becoming cocaine dependent were found at ages 23–25. Once drug use started, cocaine dependence emerged earlier and more explosively than dependence upon cannabis and alcohol, with an estimated 5–6% of cocaine users becoming cocaine dependent in the first year of use, as compared to no more than roughly 1% of cannabis and alcohol users developing dependence in the initial year after onset of use of these drugs.

A natural extension of the previous work includes descriptive analyses of male–female differences with regard to the risk of drug dependence. Here, our goal is not to explain or account for male–female differences, which we cannot accomplish in this particular survey. Rather, we seek to offer new evidence on possible male–female differences with specific focus upon elapsed time from first use to onset of dependence upon cannabis, cocaine, and alcohol among users of these drugs, based on novel analyses of survey data. If there are no such differences, then the already published estimates and survival curve estimates for all persons will serve well until estimates from new surveys are published. However, we launched this investigation with an expectation that the risks of becoming dependent might be different for these two subgroups of the population—i.e., male users versus female users. If so, future more detailed studies of observed male–female differences can be motivated by the new evidence, including analyses of more recently gathered data to see whether this study's findings can be replicated by other research teams.

2. Methods

Methods used in this study have been described elsewhere in more detail (Kessler et al., 1994; Anthony et al., 1994; Warner et al., 1995; Wagner and Anthony, 2002a). Briefly, we analyzed data from the National Comorbidity Survey (NCS), which are based upon a representative sample of all non-institutionalized people living in the US, 15–54 years old, in 1990–1992. In contrast to prior reports on prevalence of use, this work offers insights into male–female differences in the instantaneous risk of developing cannabis, cocaine, and alcohol dependence. These differences may be helpful to understand forces that have influenced the scope of drug involvement in the US for the past 10–15 years and may continue to do so. The NCS and the present study fully comply with the Declaration of Helsinki and with research ethics regulations adopted and promulgated by the US National Institutes of Health.

In an effort to constrain potential age-related relationships that could not be disentangled from recall bias, we restricted all analyses in this study to respondents 15–44 years old at the time of assessment, as explained elsewhere (Chen et al., 2002). At the time of the survey, the alcohol and other drug experiences of the 45–54 years olds in the NCS sample actually pre-dated the 1960s. (Even when age at first drug use can be recalled with accuracy, it is likely that the experience of these cohorts of drug users is quite different from the experience of the birth cohorts more recently born.)

Data on alcohol and other drug use were obtained via standardized questions in a structured, face-to-face interview. Questions on first use were those of the National Household Survey on Drug Abuse (NHSDA); diagnostic assessment of drug dependence was via the University of Michigan version of the Composite International Diagnostic Interview (UM-CIDI). Drug dependence was assessed according to diagnostic criteria described in the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (APA, 1987), with the same algorithms and associated computer programs used for the original NCS reports on drug dependence (Kessler et al., 1994; Anthony et al., 1994) as well as our more recent report (Wagner and Anthony, 2002a). As such, a diagnosis of dependence upon cannabis, cocaine, and alcohol required that the respondent had at least three of nine presenting features of dependence upon each of these drugs, with duration of at least one month, or repeatedly occurring over a long period. Whereas initiation of drug use was made operational directly from questions asking about the age of first use of cannabis, cocaine, and alcohol, the onset age of dependence was expressed as the reported age at which the third qualifying clinical feature of dependence occurred for each drug, consistent with the idea that multiple clinical features must be manifest before the dependence syndrome is established (Wagner and Anthony, 2002a).

In this study, we estimate the risk of transition from initiation of drug use to onset of drug dependence, for males and females separately, with focus upon two statistical measures: the "cumulative probability," and the "instantaneous hazard" or "time-specific risk" of an event. The cumulative probability is a measure of accumulation of risk over time. In contrast, the instantaneous hazard or risk refers to the probability of event occurrence within a particular interval of time, given that the event has not taken place previously for the individual (Willet and Singer, 1993; Obot et al., 2001; Wagner and Anthony, 2002a).

For the estimation of the cumulative probability of dependence upon cannabis, cocaine and alcohol, we set two time perspectives. According to the first perspective, time is measured chronologically in years since birth. In the second perspective, the time-scale is set as years since first use of the corresponding drug. All analyses have been conducted with attention to variation in analytical weights and clustering of respondents within sample strata (StataCorp, 1999). As an aid to assess equivalence of failure curves for males versus females, a Wald-statistic test was used via implementation of Cox regression models that allowed for the use of weights and robust variance estimation (as described in Lin and Wei, 1989). Ties were handled via the Breslow method (Breslow, 1974). In brief, the Wald statistic test compares the slopes of the hazards for males versus females taking into account robust standard errors, and then evaluates the difference using a chi-square distribution with one degree of freedom (StataCorp, 1999).

3. Results

Fig. 1 depicts estimates for the risk of first cannabis, cocaine, and alcohol use, as well as the estimated cumulative probability of first use of each of these drugs, by age. Peak estimates for the risk of cannabis and alcohol first use were observed between ages 18 and 19, and around 21–22 years for cocaine. In general, the risk of first use shows a male excess. The estimated risk of first alcohol use is greater than that for cannabis and cocaine, at each age.

Among users, for males and females separately, Table 1 presents the estimated cumulative probability for meeting criteria for dependence upon cannabis, cocaine, and alcohol among US residents up to 44 years old, with the time perspective in years since birth. As shown in panel A, among the 3558 respondents who reported cannabis use, there were 241 male cases of dependence and 102 female cases of cannabis dependence. As shown in panel B, there were fewer users of cocaine, amounting to 137 male cases and 83 female cases of dependence upon this drug. Finally, panel C shows that a similar number of male and females had become users of alcohol, but there were almost twice as many male cases of alcohol dependence compared to the number of female cases.

The main estimates from this study with respect to the risk of developing dependence are depicted in Figs. 2–4, and can