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ORIGINAL ARTICLE

A developmental model for alcohol use disorders in Swedish men

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Background. Alcohol use disorder (AUD) is a classic multifactorial syndrome and it is critical to understand the diversity of the relevant risk factors and how they inter-relate over development.

Method. We examined 21 risk factors for AUD in four developmental tiers reflecting (i) birth, (ii) childhood and early adolescence, (iii) late adolescence, and (iv) early adulthood in 47 414 Swedish men of whom 3907 (8.2%) were registered for AUD at or after age 25 with a mean length of follow-up of 33.9 (6.6) years. Structural equational model fitting was performed using Mplus.

Results. The best-fitting model provided a good fit to the data and explained 23.4% of the variance in AUD. The five strongest predictors were: externalizing behaviors, criminal behavior, father's alcohol consumption, genetic risk, and low educational attainment. Two developmentally early familial/genetic risk factors had substantial direct paths to AUD: father's alcohol consumption and genetic liability. Other broad developmental pathways to risk for AUD were evident: externalizing, psychosocial and internalizing. Overall, the externalizing pathway to AUD was the strongest. However, these pathways were substantially interwoven over time such that risk factors from one domain were commonly predicted by and/or predicted risk factors from the other broad domains of risk.

Conclusion. AUD in men is an etiologically complex syndrome influenced by familial-genetic, psychosocial, internalizing, and especially externalizing risk factors that act and interact over development and have complicated mediational pathways.

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Key words: Alcohol use disorder, development, environment, personality, path models.

Introduction

Alcohol use disorder (AUD) is a prototypical multifactorial syndrome influenced by a diversity of risk factors distributed across biological, psychological and social-cultural levels and including genetic factors (Verhulst *et al.* 2015), aspects of the rearing environment including urbanization (Grant *et al.* 2015), social class (Grant *et al.* 2015), physical abuse (Fergusson & Mullen, 1999; Kendler *et al.* 2000), parental monitoring (Dielman *et al.* 1990; Tucker *et al.* 2008), peer group deviance (Fergusson *et al.* 1995; Hawkins *et al.* 1998; Patterson *et al.* 2000; Coie & Miller-Johnson, 2001; Farrington, 2005), internalizing traits and symptoms (Kessler *et al.* 1997; Sher *et al.* 2005), intellectual functioning (Finn & Hall, 2004; Nigg *et al.* 2004), externalizing traits and behaviors [Kendler *et al.* 2003; Sher *et al.* 2005; including use of other psychoactive substances (Kandel, 1975; Grant *et al.* 2015)], and, later in development, marital and occupational status (Miller-Tutzauer *et al.* 1991; Mossakowski, 2008; Grant *et al.* 2015). Because risk for AUD in adulthood can be predicted by risk factors assessed in childhood and adolescence, (Caspi *et al.* 1996; Manzardo *et al.* 2005; Dubow *et al.* 2008; Englund *et al.* 2008; Maggs *et al.* 2008; Pitkanen *et al.* 2008) a comprehensive understanding of the pathways to AUD require adopting a developmental perspective that can help understand the complex mediational pathways of risk (Windle, 1999; Zucker, 2006).

A number of prior attempts have been made to develop empirical models for the etiology of AUDs (e.g. Fergusson *et al.* 1995; Guo *et al.* 2001; Dubow *et al.* 2008; Ohannessian & Hesselbrock, 2008; Feingold *et al.* 2015) some of which have been relatively comprehensive (Guo *et al.* 2001; Dubow *et al.* 2008; Kendler *et al.* 2011*b*; Edwards *et al.* 2015). Two prior efforts by

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our group have, however, been limited by a nearly complete reliance on retrospective data (Kendler *et al.* 2011*b*) and a follow-up ending at age 20 (Edwards *et al.* 2015). We here seek to complement and improve on these prior studies utilizing a particularly informative sample of 47 414 Swedish males born 1947 to 1953 whom we could follow into late adulthood using the available extensive Swedish registries. Detailed risk factor data 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. AUD is ascertained from the Swedish national medical, criminal and pharmacy registers.

Method

This study is based on data on men who were conscripted into military service in Sweden in 1969 and 1970 because for these years only the Swedish military made available to researchers more detailed information about the recruits evaluated. As the military service was compulsory during those years, it includes almost all Swedish men. We used several sources to collect information about the 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 in 1969 and 1970 than during other years. The information from the conscript register about the individuals was collected through questionnaires, with questions about medical, childhood and adolescent conditions, and alcohol and tobacco use. We call these variables *conscript self-report data* (CSRD). Second, during conscription a psychological function capacity assessment was also performed. We call these variables *test scores from the conscript register* (CTS). The two main aims of conscription examination were to assess the individual's capacity for military service and to prepare for appropriate posting within the military. At the time, there were six enlistment centers in Sweden, which managed the 2-day long examination of each conscript. We then linked this database to the Multi-Generation Register (MGR), providing information on family relations and to Population Registers (PoR) providing information on education and geographical status. We also linked the database to the Swedish Medical Registers (MR) consisting of the Swedish Hospital Discharge Register, containing all hospitalizations for all Swedish inhabitants from 1973 to 2011 (and partial data between 1969 and 1972); the Swedish Prescribed Drug Register, containing all prescriptions in Sweden picked up by patients from 2005 to 2010; the Outpatient Care Register, containing information from all specialist outpatient clinics from 2001 to 2010, including those for psychiatric care. Finally the database was linked to the Swedish Criminal registers (CR) consisting of the Swedish Crime Register, containing national complete data on all convictions from 1973–2011, and the Swedish suspicion register, containing national complete data on all individuals strongly suspected of crime from 1998 to 2011. The linking was done using each person's unique identification number. In order to preserve confidentiality this ID number was replaced by a serial number by Statistics Sweden that provided the linked data to us. We secured ethical approval for this study from the Regional Ethical Review Board of Lund University (No. 2008/409).

Outcome variable

AUD was defined from ICD codes for main and secondary diagnoses from Swedish medical and mortality registries for the following diagnoses: ICD9: alcohol-related psychiatric disorders (291), alcohol dependence (303), alcohol abuse (305A), alcohol-related polyneuropathy (357F), alcohol-related cardiomyopathy (425F), alcohol-related gastritis (535D), alcoholic fatty liver, alcohol hepatitis, alcoholic cirrhosis, unspecified liver damage caused by alcohol (571A-D), toxic effects of alcohol (980), alcoholism (V79B); ICD10: alcohol-related psychiatric and behavioral disorders (F10, excluding acute alcohol intoxication: F10.0), rehabilitation of a person with alcohol abuse (Z50.2), guidance and medical advice to a person with alcohol abuse (Z71.4), alcohol-related pseudo-Cushing syndrome (E24.4), alcohol-related degeneration of the nervous system and brain (G31.2), alcohol-related polyneuropathy (G62.1), alcohol-related myopathy (G72.1), alcohol-related cardiomyopathy (I42.6), alcohol-related gastritis (K29.2), liver diseases caused by alcohol (K70.0–K70.9), acute pancreatitis caused by alcohol (K85.2), chronic pancreatitis caused by alcohol (K86.0), treatment of pregnant alcoholic women (O35.4), toxic effects of alcohol (T51.0–T51.9), and based on Anatomical Therapeutic Chemical (ATC) codes in the Prescribed Drug Register: disulfiram (N07BB01), acamprosate (N07BB03), or naltrexone (N07BB04). Additionally, we identified individuals with at least two convictions of drunk driving (law 1951:649) or drunk in charge of maritime vessel (law 1994:1009) using both the Crime and Suspicion registers and insuring that each event was only counted once. AUD was treated as dichotomous variable with an assumed underlying normal liability distribution.

Sample

From the 50 529 individuals who were conscripted into military service during 1969–1970 we excluded those

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born before 1947 and after 1953 ($n = 270$) to insure our sample was all of similar age. In addition, we excluded five cases with duplicate/misclassified ID number and 1445 individuals with more than 10% missing values based on all our included covariates (see below for covariates). Of the remaining 48 539 individuals 1125 were registered for AUD prior to 1976 and were also excluded from the study (so as to allow us to include, in our model, key risk factors in early adulthood). In total, we investigated 47 414 individuals with a mean (S.D.) age at registration of 18.3 (0.6). 99.1% of the sample were ages 18–20 at conscript evaluation.

Model variables

We organized the predictor variables into four tiers that approximated four developmental periods: (1) birth (Father's Alcohol Consumption, Parental Education and Genetic Risk); (2) childhood and early adolescence (Parental Abuse, Disruption in Family, Repeat a Year in School, Parental Monitoring, Urbanization, Internalizing Behavior, Externalizing Behavior and Pro-social Behavior); (3) late adolescence (Resilience, IQ, Smoking, Alcohol Score); (4) early adulthood (Peer Deviance, Drug Use, Unemployed, Marital Status, Education, Criminal Behavior). Of the 21 final predictor variables, four were latent (internalizing behavior, externalizing behavior, alcohol score, and drug use/abuse) and were constructed, by using a measurement model, from other observed variables. Supplementary Table S1 shows a detailed definition of all variables included in the study. In addition to these 21 variables, the following other variables were included in earlier drafts of the model but were excluded because they provided minimal additional predictive power: Socioeconomic status during childhood (from CSRD); Number of moves during childhood (CSRD); Number of Alcohol Outlets in the municipality at age 20; and a Psychiatric Genetic Risk score (based on Psychiatric registrations in the MR in close relatives).

Statistical methods

Of the 47 414 individuals 35 806 had no missing values, 8323 had 2% missing values and 3285 had between 2% and 10% missing values. In order 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 six groups and performed the predicted regression method within each group. The six groups were Alcohol Score (all alcohol-related questions), Externalizing Behavior, Internalizing Behavior (all questions included in the factor analysis for internalizing behavior and Resilience), Drug Use, Education and Socioeconomic variables (Parental Education, Disruption in Family, IQ, Urbanization, Education, Marital Status, Parental Monitoring, Unemployment, and Repeat a Year in School) and Others (Smoking, Genetic Risk Score, Peer Deviance, Father's Alcohol Consumption, Prosocial Behavior, and Parental Abuse).

We analyzed these data using structural equation modeling. Our model consisted of two parts: first, a measurement model that 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 17 observed variables of the model. For the structural model, we followed an approach we developed in previous studies (Kendler *et al.* 2006; Volk & Lewis, 2010). We began with a fully saturated model and used a combination of three approaches to produce a model with the optimal balance of explanatory power and parsimony. Note that variables in the first tier are interconnected by correlations, depicted by two-headed arrows in the figures, rather than partial regression coefficients, which are depicted by one-headed arrows. In the first step, observing the significance levels of individual paths, we fixed sets of paths to zero when the associated z value was <1.96. Second, some paths that remained significant were too small to be meaningful. Therefore, the second step was to set all paths to zero with a standardized parameter estimates of <0.05, regardless of z value. Third, we added and subtracted a number of paths that were marginal by significance and/or magnitude to test if we could arrive at a better overall fit, and indeed produced a modest improvement in fit and explanatory power. We utilized two fit indices that reflect the success of the model in balancing explanatory power and parsimony: the Tucker–Lewis index (TLI) and the root mean square error of approximation (RMSEA). For the TLI and comparative fit index, values between 0.90 and 0.95 are considered acceptable, and values $\geqslant 0.95$ as good (Tanzi *et al.* 1987). For RMSEA, good models have values $\leqslant 0.05$, while values >0.10 are considered poor (Eaton *et al.* 2000). Model fitting was done by using Mplus, version 7.31 (Muthén & Muthén, 2015). The fit function was weighted least squares.

Results

Model fitting

Our final sample for model fitting included 47 414 individuals of whom 3907 (8.2%) were registered for AUD at or after age 25. Mean age (S.D.) at registration for AUD was 42.6(11.2). The mean length of follow-up of this sample was 33.9 (6.6) years. The best-fit model

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Table 1. *Main results from best-fit model for the prediction of alcohol use disorders*

Variable (and sign)	Total effect	Total direct effect	% of effect direct	Origin of variable	Two most important mediating variables[a]
Father's alcohol consumption (+)	0.171	0.051	30	CSRD	Disrupt, Urb
Parental education (−)	0.031	0.0	0	PoR	Edu, IQ
Genetic risk (+)	0.155	0.097	62	MGR, CR, MR, PR	Disrupt, IQ
Parental abuse (+)	0.044	0.0	0	CSRD	Int, Ext
Disruptive behavior (+)	0.060	0.0	0	CSRD	Urb, LR
Repeat class (+)	0.046	0.0	0	CSRD	IQ, Int
Parental monitoring (−)	0.106	0.0	0	CSRD	Ext, Int
Urbanization (+)	0.085	0.0	0	CSRD	PD, DA
Internalizing symptoms (+)	0.084	0.0	0	CSRD	LR, Ext
Externalizing behaviors (+)	0.288	0.0	0	CSRD	DA, Smoking[b], CB[b]
Pro social (−)	0.025	0.0	0	CSRD	Res, Edu
Resilience (−)	0.034	0.0	0	CTS	IQ, Married
IQ (−)	0.079	0.0	0	CTS	Edu, CB
Smoking (+)	0.119	0.116	97	CSRD	Alc Score, DA
Alcohol score (+)	0.108	0.106	98	CSRD	DA
Peer deviance[c] (+)	0.078	0.078	100	CR, MR, PR	
Drug abuse score (+)	0.013	0.0	0	CR, MR, CSRD	Married, Unemp
Unemployed (+)	0.116	0.061	54	PoR	CB, Married
Marital status (−)	0.095	0.065	68	PoR	CB
Education (−)	0.121	0.121	100	PoR	
Criminal behavior (+)	0.230	0.230	100	CR	

CSRD, Conscript self-report data; PoR, Population Register; MGR, Multi-generational Register; CR, Criminal Register; MR, Medical Register; PR, Prescription Register.

[a] Int, Internalizing Behavior; Ext, Externalizing Behavior; Urb, Urbanization; PD, Peer deviance; DA, Drug abuse; LR, Low resilience; CB, Criminal behavior.

[b] Tied.

[c] Peer deviance reflects rates of future AUD registration in community peers (see Supplementary Table S1 for details).

fitted relatively well (RMSEA = 0.03, TLI = 0.94) and explained 23.4% of the variance in liability to AUD. The observed correlations between all 21 variables in the model are seen in Supplementary Table S2.

Parameter estimates

Table 1 provides a summary of the overall modeling results, which are presented in detail in Fig. 1. The four levels of our model are color-coded in the figures: yellow – features of the proband and proband's home environment likely present *at birth*; blue – proband's experience in *childhood and early adolescence*; red – tests or current behavior measures obtained in *late adolescence*; and green – variables assessed between the conscript evaluation and age 25 that is in *early adulthood*.

We first summarize the main pattern of findings and then review, selectively, more detailed results. Our 21 predictor variables can be usefully divided into three groups based on total effect on risk for AUD: moderate ($\geqslant$0.10), modest (0.05–0.10) and small ($\leqslant$0.05). Nine variables had a moderate effect and, in order of their effect-size and direction (±), were: (i) externalizing behaviors (+), (ii) criminal behavior (+), (iii) father's alcohol consumption (+), (iv) genetic risk (+), (v) educational attainment (−), (vi) smoking (+), (vii) unemployment (+) (viii) alcohol consumption (+), and (ix) parental monitoring (−). Six variables each had modest or small effect sizes.

Table 1 also notes the direct effect on AUD from each variable and the proportion of the total effect that is direct. With structural models, the closer the predictor variable is to the outcome, the fewer indirect paths are available and, therefore, on average, the higher is the proportion of total effect that is direct. This trend is clearly seen in Table 1 with two exceptions. Despite being quite proximal in the model, both father's alcohol consumption and especially genetic risk have substantial direct effects on AUD.

Structural models are particularly useful at clarifying mediational paths. Table 1 notes the two most important mediational variables for all risk factors. A number of them are consistent with expectation. For example, the modest effect of parental education's effect on risk for AUD is largely mediated through the

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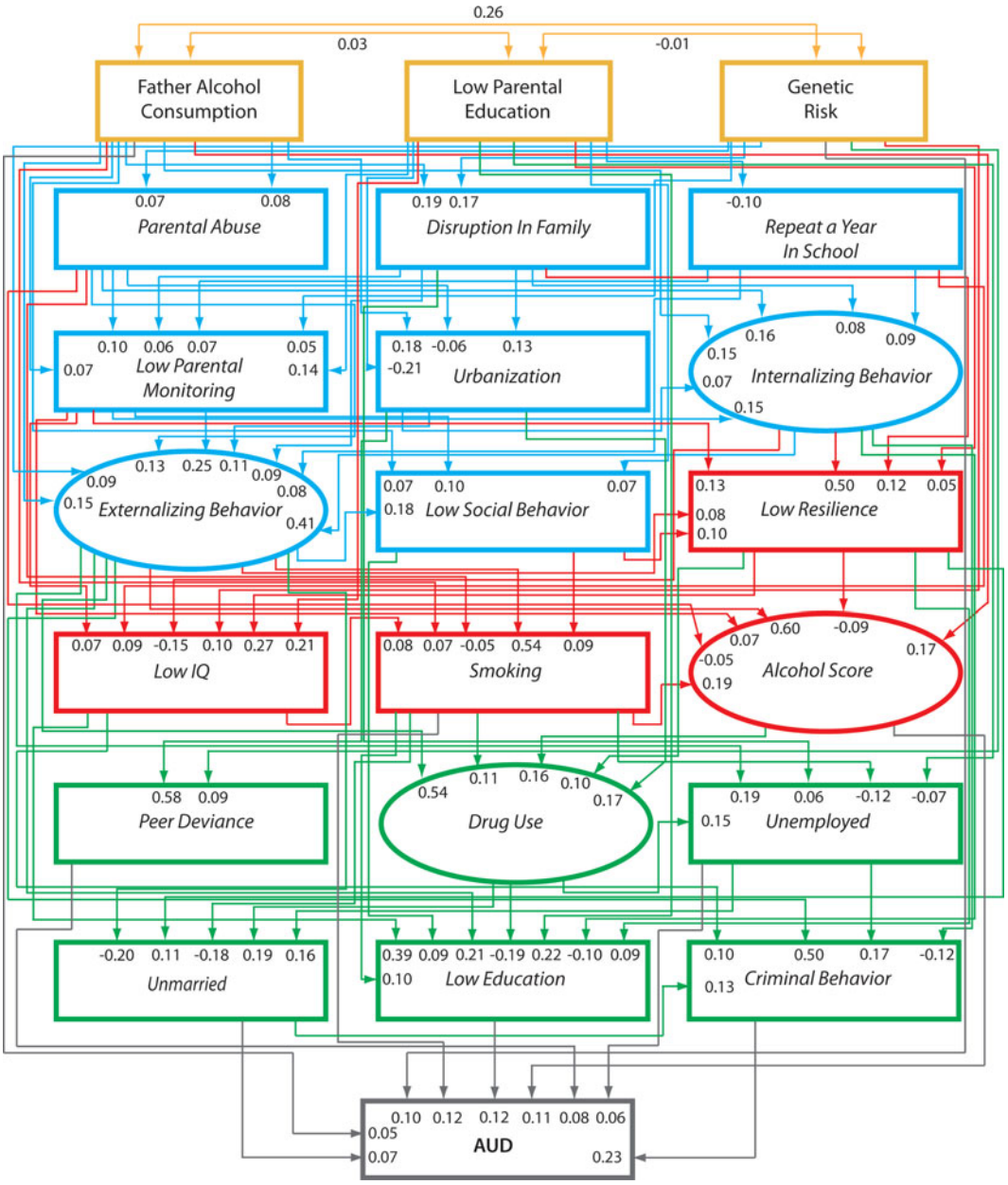

Fig. 1. Results of our best-fit model for the prediction of alcohol use disorder at or after age 25. Two-headed arrows represent correlation coefficients while one-headed arrows represent path coefficients or standardized partial regression coefficients. The variables were ordered to approximate a developmental process within four time periods which are colored coded: (1) birth – yellow, (2) childhood and early adolescence – blue, (3) late adolescence – red, (4) and early adulthood – green. Four of the 21 predictor variables were latent and constructed, using a measurement model, from other observed variables: internalizing behavior, externalizing behavior, alcohol score and drug use/abuse. See Supplementary Table S1 for a detailed description of each variable.

probands educational attainment and IQ. Parental monitoring has its strongest effect through a reduction in externalizing behavior. Urbanization increases AUD risk via increasing exposure to deviant peers and augmenting risk for drug abuse (DA). The large effect of externalizing behavior on AUD risk is via other externalizing behaviors: smoking, DA and crime. Resilience decreases risk for AUD through an association with a higher IQ and increased rates of marriage. The most important mediator of the protective effect of marital status on AUD risk is through a reduction in criminal behavior.

To further elucidate these mediational pathways, we prepared three additional figures that highlight

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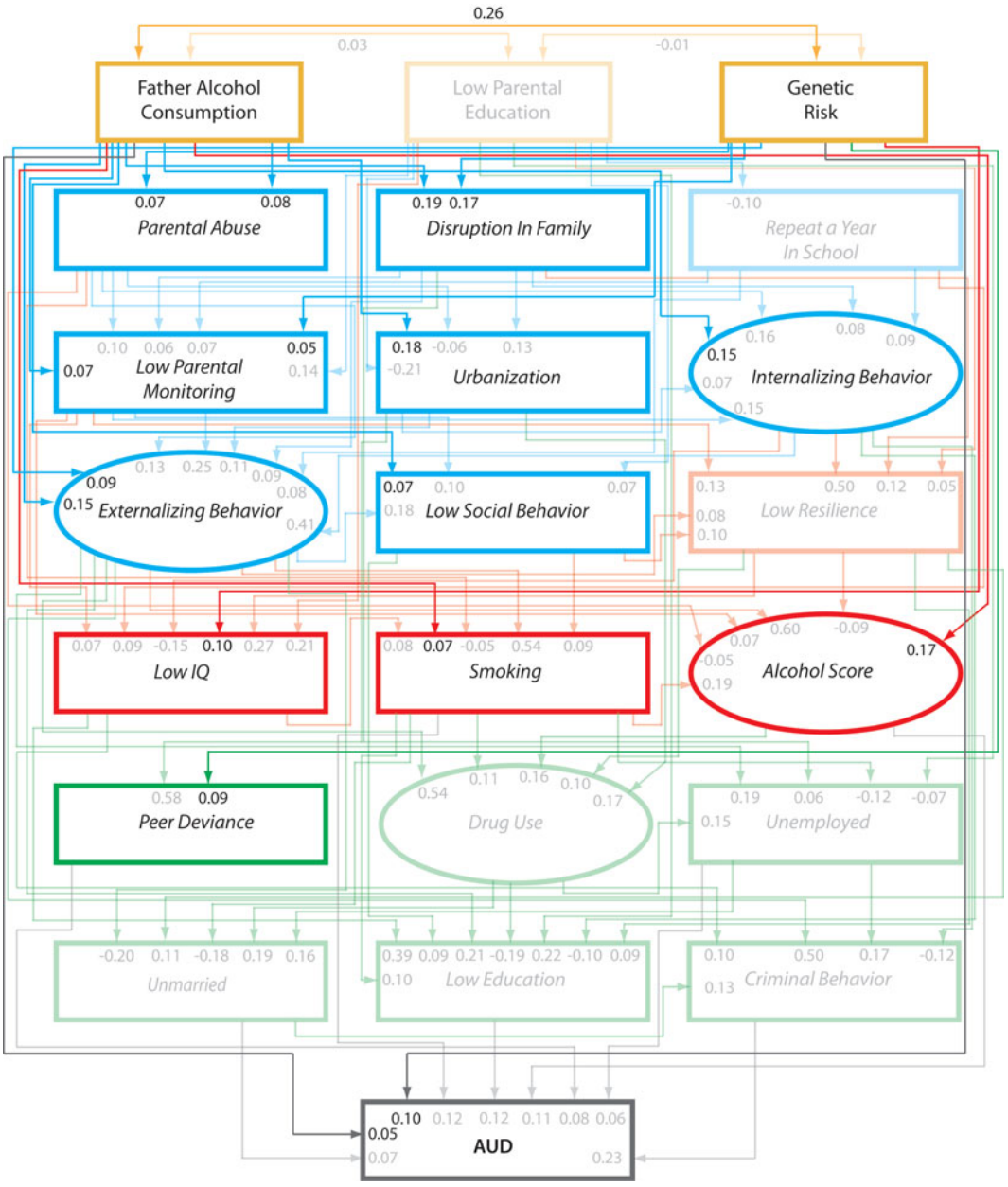

Fig. 2. Our best-fit model highlighting the impact of father's alcohol consumption and genetic risk.

different parts of our overall model. Fig. 2 illustrates the complex causal pathways from paternal alcohol consumption and genetic risk to AUD. In addition to their direct effects on AUD, these variables both predict increased rates of parental abuse, family disruption and externalizing behaviors, and reduced parental monitoring. Father's alcohol consumption predicts urbanization and reduced prosocial behaviors. Genetic risk scores are associated with increased internalizing symptoms, alcohol consumption, lower IQ, and peer deviance.

Fig. 3 illustrates the key elements of the externalizing pathway to AUD. Noteworthy are the strong paths from externalizing behavior to smoking, alcohol score, drug use, and criminal behavior, and paths from all these variables (except drug use) directly to AUD. These variables also impact on risk for AUD by generally increasing rates of unemployment, lowering the chances of being married and reducing educational attainment, all of which in turn are associated with increased rates of AUD.

Fig. 4 illustrates what might be termed inter-related psychosocial and internalizing pathways to AUD. Prominent risk paths here include: family disruption predicting internalizing behavior, low parental monitoring and unemployment, low parental monitoring and

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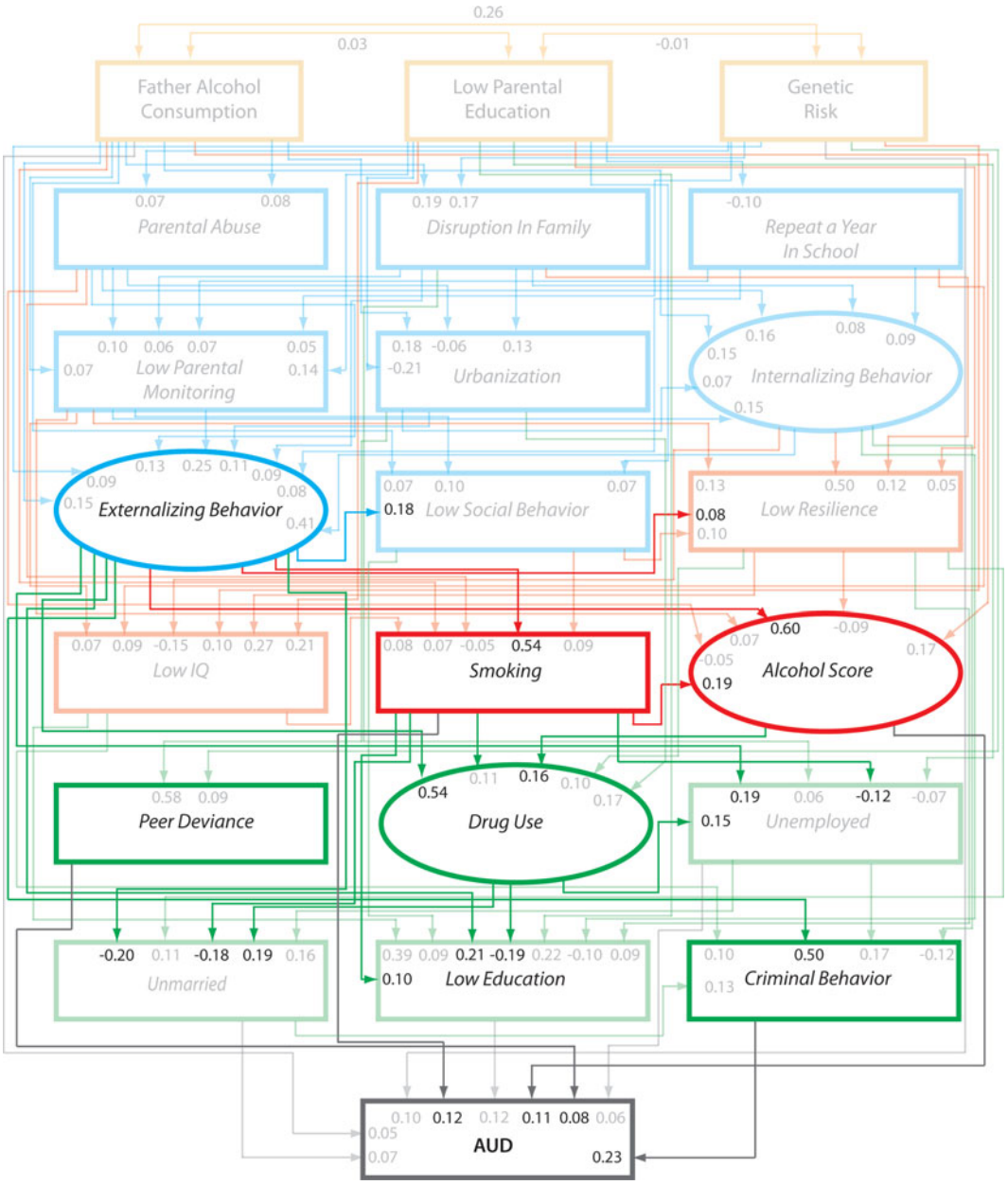

Fig. 3. Our best-fit model highlighting an externalizing pathway to alcohol use disorder.

internalizing behavior predicting low resilience, low resilience and unemployment predicting a reduced probability of marriage, and low parental education predicting low education.

Discussion

Main findings

The goal of this paper was to further improve our understanding of the etiologic pathways to AUD in men by constructing, in a large informative sample with long-term follow-up, an empirical broad-based causal model for AUD that integrates, in a single developmental framework, a wide diversity of risk factors. While a long tradition in psychiatry has advocated the importance of inclusive etiologic models, alternatively called 'biopsychosocial' (Engel, 1977), 'multi-level' (Schaffner, 1994) or 'integrative' (Kendler, 2005), the actual implementation of such approaches is challenging as it requires developing adequate samples with a sufficient diversity of risk factors and appropriate statistical approaches that avoid the extremes of dramatic over-simplification and baffling complexity. Indeed, our results provide a range of useful insights into the etiology of AUDs five of which are particularly worthy of comment.

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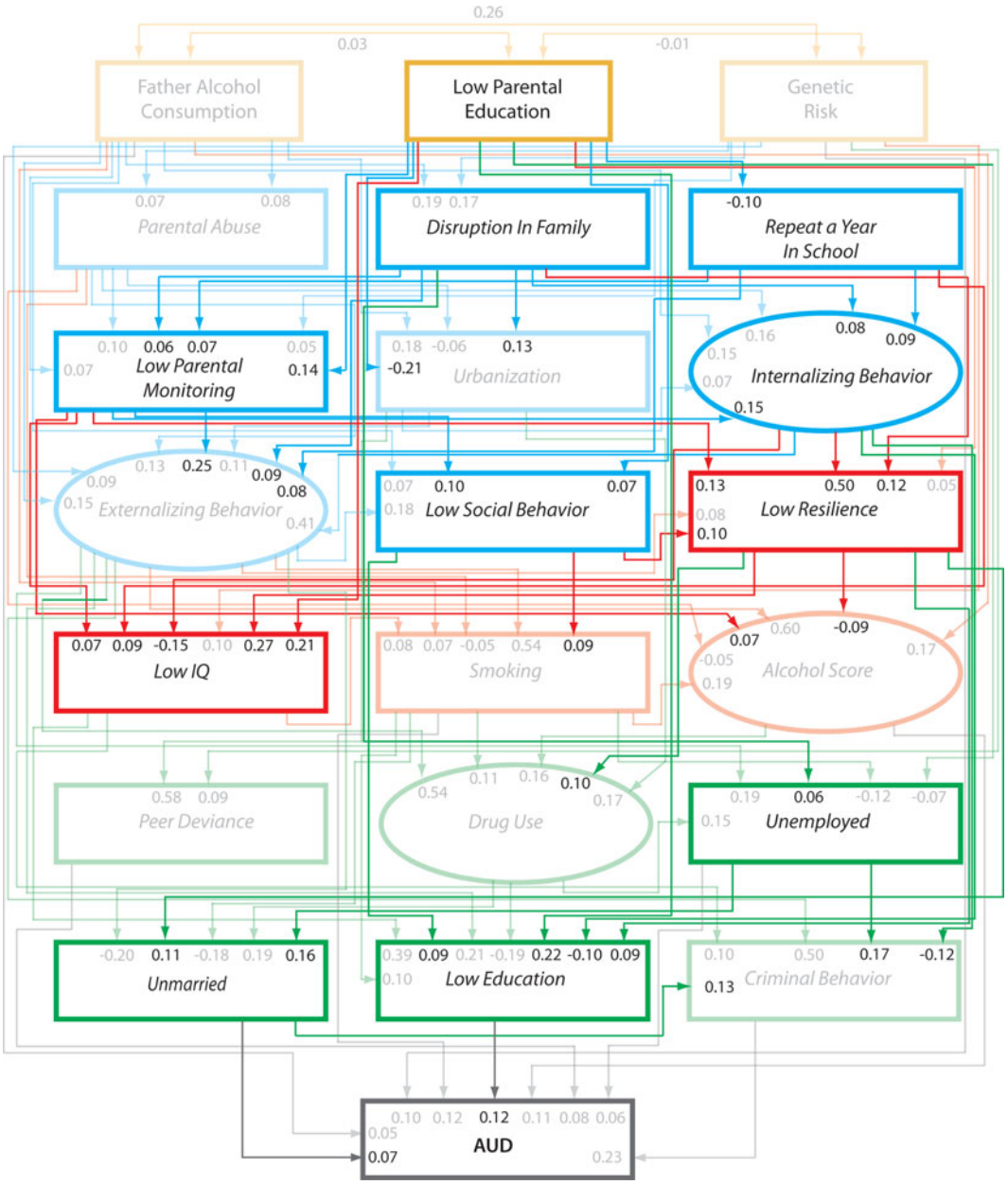

Fig. 4. Our best-fit model highlighting a psychosocial-internalizing pathway to alcohol use disorder.

First, our findings are congruent with a range of prior evidence from other longitudinal studies beginning in childhood and adolescence that the single most consistent set of risk factors for AUD can be described as reflecting an 'externalizing pathway' (Zucker, 2008). These results are in turn consistent with two other literatures – that risk for AUD is consistently associated with high levels of externalizing personality traits such as impulsivity, disinhibition, extraversion, and novelty seeking (Zuckerman, 1972; Windle, 1999; Sher *et al.* 2005; Grucza *et al.* 2006; Verdejo-Garcia *et al.* 2008), and that twin studies, including one we recently completed in a Swedish national sample (Kendler *et al.* 2016), showing substantial sharing of genetic risk factors between high alcohol intake and/or AUD, and a range of externalizing disorders and traits (Slutske *et al.* 2002; Kendler *et al.* 2003, 2011*a*; McGue & Iacono, 2008). Not surprisingly, many of the traits that constitute our externalizing pathway to AUD (Fig. 3) are part of the broad syndromes of conduct disorder and antisocial personality.

Second, while earlier studies focusing on AUD generally supported a robust internalizing pathway to AUDs (Hawkins *et al.* 1992), and there is strong evidence for co-morbidity between AUD and mood and anxiety disorders (Kendler *et al.* 1993; Grant *et al.* 2015), our results

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are in accord with recent longitudinal studies which have produced less robust findings (Zucker, 2008). This may be because some internalizing symptoms – such as social anxiety – can be protective (Dubow *et al.* 2008; Maggs *et al.* 2008) and other internalizing symptoms can predispose to risk for AUD (Caspi *et al.* 1996; Pitkanen *et al.* 2008). When measured at age 18, internalizing symptoms predicted less than one-third as much variance in AUD risk as did externalizing symptoms assessed at the same age. Also, we studied only men and the association between internalizing syndromes and AUD may be stronger in women (Cloninger *et al.* 1996). It should be noted, however, as commonly seen in other samples, that our measure of internalizing behaviors strongly predicted levels of externalizing behaviors with a path coefficient of +0.41.

Third, our results also support prior research demonstrating that AUD risk is associated with a range of adverse familial and social-environmental factors including disruption in the childhood home (Kendler *et al.* 1996, 2015), childhood abuse (Fergusson & Mullen, 1999; Kendler *et al.* 2000), poor parental monitoring (Dielman *et al.* 1990; Tucker *et al.* 2008), urban environments (Grant *et al.* 2015) and peer deviancy (Fergusson *et al.* 1995; Hawkins *et al.* 1998; Patterson *et al.* 2000; Coie & Miller-Johnson, 2001; Farrington, 2005).

Fourth, our strong predictors for AUD were widely dispersed across levels and place in the developmental cascade. Along with previous similar efforts (Kendler *et al.* 2011*b*; Edwards *et al.* 2015), our results begin to give a temporal perspective to the multifactorial nature of the etiologic pathways to AUD.

Fifth, our results well illustrate the developmental inter-weaving of genetic/biological and family/social risk factors for AUD. Such findings suggest that the attempts to subdivide pathways to risk for common psychiatric disorders into 'biological' and 'psychosocial/environmental' levels is not as feasible as is often assumed. This is particularly clearly seen in Fig. 2 where the effect of genetic risk on AUD is mediated by a range of social variables such as family disruption and low parental monitoring.

Comparison with two prior similar studies

It is of particular interest to compare our findings with two prior studies which utilized similar developmental path models to predict alcohol use, problems and symptoms of AUD in male Virginia twins from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders (VATSPSUD; Kendler *et al.* 2011*b*) and in the Avon Longitudinal Study of Parents and Children (ALSPAC; Edwards *et al.* 2015). In the VATSPSUD study, the data were retrospective, obtained from a Life History Calendar interview when the twins were in middle adulthood (mean age 40.3). The outcome variable was a count of DSM-IV criteria for Alcohol Abuse or Dependence (APA, 1994). In the ALSPAC study, the cohort, followed longitudinally since birth, included both sexes, and the key dependent measure was alcohol problems at age 20 assessed using items from the Alcohol Use Disorders Identification Test (AUDIT; Saunders *et al.* 1993) and DSM-IV alcohol dependence criteria (APA, 1994). The predictor variables were assessed in earlier waves. By contrast, our study followed men till a mean age (S.D.) of 58.2 (6.6), used registry-based diagnoses of AUD, which are likely to on average be relatively severe, and our predictor variables were a mixture of self-report measures at age 18 and registry-based information.

All three studies found important predictive effects on AUD related outcomes of (1) parental drinking, alcohol problems and or genetic risk, (2) low parental monitoring, (3) externalizing psychopathology (ADHD, sensation seeking and conduct disorder in the VATSPSUD study; conduct difficulties, low conscientiousness and sensation seeking in the ALSPAC study and externalizing and criminal behavior in this study), and (4) peer deviance. In each study, weaker effects were found for various measures of internalizing psychopathology (early onset anxiety disorders and neuroticism in the VATSPSUD, major depression symptoms in ALSPAC and internalizing behavior here). In the two studies where they were examined, child abuse (VATSPSUD and here) and other illicit substance use or abuse (ALSPAC and here) were also consistently predictive. All three studies also clearly illustrated the difficulty of cleanly disentangling genetic-temperamental and social-environmental pathways to risk. The proportion of variance in the AUD-related outcome measure was also relatively similar across studies: 30% in the VATSPSUD, 31% in the ALSPAC and 23% here. Despite major difference in the nature of the sample and the method of measurement, the similarities in findings across these studies support the robustness and generalizability of the broad results of these three studies.

Limitations

These results should be interpreted in the context of eight potentially important methodologic limitations.

First, we detected subjects with AUD from a range of official Swedish registry records obviating the need for cooperation or accurate recall. While the validity of our method is supported by high concordance for registration across our modes of ascertainment (Kendler *et al.* 2015), false-negative and false-positive diagnoses are a near certainty. Given that the prevalence of AUD in this sample is lower than estimated from interview surveys in males

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from both the United States (Kessler *et al.* 1994; Grant *et al.* 2015) and nearby Norway (Kessler *et al.* 1994; Kringlen *et al.* 2001), false negatives are likely to be a greater problem. Put another way, our AUD cases are likely to be more severely affected than those ascertained from population-based interview studies.

Second, these models assume a causal relationship between predictor and dependent variables. The validity of this assumption varies across our model. Some of the inter-variable relationships that we assume take the form of A→B may be truly either A ← B or, more likely, A ↔ B. Others may result from other (or confounding) variables that predict both A and B.

Third, some of the variables assessed at conscription involved retrospective recall and may be subject to bias. This would be particularly true of reports of father's alcohol consumption, parental abuse and parental monitoring.

Fourth, the sequence of variables in our model was only approximate. We do not claim that in all cases, this was the only valid way in which the variables could have been placed within our schema. We switched the order of several variables in our models from that of our final model (e.g. having the alcohol score precede smoking, the externalizing factor precede the internalizing symptoms, re-ordering the early adulthood risk factors so that the order was criminal behavior → low education → unemployed → unmarried). With these variations on our final model, the parameter estimates changed little and fit indices tended to deteriorate. This provides indirect evidence that our ordering of variables is not likely to seriously distort the observed associations.

Fifth, our model assumes that our predictor variables act additively and linearly in their impact on AUD risk. This is unlikely to be always true. For example, high levels of parental monitoring may modify the impact of peer group deviance on alcohol intake (Steinberg *et al.* 1994; Fletcher *et al.* 1995). However, the possible interactions between our 21 variables are too numerous to permit any tractable evaluation.

Sixth, this sample consisted of males born in Sweden. While we note many parallels above between our findings and those of prior studies, we cannot be certain our results would extrapolate to women or to other ethnic samples. In particular, among European countries, Sweden shares with Finland and Russia a relatively distinctive drinking pattern characterized by intoxication-oriented drinking with large quantities often consumed per occasion (Leifman, 2002).

Seventh, while extensive, we did not have information on some key risk factors for AUD including intra-uterine alcohol exposure (Spear & Molina, 2005), alcohol expectancies (Sher *et al.* 2005) or drinking motives (Cooper, 1994; Prescott *et al.* 2004).

Finally, we only examined first AUD registrations after age 25 which had the considerable benefit of permitting the inclusion of key risk factors in early adulthood but the down side of eliminating from our modeling the earliest onsets of AUD.

Conclusions

AUD in men is an etiologically complex syndrome influenced by familial-genetic, psychosocial, internalizing, and especially externalizing risk factors. These multiple factors act and interact over development with often complicated mediational pathways that move fluidly between measures typically conceptualized as biological, familial, temperamental, symptomatic and social. A full understanding of the etiology of AUD will in future studies require the recognition of a diversity of causes.

Supplementary material

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0033291716001409.

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Declaration of Interest

None.

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