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A developmental etiological model for drug abuse in men

Kenneth S. Kendler[a,b,c,*], Henrik Ohlsson[d], Alexis C. Edwards[a,b], Jan Sundquist[d], Kristina Sundquist[d]

[a] Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University, Richmond, VA, USA
[b] Department of Psychiatry, Virginia Commonwealth University, Richmond, VA, USA
[c] Department of Human and Molecular Genetics, Virginia Commonwealth University, Richmond, VA, USA
[d] Center for Primary Health Care Research, Lund University, Malmö, Sweden

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ABSTRACT

Background: We attempt to develop a relatively comprehensive structural model of risk factors for drug abuse (DA) in Swedish men that illustrates developmental and mediational processes.

Methods: We examined 20 risk factors for DA in 48,369 men undergoing conscription examinations in 1969–70 followed until 2011 when 2.34% (n = 1134) of them had DA ascertained in medical, criminal and pharmacy registries. Risk factors were organized into four developmental tiers reflecting i) birth, ii) childhood/early adolescence, iii) late adolescence, and iv) young adulthood. Structural equational model fitting was performed using Mplus.

Results: The best fitting model explained 47.8% of the variance in DA. The most prominent predictors, in order, were: early adolescent externalizing behavior, early adult criminal behavior, early adolescent internalizing behavior, early adult unemployment, early adult alcohol use disorder, and late adolescent drug use. Two major inter-connecting pathways emerged reflecting i) genetic/familial risk and ii) family dysfunction and psychosocial adversity. Generated on a first and tested on a second random half of the sample, a model from these variables predicted DA with an ROC area under the curve of 83.6%. Fifty-nine percent of DA cases arose from subjects in the top decile of risk.

Conclusions: DA in men is a highly multifactorial syndrome with risk arising from familial-genetic, psychosocial, behavioral and psychological factors acting and interacting over development. Among the multiple predisposing factors for DA, a range of psychosocial adversities, externalizing psychopathology and lack of social constraints in early adulthood are predominant.

1. Introduction

Drug Abuse (DA) is a multifactorial syndrome influenced by a wide range of biological, psychological and socio-cultural risk factors (Hawkins et al., 1986; West, 2006). More specifically, individual risk factors for DA include genes (Tsuang et al., 1996), aspects of the childhood environment (Grant et al., 2009) (including child abuse (Kendler et al., 2000; Fergusson and Mullen, 1999), parental loss (Hawkins et al., 1986; Kendler et al., 2012), and parental behaviors (Hawkins et al., 1992; Hawkins et al., 1986)), urbanicity (Sundquist and Frank, 2004; Grant et al., 2009), peer group deviance (Farrington, 2005; Hawkins et al., 1998; Patterson et al., 2000; Marshal et al., 2003; Hawkins et al., 1992; Hawkins et al., 1986), internalizing traits and symptoms (Kessler et al., 2005), intellectual and school functioning (Gigi et al., 2014; Hawkins et al., 1992; Hawkins et al., 1986), externalizing traits and behaviors (Kessler et al., 2005; Kendler et al., 2003; Brook et al., 1996; Hawkins et al., 1992; Hawkins et al., 1986; Blanco et al., 2013)(including use of alcohol and cigarettes (Kessler et al., 2005; Kandel, 1975; Blanco et al., 2013)), and, later in development, absence of social constraints such as marriage, employment and church attendance (Grant et al., 2009; Blanco et al., 2013).

Given the wide range of these risk factors and the diversity of developmental stages at which they impact, a comprehensive understanding of the pathways to DA requires more than their enumeration in review articles (e.g., (Hawkins et al., 1986)) or their testing in multiple regression models (Blanco et al., 2013). Optimally informative will be models that capture the dynamic relations between individuals, their behavioral and psychiatric symptoms and their social contexts across development. Particularly, such models can clarify mediational mechanisms that could be targets for intervention. As articulated by

* Corresponding author at: Virginia Institute for Psychiatric and Behavioral Genetics of VCU, Box 980126, Richmond, VA 23298-0126, USA.
E-mail addresses: kenneth.kendler@vcuhealth.org (K.S. Kendler), Henrik.ohlsson@med.lu.se (H. Ohlsson), alexis.edwards@vcuhealth.org (A.C. Edwards), jan.sundquist@med.lu.se (J. Sundquist), Kristina.sundquist@med.lu.se (K. Sundquist).

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Dodge et al. the goal of such research should be to provide "a map for how myriad genetic, biological, social, and ecological factors conspire to produce disorders in adolescence … [especially] substance abuse (Dodge et al., 2009, p. 3)".

We here present such a study utilizing a sample of 48,276 Swedish males born 1947–1953 whom we followed until 2011. Detailed information on risk factors was available for this cohort at an average age of 18 from the Conscript Registry and has been supplemented from other registry resources that can provide risk factors from earlier and later ages. DA is ascertained from the Swedish national medical, pharmacy and criminal registers.

2. Materials and methods

This study utilizes men conscripted into military service in Sweden in 1969 and 1970. In those years, only 2–3% of all Swedish men were exempt from conscription, largely due to severe handicaps or congenital disorders (Neovius et al., 2009). We collected information from several sources on these individuals. First, we used information from the conscript register. The national birth cohorts used in this study are unique among all conscript material in Sweden, as more extensive data were collected at conscription during these years. Information from the conscript register about the individuals was collected through questionnaires, with questions about medical symptoms, childhood and adolescent traits and behaviors, and alcohol and tobacco use. We call these variables conscript self-report data (CSRD). Second, during conscription direct assessments of psychological function were performed. We call these conscript test scores register. We then linked the conscript database to the Multi-Generation Register, providing information on family relations and to Population Registers providing information on education and geographical status. We also linked the database to the Swedish Medical Registers consisting of the Swedish Hospital Discharge Register, containing all hospitalizations for all Swedish inhabitants from 1969 to 2011 and the Outpatient Care Register, containing information from outpatient clinics from 2001 to 2011; to the Swedish Criminal registers consisting of the Swedish Crime Register, containing national complete data on all convictions from 1973 to 2011, the Swedish suspicion register, containing national complete data on all individuals strongly suspected of crime from 1998 to 2011; and finally to the Swedish Prescribed Drug Register, containing all prescriptions in Sweden picked up by patients from 2005 to 2010. The linking was done using each person's unique identification number. To preserve confidentiality, this ID number was replaced by a serial number. We secured ethical approval for this study from the Regional Ethical Review Board of Lund University (No. 2008/409).

2.1. Outcome variable

DA was identified in the Swedish medical and mortality registers by ICD codes (ICD8: Drug dependence (304); ICD9: Drug psychoses (292) and Drug dependence (304), Nondependent abuse of drugs (305; excluding 305.0); ICD10: Mental and behavioral disorders due to psychoactive substance use (F10-F19), except those due to alcohol (F10) or tobacco (F17)); in the Suspicion Register by codes 3070, 5010, 5011, and 5012, that reflect crimes related to DA; in the Crime Register by references to laws covering narcotics (law 1968:64, paragraph 1, point 6) and drug-related driving offences (law 1951:649, paragraph 4, Subsection 2 and paragraph 4A, Subsection 2); and in the Prescribed Drug Register in individuals (excluding those suffering from cancer) who had retrieved (in average) more than four defined daily doses a day for 12 months from either of Hypnotics and Sedatives (Anatomical Therapeutic Chemical (ATC) Classification System N05C and N05BA) or Opioids (ATC: N02A).

DA was treated as dichotomous variable with an assumed underlying normal liability distribution.

2.2. Sample

From the 50,529 individuals who were conscripted into military service during 1969–1970, we excluded those not born between 1947 and 1953, to insure our sample was of similar age; females; and cases with duplicate ID number (n = 834). Of the remaining 49,691 individuals, we excluded 1322 individuals with more than 10% missing values based on all our included covariates (see below for covariates). In total, we investigated 48,369 individuals. 99.1% of the sample were ages 18–20 at conscript evaluation.

2.3. Model variables

We organized the predictor variables into four groups approximating four developmental periods: 1) birth (Father alcohol consumption, Low parental education and genetic risk (for DA, criminal behavior or alcohol use disorder – all highly genetically correlated in the Swedish population (Kendler et al., 2016a)), 2) childhood and early adolescence (Frequency of Corporal Punishment, Disruption in family [i.e., loss of one or more parents through death or divorce before age 18], Low Parental monitoring, Move during childhood, Urbanization, Internalizing Behavior and Externalizing Behavior), 3) late adolescence (Neighborhood Socioeconomic Status, Low Resilience, Low IQ, Sniffing Glue and Drug use score), and 4) early adulthood (Low education, Unemployed, Unmarried, Criminal Behavior, Alcohol use disorder). Of the 20 final predictor variables, 4 were latent (internalizing behavior, externalizing behavior, Drug use score, and Neighborhood SES) and were constructed using a measurement model from other observed variables. Sniffing glue, assessed at conscription, loaded poorly on the drug use factor and therefore was included as an independent item in the model. See the Appendix Table A1 for a detailed definition of all variables. In addition to these 20, the following other variables were included in earlier drafts of the model but were excluded because they provided minimal additional predictive power: Peer Deviance (share of Drug Abusers in close geographical proximity during early adolescence (Kendler et al., 2015)), Prosocial Behavior (from CSRD), Familial Socioeconomic status (from CRSD), Repeat year in school (from CSRD), Psychiatric Genetic Risk Score (based on Psychiatric registrations in close relatives), Alcohol consumption during adolescence (from CSRD), Educational status (from population registers),Smoking status during adolescence (from CSRD).

2.4. Statistical methods

Of the 48,369 individuals, 37,843 had no missing values; 7271, had below 2%; and 3255 had between 2 and 10%. To impute values, we used the Predicted Regression imputation method within specific groups of questions; that is using regression models to predict missing values based on similar covariates. We divided the material into five groups and performed the predicted regression method within each group. The five groups were *Drug-related questions* (all questions for the DA score and the question on Sniffing Glue), *Externalizing Behavior, Internalizing Behavior* (all questions included in the factor analysis for internalizing behavior and Resilience), *Socioeconomic and Family-variables* (Low Parental education, Disruption in family, IQ, Urbanization, Low education, Unmarried, Parental monitoring, Unemployment, Move during childhood), and *Others* (Genetic Risk Score, Fathers Alcohol consumption and Frequency of Corporal Punishment).

Our structural equation model consisted of two parts. First a measurement model consisted of factor loadings for the observed variables that index the four latent variables and second a structural model that consisted of path and correlation coefficients connecting the four latent and the 16 observed variables of the model. For the structural model, we followed an approach developed in previous similar studies (Kendler et al., 2002; Kendler et al., 2011; Kendler et al., 2016b). We began with a fully saturated model and used a combination of three