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TESTING A LEVEL OF RESPONSE TO ALCOHOL-BASED MODEL OF HEAVY DRINKING AND ALCOHOL PROBLEMS IN 1,905 17-YEAR-OLDS

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Abstract

Background—The low level of response (LR) to alcohol is one of several genetically-influenced characteristics that increase the risk for heavy drinking and alcohol problems. Efforts to understand how LR operates through additional life influences have been carried out primarily in modest sized U.S.-based samples with limited statistical power, raising questions about generalizability and about the importance of components with smaller effects. This study evaluates a full LR-based model of risk in a large sample of adolescents from the U.K.

Methods—Cross-sectional structural equation models (SEM) were used for the approximate first half of the age 17 subjects assessed by the Avon Longitudinal Study of Parents and Children (ALSPAC), generating data on 1,905 adolescents (0 age 17.8 years, 44.2% males). LR was measured with the Self-Rating of the Effects of Alcohol (SRE) Questionnaire, outcomes were based on drinking quantities and problems, and standardized questionnaires were used to evaluate peer substance use, alcohol expectancies, and using alcohol to cope with stress.

Results—In this young and large U.K. sample, a low LR related to more adverse alcohol outcomes both directly and through partial mediation by all three additional key variables (peer substance use, expectancies, and coping). The models were similar in males and females.

Conclusions—These results confirm key elements of the hypothesized LR-based model in a large U.K. sample, supporting some generalizability beyond U.S. groups. They also indicate that with enough statistical power multiple elements contribute to how LR relates to alcohol outcomes, and reinforce the applicability of the model to both genders.

Keywords

ALSPAC; alcohol; level of response; structural equation models; adolescents

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I. Introduction

An intensive effort across multiple laboratories has focused on the need to identify genetically-influenced factors that impact on the risk for heavy drinking and alcohol problems (Ducci and Goldman, 2008; McGue, 1999; Schuckit, 2009). This is a challenging and complex task, as multiple genetic and environmental pathways are likely to contribute to a vulnerability toward repetitive alcohol problems, such as alcohol use disorders (AUDs). One major reason for this search is the hope that identifying such risk factors early in the drinking career might aid in the development of more focused and effectively targeted approaches to preventing costly and life-threatening alcohol problems in the future.

Among the heterogeneous and polygenic characteristics involved in the alcoholism risk are variations in alcohol metabolism, the presence of problematic externalizing behaviors (e.g., impulsivity), as well as the manner in which a person responds to alcohol (Li, 2000; Sher et al., 2005; Slutske et al., 2002). The latter includes differences in how alcohol affects reactions to stress and how rapidly rising blood alcohol levels (BACs) can produce an exaggerated overall response in some drinkers (Finn et al., 1990; Morzorati et al., 2002). Perhaps the most intensively studied alcohol reaction characteristic related to future AUDs, however, is the low level of response (LR) to alcohol observed at peak and falling blood levels after oral administration (Schuckit, 2009). LR refers to the intensity of response to alcohol at a specified BAC or to the retrospective recall of the number of standard drinks usually needed for a range of effects.

The need for higher amounts of alcohol for various effects (or a low LR per drink) has a heritability of 40% to 60%, with additional influences and environment contributing to the remainder of the risk (Schuckit, 2009; Heath et al., 1999). For some genetically influenced characteristics impacting on the AUD risk, especially those where many genes with small effects are likely to operate, there are advantages to looking beyond genes to see what additional prevention approaches might be appropriate (Paynter et al., 2010). This consideration contributed to the development of models that include genetically influenced characteristics (or phenotypes), life experiences, and drinking status, which have been tested for several potentially independent risk factors, including externalizing characteristics, mood disturbances, as well as the low LR to alcohol (Sher et al., 2005; Ohannessian and Hesselbrock, 2008; Schuckit and Smith, 2006).

Regarding LR, aspects of Social Information Processing, Peer Cluster, and Social Learning models led to the low LR-based model presented in Figure 1 (Bandura, 1997; Brown et al., 2008; Dodge et al., 2003; Schuckit et al., 2004). Here, it is hypothesized that: 1) an individual is likely to consume the amount of alcohol needed to achieve desired effects; 2) if more alcohol is required for such effects, they are likely to drink more per occasion; 3) the low LR contributes to association with peers who are likely to have a similar response to alcohol and who, therefore, consume similar higher doses of alcohol per occasion (Henry et al., 2005); 4) a person's low LR and the influence of similar peers is likely to affect what one should expect from alcohol during a drinking session (Brown et al., 2008; Schuckit et al., 2004); and that 5) the low LR, peer influences, and more positive alcohol expectancies are hypothesized to encourage using alcohol to cope with life problems (Veenstra et al., 2007).

Evaluations of the relationships in Figure 1 have been carried out using structural equation models (SEMs), survival analyses, and latent trajectory approaches. Most have focused on U.S. samples, and have included higher functioning adults, lower income subjects from families with a high density of AUDs, as well as several non-clinical samples of adolescents (Schuckit et al., 2004; Kramer et al., 2008; Schuckit et al., 2008c; Trim et al., 2008, 2010;

Schuckit et al., 2009a). The focus on U.S. samples raises the question of whether the model generalizes to other cultures or is a unique reflection of a U.S.-based environment.

There have been some modest differences across model results in different U.S. groups. All models to date have supported a direct link between a low LR to alcohol and heavier drinking and alcohol problems (e.g., Schuckit et al., 2004, 2008a, 2008c, 2009a, 2010), and all indicate that one or more of three additional characteristics statistically partially mediate the relationship between a low LR and adverse alcohol outcomes. Most support a significant contribution to mediation by using alcohol to cope with stress (COPE), and several have indicated that more positive expectations of the effects of alcohol (EXPECT) partially mediate how low LR relates to the drinking characteristics, but not all studies agree (Schuckit et al., 2008c, 2009a). There is similar variability regarding the possible mediational role for heavier substance using peers (PEER) (Schuckit et al., 2004, 2008a, 2008c, 2009a). The variation across studies regarding statistical partial mediators of the relationship of LR to heavy drinking and problems could reflect differences among samples, but it is also possible that some of the variability in performance of model components could be a consequence of the relatively modest sample sizes often available for these analyses.

Another issue for these models relates to possible gender effects. This could be salient because males are more likely to have higher impulsivity, itself a risk factor for heavy drinking. Also, while both sons and daughters of alcoholics demonstrate lower LRs than matched family-negative controls overall, females are likely to weigh less and have lower muscle mass with a higher BAC (Chung and Martin, 2009; Eng et al., 2005; Sher et al., 2005). Despite these differences, evaluations through invariance procedures of whether it was reasonable to combine males and females in prior models revealed few significant gender differences (Schuckit et al., 2008a, 2008c, 2009a). However, lack of statistical differences between males and females in the model (i.e., invariance) could reflect insufficient statistical power and a more definitive answer to gender effects requires a larger sample.

Most evaluations of the LR model have been cross-sectional, as those data are useful in helping to learn more about how elements of the model relate, and do not require continuity of measures over time and costly followups. Two prospective analyses have been published involving a U.S. sample of men originally studied at about age 20 and followed at about age 40, generating conclusions similar to those from cross-sectional evaluations (Schuckit et al., 2004, in press). In those men the low LR at age 20 related directly to heavy drinking and alcohol problems at age 40, with additional partial mediation of that relationship by age 35 heavier peer drinking and the use of alcohol to cope with stress, although not through more positive alcohol expectancies in these more middle aged subjects.

The current analyses address the questions regarding possible culture bound and gender effects of the LR model in the largest group for which elements of the LR-based model in Figure 1 have been evaluated, the Avon Longitudinal Study of Parents and Children (ALSPAC). In this population-based prospective study of a birth cohort (Golding et al., 2001; Schuckit et al., 2008a, b), self-report measures of the LR to alcohol along with measures of drinking patterns and problems were added to the ongoing protocol when the ALSPAC children reached about age 12 (Schuckit et al., 2005). Data generated from ALSPAC have established correlations in the range of .40 to .50 between a lower LR and heavier alcohol intake, as well as correlations of about .28 between LR and alcohol problems in children as young as age 12 (Schuckit et al., 2005). A subsequent two-year followup demonstrated significant relationships between an earlier low LR and later alcohol patterns of consumption and problems, even after controlling for baseline drinking characteristics (Schuckit et al., 2008b). Also, a SEM analysis of 688 ALSPAC offspring

demonstrated both a direct relationship between LR and adverse alcohol outcomes, as well as partial mediation of this relationship through higher quantities of alcohol consumption in peers (Schuckit et al., 2008a). However, at the time those data were gathered for that SEM, ALSPAC did not use additional measures of potentially important elements of the LR-based model, such as alcohol expectancies and the use of alcohol to cope with stress, and, thus, follow-up data testing the full model are not yet available.

This paper presents data from almost 2,000 ALSPAC offspring at the age 17 evaluation using an expanded test battery that included aspects of all elements of the model in Figure 1.

II. Materials and Methods

Subjects

Following guidelines of the relevant Law Ethics Committee and the Local Research Ethics Committee, as described in detail elsewhere, ALSPAC is a study that began in 1991 to prospectively follow a birth cohort attempting to enroll all singleton children born to 14,541 pregnant women in Avon, England between 4/1/1991 and 12/31/1992 (Golding et al., 2001). Self-administered questionnaires were regularly used to gather data from the mothers during the pregnancy and the early developmental period of the offspring. Among these subjects, a subset of about 8,000 children continued with face-to-face evaluations every 18 months beginning at age seven. The current data are based on the first of 1,905 males and females (44.2% male) who had consumed at least one full drink and who participated in personal interviews in the age 17+ assessment clinic. The large majority (98.2%) of the participants were Anglo-European, with the remainder comprised of individuals with Pakistani/Indian, Chinese, and Caribbean ancestry.

Measures used in the SEM

The **LR to alcohol**, a manifest variable in the SEM, was evaluated using the Self-Rating of the Effects of Alcohol (SRE) Questionnaire where subjects retrospectively reported the number of U.K. standard units of drinks (8 g of ethanol) they estimated had been required for each of up to four effects the approximate first five times of drinking (Schuckit et al., 2009b). All subjects who consumed ≥ 1 drink were asked to make their best estimates, but to only give estimates for effects they actually experienced in the noted time frame. The SRE includes the amount of alcohol required to begin to feel the first effects, the drinks needed to begin to feel slurring of speech, the alcohol needed to produce a stumbling gait, and the drinks required for unwanted falling asleep, with subjects instructed to only report the number of drinks for effects actually experienced during that early drinking phase (Schuckit et al., 1997). The SRE has a one-year retest reliability of .82, a Cronbach α of $> .90$, and overlaps at about .60 with another LR measure (the alcohol challenge) regarding the ability of LR to predict future drinking patterns and problems (Schuckit et al., 1997, 2009b; Ray et al., 2007). In the SRE, a greater number of drinks required for effects indicates a lower response per drink, or a lower LR as would be measured on alcohol challenges (Schuckit et al., 2001, 2010). SRE scores are generated by summing the number of drinks required across effects, and dividing that figure by the number of effects reported. Alcohol challenge and SRE-based LR's perform similarly when used to identify higher and lower LR subjects who are then evaluated in functional brain imaging, and when results from the two measures are compared in similar structural equation model (SEM) approaches (Schuckit et al., 2010).

A latent variable for **alcohol outcomes** (ALCOUT) incorporated three indicators gathered from a semi-structured questionnaire developed from the valid and reliable Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) instrument (Bucholz et al., 1994;

Hesselbrock et al., 1999). Indicators included the maximum number of standard units of drinks (~ 8 g of ethanol) ever consumed in the lifetime, the frequency of drinking ≥ 6 drinks per occasion in the prior six months, and the number of alcohol problems experienced in the prior 12 months. The 17 potential problems incorporated all of the 11 DSM-IV abuse and dependence criteria, along with additional nondiagnostic problems that include blackouts, feelings of guilt regarding drinking, complaints about drinking problems by relatives or friends, and alcohol-related fights (American Psychiatric Association, 1994).

The PEER variable used here was developed from the Important People and Activities (IPA) Scale, an instrument with retest reliabilities, as well as measures of validity that approach .80 (Longabaugh et al., 1993, 2001). While prior analyses used PEER drinking quantity because LR is more closely linked to quantities consumed per occasion, ALSPAC currently only records PEER substance frequencies. Therefore, a latent variable was created reflecting the subjects' perception of whether the relevant peer used alcohol, nicotine, cannabinoids, and/or other illicit drugs. In the IPA, four individuals felt by the subject to be important peers were noted, with subsequent questions regarding the perceived use of substances yielding a mean number of peers using each of the four substances.

Alcohol expectancies (EXPECT) were measured through questionnaire items from the Adolescent Alcohol Expectancy Questionnaire (AEQ-A) which has a Cronbach α and retest reliabilities of about .7, as well as good validities when compared to other scales (Brown et al., 1987; Goldman, 2002). In light of limited time available in the ALSPAC protocol, three items with the highest factor loadings in the four AEQ-A scales of interest were selected to be representative of the AEQ. These true/false items were scored on a 0 to 3 scale based on the number of "true" ("I think that effect occurs") answers recorded for the three items for each of the four scales of expected Changes in Social Behavior, Improved Cognitive and Motor Abilities, Sexual Enhancement, and Arousal. The scales were used as four indicators to create a latent alcohol expectancy variable in the SEM.

Finally, a **coping with stress** variable (COPE) was generated from scores of 1 (almost never) to 4 (almost always) for each of six items on the Drinking to Cope Scale, an instrument with good validities, reliabilities, and Cronbach α (Beseler et al., 2008; Cooper et al., 1988). Scores for each item were placed into three parcels of two items each that were used as indicators for the latent variable.

Data analyses

Analyses began with point-biserial and Pearson Product-Moment correlations among the manifest (e.g., LR) and latent variables used in the SEM. Subsequently, structural equation modeling was carried out based on both AMOS version 18, as well as Mplus Version 5.1, using the maximum likelihood estimation for analysis of the variance/covariance matrix (Arbuckle, 2009; Muthén and Muthén, 2007). Any violations of distributional assumptions for the model and parameter estimations were evaluated within AMOS using bootstrapping procedures which were repeated 1,000 times. Within the model, when needed, exponential and square root transformations were carried out, depending on the topography of the data (i.e., exponential transformation for EXPECT, two indicators of COPE, and for alcohol problems, while square root transformations were used for one COPE indicator and for the alcohol outcome indicator of maximum drinks lifetime). In our approach, for clarity of interpretation, the measurement model was first determined using a confirmatory factor analysis specifying correlations among the latent variables, after which the results were incorporated into the full SEM.

Evaluation of statistical mediation within the cross-sectional model used a product-of-coefficients test within Mplus, version 5.1 (Muthén and Muthén, 2007; MacKinnon et al.,

1995). Non-normal distributions in these mediational analyses were addressed using the bias-corrected bootstrapping approach with 1,000 resamples (Fritz and MacKinnon, 2007). The results are presented as the 2.5th and 97.5th percentiles, reflecting the lower and upper limits of the 95% confidence intervals where mediation is indicated when the confidence interval does not span across zero. Also, gender differences were evaluated within AMOS through the creation of separate results for males and females in order to observe possible differences in elements of the model across these groups.

The measurement model and SEM results were evaluated using the appropriate goodness of fit characteristics that included: the comparative fit index (CFI) where good fit is indicated by a value > .90; the non-normal fit index (NNFI) with a good fit defined as one that approaches 1.0; the root mean square error of approximation (RMSEA) with good fit seen with scores < .05; and the root mean squared residual (RMSR) with good fit < .08 (Bentler, 1990; Hu and Bentler, 1998; Wheaton et al., 1977). χ^2 and the χ^2/df ratio were not appropriate for these analyses because they are overly sensitive to large samples and likely to give misleading statistical results.

Invariance analyses across genders were carried out using the approach of Spillane et al. (2004) and Hoyle and Smith (1994). These involved steps of: 1) running the full model without constraints; 2) applying equality constraints to make factor loadings the same for males and females; 3) adding the requirement of using the same variances across the genders; 4) requiring the same correlations across groups; and 5) requiring the same values for structural paths across males and females. Chi squares were used to determine if each additional constraint significantly reduced model fit (Bentler, 1990).

III. Results

Data were available on 1,905 drinking subjects, including 842 males (44.2%), from ALSPAC with a mean (standard deviation) age of 17.8 (0.27) years and an age of onset for the first full drink of 13.6 (1.60) years. The correlation between LR and age of first drink was -.05 ($p = .04$). At the time of the current evaluation the males and females reported drinking alcohol on an average of 4.6 (3.90) days per month with an intake of an average 4.6 (2.55) U.K. standard units per drinking day (3.7 U.S.-based 10 gm drinks) and a lifetime maximum of 13.4 (7.34) drinks per occasion (10.7 U.S.-based drinks). Almost half (49.5%) of drinkers reported at least one repetitive (i.e., occurring more than twice) alcohol-related problem. The most common were alcohol-related blackouts (20.3%); drinking more than intended, having problems stopping drinking, spending a lot of time consuming alcohol, or the development of tolerance occurred in about 15% each; feeling guilty about drinking, neglecting obligations, or recognizing the need to cut down in about 7% each; and having heard complaints about their drinking, alcohol interfering with work or school, or alcohol-related fights in about 3% each. In this population, 8.4% related having experienced four or more life problems related to alcohol.

Regarding the major correlates (or “predictors”) used in this cross-sectional model, the mean SRE score for the LR to alcohol was 4.2 (1.37) drinks (equivalent to ~ 3.4 using U.S.-based units). Regarding the scores, 13.9% endorsed one SRE item, 11.7% two, 36.8% three, and 37.7% four effects. In addition: 1) the average for each of the four alcohol expectancy questionnaire scores were: 2.1 (0.96) for expectations of Changes in Social Behavior, 0.2 (0.54) for expectations of Improved Cognitive and Motor Abilities, 2.0 (0.95) regarding expected Sexual Enhancement, and 2.2 (0.99) regarding the expected Increased Arousal; 2) the average endorsement of the six possible drinking to cope items was 1.6 (0.49); and 3) the average endorsement of the six possible substances perceived to be used in the prior six months for the most important

peers, 80% were felt to have used alcohol, 33% tobacco, 17% cannabinoids, and 7% other illicit drugs.

Table 1 presents the correlations among latent and manifest variables used in the SEM. Here, a low LR per drink (indicated by the need for a higher number of drinks to obtain effects on the SRE) correlated significantly with alcohol outcomes, peer substance use, alcohol expectancies, and drinking to cope. LR, alcohol outcomes, and alcohol expectancies related to gender with females reporting needing fewer drinks for effects, noting lower alcohol quantities and fewer problems, and having less positive expectations of the effects of alcohol. In Table 1, more adverse alcohol outcomes also related significantly to higher scores for peer substance use, expectations of the effects of alcohol, and drinking to cope, as well as to an older age. Peer substance use, alcohol expectancies, and drinking to cope all correlated positively with each other.

Figure 2 represents the measurement model for the 1,905 males and females. Here, consistent with prior evaluations, the analyses allowed correlated residuals within constructs as a reflection of the correlation expected between some indicators within a domain (e.g., maximum lifetime drinks and recent quantities). For Figure 2, the fit statistics included: CFI = .97; NNFI = .96; RMSEA = .042 (.037 – .047); and SRMR = .037. Thus, all were in the good fit range. If residuals were not allowed to correlate, the fit indices were .93, .93, .058 (.054 – .063), and .048, respectively.

Figure 3 presents the significant ($p < .05$) paths for the SEM in a model that explains 59% of the variance (the R^2). Note that path coefficients of .05 represent $p < .04$, coefficients of .07 indicate $p < .01$, and values of .08 relate to $p < .001$. In the figure, LR related directly to alcohol outcomes, and demonstrated significant paths to peer substance use, alcohol expectancies, and using alcohol to cope with stress. All additional key variables (PEER, EXPECT, and COPE) related directly to alcohol outcomes and to each other within the model. Gender and age covariates related to key components of the model in a manner consistent with Table 1. Fit characteristics for the model were all in the good range, including: CFI = .92; NNFI = .90; RMSEA = .054 (.051 – .058); and SRMR = .042. Without correlated residuals, the indices are .92, .87, .06 (.056 – .064) and .048, respectively. All relevant relationships among key variables in the model had mediational effects, including, for LR, LR – PEER – COPE – ALCOUT (.001, .004), LR – EXPECT – COPE – ALCOUT (.005, .015), and LR – COPE – ALCOUT (.001, .016).

Reflecting the gender effects observed in Figure 3, an invariance analysis was performed across the genders. Formal evaluation of male/female invariance revealed no significant variability for path estimates ($\chi^2[10] = 10.89$, $p = .37$), for variance of exogenous variables ($\chi^2[2] = 0.55$, $p = .76$), or for factor loadings ($\chi^2[14] = 23.64$, $p = .06$). However, there was a significant gender difference for correlations ($\chi^2[5] = 13.66$, $p = .02$), reflecting differences across males and females regarding the relationships between error terms for peer substance use. Across these levels of invariance testing, the model fit indices were good and varied little [CFI = .94 for all levels, NNFI = .92 to .93 across the four invariances, RMSEA = .035 (.032 – .038) to .036 (.032 – .039), and SRMR (from .037 to .040).

IV. Discussion

These data present the first evaluation of a full LR-based cross-sectional model in a large sample of adolescents, as well as the first evaluation of a complete set of elements of the full model in a non-U.S.-based population. The results underscore several issues relevant to the cross-sectional LR-based model. First, the major conclusions regarding the importance of both the direct and partially mediated relationships between a low LR and adverse outcomes

have now been documented in both U.S. and U.K. samples. Second, variations across prior studies regarding which potential mediators of the LR to alcohol outcome relationship operate may reflect, at least in part, statistical power, as in the current large sample partial mediation was observed with more intense peer substance use, more positive alcohol expectancies, and with using alcohol to cope with stress. Third, model invariance across genders was supported in the current model, indicating that similar findings in prior analyses of smaller samples were not likely to have reflected limited statistical power.

Regarding peer substance use, the measure used here might reflect the broader construct of peer deviant behavior, which could also impact on how a low LR affects a subject's expectation of alcohol's effects, their drinking patterns, and coping style. In Figure 3, the PEER variable added significantly to the model overall, with evidence that this peer substance use measure also partially mediated the relationship between a low LR and heavier drinking and alcohol problems. However, it is not possible in this cross-sectional model to determine if higher peer substance use influenced how much a person drank, or if heavier drinkers gravitated toward peers who used substances. The zero order correlation between LR and the PEER measure and the path coefficients observed in the model were both modest.

The zero-order correlations, and both direct and indirect links between LR and EXPECT in the model, indicated a more robust contribution of alcohol expectancies than was seen for peer substance use. These findings are consistent with prior longitudinal expectancy-focused research and some prior evaluations of this model (Schuckit et al., 2008c). It is relevant to note that the overall performance of EXPECT occurred despite the fact that the ALSPAC protocol did not allow for the use of the 90-item full Adolescent Alcohol Expectancy Scale. Thus, while the current study used an abbreviated version of the Alcohol Expectancy Questionnaire, the results are consistent with the probability that similar results might have been seen if we had been able to use the full and more widely tested scale. The performance of PEER and EXPECT in these analyses, despite using shortened versions of these variables, may attest to the stability across different measures regarding the relationships among components of the LR-based model.

Invariance testing for gender in the model revealed overall similarities for path estimates, the variance of the exogenous variables (age and gender), and for factor loadings. While there was a lack of invariance (i.e., group differences existed) for correlations, these reflected relationships between error terms within latent constructs, and did not appear to have a major impact on the model overall, given that no other invariances were found. Visual inspection of the models evaluated separately for males and females corroborated their overall similarity.

The current analyses did not include additional characteristics related to alcohol problems, such as the age of onset of drinking. There are several indications that the age of onset may not be a major issue in these analyses. First, LR and the age of first full drink only correlated at -.05 in the current sample, which while significant in this large group, explains only a small proportion of the variance. Second, the cross-sectional relationship between LR and the most relevant dependent variable, the maximum number of drinks, is about .50 in both subjects as young as age 12 and for subjects almost age 20, with the latter consisting mostly of males and females with later onsets (Schuckit et al., 2008b, 2009a). This indicates that LR and heavy drinking are relatively closely linked despite differences in the age at which drinking began. Third, an early age of onset is relatively closely linked to conduct problems and similar externalizing behaviors, but there is little evidence that LR and externalizing symptoms are closely related (Schuckit and Smith, 2006; Schuckit et al., 2000). These data, however, do not definitively address the relationship of LR to age of onset, and this question

deserves further exploration. Another issue related to LR is the question of whether the performance of the score is a function of the number of SRE items endorsed. Prior work has demonstrated little or no change in LR when analyses covary for the number of items endorsed or if values are converted to z scores adjusted relative to only those subjects who endorsed the same number of items (Schuckit et al., 2005, 2006, 2008c).

The results of any model testing must be considered in light of the methodology employed. First, while results are generally similar across U.S. and U.K. samples, and while prior studies demonstrated similar results in both upper and lower socioeconomic class subjects (Schuckit et al., 2008b, 2009a), there are many similarities between the U.S. and U.K. The performance of the LR-based model still needs to be determined in additional cultures and the impact of LR may be most robust in heavier drinking environments. Second, it is important to remember that the low LR to alcohol was measured using a retrospective report, and such questions are vulnerable to memory distortions and forgetfulness. Also, LR is only one of several potential measures of how an individual responds to alcohol, and that additional intermediate phenotypes (e.g., alcohol metabolizing enzymes and externalizing conditions) also contribute to the heavy drinking risk. Third, this paper only tested one model of how LR might relate to adverse alcohol outcomes and alternative models may have done equally well in accounting for the interrelationships of variables. Fourth, the current data involve cross-sectional analyses, and, thus, the results of any mediational analyses should be considered preliminary until prospective studies are carried out. The cross-sectional approach was needed to optimize the number of subjects for the current analyses; while a prior ALSPAC paper reported data for early-onset drinkers (Schuckit et al., 2008a), that sample did not have the full set of potential mediators to allow for an optimal prospective evaluation. Fifth, the model could not evaluate the impact of peer drinking alone, and used a proxy measure of the number of substances reported to have been used by peers, while the alcohol expectancy measure used an abbreviated form of the Alcohol Expectancy Questionnaire. Despite these changes, the model performed as predicted. Finally, while significant, some of the effects presented in Figure 3 are modest in size, a factor that may have contributed to variations across smaller samples.

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Figure 1.

The hypothesized level of response (LR)-based conceptual model where low LR to alcohol is directly related to alcohol-related outcomes (ALCOUT) and indirectly related to ALCOUT via substance use in peers (PEER), higher positive expectancies for alcohol effects (EFFECT), and the use of alcohol to cope with stress (COPE). COPE is conceptualized as at least partially mediating the effect of PEER and EXPECT to ALCOUT.

Figure 2.

Measurement Model where PEER is a latent variable from a modified Important People and Activities Scale with 4 indicators of peer1 = average number of 4 peers reported as using alcohol, peer 2 = average number of 4 peers reported as using tobacco, peer3 = average number of 4 peers reported as using cannabinoids, peer4 = average number of 4 peers reported as using other drug; EXPECT is a latent variable from a modified Alcohol Expectancies Scale with 4 indicators from subscales with aeqs = Changes in Social Behavior, aeqc = Improved Cognitive and Motor Abilities, aeqx = Sexual Enhancement sexuality, and aeqat = Arousal; COPE is a latent variable from the Drinking to Cope scale with 3 indicators from parcels of 2 items each; and ALCOUT is a latent variable with 3 indicators of max = maximum drinks lifetime, drnk6 = how often 6+ drinks/occasion, and probs = number of 17 alcohol problems.

Figure 3.

Full Structural Equation Model: All domains are as defined in Figure 2; LR is the manifest variable of the level of response using the SRE, where a higher score represents a lower LR per drink; and GENDER and AGE are as reported in the interview. Only significant paths ($p < .05$) are represented, beta weights are presented for paths, and R^2 is included next to each endogenous variable.

Table 1

Correlations among Manifest and Latent Variables used in the SEM for 1905 17-Year Old Subjects*

	LR	ALCOUT	PEER	EXPECT	COPE	GENDER
ALCOUT	.35 ^c					
PEER	.07 ^b	.51 ^c				
EXPECT	.15 ^c	.50 ^c	.24 ^c			
COPE	.12 ^c	.50 ^c	.33 ^c	.50 ^c		
GENDER	-.11 ^c	-.14 ^c	.01	-.14 ^c	.04	
AGE	.02	.11 ^c	.05 ^a	-.02	.01	-.04

* LR (level of response to alcohol) is a manifest variable measured by the Self-Rating of the Effects of Alcohol Questionnaire (SRE), where a higher number of drinks for effects indicates a lower LR per drink, reflecting more drinks required for an effect; ALCOUT is a latent variable in the SEM assessing drinking quantities and problems; PEER is a latent variable representing peer use of alcohol, nicotine, and illicit drugs; EXPECT is the alcohol expectancies latent variable; COPE is a latent variable generated from the Drinking to Cope scale; GENDER (male = 1, female = 2) and AGE are both manifest variables as reported in the interviews.

^a p < .05
^b p < .01
^c p < .001