Subjective Stimulant and Sedative Effects of Alcohol During Early Drinking Experiences Predict Alcohol Involvement in Treated Adolescents*

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ABSTRACT. Objective: Research on low subjective response to alcohol has focused primarily on alcohol's sedative effects during early drinking experiences. This study examined subjective response to both stimulant and sedative effects of alcohol during initial drinking experiences as predictors of treated adolescents' severity of alcohol involvement before treatment and over 1-year follow-up. **Method:** Adolescents ($N = 169$) recruited from addictions treatment reported on the number of drinks needed to obtain stimulant and sedative effects of alcohol for early and heavy drinking periods. The number of drinks needed to obtain stimulant and sedative effects, as well as the degree of stimulant and sedative effect obtained, were examined as predictors of adolescents' alcohol involvement at baseline (before treatment) and 1-year follow-up. **Results:** During early drinking experiences, females reported a greater degree of sedative effect compared with males; there was no gender difference in degree of stimulant effect reported during early drinking experiences. Both early subjective stimulant and sedative effects of alcohol predicted the usual number of drinks needed to become intoxicated and the maximum drinking quantity per day before treatment. However, at 1-year follow-up, only early sedative effects predicted 1-year outcomes. **Conclusions:** Study findings suggest potentially important roles for both early subjective stimulant and sedative effects of alcohol in relation to adolescent alcohol involvement. (*J. Stud. Alcohol Drugs* **70:** 660-667, 2009)

INITIAL OR "INNATE" SENSITIVITY refers to an individual's level of response to alcohol during initial and very early drinking episodes. Low initial response to early drinking episodes, that is, the need to consume more alcohol to feel specific effects, has been described as "innate tolerance," "low sensitivity," or "low response" to alcohol (Li, 2000). Initial subjective effects of alcohol, particularly low response to the sedative effects of alcohol, have been investigated as a phenotype and risk factor for heavy alcohol use and alcohol dependence (e.g., Schuckit, 2000).

Two possible mechanisms, related to the biphasic effects of alcohol, have been proposed to explain the association between initial sensitivity to alcohol effects and alcohol involvement. Research indicates that greater stimulant and euphoric effects are experienced during rising blood alcohol concentrations (BACs), and greater sedative effects at relatively high BACs and across the falling limb of the BAC curve (Martin et al., 1993). Low subjective response to alcohol's sedative and aversive effects, particularly during early drinking episodes, may facilitate heavy drinking (Schuckit, 2000). Alternatively, studies of acute functional tolerance suggest that individuals at high risk for alcohol problems (i.e., family history of alcohol dependence) report greater positive feelings (e.g., euphoria, "reward") during rising BACs compared with low-risk adults and demonstrate greater acute tolerance to sedative effects during falling BACs (Newlin and Thomson, 1990, 1999). It is possible that the combination of feeling both greater "reward" (i.e., stimulant effects) and less "punishment" (i.e., sedative effects) during drinking episodes provides a potent pharmacological mechanism that drives the continuing, heavy alcohol use associated with alcohol dependence (Newlin and Thomson, 1999).

The Self-Rating of the Effects of Alcohol (SRE) questionnaire (Schuckit et al., 1997) was developed as a cost-effective means to assess level of response to alcohol when laboratory alcohol challenge is not feasible and provides a method for collecting data on subjective response to alcohol during early drinking episodes. The SRE queries four, mainly sedative, alcohol effects—(1) feeling an initial effect, (2) feeling dizzy or beginning to slur your speech, (3) stumbling or walking in an uncoordinated manner, and (4) passing out or falling asleep when not intended—in relation

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to three drinking periods, one of which refers to the first five drinking episodes (i.e., FIRST5). A key SRE variable is the minimum number of drinks needed to obtain alcohol effects during FIRST5. Higher SRE scores reflect more standard drinks needed to obtain sedative effects, that is, a "low response" to alcohol (Schuckit et al., 2003). In support of the validity of SRE FIRST5, the measure correlated with adults' reports of subjective effects and physiological response during laboratory alcohol challenge (e.g., Schuckit et al., 1997) and predicted severity of alcohol involvement in adults (e.g., King et al., 2006; Schuckit et al., 2007).

Several studies have examined SRE FIRST5 in youth. Based on SRE FIRST5, adolescents' subjective response to alcohol appears to be familial, with correlations ranging from .14 to .22 in a sample of offspring from the Collaborative Study on the Genetics of Alcoholism (COGA; Schuckit et al., 2005c). In a cross-sectional study of COGA 13- to 19-year-old offspring, FIRST5 low response mediated the association between family history of alcoholism and alcohol involvement (Schuckit et al., 2005b). In another cross-sectional study, SRE FIRST5 correlated with maximum number of drinks consumed in a day and frequency of drinking in a sample of 80 British 12- to 13-year-olds (Schuckit et al., 2005a). Importantly, in the study of British youth, FIRST5 correlated with maximum quantity of alcohol consumed when acquired chronic tolerance was less likely to account for the observed association, supporting the distinctiveness of FIRST5 from measures of chronic alcohol tolerance.

Because the SRE focuses primarily on sedative effects, a gap in knowledge exists with regard to the unique roles that stimulant and sedative effects, particularly during early drinking experiences, may play in the onset and maintenance of heavy drinking leading to alcohol dependence. To investigate associations between early response to both stimulant and sedative alcohol effects in relation to adolescent alcohol involvement, the SRE was expanded in this study to include stimulant effects, as well as to include items querying the degree of effect obtained during specific drinking periods (e.g., FIRST5).

This study extends the literature on early response to alcohol in adolescents by examining the quantity of alcohol consumed to obtain both stimulant and sedative effects during FIRST5 and examining the perceived degree of alcohol effects obtained during FIRST5 as predictors of alcohol involvement. We tested for possible gender differences in alcohol effects and tested the hypothesis that both greater "reward" (i.e., greater degree of stimulant effect) and less "punishment" or aversive effects (i.e., greater number of drinks to obtain sedative effect, and lower degree of effect obtained) during early drinking episodes predict greater alcohol involvement at baseline and 1-year follow-up. Study results have implications for understanding the role of early alcohol effects as predictors of adolescent alcohol involvement.

Method

Participant characteristics

Adolescents, ages 14-18, were recruited from five treatment sites in Western Pennsylvania offering intensive outpatient treatment (IOP) for substance-using youth. IOP treatment was provided in groups that met three times per week, 3 hours per session, for 6-8 weeks. All sites prescribed a goal of abstinence from alcohol and other drugs, with program content that covered relapse prevention skills and the facilitation of 12-step meeting attendance.

Adolescents included in these analyses ($N = 169$) reported lifetime alcohol use at a minimum frequency of at least once per month for at least 6 consecutive months. The majority of participants were male (64%) and white (90%); African-Americans represented 4% of the sample, and 6% were of other ethnicity (e.g., biracial, Hispanic, Asian). Participants had a mean (SD) age of 16.9 (1.1) and represented a range in socioeconomic status (mean years of education for the head of household was 13.3 [1.5] years, range: 8-16; 11% of the heads of household had a bachelor's degree; mean Hollingshead score = 2.5 [1.0], range: 1-5; Hollingshead, 1975). At baseline, the majority (65%) had a current (past-6-month) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994), alcohol-use disorder (30% abuse, 35% dependence). The majority (79%) had a current DSM-IV other drug-use disorder, typically involving cannabis (12% abuse, 67% dependence); 62% had a current nicotine-dependence diagnosis. In the year before treatment, the average frequency of alcohol use was once per week, and for marijuana, it was three to four times per week.

Comparison of retained and attrited participants (90% retention: 153 vs 16 adolescents, respectively) indicated that those who were not followed at 1 year had higher socioeconomic status (3.1 vs 2.4; $t = 2.7$, 17.6 df, $p < .05$). No differences between retained and attrited youth on other baseline variables used in the analyses were identified (p's > .07).

Procedure

Shortly after treatment admission, adolescents were provided with a brief description of a longitudinal study on the course of alcohol and drug problems to determine their interest in research participation. The majority (77%) of youth who were approached agreed to participate. Adolescents enrolled in the study are generally comparable on demographic and substance-use characteristics to youth in addictions treatment (Substance Abuse and Mental Health Services Administration, 2007).

Following a description of study procedures and before data collection, written informed consent or assent was obtained from the adolescent and his/her guardian. Participants

completed baseline (usually within 2 weeks of starting treatment) and 1-year follow-up protocols that were administered by highly trained research interviewers. Each assessment lasted 2-3 hours and collected data on the adolescent's substance-use history, self-reported subjective effects of alcohol, and DSM-IV substance-use disorders. Youth completed a urine drug screen at each assessment, and discrepancies between self-report and test results were discussed with the adolescent to ensure high data quality. Adolescents received compensation on completion of the assessment. The university's institutional review board approved the study protocol.

Measures

Subjective Effects of Alcohol Questionnaire (*SEAQ*). Pilot testing was conducted in a separate sample of adolescents recruited from treatment (see Chung and Martin, 2005) to determine the specific alcohol effects and drinking periods to be included in the SEAQ. The SEAQ extends the SRE (Schuckit et al., 1997) in several ways. Specifically, the SRE's four, largely sedative, alcohol effects were expanded to cover a total of seven stimulant and sedative alcohol effects. Alcohol effects selected for inclusion were derived from effects used in the Biphasic Alcohol Effects Scale (Martin et al., 1993). Two effects were selected to represent effects that occur on the ascending limb of the blood alcohol curve (i.e., stimulant effects): (1) "warm, glow" and (2) "talkative, excited, high, energized." Five effects were selected to represent sedative effects that are typically experienced at high BACs and on the descending limb of the blood alcohol curve: (1) "slurred speech, thinking was fuzzy"; (2) "sleepy, slow, tired"; (3) "nauseous"; (4) "stumbling, bump into things, uncoordinated"; and (5) "pass out or fall asleep when didn't want to." The SEAQ's four drinking periods were as follows: (1) early (first five) drinking experiences (FIRST5), (2) a period of drinking at least once per week (for at least 4 weeks), (3) heaviest drinking period, and (4) current drinking period (past 6 months). The SEAQ also obtained information on the age at onset of each drinking period. For FIRST5, the individual reported the age at onset for consuming at least one standard drink (i.e., the equivalent of 10 g of ethanol: one 12 oz beer, 4 oz wine, or 1.5 oz of 80-proof distilled spirits) and the age at which the fifth drinking episode (at least 1 standard drink) occurred.

For each drinking period, the SEAQ obtained information on the typical amount consumed per occasion. In addition, for each drinking period, the individual reported the smallest number of standard drinks needed to obtain a specific effect. SEAQ instructions stated that alcohol effects that were not experienced during a given drinking period were to be marked with an "X." Based on the SRE method for deriving a summary alcohol effects score for a drinking period (Schuckit et al., 1997), the number of drinks reported for each effect was summed, and the sum was then divided by the number of effects endorsed for that drinking period.

After completion of the SEAQ, interview items were administered to obtain data on the degree to which the reported alcohol effects were experienced, when the adolescent was feeling the effect "the most," on a 4-point scale (0 = "not at all" to 3 = "a lot"), for each drinking phase. The score for degree of effect experienced was computed for each drinking period, separately for stimulant and sedative effects. For degree of stimulant effect, the mean of the two stimulant degree of effect items was divided by the usual number of drinks consumed during the drinking period of interest. Likewise, for sedative effects, the mean of the five sedative effect items was divided by the usual number of drinks consumed for a given drinking period.

Because the "current" (6 months before baseline) drinking period typically also was the period of heaviest lifetime use in this sample, data for the current drinking period are not presented. Satisfactory internal consistency reliabilities were obtained for the two stimulant items (FIRST5 α = .79, weekly use = .90, heaviest use = .91) and for the five sedative items (FIRST5 α = .93, weekly use = .94, heaviest use = .96).

To characterize the retest reliability of the SEAQ, a subsample of 50 adolescents completed the SEAQ and other substance-use measures at baseline and at a 2-week retest. The demographic and substance-use characteristics of the retest sample were comparable to the total sample. Two-week test-retest (n = 50) for SEAQ items on the smallest number of drinks needed to obtain specific effects for each drinking period was good: FIRST5 intraclass correlation (ICC) = .84, weekly drinking ICC = .86, and heaviest use ICC = .83. Test-retest was also good for reports of the magnitude of effects experienced for each drinking period (ICC = .70-.89).

Consistent with other reports (e.g., Schuckit and Smith, 2000), FIRST5 sedative and stimulant effects do not appear to be proxies for constructs such as impulsivity (partial r, controlling for gender, age, and ethnicity = .13 and -.04 for sedative and stimulant effects, respectively, $p > .1$) as measured by the Eysenck Impulsivity Questionnaire (Eysenck and Eysenck, 1977) or sensation seeking (partial r = .03 and -.15 for sedative and stimulant effects, respectively, $p > .07$) as determined by the Sensation Seeking Scale total score (Zuckerman, 1971).

The alcohol-use questionnaire given at baseline and follow-up collected data on past-year frequency of alcohol use, frequency of drinking five or more drinks in a day (frequency codes for questionnaire items were as follows: 0 = never, 1 = less than once a month, 2 = once a month, 3 = twice per month, 4 = three times per month, 5 = once per week, 6 = twice per week, 7 = three times per week, 8 = four times per week, 9 = five times per week, 10 = six times per week, 11 = daily, 12 = twice or more per day), and the largest number of drinks consumed in a day in the past year. The Alcohol-Dependence Scale (Ross et al., 1990) assessed alcohol-dependence severity in the past year at baseline and 1-year

TABLE 1. Descriptive statistics for stimulant and sedative effects during early (FIRST5) and heavy drinking periods by gender

Variable	% reporting	Females (n = 61) Mean (SD) no. of drinks	Males (n = 108) Mean (SD) no. of drinks	t, p
FIRST5 episodes				
Age at 5th use episode		13.2 (1.5)	13.4 (1.6)	NS
Average quantity/occasion		4.0 (2.0)	4.7 (2.6)	NS
Feel warm	83.4	1.8 (1.1)	2.5 (1.6)	-2.78†
Talkative	89.9	2.7 (1.6)	3.1 (1.4)	NS
Slurred speech	89.9	4.2 (1.9)	4.9 (2.3)	NS
Feel sleepy	78.7	4.9 (2.6)	5.5 (2.8)	NS
Nauseous	74.0	5.7 (2.7)	6.7 (3.1)	NS
Stumble	85.8	5.3 (2.3)	6.8 (3.2)	-2.93†
Pass out	67.5	7.3 (4.1)	9.0 (4.6)	-2.00*
Stimulant effect		2.3 (1.2)	2.8 (1.4)	-2.63†
Sedative effect		5.3 (2.5)	6.3 (2.8)	-2.27*
Heaviest drinking period before treatment				
Age at onset		15.1 (1.1)	15.3 (2.0)	NS
Average quantity/occasion		9.5 (5.0)	10.4 (4.4)	NS
Feel warm	84.0	4.1 (2.2)	4.5 (2.6)	NS
Talkative	90.5	5.4 (3.6)	5.5 (2.7)	NS
Slurred speech	92.9	7.1 (4.0)	7.4 (3.3)	NS
Feel sleepy	82.8	8.0 (4.9)	8.6 (3.7)	NS
Nauseous	77.5	9.6 (5.8)	9.7 (4.0)	NS
Stumble	89.9	9.3 (4.9)	9.9 (3.7)	NS
Pass out	76.9	12.0 (5.9)	12.3 (4.5)	NS
Stimulant effect		5.0 (3.5)	5.1 (2.7)	NS
Sedative effect		8.9 (5.0)	9.4 (3.6)	NS

Notes: Stimulant effect = total number of drinks to obtain stimulant effects divided by the number of effects reported during that drinking period; sedative effect = total number of drinks to obtain stimulant effects divided by the number of effects reported during that drinking period (cf. Schuckit et al., 1997).
*$p < .05$; †$p < .01$; NS = not statistically significant at $p < .05$

follow-up. Twenty-five items were either rated "yes" or "no" or according to a three-point response format—(1) no, (2) sometimes, or (3) almost every time. Alcohol Dependence Scale items were summed to generate a total score (α = .88 at baseline and 1 year).

DSM-IV substance-use disorder diagnoses and symptoms. A modified version of the Structured Clinical Interview for DSM-IV (SCID) substance-use disorders (First et al., 1997; Martin et al., 1995) was used to evaluate the presence of substance-use disorder diagnoses. The modified SCID included an item, used as an alcohol outcome variable, that asked about the usual number of drinks needed to get drunk ("intoxication quantity") during the period of heaviest drinking at each time point. The modified SCID demonstrated moderate to high interrater reliability for symptom ratings, as well as satisfactory concurrent validity in adolescents (Chung et al., 2004; Martin et al., 2000).

Results

Gender differences in stimulant and sedative effects for FIRST5 and heavy drinking periods

For the FIRST5 drinking period, males reported consuming, on average, a larger number of drinks to obtain both sedative and stimulant effects compared with females (Table 1). With regard to degree of effect, there was no gender difference in the degree of stimulant effect reported (females = 0.7 [0.4]; males = 0.6 [0.5]). However, females reported, on average, a greater degree of FIRST5 sedative effect than males (females = 0.4 [0.4]; males = 0.3 [0.3]; t = 2.48, $p < .05$). For the heaviest drinking period before treatment, there was no gender difference in the stimulant and sedative effect scores (Table 1), reported degree of stimulant effect (females = 0.3 [0.3]; males = 0.2 [0.1]), or reported degree of sedative effect (females = 0.2 [0.2]; males = 0.2 [0.1]).

Although sedative and stimulant scores increased from FIRST5 to the heavy drinking period (Table 1), repeated measures analysis of covariance—controlling for gender, age, and ethnicity—did not indicate a statistically significant increase over time. There was also no statistically significant change in the degree of stimulant and sedative effects experienced over time (p's > .05). Given the absence of statistically significant differences across drinking periods, and because subjective alcohol effects during FIRST5 are less likely to reflect the influence of acquired tolerance on self-reported effects, the following analyses focus on the FIRST5 period.

TABLE 2. Zero-order correlations among FIRST5 stimulant and sedative effects, parental alcoholism, and indicators of alcohol involvement at baseline (BL) and 1-year follow-up (1-yr) (*n*'s = 123-169)

Variable	Mean (SD)	Stimulant effect	Sedative effect	Stimulant degree	Sedative degree
Gender	–	.21†	.18*	-.10	-.19*
Age	16.9 (1.1)	-.14	-.16*	.16	.05
Ethnicity	–	-.12	-.16*	.14	.08
FIRST5 age at 5th episode	13.3 (1.6)	-.02	-.01	.05	.00
BL other drug diagnosis	–	.18*	.13	-.05	-.15
BL nicotine dependence	–	.08	.12	-.01	.00
BL intoxication quantity	9.0 (4.3)	.34†	.43†	-.30†	-.16*
BL maximum quantity	8.7 (2.1)	.18*	.33†	-.25†	-.14
BL frequency of heavy episodic drinking	4.8 (2.7)	.02	.09	-.04	.06
BL ADS score	16.9 (8.1)	-.06	.09	.06	.07
1-yr intoxication quantity	7.7 (5.2)	.33†	.37†	-.22†	-.10
1-yr maximum quantity	7.8 (3.6)	.18*	.20*	-.11	-.05
1-yr frequency of heavy episodic drinking	3.4 (2.7)	.19*	.17*	-.02	.10
1-yr ADS score	12.8 (7.4)	-.06	-.02	-.08	.17
Mean (SD)	–	2.6 (1.4)	5.9 (2.8)	0.6 (0.4)	0.4 (0.3)

Notes: Other drug and nicotine dependence are dichotomous variables. FIRST5 = first five drinking experiences; stimulant effect = total number of drinks to obtain stimulant effects divided by the number of effects reported during FIRST5; sedative effect = total number of drinks to obtain stimulant effects divided by the number of effects reported during FIRST5; stimulant degree = mean degree of stimulant effects divided by the number of drinks typically consumed during FIRST5; sedative degree = mean degree of sedative effects divided by the number of drinks typically consumed during FIRST5. ADS = Alcohol Dependence Scale.
*$p < .05$; †$p < .01$

FIRST5 alcohol effects as predictors of alcohol involvement at baseline

Zero-order correlations (Table 2; the full matrix is available on request) indicated that a greater number of drinks consumed during FIRST5 to obtain stimulant and sedative effects was associated with greater intoxication quantity and maximum quantity consumed in the year before treatment entry. However, quantity consumed during FIRST5 was not correlated with past-year frequency of heavy episodic drinking or Alcohol Dependence Scale total score. Regarding degree of effect, lower FIRST5 degree of stimulant effect was associated with greater intoxication quantity and maximum quantity, and lower degree of FIRST5 sedative effect was associated with greater intoxication quantity at baseline.

Simultaneous linear regression analyses were used to examine FIRST5 effects and degree of effect as predictors of indicators of alcohol involvement, controlling for age, gender, ethnicity, age at fifth drinking episode, lifetime drug diagnosis, and lifetime nicotine dependence. Results (Table 3) indicated that FIRST5 sedative effects and FIRST5 degree of stimulant effect each uniquely predicted intoxication quantity before treatment (standardized beta [β] = .30 and -.23, respectively, $p < .01$), as well as maximum drinking quantity in the past year (β = .38, $p < .01$, and β = -.21, $p < .05$, respectively). Specifically, greater number of drinks needed to obtain FIRST5 sedative effects and feeling less FIRST5 stimulant effect were uniquely associated with consumption of greater quantity per occasion during the heavy drinking period. In addition, lower number of drinks to obtain stimulant effects (β = -.30, $p < .05$) and greater number of drinks to obtain FIRST5 sedative effects (β = .31, $p < .05$) predicted higher Alcohol Dependence Scale score. FIRST5 effects were not uniquely predictive of frequency of heavy episodic drinking at baseline.

FIRST5 alcohol effects as predictors of alcohol involvement at 1-year follow-up

Zero-order correlations (Table 2) indicated that greater number of drinks to obtain FIRST5 stimulant and sedative effects was associated with greater intoxication quantity, maximum quantity consumed in a day, and frequency of heavy episodic drinking at follow-up. Regarding degree of effect, lower degree of FIRST5 stimulant effect was associated with greater intoxication quantity at follow-up.

In simultaneous linear regression analyses predicting 1-year alcohol outcomes, report of a larger number of drinks to obtain FIRST5 sedative effects uniquely predicted greater intoxication quantity over follow-up (β = .25, $p < .05$; Table 3). In addition, greater degree of FIRST5 sedative effect (i.e., greater early sensitivity to sedative effects) predicted greater frequency of heavy episodic drinking over follow-up (β = .20, $p < .05$). In the regression model predicting maximum

TABLE 3. Simultaneous regression analysis predicting baseline and 1-year alcohol involvement from FIRST5 sedative and stimulant effects

	Baseline[a]						1-year follow-up[b]					
	Intoxication quantity		Max. drinking quantity		ADS total score		Intoxication quantity		Max. drinking quantity		Frequency of HED	
Predictor	*B* (SE)	β	*B* (SE)	β	*B* (SE)	β	*B* (SE)	β	*B* (SE)	β	*B* (SE)	β
Gender	0.33 (0.67)	.04	-0.16 (0.35)	-.04	-3.28 (1.31)	-.20*	1.29 (0.93)	.12	1.76 (0.66)	.24†	1.34 (0.50)	.23†
Age	0.70 (0.31)	.17*	0.26 (0.16)	.13	0.35 (0.61)	.05	-0.42 (0.42)	-.09	-0.54 (0.30)	-.16	-0.54 (0.23)	-.21*
Ethnicity	-0.59 (0.27)	-.16*	-0.24 (0.14)	-.14	-0.98 (0.54)	-.15	-0.24 (0.36)	-.06	-0.27 (0.26)	-.09	-0.42 (0.20)	-.19*
FIRST5 stimulant	0.10 (0.33)	.03	-0.25 (0.17)	-.16	-1.69 (0.65)	-.30*	0.39 (0.45)	.10	0.20 (0.32)	.07	0.29 (0.24)	.14
FIRST5 sedative	0.47 (0.16)	.30†	0.29 (0.08)	.38†	0.86 (0.32)	.31*	0.48 (0.22)	.25*	0.11 (0.16)	.08	-0.00 (0.12)	-.00
FIRST5 stimulant degree of effect	-2.12 (0.77)	-.23†	-0.95 (0.40)	-.21*	-0.07 (1.50)	-.00	-0.83 (1.03)	-.07	-0.02 (0.73)	-.00	0.10 (0.55)	.02
FIRST5 sedative degree of effect	0.14 (0.97)	.01	0.00 (0.52)	.00	0.35 (1.91)	.02	0.69 (1.35)	.04	0.67 (0.96)	.06	1.60 (0.73)	.20*
Age at 5th drinking episode	-0.38 (0.20)	-.14	-0.20 (0.10)	-.15	-0.48 (0.39)	-.10	-0.33 (0.27)	-.10	0.01 (0.19)	.00	-0.11 (0.15)	-.06
Other drug dx	-1.46 (1.22)	-.09	-0.06 (0.63)	-.01	3.30 (2.38)	.11	1.46 (0.89)	.13	1.23 (0.63)	.16	0.75 (0.48)	.13
Nicotine dx	1.58 (0.66)	.18*	0.23 (0.35)	.05	3.68 (1.30)	.23†	1.84 (0.95)	.16	0.43 (0.67)	.05	0.13 (0.52)	.02
Model statistics	$F = 7.26$,† 10/139 df $R^2 = .34$		$F = 4.18$,† 10/136 df, $R^2 = .24$		$F = 3.82$,† 10/138 df, $R^2 = .22$		$F = 3.83$,† 10/127 df, $R^2 = .23$		$F = 2.45$,* 10/127 df, $R^2 = .16$		$F = 3.08$,* 10/127 df, $R^2 = .20$	

Notes: FIRST5 = average number of drinks needed to obtain specific alcohol effects during the first five drinking episodes, divided by the number of specific effects endorsed; max. = maximum; ADS = Alcohol Dependence Scale; HED = heavy episodic drinking (five or more drinks at a sitting); dx = diagnosis.
[a]For the baseline analyses, lifetime diagnoses were used; [b]for 1-year analyses, diagnoses were present in the past 6 months.
*$p < .05$; †$p < .01$.

drinking quantity at follow-up, FIRST5 effects were not unique predictors of outcome. The model predicting Alcohol Dependence Scale score at 1 year was not statistically significant overall. FIRST5 stimulant effect score and FIRST5 stimulant degree of effect did not uniquely predict any of the 1-year alcohol outcomes.

Discussion

An expanded version of the SRE—which includes assessment of both stimulant and sedative effects, as well as degree of alcohol effect obtained, in relation to specific drinking periods—demonstrated good reliability and psychometric properties. Results of tests for gender differences in alcohol effects highlight the importance of alcohol effects during early drinking experiences (FIRST5), because gender differences that were observed for FIRST5 were not found during the heavy drinking period in this adolescent treatment sample. Both early stimulant and sedative effects predicted certain indicators of alcohol involvement before treatment. In contrast, at follow-up, only quantity consumed to obtain FIRST5 sedative effects and FIRST5 degree of sedative effects predicted 1-year outcomes. Study findings suggest important roles for both stimulant and sedative effects in relation to an individual's level of alcohol involvement.

The consistency of findings across studies with regard to associations between FIRST5 and certain indicators of alcohol involvement (e.g., maximum quantity consumed in a day) support the validity of retrospective reports of early alcohol effects, particularly given differences across studies in the type of early alcohol effects queried, use of adolescent and adult samples, and high-risk (e.g., COGA offspring) and treated adolescents. Although it may not be possible to determine the validity of self-reported alcohol effects in adolescents by laboratory alcohol challenge, studies involving adults have validated self-reported alcohol effects against laboratory alcohol challenge (e.g., Schuckit et al., 1997). Furthermore, FIRST5 stimulant and sedative effects, as assessed by the SEAQ, do not appear to be proxies for impulsivity and sensation seeking (cf. Schuckit and Smith, 2000). The consistency of findings across measures and studies supports the utility of self-reported early alcohol effects as a potential phenotype in research examining genetic and environmental factors associated with alcohol dependence.

With regard to gender differences in alcohol effects, although there was no gender difference in degree of stimulant effect experienced during FIRST5, females reported a greater degree of FIRST5 sedative effect compared with males. During the period of heaviest drinking before baseline, however, there were no gender differences in the number of drinks needed to obtain stimulant and sedative effects or in the degree of effect experienced. The absence of a gender difference in degree of sedative effect during the heavy drinking period suggests that although adolescent females may have had greater sensitivity, on average, to the degree of sedative effects during FIRST5, intervening alcohol use during a period of heavy drinking and acquired tolerance may have reduced the degree of alcohol effects obtained, even in the context of a general increase in quantity consumed per occasion. The influence of acquired tolerance on degree of effect obtained highlights the importance of FIRST5 effects as an early marker of risk.

Results provided some support for both FIRST5 stimulant and sedative effects as predictors of alcohol involvement.

Greater quantity of alcohol needed to obtain sedative effects during FIRST5 and lower degree of FIRST5 stimulant effect both uniquely predicted greater drinking quantity before treatment (i.e., quantity to become intoxicated, maximum quantity in the past year). These findings provide some support for the hypothesis that individuals at risk for alcohol problems show less sensitivity to alcohol effects generally, that is, need a larger number of drinks to obtain both stimulant and sedative effects (Pollock, 1992). It is of interest that degree of FIRST5 stimulant effect (i.e., lower degree of effect), rather than number of drinks to obtain FIRST5 stimulant effect, uniquely predicted greater drinking quantity per occasion before treatment. Because stimulant effects emerge earlier than sedative effects during a drinking session, attempts to maintain or enhance a certain degree of stimulant effect during a drinking session may underlie the greater quantity of alcohol consumed per occasion for some youth.

In contrast to the pattern of findings for drinking quantity before treatment, the number of drinks needed to obtain FIRST5 stimulant and sedative effects (rather than degree of effect) both uniquely predicted baseline Alcohol Dependence Scale score. These results suggest, with regard to the prediction of alcohol-related problems, the relative importance of greater average quantity needed to obtain early alcohol effects (both stimulant and sedative) compared with the degree of effect obtained. Findings regarding the number of drinks needed to obtain FIRST5 effects as a predictor of alcohol-related problems replicate results reported for SRE FIRST5 (e.g., Schuckit et al., 2005b). However, results from this study also suggest a more complex pattern of findings that involves drinking quantity needed to obtain certain effects, degree of effect obtained, and specific alcohol outcomes. Further research is needed to replicate the pattern of findings obtained in this study and to further test hypotheses regarding differential sensitivity to stimulant and sedative effects (e.g., Newlin and Thomson, 1999) versus lower sensitivity to alcohol effects more generally (e.g., Pollock, 1992) among individuals at risk for heavy drinking.

Another relatively novel aspect of this study involves an examination of the extent to which FIRST5 alcohol effects predict treatment response among adolescent substance users. Results suggest the importance of quantity consumed to obtain FIRST5 sedative effects and the degree of FIRST5 sedative effect in predicting 1-year outcomes relative to FIRST5 stimulant effects. As found at baseline, greater quantity to obtain FIRST5 sedative effects predicted greater intoxication quantity over follow-up, suggesting that individuals who need more drinks to obtain sedative effects during early drinking experiences may maintain a high quantity to become intoxicated over follow-up (possibly reflecting chronic tolerance). The finding that greater degree of sedative effect during FIRST5 predicted greater frequency of heavy episodic drinking at 1 year stands in contrast to hypotheses that associate lower FIRST5 sedative effects with greater alcohol involvement and warrants replication and further study in other samples.

Certain study limitations require consideration. The generalizability of study results is limited with respect to adolescents recruited from addiction treatment, the majority of whom were male, white, and primarily marijuana users. Study measures relied on self-reported alcohol effects and substance use. However, care was taken to ensure valid self-report of substance use (e.g., comparison of self-report with urine drug screen). The measure of alcohol effects developed in this study included only two stimulant effects, which may have limited the predictive power of the stimulant effect scales.

Early stimulant and sedative alcohol effects, as assessed by the SEAQ, are relatively robust predictors of some indicators of alcohol involvement, particularly quantity of alcohol consumed. Further research is needed to investigate associations between FIRST5, drinking quantity, and alcohol dependence, because genetic and environmental influences on measures of alcohol intake (e.g., quantity consumed per occasion) may be independent of factors influencing dependence (Whitfield et al., 2004). Both stimulant and sedative subjective effects of alcohol represent potentially important markers of risk for heavy drinking in research on genetic and environmental influences on the development of adolescent-onset alcohol involvement.

References

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), Washington, DC, 1994.

Chung, T. and Martin, C.S. What were they thinking? Adolescents' interpretations of DSM-IV alcohol dependence symptom queries and implications for diagnostic validity. Drug Alcohol Depend. **80:** 191-200, 2005.

Chung, T., Martin, C.S., San Pedro, R., Shriberg, R.F., and Cornelius, J.R. Retest reliability and discrepancy interview for DSM-IV alcohol, cannabis, and nicotine diagnoses in treated adolescents (abstract). Alcsm Clin. Exp. Res. **28** (5 Supplement): 111A, 2004.

Eysenck, S.B. and Eysenck, H.J. The place of impulsiveness in a dimensional system of personality description. Brit. J. Social Clin. Psychol. **16:** 57-68, 1977.

First, M.B., Spitzer, R.L., Gibbon, M., and Williams, J.B.W. Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version, Non-Patient Edition (SCID-I/NP), New York: Biometrics Research, New York State Psychiatric Institute, 1997.

Hollingshead, A.B. Four-Factor Index of Social Status, New Haven, CT: Department of Sociology, Yale University, 1975.

King, A.C., Houle, T., de Wit, H., Holdstock, L., and Schuster, A. Biphasic alcohol response differs in heavy versus light drinkers. Alcsm Clin. Exp. Res. **26:** 827-835, 2002.

Li, T.-K. Pharmacogentics of responses to alcohol and genes that influence alcohol drinking. J. Stud. Alcohol **61:** 5-12, 2000.

Martin, C.S., Earleywine, M., Musty, R.E., Perrine, M.W., and Swift, R.M. Development and validation of the Biphasic Alcohol Effects Scale. Alcsm Clin. Exp. Res. **17:** 140-146, 1993.

Martin, C.S., Kaczynski, N.A., Maisto, S.A., Bukstein, O.M., and Moss,

H.B. Patterns of DSM-IV alcohol abuse and dependence symptoms in adolescent drinkers. J. Stud. Alcohol **56:** 672-680, 1995.

Martin, C.S., Pollock, N.K., Bukstein, O.G., and Lynch, K.G. Inter-rater reliability of the SCID alcohol and substance use disorders section among adolescents. Drug Alcohol Depend. **59:** 173-176, 2000.

Newlin, D.B. and Thomson, J.B. Alcohol challenge with sons of alcoholics: A critical review and analysis. Psychol. Bull. **108:** 383-402, 1990.

Newlin, D.B. and Thomson, J.B. Chronic tolerance and sensitization to alcohol in sons of alcoholics: II. Replication and reanalysis. Exp. Clin. Psychopharmacol. **7:** 234-243, 1999.

Pollock, V.E. Meta-analysis of subjective sensitivity to alcohol in sons of alcoholics. Amer. J. Psychiat. **149:** 1534-1538, 1992.

Ross, H.E., Gavin, D.R., and Skinner, H.A. Diagnostic validity of the MAST and the Alcohol Dependence Scale in the assessment of DSM-III alcohol disorders. J. Stud. Alcohol **51:** 506-513, 1990.

Schuckit, M.A. Biological phenotypes associated with individuals at high risk for developing alcohol-related disorder. Part 2. Addict. Biol. **5:** 23-36, 2000.

Schuckit, M.A., Mazzanti, C., Smith, T.L., Ahmed, U., Radel, M., Iwata, N., and Goldman, D. Selective genotyping for the role of 5-HT_{2A}, 5-HT_{2C}, and $GABA_6$ receptors and the serotonin transporter in the level of response to alcohol: A pilot study. Biol. Psychiat. **45:** 647-651, 1999.

Schuckit, M.A. and Smith, T.L. The relationships of a family history of alcohol dependence: A low level of response to alcohol and six domains of life functioning to the development of alcohol use disorders. J. Stud. Alcohol **61:** 827-835, 2000.

Schuckit, M.A., Smith, T.L., Beltran, I., Waylen, A., Horwood, J., Davis, J.M., and the ALSPAC Study Team. Performance of a self-report measure of the level of response to alcohol in 12- to 13-year-old adolescents. J. Stud. Alcohol **66:** 452-458, 2005a.

Schuckit, M.A., Smith, T.L., Danko, G.P., Anderson, K.G., Brown, S.A., Kuperman, S., Kramer, J., Hesselbrock, V., and Bucholz, K. Evaluation of a level of response to alcohol-based structural equation model in adolescents. J. Stud. Alcohol **66:** 174-184, 2005b.

Schuckit, M.A., Smith, T.L., Danko, G.P., and Isacescu, V. Level of response to alcohol measured on the Self-Rating of the Effects of Alcohol Questionnaire in a group of 40 year old women. Amer. J. Drug Alcohol Abuse **29:** 191-201, 2003.

Schuckit, M.A., Smith, T.L., Danko, G., Kuperman, S., Bierut, L.J., and Hesselbrock, V. Correlations among first-degree relatives for responses on the Self-Rating of the Effects of Alcohol Questionnaire in teenagers. J. Stud. Alcohol **66:** 62-65, 2005c.

Schuckit, M.A., Smith, T.L., Danko, G.P., Pierson, J., Hesselbrock, V., Bucholz, K.K., Kramer, J., Kuperman, S., Dietiker, C., Brandon, R., and Chan, G. The ability of the Self-Rating of the Effects of Alcohol (SRE) Scale to predict alcohol-related outcomes five years later. J. Stud. Alcohol Drugs **68:** 371-378, 2007.

Schuckit, M.A., Smith, T.L., and Tipp, J.E. The Self-Rating of the Effects of Alcohol (SRE) form as a retrospective measure of the risk for alcoholism. Addiction **92:** 979-988, 1997.

Substance Abuse and Mental Health Services Administration (Office of Applied Studies). Results from the 2006 National Survey on Drug Use and Health: National Findings, DHHS Publication No. SMA 07-4293, Rockville, MD: Substance Abuse and Mental Health Services Administration, 2007.

Whitfield, J.B., Zhu, G., Madden, P.A., Neale, M.C., Heath, A.C., and Martin, N.G. The genetics of alcohol intake and of alcohol dependence. Alcsm Clin. Exp. Res. **28:** 1153-1160, 2004.

Zuckerman, M. Dimensions of sensation seeking. J. Cons. Clin. Psychol. **36:** 45-52, 1971.