Evaluation of a Level of Response to Alcohol-Based Structural Equation Model in Adolescents*

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ABSTRACT. Objective: A low level of response (LR) to alcohol relates to a family history of alcoholism and predicts future heavier drinking and alcohol-related problems. The current analyses evaluate how LR functions within the context of a Social Information Processing Model, using 238 subjects aged 13 to 19 years from the Collaborative Study on the Genetics of Alcoholism (COGA). **Method**: A structural equation model (SEM) was used to evaluate the relationship among (1) a family history (FH) of alcoholism, (2) the LR to alcohol, (3) expectations as measured by the Alcohol Expectancy Questionnaire and (4) the recent pattern of drinking among parents in the home as predictors of the maximum recent quantity of drinking, the maximum number of drinks ever consumed in 24 hours and the number of alcohol problems in the teenage subjects. **Results**: When tested in the SEM, LR functioned as a mediator of the relationship between an FH of alcoholism and alcoholic outcome, and expectancy functioned as a partial mediator of the relationship between LR and outcome. Invariance testing revealed that the SEM performed similarly in light and heavy drinkers, the two sexes, and older versus young subjects. Both the measurement model and SEM had good characteristics of fit, and direct paths within the model explained 49% of the variance of outcome. **Conclusions**: Consistent with results from the San Diego Prospective Study, when tested in the more heterogeneous COGA population, LR functioned as a mediator of the relationship between the FH and alcoholic outcome. In these adolescents, LR not only had a direct relationship to alcoholic outcome but, in contrast to prior results in adults, also appeared to operate through expectations of the effects of alcohol in predicting heavier drinking and a higher rate of alcohol-related problems among teenagers. (*J. Stud. Alcohol* **66**:174-184, 2005)

ALCOHOL USE DISORDERS (AUDs) are complex, genetically influenced conditions (Heath et al., 1997; Newlin et al., 2000; Rose et al., 2001; Schuckit, 2002; Zucker et al., 2000). Multiple phenotypes contribute to the risk, including alcohol-metabolizing enzymes, disinhibition, independent psychiatric disorders such as schizophrenia and bipolar disorder and the level of response to alcohol (Goldman, 1996; Li, 2000; Schuckit, 2002; Slutske et al., 1998). These characteristics that impact on the vulnerability toward alcoholism appear to operate relatively independently of each other, and all genetic factors together are likely to explain about 40% to 60% of the risk for AUDs (Prescott and Kendler, 1999; Schuckit et al., 2000a). Recognizing that environmental and cultural influences also contribute to approximately 50% of the vulnerability toward these disorders, and considering the polygenic nature of most genetic influences, it is not likely that any one gene or combination of genes directly causes AUDs (Jacob et al., 2001; McGue, 1997). A logical approach to improving our understanding of causative mechanisms in such conditions is to evaluate specific genetically influenced phenotypes in the context of environmental and cultural influences.

One of the more widely studied phenotypes relating to the AUD risk is a low level of response (LR) to alcohol. LR can be measured after administrating alcohol and evaluating levels of change at a specific blood alcohol level

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(BAL) (Schuckit and Gold, 1988; Schuckit and Smith, 2000; Schuckit et al, 2000b). Most studies indicate that a low LR to alcohol (i.e., less response at a specific BAL) relatively early in life is more likely to be observed in 18- to 25-year-old sons and daughters of alcoholics than in family history-negative (FHN) controls (DeWit and McCracken, 1990; Eng et al., in press; Newlin and Thomson, 1991; Schuckit and Gold, 1988; Schuckit et al., 1996, 2000b; Vogel-Sprott and Chipperfield, 1987). In addition, a low LR predicts heavier drinking, alcohol-related problems, and AUDs during 5- to 20-year follow-ups (Heath et al., 1999; Rodriguez et al., 1993; Schuckit and Smith, 2000; Volavka et al., 1996). Alcohol challenges in twin pairs, first-degree relatives and studies in animals have established a 50% to 60% heritability for this complex characteristic (Davies et al., 2003; Heath et al., 1997; Schuckit et al., 1999; Schuckit et al., 2005). An alternate approach is to measure the intensity of response to alcohol through self-reports where subjects are asked the usual number of standard drinks required to achieve each of four effects ranging from first feelings of intoxication through unwanted falling asleep (i.e., passing out) (Daeppen et al., 2000; Schuckit et al., 1997a, b, 2001b, 2003a). The correlation between the laboratory alcohol challenges and the self-report relating to the first five or so times drinking (the "First 5") on the Self-Rating of the Effects of Alcohol (SRE) measure is approximately 0.6 for those with clearly high and low LRs. SRE values (where more drinks required for an effect indicates a low LR) relate positively to a family history (FH) of alcoholism, correlate with alcohol-related problems, have heritabilities of approximately 0.4 and appear to work well in both adolescents and in adults (Schuckit et al., 2001a, 2005).

While evaluating the potential importance of a low LR to alcohol as a genetically influenced risk factor for AUDs (Schuckit et al., 1999, 2001a; Wilhelmsen et al., 2003), our group is also testing models of how this phenotype might contribute to the alcoholism risk in the context of additional characteristics. We have hypothesized that a person who early in the drinking career needs more drinks to have an effect (i.e., who has a low LR) and who strives to achieve his/her desired level of intoxication is more likely to consume more alcohol during a drinking evening (Schuckit and Smith, 2000; Schuckit et al., 2004). This overall theory can be placed in the context of the Social Information Processing Model of Dodge et al. (2002, 2003). Here, a preexisting characteristic (i.e., a low LR to alcohol) can impact how a person interprets alcohol-related experiences and the subsequent feedback they receive. In a heavy-drinking society, the need for higher doses of alcohol to achieve desired effects might produce a social information-processing bias that primes an individual to use alcohol in specific ways and to search for specific aspects of social interactions. Earlier in the drinking career, the low LR could contribute to beginning to drink more per occasion through learning to expect that more drinks are required for the desired effect, while subsequently also acquiring tolerance that leads to even higher alcohol intake. In the full model (Schuckit et al., 2004), the lower LR is likely to contribute to the choice to associate with individuals who drink similar amounts (i.e., heavy drinkers), and this peer group may also contribute to what the person expects to experience when drinking and to a higher probability of developing heavier drinking and alcohol-related problems. Depending on the age of the individual, it is also hypothesized that heavier drinking and other characteristics in the home of upbringing might similarly affect expectations of the effects of alcohol and enhance the likelihood of alcohol-related problems. Expectations of the effects, a low LR and an adverse home environment might contribute to developing less appropriate mechanisms for coping with stress, including a higher probability of using alcohol to deal with life difficulties (Schuckit et al., 2004).

This model is being tested in members of the 453 families in the San Diego Prospective Study (Schuckit and Smith, 2000; Schuckit et al., 2004). A preliminary evaluation of a model used a structured series of regressions at the 15-year follow-up for 315 probands who had been originally selected as 20-year-old healthy subjects (Schuckit and Smith, 2000). The results confirmed a relationship between an FH of alcoholism and a lower LR to alcohol, and LR related well to alcoholic outcome in the model, even in the context of the additional life domains. The analyses also pointed to the importance of alcohol expectancies, ways of coping with stress and drinking in the environment as contributors toward the risk for AUDs, but these variables did not link closely to LR in these 35-year-old men (Schuckit and Smith, 2000).

At the 20-year follow-up, it was possible to apply structural equation modeling (SEM) approaches to test aspects of the LR-based model in the first 297 original probands from the San Diego protocol (Schuckit et al., 2004). Data were available from both the 15- and the 20-year follow-ups of these subjects (at about ages 35 and 40 years). Because multiple time points were involved and there were limitations on the number of parameters appropriate for testing a sample of this size, the analyses were limited to domains of the FH of alcoholism, LR determined through alcohol challenges at approximately age 20, expectations of the effects of alcohol, drinking among peers and a coping measure. For these adults, drinking in the home of upbringing was not felt to be as salient, and the relative homogeneity of this Caucasian male sample did not require that age, gender, or ethnic group be used as covariates. The SEM results revealed the expected relationship between FH and LR, and indicated that LR appeared to operate primarily through coping in enhancing the risk of symptoms of alcohol abuse or dependence at both the 15- and 20-year follow-ups. While expectations of the effects of alcohol

and drinking among peers at the 15-year follow-up contributed significantly to the model, neither was closely tied to FH or LR in these adults. The direct paths within the overall SEM explained 58% of the variance regarding AUD-related outcomes at age 40 and contributed to 35% of the variance at age 35. The overall model demonstrated good fitness characteristics.

Because the impact of domains might differ with age, it is important to also test the model in younger groups. This offers the opportunity to measure LR close to the time of onset of drinking, which optimizes the probability that the LR reflects the initial sensitivity to alcohol rather than differences in how a person adapts to alcohol during the drinking career. As shown in the hypothesized model in Figure 1, we propose that among adolescents the expectations of the effects of alcohol might be more closely tied to the FH of alcoholism and to LR than in adults, because parental personality characteristics and attitudes might be more salient at this age, and because adolescents are just beginning to experiment with alcohol and to develop their attitudes and expectations of the effects of this drug (Colder et al., 1997; Curran et al., 1997; Duncan et al., 1998; Shen et al., 2001; Tarter, 2002; Zucker et al., 2000). At this age, models of drinking in the home environment may be more closely related to the FH of AUDs, and could also affect both alcohol expectancies and an offspring's drinking pattern and problems.

Although there are over 500 offspring of the probands in the San Diego Prospective Study and data relevant to the LR-based model are being gathered on this group, most children are currently too young to generate information relevant to LR and to alcoholic outcomes. However, several key domains in the LR-based model are also available from the ongoing Collaborative Study on the Genetics of Alcoholism (COGA) (Bucholz et al., 1994; Schuckit et al., 2003b). The current analyses test aspects of the LR Social Information Processing Model presented in Figure 1 in 238 subjects aged 13 through 19 in the COGA investigation. Reflecting the heterogeneity of the sample, the applicability of the findings to subgroups will use multigroup and invariance testing across the sexes, older versus younger subjects and lighter versus heavier drinkers, and compare results when analyses are limited to one offspring per family versus families with more than one offspring. A more complete model in teenagers would also include drinking among peers and deficient coping mechanisms (Schuckit et al., 2004), but these domains had not been measured in the COGA sample.

Method

The subjects were 13- to 19-year-old offspring who had ever consumed alcohol and who were from families who gave written informed consent to participate in the six-center COGA project (Bucholz et al., 1994; Schuckit et al., 2003b). These families were selected through a proband identified in treatment programs as an individual who met criteria for alcohol dependence as defined in several approaches

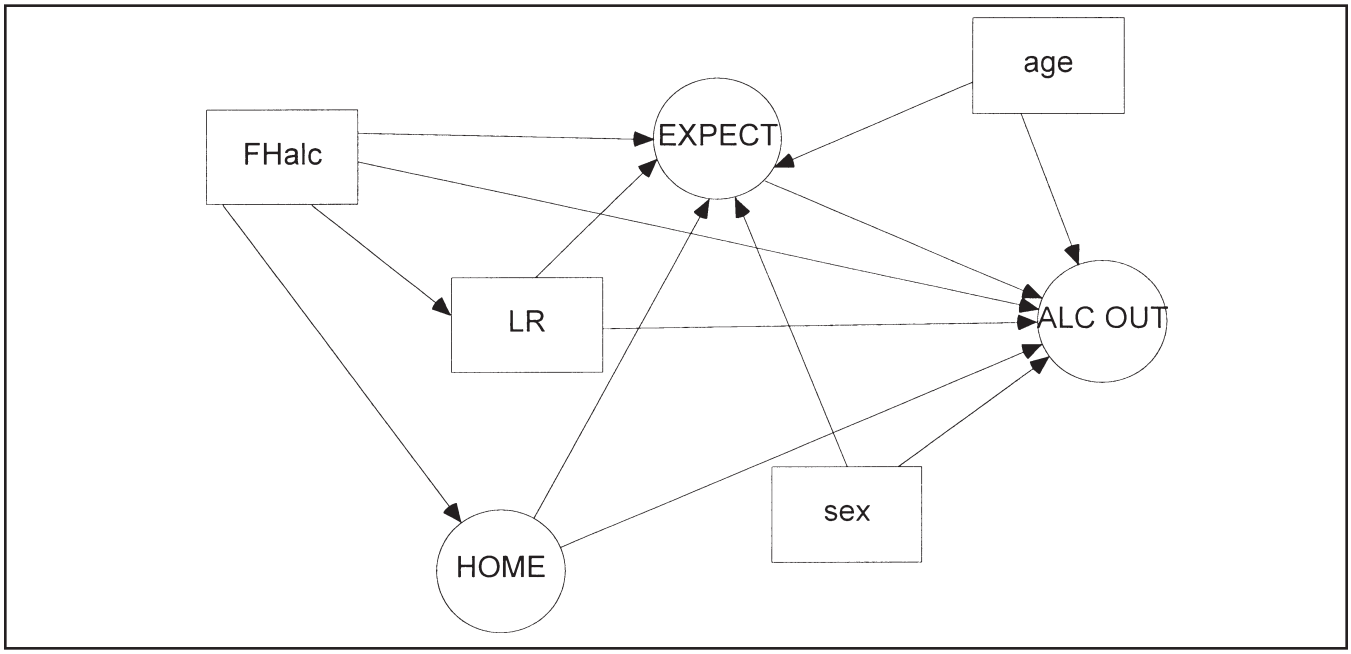

FIGURE 1. This figure presents the hypothesized model. Here, and in Figures 2 and 3: FHalc is the offspring family history of alcoholism; LR is the offspring level of response to alcohol (higher SRE = lower LR on alcohol challenge); HOME is the offspring home environment; EXPECT represents the offspring expectations of the effects of alcohol using the Alcohol Expectancies Questionnaire; age is that of the offspring at the time of interview; sex is that of the offspring; ALC OUT is the alcohol outcome for the offspring.

including the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised, (DSM-III-R; American Psychiatric Association, 1987; Feighner et al., 1992) and who had multiple alcoholic relatives available for testing. Control families were identified using a variety of mechanisms across the centers, including dental and medical clinic visits, driver's license registers and mailed questionnaires. After excluding subjects with life-threatening illnesses, with intense recent intravenous drug use, and who were unable to speak English or cooperate in the interview, original probands were evaluated using the Semi-Structured Assessment of the Genetics of Alcoholism (SSAGA) interview as described below (Bucholz et al., 1994; Hesselbrock et al., 1999). Available relatives aged 18 and older were evaluated using the adult version of the SSAGA, with age-appropriate instruments given to children ages 7 through 12 and adolescents ages 13 through 17. The adolescent and adult forms generate information on up to 17 DSM syndromes and gather detailed data about alcohol- and drug-related problems. The adolescent SSAGA has a 1-week kappa statistic of 0.86 for alcohol-related problems (Kuperman et al., 2001). Diagnostic information regarding the parents of the offspring was established through direct SSAGA interviews with the mother and father. Outcome data regarding the adolescents were generated through direct age-appropriate SSAGA interviews. In these analyses, FH was indicated by a score of 0 if neither parent had alcohol abuse or dependence, 1 if only one parent had ever had either of these disorders and 2 if both parents ever fit the criteria.

LR values were established using the 12-item SRE questionnaire (Schuckit et al., 1997a, 1997b). The relevant score for these adolescents was their estimates of the number of drinks required for effects for approximately the first five times of drinking, using the sum of the number of drinks required for any of the up to four possible effects they had actually experienced (first feeling intoxication, slurring speech, stumbling gait or unwanted falling asleep), divided by the number of effects endorsed. The SRE correlates with LR from alcohol challenges as high as 0.6, has a test/retest reliability over several years of 0.8 and has been demonstrated to relate to heavier drinking and alcohol-related problems in studies in both the United States and Europe (Daeppen et al., 2000; Schuckit et al., 1997a, 1997b, 2001b).

Alcohol expectancies were evaluated using the Alcohol Expectancy Questionnaire-Adolescent (AEQ-A) for offspring ages 13 through 17, and the adult AEQ for those ages 18 and 19 (Christiansen et al., 1989; Kline, 1996). These two forms have between 90 and 120 self-administered questions used to generate up to seven scale scores (including a total). The expectancy scores for these analyses used the four scales that overlap between the adolescent and adult forms, including sexual enhancement, social behavior or assertiveness, relaxation and tension reduction and global positive scores. For each subject, z-scores for the scales are generated relative to his/her age group.

The home environment values were developed through the mothers' and fathers' average alcohol quantity per drinking occasion and their maximum number of drinks over the prior 6 months. These data were extracted directly from the parents' SSAGA interviews.

Alcohol-related outcomes for these teenagers were determined by combining scores for the maximum number of drinks in 24 hours in their lives, the maximum quantity of drinks per drinking day in the prior 6 months and the number of alcohol problems they ever had as reported at the time of the SSAGA interview. The 23 problem items included those related to DSM abuse and dependence, as well as blackouts, morning drinking, fights and seeking help for alcohol-related problems. Data were available from both the parent report on the offspring as well as the adolescent SSAGA interviews, with endorsement of an item by either informant considered as a positive report.

Finally, regarding the analyses described below, the adolescents' ages and genders were determined from their personal SSAGA interview. Unfortunately, data on coping mechanisms and peer drinking practices were not included in the COGA protocol, and only one time point (the Phase II interview) incorporated the SRE.

The evaluation of the performance of domains was first determined through zero order Pearson Product Moment correlations. Then an SEM approach was carried out using the AMOS Structural Equation Program with the analysis of the variance/covariance matrix invoking maximum likelihood estimation (Arbuckle and Wothke, 1999). Measurement models were first evaluated via confirmatory factor analysis allowing for correlations among the latent variables, after which the measurement model was incorporated into the structural model. Our final model is a respecification of the hypothesized model via modification indices that also make theoretical sense. Initial goodness of fit was evaluated through multiple approaches (McDonald and Ho, 2002) including: the ratio of χ^2 to the degrees of freedom, with good fit indicated as from 2 to 1 to 3 to 1 (the smaller the ratio the better) (Wheaton et al., 1997) the Comparative Fit Index (CFI), with better fits indicated by scores greater than 0.95 (Hu and Bentler, 1999); the Bentler-Bonnett Non-Normal Fit Index (NNFI) (Bentler and Chou, 1995), with a good model indicated by values close to 1.0; the Root Mean Square Error of Approximation (RMSEA), where values less than 0.05 indicate good model fit (Hu and Bentler, 1999; McDonald and Ho, 2002); and the Standardized Root Mean Squared Residual (SRMR), where values less than 0.08 indicate good model fit (Hu and Bentler, 1999). We also follow Hu and Bentler's (1999) recommendations for use of a two-index presentation strategy for assessing fit using SRMR in tandem with a second index such as RMSEA requiring, for example, both that SRMR

be less than 0.08 and RMSEA be less than 0.06 for good fit.

Tests of mediation relied on two procedures. The first was the Preacher and Leonardelli (2003) interactive calculation tool for mediation tests, which yields z-scores for evaluating significance. Here, we incorporated the Goodman (1960) version of the Sobel test suggested by Baron and Kenny (1986). Second, we ran the SEM models with and without the direct effect involved in each of our two mediation tests, comparing the resulting chi-squares. The steps for testing invariance here (e.g., across boys and girls) have been described by Hoyle and Smith (1994) and by Spillane et al. (2004). First, the full model is run without any invariance constraints, allowing the two groups to be run at the same time but to function independently in estimating all parameters. Second, equality constraints then require that the factor loadings be the same across the two groups. Third, the specification is made so that, in addition, variances across the two groups are the same. Fourth, correlations are required to be the same across the two groups. Fifth and finally, equality constraints require that the structural paths have the same values across the two groups. A chi-square test is used to determine whether each additional set of constraints across the two groups reduced how well the model fits the data. Bentler (1990) noted that this chi-square test is overly sensitive, so an additional evaluation is needed to determine whether there are marked changes in the overall fit indices (Spillane et al., 2004).

Results

The 238 teenagers evaluated in this protocol include 48.7% males and had a mean (SD) age of 17.2 (1.51) years. Among these subjects, 4.7% were ages 13 or 14, 26.9% were 15 or 16, 21.0% were 17 and 47.5% were 18 or 19, and 25.7% were children of probands. The racial breakdown for this population was 77.3% white, 10.1% black, 2.5% Latino and 10.1% mixed race or other; religious background included 41.2% Catholic, 42.4% other Christian denominations, 12.6% reporting no religion, and 3.8% other faiths.

Among these offspring, 38.1% had a father alone who ever fulfilled criteria for alcohol abuse or dependence. The figure for mothers alone was 8.4%; 29.8% had both parents with abuse or dependence, and for 22.7%, neither parent had ever fulfilled criteria for these conditions. Regarding LR, the First-5 SRE score was 3.9 ± 2.30; for drinking in the home environment, the fathers' mean quantity per drinking day in the last 6 months was 2.8 ± 3.48 drinks, and his maximum number of drinks over the same time span was 5.8 ± 7.30. Figures for the mothers' mean and maximum quantities were 1.9 ± 2.51 and 3.6 ± 5.31, respectively. Expectancy in the teenagers was measured through z-transformation of the four relevant AEQ scores, which included 0.2 ± 0.97 for sexual enhancement, 0.4 ± 1.05 for social behavior or assertiveness (the scale is called "social behavior" for adolescents), 0.2 ± 0.90 for relaxation and tension reduction and 0.1 ± 0.99 as the global positive score. Regarding the dependent variable in the analyses, the offsprings' maximum number of drinks ever consumed in 24 hours was 11.7 ± 9.65, and the maximum quantity of drinking per drinking day in the prior 6 months was 4.7 ± 4.58. Only 54% had four or more drinks in an evening in the recent time frame. Finally, relating to outcomes, the subjects reported 2.1 ± 2.84 alcohol-related life problems from among the 23 possible items. These included blackouts, interpersonal problems and questions relating to the 11 DSM-III-R alcohol abuse and dependence items (American Psychiatric Association, 1987). Because of distribution properties, log transformations were used for LR, indicators for Home, and alcohol-related outcomes.

Table 1 presents the zero order Pearson Product-Moment correlations among the variables relevant to the model. Beginning with the key domain, as predicted LR correlated (r = .16) with FH (i.e., a higher SRE score—the equivalent of a low LR on alcohol challenges—correlated with a positive FH of AUDs), with the offsprings' alcohol-related outcomes (0.39-0.55), and with Expect measures (0.15-0.27). FH related, as anticipated, to three of the four Home measures (0.16-0.18), and to two of the three outcomes (0.15). Expect items correlated with outcome (0.21-0.30), and although only some of the four Expect items correlated with Home measures (e.g., the social behavior or assertiveness score with three of the four parent drinking scores [r = 0.13-0.18], most other correlations were at least 0.10. Regarding covariates, gender related to LR (-0.20, with lower SRE scores for females), to some aspects of Home (e.g., fathers' quantity; 0.14-0.15), and to only one Expect measure (global positive AEQ), as well as to all three outcome measures (higher outcome scores for males). Age related to one outcome measure (0.19 to the lifetime maximum number of drinks) and to one AEQ score (0.19 to social behavior or assertiveness) but did not significantly correlate with any additional domains.

The results of the measurement model are presented in Figure 2. Here, the overall χ^2 = 43.04, 40 df, p = .35, with a χ^2/df ratio of 1.08. The CFI value was 0.99, NNFI = 0.99, RMSEA = 0.018 (90% confidence interval [CI] 0.00-0.049) and SRMR = 0.04. These indices also meet the criteria for the two-index presentation strategy, as do all sets of indices reported below. In addition, regarding the measurement model, all factor loadings were significant (p <.001). As can be seen in Figure 2, despite similarities among parents for zero order correlations, regarding drinking practices factor loadings for mothers' drinking, variables were more highly loaded on Home than those for fathers. For Expect, the factor loadings were generally similar. For Alc Out, the more recent maximum quantity drinking variable was less highly loaded on the latent variable.

TABLE 1. Zero-order correlations among domains and outcome

	FH	LR	Father usual quant.	Father max. quant.	Mother usual quant.	Mother max. quant.	AEQ: Sex	AEQ: Social	AEQ: Relax	AEQ: Global	Outcome: Recent max.	Outcome: Max. ever	Outcome: problems	Age
LR	.16†													
Father usual quant.	.12	-.00												
Father max. quant.	.17*	.02	.93‡											
Mother usual quant.	.16†	.06	.28‡	.28‡										
Mother max. quant.	.18†	.03	.33‡	.34‡	.91‡									
AEQ: Sex	.08	.17†	.09	.05	.10	.13								
AEQ: Social	.07	.15*	.14*	.11	.16*	.18†	.59‡							
AEQ: Relax	.04	.18†	.12	.12	.11	.13*	.69‡	.60‡						
AEQ: Global	.01	.27‡	.06	.05	.11	.11*	.69‡	.61‡	.72‡					
Outcome: Recent max.	.08	.39‡	.12	.12	.14*	.10	.26‡	.24‡	.23‡	.24‡				
Outcome: Max. ever	.15*	.55‡	.04	.06	.04	.06	.25‡	.24‡	.25‡	.28‡	.55‡			
Outcome: Problems	.15*	.45‡	.03	.04	.01	-.01	.26‡	.24‡	.21‡	.30‡	.44‡	.67‡		
Age	-.13	.03	-.05	.01	-.10	-.07	-.09	-.19†	-.06	-.10	.05	.19‡	.07	
Sex	.02	-.20†	.15*	.14*	.06	.09	-.05	.06	.03	-.17†	-.16*	-.28‡	-.12	-.03

Notes: FH = offspring family history of alcoholism; LR = offspring level of response to alcohol where higher SRE scores = a lower LR on an alcohol challenge; Father usual quant. = father average quantity alcohol/drinking day last 6 months; Father max. quant. = father maximum quantity alcohol last 6 months; Mother usual quant. = mother average quantity alcohol/drinking day last 6 months; Mother max. quant. = mother maximum quantity alcohol last 6 months; AEQ: Sex = sex factor; AEQ: Social = social factor; AEQ: Relax = relaxation factor; AEQ: Global = global factor; Outcome: Recent max. = offspring maximum quantity alcohol last 6 months; Outcome: Max. ever = offspring lifetime maximum quantity alcohol in 24 hours; Outcome: Problems = offspring no. (of 23) alcohol-related problems; Age = age of offspring at time of interview; Sex = sex of offspring.
*$p < .05$; †$p < .01$; ‡$p < .001$.

Figure 3 presents the significant path coefficients ($p < .05$) for the structural model. Here, the direct paths within the model explained 49% of the variance of outcome, with $\chi^2 = 106.37$, 76 df, $p = .02$; χ^2/df ratio = 1.40; CFI = 0.98, NNFI = 0.98, RMSEA = 0.041 (90% CI = 0.020-0.059) and SRMR = 0.04. Consistent with predictions, FH related to LR (path = 0.25) and Expect scores were also tied to alcohol-related outcomes (coefficient = 0.24). Home related to FH (coefficient = 0.29) and to Expect (path = 0.24) but not to outcome. Regarding covariates, in the SEM age related only to outcome, whereas gender performed as predicted regarding outcome, Home, and LR. Analyses of mediation revealed that LR mediated the relationship between FH and alcohol-related outcome. The Sobel test yielded a z of 2.57 ($p < .02$), and the χ^2 difference between the χ^2 for the SEM model with and without the direct FH to alcohol-related outcome path was nonsignificant ($\chi^2 = 1.57$, 1 df, $p = .18$). The evaluation of Expect as mediating the relationship between LR and outcome suggests partial mediation. The Sobel test yielded a z of 2.50 ($p < .02$), but the χ^2 difference was significant ($\chi^2 = 65.23$, 1 df, $p < .001$). Therefore, although the Sobel test result was consistent with mediation, the significant χ^2 indicated that the direct path had a significant effect.

The model (excluding the age variable) was reevaluated for older and younger offspring groups, testing for invariance. Here, tests were run for invariance in five steps as described in Methods: the full model for two groups with no equality constraints, adding constraints requiring the same factor loadings across the two groups, adding constraints requiring the same variances then requiring the same correlations and finally the same structural path values. The age break for older and younger offspring groups was a priori selected as reflecting the youngest usual time of graduation from high school, with the result that the model was tested for invariance for the 125 subjects aged 17 or younger (16.0 ± 1.05 years) and the 113 subjects aged 18 and 19 (18.5 ± 0.50 years). The younger and older groups had an average of 4.5 ± 4.15 and 4.9 ± 5.00 ($t = -0.62$, $p = .54$) maximum drinks per occasion in the prior 6 months and drank an average of 1.3 ± 1.00 and 1.8 ± 1.44 times per week ($t = -3.27$, $p<.001$). Invariance testing revealed nonsignificant χ^2s, indicating invariance between groups for factor loadings ($\chi^2 = 6.94$, 8 df, $p = .60$), variances ($\chi^2 = 0.004$, 2 df, $p = .99$), correlations ($\chi^2 = 1.60$, 2 df, $p = .45$) and path values ($\chi^2 = 12.70$, 13 df, $p = .45$). Also, the fit indices were the same across all levels (CFI = 0.98, NNFI = 0.98, RMSEA = 0.03 [CI = 0.000-0.04], SRMR = 0.05).

Testing for invariance (excluding the sex variable) was also used to compare the functioning of the model in 122 girls versus 116 boys. The girls and boys had a maximum of 3.5 ± 3.01 and 5.0 ± 4.74 drinks on any occasion in the prior 6 months ($t = 2.89$, $p < .004$), with an average frequency of 1.8 ± 1.42 and 1.4 ± 2.43 times per week ($t = 2.43$, $p < .02$). Here again there were no significant χ^2s for any step difference indicating invariance between groups for factor loadings ($\chi^2 = 2.12$, 8 df, $p = .98$), variances ($\chi^2 = 2.32$, 2 df, $p = .30$), correlations ($\chi^2 = 0.77$, 3 df, $p = .85$) and path values ($\chi^2 = 11.44$, 11 df, $p = .40$). Also, the fit indices were generally the same across levels (CFI = 0.98 to 0.99, NNFI = 0.98 to 0.99, RMSEA = 0.02 to 0.03 [CI = 0.000-0.04], SRMR = 0.06).

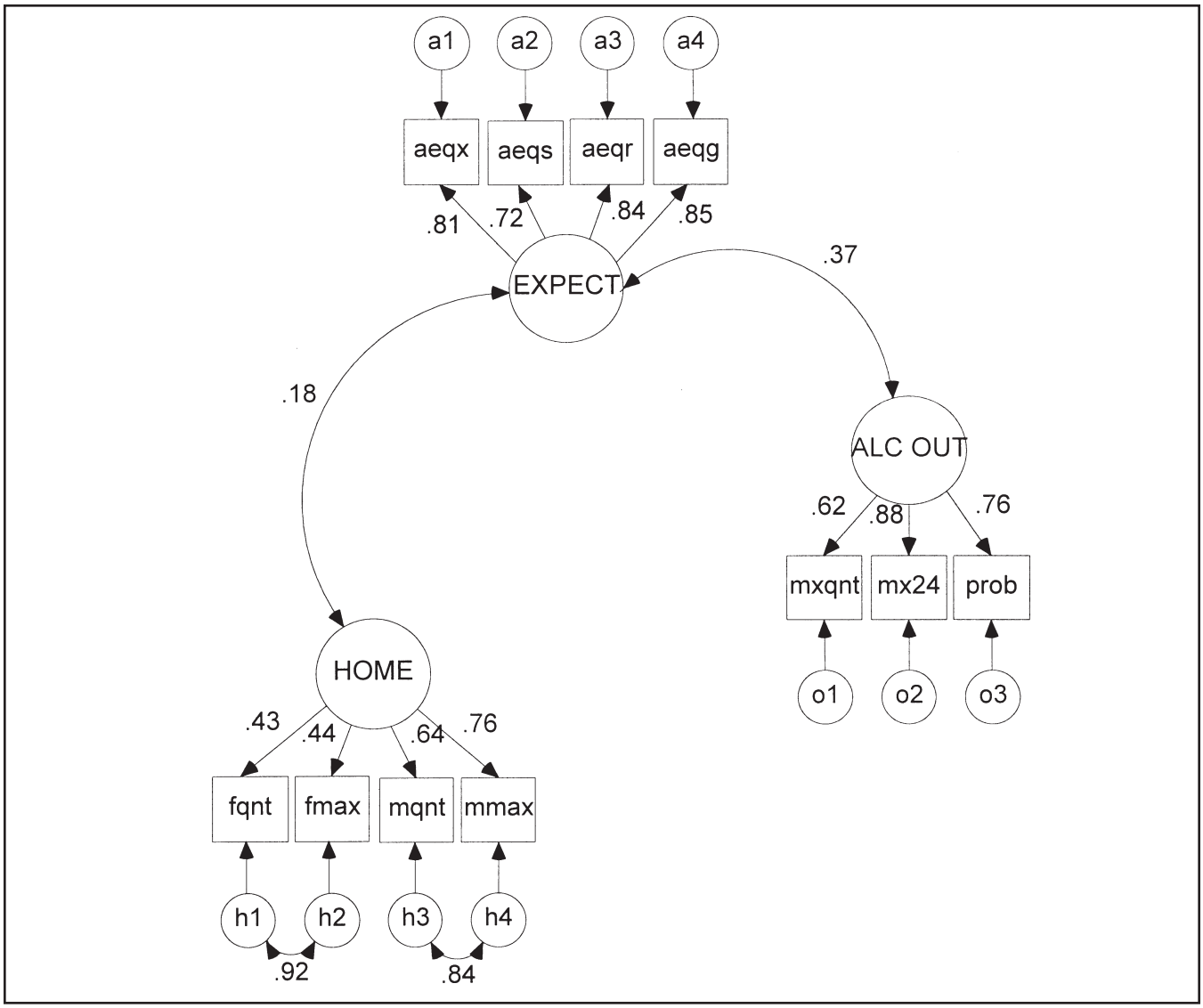

FIGURE 2. This figure presents the measurement model evaluated outside the structural equation model (SEM). HOME, EXPECT and ALC OUT are used as defined for Figures 1 and 3. The measurement model for HOME is represented by four indicators (fqnt = father average quantity alcohol/drinking day, fmax = father maximum quantity alcohol last 6 months, mqnt = mother average quantity alcohol/drinking day, mmax = mother maximum quantity alcohol last 6 months) with error correlations allowed. EXPECT is represented by four indicators for the offspring (aeqx = sex factor, aeqs = social factor, aeqr = relaxation factor, aeqg = global factor). ALC OUT is represented by three indicators for the offspring (mxqnt = maximum quantity alcohol in a day last 6 months, mx24 = lifetime maximum quantity alcohol in 24 hours, prob = no. of 23 alcohol-related problems).

Invariance was also evaluated for 120 lighter versus 118 heavier drinkers. The former were defined as drinking less than four drinks as their maximum consumption on the usual drinking day over the prior 6 months. Regarding drinking variables, lighter versus heavier drinkers differed significantly on the maximum number of drinks per occasion in the prior 6 months (1.6 ± 1.14 vs 7.8 ± 4.59, t = 14.55, 236 df, $p < .001$), the mean number of drinks per occasion (1.0 ± 1.03 vs 5.04 ± 4.62, t = -9.40, 236 df, $p < .001$), and the maximum number of drinks ever consumed in 24 hours (7.7 ± 7.02 vs 15.8 ± 10.24, t = -7.18, 236 df, $p < .001$). The invariance testing here did identify a significant χ^2 (χ^2 = 31.00, 8 df, $p < .001$) for factor-loading invariance, suggesting that the factor loadings are not completely invariant across lighter and heavier drinking groups. Specifically, an examination of factor loadings for the two groups run without equality constraints revealed that for the alcohol outcome latent variable, heavier drinkers had more equal loadings across the three indicators, whereas lighter drinkers had a lower loading on the recent drinking indicator, compared with the other two indicators. Despite this, the fit indices did not change much from an unconstrained

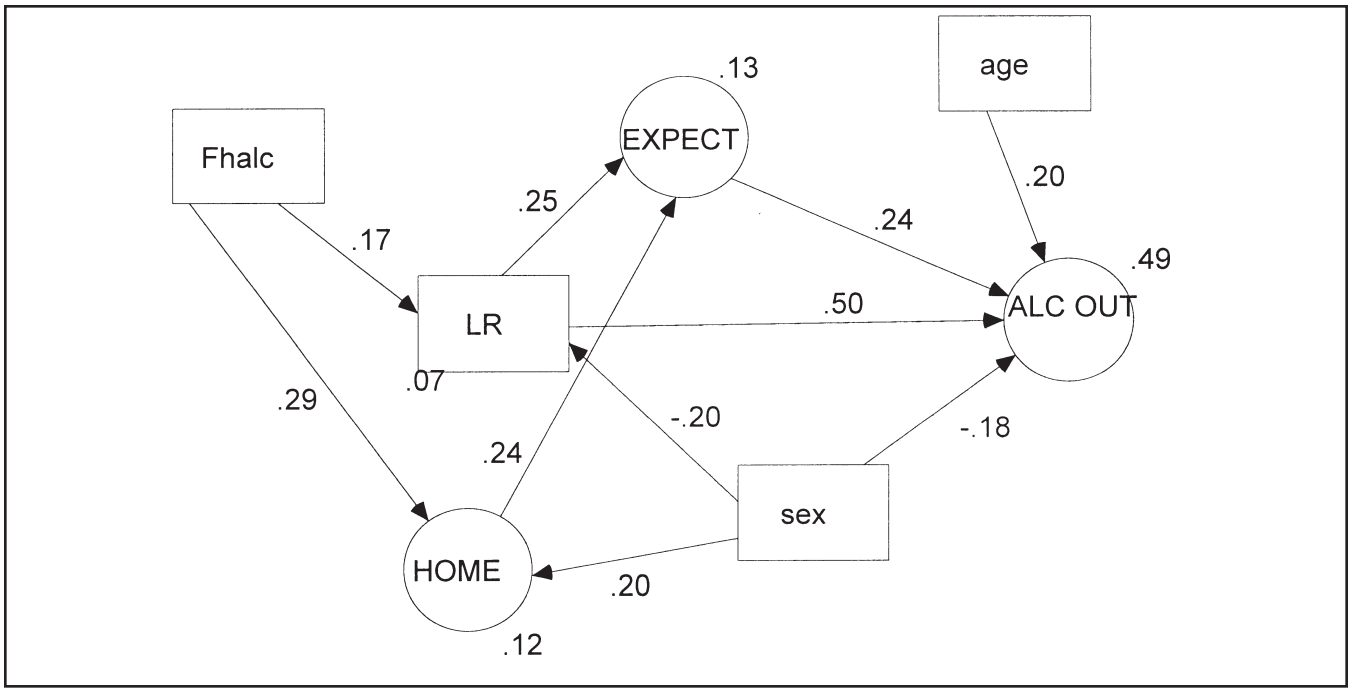

FIGURE 3. This figure presents the result of the SEM with 49% of the variance explained for ALC OUT. Only significant path coefficients ($p < .05$) are presented. R^2's are provided for endogenous variables. Manifest and latent variables are as defined for Figures 1 and 2.

model (CFI = 0.97, NNFI = 0.96, RMSEA = 0.04 [CI = 0.025-0.052], SRMR = 0.06) to the factor loading for equality constraints (CFI = 0.96, NNFI = 0.94, RMSEA = 0.05 [CI = 0.033-0.057], SRMR = 0.06). Nonetheless, paying attention to the potential for different factor loadings on alcohol outcome for these two groups could be important. For example, a measurement model for outcome in lighter drinkers, whose intake may be more variable, might exclude a recent drinking indicator. There were no significant χ^2s for invariance at the other levels, nor were there markedly different fit indices at these levels of variances (χ^2 = 0.75, 3 df, p = .99, CFI = 0.96, NNFI = 0.94, RMSEA = 0.04 [CI = 0.032-0.056], SRMR = 0.06), correlations (χ^2 = 7.32, 3 df, p = .07, CFI = 0.95, NNFI = 0.94, RMSEA = 0.04 [CI = 0.033-0.057], SRMR = 0.06) and path values (χ^2 = 9.98, 15 df, p = .85, CFI = 0.96, NNFI = 0.95, RMSEA = 0.04 [CI = 0.028-0.053], SRMR = 0.07).

In these analyses, nonindependence among siblings in families was also evaluated. Here, 116 offspring had no siblings, whereas the remaining 122 subjects came from families with more than one child (38 families had two children in the analyses, 12 three, and 2 with four or more). An invariance procedure was conducted comparing the two groups with and without siblings in the home. There were no significant χ^2s for any step difference indicating invariance between groups for factor loadings (χ^2 = 7.42, 8 df, p = .49), variances (χ^2 = 2.43, 3 df, p = .46), correlations (χ^2 = 1.06, 3 df, p = .80) and path values (χ^2 = 15.40, 15 df, p = .43). Also, the fit indices were the same across levels (CFI = 0.98 to 0.97, NNFI = 0.98 to 0.99, RMSEA = 0.03 [CI = 0.02-0.05], SRMR = 0.06).

Discussion

The level of response to alcohol has been well established as a genetically influenced phenotype related to the alcoholism risk (Schuckit, 2002; Erblich and Earleywine, 1999; Pollock, 1992). Although a search is under way for genes that contribute to LR (Schuckit et al., 1999; Wilhelmsen et al., 2003), it is also important to gather data regarding how the LR to alcohol relates to other key domains of influence in enhancing the risk of heavy drinking and alcohol-related problems. We have hypothesized that LR might operate within a Social Information Processing Model, where a low LR, along with models of heavy drinking in the family, might alter an individual's cognitive set regarding expectations of the effects of alcohol, with subsequent higher risks of repetitive heavy drinking (Schuckit et al., 2004). Aspects of the model have been shown to operate primarily as predicted in 40-year-old, relatively well functioning adult males, but we proposed that some elements might function differently during adolescence.

The current analyses used domains available in adolescents from COGA to explore aspects of the model in 13- to 19-year-old subjects who came primarily from less educated and less affluent families (Schuckit et al., 2002). The

direct paths within the SEM explained 49% of the variance of outcome, with most domains functioning in the predicted manner. Central to our hypothesis, LR related to FH and predicted outcome operating both directly and through alcohol expectancies in the SEM. Here, LR mediated the relationship between FH and alcoholic outcome, and there were indications that Expect might have partially mediated the link between LR and outcome. These results are distinct from model testing in adults, where LR was not related to expectancies, and appeared to operate through using alcohol to cope with stress (drinking to cope) instead (Schuckit et al., 2004). Although it was not possible to evaluate a more complete model in these adolescents because of the absence of data on peer drinking and using alcohol to cope, the current results do support the conclusion that expectancies may be an important mechanism through which LR influences alcohol-related outcomes in adolescents, but not in middle-aged adults.

There are several reasons why the central role of LR within the model in these teenagers was not likely to have been explained by acquired tolerance. First, the model appeared to work with equality constraints across light and heavy drinkers, suggesting that these two groups functioned similarly regarding parameter estimation. The lighter-drinking group had a significantly lower maximum number of drinks per occasion in the prior 6 months (1.6 ± 1.14 vs 7.8 ± 4.59) and a lower average number of drinks per occasion (1.0 ± 1.03 vs 5.04 ± 4.62). It would be difficult to explain the acquisition of physiological tolerance as an explanation for the performance of LR with maximum recent drinks of 1.6 and a usual average of 1 drink per occasion. Second, invariance testing supported similarities regarding performance of the model in younger versus older teenagers, and in this sample age as a covariate was not significantly related to LR. In the prior 6 months, younger drinkers consumed alcohol about once per week with a maximum of four drinks, a pattern unlikely to result in significant tolerance. Regarding covariates, although both LR and alcohol-related outcomes were related to sex, the invariance procedure supported the similarity of boys and girls in both the measurement and full models.

It is interesting to note that several predictions presented in the hypothetical model were not supported by empirical testing. The FH did not relate to measures of expectancy either on a zero-order level or within the SEM. However, recent quantities of drinking in the mother and father (as measured in the Home domain) did relate to Expect within the model, indicating that expectations might reflect models of drinking in the home, rather than general genetic or environmental influences flowing in families of alcoholics independent of recent drinking practices of parents. It is noteworthy that, on a zero order level, whereas only 4 of a possible 16 correlations were significant (.13 to .18) between the four Home and the four Expect indicators, an additional 8 were between .10 and .13. Also, it is possible that the significant path between Home and Expect in the SEM may reflect removal of measurement error in testing the full model.

With the current model, although FH did relate on a zero-order level to two of the three alcohol-related outcomes, within the SEM the only notable link between FH and outcome operated through LR. These findings underscore the potential role of LR as a mediator of part of the risk for AUDs associated with an FH of these disorders. However, it is important to remember that FH is also likely to impact the risk of heavier drinking and alcohol-related problems through disinhibition and other externalizing symptoms, as well as via mood and anxiety problems (i.e., internalizing symptoms) (Pandina et al., 1992; Slutske et al., 1998). Reflecting the size of the current sample and the need to limit the number of domains (and thus parameters) being tested, along with our focus on specific aspects of the LR Social Information Processing Model, these additional domains were not included in the SEM. It is hoped that both a Deviance-Prone Model and the Affect-Related Model can also be tested in the COGA population in the future. Once the attributes associated with each model are better understood, one might be able to best choose specific domains to enter in an overall SEM considering elements of all three models simultaneously.

The Home domain did not link directly to alcohol-related outcomes in the SEM, nor did drinking in the home have a consistent pattern of zero-order relationships. Home appeared to operate primarily in the model through its impact on expectancies. The absence of a measurable effect on drinking practices in these teenagers may reflect the fact that, despite the selection of COGA families, only a minority of the parents were alcohol-dependent probands.

Invariance testing established invariances for the sexes, younger versus older offspring, and subjects with and without siblings. The model generally functioned similarly in lighter versus heavier drinkers, with the single exception that recent drinking quantity did not work as well in the measurement model in the former, perhaps because light drinkers may be more variable in the amount they consume week by week.

Of course, the results must be interpreted in light of the methods used. First, COGA families are predominantly blue-collar whites and have a greater proportion of alcoholics than usual families (Schuckit et al., 2002). The generalizability of results to other populations will need to be determined. Second, the LR to alcohol was measured with the self-report SRE. Although such LR rankings appear to be stable, function in a manner consistent with genetic influences and correlate moderately well with alcohol challenge-based findings (Schuckit et al., 1997a,b, 2005), it would be of interest to observe how this model functions in adolescents with LR determined by alcohol challenges.

Unfortunately, this would be a difficult step to carry out and, reflecting the need for informed consent, would likely be limited to drinkers ages 18 and older. Third, the size of the current sample required that only a limited number of domains could be tested, and COGA did not have data available on two additional relevant areas—drinking among peers and ways of coping with stress. Similarly, although the development of heavier drinking and alcohol-related problems during adolescence is likely to reflect the pattern of influences of domains over time, only cross-sectional data were available at the present time. Finally, reflecting the age range of the subjects, the emphasis was on drinking quantities and problems, rather than DSM-based diagnoses of alcohol abuse and dependence. Future follow-ups will hopefully help to add to our understanding of how the LR to alcohol earlier in life predicts later AUDs.

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