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Heritability of Level of Response and Association with Recent Drinking History in Non-Alcohol Dependent Drinkers

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Abstract

Background—Level of response to alcohol (LR) has been shown to be associated with the risk for developing alcohol dependence and can be measured using the Self-Rating of the Effects of Alcohol (SRE) questionnaire. This study examined the heritability of the SRE-measured level of response and the relationship between LR and recent alcohol drinking history (RDH) in a predominantly African American non-alcohol dependent population.

Methods—This was a sibling study of 101 social drinkers aged 21–35 years recruited from the Washington DC metropolitan area. Participants were administered the SRE to assess LR and the Timeline Followback (TLFB) to assess RDH. The indices of SRE used were Total SRE score (SRTT), Early Drinking SRE score (SRED), Regular Drinking SRE score (SRRD), and Heavy Drinking SRE score (SRHD). Pearson's product-moment correlation and linear regression was used to analyze SRE indices and RDH variables (quantity and drinks per drinking occasion). Heritability analysis was conducted using Sequential Oligogenic Linkage Analysis Routines (SOLAR) software with SRE indices as traits of interest.

Results—There was a significant relationship between SRE and RDH measures. Drinks per drinking day, maximum drinks, and quantity of drinks were significantly associated with SRTT, SRHD and SRRD (all $p<0.05$). SRTT showed significant heritability ($h^2=.67$, $p=.025$), however, the SRE sub-indices (SRED, SRRD, SRHD) were not significantly heritable. Analysis performed in the subset consisting of only African Americans (n=86) showed similar trends.

Conclusion—Level of response, as measured by the SRE, is associated with recent alcohol drinking history. The high level of heritability of the SRE total score suggests that genetics accounts for a significant proportion of the variation in the level of response to alcohol in social drinkers.

Keywords

Self-Rating of the Effects of Alcohol; Timeline Followback; Alcohol Infusion Challenge; Level of Response; Heritability in Predominantly African American Cohort

Introduction

Alcohol dependence is a complex disorder arising from a variety of predisposing factors. One such factor is an intermediary phenotype, or endophenotype, that represents an

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individual's level of response to alcohol (Schuckit, 1994). Individuals who require higher doses of alcohol to achieve an effect have a low level of response (low LR) and tend to escalate their alcohol intake, increasing their risk for dependence (Schuckit et al., 1997b; Schuckit et al., 2006; Schuckit et al., 2007).

Genetics can account for up to 30–60% of LR (Schuckit, 1999; Heath et al., 1999; Viken et al., 2003, Schuckit et al., 2005a). LR may also occur more in those with a family history of alcohol dependence (FHA) and is lower in males than females (Schuckit and Smith, 2004; Eng et al., 2005; Schuckit et al., 2005a; Schuckit et al., 2006).

Many of the characteristics that influence LR also have an effect on recent drinking history (RDH) in terms of number of alcohol drinks (quantity), the lifetime maximum number of drinks consumed (Schuckit et al, 2006), and number of alcohol drinks per drinking occasion. Males, for instance may consume more alcohol, more often, than females (Schuckit et al., 2007; Pedersen and McCarthy, 2009). Body weight may influence quantity and frequency of drinks (Schuckit et al., 2005b; Schuckit et al., 2006) with lower body weight participants consuming less alcohol, less often. FHA alone, however, may not have any effect on the quantity, drinks per drinking occasion, or frequency of drinks consumed (deWit and McCracken, 1990). The interaction of gender, FHA, and body weight, with low LR may produce higher quantity (Schuckit et al., 2006) and drinks per drinking occasion among individuals with low LR, and vice versa among those with high LR.

LR can be assessed in an alcohol challenge using a subjective high scale (Schuckit, 1994; Schuckit et al., 1997a; Schuckit et al., 2009), or a sensation scale (King et al., 2002) These scales capture the degree to which an individual experiences a response after consuming alcohol. An additional method for assessing the level of response is the Self Reported Effects of Alcohol (SRE) scale developed by Schuckit et al (1997a). The SRE is a 12-item instrument used to retrospectively assess the degree to which an individual experiences physiological consequences of elevated alcohol intake (Schuckit et al., 1997a; Schuckit et al., 1997b). It acts as a measure of response to alcohol by recording information on the number of standard drinks needed to evoke a sensation associated with alcohol, such as feeling different, dizziness, stumbling when walking or blackouts (Schuckit et al., 1997a). This is recorded for three periods in the individual's lifetime – period of first five times the individual had a drink, period of regular drinking, and period of heaviest drinking.

Studies on the SRE have examined how it compares to other measures of LR such as the Subjective High Assessment Scale (SHAS; Schuckit et al., 1997a; Schuckit et al., 1997b; Eng et al., 2005). While a low LR is indicated in SHAS by a low score SHAS at a particular blood alcohol level, in SRE the same effect is shown by a high score. Due to the retrospective nature of the scale, SRE data may be obtained long after an individual has had their first alcoholic drink. LR observed through these SRE scores could be a function of an individual's level of alcohol tolerance. The development of tolerance to alcohol over time could result in higher (over-estimated) numbers of drinks reported on the SRE scale (Morean and Corbin, 2008). Nevertheless, studies have found that the SRE is comparable to the level of response measured following an actual alcohol challenge study and can serve as a substitute for measuring level of response in those that cannot consume alcohol such as minors or sober alcoholics (Schuckit et al., 1997a; Schuckit et al., 2009).

Literature suggests there is a significant relationship between recent alcohol drinking history and SRE measures (Schuckit et al., 1997a; Schuckit et al., 2003; Schuckit and Smith, 2004; Schuckit et al., 2005b; Schuckit et al., 2006; Schuckit et al., 2007; Ray et al., 2011). Most of these studies have focused on cohorts of European descent. Although rates of alcohol dependence currently hold constant for all racial groups (SAMHSA, 2010), African

Americans have in the past become more alcohol dependent, at faster rates, within the ages of 18–29 years (Grant et al., 2004; Breslau et al., 2006). The heritability of LR and its association with RDH may explain such trends in alcohol dependence among African Americans. There is limited data on the association of the SRE with alcohol-related problems in African Americans. To our knowledge there is only one study that related increased drinking, alcohol related problems, and DSMIV alcohol use disorders to SRE (Pedersen and McCarthy, 2009). One of their findings, that SRE and acute response were unrelated, differed from previous research on alcohol response. This present study examines (1) how the SRE as a measure of LR influences RDH in terms of quantity of alcohol and/or drinks per drinking occasion, and (2) the heritability of LR in non-alcohol dependent drinkers within a predominantly African American cohort. This paper hypothesizes that LR is heritable and influences current quantity of alcohol consumed and drinks per drinking day.

Materials and Methods

Participants

The participants were part of a larger study, *Ethno-Genetic Diversity and Alcohol Elimination Rates: the Utility of Alcohol Clamping,* which evaluated the heritability of acute responses to an alcohol clamp technique. Recruitment techniques used for the parent study included advertising in local newspapers, radio ads, posted flyers, and self referrals within the Washington, DC metropolitan area. Advertising directed potential participants to call the Howard University Alcohol Research Center (HUARC) pre-screening hotline.

Pre-Screening

Inclusion criteria consisted of physically healthy sibling pairs from all ethnic groups aged 21 through 35 years, who were able to read and speak conversational English. Social alcohol drinkers, defined as drinking less than 7 drinks per week (for females) and 14 drinks a week (for males) per guidelines from the National Institutes of Alcohol Abuse and Alcoholism (NIAAA, 2003), were selected to avoid influence of heavy drinking history on the metabolism or responses to alcohol administration during the study. The diagnosis of alcohol dependence was based on a best final diagnosis derived from concurrence of criteria based on: (1) revised Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV; American Psychiatric Association [DSM-IV-TR], 2000), (2) Diagnostic and Statistical Manual of Mental Disorders III (DSMIII-R; American Psychiatric Association, 1987), and (3) International Statistical Classification of Diseases and Related Health Problems-10 (ICD-10; World Health Organization, 1992).

Participants could not use any medications (other than multivitamins or oral contraceptives) within 30 days of study enrollment in order to avoid any interactions with the alcohol administration. Eligible participants needed to have the ability to have an intravenous catheter inserted in a peripheral vein. Persons not meeting the above criteria, having a history of alcohol dependence, current drug use, or serious mental illness were excluded from participation in the study.

Brief Description of the Study

The study consisted of three sessions. The first study session consisted of a screening interview with the participant in order to obtain a detailed medical history. Subsequently, qualified participants returned for two more sessions of intravenous infusion of either (1) 95% ethanol diluted to 6% v/v ethanol solution or (2) Lactated Ringer's placebo solution. Participants were compensated upon completion of each session of the study. The study

protocol was approved by the Howard University Institutional Review Board and General Clinical Research Center (GCRC) Advisory Board.

Screening and Interview Session of the Study

The data presented in this analysis represents the information collected during the screening and interview session only. During this session, demographic information, individual and family medical history, and substance use history were obtained from study questionnaires, Participants provided urine and blood samples for various tests including pregnancy (in females) and hepatic function. Finally, a detailed medical history and physical examination was performed by a licensed physician to rule out medical or health problems which may exclude participation in the infusion sessions of the study.

Data Collection Instruments

Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA): was used to ascertain alcohol dependency status (Bucholz et al., 1994). The SSAGA is a validated instrument with a mean reliability score of 0.7 or higher for alcohol and other substance dependencies (Bucholz et al., 1994).

Self-Reported Effects of Alcohol (SRE): SRE is an instrument used in numerous studies to assess level of response. SRE scores taken over a year apart have 0.82 correlation (ranging from 0.60 to 0.99) showing high test/retest reliability (Schuckit et al., 1997a). The SRE, completed during screening and interview, assessed the indices of early alcohol use (SRED), regular alcohol use (SRRD), and heavy alcohol use (SRHD). SRE produced 12 possible cells of data – 3 periods of drinking (early, regular, and heavy) by 4 physiological effects of drinking (feeling different, slurring speech, begin stumbling, and pass out when not want to). Each score was an average, generated by dividing the total number of standard drinks reported in cells of a particular period, by the number of cells of physiological effects endorsed within that period. A standard drink was the equivalent of 13.6gm of alcohol such as 12oz beer, 5–6 oz table wine or 1.5oz 80-proof spirit. Outlying SRE scores were unadjusted in the analysis. Total effect score (SRTT) was the mean score obtained by adding the number of drinks from the three indices and dividing by the number of cells for which standard drinks were reported (Schuckit et al., 1997a). Data on the period of heaviest drinking was used to derive a variable on maximum drinks, as this data was not collected during the study. Maximum drinks were estimated as the highest number of standard drinks consumed during the period of heaviest drinking.

Timeline-Followback (TLFB): A Timeline Followback (TLFB) was completed by each subject during screening and interview. The TLFB offers a daily retrospective report of alcohol consumption over a specific time interval, from which quantity, drinks per drinking occasion, and pattern of drinking can be obtained (Sobell and Sobell, 1992; Sobell and Sobell, 2003). Participants completed a log based on a monthly calendar to indicate daily alcohol drinking to provide the total number of alcoholic drinks consumed in the last 28 days prior to SRE administration (quantity). This quantity was then divided by the total number of drinking days, also within the last 28 days, to calculate Drinks per drinking day. Studies have shown that this is an adequate period of assessment and TLFB is established as an effective measure of drinking patterns among normal drinkers in short time intervals (Sobell et al., 1988; Ramchandani et al., 2002; Collins et al., 2008). TLFB demonstrates a test-retest reliability correlation ranging from 0.86 to 0.90 for normal drinkers within the last 30 drinking days (Sobell et al., 1988).

Family History of Alcoholism: Family history of alcohol problems was assessed using the Family History Assessment Module (FHAM) and the Individual Assessment Module (IAM)

of the FHAM (Janca et al., 1997). FHAM measures psychiatric disorders including alcohol dependence based on information from relatives. It has a specificity of up to 97% among siblings and offspring implicated of dependence (Rice et al, 1995). Participants indicated the number of first and second degree biological relatives that were diagnosed with alcohol dependence. If one or more relatives were implicated as alcohol dependent, participants were designated as family history positive. Among the family history positive, a second variable, family history density (FHD) was adapted from Stoltenberg and colleagues weighting of family history measures (Stoltenberg et al., 1998). First degree alcohol dependent relatives (parents and siblings) were assigned a score of 0.5, alcoholic second degree relatives (grandparents, aunts, uncles, and cousins) were assigned a score of 0.25, and all other relatives were assigned a score of 0. FHD was then computed from the sum of these weights per participant.

Data Analysis

In this cross sectional study, independent samples t-test and Chi-squared test were used to detect significant differences in continuous and discrete socio-demographic variables across gender. Pearson's correlation was performed to analyze associations between RDH (quantity and drinks per drinking day) and LR variables (SRTT, SRED, SRRD, SRHD), as well as maximum drinks consumed and FHD. Linear regression was used to examine the relationship between LR and RDH with each SRE index (SRED, SRRD, SRHD, SRTT) loaded separately as contributing factors for each RDH dependent variable (total quantity of drinks consumed, and drinks per drinking day). Regression model covariates included gender, age, and body weight to control for the effect of demographics on the relationship between SRE and drinking history. Forty-eight of the 51 parent study sibling pairs were represented within the cohort including three twin pairs (data on zygosity of twin sib pairs was not collected during this study, however). Regression models were weighted with sib ship as a covariate to take into account the non-independence in LR among siblings compared to non-related participants (Schuckit et al., 2005a), and the mixed effects of variables in the regression model. Data was tested for normality using the 1-sample Kolmogorov-Smirnov test. While a few study variables were not normally distributed, all residuals were within limits of normality with $p > 0.05$. Non-normal variables were log transformed and re-analyzed with the appropriate inferential test such as linear regression. SPSS version 17.0 (SPSS, 2008) was used in this analysis with significance established at $p<0.05$. Regression analysis was repeated in a sub-sample comprised of only the African Americans (86% of the sample) to examine the effect of race/ethnicity on LR and RDH. Heritability was determined using polygenic commands for variance component modeling in Sequential Oligogenic Linkage Analysis Routine software (SOLAR, 2009). Pedigree and multiple trait files were loaded into SOLAR. Pedigree files included singleton and twin sib pairs. Separate covariate screening commands were initiated for each LR trait (SRED, SRRD, SRHD and SRTT), with age, gender, body weight, quantity of drinks, and drinks per drinking day as covariates. During covariate screening, only significant covariates were included in the final analysis of each LR trait. Heritability analysis was also repeated on a sub-sample comprised of only African Americans. Residuals were within a standard deviation of 0.5 and kurtosis of 0.8 as required by SOLAR.

Results

Demographics

The study cohort consisted of 101 non-alcohol dependent siblings, aged 21–35 years old who were predominantly of African descent. Other ethnicities represented include persons of European (9.9%), Asian (2%), and other (2%) descent. The mean body weight and height were 81kg and 170cm respectively. Females reported more alcohol dependent relatives.

Average SRE scores, drinks per drinking day, maximum drinks, and quantity of drinks are presented in Table 1.

Recent Drinking History and Level of Response

Table 2 illustrates the relationship between SRE and RDH. All SRE variables correlate with each other and with the RDH variables except for SRED and quantity of drinks (see Table 2). SRED correlated with quantity of drinks in the African American sample but not in the entire sample.

Although gender and body weight were used as covariates in the regression model, only gender significantly contributed to both quantity and drinks per drinking day (see Table 3). Gender was a significant predictor of drinks per drinking day during the period of earliest drinking, and also a significant predictor of quantity of alcohol drinks for earliest, regular, and heaviest drinking. Body weight had no effect on quantity of alcohol and drinks per drinking day when loaded with other covariates, despite differences in body weight between genders.

Regression models on a sub-sample of African Americans revealed similar trends as with all ethnicities included. Significant differences seen in SRRD and SRTT across gender disappeared in the African American sample, compared to the all ethnicity sample.

Heritability of Level of Response

Heritability was significantly demonstrated in SRTT (see Table 4). The genetic variation in overall LR due to genetics was 67% ($p=0.025$). However, there was no significant genetic variation in LR shown during the periods of early alcohol drinking, regular alcohol drinking, and heaviest alcohol drinking, although period of regular drinking did trend towards significance ($h^2=0.52$, $p=0.068$). Heritability analysis of African Americans in the sample indicated that similar to the entire sample, the African Americans also have a significant SRTT score.

Discussion

This study investigated 101 non-dependent drinkers, specifically looking at SRE as a measure of LR for three time periods, its influence on RDH as measured by TLFB, as well as heritability of LR. This analysis supported the hereditary nature of LR which influences current quantity of alcohol drinking, maximum drinks consumed, and drinks per drinking day.

As demonstrated in other studies (Schuckit et al., 1997a; Schuckit et al., 2003; Schuckit and Smith, 2004; Schuckit et al., 2005b; Schuckit et al., 2006; Schuckit et al., 2007; Ray et al., 2011), we found a robust relationship between RDH and SRE measures. There was an additional gender-related influence on drinks per drinking day and quantity of alcohol drinks. As demonstrated in other studies (Schuckit et al., 2005a), male participants in this study were more likely to have higher SRE scores which, in turn, may translate into a lower LR. Generally, this is to be expected since males and females differ in quantity of alcohol, maximum drinks consumed, and amount consumed per drinking day. Decreased alcohol dehydrogenase enzymes, reduced alcohol volume distribution, higher hepatic oxidation levels, and diminished gastric emptying in females, compared to males, may contribute to fewer drinks per drinking day and quantity of alcohol consumption (Baraona et al., 2001). This influence of gender did not diminish even after accounting for body weight in the sample.

Similar to a study by de Wit and McCracken (1990), the present study did not observe FHA as a contributing factor to RDH. This suggests that FHA (FHD in present study) influences on the response to alcohol may be independent of recent alcohol drinking history. In contrast, Pedersen and McCarthy (2009) observed a relationship between LR and FHA, which was within the context of FHA among second degree relatives, and was only observed for period of regular drinking.

Heritability analysis indicated significant genetic contribution to variation in LR. The estimate of 67% heritability of overall SRE observed in this study was slightly above the range seen in literature. Research studies observed 40–60% heritability when SRE alone was administered (Schuckit, 1999), and 44–60% following alcohol challenge (Heath et al., 1999; Viken et al., 2003; Agrawal et al., 2009). In the present study, SRE measures for individual time frames were not found to be heritable. During a period of regular drinking (SRRD), there was a trend toward heritability (p=0.068), which, perhaps with a larger sample size, may reveal a heritable association of LR with regular alcohol consumption. The observed heritability of LR may be related to the number of genes associated with LR. Preliminary findings that genes located on chromosome 10 were associated with LR (Wilhelmsen et al., 2003; Schuckit et al., 2005c) were further confirmed in a later study by Webb et al. (2011). Webb and colleagues discovered that loci coding for CYP2E1 were highly correlated with LR measured after an alcohol challenge. Kuo and colleagues observed an association between GABAnergic enzyme gene markers, linked with sedative and depressant effects of alcohol, and SRED (Kuo et al., 2009). In a sample of Native Americans, loci on six chromosomes were found to overlap with genes associated with SRED (Ehlers et al., 2010). SRE measured during the early drinking phase (SRED) has been found to be heritable among a sample of adolescents (Schuckit et al., 2005a). However, within that sample, SRED may represent total SRE as they may not yet be regular drinkers (in order to measure SRRD) or experienced their period of heaviest drinking (SRHD). The lack of significant heritability of the SRED score in the present study suggests that genetic influence on initial response to alcohol may be limited (Rose et al., 2001). Alternatively, a lapse in time between initiation of drinking and the study could have resulted in over-estimation of LR, and consequently affected the interpretation of the results (Morean and Corbin, 2008).

Overlap is expected as the composite indices (SRED, SRRD, and SRHD) make up the total SRE score SRTT, making it difficult to tease out the significant heritability of SRTT without considering the individual indices. SRED was lower than SRRD which in turn was lower than SRHD, showing a progressive increase in alcohol consumption and a consequent decrease in level of response. A significant heritability of SRTT could then indicate that the total score is not only heritable, but indicative of a progression to lower LR with time, in this sample.

This analysis demonstrated that among non-alcohol dependent drinkers, LR is heritable, and has an inverse relationship with the amount of alcohol consumed and drinks per drinking day. There were a few limitations to the present study. This study was an evaluation of retrospective measures of drinking history as well as self-reported measures of LR across individuals collected at a single point in time. Longitudinal evaluations of cohorts of young individuals, assessed for their level of response to alcohol as young adults and then followed over 5 to 25 years, have shown consistent relationships between level of response and development of alcohol use problems (Schuckit et al., 2007; Trim et al., 2009). Future research may involve following the present cohort of participants to determine if any develop alcohol use disorders. A second limitation was the reliance on participants' recall of individual and family history of alcohol use. As mentioned above, even though the sample size was relatively larger than previous studies, an even larger sample size may reveal a heritable association of LR with regular alcohol consumption. Participants were randomly

recruited, but eligibility criteria may have also limited the extrapolation of the study findings to the general population. For instance, the sample may have lower drinking levels than the general population within the restricted age range used in this study. Despite these limitations, this analysis possesses a number of strengths. This analysis focused on examining a predominantly African American sibling pair cohort for the predictive nature of SRE on current alcohol drinking patterns as well as levels of heritability, adding to existing knowledge of heritability of LR in a particular ethnic minority group. In contrast to twin studies, the current study observed genetic effects interacting with both shared and unique environmental effects without excluding members of a sib pair who lacked data that the other sibling provided. The age range of participants and their siblings (21–35 years) represented both college students and adults in the community and complemented the diversity to the study cohort. Finally, this cohort displayed many similarities in LR and LR heritability seen in other studies, further validating the utility of SRE in this population.

In conclusion, the results obtained in this study confirm the validity of the screening instruments and diagnostic tools, while illustrating how LR is heritable and influences current quantity and drinks per drinking day in a predominantly African American cohort. This manuscript focused on LR as one of the possible reasons behind the incidence of alcohol dependence by eliciting the participation of a community sample including college students. The study met and exceeded expectations as authors did not expect heritability to be as high as 67%. This was a strong indication that level of response plays a significant role in the development of alcohol dependence among African Americans. The reason why heritability estimates are higher in this sample compared to other samples is uncertain. It may be intrinsic to the predominantly African American ethnicity in the sample.

Future studies may explore the intricacies of this relationship using larger, more culturally diverse populations. Further study may also undertake an examination of the association of alcohol LR to other substances linked with alcohol use such as nicotine.

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Table 1

Demographics and Drinking History Stratified by Gender

		Male	Female	Total
		(n=45)	(n=56)	(n=101)
	Age in years (mean±SD)	25.49±4.11	26.39±4.26	25.99±4.20
	** **Weight in kg (mean±SD)**	87.59±16.16	76.27±20.42	81.31±19.40
	** **Height in cm (mean±SD)**	177.16±10.13	164.33±6.85	170.04±10.59
SRE Scores During period of	** **Early Alcohol Use (mean±SD)**	3.40±1.82	2.59±1.20	2.94±1.55
	* **Regular Alcohol Use (mean±SD)**	3.98±2.02	3.04±1.99	3.45±2.05
	Heavy Alcohol Use (mean±SD)	4.56±2.29	3.82±2.57	4.14±2.47
	* **Total Score (mean±SD)**	3.91±1.75	3.14±1.65	3.48±1.73
Recent Drinking History	[1]* **Drinks/Drinking Day (mean±SD)**	2.62±1.26	1.89±1.03	2.25±1.20
	[2]** **Quantity (mean±SD)**	14.23±14.96	6.66±6.93	10.27±12.03
	[3]* **Family Density of Alcohol Dependence (mean±SD)**	0.03±0.11	0.16±0.28	0.10±0.23
	[4] **Maximum drinks (mean±SD)**	6.53±3.31	4.95±4.24	5.61±3.93

* p<.05

** p<.01

[1] Drinks per drinking occasion is expressed as number of alcohol drinks consumed per drinking day

[2] Quantity represents number of alcohol drinks consumed

[3] Based on first or second degree relatives diagnosed with alcohol dependence in FHAM/IAM

[4] Mean maximum drinks consumed during period of heaviest drinking

Table 2

Correlation of Level of Response with Drinking History

	All Participants				African American Participants			
	SRED	**SRRD**	**SRHD**	**SRTT**	**SRED**	**SRRD**	**SRHD**	**SRTT**
SRRD [1,2]	0.601†				0.594†			
SRHD	0.599†	0.802†			0.629†	0.824†		
SRTT [1]	0.746†	0.873†	0.880†		0.705†	0.836†	0.899†	
Quantity [1,2]	0.213	0.343†	0.334†	0.354†	0.256*	0.318*	0.300*	0.357†
Drinks/Drinking Day	0.346†	0.484†	0.474†	0.389†	0.383†	0.409†	0.410†	0.420†
Maximum Drinks Consumed [1,2]	0.648†	0.809†	0.887†	0.923†	0.633†	0.808†	0.967†	0.883†
Family History Density	−0.085	−0.062	−0.094	−0.115	−0.089	−0.071	−0.138	−0.126

SRED: Early drinking period SRE score; SRRD: Regular drinking period SRE score; SRHD: Heavy drinking period SRE score; SRTT: Total SRE score

[1] Log transformed for all participants

[2] Log transformed for African American subset

* $p<0.05$

† $p<0.01$

Table 3

Association of Level of Response and Recent Drinking History

Recent Drinking History Variable	Contributing Factors	All Participants			African American		
		β[1]	p	95% CI[2]	β[1]	p	95% CI[2]
Drinks/Drinking Day							
	SRTT[3]	0.331	0.007†	0.511, 3.027	0.342	0.008†	0.067, 0.433
	Gender	−0.217	0.099	−1.138, 0.100	−0.196	0.160	−1.087, 0.184
	Body Weight	−0.071	0.567	−0.021, 0.011	−0.006	0.965	−0.018, 0.017
	SRHD[4]	0.417	0.001†	0.090, 0.355	0.379	0.015†	0.366, 3.233
	Gender	−0.197	0.154	−1.165, 0.189	−0.095	0.555	−0.965, 0.525
	Body Weight	−0.090	0.509	−0.023, 0.012	−0.052	0.748	−0.023, 0.017
	SRRD[3,4]	0.495	<0.001††	1.367, 3.722	0.399	0.004†	0.686, 3.367
	Gender	−0.137	0.273	−0.923, 0.265	−0.148	0.295	−0.991, 0.307
	Body Weight	−0.099	0.401	−0.022, −0.009	−0.048	0.726	−0.021, 0.015
	SRED	0.249	0.040†	0.009, 0.370	0.312	0.016†	0.048, 0.443
	Gender	−0.278	0.034†	−1.281, −0.050	−0.212	0.131	−1.127, 0.150
	Body Weight	−0.101	0.433	−0.023, 0.010	−0.005	0.969	−0.018, 0.018
Quantity[3,4]							
	SRTT[3]	0.361	0.001†	0.289, 1.150	0.369	0.001†	0.044, 0.160
	Gender	−0.366	0.003†	−0.537, −0.114	−0.509	<0.001††	−0.645, −0.240
	Body Weight	−0.286	0.015†	−0.012, −0.001	−0.413	0.001†	−0.016, −0.005
	SRHD[4]	0.365	0.004†	0.022, 0.110	0.380	0.005†	0.198, 1.066
	Gender	−0.337	0.014†	−0.505, −0.059	−0.448	0.002†	−0.589, −0.138
	Body Weight	−0.289	0.032†	−0.012, −0.001	−0.469	0.002†	−0.016, −0.004
	SRRD[3,4]	0.370	0.002†	0.270, 1.128	0.377	0.002†	0.282, 1.144

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Recent Drinking History Variable	Contributing Factors	All Participants			African American		
		β[1]	p	95% CI[2]	β[1]	p	95% CI[2]
	Gender	−0.341	0.007†	−0.523, −0.086	−0.472	<0.001††	−0.623, −0.201
	Body Weight	−0.307	0.010†	−0.013, −0.002	−0.451	<0.001††	−0.017, −0.005
	SRED	0.220	0.053	−0.001, 0.126	0.297	0.008†	0.024, 0.153
	Gender	−0.442	0.001†	−0.610, −0.178	−0.534	<0.001††	−0.673, −0.256
	Body Weight	−0.310	0.012†	−0.013, 0.002	−0.408	0.001†	−0.016, −0.004

SRED: Early drinking period SRE score; SRRD: Regular drinking period SRE score; SRHD: Heavy drinking period SRE score; SRTT: Total SRE score

Weighted Least Squares Regression - Weighted by Sib pair number

[1] Standardized β

[2] CI - Confidence Interval

[3] Log transformed for all participants

[4] Log transformed for African American participants

† p<0.05

†† p<.001

Table 4

Heritability of Level of Response

	All Participants				African American Participants			
	h^2r	SE[a]	p	95% CI[b]	h^2r	SE[a]	p	95% CI[b]
SRED[c]	0.13	0.31	0.339	(−0.48, 0.74)	0.44	0.33	0.095	(−0.21, 1.09)
SRRD[c,d]	0.52	0.33	0.068	(−0.13, 1.17)	-	-	-	-
SRHD[c]	0.19	0.39	0.318	(−0.57, 0.95)	0.22	0.30	0.238	(−0.37, 0.81)
SRTT	0.67	0.31	0.025	(0.06, 1.28)	0.70	0.37	0.045	(−0.03, 1.43)

SRED: Early drinking period SRE score; SRRD: Regular drinking period SRE score; SRHD: Heavy drinking period SRE score; SRTT: Total SRE score

[a] Standard Error

[b] Confidence Interval

[c] Log transformed for African American subset

[d] SRRD was not determined for the African American subset in this analysis