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Predictors of Subgroups Based on Maximum Drinks per Occasion Over Six Years for 833 Adolescents and Young Adults in COGA

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ABSTRACT. Objective: A person's pattern of heavier drinking often changes over time, especially during the early drinking years, and reflects complex relationships among a wide range of characteristics. Optimal understanding of the predictors of drinking during times of change might come from studies of trajectories of alcohol intake rather than cross-sectional evaluations. **Method:** The patterns of maximum drinks per occasion were evaluated every 2 years between the average ages of 18 and 24 years for 833 subjects from the Collaborative Study on the Genetics of Alcoholism. Latent class growth analysis identified latent classes for the trajectories of maximum drinks, and then logistic regression analyses highlighted variables that best predicted class membership. **Results:** Four latent classes were found, including Class 1 (69%), with about 5 maximum drinks per occasion across time; Class 2 (15%), with about 9 drinks at baseline that increased to 18 across time; Class 3 (10%), who began with a maximum of 18 drinks per occasion but decreased to 9 over time; and Class 4 (6%), with a maximum of about 22 drinks across time. The most consistent predictors of higher drinking classes were female sex, a low baseline level of response to alcohol, externalizing characteristics, prior alcohol and tobacco use, and heavier drinking peers. **Conclusions:** Four trajectory classes were observed and were best predicted by a combination of items that reflected demography, substance use, level of response and externalizing phenotypes, and baseline environment and attitudes. (*J. Stud. Alcohol Drugs, 75,* 24–34, 2014)

HEAVY DRINKING AND ALCOHOL-RELATED problems are prevalent and complex conditions that reflect age-related influences of multiple characteristics (Casswell et al, 2002; Mason and Spoth, 2012). By the end of high school (age ~17 years), 80% of students have had experience with alcohol, and more than 20% consumed five or more drinks in an evening in the prior 2 weeks (Johnston et al, 2012). Between ages 18 and 22, almost 75% of men and women had been intoxicated, and their patterns of alcohol quantities and frequencies continued to increase with age. As a consequence, the period of heaviest drinking was usually seen in the late teens to early 20s, after which the quantities per occasion typically decreased (Auerbach and Collins, 2006; Bates and Labouvie, 1997; Ellickson et al., 2001; Hasin et al., 2007; Huckle et al., 2001; Johnston et al., 2012; Mason and Spoth, 2012). In contrast to quantity-related patterns, drinking frequencies tended to continue to increase until the late 20s without the downward trend observed for quantities, with the latter more closely linked to alcohol problems than drinking frequencies (Auerbach and Collins, 2006; Casswell et al., 2002).

Drinking patterns and related problems across ages reflect complex interrelationships among many characteristics that are associated with later heavy drinking (Colder et al., 2002; Ellickson et al., 2001; Hawkins et al., 1992; Sher et al., 1991). These include the demographic factors of male sex (Ellickson et al., 2001; Mason and Spoth, 2012; Muthén and Muthén, 2000), age, educational achievement (Casswell et al., 2002), and European American background (Compton et al., 2006; Muthén and Muthén, 2000; Wu et al., 2011). Heavier drinking and related problems also reflect earlier alcohol-related experiences, including prior heavier drinking (Li et al., 2001; Schuckit and Smith, 2011; Trim et al., 2009), earlier onsets of drinking and drunkenness (Casswell et al., 2002; Ellickson et al., 2001; Grant and Dawson, 1997; Kuntsche et al., 2013; Kuperman et al., 2005), the absence of an alcohol-related facial flush (Eng et al., 2007; Li et

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al., 2011; Muñoz et al., 2012), a family history of alcohol use disorders (AUDs) (Mason and Spoth, 2012; Schuckit, 2009), and elements of parental alcohol use and levels of permissiveness along with easy access to alcoholic beverages (Bennett et al., 1999; Casswell et al., 2002; Casswell and Zhang, 1997; Li et al., 2001; Muthén and Muthén, 2000; Trim and Chassin, 2008). A third correlate of future heavy drinking and problems includes prior tobacco and illicit drug use (Costello et al., 2008; Ellickson et al., 2001; Lessov-Schlaggar et al., 2012; Schuckit et al., in press).

Heavier drinking also relates to several genetically influenced intermediate phenotypes that have been the focus of our work and associated environmental mediators of their effects (Schuckit, 2009, 2011a). These include externalizing attributes of impulsivity, sensation seeking, and disinhibition (Bates and Labouvie, 1997; Colder and Chassin, 1999; Colder et al., 2002; Li et al., 2001; Mason and Spoth, 2012; Schuckit et al., 2008a; Slutske et al., 1998), and internalizing characteristics of mood and anxiety-related symptoms (Bates and Labouvie, 1997; King and Chassin, 2008). Another key intermediate phenotype is how a person reacts to alcohol (Newlin and Renton, 2010; Quinn and Fromme, 2011), including a low level of response (low LR) to alcohol that reflects the need for higher blood alcohol concentrations for effects. Whether measured as the response at a specific blood alcohol concentration or through the number of drinks needed for effects (Schuckit et al., 2009, 2012b), the low LR is observed before heavy drinking develops and predicts higher consumption per occasion (Chung and Martin, 2009; Quinn and Fromme, 2011; Schuckit et al., 2007a, 2008b, 2009, 2011b; Volavka et al., 1996). The impact of a low LR on later heavier drinking is partially mediated by environmental and attitudinal characteristics, including higher peer drinking (Bates and Labouvie, 1997; Schuckit et al., 2011a, 2012b), stress and using alcohol to cope (Ellickson et al., 2001; King and Chassin, 2008; Moberg and Curtin, 2009), and positive expectations of alcohol's effects (Agrawal et al., 2008; Pabst et al., 2010).

The interrelationships among demography, alcohol experiences, substance use, intermediate phenotypes, and environment/attitudes on the one hand, and changes in patterns of drinking and problems on the other, might be optimally studied as trajectories, especially when drinking practices are increasing (Brown et al., 2008; Jacob et al., 2012). There are likely to be multiple trajectories of alcohol-related characteristics, and although these can be estimated a priori, several statistical approaches might better model subclasses of trajectories as latent variables and set the stage for more accurate identification of predictors of those patterns (Auerbach and Collins, 2006; Bates and Labouvie, 1997; Casswell et al., 2002; Colder et al., 2002; Li et al., 2001; Muthén and Muthén, 2000; Trim and Chassin, 2008). Most relevant investigations included a measure of drinks consumed per occasion in their dependent variable. When applied to adolescents or young adults, these studies often identified two to five classes of trajectories, with most analyses recognizing a class of individuals who had relatively light substance intake across time and a class with a sustained high alcohol-related pattern. A third class seen in some studies involved individuals with relatively stable levels of moderate or moderately high substance intake patterns (Casswell et al., 2002; Colder et al., 2002). The remaining classes involved individuals who demonstrated significant changes in alcohol use patterns over the follow-up, with some beginning at relatively low levels of intake and progressing to higher values over time (Casswell et al., 2002; Li et al., 2001) and others with high initial substance-related values that decreased during the follow-up (Bates and Labouvie, 1997). Across latent growth mixture model–related evaluations of teenagers and young adults, common predictors of trajectories with higher alcohol involvement included male sex and European American heritage, high externalizing characteristics, poorer coping mechanisms, and higher levels of stress, whereas findings regarding internalizing attributes were less consistent. Individuals in the class with the lowest levels of substance involvement tended to have the opposite characteristics.

Although these results are impressive and many findings were consistent across investigations, each study used a limited number of predictors. Few investigations evaluated the span of characteristics that covered all five potential baseline domains of demography, alcohol use patterns, drug use–related characteristics, genetically influenced intermediate phenotypes (externalizing, internalizing, and alcohol-sensitivity measures), and environmental characteristics. The current article takes advantage of data available from the ongoing prospective panel of every-2-year evaluations of young members of families participating in the six-center Collaborative Study on the Genetics of Alcoholism (COGA), using data across a broad range of predictors of the trajectories of maximum drinks per occasion through adolescence and young adulthood. We hypothesized that multiple outcome classes for maximum drinks per occasion would be observed, aspects of all five domains of predictors would contribute to an optimal understanding of different trajectories of maximum drinks per occasion over time, and different patterns of predictors would be associated with each class. Maximum drinks per occasion was chosen as the outcome because it is most closely associated with one key phenotype being evaluated, the low LR to alcohol, and because this variable is both relevant to all drinkers and likely to change during the timeframe being evaluated (Schuckit et al., 2007a, 2008b, 2011a, 2011b).

Method

The subjects were 833 males and females from COGA families who gave informed consent or, for those younger than age 18, assent plus parental consent, to participate in

this prospective investigation. COGA originally began in 1989 with alcohol-dependent subjects from alcohol treatment programs who reported multiple alcoholic relatives (Bucholz et al., 1994; Hesselbrock et al., 1999; Schuckit et al., 2007a). Original comparison subjects were chosen without restrictions regarding AUDs through a range of methods across COGA centers, including driver's license applications, visits to medical clinics, and respondents to questionnaires at a university (Bucholz et al., 1994).

For the current analyses, young subjects from these families were selected using several criteria from among 1,132 12- to 24-year-old children, grandchildren, nieces, and nephews of original subjects, with no restrictions for prior diagnoses. To be included in these trajectory analyses, individuals were required to have drinking variables for at least two of the four time points among the every-2-year follow-ups; 70.6% of subjects had three or four completed time points, including 34.8% completing all four. Although the statistical methods are capable of imputing outcomes from subjects with only one follow-up, we preferred that at least two data points be available to estimate a trajectory. Also, to focus on the trajectory of drinking among drinkers, subjects were required to have reported alcohol intake in the 6 months before each evaluation. Baseline (T1) (M_{age} ~18 years) demographic information, prior drinking patterns, drug use histories, externalizing and internalizing characteristics, and psychiatric syndromes based on the *Diagnostic and Statistical Manual of the Mental Disorders, Fourth Edition* (DSM-IV; American Psychiatric Association, 1994), were gathered through age-appropriate versions of the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) interview (Bucholz et al., 1994). The dependent variable for these analyses was generated from the SSAGA question, "In the past 6 months, what was the largest number of (standard) drinks you've drunk in a 24-hour period?"

The diagnoses evaluated included conduct disorder (CD), antisocial personality disorder (ASPD); major depression; and panic, obsessive–compulsive, social phobic, and agoraphobic disorders. The SSAGA instrument has sensitivity for diagnoses of ~90%, a specificity of ~75%, and positive and negative predictive values of 65% and 90% compared with another standardized interview schedule (Hesselbrock et al., 1999). One-week retest reliabilities (κ) for the SSAGA regarding the relevant diagnoses are .64 to .86 for alcohol-related items, other drugs, and most major psychiatric histories (Bucholz et al., 1994). Data for subjects younger than 18 years old were also evaluated using the parent version of the SSAGA with, when the two informants disagreed, the worst-case scenario (e.g., the larger number of alcohol problems) used in the analyses. SSAGAs also recorded six alcohol-flushing phenomena that were ever experienced with two or fewer standard (10 g) drinks (flush, rash, sleepy, nauseous, headache, palpitations). Family histories of AUDs were determined through the Family History Assessment Module, with a specificity of 90% and a positive predictive value of ~50%, with a positive indication of an AUD associated with a 14-fold enhanced odds ratio (OR) of a diagnosis being confirmed if the relative was personally interviewed (Rice et al., 1995).

At T1, the participants filled out the Self-Report of the Effects of Alcohol Questionnaire (SRE). This form determines an individual's LR to alcohol through the number of standard drinks required for up to four effects actually experienced during a drinking evening (i.e., drinks to first feel any effects, to slur speech, to cause unsteadiness when walking, or to cause unintended falling asleep) (Ray et al., 2011; Schuckit et al., 1997, 2006). SRE values, including those for the approximate first five times of drinking (SRE5), were generated by summing the drinks needed for effects and dividing that figure by the number of effects reported, with the result that the need for more drinks for effects indicated a lower effect (or a lower LR) per drink.

Subjects at T1 also completed several personality questionnaires regarding aspects of externalizing and internalizing characteristics. These included the NEO-Five Factor Inventory consisting of 60 items and recording separate scores for neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness (McCrae and Costa, 2010; McCrae and John, 1992). Additional standardized questionnaires included the total score for the Barratt Impulsiveness Scale (Stanford et al., 2009), with sensation seeking evaluated using the Zuckerman Sensation Seeking Scale (Zuckerman, 1978) for those age 18 or older and the Sensation Seeking Scale for Children for younger subjects (Russo et al., 1993). Last, information was also gathered for environmental characteristics and attitudes regarding a person's perception of the maximum drinks per occasion among peers using the Important People and Activities Scale (Longabaugh et al., 2001), the sum for positive expectations of the effects of alcohol from the adult and child forms of the Alcohol Expectancy Questionnaire (Goldman, 2002), drinking alcohol to deal with stress using the total score from the Drinking to Cope adaptation of Carver's COPE Scale (Carver et al., 1989; Park and Levinson., 2002), and the levels of life stress from the Hassles and Uplifts Scale (DeLongis et al., 1988) for those 18 and older and the Children's Hassles Scale for those younger than 18 (Kanner et al., 1987).

The first stage of analyses used latent class growth analysis (LCGA). This approach incorporates growth mixture modeling, where the optimal number of latent trajectory classes is determined using maximum likelihood estimates in Mplus (Muthén and Muthén, 2006) with LCGA used to evaluate class intercepts and linear as well as quadratic trends. The criteria for the optimal number of classes included that the Bayesian information criterion continued to decrease with additional classes, the Lo–Mendell–Rubin Likelihood Ratio Test became nonsignificant, and the classes remained interpretable (Nagin and Tremblay, 2001; Schwarz, 1978).

Next, T1 predictor characteristics were evaluated across the classes, with the overall level of statistical significance determined by chi square for categorical data and analysis of variance for continuous variables. Missing data were dealt with using full information maximum likelihoods (Muthén and Muthén, 2006). In the third step, to highlight the optimal combination of predictors for each class, all T1 variables that were significantly different across the classes were entered into a series of backward elimination regression analyses for each of the four classes where Class 1 was compared with combined Class 2–4; Class 2 was contrasted with combined Classes 1, 3, and 4; and so on.

Results

As shown in Table 1, half of the 833 adolescents and young adults were female, they were primarily European American or African American, and they entered the study at 18 years of age with 12 years of education. All subjects included here had experience with alcohol by T1, with their first full drink at age 15. In the 6 months before T1, they drank 1 day per week with usual and maximum quantities of three and eight standard drinks per occasion, respectively; 8% had ever met DSM-IV criteria for alcohol dependence, with 23% for abuse. Reflecting the COGA proband selection criteria, two thirds had a father and/or mother who ever had an AUD, more than 40% of the subjects ever consumed an illicit drug (primarily cannabis) more than 10 times, 27% ever had a substance use disorder (SUD) of drug abuse or dependence, and 34% had smoked more than 100 cigarettes (lifetime). Focusing on provisional endorsement of any of the 15 DSM-IV conduct problems without the requirement for repeated occurrences or significant impairment, 86% reported more than one lifetime conduct problem, with 44% reporting more than three such behaviors. When the full DSM-IV criteria were used, 6% met criteria for ASPD, and

Table 1. Time 1 background information on 833 drinking adolescents/young adults from COGA in percentages and means (with standard deviations in parentheses)

Demography		Externalizing related	
Female	49.5%	Mean no. 15 conduct items	2.6 (2.04)
Ethnicity		≥1 conduct items	85.5%
European American	67.6%	≥3 conduct items	44.3%
African American	18.5%	Personality scores	
Hispanic	10.8%	Barrett impulsivity	65.4 (10.56)
Other	3.1%	*z* sensation seeking	0.01 (0.96)
Age, in years	18.3 (2.03)	NEO extraversion	53.7 (9.03)
Years of education	11.8 (1.69)	NEO conscientiousness	42.9 (10.14)
6-month alcohol related history		NEO agreeableness	43.2 (10.14)
Age at onset drinking	15.0 (2.31)	NEO openness	49.6 (9.32)
Frequency/week	1.2 (1.22)	ASPD diagnosis	6.4%
Quantity/time	3.4 (3.73)	CD diagnosis (not ASPD)	4.1%
Maximum quantity	8.0 (6.38)	Internalizing related	
First 5 SRE (LR)	3.7 (1.85)	Ever depressed ≥2 weeks	33.3%
Flush score (of 6 items)	1.0 (1.13)	Yes for ≥1 possible anxiety screens	23.8%
Lifetime abuse	22.9%	NEO neuroticism	52.1 (9.35)
Lifetime dependence	7.6%	Lifetime MDE	13.3%
Parental AUD	66.6%	Lifetime anxiety diagnosis	1.8%
Lifetime substance history		Environment/attitudes measures	
(>10 times)		Perceived peer maximum drinks	1.8 (0.87)
≥1 drug used	43.1%	*z* alcohol expectancy	0.0 (0.97)
Cannabinols	37.2%	*z* hassles	0.0 (0.80)
Cocaine	14.2%	Drink to cope	9.9 (3.00)
Amphetamines	9.4%	Raw scores adult/adolescents	
Opiods	14.4%	Sensation seeking adult	19.5 (6.51)
Hallucinogens	15.1%	Sensation seeking adolescent	17.2 (4.15)
Sedative–hypnotics	11.9%	Alcohol expectancy adult	136.9 (38.99)
Other drug	14.4%	Alcohol expectancy adolescent	29.5 (9.89)
Used 1 drug	19.4%	Hassles adult	35.4 (21.48)
Used 2 drugs	5.5%	Hassles adolescent	37.2 (15.74)
Used ≥3 drugs	18.1%		
Tobacco > 100 times	34.0%		
Substance use disorder	26.8%		

Notes: COGA = Collaborative Study on the Genetics of Alcoholism; SRE = self-report measure of the number of drinks need for effects the first five times drinking; LR = level of response; AUD = alcohol use disorder; no. = number; sensation seeking = Zuckerman Sensation Seeking Scale for Adults and the Russo Sensation Seeking Scale for Children; *z* sensation seeking = scales *z* scored within adults and adolescents; NEO = NEO Five-Factor Inventory personality inventory with scores presented as *T* values where 50 indicates an average score regarding the literature; ASPD = antisocial personality disorder; CD = conduct disorder; MDE = major depression episode; peer maximum drinks = from Important Persons and Activity Scale; alcohol expectancy = Alcohol Expectancy Questionnaire (adult and adolescent); *z* alcohol expectancy = scales *z* scored within adults and adolescents; hassles = Daily Hassles & Uplifts Scale (adult) and the Children's Hassles Scale; *z* hassles = scales *z* scored within adults and adolescents.

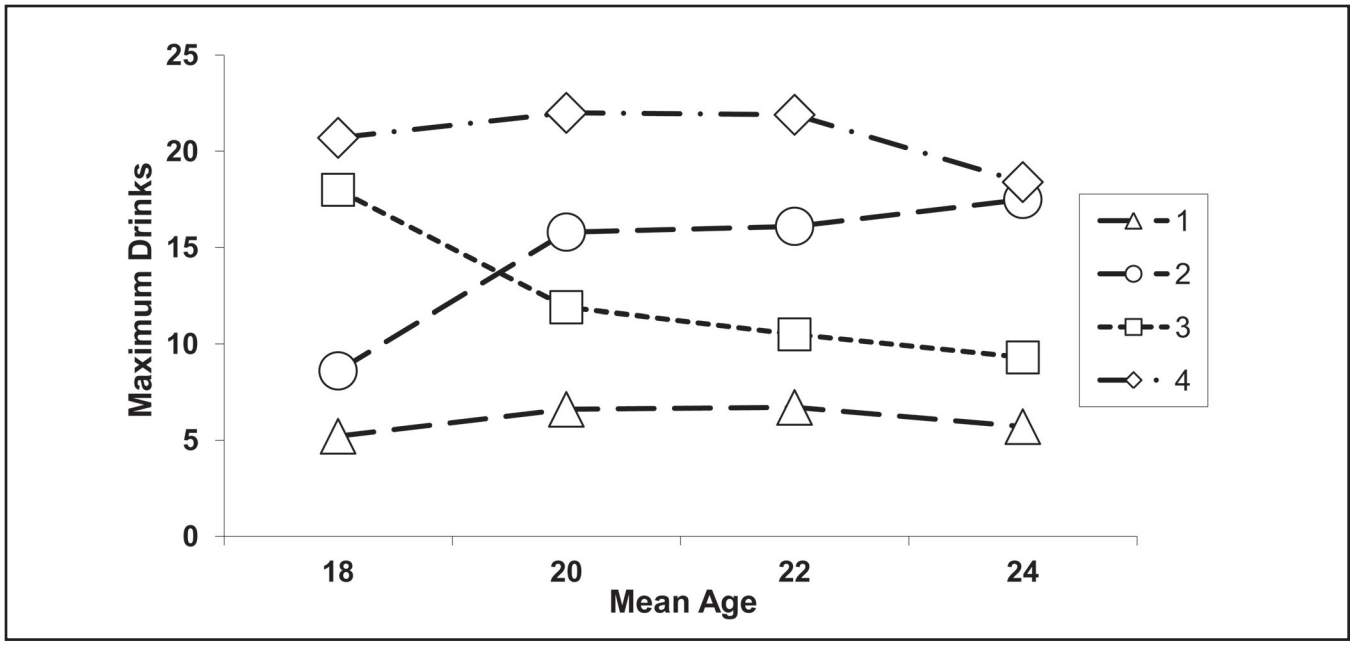

FIGURE 1. Maximum drinks per occasion in the 6 months before each follow up between mean age 18 and 24 for 833 Collaborative Study on the Genetics of Alcoholism adolescent and young adult men and women: Four classes, four time points. Class 1 = 571 subjects; Class 2 = 123; Class 3 = 86; and Class 4 = 53 subjects.

an additional 4% had CD alone. Results were similar across the 4.9% of the subjects from comparison versus original COGA families regarding demography (except for AUD family histories and proportions of European Americans), and the two groups demonstrated similar relationships of predictors to trajectory class membership, including how the class related to a subject's AUD, SUD, CD, and ASPD diagnoses.

LCGA identified the four trajectory classes shown in Figure 1 and Table 2. The entropy for the LCGA classes was .82 and the mean posterior probabilities ranged from .79 to .94, where 64.0% to 94.4% of the subjects had class probabilities of .70 or greater. The 571 individuals in Class 1 (consistent low) reported between 5 and 7 maximum drinks per occasion across time, and the 123 subjects in Class 2 (low to high) reported 9 maximum drinks at T1, increasing to almost 18 at age 24. Class 3 (high to low) consisted of 86 individuals who began at about 18 maximum drinks per occasion and decreased to 9 maximum drinks by age 24. The 53 participants in Class 4 (consistently high) reported about 21–22 maximum drinks per occasion between the average ages of 18 and 22, with a slight decrease to 18 maximum drinks at the final time point. The patterns for the four classes were similar if analyses were limited to the 588 subjects with three or four follow-ups.

Table 3 presents the patterns of T1 characteristics across the four classes reflecting maximum drinks per occasion. Focusing on items that were significantly different across the four classes, Class 1 (consistently low) subjects were likely to be nonsmoking females with a relatively low proportion of European Americans who had a relatively late onset of drinking, had the lowest SRE values (highest LR per drink), and were the least likely to have a personal or family history of an AUD. They were also the least likely to have used drugs or tobacco by T1, had the lowest externalizing characteristics and lower NEO neuroticism values, reported low maximum drinks among peers, had the lowest positive alcohol expectancies, and had the lowest Drinking to Cope Scale scores. In contrast, members of Class 4 (consistently high) had a pattern for most predictors that was the opposite of Class 1, including a low proportion of females, the highest SRE scores (lowest LRs), higher externalizing

TABLE 2. Mean maximum drinks in the 6 months before interview across four time points, separated by 2 years each across four classes for 833 adolescents/young adults

Variable	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
Age, in years	18.3 (2.03)	20.8 (2.23)	22.8 (2.18)	24.5 (2.06)
Class (*n,* %)				
1 (571, 68.5%)	5.2 (3.32)	6.6 (3.84)	6.7 (3.72)	5.7 (3.20)
2 (123, 14.8%)	8.6 (3.55)	15.8 (5.82)	16.1 (5.83)	17.5 (5.09)
3 (86, 10.3%)	18.0 (3.95)	11.9 (4.96)	10.5 (4.18)	9.3 (3.64)
4 (53, 6.4%)	20.7 (4.07)	22.0 (3.76)	21.9 (4.00)	18.4 (5.84)

values, and low flushing with alcohol. Class 2 (low to high) had the youngest subjects who were more similar to Class 4 (consistently high) than to Class 1 (consistently low) on the low proportion of females, the relatively high SRE scores (low LR per drink), the family history of AUDs, and the relatively high proportion with ASPD or CD diagnoses; they also were higher on positive alcohol expectancies and Drinking to Cope with stress. However, Class 2 subjects were more like those in the light-drinking Class 1 with respect to the lower proportion of European Americans, higher flushing, low extraversion, and low peer maximum drinks. On most other baseline variables, those in Class 2 were about midway between Class 1 and Class 4 subjects. Individuals in Class 3, who resembled Class 4 at T1 but were similar to Class 1 by age 2, resembled Class 4 on the relatively low proportion of females and high percentage of European Americans, the higher proportion with AUDs and other drug use at T1, their moderately higher scores on several externalizing characteristics, and on their higher values for most environmental/attitudinal variables. However, the Class 3 subjects resembled those of Class 1 in their higher flushing, lower proportion with an SUD history, and higher NEO openness scores, and they were unique in having the highest baseline mean age and education.

The wide range of items that differed significantly across the classes, along with the likely intercorrelations among

Table 3. Time 1 background characteristics as mean or percentage across four latent trajectory classes for maximum drinks

Variable	Class 1 Consistent low (n = 571; 68.5%) M (SD) or %	Class 2 Low to high (n = 123; 14.8%) M (SD) or %	Class 3 High to low (n = 86; 10.3%) M (SD) or %	Class 4 Consistent high (n = 53; 6.4%) M (SD) or %	F or χ^2
Demography					
Sex, female	60.1%	27.6%	33.7%	11.5%	88.50***
European American	63.0%	70.0%	82.6%	86.8%	23.40***
Age	18.4 (2.05)	17.6 (1.97)	19.05 (1.63)	18.4 (2.08)	9.54***
Education highest grade	11.8 (1.73)	11.1 (1.47)	12.3 (1.39)	11.7 (1.69)	9.58***
Alcohol					
Age onset first drink	15.4 (2.28)	14.3 (1.96)	14.5 (2.35)	13.5 (2.09)	18.89***
First 5 SRE (LR)	3.2 (1.60)	4.6 (1.79)	4.5 (1.80)	5.9 (1.72)	68.46***
Flush score no.	1.1 (1.15)	1.0 (1.14)	1.1 (1.13)	0.5 (0.76)	4.40***
AUD	19.6%	35.8%	62.8%	83.0%	144.82***
Family history of AUD	62.6%	75.6%	68.6%	75.5%	8.88*
Drugs					
Used any drug > 10 times	35.0%	52.0%	61.6%	79.2%	59.45***
≥1 SUD	19.3%	35.0%	38.4%	69.8%	76.60***
Used tobacco > 100 times	26.1%	47.2%	48.8%	64.2%	55.32***
Externalizing					
No. of conduct disorder symptoms	2.2 (1.94)	3.2 (2.14)	3.0 (1.76)	4.3 (2.00)	25.17***
Barrett impulsivity	63.5 (10.28)	68.4 (10.20)	69.2 (9.41)	71.6 (10.70)	20.26***
z sensation seeking	-0.2 (0.94)	0.2 (0.92)	0.5 (0.86)	0.7 (0.70)	29.49***
NEO extraversion	53.4 (9.09)	52.1 (8.94)	56.3 (7.76)	55.9 (9.47)	4.94**
NEO conscientiousness	44.1 (10.29)	40.5 (8.58)	40.5 (9.13)	40.0 (10.32)	8.34***
NEO agreeableness	44.5 (10.40)	39.8 (9.22)	41.2 (9.22)	41.0 (8.00)	9.88***
NEO openness	50.0 (9.57)	48.0 (9.25)	50.9 (8.34)	47.0 (7.22)	3.64*
ASPD diagnosis	4.6%	7.3%	10.5%	17.0%	15.78***
Conduct disorder diagnosis	2.8%	8.1%	7.0%	3.8%	9.39*
Internalizing					
Depression screen, % yes	32.2%	35.8%	36.0%	34.0%	0.94
Anxiety screen, % yes	23.8%	26.0%	20.9%	22.6%	0.76
NEO neuroticism	51.0 (9.16)	56.2 (9.15)	54.2 (9.05)	50.9 (9.29)	12.82***
MDE diagnosis	13.7%	13.0%	15.1%	7.5%	1.84
Anxiety diagnosis	1.9%	2.4%	1.2%	0.0%	1.50
Environment/attitudes					
Perceived peer maximum drinks	1.7 (0.80)	1.7 (0.86)	2.3 (0.85)	2.5 (0.93)	29.48***
z alcohol expectancy	-0.2 (0.94)	0.3 (1.06)	0.4 (0.80)	0.4 (0.91)	18.72***
z hassles	0.0 (0.78)	-0.1 (0.84)	0.0 (0.72)	0.2 (0.90)	1.83
Drink to cope	9.2 (2.68)	11.1 (3.21)	11.2 (3.01)	11.9 (3.25)	33.35***

Notes: SRE = self-report measure of the number of drinks need for effects the first five times drinking; LR = level of response; no. = number; AUD = alcohol use disorder; sensation seeking = Zuckerman Sensation Seeking Scale for Adults and the Russo Sensation Seeking Scale for Children; z sensation seeking = scales z scored within adults and within adolescents; NEO = NEO Five-Factor Inventory personality inventory with scores presented as T values where 50 indicates an average score regarding the literature; ASPD = antisocial personality disorder; MDE = major depression episode; peer maximum drinks = from Important Persons and Activity Scale; alcohol expectancy = Alcohol Expectancy Questionnaire (adult and adolescent); z alcohol expectancy = scales z scored within adults and within adolescents; hassles = Daily Hassles & Uplifts Scale (adult) and the Children's Hassles Scale; z hassles = scales z scored within adults and within adolescents.
*p < .05; **p < .01; ***p < .001.

TABLE 4. Logistic regression analyses odd ratios (with 95% confidence intervals [in brackets]) using baseline (Time 1) items significantly different across trajectories of maximum drinks classes in Table 3 to predict each of Class 1 through 4

Baseline (Time 1) predictors	Class 1 Consistent low	Class 2 Low to high	Class 3 High to low	Class 4 Consistent high
Demography				
Sex, female, %	3.60 [2.47, 5.31]	0.37 [0.23, 0.59]	0.59 [0.35, 0.97]	0.22 [0.08, 0.64]
Age		0.63 [0.51, 0.78]	1.67 [1.73, 2.26]	
Alcohol				
Age onset drinking	1.32 [1.08, 1.60]			
First 5 SRE [LR]	0.45 [0.37, 0.55]	1.70 [1.38, 2.11]		3.01 [2.07, 4.38]
Flush score no.				0.57 [0.36, 0.91]
AUD, %	0.40 [0.27, 0.60]		2.68 [1.62, 4.46]	6.97 [2.98, 16.26]
Drugs				
Used tobacco > 100 times %	0.56 [0.38, 0.83]	1.64 [1.04, 2.58]		3.25 [1.44, 7.34]
Externalizing				
No. of conduct disorder symptoms				1.45 [1.02, 2.06]
Barrett impulsivity	0.80 [0.64, 0.98]			1.64 [1.08, 2.42]
NEO extraversion	0.81 [0.67, 0.99]		1.56 [1.18, 2.08]	
NEO conscientiousness			0.75 [0.57, 0.99]	
NEO openness	1.25 [1.02, 1.52]			
Internalizing				
NEO neuroticism	0.80 [0.65, 0.98]	1.55 [1.23, 1.95]		0.64 [0.44, 0.94]
Environment/attitudes				
Peer maximum drinks		0.64 [0.51, 0.81]	1.33 [1.02, 1.73]	
z alcohol expectancy			1.37 [1.03, 1.83]	
Drink to cope	0.40 [0.27, 0.60]	1.42 [1.14, 1.77]		
Pseudo R^2	.45	.23	.20	.51

Notes: Blank cells = nonsignificant; continuous variables were entered as standardized variables. SRE = self-report measure of the number of drinks need for effects the first five times drinking; LR = level of response; no. = number; AUD = alcohol use disorder; NEO = NEO Five-Factor Inventory personality inventory with scores presented as *T* values where 50 indicates an average score regarding the literature; peer maximum drinks = from Important Persons and Activity Scale; alcohol expectancy = Alcohol Expectancy Questionnaire (adult and adolescent); *z* alcohol expectancy = scales *z* scored within adults and within adolescents.

many of these T1 characteristics, raised the question of which of the items in Table 3 best predicted each trajectory class. Thus, Table 4 presents the standardized ORs for logistic regression analyses regarding how significant items from Table 3 predicted each trajectory when considered in the context of all other significant items, along with an estimate of the proportion of the variance explained (pseudo R^2). Significant items from Table 3 that did not enter any regression equation are not shown in Table 4 (i.e., European American background, education, family history of AUDs, all illicit substance use items, sensation seeking, NEO agreeableness, ASPD/CD diagnoses, and all internalizing items except NEO neuroticism). The T1 characteristics that added significantly to the equation predicting the consistently low Class 1 (pseudo R^2 = .45) were nonsmoking females with a later onset of drinking, low SRE scores (a high LR per drink), and the absence of a T1 AUD, who had low impulsivity, extraversion, and neuroticism but high openness, and they did not use alcohol to cope with stress. At the other extreme, the regression analyses for the consistently high-drinking Class 4 (pseudo R^2 = .51) identified smoking males with a very high SRE (a low LR per drink), low flushing, and high T1 AUDs, who had high conduct symptoms and impulsivity but low neuroticism. Class 2 subjects (low to high; pseudo R^2 = .23) represented younger smoking males who had high SRE values (a low LR per drink) with (in contrast to Classes 1 and 4) high neuroticism, who reported low perceived peer drinking at T1 but a tendency to drink to cope with stress. Last, subjects in Class 3 who went from high to low maximum drinks per occasion (pseudo R^2 = .20) were likely to be older males who had baseline histories of AUDs, high extraversion, and low conscientiousness, who (in contrast to Class 2) reported high T1 peer drinking and high positive alcohol expectancies. For Class 3, if T1 AUD was excluded from the regression equation, SRE became significant (OR = 1.32, 95% confidence interval [1.03, 1.68]) and the resulting pseudo R^2 for the equation became .17.

Although the analyses in Table 4 offer information regarding the pattern of predictors for each of the classes, the data were also evaluated using multinomial regressions where the same items used in Table 4 were used to discriminate Class 1 from each of the remaining three classes. The results (pseudo R^2 = .53) were similar to those in Table 4 in that elements of all five domains contributed significantly to the equation: SRE, female sex, and prior AUD diagnoses were significant for all three comparisons to Class 1; elements of NEO extraversion and/or openness also contributed to all three comparisons; and smoking, NEO neuroticism, drinking to cope, and peer drinking contributed significantly only to the comparison of Class 1 versus Class 2.

Discussion

Heavy drinking is a complex characteristic that tends to peak in the late teens to early adulthood (Casswell et al., 2002; Mason and Spoth, 2012). Such heavier alcohol intake relates to at least five types of life characteristics, including demography, prior alcohol use patterns, earlier use of illicit substances and nicotine, several preexisting genetically influenced phenotypes, and environmental/attitudinal influences. The current analyses used data from all five of these domains to evaluate trajectories of maximum drinks per occasion between the average ages of 18 and 24 in a well-characterized sample. The overarching conclusions are that different drinking trajectories were identified and their prediction reflected components of all five domains.

The four trajectory classes for the 833 subjects reflected different patterns of predictors. On a multivariate level, members of Class 1 (consistently low) were typically nonsmoking females with a late drinking onset, a high LR, low externalizing characteristics, and low neuroticism, who were unlikely to use alcohol to cope with stress. Class 4 (consistently high) had predominantly the opposite pattern of trajectory predictors. The key findings here demonstrate that low LR, externalizing, and internalizing domains related not only to whether heavy drinking developed but also to the course of alcohol intake over a life period where drinking practices are in great flux. The unique contributions of all three phenotypes underscore the conclusion that trajectories of drinking do not just reflect a single underlying characteristic but that the predictors operate together in the context of demographic and environmental/attitudinal factors to influence the course of heavy drinking over time.

Our research group has been interested in a range of genetically influenced phenotypes that relate to future adverse alcohol outcomes, especially the low LR to alcohol and externalizing characteristics (Schuckit, 2009). The current results indicate that these phenotypes are relatively separate phenomena (Schuckit and Smith 2006; Schuckit et al., 2000) and demonstrate that each is related to the trajectories of heavy drinking in these young subjects. The contribution of a lower LR to three of the four regression equations is consistent with prior research documenting the ability of this phenotype to predict later heavy drinking in both males and females of different ages and from different populations (Chung and Martin, 2009; Schuckit and Smith, 2013; Schuckit et al., 2008b, 2011b). T1 externalizing characteristics, especially extraversion and impulsivity, each contributed to the prediction of two of the four trajectory classes, although sensation seeking as well as CD and ASPD diagnoses did not contribute to class membership in the regressions. These results underscore the heterogeneity among externalizing characteristics as well as the importance of evaluating the relationship of these phenomena to heavy drinking while also considering sex and additional subject characteristics that also relate to drinking patterns.

The separate contributions of LR and externalizing characteristics to whether alcohol intake increased, decreased, or remained unchanged have potential implications regarding prevention approaches. A recent study indicated that a prevention approach based on incorporating information about the low LR to alcohol into a program to decrease the risk for heavy drinking in 18-year-olds significantly improved the outcome for subjects with a low LR (Schuckit et al., 2012a). That work needs to be expanded to evaluate whether the program affects the trajectories of heavy drinking, and if the outcomes are promising, it might be the basis for developing similar programs for subjects with externalizing phenomena.

Perhaps the most interesting trajectories were seen for members of Classes 2 and 3, who evidenced large changes in their maximum drinks per occasion over the 6 years. At T1, Class 2 resembled the light-drinking Class 1 in several ways, demonstrating similar later onsets of drinking, lower externalizing scores, and lower drinking among friends. Class 2 subjects subsequently increased their maximum drinks over time to become similar to subjects in the heavy-drinking Class 4, with whom they shared a predominance of males, a lower LR to alcohol, and smoking histories. The T1 lower drinking might have reflected the relatively younger age and lower peer drinking at T1. Members of Class 2 also had higher NEO neuroticism scores, which indicated more anxiety, depression, self-consciousness, and feelings of vulnerability, mood states that can change over time and that may have contributed to the altered levels of drinking with age (Lima et al., 2013; Schuckit et al., 2007b, 2013). Class 3 members had a trajectory that was the mirror image of Class 2, resembling the heavy-drinking Class 4 at T1 but decreasing their drinking over time to levels similar to the persistently low-drinking Class 1. Class 3 subjects were older and had higher education at T1, and their enhanced maturity may have contributed to an ability to subsequently moderate their drinking. On a univariate level, Class 3 also had the second highest proportion of females, a later age at onset of drinking, and a lower proportion with SUDs or smoking at T1 compared with Class 4 members. Each of these might have reflected higher levels of life functioning associated with a better prognosis for their heavier drinking. Class 3 also shared with Class 2 a relatively high neuroticism score, which could have affected the changes in drinking practices for the reasons described above.

Overall, the characteristic that most consistently predicted the four trajectories of maximum drinks per occasion in this study was female sex. This variable has been linked in prior research to lower quantities of alcohol consumed (Ellickson et al., 2001; Mason and Spoth, 2012; Muthén and Muthén, 2000; Schuckit et al., 2012c) and is likely to relate to the smaller physical size, lower percentage of body water, and

moderately slower alcohol metabolism in females (Schuckit et al., 2012c).

It is also noteworthy that T1 AUDs also contributed to three of the regression equations. This variable was included because an analysis of trajectories of maximum drinks per occasion among drinkers might be best understood when subjects with higher T1 maximum drinking were not excluded. By including the T1 AUDs diagnosis in the regression equations, the analyses were able to demonstrate that the predictors of the trajectory classes contributed significantly to the classes even when evaluated in the context of T1 alcohol diagnoses. Smoking was also significant in three regressions, and on a univariate level drug use and SUDs demonstrated a similar pattern across groups as tobacco use.

Several of the issues raised here highlight the need to keep in mind the methods used to generate these data. First, the original COGA probands were from families with multigenerational AUDs with subsequent high rates of alcohol problems, and thus the results might not generalize to other populations with lower risks for heavy drinking. Second, because all data were generated from the COGA protocol, the timeframes for the follow-up, the focus on the 6 months before each evaluation as the timeframe for the drinking, the wording of the single question used for maximum drinking, etc., were already established before the current analyses. Other definitions and alternative follow-up procedures might have generated different results. Third, our goal was to evaluate the maximum drinks among drinkers, and additional evaluations are needed to determine patterns associated with drinking versus nondrinking. Fourth, although a broad range of potential predictors representing five domains was included, with our emphasis on the three phenotypes of long-term interest to our group, many potentially interesting items were not analyzed, including marital status, occupation, living arrangements, childhood environment, parental monitoring, and exposure to treatment. Thus, additional study is needed regarding potential contributions to trajectories for these and other environmental, attitudinal, and genetically related phenotypes. Fifth, we used LCGA because this is a relatively simple approach that can be implemented with modest-sized samples and produces results that are relatively straightforward to interpret. However, LCGA may unrealistically constrain variance within identified classes, although the approach also diminishes problems with convergence and increases model stability. Sixth, consistent with our usual approach to evaluating complex phenomena related to phenotypes in a way that facilitates clinically useful information and diminishes model instability, we decided not to include potential predictors as covariates within the model itself. Instead, we evaluated relationships between predictors and class membership using univariate statistics followed by logistic regressions. However, issues of classification error here are mitigated by the relatively high entropy for this model (.82). Seventh, in contrast to multinomial regression, we elected to run a series of binary logistic regressions allowing for evaluation of predictors of each class separately. Although we recognize some problems with this approach, we feel that the clearer presentation of results is important and the overall results were consistent with results of a multinomial regression. Last, the average age of these subjects was 18–24 years, and findings may be different in earlier adolescence or later adulthood.

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