HHS Public Access

Author manuscript

Alcohol Clin Exp Res. Author manuscript; available in PMC 2020 July 01.

Published in final edited form as:

Alcohol Clin Exp Res. 2019 July ; 43(7): 1384–1390. doi:10.1111/acer.14038.

Performance of the Self-Report of the Effects of Alcohol (SRE) Questionnaire Across Sexes and Generations

Marc A. Schuckit, M.D[1], **Tom L. Smith, Ph.D**[1], **Brinda Rana, M.S**[1], **Lee Ann Mendoza, B.S**[1], **Dennis Clarke, B.A**[1], and **Mari Kawamura, B.S**[1]

[1]University of California, San Diego, Department of Psychiatry, 8950 Villa La Jolla Dr, Suite B-218, La Jolla, California, United States, 92037

Abstract

Background: Low responses (low LRs) to alcohol established using the Self Report of Effects of alcohol (SRE) questionnaire are genetically-influenced phenotypes related to heavy drinking and alcohol problems. To date, most studies using SREs focused on scores for the number of drinks needed for effects the first five times drinking (SRE-5), and few evaluated scores that also included the prior 3-months and heaviest drinking periods (SRE-T). This paper evaluates characteristics of SRE-5 and SRE-T within and across generations.

Methods: Data were extracted from 407 participants across two generations of 107 families in the San Diego Prospective Study (SDPS). Pearson Product Moment correlations for SRE-5 and SRE-T were determined across first degree relatives both within and across generations and sexes, as well as correlations of each measure to maximum drinking quantities and alcohol problems.

Results: Responding to four hypotheses, the analyses first demonstrated significant within-generation positive correlations for both SRE measures across brother-brother and sister-sister pairs as well as for cross-generation correlations for fathers and sons, although correlations for mothers and daughters were not robust. Second, both SRE-5 and SRE-T correlated with maximum drinks and alcohol problems for both sexes and both generations. Third, within parental and offspring generations SRE-T correlated more robustly than SRE-5 to maximum drinks and alcohol problems. Fourth, across generations SRE values for sons were more closely related to drinking quantities and problems than for their fathers, but the mother-daughter SRE relationships to adverse alcohol characteristics were not different.

Conclusions: Both the SRE-5 and SRE-T offered useful information about propensities toward heavier drinking and alcohol problems in SDPS families. Correlations with adverse alcohol outcomes were greater for the more broad-based SRE-T, but both scores appeared to be genetically influenced and continue to operate in a robust manner in both generations of these families.

Keywords

heavy drinking; alcohol problems; level of response; self-report of the effects of alcohol questionnaire

Corresponding Author: Marc A. Schuckit, M.D., Distinguished Professor of Psychiatry, School of Medicine, University of California, San Diego, 8950 Villa La Jolla Drive, Suite B-218, La Jolla, CA 92037, Tel: (858) 822-0880; Fax: (858) 822-1002, mschuckit@ucsd.edu.

Introduction

A low level of response (low LR) to alcohol as measured at peak and declining blood alcohol concentrations (BACs) is one of several genetically-influenced characteristics that can be identified early in a person's drinking career and that predict later heavier drinking and alcohol problems (King et al., 2014; Schuckit, 2018). Low LRs can be determined through alcohol challenges where individuals carrying an elevated risk for alcohol problems and appropriate controls are given alcohol and the intensity of responses over time are observed regarding subjective feelings of intoxication as well as alcohol-related changes in physiological measures (e.g., Ehlers et al., 1999; King et al., 2014; Paulus et al., 2012; Schuckit and Gold, 1988; Schuckit et al, 1988). Alcohol-challenge based LR values have been reliably shown to relate to future heavier drinking, alcohol problems and alcohol use disorders (AUDs) (Schuckit et al., 2016; Schuckit and Smith, 1996).

However, alcohol challenges are expensive and time-consuming to carry out, characteristics that preclude large scale studies of LR. In response to this problem, our group developed a 12-item retrospective self-report measure of LR, the Self-Report of the Effects of Alcohol (SRE) questionnaire, where a person records the number of standard (10–12 ounces of ethanol) drinks required across four possible effects as measured across three timeframes (Schuckit et al., 2018). The effects evaluated include the number of drinks to first feel any effect of alcohol, drinks required to actually experience slurring speech, unsteady gait, and unwanted falling asleep. The three timeframes evaluated are the approximate first five times of ad lib drinking, the period of heaviest alcohol consumption, and the most recent 3 months. The SRE instrument can be found in PhenX.

The most commonly used SRE score is the value for the approximate first five times of drinking, the SRE-5, that potentially reflects alcohol sensitivity observed before the development of repetitive heavier drinking that might contribute to intersession tolerance (Schuckit, 2018). Less often mentioned in the literature is the more broad-based SRE Total (SRE-T) score that is based on the average drinks needed for up to four effects across all three timeframes (first five times, period of heaviest drinking, and recent three months), an approach that potentially reflects both sensitivity and the development of tolerance related to repeated drinking (e.g., Lai et al., submitted; Schuckit, 2018). Using the SRE, a higher number of drinks required for effects indicates a lower LR per drink.

SRE values have retest reliabilities and predictive validities regarding drinking quantities and alcohol-related problems of 0.70 or higher (Kalu et al., 2008; Ray et al., 2011; Schuckit et al, 1997), and lower or higher designations of LR remain relatively consistent as drinkers age (Schuckit and Smith, 2012). Because a low LR is hypothesized to impact on how much a person drinks per occasion and does not relate closely to impulsivity, LR does not correlate highly with drinking frequency (Schuckit, 2018). Examples of significant positive correlations between SRE scores and future heavier alcohol intake and alcohol problems include data from the San Diego Prospective Study (SDPS), the Collaborative Study of the Genetics of Alcoholism (COGA), the U.K.-based Avon Longitudinal Study of Parents and Children (ALSPAC), and others (e.g.,Chung and Martin, 2009; Goncalvez et al., 2017a,

2017b; Schuckit et al., 2007a; 2008; Schuckit and Smith, 1996). SRE-based LR values are higher in men than women (i.e., men have a lower LR per drink) (Eng et al., 2005; Schuckit et al., 2000; 2011; 2012b, 2016) and European Americans (EAs) compared to African Americans (AAs) and Asian individuals (Luczak et al 2002; 2006; Park et al., 2018; Pederson et al, 2009). However, within each sex and ethnic/racial group lower LR values (higher SRE scores) correlate with heavier drinking and alcohol problems (e.g., Schuckit et al., 2004; 2012). Several cross-sectional and longitudinal studies of drinkers indicate higher values for SRE-T than for SRE-5 (e.g., Schuckit and Smith, 2012).

LR values measured by either alcohol challenges or retrospective questionnaires are genetically influenced. This conclusion is supported by family, sibling-pair, and twin studies that together indicate a heritability between 40% and 60% (Lai et al., submitted; Heath et al., 1999; Kalu et al 2012; Schuckit et al, 2001; Viken et al., 2003).

To date, relatively few studies have directly evaluated SRE-5 and SRE-T correlations across men and women in the same families or whether the correlates of those LR values are consistent from one generation to the next. Such evaluations are important because they could add to our understanding of whether SRE scores and correlates were limited to the original generation, perhaps reflecting the impact of the second parent's genes and the differences across cohorts regarding drinking norms and practices (Seglem et al., 2016; White et al., 2015). In order to begin to evaluate aspects of the relative performance of SRE-5 and SRE-T across sexes and across generations, our group published data from the 25-year follow-up of SDPS families regarding drinking offspring at an average age of 20 years (Schuckit et al., 2007b; 2012a). Structural equation model evaluations of potential mediators of the relationship of SRE-based LR to later heavier drinking and alcohol problems were similar across generations (Schuckit et al., 2012a). However, the analyses were carried out when offspring were relatively young, did not include SRE-T scores, did not include direct comparisons of SRE-related attributes across the two generations, and analyses focused on fathers of these offspring but did not consider data regarding the offsprings' mothers.

The current analyses extend prior work to an older sample of drinking SDPS offspring while directly evaluating both SRE-5 and SRE-T performance and correlates across the generations and across the sexes. The goal is to address four hypotheses. Hypothesis 1 proposes that SRE-5 and SRE-T scores will correlate positively and significantly among first-degree relatives. This will be true both within and across generations. In Hypothesis 2, because SRE-T values potentially relates to both alcohol sensitivity and intersession tolerance, correlations to maximum drinks and alcohol problems will be greater for SRE-T than SRE-5. Hypothesis 3 states that within both the parent and offspring generations higher SRE-5 and SRE-T scores will positively and significantly correlate with higher maximum drinking quantities and the number of alcohol-related problems. Finally, Hypothesis 4 proposes that correlations of SRE scores with maximum drinks and alcohol problems will be similar in parental and offspring generations.

Methods

Subjects, interviews, and questionnaires

Using procedures approved by the University of California, San Diego (UCSD), Human Research Protections Committee, the data described below were gathered during several phases in the course of the SDPS. Between 1978 and 1988, each year the original probands were identified from a mailed questionnaire that asked students to report their demography and substance use patterns and problems (Schuckit and Gold, 1988). To be eligible for the next stage of the study, a student had to be age 18 to 25 years (old enough to give consent but not too old as to have passed through the usual age of onset of alcohol dependence), with exclusions for potential participants who ever met criteria for alcohol or illicit drug dependence, bipolar disorder or schizophrenia using the Diagnostic and Statistical Manual (DSM) criteria (e.g., American Psychiatric Association, 1994). Appropriate probands were originally evaluated using alcohol challenges where, on rising, peak and falling BACs (peak BAC averaged about 60 mg/dl), they reported subjective feelings of intoxication, and were evaluated for changes in standing steadiness (body sway), and, depending on the specific paradigm, the research team recorded physiological measures (e.g., blood cortisol, background electroencephalograms, event related potentials) (Ehlers et al.,1999; Schuckit and Gold, 1988; Schuckit et al., 1988).

Probands were then followed about every five years regarding demography as well as alcohol, smoking and illicit drug use and related problems using questions derived from the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) instrument. The SSAGA has validity, retest reliabilities, and cross-interviewer reliabilities of .7–.8 regarding alcohol-related items (Bucholz et al.,1994; Hesselbrock et al.,1999).

The age 35 evaluation of probands (i.e., 15 years after recruitment) included the then recently developed SRE regarding drinks required across effects the approximate first five times of drinking, the time of heaviest drinking, and drinks required for effects during the three months prior to interview (Schuckit, 2018; Schuckit et al., 1997). The instrument was developed to facilitate collecting LR data on large numbers of individuals at relatively little cost and without requiring travel to a research center to undergo a time-consuming laboratory-based alcohol challenge. The SRE score for any timeframe is the sum of the number of drinks reported across the range of effects actually experienced in that timeframe (e.g., first five times or the combined first five times, recent three months, and period of heaviest drinking) divided by the number of effects reported. This questionnaire has a literature-based Cronbach's α >.95, retest reliabilities as high as .8, correlates with the alcohol challenge in predicting future heavy drinking at about .60 (Ray et al., 2011; Schuckit et al., 1997), and, as described in the Introduction, performs similarly to the alcohol challenge-based LR in predicting alcohol outcomes.

Over time, probands' spouses and children age 18 or older were asked to participate in the SDPS protocol. Beginning at the time of the proband's age 35 interview these spouses and offspring age ≥ age 18 were interviewed with an adult SSAGA-based instrument similar to the one used with probands to evaluate their own demography, alcohol, and drug-related

histories. If that relative had consumed at least a full drink on any occasion they also filled out the SRE questionnaire.

Data analyses

The sample reported here was limited to offspring age 18 or older who had consumed alcohol for optimal interpretation of the SRE. The data regarding the offspring presented in the tables were collected during the most recent interview when the proband was approximately age 57, a step required to include the sons and daughters who met the age requirement for informed consent and who had a drinking history that was appropriate for the SRE. Once an offspring was selected, data were gathered from the relevant proband and offsprings' mothers. Among the 407 individuals included in these analyses, results were evaluated separately for the 107 original probands (fathers of the offspring) and the 88 mothers as the parental generation, and the 115 sons and 97 daughters as the offspring generation. Statistical analyses across groups were carried out using ANOVA for means and standard deviations (SD) for continuous variables and chi square (x^2) for categorical data. The statistical evaluations were conducted on appropriately transformed variables.

The following approach for Tables 3 and 4 used a modified bootstrap procedure without replacement in R (R Core Team, 2013). In this approach the procedure was the same whether the analyses required separating data for sex of parents, sex of offspring or when combining both sexes within parents or offspring. Here, subjects were first grouped by family, after which a subset of data was generated based on the desired family members (e.g., fathers and sons) and the relevant variable (e.g., SRE-5). Two samples were then generated by using the sample _n function from the dplyr library in R (Wickham et al., 2018), which selected a target parent and a random offspring or randomly selected pairs of offspring. Then, Pearson Product Moment correlations were run with rcorr (Harrell, 2018). The sampling and correlations were done 1000 times. Finally, using the fisherz2r function for Fisher Z transformations (Revell, 2018), an average Pearson Product Moment correlation was computed. Analyses were done using the Statistical Package for the Social Sciences (SPSS Inc, 2009) and R (R Core Team, 2013).

Results

To help place the SRE findings into perspective, the analyses began with a comparison of demography across fathers, mothers, sons and daughters in the 107 families that contributed to these data. As shown in the upper portion of Table 1, the large majority of subjects self-reported an EA heritage. Within generations, fathers and mothers were about age 40 at the time of filling out the SRE (mothers filled out the SRE about three years later than fathers), and sons and daughters about age 28. In these relatively highly educated families, fathers had more years of education than mothers, and daughters more years of education than sons. Looking across generations, the fathers were more highly educated than sons, although mothers and daughters reported similar years of education.

Turning to alcohol-related variables in the lower portion of Table 1, within generations both SRE-5 and SRE-T values were higher in males than females (i.e., males reported needing more drinks for effects, or a lower LR per drink). Similarly, within each generation, males

reported higher lifetime maximum drinking quantities, more of the 11 DSM-IV alcohol problems (American Psychiatric Association, 1994), and were more likely to fulfill criteria for lifetime alcohol dependence or abuse. These drinking figures are for lifetime up to the time of the interview used here.

Across generations, SRE-T scores were similar for sons and fathers, but daughters had significantly higher SRE-T values than mothers. For both sexes offspring had higher values than the same sex parent for maximum drinking quantities, the number of alcohol problems, and for alcohol dependence and abuse (statistical analyses focused on abuse and dependence combined).

Relevant to Hypothesis 1, the data in Tables 2 and 3 use Pearson Product Moment correlations to compare SRE-5 and SRE-T values across first degree relatives. Within generations, Table 2 indicates that brother-brother and sister-sister pairs correlated at between .35 and .55 for SRE-5 and SRE-T, but SREs for unrelated offspring correlated about zero. These same-sex sibling correlations indicate a possible heritabiliy of 53% for SRE-5 and 39.5% for SRE-T. Across generations, Table 3 demonstrates that father-sons SRE-T values correlated significantly, with nonsignificant differences for SRE-5 correlations across generations. Mother-daughter SRE-5 and SRE-T scores were positive in sign but correlations were not significant. Neither parent's SRE values correlated significantly with SRE scores for opposite sex offspring. Note that cross-generation SRE correlations were mostly close to zero for unrelated parent-offspring pairs, and none were significant.

The data in Table 4 evaluate Hypotheses 2–4. Related to Hypothesis 2, as shown in the columns labeled SRE-5 vs SRE-T difference, SRE-T correlations with maximum drinks and the number of alcohol problems were higher than SRE-5 correlations in all but one of the correlations. Hypothesis 3 predicted that higher SRE-5 and SRE-T values will correlate significantly with higher maximum drinks and more alcohol problems in both sexes and both generations. That prediction was supported with significant correlations of SRE-5, with maximum drinks of .28 to .67 and SRE-T correlations of .54 to .84.

Table 4 data also address Hypothesis 4, which predicted that the correlations of SRE scores with heavier drinking and alcohol problems would be similar across generations. However, contrary to the hypothesis, correlations of the two SRE scores with drinking-related outcomes were higher for the combined offspring compared to the combined parents. Closer inspection of the table indicates that this pattern appears to apply to fathers versus sons where SRE-5 differences and SRE-T differences were both significant ($z=3.72$, $p=.002$ and $z=3.80$, $p<.001$, respectively) but not mothers versus daughters ($z=0.39$. $p=.70$ and $z=0.05$, $p=.62$ for SRE-5 and SRE-T, respectively).

Discussion

These analyses evaluated how a relatively simple retrospective measure of a genetically influenced phenotype, the low LR to alcohol, operates across sexes and across generations. The results offered support for three of the hypotheses, and demonstrated unpredicted results for the fourth. In these evaluations the SRE continued to relate to heavier drinking and the

number of alcohol problems in both men and women in both generations and correlated significantly across first degree relatives. These analyses represent the first extensive comparison of the performance of SRE-T with SRE-5 in the same subjects.

Supporting Hypothesis 1, both SRE-5 and SRE-T scores correlated positively and significantly across first-degree relatives. This was most robust within generations, with positive and significant but less consistent relationships across generations. This is one of the first evaluations of this question for SRE-T (see also Lai et al., submitted) and the SRE-5 results are consistent with several prior reports from the SDPS, COGA, and ALSPAC (Schuckit et al., 2001; 2005; 2008).

The confirmation in a study of cross-generation correlations for SRE-5 and the expansion of these data to SRE-T are important for several reasons. First, these data add confidence to the conclusion that both scores from a simple retrospective measure of LR are familial and genetically influenced. Second, the demonstration of relatively robust correlations among brother-brother, sister-sister and father-son pairs, with a similar but nonsignificant pattern for mother-daughter pairs also indicates a genetic influence for SRE-T scores. Estimated heritability SRE-5 and SRE-T for same sex siblings were 53% and 39.5%, respectively. The conclusion that SRE-T scores are genetically influenced is also supported by a recent large-scale genome-wide association study (GWAS) that reported significant heritability for this measure and identified several gene variations with significance values of 10^{-8} or better (Lai et al, in submission).

Regarding Hypothesis 2, SRE-T scores correlated more closely with heavy drinking and alcohol problems than SRE-5. This result is consistent with the concept that SRE-5 might primarily reflect a person’s sensitivity to alcohol, whereas SRE-T values are also likely to reflect the depth of development of intersession alcohol tolerance. It is also possible that the stronger association of SRE-T to alcohol problems might reflect the combination of three timeframes in that measure compared to the single timeframe for SRE-5. While the relative performance of the two SRE measures had been noted in a few prior studies (e.g., Schuckit and Smith, 2012), a direct comparison of the two scores across multiple generations and across men and women had not been reported before. Hopefully, these results will encourage future investigators to include both measures in future studies.

Positive results regarding Hypothesis 2 raise the possibility that the difference between SRE-5 and SRE-T might be evaluated as a potentially more standardized way to retrospectively and relatively inexpensively evaluate acquired tolerance. Major diagnostic manuals include tolerance as an important criterion for AUDs (e.g., American Psychiatric Association,1994; World Health Organization 1992). Those diagnostic systems currently often depend on unstructured, retrospective, subjective evaluations of whether tolerance occurred, and, to date, there is no gold standard of how to retrospectively evaluate the change in intensity of response to alcohol over time. Rather than asking a person if they ever required more drinks to get the effect previously experienced with fewer drinks, the SRE potentially quantitatively assesses tolerance by recording a person’s perception of actual quantities required for specific effects at different periods in their lives.

Hypothesis 3 addressed a key question regarding the potential clinical and research-related usefulness of SRE scores, the correlations of these measures with heavier drinking and alcohol problems. These outcomes are the two major correlates of LR. In the current analyses those two outcomes were correlated with both SRE-5 and SRE-T in members of both generations and in both men and women.

Regarding Hypothesis 4, our group was concerned that the relationships of SRE scores to maximum drinks and alcohol problems might diminish in a second generation. This could have reflected cohort-related changes in attitudes about drinking and related problems and occurred because the SRE values related to either parent would be diluted by characteristics of the second parent. The results, however, revealed unexpected higher offspring SRE-5 and SRE-T correlations with maximum drinks and alcohol problems compared to the parent generation. That observation is reassuring regarding the potential clinical usefulness of the SRE scores as correlates of problematic drinking in new generations of drinkers.

When cross-generation correlations of SRE scores with maximum drinks and alcohol problems were broken down by sex, most of the cross-generation findings were explained by father-son pairs, with only non-significant mother-daughter differences. Potential explanations for these sex differences might be the higher absolute values for drinking quantities and problems in males which resulted in a wider range of values for correlations, or potential cross-generational sex-related differences in attitudes such as levels of permissiveness for heavier drinking in males versus females (McCabe, 2002; Nichol et al., 2007; Salvatore et al., 2017; Weisbeck, 2003). Such possibilities are supported by data regarding secular trends in the lifetime prevalence of heavy drinking and alcohol problems (Grucza, et al., 2008) and cohort effects for drinking practices over the years (Kapoor et al., 2017). Also, sex differences in attitudinal influences (e.g., the impact of heavier drinking peers and more positive alcohol expectancies) might help explain the greater relationship of a low LR to heavier drinking in males in the younger generations as the impact of heavier drinking peers and more positive alcohol expectancies have been shown to mediate how a low LR relates to higher drinking maximums and alcohol problems (Salvatore et al.,2017; Schuckit et al., 2017). Another possible explanation might rest with the fact that more than half of a person's LR values relate to the environment and that in these families 19% of the fathers but only 5% of the mothers were alcohol dependent, with the possibilities that the model of heavy drinking in the same sex parent might have had a greater impact on sons than daughters.

As with all studies, the current results must be considered in the context of the methods used. First, the subjects in the SDPS are almost all of EA descent and most offspring come from families with relatively highly educated parents, raising the question of whether the results are likely to generalize to less educated subjects. However, support for the current findings regarding SRE-5 comes from two COGA- based papers reporting data across two generations of what are generally lower educated and lower socioeconomic families (Schuckit et al., 2001, 2005). Second, all correlations reported here are cross sectional and it will be important to evaluate similar hypotheses in a prospective model. Third, a caveat inherent in all measures of LR is that this characteristic can only be evaluated in individuals who have had experience with alcohol. Fourth, the distinction between the aspects of

drinking reaction related to SRE-5 versus SRE-T (i.e., more sensitivity for the former but both sensitivity and intersession tolerance for the latter) are hypothetical and difficult to prove. Fifth, it is important to remember that a person's response to alcohol can be measured several ways (King et al., 2014; Schuckit, 2018), including the level of stimulation experienced early in a drinking occasion which is also related to future escalations in drinking quantities and problems (King et al., 2014). Alcohol stimulation during rising blood alcohol concentrations (BACs) cannot be measured with the SRE. Sixth, the sample reported on here is modest in size, and some of the non-significant findings in Tables 3 and 4 might be significant in larger studies. Finally, the heritability estimates for same-sex siblings offered here do not fully consider the impact of shared family environment.

In conclusion, both the SRE-5 and SRE-T scores from the simple retrospective measure of LR offered useful information about the propensity to heavier drinking and alcohol problems in these families for the SDPS. Correlations with adverse alcohol outcomes are greater from the more broad-based SRE-T, but both scores are likely to be genetically influenced and continue to operate in a robust manner in both generations of these families.

Acknowledgments

This work is supported by a NIH/NIAAA grant number R01 AA021162

References

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

Baraona E, Abittan CS, Dohmen K, et al. (2001) Sex differences in pharmacokinetics of alcohol. Alcohol Clin Exp Res 25:502–507. [PubMed: 11329488]

Bucholz KK, Cadoret R, Cloninger CR, Dinwiddie SH, Hesselbrock VM, Nurnberger JI Jr, Reich T, Schmidt I (1994) A new, semi-structured psychiatric interview for use in a genetic linkage studies: a report on the reliability of the SSAGA. J Stud Alcohol 55:149–158. [PubMed: 8189735]

Chermack ST, Stoltenberg SF, Fuller Be, Blow FC (2000) Sex differences in the development of substance-related problems: the impact of family history of alcoholism, family history of violence and childhood conduct problems. J Stud Alcohol 61:845–852. [PubMed: 11188490]

Chung T, Martin CS (2009) Subjective stimulant and sedative effects of alcohol during early drinking experiences predict alcohol involvement in treated adolescents. J Stud Alcohol Drugs 70:660–667. [PubMed: 19737489]

Ehlers CL, Garcia-Andrade C, Wall TL, Cloutier D, Phillips E (1999) Electroencephalographic responses to alcohol challenge in Native American Mission Indians. Biol Psychiatry 45:776–787. [PubMed: 10188009]

Eng MY, Schuckit MA, Smith TL (2005) The level of response to alcohol in daughters of alcoholics and controls. Drug Alcohol Depend 79:83–93. [PubMed: 15943947]

Goncalves PD, Smith TL, Anthenelli RM, Danko G, Schuckit MA (2017) Alcohol-related blackouts among college students: impact of low level of response to alcohol, ethnicity, sex and environmental characteristics. Rev Bras Psiquiatr 40:128–137. [PubMed: 28876407]

Goncalves PS, Schuckit MA, Smith TL (2017) Drinking Status Between Ages 50 and 55 for Men from the San Diego Prospective Study who Developed DSM-IV Alcohol Abuse or Dependence in Prior Follow-Ups. J Stud Alcohol Drugs 78:512–520. [PubMed: 28728633]

Grucza RA, Bucholz KK, Rice JP, Bierut LJ (2008) Secular trends in the lifetime prevalence of alcohol dependence in the United States: a re-evaluation. Alcohol Clin Exp Res 32:763–770. [PubMed: 18336633]

Harrell FE Jr, Dupont C, et al. (2018) Hmisc:Harrell Miscellaneous. R package version 4.1–1 https://CRAN.R-project.org/package=Mmisc.

Heath AC, Madden PF, Bucholz KK, Dinwiddie SH, Slutske WS, Bierut LJ, Rohrbaugh JW, Statham DJ, Dunne MP, Whitfield JB, Martin NG (1999) Genetic differences in alcohol sensitivity and the inheritance of alcoholism risk. Psychol Med 29:1069–1081. [PubMed: 10576299]

Hesselbrock M, Easton C, Bucholz KK, Schuckit M, Hesselbrock V (1999) A validity study of the SSAGA – a comparison with the SCAN. Addiction 94:1361–1370. [PubMed: 10615721]

Kalu N, Ramchandani VA, Marshall V, Scott D, Ferguson C, Cain G, Taylor R (2012) Heritability of level of response and association with recent drinking history in non-alcohol dependent drinkers. Alcohol Clin Exp Res 36:1034–1041. [PubMed: 22235947]

Kapoor E, Collazo-Clavell ML, Faubion SS (2017) Weight Gain in Women at Midlife: A Concise Review of the Pathophysiology and Strategies for Management. Mayo Clin Proc 92:1552–1558. [PubMed: 28982486]

King AC, McNamara PJ, Hasin DS, Cao D (2014) Alcohol challenge responses predict future alcohol use disorder symptoms: a 6-year prospective study. Biol Psychiatry 75:798–806. [PubMed: 24094754]

Lai D, Wetheril L, Kapoor M, Johnson EC, Schwandt M, Ramchandani VA, Goldman D, Joslyn G, et al. (2018) Genome wide association studies of the Self-Rating of Effects of Ethanol (SRE). Neuropsychopharmacology, submitted

Luczak SE, Elvine-Kreis B, Shea SH, Carr LG, Wall TL (2002) Genetic Risk for Alcoholism Relates to Level of Response to Alcohol in Asian-American Men and Women. J Stud Alcohol 63:74–82. [PubMed: 11925062]

Luczak SE, Glatt SJ, Wall TL (2006) Meta-Analyses of ALDH2 and ADHIB with Alcohol Dependence in Asians. Psychological Bulletin 132:607–621. [PubMed: 16822169]

McCabe SE (2002) Sex differences in collegiate risk factors for heavy episodic drinking. J Stud Alcohol 63:49–56. [PubMed: 11925058]

Nichol PE, Kreuger RF, Iacono WG (2007) Investigating sex differences in alcohol problems: a latent trait modeling approach. Alcohol Clin Exp Res 31:783–794. [PubMed: 17386067]

Park Y, Stadlin A, Lee B, Kim S, Schuckit MA (2018) Korean version of the level of response to alcohol measured on the Self-Rating of the Effects of Alcohol Questionnaire in Korean medical students. J Korean Academy of Addiction Psychiatry 22:19–25.

Paulus MP, Schuckit MA, Tapert SF, Tolentino NJ, Matthews SC, Smith TL, Trim RS, Hall SA, Simmons AN (2012) High versus low level of response to alcohol: evidence of differential reactivity to emotional stimuli. Biol Psychiatry 72:848–855. [PubMed: 22608014]

Pedersen SL, McCarthy DM (2009) An Examination of Subjective Response to Alcohol in African Americans. J Stud Alcohol Drugs 70:288–295. [PubMed: 19261241]

R Core Team (2013) R: A language and environment of statistical computing R Foundation for Statistical Computing, Vienna, Austria http://www.R-project.org/.

Ray LA, Hart EJ, Chin PF (2011) Self-rating of the Effects of Alcohol (SRE): predictive utility and reliability across interview and self-report administrations. Addict Behav 36:241–243. [PubMed: 21095629]

Revelle W (2018) psych: Procedures for Personality and Psychological Research, Northwestern University, Evanston, Illinois, USA, https://CRAN.R-project.org/package=psychVersion=1.8.4.

Salvatore J, Sho S, Dick D (2017) Genes, environments, and sex differences in alcohol research. J Stud Alcohol Drugs 78:494–501. [PubMed: 28728631]

Schuckit MA (2018) A critical review of methods and results in the search for genetic contributors to alcohol sensitivity. Alcohol Clin Exp Res 42:822–835. [PubMed: 29623680]

Schuckit MA, Edenberg HJ, Kalmijn J, Flury L, Smith TL, Reich T, Bierut L, Goate A, and Foroud T (2001) A genome-wide search for genes that relate to a low level of response to alcohol. Alcohol Clin Exp Res 25:323–329. [PubMed: 11290841]

Schuckit MA, Gold EO (1988) A simultaneous evaluation of multiple markers of ethanol/placebo challenges in sons of alcoholics and controls. Arch Gen Psychiatry 45:211–216. [PubMed: 3422553]

Schuckit MA, Gold EO, Croot K, Finn P, Polich J (1988) P300 latency after ethanol ingestion in sons of alcoholics and in controls. Biol Psychiatry 24:310–315. [PubMed: 3401524]

Schuckit MA, Smith TL (1996) An 8-year follow-up of 450 sons of alcoholic and control subjects. Arch Gen Psychiatry 45:647–651.

Schuckit MA, Smith TL (2012) Stability of scores and correlations with drinking behaviors over 15 years for the Self-Report of the Effects of Alcohol Questionnaire. Drug Alcohol Depend 128:194–199. [PubMed: 22980675]

Schuckit MA, Smith TL (2017) Mediation of effects of the level of response to alcohol and impulsivity 15 years later in 36-year-old men: Implications for prevention efforts. Drug Alcohol Depend 180:356–362. [PubMed: 28954250]

Schuckit MA, Smith TL, Danko G, Kuperman S, Bierut LJ, Hesselbrock V (2005a) 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. [PubMed: 15830904]

Schuckit MA, Smith TL, Danko GP, Pierson J, Hesselbrock V, Bucholz KK, Kramer J, Kuperman S, Dietiker C, Brandon R, Chan G (2007a) 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. [PubMed: 17446976]

Schuckit MA, Smith TL, Eng MY, Kunovak J (2002) Women who marry men with alcohol-use disorders. Alcohol Clin Exp Res 26:1336–1343. [PubMed: 12351927]

Schuckit MA, Smith TL, Goncalves PD, Anthenelli R (2016) Alcohol-related blackouts across 55 weeks of college: Effects of European-American ethnicity, female sex, and low level of response to alcohol. Drug Alcohol Depend 169:163–170. [PubMed: 27835824]

Schuckit MA, Smith TL, Heron J, Hickman M, Macleod J, Lewis G, Davis JM, Hibbeln JR, Brown S, Zuccolo L, Miller LL, Davey-Smith G (2011) Testing a level of response to Alcohol-Based Model of Heavy Drinking and alcohol problems in 1,905 17-year-olds. Alcohol Clin Exp Res 35:1897–1904. [PubMed: 21762180]

Schuckit MA, Smith TL, Kalmijn J (2004) Findings across subgroups regarding the level of response to alcohol as a risk factor for alcohol use disorders: a college population of women and Latinos. Alcohol Clin Exp Res 28:1499–1508. [PubMed: 15597082]

Schuckit MA, Smith TL, Kalmijn J, Trim RS, Cesario E, Saunders G, Sanchez C, Campbell N (2012a) Comparison across two generations of prospective models of how the low level of response to alcohol affects alcohol outcomes. J Stud Alcohol Drugs 73:195–204. [PubMed: 22333327]

Schuckit MA, Smith TL, Kalmijn JA, Tsuang J, Hesselbrock V, Bucholz K (2000) Response to alcohol in daughters of alcoholics: a pilot study and a comparison with sons of alcoholics. Alcohol Alcohol 35:242–248. [PubMed: 10869242]

Schuckit MA, Smith TL, Pierson J, Danko GP, Allen RC, Kreikebaum S (2007b) Patterns and correlates of drinking in offspring from the San Diego Prospective Study. Alcohol Clin Exp Res 31:1681–1691. [PubMed: 17651467]

Schuckit MA, Smith TL, Tipp JE (1997) The Self-Rating of the Effects of Alcohol (SRE) form as a retrospective measure of the risk for alcoholism. Addiction 92:979–988. [PubMed: 9376780]

Schuckit MA, Smith TL, Trim RS, Heron J, Horwood J, Davis J, Hibbeln J, ALSPAC Study Team (2008) The Self-Rating of the Effects of Alcohol Questionnaire as a predictor of alcohol-related outcomes in 12-year-old subjects. Alcohol and Alcoholism 43:641–646. [PubMed: 18845530]

Schuckit MA, Smith TL, Trim RS, Kuperman S, Kramer J, Hesselbrock V, Bucholz KK, Nurnberger JI Jr, Hesselbrock M, Saunders G (2012) Sex differences in how a low sensitivity to alcohol relates to later heavy drinking. Drug and Alcohol Review 31:871–880. [PubMed: 22708705]

Seglem K, Waaktaar T, Ask H, Torgersen S (2016) Sex differences in genetic and environmental contributions to alcohol consumption from early adolescence to young adulthood. J Stud Alcohol Drugs 111:1188–1195.

Viken RJ, Rose RJ, Morzorati SL, Christian JC, Li TK (2003) Subjective intoxication in response to alcohol challenge: heritability and covariation with personality, breath alcohol level, and drinking history. Alcohol Clin Exp Res 27:795–803. [PubMed: 12766624]

Weisbeck G (2003) Gender-specific Issues in Alcoholism – Introduction. Arch Women's Ment Health 6:223–224. [PubMed: 14628172]

White A, Castle I-J, Shirley M, Roach D, Hignson R (2015) Converging patterns of alcohol use and related outcomes among females and males in the United States, 2002 to 2012. Alcohol Clin Exp Res 39:1712–1726. [PubMed: 26331879]

Wickham H, Francois R, Henry L, Muller K (2018) dplyr: A Grammar of Data Manipulation. R package version 0.7.6 https://CRAN.R-project.org/package=dplyr.

Wilsnack RW, Vogeltanz ND, Wilsnack SC, et al. (2000) Sex differences in alcohol consumption and adverse drinking consequences: cross-cultural patterns. Addiction 95:251–265. [PubMed: 10723854]

World Health Organization (1992) The ICD-10 Classification of Mental and Behavioral Disorders Geneva, World Health Organization.

Table 1

Demography and Alcohol Related Characteristics for Fathers, Mothers, and Offspring [% or Mean [(SD)]

Groups	1 Fathers (N=107)	2 Mothers (N=88)	3 Sons (N=115)	4 Daughters (N=97)	Statistics t-value or x^2 Within Generations Across Generations			
Demography					1 vs. 2	3 vs. 4	1 vs.3	2 vs. 4
Age (years)	38.2 (2.86)	41.6 (4.03)	27.6 (5.1)	28.1 (5.0)	−6.86^{c}	−0.74	18.90^{c}	20.01^{c}
Years of Education	17.9 (2.33)	16.0 (2.43)	15.2 (2.50)	16.1 (2.13)	5.64^{c}	−2.70^{b}	8.42^{c}	−0.18
Ever Married (%)	99.1	100	32.2	41.2	0.83	1.87	108.20^{c}	74.74^{c}
European-American [EA] %	96.3	93.2	93.9	95.9	0.94	0.41	0.65	0.66
Alcohol								
SRE-5	3.2 (1.45)	2.4 (1.23)	3.3 (1.39)	2.6 (1.20)	4.37^{c}	3.89^{c}	−0.81	−1.38
SRE-T	4.1 (1.60)	2.9 (1.31)	4.4 (1.86)	3.2 (1.23)	6.21^{c}	4.87^{c}	−0.94	−2.13^{a}
Maximum Drinks/Occasion *	6.9 (3.78)	3.5 (2.18)	9.8 (4.57)	6.8 (3.02)	8.31^{c}	4.73^{c}	−4.74^{c}	−8.86^{c}
Number of 11 DSM-IV Alcohol Problems *	1.8 (2.30)	0.6 (1.66)	3.2 (2.91)	2.1 (2.42)	5.39^{c}	2.66 ^{b}	−3.38^{c}	−5.65^{c}
DSM-IV Alcohol Disorder * Dependent (%) Abuse (%)	18.7 10.3	4.5 6.8	43.5 18.3	22.7 17.5	10.41^{b}	11.79^{b}	24.26^{c}	20.27^{c}

DSM-IV = Fourth Diagnostic and Statistical Manual (American Psychiatric Association, 1994); SRE-5 = the Self Report of the Effects of Alcohol questionnaire score for the approximate first 5 times drinking; SRE-T = the total SRE score.

Statistics conducted on appropriately transformed values.

Superscripts:

^{a} = p < .05

^{b} = p < .01

^{c} = p < .001

* = Lifetime

Table 2

Pearson Product Moment Correlations of SRE-5 and SRE-T Among Brother-Brother, Sister-Sister, and Unrelated Sibling Pairs

Pairs of Offspring	SRE-5	SRE-T
Brother-Brother (N=32)	.55[a]	.35[a]
Sister-Sister (N=22)	.51[b]	.44[a]
Unrelated Males (N=40)	−.00	.00
Unrelated Females (N=40)	.01	.00

Abbreviations are described in Table 1.

Statistics conducted on square root transformed values.

Superscript:

[a] = $p < .05$

[b] = $p < .01$.

Table 3

Pearson Product Moment Correlations of SRE-5 and SRE-T for Fathers and Mothers with Sons and Daughters

	Fathers (N=107)		Mothers (N=88)	
Group	**SRE-5**	**SRE-T**	**SRE-5**	**SRE-T**
Sons (N=115)	.16[x]	.22[a]	.01	−.01
Daughters (N=97)	.02	.04	.19[xx]	.15
Unrelated Sons	−.00	.00	−.00	.03
Unrelated Daughters	−.01	−.11	.04	−.00

Abbreviations are described in Table 1.

Statistics conducted on square root transformed values.

Superscript:

[a] = p < .05

[b] = p < .01

[c] = p < .001

[x] = p < .08

[xx] = p < .07

Table 4

Pearson Product Moment Correlations of SRE-5 and SRE-T values to Maximum Drinks and Number of DSM-IV Alcohol Problems for Fathers, Mothers, Sons and Daughters

Group	Maximum Drinks			Alcohol Problems		
	SRE-5	SRE-T	SRE-5 vs. SRE-T Difference*	SRE-5	SRE-T	SRE-5 vs. SRE-T Difference*
Parents						
Fathers (N=107)	.28^{b}	.54^{c}	3.91^{c}	.10	.33^{c}	3.15^{b}
Mothers (N=88)	.37^{c}	.64^{c}	5.00^{c}	.42^{c}	.53^{c}	1.91^{x}
Parent Combined (N=195)	.41^{c}	.66^{c}	7.56^{c}	.31^{c}	.49^{c} .55^{c}	4.78^{c}
Offspring						
Sons (N=115)	.67^{c}	.84^{c}	4.72^{c}	.60^{c}	.72^{c}	2.71^{b}
Daughters (N=97)	.43^{c}	.69^{c}	5.51^{c}	.42^{c}	.64^{c}	4.43^{c}
Offspring Combined (N=212)	.61^{c}	.81^{c}	8.22^{c}	.54^{c}	.69^{c}	5.12^{c}
Parents Combined vs. Offspring Combined	2.73^{b}	3.34^{c}		2.84^{b}	3.12^{b}	

Abbreviations are described in Table 1.

Both SRE variables were square root transformed, maximum drinks variable was log transformed, and alcohol problems variable was inverse transformed.

*Difference between SRE-5 and SRE-T correlations with maximum drinks and (separately) for number of alcohol problems for fathers, mothers, parents combined and sons, daughters and offspring combined as evaluated by z-scores for the differences.

Superscript:

^{a}= p < .05

^{b}= p < .01

^{c}= p < .001

^{x}= p <.057.