

RESEARCH REPORT

The Self-Rating of the Effects of Alcohol (SRE) form as a retrospective measure of the risk for alcoholism

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Abstract

Aims. A low level of response (LR) to alcohol is a characteristic of sons of alcoholics and predicts an elevated future alcoholism risk. A 12-question Self-Rating of the Effects (SRE) of alcohol form has been shown to correlate cross-sectionally with a designation of a low LR determined by alcohol challenges. **Design.** This study evaluates the potential usefulness of the SRE as a retrospective measure of both the response to alcohol and of subsequent alcoholism in two samples. **Setting.** All subjects were studied in the United States, most in California. **Participants.** First, 94 sons of alcoholics and controls completed the SRE 15 years after an alcohol challenge, and SRE values were compared to their prior LR results and their alcoholic outcomes. Secondly, the relationship between SRE results and alcoholic status was determined in 551 men and women alcoholics, their relatives, and controls. **Measurements.** Subjects were evaluated with face-to-face interviews. **Findings.** Despite the interval of 15 years, the correlation between the SRE and the subjective high feelings on the alcohol challenge was between -0.3 and -0.4 . For those 94 subjects the full SRE correlated with a diagnosis of alcohol dependence at 0.5, a figure that remained at 0.3 even when only the estimates related to the earliest drinking experiences were considered. For the 551 men and women, the correlation between the SRE and alcohol dependence diagnoses was 0.6, including 0.3 for the estimates of the first five times of drinking. All major findings in both samples remained robust when the recent drinking history or the number of items endorsed was considered, or when the most severe alcohol problem, passing out, was deleted from the analysis. **Conclusions.** When alcohol challenges are not possible, these retrospective reports indicate that the SRE is a potentially useful surrogate for determining a subgroup of people who might carry a low level of response to alcohol and a subsequent elevated risk for alcoholism.

Introduction

It is likely that a variety of genetic factors increase the risk for developing alcoholism (alcohol abuse or dependence).^{1,2} For example, some alcoholics might have experienced a vulnerability toward their disorder as a consequence of pre-existing major psychiatric conditions such as

schizophrenia or mania. Also, perhaps 20% of alcoholic individuals might have developed alcoholism as a consequence of a pre-existing high level of impulsivity and an inability to form close meaningful relationships as seen in the antisocial personality disorder (ASPD).^{2,3} As a result of this heterogeneity, it is likely that a variety of

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biological characteristics correlate with the future risk for severe alcohol-related life problems, including several electrophysiological and some biochemical measures.⁴⁻⁷ An additional physiological characteristic, the relative absence of the low K_m aldehyde dehydrogenase enzyme with the resulting flushing response, has been shown to be related to a relatively low alcoholism risk among Asians.^{8,9}

In an effort to search for trait markers of the alcoholism risk while minimizing the impact of genetic heterogeneity, our research group has primarily studied Caucasian men whose predisposition toward alcoholism was documented in the absence of ASPD, schizophrenia or mania in themselves or a close relative.^{1,2} The major finding of this prospective investigation of 453 subjects has been the documentation that a low level of response to alcohol (LR) at approximately age 20 years was observed significantly more often in the offspring of alcoholics than controls (about 40% vs. <10%), with LR also acting as a significant predictor of alcoholism almost a decade later.^{1,10} Regarding the latter finding, the correlation between LR at age 20 and the future development of alcoholism was between 0.4 and 0.5, at least among subjects with clearly high or low LR scores.¹ The ability of LR to predict alcoholic outcome almost a decade later remained robust after covarying for the quantity and/or frequency of drinking at approximately age 20.¹ Finally, LR acted as an apparent mediator of the alcoholism risk, explaining a significant portion of the relationship between family history and future alcoholism in this population.^{1,10}

The level of response to alcohol is a complex phenomenon that has been demonstrated in animal studies both to be related to genetic factors and to affect voluntary alcohol intake patterns.¹¹⁻¹³ The importance of genetic influences in LR is also supported, at least in part, by human twin research.¹⁴ However, it is likely that different aspects of the intensity of reaction to alcohol are mediated by different genetic influences.^{15,16}

In our own studies of humans, LR was measured through relatively costly alcohol challenge paradigms.^{1,10,17} In an effort to find an alternative, less costly approach to determining an individual's level of response to alcohol, we developed a Self-Rating of Effects of Alcohol (SRE) form.¹⁸ The purpose of the SRE is to evaluate subjects for whom an alcohol challenge

is too costly or for whom results would be difficult to interpret (e.g. older individuals or subjects with active alcohol dependence). This form asks a subject to estimate the number of standard drinks required to produce each of four potential effects (the recognition of "any effect", the development of dizziness or slurred speech, a stumbling gait, or passing out). The four specific effects were chosen because, a priori, they are likely to mirror the reactions to alcohol measured on the Subjective High Assessment Scale (SHAS) and the body sway measures of the alcohol challenge, while representing experiences the subjects might remember. Information is gathered for three separate time points including the first five times on which alcohol was imbibed, the period of heaviest drinking, and the most recent 3 months. The three time frames were selected to represent a period that might reflect aspects of the initial sensitivity to alcohol, a period of heaviest drinking likely to relate to the usual ages in which alcohol challenges are carried out (late teens to mid-twenties), and a recent period relatively easy to recall.

To evaluate the potential usefulness of this measure, 98 18-29-year-old drinking but not alcohol-dependent men were both tested in the laboratory using a challenge with 0.9 ml/kg of ethanol and asked to fill out the SRE.¹⁸ The test-retest correlation for the full SRE administered almost a year apart in a subset of 40 of these 98 subjects was 0.82, and the correlation between the average number of drinks reported on the SRE and the alcohol challenge results at the time of peak alcohol effect was -0.36. In addition, the SRE correctly identified almost 80% of the individuals whose level of response fell into the lowest third of intensity during the alcohol challenge, along with 60-67% of the subjects who clearly did not exhibit a low LR (i.e. their results were above the median compared to other men).¹⁸

To date, all of the alcohol challenges have used non-alcoholic young men, and only the cross-sectional relationships between the SRE and alcohol challenge results have been studied. Thus, the potential usefulness of the SRE as a retrospective measure of a person's LR earlier in life, and the results in older men and women have not been reported. The present analyses test three hypotheses. First, the SRE scores generated at about age 40 accurately reflect the actual intensities of response to alcohol that had

been measured 15 years earlier. Secondly, the relationships between SRE scores, on one hand, and alcohol challenge results or the diagnoses of alcoholism, on the other hand will not be greatly affected by the recent drinking history. Finally, using a population heterogeneous in regard to gender and age, the SRE will still relate to the risk for alcoholism.

Methods

The data reported in this paper come from two studies. For each investigation, written informed consent was obtained after the procedures had been fully explained.

SRE results in subjects with alcohol challenges 15 years earlier

The first investigation uses information from the first 94 men who took part in the 15-year follow-up of the 453 sons of alcoholics and controls, subjects who had originally been tested at approximately age 20.^{1,10} As described in more detail elsewhere, between 1978 and 1988 mailed questionnaires and subsequent personal interviews were used to identify Caucasian, drinking, but non-alcohol-dependent 18–25-year-old men who had an alcohol-dependent first-degree relative, usually the father.^{1,2,10} Neither the alcoholic relative nor the subject had ASPD, schizophrenia nor mania. Each family history positive (FHP) individual was matched with a family history negative (FHN) control, with the two subgroups chosen to be similar on age, religion and education, as well as on smoking, alcohol and other drug use histories.

At about age 20 these subjects participated in an alcohol challenge experiment where they consumed (over a 10-minute period) 0.75 to 1.1 ml/kg of ethanol, with subsequent repeated evaluations approximately every half hour over the next 3 hours.^{1,10,17} One available measure from these sessions, the SHAS, relates to the types of information gathered on the SRE, and has been shown to discriminate between subjects on responsiveness to alcohol.^{1,10} The SHAS is a self-rating form used to record levels of feelings of intoxication on a 36-point analog scale at baseline (before administration of the beverage) and every 30 minutes throughout the experiment.^{1,10,17} Although not administered at the earliest stages of this study, SHAS data were

available on 68 of the 94 men from the alcohol challenge protocol. As in previous work, the analyses of the SHAS focus on the measure relating to “feeling high” at the time of peak intoxication (60 minutes post baseline). The data reported below compare the results of this measure of feelings of intoxication during the alcohol challenge with the SRE ratings of the usual effects of alcohol.

All 453 subjects from this experiment were successfully located an average of 8.2 years after initial testing, with complete follow-up data gathered on 450 (99.3%).¹ Subsequently, all subjects have been located once again and scheduled for the next stage of work, approximately 5 years after the first follow-up (i.e. about 15 years after the alcohol challenge).^{1,10} This second protocol incorporated the SRE form for all 94 subjects interviewed to date. The follow-up evaluations were carried out by interviewers who were blind to the subjects’ original family history, level of response to alcohol at approximately age 20, and the diagnostic information gathered at the first stage follow-up.^{1,10} A structured interview, developed from the Alcohol Research Center Interview and the Structured Clinical Interview for DSM-III-R (SCID),^{19,20} was administered separately to subjects and at least one additional informant (usually the spouse). All relevant medical records were obtained, blood samples were drawn for the evaluation of state markers of heavy drinking, and urine samples were obtained for a drug toxicology screen.^{1,21} From these data, a clinician blind to the subject’s background (MAS) established an Axis I diagnosis using DSM-III-R criteria,²² including alcohol dependence.

The SRE form administered as part of the second stage follow-up, as shown in the Appendix, asked each subject to estimate the number of standard drinks required to produce each of four potential conditions during three periods in their lives.¹⁸ As part of the form, a drink was defined as the amount of alcohol contained in a 12-ounce beer, a 4-ounce glass of wine, or a single “shot” (1–1.5 ounces) of 80 proof beverage. In order to generate the most simple single score that reflects an overview of the SRE values, an overall score was created by dividing the sum of the number of drinks recorded in the 12 possible cells of the SRE by the number of cells endorsed. In the present analyses, in order to test the potential importance of very early experi-

ences, an Early Drinking SRE score was also generated using a similar formula but based only on the first five times of drinking.

Cross-sectional SRE results in a more heterogeneous group

The second sample involved 551 subjects (279 women) who took part in the San Diego component of Collaborative Study on the Genetics of Alcoholism (COGA) between September 1991 and October 1995.²³⁻²⁶ As described in additional publications, this is a family pedigree study that begins with an alcohol dependent proband and gathers data from that subject and all available appropriate relatives.^{25,26} Data were generated through face-to-face administration of the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) which was based on the Diagnostic Interview Schedule, the Composite International Diagnostic Interview, and the Schedule for Affective Disorders and Schizophrenia, as well as the SCID.^{20,23,27,28} For these subjects, the information from the SSAGA was used to determine the life-time history of alcohol dependence as defined by DSM-III-R. In addition to the SSAGA, the 551 subjects interviewed in San Diego presented here also filled out the SRE, using the form described above.

Statistical analyses were carried out using correlations established as either point bi-serial analyses when dichotomous variables were involved or Pearson's product moment correlations for continuous variables. When

appropriate, χ^2 values for comparisons across groups on categorical data were determined.

Results

The prospective evaluation

The first group of subjects for whom relevant data were available were the 94 men in the 15-year follow-up of sons of alcoholics and controls. They were all Caucasian, had a mean (\pm SD) of 38.7 ± 2.00 years of age at the most recent follow-up (a range of 35-45 years), and were composed of 32 sons of alcoholics and 62 controls. The average years of education was 18.6 ± 2.45 years, with a range of 14-22 years. By the time of filling out the form, 18.1% had fulfilled criteria for alcohol dependence plus 9.6% for abuse. In these 94 men, the full SRE scores had a mean of 3.8 ± 1.94 drinks, a range of 1.0-12.83, and 13.6% of the mean values were 3.0 or less. In contrast, the Early Drinking SRE scores had a mean of 2.5 ± 1.22 drinks, a range of 1.0-8.75, and 78.7% of the scores were 3.0 or less.

Relevant to the first hypothesis, the alcohol challenge follow-up sample offered the opportunity of evaluating the relationship between the SRE scores generated at about age 39 years, and the alcohol challenge results determined when the subjects had first been tested in the laboratory at about age 20. SHAS high scores were only available on a subset of 68 of these initial men. As shown in the lower half of Table 1, the correlations between the SRE and diagnoses of alcohol dependence for this subset were similar

Table 1. Correlations between SRE full and early drinking scores and alcohol dependence or alcohol challenge results

<i>n</i>	Full sample 94	Complete data 68
<i>Correlation SRE to SHAS high</i>		
Full SRE	N/A	-0.39**
Partialing for quantity		-0.37**
Early Drinking SRE		-0.28 ⁺
Partialing for quantity		-0.23 ⁺
<i>Correlation SRE to alcohol dependence</i>		
Full SRE	0.52**	0.55**
Partialing for quantity	0.42**	0.48**
Early Drinking SRE	0.29*	0.34*
Partialing for quantity	0.25*	0.30*

** , Correlation significant at $p < 0.001$; * , Correlation significant at $p < 0.01$;
⁺ , correlation significant at $p < 0.05$.

to those reported for the full group of 94 men. Despite the passage of an average of 15.0 ± 0.96 years since the alcohol challenge, the full SRE results correlated with the SHAS high score at -0.39 ($p < 0.001$). Related to the second hypothesis, this figure was not affected by covarying, or partialing, for the drinking pattern in the period immediately prior to follow-up. The evaluation of the impact of recent drinking was carried out because the SRE score also correlated with the usual number of drinks consumed per drinking day in the 6 months prior to follow-up (quantity) at 0.28 ($p = 0.007$), although it did not relate to the frequency of consumption ($r = 0.07$, $p = 0.50$).

The Early Drinking SRE score, figures that involved estimates of effects of alcohol at a time that clearly antedated the onset of alcohol dependence, correlated with the SHAS at -0.28 ($p < 0.02$), and was not closely related to or "colored" by recent drinking experiences, as the value was only slightly diminished when partialled for recent drinking quantity ($r = -0.23$, $p < 0.04$). These lower correlations for the Early Drinking as opposed to the full SRE scores reflect the relatively restricted range of the number of drinks required for effects the first five or so times of consumption.

Finally, while not shown in the table, the correlations of the full SRE to the alcohol challenge results remained robust when two additional aspects of this form were manipulated. First, to evaluate the usefulness of the SRE in people who never experienced severe alcohol effects, the "passing out" item was deleted from the analyses. In this instance, the correlation of SHAS to SRE was unchanged ($r = -0.38$, $p < 0.001$). Even when the Early SRE score was used, correlations remained significant ($r = -0.22$, $p < 0.04$). Secondly, to determine if the number of the twelve potential SRE boxes endorsed by the subjects had an impact on the results, the full SRE-SHAS correlations were re-evaluated after covarying for the number of endorsed items, with the resulting $r = -0.29$ ($p < 0.008$).

An additional step was taken to evaluate the second hypothesis regarding the possible impact of the drinking history on these SRE results. The goal was to see if the SRE still functioned in a useful way among a subgroup with more homogeneous drinking histories, i.e. alcoholics. Thus, among the 14 alcohol dependent subjects with

full SHAS data the correlation between the level of subjective intoxication observed during the alcohol challenge at approximately age 20 and the full SRE was -0.49 ($p < 0.05$), while the SRE Early Drinking score was shown to correlate at -0.22 ($p < 0.23$). Although the last correlation was not significant, this was most likely due to low power because of the small sample size here ($n = 14$). Supporting this interpretation is the effect size which is similar to those obtained above.

The ability of the SRE to serve as a test for identifying the subgroup of subjects with low LR scores during their alcohol challenges 15 years previously was evaluated from another perspective. The goal was to establish the sensitivity and specificity of the current SRE as a measure of a low LR score as established in the prior alcohol challenge in this older population. Consistent with the approach used in published papers, SHAS scores were used to identify the men whose intensity of response to alcohol had fallen into the lowest third of results (i.e. the 21 subjects labeled by the SHAS as being at high risk for future alcoholism) and the 30 subjects whose SHAS results fell above the median (i.e. those lacking a clearly high alcoholism risk as determined by the alcohol challenge).^{1,18,24} Using a cut-point of an average of 4.5 or more drinks on the full SRE as an indicator of a low level of response to alcohol,¹⁸ 11 of the 21 subjects considered high risk by their SHAS score were correctly identified (a sensitivity of 52.4%). The same cut-off correctly identified 26 of the 30 subjects labeled as low risk on the alcohol challenge (a specificity of 86.7%). Decreasing the full SRE cut-point to 4.0 for high risk resulted in a sensitivity of 61.9% and a specificity of 80.0%.

Similar evaluations of sensitivity and specificity were carried out using the Early Drinking SRE scores. Here a mean of 3.0 or more drinks to have any of the four possible effects the first five times of drinking correctly identified 42.9% of the alcohol challenge high risk subjects and 73.3% of those at low risk. The sensitivity and specificity were 47.6% and 66.7% if a cut-point of 2.5 drinks was used, and became 81.0% sensitivity and 40% specificity at 2.0 drinks.

Data were also available for all 94 subjects regarding the development of alcohol dependence during the follow-up. As shown in Table 1, the correlation between a diagnosis of alcohol

Table 2. Correlations of SRE measures to alcohol dependence for 551 COGA subjects

<i>n</i>	Full sample 551	Male 272	Female 279
<i>Correlation SRE to alcohol dependence</i>			
Full SRE	0.63**	0.62**	0.51**
Partialing for quantity	0.61**	0.60**	0.49**
Early drinking SRE	0.28**	0.23**	0.18*
Partialing for quantity	0.27**	0.22**	0.19*

** , correlation significant at $p < 0.001$; *, + correlation significant at $p < 0.01$.

dependence at any time during the 15 years and the full SRE was 0.52 ($p < 0.001$). Regarding the possible impact of recent drinking practices, the correlation between the full SRE and a diagnosis of alcohol dependence was also determined after covarying, or partialing, for the impact of the quantity of drinking in the 6 months before filling out the SRE, with a resulting $r = 0.42$ ($p < 0.001$). Despite the relatively narrow range of scores on the Early Drinking SRE, the correlations with a diagnosis of alcohol dependence here were 0.29 ($p = 0.005$) overall, and 0.25 ($p = 0.008$) after partialing for the recent quantity of drinking. Once again, for the full SRE the correlations remained robust even after excluding the results relating to passing out, with $r = 0.53$ ($p < 0.001$) for the full sample. The correlations of SRE to alcohol dependence continued to remain significant after controlling for the SRE boxes endorsed ($r = 0.47$, $p < 0.001$).

Finally, regarding this group of 94 men, the SRE values were evaluated for the sensitivity and specificity of this test in identifying alcohol dependence. Focusing on the full SRE score and using the cut-off of 4.5 or more drinks, the ability of the SRE to correctly identify alcohol dependent subjects had a sensitivity of 58.8% and a specificity of 81.8%. The figures were 64.7% and 64.9% with a cut-point of 4.0 drinks on the full SRE score. Regarding the Early Drinking SRE value, if the subject reported a mean of 3.0 or more drinks for the various effects the first five times of drinking, 47.1% of the alcohol dependent individuals were correctly identified (the sensitivity), while 72.7% of the non-alcoholics were correctly noted (the specificity). These figures changed to a 52.9% sensitivity and a 61.0% specificity if a cut-point of 2.5 drinks was used and 82.4% sensitivity and 29.9% specificity if 2.0 drinks was the cut-point.

Cross-sectional SRE results

The second group for whom SRE scores were examined also helped establish the potential usefulness of the SRE in a more heterogeneous population. The subjects were the 551 men and women who were alcohol-dependent probands, their alcoholic and non-alcoholic relatives, and controls from the San Diego portion of the COGA study. Here, the subjects had an average of 40.6 ± 14.17 years of age (a range of 18–78 years), had completed an average of 13.5 ± 2.31 years of education (a range of 1–17 years), and exhibited a racial distribution of 69.5% Caucasian, 10.3% black, 15.8% Hispanic and 4.3% other. This population incorporated 37.4% of individuals with alcohol dependence, and subjects were included regardless of additional psychiatric disorders, including 12.7% who fulfilled criteria for the antisocial personality disorder and 26.1% who demonstrated dependence on some drug other than alcohol.

For these subjects, data were available on the SRE results filled out at the time of interview and on alcoholic status. As shown in Table 2, within this group the correlation between the full SRE (with a mean of 5.1 ± 3.42 and a range of 1.0–21.2) and a diagnosis of alcohol dependence was 0.63 ($p < 0.0001$). Here 30.6% had SRE values of 3.0 or less. This figure remained at 0.61 ($p < 0.0001$) when the effect of the recent quantity of drinks was partialled. The Early Drinking SRE results (a mean of 3.06 ± 1.88 and a range of 1.0 to 18.0 and 61.5% had SRE values of 3.0 or less) correlated with a diagnosis of alcohol dependence at 0.28 ($p < 0.0001$), and remained at 0.27 ($p < 0.0001$) when the recent quantity of consumption was partialled. The results were fairly similar for men and women and appeared to be independent of age, as there was no significant correlation between SRE Early

Drinking estimates and age ($r = -0.05$, $p = 0.23$).

Similar to analyses described for Table 1, the figures in Table 2 did not change greatly for the full sample for the full SRE when "passing out" was deleted from the analysis ($r = 0.58$, $p < 0.001$), nor when the number of SRE endorsed boxes were partialled ($r = 0.49$, $p < 0.001$). Nor did these covariates impact greatly on the correlations between the Early Drinking SRE and an alcohol dependence diagnosis. The results also remained robust when men and women were analyzed separately.

An additional step was taken to evaluate the potential impact of the more recent drinking history on SRE scores. The correlations between the SRE estimates and alcoholic outcome were evaluated separately for the 307 (55.7%) men and women who had been abstinent or near-abstinent during the 6 months prior to interview, and for whom no severe alcohol problems were observed during that time frame. Here, the full SRE score and a diagnosis of alcohol dependence correlated at 0.67 ($p < 0.0001$), and the correlation between SRE Early Drinking score and the alcoholic diagnosis was 0.27 ($p = 0.0001$).

The COGA generated SRE results could also be evaluated to see how well this score correctly classified subjects as having alcohol dependence. Focusing on the full SRE score and using the figure of 4.5 or more drinks as a measure of high risk as reported in an earlier paper,¹⁸ the ability of the SRE to identify correctly the alcohol-dependent subjects demonstrated a sensitivity of 84.5% and a specificity of 76.2%. The figures were 89.3% and 66.7% with a cut-point of 4.0 drinks. Using the Early Drinking SRE score with its more narrow range of values, if the subject reported a mean of 3.0 or more drinks for the various effects the first five times of drinking, 64.1% of the 206 alcohol-dependent individuals were correctly identified (the sensitivity), while 59.7% of the 345 non-alcoholics were correctly identified (the specificity). These figures changed to a 75.2% sensitivity and a 51.3% specificity if a cut-point of 2.5 drinks was used and 87.9% and 30.4% if 2.0 drinks was the cut-point.

Discussion

A low level of response to alcohol has been shown to be a characteristic of sons of alcoholics

and to predict alcoholism almost a decade later.^{1,10} These prospective studies used a relatively time-consuming and costly alcohol challenge protocol to determine LR among young, Caucasian, relatively highly functioning subjects. This paper evaluates the characteristics of a simple SRE form developed to help measure levels of reaction to alcohol in subjects for whom alcohol challenges are not practical. The goal is to test a tool that can be used in research settings, and that might also serve as an aid in educating people that their reaction to alcohol might relate to their alcoholism risk.

While there is no proven adequate substitute for an alcohol challenge in determining LR, a prior investigation has shown some potential promise for the SRE.¹⁸ The present study expands upon these prior findings. First, as hypothesized, SRE values generated at about age 40 correlated at -0.39 ($p < 0.001$) with the results of alcohol challenges carried out almost 15 years previously. Secondly, the correlations between the SRE and the earlier alcohol challenge results or the diagnosis of alcoholism were not greatly affected by the recent drinking history. Thirdly, the results are not likely to merely reflect more severe alcohol experiences predicting later alcoholism or SHAS results as the correlations remained robust even after excluding the most severe alcohol effect, passing out. Regarding the third hypothesis, the full SRE score performed well in identifying subjects with clearly high or low LR values on the alcohol challenge, even in a sample that is outside the age range of the prior studies. These results indicate a potential stability of SRE values, at least regarding their relationship to alcohol challenge results and alcoholism diagnoses.

While the correlation between the full SRE values and the earlier alcohol challenge LR designation appeared to be independent of the quantity and frequency of recent drinking, several other steps were taken to further evaluate the second hypothesis regarding the potential impact of drinking experiences on the SRE. One approach was to analyze separately SRE data regarding the first five occasions on which drinking occurred, results which focus on a time period that was likely to have antedated the onset of very heavy drinking or alcohol dependence. However, the Early Drinking SRE scores were in a relatively narrow range, with the large majority of subjects reporting an average of three or less

drinks as the average score. Despite this problem, the results from the Early Drinking SRE scores were in the same direction as the full SRE, with a correlation to the alcohol challenge results of 15 years previously of about -0.30 ($p < 0.02$), and a sensitivity and specificity of almost 48% and 67% regarding the LR category generated from the alcohol challenge when a cut-point of 2.5 drinks on the SRE was used. Also, the relationship between the SRE and an alcohol dependence diagnosis was not greatly affected by partialing for the recent drinking history, and remained robust when a subgroup which had been abstinent for 6 or more months prior to filling out the SRE was evaluated.

In interpreting these findings, it is important to recognize the limitations of the work. First, the ideal evaluation of the relationships among SRE, LR and the development of alcoholism can only be determined through prospective studies. Although such studies are planned for the future, all the data reported here regarding alcohol dependence were retrospective. Thus, it is possible that some of the SRE values might have developed as a result of prior drinking experiences. On the other hand, the correlation between SRE results and alcohol challenge values generated before the onset of alcohol dependence, an average of 15 years earlier, was almost, -0.4 . All results remained robust after partialing or covarying for recent drinking histories, and the relationship between SRE and alcohol dependence remained strong even among individuals who had abstained for 6 or more months prior to the time of filling out the SRE.

Another caveat is the relatively blunt dissection of alcohol reaction achieved by the SRE. Future research will evaluate possible ways of looking more precisely at the combination of the number of drinks consumed over specific periods of time (e.g. 1 hour vs. 3 hours) to achieve the measured effects. Such distinctions could be important in differentiating subgroups of alcohol dependent individuals, such as those predisposed toward intensive binge drinking or those with very early onset disorders.

It is also important to remember that while a low level of response to alcohol on an alcohol challenge has been shown to predict alcoholism almost a decade later,^{1,10} the SRE is an indirect and relatively unproven measure of both LR and the alcoholism risk. There is no current adequate substitute for an alcohol challenge protocol in

determining LR. However, when alcohol challenges cannot be carried out, the SRE is a reasonable alternative to establishing the intensity of response to alcohol. This measure appears to be relatively stable in its relationship to LR, and has demonstrated a significant relationship with a past history of alcohol dependence in men and women of a fairly wide range of ages.

Thus, despite the potential caveats, the high levels of correlation between the SRE and alcohol challenge results and the stability of this relationship over time indicate the possible usefulness of the SRE in research settings. At the same time, it is important to remember that neither the alcohol challenge nor the SRE is a way to diagnose alcohol dependence. That requires a careful clinical interview gathering information from subjects and additional informants. Nor is this a test to identify the condition, or state, of current heavy drinking or associated problems. That task rests with state markers of heavy drinking such as gamma glutamyl transferase (GGT), or questionnaires dealing with alcohol problems such as the Michigan Alcohol Screening Test (MAST)²⁹⁻³¹ or the CAGE.²⁹⁻³¹

In the absence of additional simple measures of the intensity of reaction to alcohol, one specific application of this self-rating form is in genetic linkage analyses such as the COGA study, where multiple relatives from diverse generations can fill out the SRE and the relationship between clearly low levels of response to alcohol and genetic material can be determined. In more clinical and educational settings, the form might help educate drinkers about the impact alcohol is having on them. The SRE might also be useful in attempting to prevent alcoholism through educating relatives of alcoholics, individuals arrested for driving while intoxicated, and groups of young drinkers regarding the relationship between "being able to hold your liquor well" and a significantly elevated future risk for alcoholism.

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References

1. SCHUCKIT, M. A. & SMITH, T. L. (1996) An 8-year follow-up of 450 sons of alcoholic and

- control subjects, *Archives of General Psychiatry*, **53**, 202–210.
2. SCHUCKIT, M. A. (1994) A clinical model of genetic influences in alcohol dependence, *Journal of Studies on Alcohol*, **55**, 5–17.
 3. HESSELBROCK, M. N. (1991) Gender comparison of antisocial personality disorder and depression in alcoholism, *Journal of Substance Abuse*, **3**, 205–219.
 4. BEGLEITER, H. & PORJESZ, B. (1988) Potential biological markers in individuals at high risk for developing alcoholism, *Alcoholism, Clinical and Experimental Research*, **12**, 488–493.
 5. ANTHENELLI, R. M., SMITH, T. L., CRAIG, C. E., TABAKOFF, B. & SCHUCKIT, M. A. (1995) Platelet monoamine oxidase activity levels in subgroups of alcoholics: diagnostic, temporal, and clinical correlates, *Biological Psychiatry*, **38**, 361–368.
 6. TABAKOFF, B., HOFFMAN, P. L., LEE, J. M., SAITO, T., WILLARD, B. & DE LEON-JONES, F. (1988) Differences in platelet enzyme activity between alcoholics and nonalcoholics, *New England Journal of Medicine*, **318**, 134–139.
 7. EHLERS, C. L. & SCHUCKIT, M. A. (1991) Evaluation of EEG alpha activity in sons of alcoholics, *Neuropsychopharmacology*, **4**, 199–205.
 8. WALL, T. L., THOMASSON, H. R., SCHUCKIT, M. A. & EHLERS, C. L. (1992) Subjective feelings of alcohol intoxication in Asians with genetic variations of ALDH2 alleles, *Alcoholism, Clinical and Experimental Research*, **16**, 991–995.
 9. HARADA, S., AGARWAL, D. P., GOEDDE, H. W. & ISHIKAWA, B. (1983) Aldehyde dehydrogenase isozyme variation and alcoholism in Japan, *Pharmacology, Biochemistry and Behavior*, **18**, 151–153.
 10. SCHUCKIT, M. A. (1994) Low level of response to alcohol as a predictor of future alcoholism, *American Journal of Psychiatry*, **151**, 184–189.
 11. BALDWIN, H. A., WALL, T. L., SCHUCKIT, M. A. & KOOB, G. F. (1991) Differential effects of ethanol on punished responding in the P and NP rats, *Alcoholism, Clinical and Experimental Research*, **15**, 700–704.
 12. LI, T., LUMENG, L. & DOOLITTLE, D. P. (1993) Selective breeding for alcohol preference and associated responses, *Behavior Genetics*, **23**, 163–170.
 13. MARKEL, P. E., BENNETT, B., BEESON, M., GORDON, L. & JOHNSON, T. E. (1997) Confirmation of quantitative trait loci for ethanol sensitivity in long-sleep and short-sleep mice, *Genome Research*, **7**, 92–99.
 14. HEALTH, A. C. & MARTIN, N. G. (1992) Genetic differences in psychomotor performance decrement after alcohol: a multivariate analysis, *Journal of Studies on Alcohol*, **53**, 262–271.
 15. MUNDT, J. C., PERRINE, M. W. & SEARLES, J. S. (1997) Individual differences in alcohol responsiveness: physiological, psychomotor, and subjective response domains, *Journal of Studies on Alcohol*, **58**, 130–140.
 16. CRABBE, J. C., GALLAHER, E. S., PHILLIPS, T. J. & BELKNAP, J. K. (1994) Genetic determinants of sensitivity to ethanol in inbred mice, *Behavioral Neuroscience*, **108**, 186–195.
 17. SCHUCKIT, M. A. & GOLD, E. O. (1988) A simultaneous evaluation of multiple markers of ethanol/placebo challenges in sons of alcoholics and controls, *Archives of General Psychiatry*, **45**, 211–216.
 18. SCHUCKIT, M. A., TIPP, J. E., SMITH, T. L., WIESEBECK, G. A., KALMIJN, J. (1997) The relationship between self-rating of the effects (SRE) of alcohol and alcohol challenge results, *Journal of Studies on Alcohol*, **58**, 397–404.
 19. SCHUCKIT, M. A., IRWIN, M., HOWARD, T. & SMITH, T. (1988) A structured diagnostic interview for identification of primary alcoholism: a preliminary evaluation, *Journal of Studies on Alcohol*, **49**, 93–99.
 20. SPITZER, R. L., WILLIAMS, J. B. W., GIBBON, M. & FIRST, M. B. (1992) The structured clinical interview for DSM-III-R (SCID): I. History, rationale and description, *Archives of General Psychiatry*, **49**, 624–629.
 21. IRWIN, M., BAIRD, S., SMITH, T. L. & SCHUCKIT, M. (1988) Use of laboratory tests to monitor heavy drinking by alcoholic men discharged from a treatment program, *American Journal of Psychiatry*, **145**, 595–599.
 22. AMERICAN PSYCHIATRIC ASSOCIATION (1987) *Diagnostic and Statistical Manual of Mental Disorders*, 3rd edn revised (Washington, American Psychiatric Press).
 23. BUCHOLZ, K. K., CADORET, R., CLONINGER, C. R. *et al.* (1994) A new, semi-structured psychiatric interview for use in genetic linkage studies: a report on the reliability of the SSAGA, *Journal of Studies on Alcohol*, **55**, 149–158.
 24. SCHUCKIT, M. A., TSUANG, J. W., ANTHENELLI, R. M., TIPP, J. E. & NURNBERGER JR, J. I. (1996) Alcohol challenges in young men from alcoholic pedigrees and control families: a report from the COGA project, *Journal of Studies on Alcohol*, **57**, 368–377.
 25. SCHUCKIT, M. A., TIPP, J. E., REICH, T., HESSELBROCK, V. M. & BUCHOLZ, K. K. (1995) The histories of withdrawal convulsions and delirium tremens in 1648 alcohol dependent subjects, *Addiction*, **90**, 1335–1347.
 26. SCHUCKIT, M. A., TIPP, J. E., ANTHENELLI, R. M., BUCHOLZ, K. K., HESSELBROCK, V. M. & NURNBERGER, JR, J. I. (1996) Anorexia nervosa and bulimia nervosa in alcohol-dependent men and women and their relatives, *American Journal of Psychiatry*, **153**, 74–82.
 27. ROBINS, L. N., WING, J., WITTICHE, H. U. *et al.* (1988) The composite international diagnostic interview: an epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures, *Archives of General Psychiatry*, **45**, 1069–1077.
 28. ROBINS, L. N., HELZER, J. E., ORVASCHEL, H. *et al.* (1985) The diagnostic interview schedule, in: EATON, W. W. & KESSLER, I. G. (Eds) *Epidemiologic Field Methods in Psychiatry: the NIMH*

epidemiologic catchment area program, pp. 143–170 (New York, Academic Press).

29. GREEN, S. J. & WHICHELOW, M. J. (1994) Longitudinal validity of the CAGE questionnaire, *Addiction Research*, 2, 195–201.

30. ROSS, H. E., GAVIN, D. R. & SKINNER, H. A. (1990) Diagnostic validity of the MAST and the alcohol dependence scale, *Journal of Studies on Alcohol*, 51, 506–513.

31. HELANDER, A., CARLSSON, A. V. & BORG, S. (1996) Longitudinal comparison of CDT and GGT, *Alcohol and Alcoholism*, 31, 101–107.

Appendix

The SRE form to be filled out by subjects regarding the number of standard drinks required to produce four possible type of effects at three different time points.

ID: -----/----

SRE FORM

Date: --/--/---

On this form, please tell us about your *ACTUAL* experiences drinking alcohol. Please answer each question as accurately as possible. Give only one answer for each question. Please do not give ranges (i.e: don't list 4–6 drinks; write 5).

To fill out this form:

- One drink of alcohol = 12 oz. beer, 4 oz. glass of wine, or a single shot of hard alcohol alone or in a mixed drink.
 - If a question does not apply to you, write N/A in the space provided and move on to the questions that relate to you.
- (1) Begin with Column A: How many drinks did it *actually* take “for you to begin to feel any different” *the first 5 times (or so) you ever drank alcohol?* DO NOT count sips taken as a child. Place your answer in column A, just to the right of Question 1.
 - (2) How many drinks did it *actually* take “for you to feel a bit dizzy, or to begin to slur your speech” *the first 5 times you ever drank?* Place your answer in Column A, next to Question 2.
 - (3) Now, complete column A for Questions 3 and 4, filling in the number of drinks it *actually* took for you to feel the effect listed in on the left side of the Table.
 - (4) Next, fill in the same information for: Column B: for your *most recent period of drinking at least once a month for 3 consecutive months.*
 - (5) Finally, fill in Column C: How many drinks did it *actually* take to feel the effects listed at the left during your *period of heaviest drinking?*

	A	B	C
Effect of drinking alcohol (answer only those which apply to your <i>actual</i> drinking experiences	First 5 times you ever drank	3 months drinking once a month	Period heaviest drinking
(1) How many drinks did it take <i>for you to begin to feel different?</i> (where you could feel an effect)			
(2) How many drinks did it take <i>for you to feel a bit dizzy, or to begin to slur your speech?</i>			
(3) How many drinks did it take you to <i>begin stumbling, or walking in an uncoordinated manner?</i>			
(4) How many drinks did it take you to <i>pass out, or fall asleep when you did not want to?</i>			