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Progression to regular heroin use: Examination of patterns, predictors, and consequences

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HIGHLIGHTS

- Strongest predictor of earlier regular heroin use was earlier initial heroin use.
- Earlier-onset regular alcohol and tobacco use predicted earlier regular heroin use.
- Earlier regular heroin use was associated with more severe heroin use characteristics.
- Most subjects reported substance progression consistent with the gateway hypothesis.
- Gateway-inconsistent progression was associated with heroin use characteristics.

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ABSTRACT

Background: The present study retrospectively evaluated the chronology and predictors of substance use progression in current heroin-using individuals.
Methods: Out-of-treatment heroin users (urinalysis-verified; $N = 562$) were screened for laboratory-based research studies using questionnaires and urinalysis. Comprehensive substance use histories were collected. Between- and within-substance use progression was analyzed using stepwise linear regression models.
Results: The strongest predictor of onset of regular heroin use was age at initial heroin use, accounting for 71.8% of variance. The strongest between-substance predictors of regular heroin use were ages at *regular* alcohol and tobacco use, accounting for 8.1% of variance. Earlier onset of regular heroin use (≤20 years) vs. older onset (≥30 years) was associated with a more rapid progression from *initial* to *regular* use, longer duration of heroin use, more lifetime use-related negative consequences, and greater likelihood of injecting heroin. The majority of participants (79.7%) reported substance use progression consistent with the gateway hypothesis. Gateway-inconsistent individuals were more likely to be African-American and to report younger age at initial use, longer duration of heroin use, and more frequent past-month heroin use.
Conclusions: Our findings demonstrate the predictive validity and clinical relevance of evaluating substance use chronology and the gateway hypothesis pattern of progression.

1. Introduction

1.1. Background

Global opioid use increased significantly in the past decade (SAMHSA, 2013; UNODC, 2013). Opioid use is implicated in more substance use-related overdose deaths than any other drug class (UNODC, 2013). Moreover, an estimated 14 million people worldwide administer drugs via injection (common among heroin users) which is associated with increased risk of contracting HIV and blood-borne diseases (Chitwood, Comerford, & Sanchez, 2003; UNODC, 2013). Heroin use is associated with severe health consequences and, for purposes of this study, will be conceptualized as an 'end-point' substance-use phenotype.

Previous research characterized substance-use progression and identified accurate predictors of future substance use disorders that can inform prevention and/or early intervention strategies (Hser, Longshore, & Anglin, 2007; Lee, Winters, & Wall, 2010; Vanyukov et al., 2012). One robust predictor of earlier future substance use disorders is earlier age at initial use of that substance (Chen, Storr, & Anthony, 2009; Windle & Windle, 2012). This intuitive finding has been

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repeatedly observed for use of alcohol (Brook, Brook, Zhang, Cohen, & Whiteman, 2002; DeWit, Adlaf, Offord, & Ogborne, 2000; Grant & Dawson, 1997; Grant, Stinson, & Harford, 2001; Nelson & Wittchen, 1998); nicotine (Breslau, Fenn, & Peterson, 1993; Hu, Griesler, Schaffran, Wall, & Kandel, 2012); and marijuana (Chen, O'Brien, & Anthony, 2005; Ellickson, Martino, & Collins, 2004). While informative, these findings are limited to within-substance progression. The majority of substance using individuals reported initial poly-substance experimentation that progressed to problematic use and dependence (Moss, Chen, & Yi, 2013; Olthuis, Darredeau, & Barrett, 2013; Sartor, Kranzler, & Gelernter, 2014b; Trenz et al., 2012); thus, characterization of within-substance progression may not capture important between-substance relationships. One recent study examined between-substance progression in current "hard" (e.g., heroin) substance users and found age at regular use of "soft" (e.g. alcohol, marijuana) substances predicted future "hard" substance use better than age at initial use (Baggio, Studer, Mohler-Kuo, Daeppen, & Gmel, 2013).

Substance-use progression research has also focused on the pattern of between-substance use. The 'gateway hypothesis' (Kandel, 1975) postulated two transitions in substance use progression: legal substance use (alcohol, tobacco) preceding marijuana use, and marijuana use preceding "hard" illegal substance use (e.g., cocaine, heroin). The gateway hypothesis implicated initial marijuana use as the critical transition step between legal and "hard" illegal substance use (Kandel, 1975). Experimental evidence for this hypothesis is mixed (Mackesy-Amiti, Fendrich, & Goldstein, 1997) and criticism has generated debate regarding its continued relevance (Golub & Johnson, 2002; Tarter et al., 2012). A novel application of the gateway hypothesis differentiates individuals based on their gateway-pattern agreement (Tarter, Vanyukov, Kirisci, Reynolds, & Clark, 2006; Wells & McGee, 2008; Agrawal et al., 2011; Sartor, Kranzler, & Gelernter, 2014a). A substance-use progression pattern that is inconsistent with the gateway hypothesis has been associated with environmental factors including: poorer physical environment, greater access to drugs in a neighborhood, and more neglectful parenting (Tarter et al., 2006). In addition, a gateway-inconsistent pattern of progression has been associated with psychiatric dysfunction (DSM-IV diagnoses of internalizing disorders [e.g. depression, anxiety disorders]; Degenhardt et al., 2009; Wells & McGee, 2008) and greater likelihood of progression to substance dependence (Degenhardt et al., 2009; Sartor et al., 2014a).

1.2. Aims and hypotheses

Within a large sample of regular heroin-using, out-of-treatment volunteers, the present study retrospectively examined: (1) age at onset of initial and regular use of tobacco, alcohol, marijuana, and cocaine as predictors of age at onset of regular heroin use; (2) age at regular heroin use as a predictor of current and lifetime heroin use characteristics; and (3) phenotype individuals by agreement (or not) with the gateway pattern of progression. Consistent with recent trends in the literature, we hypothesized that earlier age at onset of regular substance use (as opposed to initial use) would predict earlier regular heroin use. Additionally, we hypothesized that earlier age at onset of regular heroin use and deviating from the gateway pattern of substance use progression would predict heroin use characteristics indicative of a more severe condition.

2. Methods

2.1. Participant selection

Screening data from out-of-treatment, heroin-using adults (18–55 years old) recruited using media advertisements and word-of-mouth referral for several behavioral pharmacology studies (1998–2014) were used in the present analysis. All studies were approved by the local Institutional Review Board and conducted in accordance with the Declaration of Helsinki (1964). Candidates who denied major medical or psychiatric contraindications (e.g., heavy alcohol use, major depression, cardiovascular disease) during the initial structured phone interview were invited to undergo comprehensive in-person screening procedures following written informed consent. Opioid-positive (>300 ng/ml), alcohol-free (<.002%; Alco Sensor III Breathalyzer), and cognitively-intact (IQ score >80; Shipley Institute of Living Scale; Zachary, 1991) individuals were included in the analysis.

2.2. Outcome measures

Lifetime and current substance use characteristics were assessed across five substances (alcohol, tobacco, marijuana, cocaine, and heroin) via a standardized, self-report battery: Drug History and Use Questionnaire (created in our laboratory; available upon request). Age at initial use of a substance is defined as age at first consumption, whereas age at regular use is defined as age when first using at least 3 times per week. Lifetime heroin-use consequences were assessed via an 18-item checklist of items (e.g., overdose, financial problems) not biased by age-specific consequences (problems in school, high at school, and missed school; Woodcock, Lundahl, Burmeister, & Greenwald, in press). Given that one focus of the present investigation is to explore the effects of age at onset with current and lifetime heroin use characteristics, these age-specific items were excluded to prevent biasing the analysis. Participants indicated (ever/never) each consequence they experienced as a direct result of heroin use in their lifetime. Summed number of items endorsed yielded a total score for analysis (range 0–18). Lifetime consequences for the other substances examined herein were also assessed and computed using similar scales specific to each substance (alcohol: 20 items; tobacco: 16 items; marijuana: 22 items; and cocaine: 18 items). Self-reported lifetime number of attempts to stop using heroin was assessed via a single item score (maximum: 100). Past-month heroin use frequency was calculated as the product of mean daily past-week heroin use and number of past-month days using heroin (maximum: 30 days). Duration of regular heroin use was calculated as age at screening *minus* age at regular heroin use. Each participant's pattern of substance use progression was evaluated for gateway hypothesis agreement. Deviation from the gateway hypothesis was operationally defined as:

(1) *use of marijuana prior to legal substances (tobacco and alcohol); or*
(2) *use of cocaine or heroin prior to marijuana; or*
(3) *use of cocaine or heroin prior to legal substances (tobacco and alcohol).*

Temporal measurement sensitivity was limited, as participants were asked to describe age of initial substance use in calendar-year format. Thus, to qualify as gateway-inconsistent, violators would need to report use of a substance one calendar year out of order (e.g., initial marijuana use at age 12, and tobacco and alcohol use at age 13 or later).

2.3. Data analyses

Variables were assessed for normality (West et al., 1995) and outliers (z-scores $\geq$ 3.3). Non-normally distributed variables were transformed ($\log_{10}$ or square root) and outliers omitted. Substance use data were characterized using descriptive statistics, frequencies, and one-way analyses of variance (ANOVA). To protect against Type I error inflation due to unequal sample sizes, Levene's Test of Equality of Error Variances was used to confirm ($p > .05$) homogeneity of variance for each outcome variable examined for group differences. Any substance-use measures (e.g., quit attempts) that correlated with duration of use (which could bias interpretation of results) were evaluated using analyses of covariance (ANCOVA) with heroin use duration