Comparison Across Two Generations of Prospective Models of How the Low Level of Response to Alcohol Affects Alcohol Outcomes

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ABSTRACT. Objective: This article presents the first direct comparison of level of response (LR)–based prospective models in two generations of the same families. To accomplish this, we describe results from the first prospective evaluation of potential mediators of how an earlier low LR to alcohol relates to adverse alcohol outcomes in offspring from the San Diego Prospective Study (SDPS). **Method:** To compare with data from probands in the SDPS, new data were gathered from 86 drinking offspring (age ~20 years) during the 25-year follow-up of these families. Consistent with the usual effect of a low LR, outcomes 5 years later for both generations focused on drinking quantities as well as alcohol problems during the follow-up. A structural equation model (SEM) was used to analyze the relationships among variables, and the models in proband and offspring generations were compared using direct observations of the model results and through invariance procedures. **Results:** In these drinking offspring, LR correlated with 5-year outcomes ($r = .48$, $p < .001$) and the SEM R^2 was .48, with good fit statistics. As predicted, the LR relationship to alcohol-related outcomes was both direct and partially mediated by heavier peer drinking, positive alcohol expectancies, and using alcohol to cope with stress. These results were similar to a previously published prospective model in SDPS probands, although path coefficients were generally higher in the younger group. **Conclusions:** The LR-based model of heavier drinking operated similarly across generations, with some modest differences. These results indicate that the model may be meaningful in both younger and middle-age groups. (*J. Stud. Alcohol Drugs, 73,* 195–204, 2012)

FACTORS THAT RELATE TO THE RISK for heavy drinking and alcohol problems operate primarily through genetically influenced intermediate characteristics (endophenotypes) (Schuckit, 2009). These include a protective effect for variations in alcohol-metabolizing enzymes related to the alcohol flush and increased vulnerabilities associated with externalizing conditions (e.g., impulsivity and disinhibition), as well as a low level of response (LR) to alcohol (Morean and Corbin, 2010; Quinn and Fromme, 2011; Schuckit, 2009). The low LR, or low sensitivity to alcohol, is a genetically influenced characteristic reflecting the need for higher doses of alcohol to experience effects of ethanol other people garner at lower doses. Each of these sources of vulnerability also relates to environmental characteristics that could partially mediate or moderate how the phenotype affects heavy drinking and associated problems (Schuckit, 2009). Increasing our understanding of how the predisposing factors operate through environmental mediators might generate clues that can help create intervention programs to diminish that risk (Carey et al., 2007). Such potential mediators can be preliminarily identified through cross-sectional studies, but a more direct test of mediation requires the relatively time-consuming and costly prospective evaluations.

There are two ways to measure LR. The first is to evaluate changes in characteristics from pre-drinking to a specific blood alcohol concentration (BAC) following alcohol challenges (e.g., Schuckit and Gold, 1988; Schuckit and Smith, 2000), and the second is to gather self-reports of the number of standard drinks usually needed for a range of alcohol (Schuckit et al., 1997a, b). LR values generated from alcohol challenges and those from the retrospective Self-Report of the Effects of Alcohol (SRE) questionnaire correlate at about .6 in predicting future heavy drinking and alcohol problems (Schuckit et al., 2009b) and operate similarly in structural equation models (SEMs) regarding how a low LR relates to problematic drinking (Schuckit et al., 2009b, 2010).

The hypothetical model of how a lower LR might contribute to adverse alcohol outcomes is shown in Figure 1. In a heavy drinking environment, a person's earlier alcohol involvement and his or her LR could contribute to

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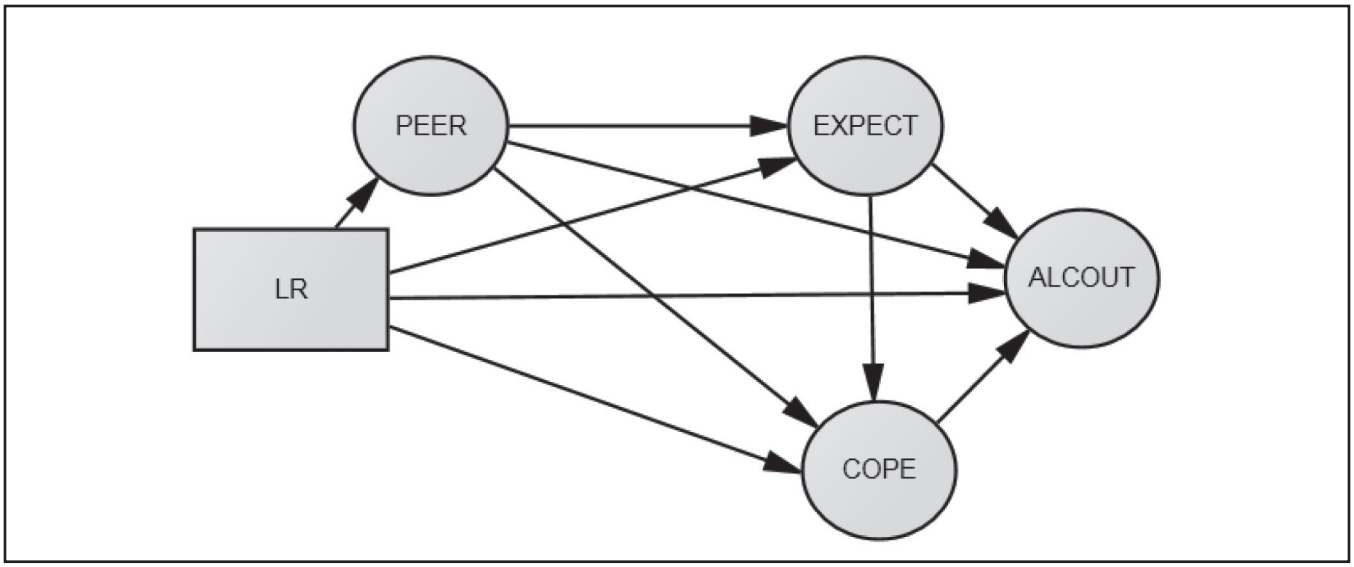

FIGURE 1. Hypothesized model. A low level of response to alcohol (LR) is hypothesized to be directly related to alcohol-related outcomes (ALCOUT) and indirectly related through drinking in peers (PEER), positive alcohol expectancies (EXPECT), and drinking to cope with stress (COPE). The domains are as defined in Table 1.

a bias in how he or she processes social information and feedback regarding the acceptability and desirability of heavy drinking, in a manner similar to the social information processing model (Dodge et al., 2003; Trucco et al., 2011). Through peer cluster theories, the lower LR and subsequent heavier drinking may contribute to a person being rejected by lighter drinking peers and welcomed by heavier drinking associates (Henry et al., 2005; Vroom, 1964). Related to expectancy and social cognitive theories, the lower LR and peers who encourage heavier drinking may contribute to expectations that inappropriately exaggerate positive attitudes that drinking is beneficial and that drunkenness is a desirable and socially acceptable behavior (Bandura, 2001; Lawler, 1991). These expectancies might not directly drive alcohol use but could override a person's recognition that problems are developing and, thus, decrease the effect of consequences on diminishing further drunkenness. LR, peer drinking, and observations of the use of alcohol in the context of stress by heavy drinking friends may combine with inaccurate expectations of the benefits of heavy drinking (from the health benefit model) to reinforce the use of alcohol to cope with stress (Rosenstock, 1974; Veenstra et al., 2007).

All cross-sectional LR-based models using adult and adolescent populations have shown significant direct links between LR and heavy drinking and associated problems. Evaluations have been carried out with subjects from a range of socioeconomic strata in the United States and an investigation of 1,905 17-year-olds in the United Kingdom (Schuckit et al., 2008a, 2009a, 2011a). All SEMs had good fit characteristics and most explained about 50% of the variance of risk for adverse alcohol outcomes (Schuckit et al., 2009a, 2011a). These cross-sectional models all supported both direct and partially mediated associations between LR and enhanced alcohol use through one or more of the following: heavier peer drinking, higher positive expectations of the effects of alcohol, and using alcohol to cope with stress (Schuckit et al., 2008b, 2009a, 2011a; Schuckit and Smith, 2000). However, the salience of specific partial mediators of the impact of LR on outcomes has differed a bit across modest-sized groups, although all partial mediators were shown to have significant effects once a relatively large sample was used (Schuckit et al., 2011a).

While longitudinal analyses are needed to confirm mediation, to date no prospective SEMs have been published in younger populations, although two prospective analyses from the San Diego Prospective Study (SDPS) have been published regarding adults from that protocol. In these evaluations of probands, although LR was measured earlier in life, mediators of LR to outcome were not evaluated until age 35 and outcomes determined at age 40 (Schuckit et al., 2004, 2011b). Focusing on the more recent analysis with a larger sample (378 men, as shown in Figure 2), the prospective 20-year model explained 32% of the variance and had good-fit characteristics (Schuckit et al., 2011b). Here, on a zero-order level, LR at age 20 correlated with alcohol outcomes at age 40 at -.20, with a significant path coefficient between the two variables within the SEM of -.11. Note that a lower LR directly measured on the alcohol challenge is predicted to relate to higher alcohol intake and problems at follow-up (i.e., the relationship is negative in sign). Within this prospective analysis (Schuckit et al., 2011b), both peer drinking and suboptimal coping mechanisms functioned as partial mediators of the LR to

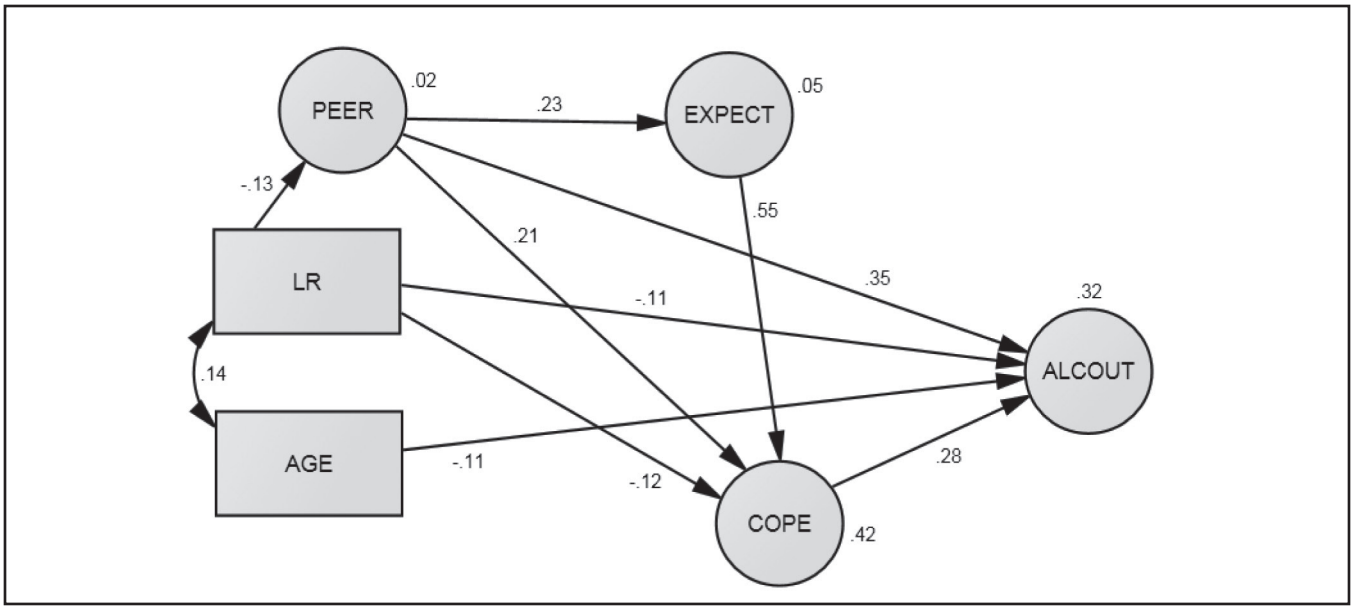

FIGURE 2. Structural equation model for 378 probands. All shown relationships are significant ($p < .05$). The domains are based on those described in Figure 1 and Figure 3. Figure 2 was taken from Schuckit et al. (2011b), with LR measured using alcohol challenges at about age 20, mediators measured at about age 35, and outcomes at about age 40.

alcohol outcomes, but there was no significant similar role in these middle-aged adults for alcohol expectancies.

The current study compares prospective evaluations of how an earlier LR and associated characteristics relate to later alcohol outcomes in offspring from the same families. The data also present the first LR-based prospective SEM results from a younger group at a time when heavy drinking and alcohol problems are likely to be increasing. We hypothesized that the LR-based models in the offspring would demonstrate similar patterns as in the parental generation regarding the relationship between a low LR and later adverse alcohol outcomes and the demonstration that the low LR/outcome relationship will be both direct and be partially mediated by one or more of heavier peer drinking, more positive alcohol expectancies, and drinking to cope with stress.

Method

The comparisons presented here are based on the recently published prospective evaluation of 378 original probands from the SDPS that began in 1978 (Schuckit et al., 2011b). Here, using procedures approved by the University of California, San Diego (UCSD), Human Research Protections Program, LR was measured in non-alcohol-dependent 20-year-old men using an alcohol challenge. Subjects in the lower and higher thirds for LR values were documented as having lower or higher LRs through alcohol-related changes from baseline to a BAC of approximately .60 mg/dl regarding subjective feelings, standing steadiness, and physiological measures (e.g., blood cortisol) (Schuckit and Gold, 1988; Schuckit and Smith, 2000). All probands were followed up at about age 30, 35, and 40 (noted as Time 10 [T10], T15, and T20, respectively). At T15 measures of peer drinking, alcohol expectancies, drinking to cope with stress, and alcohol quantities and problems were gathered using the measures described below for offspring and presented in more detail in a recent article (Schuckit et al., 2011b). When entered into an SEM, the model shown in Figure 2 explained 32% of the variance and exhibited both direct and partially mediated relationships between LR and alcohol outcomes 5 years later (Schuckit et al., 2011b).

Regarding the adolescent and early adult model, the 86 offspring gave informed consent or assent to participate in this project, as approved by the UCSD Human Research Protections Program. All data were gathered from the SDPS protocol during the 25-year (T25) evaluations that began in 2004 and the ongoing 30-year (T30) evaluations that began in 2009 (Schuckit and Gold, 1988; Schuckit and Smith, 2000).

Data from offspring were evaluated using the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) instrument, which has validity, retest reliabilities, and cross-interviewer reliabilities of .7–.8 regarding alcohol-related items (Bucholz et al., 1994; Hesselbrock et al., 1999). For offspring age 18 years or younger, a parental report on adolescents (C-SSAGA-P) was also administered to corroborate the younger offspring's self-report. When parent and offspring disagreed, the worst-case scenario (e.g., higher number of alcohol problems) was used in the

analyses. Those offspring who at T25 reported drinking on their own on multiple occasions were asked to fill out the SRE regarding the approximate first five times of drinking (Schuckit et al., 1997a, b, 2007). At T25, subjects reported the number of standard drinks (~10 g of ethanol) required to first feel the effects of alcohol, the drinks needed to produce slurring of speech, the alcohol required to feel unsteady or uncoordinated, and the amount of alcohol ingested before unwanted falling asleep (passing out), taking care to report only the drinks required for actual effects experienced. The SRE score for any time frame is the sum of the number of drinks reported across the range of effects actually experienced divided by the number of effects reported. This questionnaire has a literature-based Cronbach's α of .97, has retest reliabilities as high as .8, correlates with the alcohol challenge in predicting future heavy drinking at about .60, and performs similarly to the alcohol challenge-based LR when incorporated in SEM analyses (Daeppen et al., 2000; Ray et al., 2011; Schuckit et al., 2009b, 2010, 2011a; Trim et al., 2009).

The T25 evaluation also included measures related to the hypothesized mediators of LR to outcome. Drinking among peers was measured as a latent variable (PEER) constructed from the Important People and Activities scale, an instrument with α's of .80–.95 and external validities compared with other measures of .8 in the literature (Longabaugh et al., 2001). Here, offspring were asked to identify up to 12 closest peers and to report for each their perception of drinking status (a 5-point scale ranging from *abstainer* to *heavy drinker*), drinking frequency (a 7-point scale ranging from *only once in their lives* to *daily drinking*), and a maximum drinks score (a 4-point scale ranging from *1 or 2 drinks per occasion* to *≥10 drinks per session*).

A latent variable regarding alcohol expectancies (EXPECT) was generated from the adolescents up to age 18 (17 subjects) and for adults age 18 and older (69 subjects) using age-appropriate forms of the Alcohol Expectancy Questionnaire (AEQ) and combining results by converting data to *z* scores for each form (Christiansen et al., 1989; Goldman et al., 1997). Although there are some differences between adolescent and adult AEQs in structure and whether questions are answered as they specifically related to the respondent or to his age group in general, the step of combining the two forms has performed well in previous studies (e.g., Schuckit et al., 2008b, 2009a). The AEQ scores included global positive, social behavior, sexual enhancement, and relaxation-related variables. The literature-based Cronbach's α for the AEQ is greater than .8, and scores correlate in the predicted direction with additional measures of expectancy.

Coping (COPE) was a latent variable generated from the Drinking to Cope scale with literature-based Cronbach's α of .85 and similar levels of reliability (Cooper et al., 1995; Park and Levinson, 2002). This questionnaire records a person's usual pattern on a 4-point scale (*never* to *almost always*) of using alcohol to cope with six stressful situations. The latent variable was created by producing three parcels as indicators composed of two items each.

The alcohol-outcome latent variable was generated from the T30 SSAGA interviews using three indicators, including the maximum drinks in the prior 5 years, the usual drinks in the prior 6 months, and the number of 18 alcohol-related problems recorded over the interval since the prior evaluation. The problems included nondiagnostic items such as blackouts, arguments with friends, drinking before noon, etc., as well as the 11 abuse and dependence criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (American Psychiatric Association, 1994). Reflecting financial constraints, these T30 interviews were conducted by phone.

Data were evaluated using Pearson's product-moment and point-biserial correlations among the manifest variables (LR, age, and gender, with the latter scored as males = 1 and females = 2) along with the latent variables for PEER, EXPECT, COPE, and alcohol-related outcomes (ALCOUT). Values were entered into an AMOS 18-based analysis of variance/covariance matrix with maximum likelihood estimations for the SEM (Arbuckle, 2006) using confirmatory factor analyses first carried out outside the SEM, with the results then incorporated into the SEM itself. Except for dropping nonsignificant paths, no respecifications of the hypothesized models were made. The results were evaluated using the comparative fit index (CFI), where a good fit was considered greater than .90; the nonnormed fit index (NNFI), with about 1.0 indicating good fit; the root mean square error of approximation (RMSEA), with less than .05 considered good fit; and the standardized root mean square residual (SRMR), with less than .08 considered good fit (Bentler, 1990; Hu and Bentler, 1998; Wheaton et al., 1977). Mediation used the product-of-coefficients test within Mplus, version 5.1 (Muthén and Muthén, 2007; MacKinnon et al., 1995). Nonnormal distributions for these analyses were evaluated through 1,000 resamples in a bootstrapping approach, with results presented as the 2.5th and the 97.5th percentiles representing limits of the 95% confidence intervals. Mediation was indicated when confidence intervals did not span across zero (Fritz and MacKinnon, 2007).

Invariance across SEMs for probands in Figure 2 and the current results for offspring followed the approach of Hoyle and Smith (1994) and Spillane et al. (2004). Steps included (a) evaluating the full model that incorporates all probands and offspring with no constraints, (b) adding equality constraints to ensure that factor loadings were the same across the two samples, (c) adding the same variances across probands and offspring, and (d) using the same structural path values across probands and offspring. Results were evaluated using chi-square to determine if each additional step significantly reduced the model fit (Bentler, 1990).

Results

The 86 younger subjects represent approximately the first half of the SDPS offspring who reported drinking at T25 and who participated to date at T30. LR was based on the SRE regarding approximately the first five times of drinking, which had occurred a mean of 4.0 (*SD* = 2.99) years before T25, with higher numbers of drinks for effects indicating a lower LR per drink. The time frames for T25 PEER, EXPECT, and COPE and the T30 outcomes related to the 5-year and/or 6-month preceding periods. Among these offspring, 92 individuals met these criteria for inclusion, 93.3% of whom agreed to participate in the T30 evaluation.

At T25, the offspring were 20.2 (3.20) years old (range: 13–30 years), 53.5% were female, with racial characteristics of 91.9% White, 5.8% White Hispanic, and 2.3% other racial backgrounds. These subjects included 56.3% where only one offspring was used per family, 32.7% with two, and 10.9% with three, for 1.6 children per family and a small design effect (1.01–1.27). At T25, 17 offspring were age 17 years or younger (including 5 age ≤15), 40 were age 18–21, 26 age 22–25, and 3 age 26–30. The average SRE was 3.3 (1.88), and the prior 6-month mean and maximum drinking quantity per occasion was 3.1 (2.46) and 6.4 (5.69) standard drinks, respectively, with mean and maximum drinking frequencies of 6.8 (7.22) and 8.8 (9.10) days per month, respectively. At T25, half (50.0%) reported any of the 18 possible alcohol problems in the prior 5 years, with a mean of 1.7 (2.67) problems. The age at onset of regular drinking was 15.3 (3.06) years.

When evaluated at T30 at age 24.6 (3.15), all subjects had interval experience with alcohol, with prior 6-month usual and 5-year maximum quantities per occasion of 2.90 (2.36) and 7.8 (5.43) standard drinks, respectively, and usual and maximum drinking days per month of 8.3 (8.57) and 11.5 (8.54), respectively. About 60% reported alcohol-related problems (mean of 2.6 [3.33], including those who had no problems). Although 22.1% of the offspring met criteria for alcohol dependence at T25, by T30, 37.2% had fulfilled those criteria.

Table 1 presents the correlations among SRE scores; latent variables for T25 PEER, EXPECT, and COPE; and T30 outcomes. For T25 PEER, maximum peer drinks on the 0–4 scale was 2.5 (1.33), the maximum frequency was 4.0 (0.82) on the 0–7 scale, and 4.7% listed only peers who were abstainers. The *z*-scored T25 AEQ values for EXPECT were 0.1 (0.92) for global positive, 0.3 (0.87) for social behavior, 0.2 (1.00) for sexual enhancement, and 0.3 (0.36) for relaxation. The T25 Drinking to Cope (COPE) score was 1.8 for six items, with each rated from 1 to 4. Regarding correlations, LR values related to alcohol outcomes about 5 years after T25 at .47, with lower LR (i.e., higher SRE scores) correlating with heavier drinking and more alcohol problems at T30. LR correlated significantly with higher scores for PEER, COPE, and EXPECT. All three potential mediators also correlated significantly with ALCOUT and with each other. For covariates, the offspring's ages did not correlate significantly with most variables in Table 1. A robust correlation was noted for older offspring having peers with greater alcohol involvement, but no other domain correlated significantly with age. Although the data are not shown, at baseline younger drinking subjects had lower alcohol intake; for example, usual drinks per occasion were a mean of 1.2 (2.14) for 13- to 17-year-olds and 2.9 (1.98) for those ages 22–30, $F(2, 83) = 8.84$, $p < .001$. No significant differences between those age groups were seen at follow-up, for example, a mean of 3.5 (2.50) versus 2.9 (3.03), $F(2, 85) = 0.72$, $p = .50$. Gender related negatively to the SRE (i.e., females needed fewer drinks for effects) and to alcohol outcomes and demonstrated a trend for a negative relationship to peer drinking ($r = -.24$, $p = .055$). When the data in Table 1 were repeated for the 67 offspring who had not been alcohol dependent by T25, the correlations of LR to additional values did not change much, nor did the correlations between outcomes and EXPECT and gender, although PEER to ALCOUT was lower and age to ALCOUT was higher in the subset.

Figure 3 presents the measurement model. Here, the fit statistics included CFI = .97, NNFI = .96, RMSEA = .055 (90% CI [.000, .091]), and SRMR = .059. The SEM is presented in Figure 4, with 48% of the variance explained (R^2), and good fit indices (CFI = .92, NNFI = .90, RMSEA = .073 [.045, .099], and SRMR = .082). In this model, the path coefficient for the direct link between LR and ALCOUT was .26, which, when considered in light of the zero-order correlation between these variables of .47, indicates probable partial mediation by additional model components. There were also significant direct paths between LR and PEER, and, in light of the zero-order correlations, probable indirect relationships between LR and COPE operating through PEER and EXPECT, and between LR

Table 1. Product-moment and point-biserial correlations among manifest and latent variables for 86 offspring

	LR	ALCOUT	PEER	EXPECT	COPE	GENDER
ALCOUT	.47***					
PEER	.45***	.37**				
EXPECT	.25*	.49***	.26*			
COPE	.34**	.55***	.48***	.69***		
GENDER	-.32**	-.38**	-.24	-.11	-.19	
AGE	.04	-.16	.34**	-.12	.13	-.09

Notes: LR = level of response, based on the Self-Report of the Effects of Alcohol score (higher drinks needed for effects = lower LR per drink); ALCOUT = alcohol outcomes; PEER = perceived drinking status, frequency, and quantities of peers; EXPECT = scores in subscales of global positive, social behavior, sexual enhancement, and relaxation with alcohol; and COPE = scores on three parcels composed of two items each from the six-item Drinking to Cope scale.
*$p < .05$; **$p < .01$; ***$p < .001$.

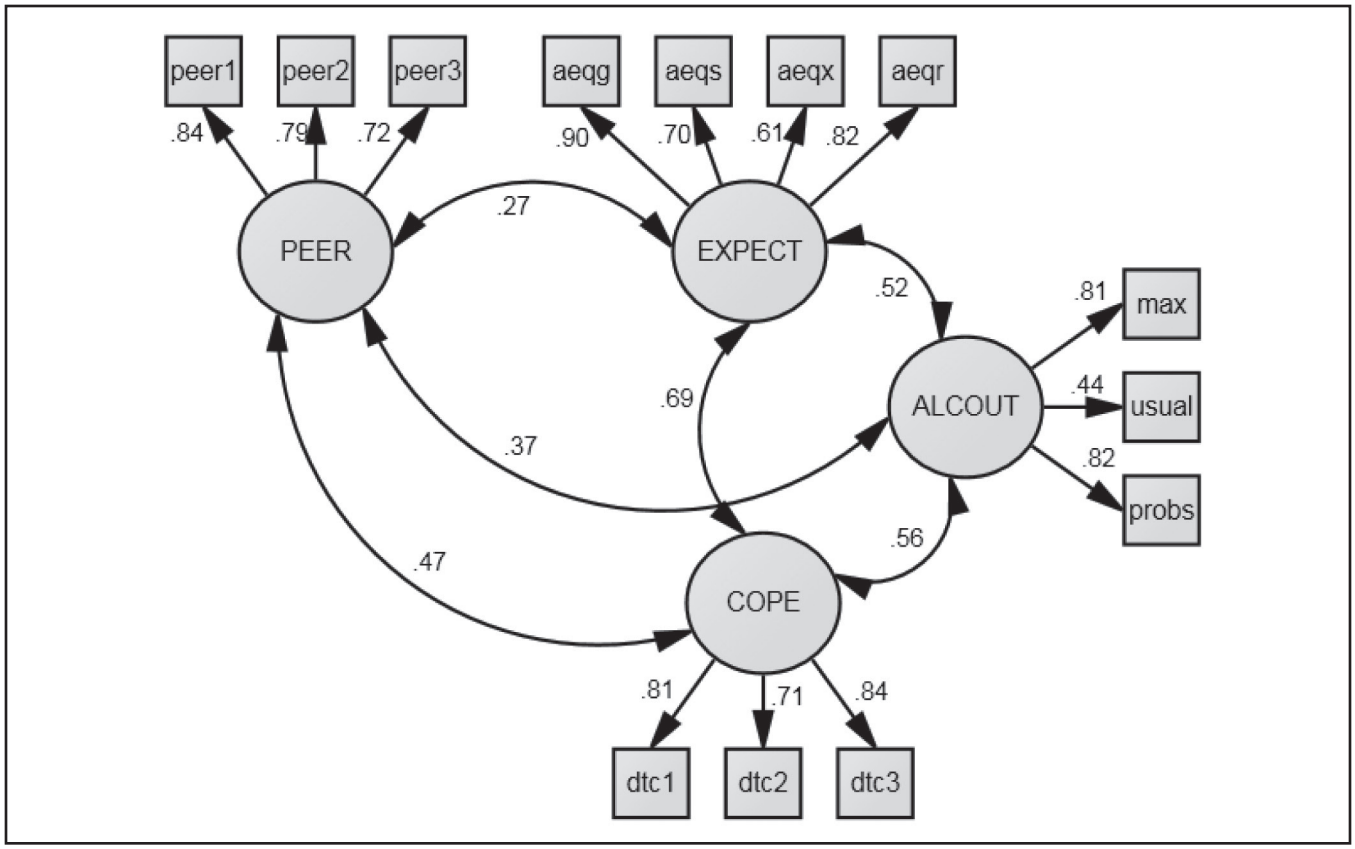

FIGURE 3. Measurement model for the 86 offspring. Here, ALCOUT during the follow-up interval includes three indicators of the offspring's maximum drinks per day (max), usual number of drinks per day (usual), and the number of the 18 potential alcohol-related problems (probs). PEER was generated using the Important People and Activities scores of peer alcohol use pattern (peer1), peer frequency (peer2), and peer maximum drinks (peer3). EXPECT consists of the four AEQ scores of the global positive (aeqg), social behavior (aeqs), sexual enhancement (aeqx), and relaxation with alcohol (aeqr). The COPE domain was generated by placing the six Drinking to Cope items into three parcels of two items each.

and EXPECT operating through PEER. COPE related directly to ALCOUT, whereas PEER and COPE had indirect links to outcomes through COPE. In the SEM, there was a negative relationship between gender and the LR measure (females had lower SRE scores), as well as between gender and alcohol outcomes. Age related positively to heavier peer drinking and negatively to higher alcohol-related outcomes but did not affect the relationships between LR, mediators of its effects, and alcohol outcome, results that are consistent with the zero-order correlations reported in Table 1.

Formal mediational analyses in Table 2 demonstrated partial mediation of how LR related to later outcome through all three domains of PEER, EXPECT, and COPE. The impact of PEER on alcohol outcomes was also mediated through EXPECT and COPE, with EXPECT operating through COPE as well.

The SEM process was also repeated using all paths from the hypothesized model in Figure 1. Here, 41% of the variance was explained (CFI = .94; NNFI = .92; RMSEA = .073 [.038, .102]; SRMR = .073).

Although not shown, LR values relating to the approximately first five times of drinking also correlated (r = .55, $p \leq .001$) with the latent variable for the T25 outcome that used the same indicators as at T30, and the correlation between T25 ALCOUT and T30 ALCOUT was .64 ($p <$ .001). When the SEM in Figure 4 was rerun after including the autoregressive T25 alcohol use characteristics, most of the impact of the earlier LR on T30 outcomes operated through T25 drinking parameters. For that extended model R^2 = .36, and the fit indices included CFI = .87, NNFI = .84, RMSEA = .09 [.070, .110], and SRMR = .10.

The current data were developed to facilitate a direct comparison of prospective models in these offspring with the prior published results for the original probands. A visual examination of the prospective SEM for the probands in Figure 2 and the results for the offspring (Figure 4) show many similarities. The structures for both indicated direct and mediated links of LR to ALCOUT, another direct link to outcome only for COPE, and significant mediation of the LR–outcome link by both PEER and COPE. Note that a

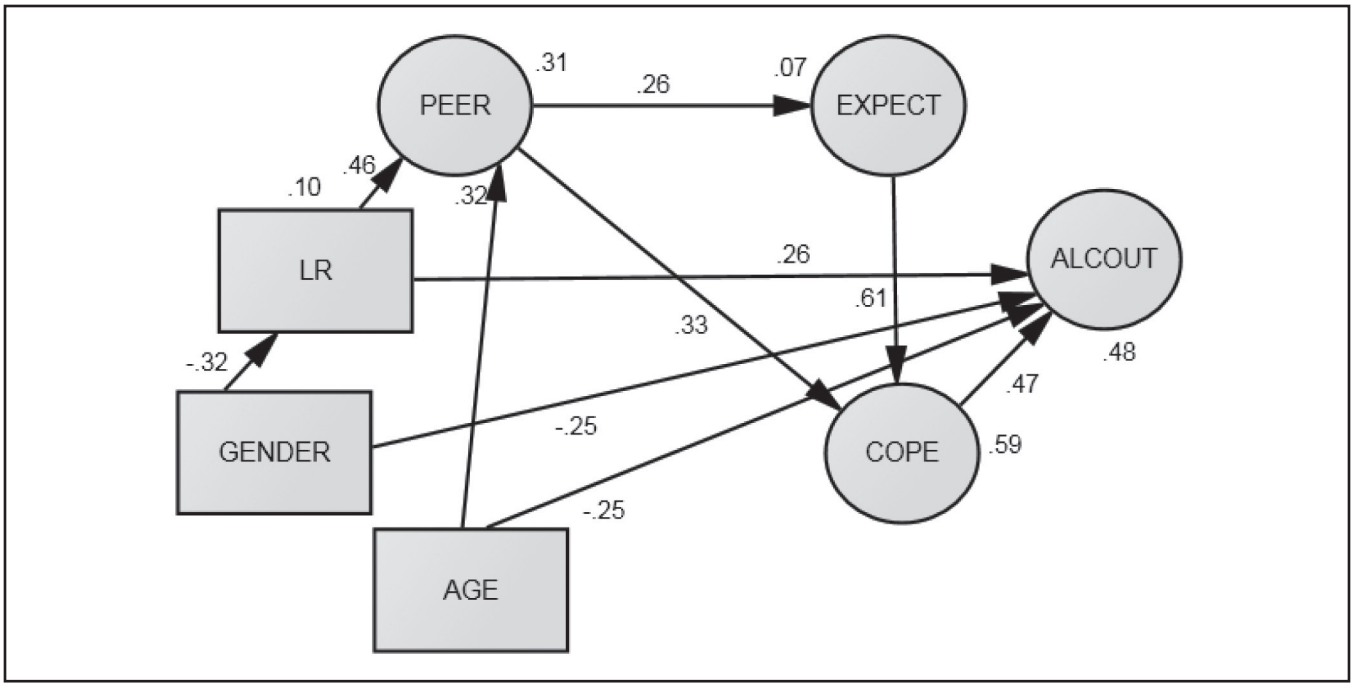

FIGURE 4. Structural equation model for 86 offspring. The latent variables here use the indicators from the measurement model in Figure 3 and the abbreviations from Table 1. Only significant paths ($p < .05$) are presented here with beta weights for path values, and the R^2 is reported for each endogenous variable. Here, LR is a retrospective report on the SRE regarding a time 4 years earlier; PEER, EXPECT and COPE relate to the data evaluated at the T25 follow-up of these families; and ALCOUT is from the T30 follow-up.

lower LR on an alcohol challenge is the same as requiring a higher number of drinks for effects in the SRE; thus, the sign of the path coefficients in Figures 2 and 4 have opposite polarity. In the offspring, EXPECT also partially mediated the impact of LR on later drinking, and the path coefficients for the direct paths of LR and COPE to ALCOUT appear to be generally more robust for the younger group.

The many similarities in the methods used for the prospective studies of probands and offspring potentially allowed for consideration of an invariance procedure. However, the results of such analyses are only tentative because invariance requires close similarity across the models for probands and offspring for how all elements of the model were measured. In the current comparison, LR was evaluated by alcohol challenges in probands and SRE in offspring; proband EXPECT came from adult AEQ but was generated in offspring by combining the adolescent and adult AEQs; and for probands, follow-ups reflected 5 years, whereas for offspring the drinking period was shorter.

Heuristic results from an invariance procedure were generated by combining the 378 probands and 86 offspring ($N = 464$) into a single SEM, after which changes in model fit were determined across probands and offspring in a series of steps. In the new combined model, the two groups were similar for measures of variance, $\chi^2 = 0.005$, $p = .95$, but there were significant differences regarding how well the indicators fit together in the latent variables, $\chi^2(9) = 43.44$, $p < .0001$. The most obvious difference across probands and offspring occurred for ALCOUT, where the factor loadings for alcohol problems were .57 for probands and .27 for offspring (while the loadings for the two drinking quantity measures were similar across the samples). Factor loading differences were also seen for the sexual enhancement indicator for EXPECT (loadings of .75 for probands and .65 for offspring), as well as for COPE (.43–.52 across the three parcels for probands and .57–.72 for offspring). In addition, significant variations across the two samples were also noted in some of the path coefficients, $\chi^2(10) =$

TABLE 2. Test of mediation between LR at age ~20 and alcohol outcomes at age ~25[a]

Indirect effects of interest	
LR → PEER → COPE → ALCOUT T30	[.007, .060]
LR → PEER → EXPECT → COPE → ALCOUT T30	[.0001, .034]
EXPECT → COPE → ALCOUT T20	[.099, .278]

Notes: LR = level of response, based on the Self-Report of the Effects of Alcohol score (higher drinks needed for effects = lower LR per drink); PEER = perceived drinking status, frequency, and quantities of peers; COPE = scores on three parcels composed of two items each from the six-item Drinking to Cope scale; ALCOUT = alcohol outcomes; T= Time; EXPECT = scores in subscales of global positive, social behavior, sexual enhancement, and relaxation with alcohol. LR, PEER, EXPECT, and COPE are from the 25-year (T25) follow up, and ALCOUT is from the 30-year (T30) follow up. [a]Mediation: Bias-corrected bootstrap 95% confidence intervals (with 1,000 resamples) for sequential multiple mediation coefficients (indirect effects).

32.04, $p < .001$. Here, although the SEMs for the probands and offspring looked similar in Figures 2 and 4, there were differences in path coefficients for LR to ALCOUT (.20 vs. .24 for probands and offspring), EXPECT to COPE (.56 vs. .43), and LR to PEER (.15 vs. .19), with relatively small differences of .03 or less for several other paths (e.g., PEER to EXPECT of .23 and .26).

Discussion

There are two major take-home messages from these analyses. First, to prepare for a comparison of the model across generations, we report results from the only prospective LR-based SEM model of risk for later heavy drinking and alcohol problems in adolescents and young adults from the SDPS. Here, SRE-based LR correlated with adverse alcohol outcomes about 5 years later at .47 ($p < .001$). In the SEM, the path coefficient between LR and later alcohol outcomes was .28, with results indicating that much of the link of LR to ALCOUT was partially mediated by heavier drinking peers, more positive alcohol expectancies, and using alcohol to cope with stress. All prior cross-sectional SEM analyses in adolescents and young adults supported similar possible meditational roles for adverse coping styles, and most suggested mediation by more positive alcohol expectancies (e.g., Schuckit et al., 2008b, 2009a, 2011a). Most also indicated potential mediation by heavier peer substance use, although there were some differences in the indicators available for the PEER domain (e.g., Schuckit et al., 2011a). Despite the modest sample size, the current prospective evaluation indicated significant mediation by all three relevant latent domains, perhaps reflecting a greater ability of the prospective approach to document these relationships. However, whereas the first 5 LR value for offspring related to a period of about 5 years before T25, the potential mediators of LR to outcome were measured at T25, and the outcome determined at T30, it is important to remember that the LR measure was retrospective and the LR data were gathered at T25. Thus, the model is not fully prospective.

The central unique contribution of the current study was our ability to compare LR-based prospective SEMs across two generations of the same families. It is worthwhile to note how similar the results in Figures 2 and 4 were despite different measures for LR. This finding is consistent with the previously reported overlap across the alcohol challenge and SRE-based LR values in predicting outcomes and regarding the similar performance of the two LR measures in SEMs (Schuckit et al., 2009b, 2010). Fortunately, similar indicators were available in offspring and proband generations for the latent variables (PEER, EXPECT, COPE, and ALCOUT). The opportunity to compare probands and offspring is particularly valuable because potential mediators of LR at about age 20 to ALCOUT at about age 40 for probands were based on mediators evaluated at about age 35, making it difficult to determine whether the same variables might have operated similarly when measured earlier in life. However, there were sufficient differences in the proband and adolescent protocols (e.g., LR and AEQ measures), such that the comparison across generations is best viewed as descriptive, and the results of the formal invariance analysis should be seen as primarily heuristic. Also, although the use of two generations helped control the possible impact of socioeconomic stratum, type of neighborhood, race, and family education levels, even though the design effect among offspring was small, the genetic relationships between offspring and probands could inflate the similarity across these two SEM results. Thus, the results might be different if models for unrelated 40-year-olds and adolescent/young adult samples are compared.

Visual inspection of the proband-based (Figure 2) and offspring-based (Figure 4) prospective models indicates similar relationships of LR to outcomes and LR to relevant mediators for both generations. However, the SEM R^2 was higher for the offspring, perhaps related to their shorter period of follow-up. Although Figures 2 and 4 both show direct LR to ALCOUT paths as well as LR to PEER, PEER to EXPECT, EXPECT to COPE, and COPE to ALCOUT, the path coefficients are a bit higher in offspring, and only the evaluation of probands demonstrated that LR and PEER related directly to COPE. These informal comparisons were generally consistent with the formal invariance analyses. The higher path coefficients in Figure 4 might indicate benefits for early prevention aimed at altering the relationships among mediators in an effort to decrease the impact of a lower LR on heavier drinking. This conclusion is the basis for a pilot prevention trial working to decrease heavy drinking in adolescents by attempting to diminish the relationships between a lower LR, the three mediators evaluated here, and adverse alcohol outcomes (Schuckit et al., in press).

The invariance testing also indicated differences across probands and offspring regarding factor loadings for indicators within some latent variables. These included the manner in which alcohol problems fit into ALCOUT, a result that might reflect the usual greater severity of alcohol consequences with advancing age regarding jobs, health, and family responsibilities that could contribute to a closer link between quantities and problems in the middle-aged probands (Schuckit and Smith, 2011). Similarly, the expectations of alcohol effects on sexual enhancement as an indicator for EXPECT could be different regarding levels of sexual activity and how alcohol impairs sexual performance in 40-year-olds versus 20-year-olds. Despite these modest differences in path coefficients and factor loadings, the pattern in both generations of how LR related to outcome and operated through mediation demonstrates the potential application of these models across a range of age groups.

Although not directly included in the models, it was not surprising that the drinking patterns and problems at T25 correlated significantly with the outcome measures at T30 (i.e., there were autoregressive effects). Thus, in a prospective model, any predisposing factor such as LR is likely to affect later heavier drinking, at least in part, through its relationship to current drinking patterns and problems. However, the adult model to which the offspring SEM is being compared did not include the autoregressive effects related to the earlier outcome. Also, our goal in both generations was to evaluate if LR and mediators related to future alcohol outcomes, and the question of whether the link is through the predictable autoregressive effect of current drinking was not of central importance.

Regardless of autoregressive effects, clinicians and prevention researchers can use the data on LR and potential mediators of its effects on later drinking to develop and test approaches for diminishing the impact of LR on outcomes through working to change the roles of the T1 partial mediators of earlier LR to later outcomes in Figures 2 and 4, as was done in a recent pilot study (Schuckit et al., in press). Regarding the relationship of earlier LR to later outcomes, a prospective evaluation in the probands indicated that a low LR at about age 20 predicted heavier drinking and alcohol problems even for individuals who did not develop their problematic drinking until after age 35, and for whom age-20 and age-30 drinking parameters were relatively benign (Schuckit and Smith, 2011). In addition, in both older and younger populations, the ability of a lower LR to predict heavier drinking and alcohol problems 2 to 5 years later remained significant even when drinking patterns and problems at the time of initial evaluation were covaried (Schuckit et al., 1997a, b, 2007, 2008a; Trim et al., 2009). These included findings of the ability of a low LR to predict adverse outcomes in very light drinking early adolescents and in adults for whom earlier drinking patterns were quite modest (e.g., Schuckit et al., 2011a).

Additional caveats must also be kept in mind. These include the relatively small number of offspring in the current dataset, although the significant results observed here are similar to those reported in prior cross-sectional analyses. Another caveat relates to our decision in 1978 at the start of the SDPS to select probands who were likely to represent the majority of heavy and problematic drinkers who did not have a teenage onset of alcohol use disorders related to conduct problems. This, combined with the fact that SDPS families are primarily White and have higher levels of education than some other studies, may limit the generalizability of the results to other populations. Third, the probands were all males, whereas the offspring had both males and females, and, thus, gender could not be incorporated into the invariance analysis, although use of gender in the offspring SEM did not greatly affect the results. Fourth, whereas the offspring model uses a retrospective evaluation of LR regarding a time before T25, potential mediators from T25, and outcomes 5 years later, the retrospective LR report was given at the same time that the mediators were measured. In addition, only one measure was used for each domain, and these had limitations (e.g., AEQ characteristics were not identical for adolescents and adults, and the peer drinking measure reflected the offspring's perception). Also, although age was used as a covariate in the SEM and age did not correlate significantly with LR, ALCOUT, EXPECT, or COPE, the age range of offspring was 13–30 years and still might have affected the results. Finally, to be consistent with our prior approaches, the model paths were assessed in only one direction, and there is variation across subjects regarding the number of years of drinking before T25 and regarding life experiences that relate to stresses, years of drinking, and alcohol problems.

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