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Blood Ethanol Levels, Self-Rated Ethanol Effects and Cognitive-Perceptual Tasks

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LEX, B W , N E GREENWALD, S E LUKAS, J P SLATER AND J H MENDELSON *Blood ethanol levels, self-rated ethanol effects and cognitive-perceptual tasks* PHARMACOL BIOCHEM BEHAV **29**(3) 509–515, 1988 — Family history of alcoholism influences the acute effects of ethanol in young men We expanded these findings by concomitantly measuring plasma ethanol levels (BALs), subjective intoxication effects, and task performance in young women Healthy subjects with no familial alcoholism provided informed consent and received 0 75 ml/kg ethanol or isocaloric placebo (n=10 per group) under randomized double-blind conditions Assessments were made at 90, 60 and 30 min before, and 15, 30, 45, 60, 90, 120, 150 and 180 min after beverage administration BALs reached 80 mg/dl 45–60 min following ethanol Dizziness and clumsiness ratings correlated strongly with BAL, but clumsiness and confusion were the strongest effects associated with placebo Impaired visual selectivity and hand-eye coordination covaried with BAL ($p<0$ 05) on written tests Deficits in abstract instruction and symbol comprehension almost attained statistical significance ($p<0$ 06) Compared with previous findings for males, data from the present report suggest that ethanol may have gender-related effects

Ethanol Women Blood alcohol levels Cognitive-perceptual tasks Expectancy effects Subjective intoxication levels

CURRENT alcohol consumption rates promote alcohol dependence among approximately 5% of women who drink [6] Although alcohol abuse by women is now seen as an important problem, there have been few systematic studies of its antecedents [2, 3, 12, 21, 29, 44, 46] No single factor explains or predicts development of alcohol problems [27, 29, 30] The prevailing consensus holds that alcoholism in men and women stems from interacting biological, behavioral and sociocultural variables [21,28].

One incisive strategy for disentangling contributory factors examines specific variables in high risk populations prior to onset of alcohol abuse [40,41]. Offspring of alcoholics are 3 to 4 times as likely to become alcoholic as persons in the general population [5, 7, 9, 13, 15, 20, 30, 43] To identify mechanism(s) possibly underlying a putative genetic component, Schuckit [39–41] compared 2 groups of young men (21 to 25 years of age) with no histories of alcohol abuse, drug abuse, or psychological disturbance. Subjects were screened for positive (FHP) or negative (FHN) histories of alcoholism in first degree relatives (85% of whom were the father) and matched for age, socioeconomic status and height-weight ratio. Matched FHN and FHP males participated in random assignment acute studies after consuming alcohol placebo, 0 75 ml/kg of 95% ethanol, and 1.1 ml/kg of 95% ethanol beverages At a typical social dose (0 75 ml/kg), FHP subjects attained equivalent blood alcohol levels (BALs) but rated themselves significantly ($p<0$ 01) less intoxicated and showed less static ataxia ($p<0$ 001) than FHN controls [40,41]

In some way FHP men may be less sensitive or responsive to subjective and physiologic effects of moderate doses of ethyl alcohol [40,41] It is hypothesized that subjective assessments of intoxication and alcohol-related motor impairment are cues to reduce or cease drinking [23, 40, 41] Alcohol consumption episodes may persist if such cues are lacking or delayed, and chronic exposure to excessive alcohol intake may promote increased tolerance and physiological dependence in FHP individuals [23, 40, 41]

Paternal alcoholism may be particularly important for women In a national survey sample more women than men reported having alcoholic fathers [32] Alcoholic women generally are more likely to have alcoholic fathers than alcoholic men [2, 9, 14], and prevalence of alcoholism in fathers of female alcoholics in treatment is as high as 61% [8].

Previous studies of sensitivity to alcohol in young men have focused on self-reports of intoxication levels and correlated simple motor performance measures with rising blood alcohol levels following moderate (e g , 0 75 ml/kg 95% ethanol) or lower doses of ethyl alcohol or placebo [16] Psychomotor tasks such as hand steadiness and finger tapping speed (cf [50]) or static ataxia (i.e , body sway) [4, 23, 35, 41, 45] are typical measures. Test batteries also have

included more complex psychomotor and cognitive-perceptual tasks, such as an automated version of the Digit Symbol Substitution Test (DSST) (cf [25])

However, gender differences have been observed in reaction times following administration of 0 76 ml/kg ethanol [47], and after comparable doses females have shown more impairment on batteries of performance and cognitive tasks [33] This paper is one of a series that reports findings from studies of subjective, cognitive-perceptual, and performance effects following a moderate dose of alcohol (0 75 ml/kg 95% ethanol) in young (ages 21 to 25 years) FHP and FHN women Results of psychomotor tasks (static ataxia, finger tapping, hand steadiness, and DSST) administered to these subjects will be reported separately (Lukas, S E , B W Lex and J P Slater, in preparation) To avoid possible confounding effects, this report presents results of measures that discriminated between placebo and alcohol conditions in female subjects with no positive family history of alcoholism (cf [40, 41, 50])

TABLE 1

BACKGROUND CHARACTERISTICS AND SUBSTANCE USE HISTORY OF 20 FEMALE SOCIAL DRINKERS

Variable	Alcohol (N=10) Mean ± S D	Placebo (N=10) Mean ± S D
Age (years)	21 9 ± 0 9	23 4 ± 0 9
Height (cm)	164 0 ± 4 4	163 0 ± 4 4
Weight (kg)	57 0 ± 8 1	62 7 ± 8 3
Formal education (years)	16 3 ± 0 4	16 3 ± 1 3
Years alcohol use (total)	7 7 ± 2 3	7 1 ± 2 3
Years regular alcohol use (total)	4 4 ± 1 9	3 1 ± 1 8
Alcohol use per month[1]	9 4 ± 6 4	11 3 ± 6 7
Cocaine use (lifetime)[2]	5 1 ± 12 4	5 9 ± 10 8
Marihuana use (lifetime)[2]	19 2 ± 20 1	7 7 ± 14 8

[1]During the month prior to the study
[2]Number of times used this drug during subject's lifetime

METHOD

Subjects

Twenty healthy adult female volunteers (weight range 49 8 to 77 9 kg) between the ages of 21 and 25 (mean=22 6 years) were recruited via newspaper advertisements and provided informed consent for paid participation in a study of acute alcohol sensitivity effects on women All volunteers were examined by a physician Only women whose physical examinations, medical and mental health histories and blood hemogram and chemistry studies were within normal limits participated No subject selected had a positive urinalysis at screening or a history of drug or alcohol abuse Subjects also were screened for history of alcohol or drug abuse or dependence or other psychiatric disorders as ascertained by the Hamilton Depression and Anxiety Scales [17] and the Schedule for Affective Disorders and Schizophrenia-Lifetime version (SADS-L) [11] using DSM-III criteria [1] Only subjects who reported no alcoholic primary relatives were assigned to the FHN category All subjects were social drinkers who drank 1 or 2 alcoholic drinks (between 45 and 90 ml of absolute alcohol) from 2 times per month to 2 times per week Subtests of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) [49] and the Wechsler Memory Scale (WMS) [48] were used as a battery to screen for clinically-obvious verbal or performance deficits (cf [22]) Each subject was tested individually All subjects were tested during the follicular menstrual cycle phase to avoid possible confounding effects of hormonal fluctuation [28]

Subjects were randomly assigned to either of two conditions Alcohol (n=10) or placebo (n=10) After completion of the study series, background characteristics of subjects assigned to the alcohol and placebo groups were contrasted using *t*-tests for independent samples No statistically significant differences were found between the two groups of subjects Table 1 summarizes pertinent background variables

Treatments

The effects of ethanol (0 75 ml/kg) were compared with placebo in a group design (n=10 per group) under randomized, double-blind conditions Body weight determined the volume of ethanol in the experimental beverage The amount calculated was mixed with grapefruit juice to yield a ratio of 20% ethanol to total volume The placebo beverage contained a mixture of grapefruit juice and Karo® syrup to provide an isocaloric beverage

Apparatus

Both alcohol and placebo beverages were administered in a modified thermos bottle with attached straw [31] A strong initial gustatory cue was provided by placing 3 ml of 30% ethanol and grapefruit juice solution in a 10 ml reservoir at the end of the straw This small amount of ethanol produces no discernible blood alcohol level in placebo subjects [24,31] A strong olfactory cue emanates from gauze saturated with 95% ethanol placed in the bottom of the container Combined gustatory and olfactory cues ensure that similar expectancy effects are associated with both ethanol and placebo mixtures Subjects drank the beverage at a relatively constant rate over a 15 min interval

Test Battery

On Day 1 of the 2-day experiment subjects came to the laboratory and were given 3 trials of the test battery to familiarize themselves with the tests to be administered under experimental conditions and to minimize the effects of learning under experimental conditions All subjects were instructed to refrain from alcoholic beverages on the day prior to the experiment, and no solid food, caffeinated beverages or tobacco cigarettes could be consumed after midnight on the day of the experiment

Experiments were conducted on Day 2 Subjects arrived at the laboratory in the morning, two hours before beverage administration Subjects were screened for recent alcohol or drug use and acclimated to the laboratory All subjects completed a 23-item alcohol-effects expectancy scale [40] 30 min before receiving the experimental beverage Items on this scale included emotional states (e g , elation, happiness, tension), physical symptoms (palpitations, weakness, sleepiness), and task performance (concentration, memory and ability to play a sport or drive a car) Responses on this scale range from 0 (least) to 10 (normal) to 20 (most) Item scores for subjects in each group were contrasted using *t*-tests for independent samples Subjects in the alcohol and placebo

groups did not differ significantly in any of their expectancies of alcohol effects

After swallowing the experimental beverage, subjects provided a breath sample for measurement of blood alcohol levels (BALs), pulse rates were obtained and subjects completed the revised Subjective High Assessment Scale (SHAS) questionnaire [40] at 15, 30, 45, 60, 90, 120, 150, and 180 min after beverage administration Subjects also performed 3 cognitive-perceptual tasks and 5 psychomotor tasks at 15, 30, 60, 90, 120, 150, and 180 min (cf [50]) Test presentation order was randomized at every assessment time to minimize possible confounding of learning effects with performance responses

Blood Ethanol Levels

A pocket sized breath monitor device (Alco-Sensor, Model IV, Intoximeters, Inc , St Louis, MO) measured BALs Subjects provided breath samples during the baseline interval Subjects rinsed their mouths with water before the first breath sample was taken (+15 min)

Pulse Rates

Heart rate was measured by peripheral pulse Subjects were seated during each rating

Subjective High Assessment Scale (SHAS)

The revised SHAS [40] measures 3 subjective affective (e g , "high," "drunk" and "confused") and 9 subjective physical (e g , "dizzy," "clumsy," "feel terrible," etc) responses to alcohol Subjects indicated their perceived level of intoxication response for each item by placing a mark on an unnumbered 36 point scale that ranged from "normal" to "extremely "

Cognitive-Perceptual Tasks

Timed paper-and-pencil cognitive-perceptual tasks were selected from a battery adapted by Wilson and colleagues [50] from tests similar to those developed by Thurstone [34] Tasks included

(1) Card Rotations [10,50] This test commonly has been used to measure visuospatial ability Each item consists of a sample shape followed by 8 rotations or mirror-image rotations of that shape Subjects are presented with a prototype and asked to compare, select and circle all rotations within the plan but to avoid choosing any mirror-image rotations (time 60 sec)

(2) Sentence Completion [50] This test measures shape (symbol) recognition, hand-eye coordination and motor speed A series of abstract sentences are presented, e g , "i before e " Subjects selected and circled one of two pairs of letters according to the instruction embedded in the abstract sentence (time 30 sec)

(3) Perceptual Speed [34,50] This test measures visual discrimination, hand-eye coordination and motor speed Subjects identify repetitions of sample digits (abstract symbols) in rows of other digits (time 30 sec)

Statistical Analysis

The 2 most similar scores for cognitive-perceptual tasks performed during the baseline interval were averaged for each subject Change scores were obtained by contrasting scores for each post-administration assessment time with baseline values Repeated measures analysis of variance of group (dose), time, and group-by-time effects were performed Pearson product-moment correlation coefficients were calculated for BAL levels versus SHAS item scores, pulse rate changes, and cognitive-perceptual test scores

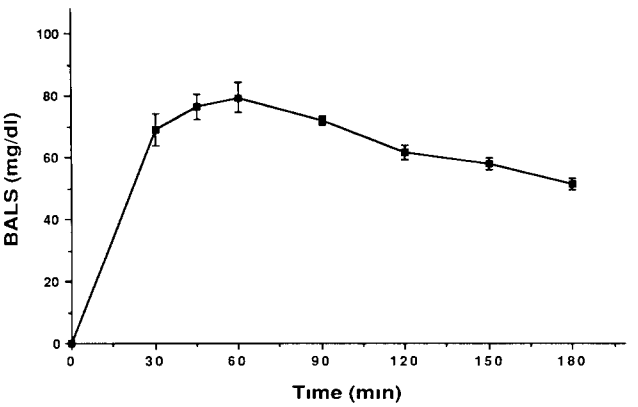

FIG 1 Mean (±SEM) blood alcohol levels in 10 female subjects after administration of 0 75 mg/kg 95% ethanol

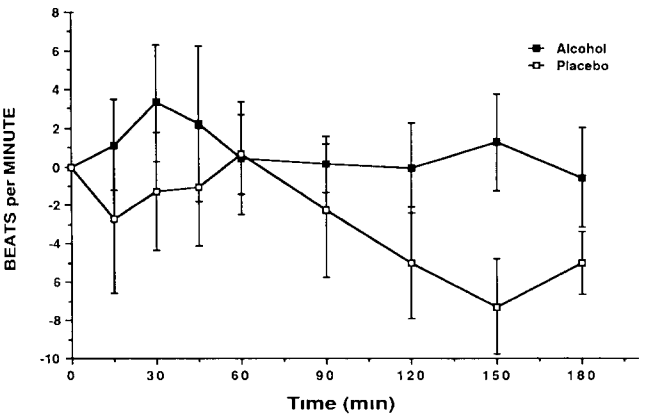

FIG 2 Mean (±SEM) peripheral pulse rate changes from baseline for 10 female subjects after administration of 0 75 mg/kg 95% ethanol and 10 female subjects after administration of isocaloric placebo

RESULTS

Blood Alcohol Levels and Subjective Levels of Intoxication

No subject in either group had a measurable BAL during baseline, and no subject who received placebo had a measurable BAL at any time after beverage administration BALs for all subjects who received alcohol were averaged for each post-administration assessment time and analyzed using one-way ANOVA $F(9,54)=11\ 951$, $p<0\ 001$ Mean BALs are shown in Fig 1

Pulse Rates

Pulse rate data were obtained at baseline and at all post-administration assessment times There were no significant relationships observed between pulse rate changes (increments or decrements from baseline) and BALs in the alcohol group Figure 2 displays almost mirror-image pulse rate patterns for alcohol versus placebo subjects Large variances

TABLE 2
CORRELATIONS

Blood Alcohol Levels Versus SHAS* Questions

Rank	r	R^2	Q*	Content	*p* Value (1-tailed)	(2-tailed)
1	82	67	8	Dizzy	0 05	0 025
2	79	62	3	Clumsy	0 05	0 025
3	78	61	10	Drunk	0 05	0 025
4	75	56	7	Floating	0 10	0 05
5	75	56	6	Alcohol Effects	0 10	0 05
6	74	55	1	Uncomfortable	0 10	0 05
7	73	53	2	High	0 10	0 05
8	72	52	4	Confused	0 10	0 05
9	71	50	12	Feel Great	0 10	0 05
10	69	48	5	Slurred Speech	0 10	0 05

*See [40] Scales range from 0 ("normal") to 36 ("extremely")

TABLE 3
PLACEBO RESPONSE TO SHAS* QUESTIONS

Rank	Q*	Mean Value	Content
1	3	1 1	Clumsy
2	4	0 9	Confused
3	7	0 7	High
4	6	0 4	Alcohol Effects
5	1	0 3	Uncomfortable
6	7	0 2	Dizzy
7	8	0 2	Floating
8	10	0 2	Drunk
9	5	0 0	Slurred Speech

*See [40] Scales range from 0 ("normal") to 36 ("extremely")

among scores in each group occurred at each assessment time. Differences in change scores attained statistical significance ($p<0.05$) only at 150 min after beverage administration

Subjective High Assessment Scale Scores

Subjects reported increased subjective levels of intoxication and associated physical drug effects following acute ethanol administration. Table 2 displays the 10 (out of 12) revised SHAS items that correlated significantly with BALs Items with statistically-significant Pearson product-moment correlation coefficients were rank-ordered according to strength The separate contribution (i.e , variance) of scores for each item and BALs can be ascertained by examining the value R^2

Adjectives that subjects used to describe their subjective intoxication experience and related ethanol effects ranged from "dizzy," "clumsy" and "drunk" (which most strongly correlated with BAL) to feeling "confused" and "great" or "slurred speech" (which least strongly correlated with BAL).

Table 3 shows that rank ordering of SHAS items differed for placebo subjects The rank order of SHAS items for placebo subjects ranged from "clumsy," "confused" and

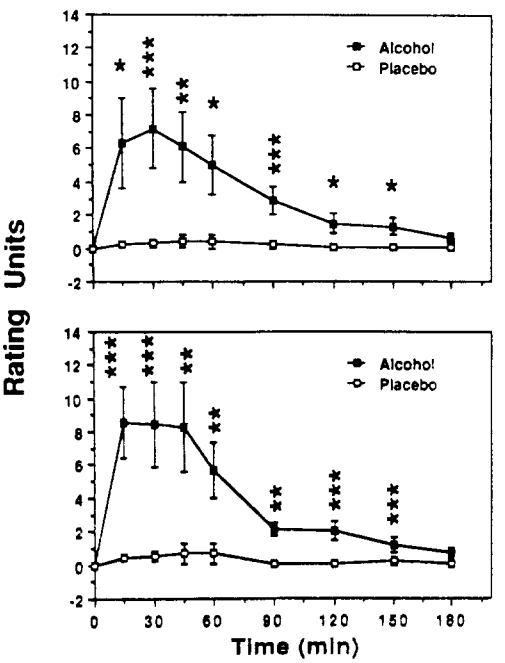

FIG 3 Mean (±SEM) SHAS rating unit changes on a 36-point scale for 10 female subjects after administration of 0 75 mg/kg 95% ethanol and 10 female subjects after administration of isocaloric placebo The upper panel displays subjective evaluation of feeling "drunk", the lower panel displays subjective evaluation of feeling "high " ***$p<0$ 01, **$p<0$ 02, *$p<0$ 05

"high" to "floating" and "drunk " Figure 3 displays the magnitude and pattern of responses for 2 SHAS items, "alcohol effects" and feeling "drunk," for each group

Cognitive-Perceptual Tasks

To assess effects of alcohol on the 3 pencil-and-paper tests, the two most similar baseline scores were averaged for each subject and change scores calculated from those values Despite Day 1 practice sessions for all tests in the battery, Card Rotation performance showed a learning effect on Day

TABLE 4
BLOOD ALCOHOL LEVELS VERSUS COGNITIVE-MOTOR TEST SCORES

Rank	r	R^2	Test	Time Samples	p-Value (2-tailed)	p-Value (1-tailed)
1	92	85	Perceptual Speed	4	0 10	0 05
2	81	67	Perceptual Speed	6	0 05	0 025
3	28	08	Sentence Completion	4	n s	n s
4	27	07	Sentence Completion	6	n s	n s
5	23	05	Card Rotations	4	n s	n s
6	15	01	Card Rotations	6	n s	n s

2 Subjects' average performance across all assessment times showed more improvement following alcohol than following placebo (mean=112.7 versus 104.5, $p<0$ 001)

Significant dose-by-time effects ($p<0.047$) were apparent in results of analysis of variance of responses for the Sentence Completion test Comparison of mean error scores for subjects who received alcohol and subjects who received placebo initially showed similar decrements (33% versus 25%, respectively) Scores subsequently improved for subjects who received placebo and declined for subjects who received alcohol and only approached statistical significance. $F(1,70)=4.402$, $p<0$ 06

Responses for Perceptual Speed were more robust and sensitive to ethanol: $F(1,70)=7$ 549, $p<0.019$, time ($p<0$ 001), and dose-by-time ($p<0$ 023) effects Relationships between the 3 cognitive-perceptual test scores and BALs are shown in Table 4. Pearson product-moment correlations were calculated between performance decrements and BAL for both 4 and 6 consecutive assessment times Only Perceptual Speed scores showed significant impairment correlated with BALs ($p<0.05$)

DISCUSSION

The implications of these findings are important for assessment of ethanol effects in women. Comparison of scores on the 23-item alcohol effects expectancy inventory developed by Schuckit [40] showed no significant differences in alcohol expectancy effects for 2 drinks between alcohol and placebo groups of women with no alcoholic first degree relatives. Further, young women significantly differed in both subjective and performance effects following administration of a social dose of alcohol versus a placebo beverage.

As measured by the revised SHAS [40], blood alcohol level increments were associated most strongly with feeling dizzy and clumsy, and least associated with feeling confused, feeling euphoric ("great") and experiencing slurred speech. Notably, subjects who received placebo were more likely to label their subjective response to beverage administration as being "high," while subjects who received alcohol were more likely to assess their subjective experience as feeling "drunk." Placebo subjects also had a slightly different rank ordering of perceived ethanol effects with "clumsiness" and "confusion" rated highest.

At all assessment times the mean BALs for the 10 FHN female subjects who received alcohol were comparable to those reported for young male subjects with no alcoholic first degree relatives [40] For women who received alcohol, these subjective assessments exhibited almost linear covariance with rapidly rising plasma ethanol levels. In comparison with findings for male subjects [40], response patterns for the intoxication level ("drunk") and the drug ("alcohol") effect SHAS item scores show less subjective assessment of impairment at virtually identical BALs. However, in contrast to the studies of young men conducted by Schuckit [40–42], our female subjects did not serve as their own controls in a random assignment design Mills and Bisgrove [33] had both male and female subjects serve as their own controls in a random assignment design which assessed both self-ratings of ethanol effects and tests of cognitive impairment Although the investigators did not ascertain family history of alcoholism, at a comparable dose (0 76 ml/kg) female subjects generally rated themselves less impared than males but exhibited greater cognitive impairment on a divided attention task Similarly, after 0 76 ml/kg ethanol Taberner [47] found young women to have slower reaction time on a visual task than young men Thus, our findings could reflect gender differences in response to alcohol as well as differences in experimental design, alcohol or other drug use histories, drinking patterns, or other intervening variables

Pulse rate data revealed no reliable significant differences between subjects in the alcohol versus placebo conditions The almost mirror-image mean pulse rate response patterns and large variances for subjects in the alcohol versus placebo groups could be attributable to individual differences in pulse rate changes following alcohol administration [51] Because there was no difference in activity level between the 2 groups, this pattern is unlikely to reflect differences associated with the physical movements of subjects during test battery administration In constrast to the large variance in pulse rate changes exhibited by subjects in each group at all other assessment times, the significant difference at 150 min after beverage administration may simply reflect a return to baseline rates or result from merely chance association

Three pencil-and-paper tests were presented No significant decrements were seen on Card Rotations This test was utilized to measure possible alterations in short term visual memory, ability to assess spatial relations, and ability to perform serial operations in spatial orientation Card Rotations also tests visual recognition, accurate perception of angulation, and discrimination of a prototype shape from a mirror-image Improved performance under ethanol conditions resembled responses of the young male subjects studied by Wilson and co-workers [50] Female subjects may have improved their scores by quickly grasping the "key"

idea—that mirror-image forms were incorrect (cf [19])—or, as Wilson and co-workers have suggested for young men [50], they may have responded to the alcohol beverage with risk-taking behavior

Effects of learning exhibited by female subjects who performed the Sentence Completion task following alcohol appear greater than those observed for males by Wilson and co-workers [50] Since this test assesses ability to abstract meaning from written instructions, employ visual selectivity, and work rapidly at a repetitive motor task, this finding might be related to the generally stronger verbal abilities attributed to females, or it simply reflects differences between male and female subjects in educational levels or occupational experience

Increments in BALs were significantly correlated with impaired performance on Perceptual Speed, a task which measures visual selectivity and scanning for a target symbol, attentional shifts, activation of rapid responses, and speed of hand-eye coordination The strong relationship between BALs and decrements in Perceptual Speed scores is indicated by the persistence of effects across all post-administration assessment intervals Scores for subjects who received alcohol showed impairments, but subjects who received placebo showed improvement Values for changes in performance scores for the ethanol-treated group closely paralleled BALs Considering the relatively small number of observations, the correlation coefficients for Perceptual Speed and BAL values presented in Table 4 show strong significance Responses by female subjects for Perceptual Speed appeared sensitive to dose ($p<0$ 019), time ($p<0$ 001), and dose-by-time ($p<0$ 023) effects These findings suggest that a more complex test of cognitive-perceptual capacities should be employed (cf [16,18]) Simple tasks have been reported to be insensitive to ethanol effects at comparable doses [26, 36–38] Accordingly, we have selected a divided attention task (DAT) [36,38] to replace simple motor tasks and pencil-and-paper tests that did not prove robust under alcohol versus placebo conditions Further examination of cognitive-perceptual responses in young women following alcohol will be investigated using a more complex divided attention task within our repeated measures design

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