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Pharmacology, Biochemistry and Behavior 78 (2004) 603–610

PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR

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No difference in responsiveness to a low dose of alcohol between healthy women and men

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Received 12 January 2004; received in revised form 23 March 2004; accepted 29 March2004

Abstract

The purpose of the current study was to examine gender-related differences in alcohol responsiveness by comparing the effect of a low-dose intravenous alcohol infusion upon saccadic eye movements, self-rated sedation and intoxication scores. The functional sensitivity to a low dose of alcohol in 12 healthy women and 12 healthy men was evaluated by comparing the effects of an intravenous alcohol infusion on a number of saccadic eye movement measures, including saccadic eye velocity (SEV), saccade latency, saccade accuracy, saccade deceleration and self-rated levels of intoxication and sedation. The infusion of a low dose of alcohol induced a decrease in SEV and increased saccade deceleration and self-rated scores of intoxication in both males and females. Saccade accuracy was also significantly deteriorated by alcohol in both groups. The alcohol infusion did not induce any main gender-related differences in the saccade or visual analogue scale measurements. According to the findings of the present study, no gender differences in the responsiveness to a low-dose alcohol infusion were found.

Keywords: Gender; Alcohol; Saccadic eye velocity; Clinical trial

1. Introduction

Women appear to be more susceptible than men are to many of the adverse effects of alcohol use and abuse. Because of more body fat and less body water, and because alcohol is dispersed in body water, women achieve higher peak blood alcohol concentration than men do after consuming equal amounts of alcohol (Jones and Jones, 1976a,b; Frezza et al., 1990). However, studies investigating gender-related differences in alcohol-induced cognitive and psychomotor performance have yielded disparate findings. Prior studies, where equivalent blood alcohol concentrations have been emphasized, have indicated that women show significantly more cognitive impairment in divided attention (Mills and Bisgrove, 1983; however, see Niaura et al., 1987) and memory tasks compared with male subjects (Jones and Jones, 1976a,b; Niaura et al., 1987), whereas reaction time (Mulvihill et al., 1997), flight simulator tasks (Taylor et al., 1996), body sway and pursuit tracking (Mills and Bisgrove, 1983; Niaura et al., 1987) were not influenced by gender.

As a potential explanation for the differences in alcohol-induced impairment between men and women, despite similar blood alcohol concentrations, prior research has suggested that alcohol pharmacokinetics or the physiological responsiveness of women to alcohol may vary with the cyclical changes in ovarian steroids throughout the menstrual cycle. However, there is a general consensus on the lack of evidence for significant effects of the menstrual cycle on alcohol pharmacokinetics (Lammers et al., 1995), and the majority of prior studies on alcohol-related cognitive, behavioral and sedative effects have not demonstrated any significant influences of ovarian steroids and menstrual cycle phase in healthy women. Although alcohol consistently induced changes in measurements of drug effect, sedation, stimulant-like effect, drug-induced euphoria, dysphoria/somatic effect and mood, no variation across

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doi:10.1016/j.pbb.2004.03.027

the menstrual cycle was reported (Holdstock and de Wit, 2000; Nyberg et al., 2004). Likewise, a number of studies have failed to demonstrate menstrual-cycle-related effects on alcohol-induced impairment of memory or attention (Brick et al., 1986; Niaura et al., 1987) and flight simulator performance tests (Mumenthaler et al., 2001a,b). However, in patients with premenstrual dysphoric disorder, which is a subgroup of women with a differential behavioral response to their endogenous gonadal hormones, decreased luteal phase sensitivity to alcohol has been reported (Nyberg et al., 2004).

Saccadic eye movements can be used to evaluate the sedative effect of alcohol, even at moderate blood alcohol concentrations. Alcohol, in doses resulting in blood alcohol concentrations between 0.4 and 1.0 mg/ml, has consistently been shown to decrease saccadic eye velocity (SEV) in a dose-dependent manner, (Lehtinen et al., 1979; Jäntti et al., 1983; Stapleton et al., 1986; Steveninck von et al., 1993; Gale et al., 1996; Moser et al., 1998; Holdstock and de Wit, 1999; Blekher et al., 2002; Nyberg et al., 2004). Furthermore, alcohol reduces the SEV, regardless of the evaluation of subjective sedation (Holdstock and de Wit, 1999). Saccade latency, which represents the time lap between target movement and saccade initiation, has, in some studies, been reported to increase in response to alcohol (Jäntti et al., 1983; Stapleton et al., 1986; Steveninck von et al., 1993; Gale et al., 1996; Moser et al., 1998; Blekher et al., 2002), whereas other studies have not been able to detect any alcohol-induced increase in saccade latency (Lehtinen et al., 1979; Holdstock and de Wit, 1999; Nyberg et al., 2004). However, the limit for detection of alcohol-induced changes in saccade parameters remains to be determined, and also, which saccadic variables are the most sensitive ones to the alcohol-induced effects.

The purpose of the current study was to examine the effect of a low dose of alcohol, approximately corresponding to 0.2–0.3 mg/ml, on SEV, saccade latency, saccade deceleration and saccade accuracy. In addition, the study aimed at investigating gender-related differences in alcohol responsiveness to a low dose of intravenous alcohol infusion by comparing the effect of alcohol on saccadic eye movements, self-rated sedation and intoxication scores.

2. Material and methods

2.1. Participants

Twelve physically healthy women between the ages of 25 and 45 previously described in Nyberg et al. (2004), and 12 healthy men between the ages of 20 and 45 were recruited for the study. All participants were recruited through newspaper advertisement and local flyers. Women had regular menstrual cycles (cycle length 28.5 ± 0.6, range 25–33) and were not taking oral contraceptives or any other hormones.

Menstrual cycle phase was confirmed by the measurement of plasma progesterone >15 nmol/l on at least one of the two late luteal phase testing days and by records of the onset of menstrual bleeding. The primary measure of recent drinking history was a retrospective report of the total amount of alcohol consumption during the last 4 weeks preceding the inclusion of the study. Only light and moderate consumers (intake of less than 25 g alcohol/day; Eckardt et al., 1998) were included. Furthermore, all participants completed a semistructured interview, and those taking benzodiazepines or other psychotropic drugs were excluded. Physical examination and routine blood determination prior to testing were within normal range. The participants gave written informed consent, and the study, which was carried out according to the Declaration of Helsinki, was approved by the Ethics Committee, University of Umeå, Sweden.

2.2. Experimental design

In the female group measurements were made on four occasions during the menstrual cycle, twice in the midfollicular phase (6–12 days after the onset of menstrual bleeding) and twice in the late luteal phase (1–7 days prior to the onset of the menstruation). Within each cycle phase, an alcohol and a placebo infusion were given in randomized order, with an interval of 48 h. Male participants were examined on two occasions, with 48-h interval, and as in the female group, alcohol and placebo infusions were given in randomized order.

Testing was carried out in the gynecological outpatient department. Participants arrived in the morning or early afternoon. No participant consumed alcohol within 24 h of the test sessions, and they were furthermore encouraged not to consume alcohol during the study period (female participants) or the week preceding the alcohol challenge (men). An intravenous cannula was inserted in each forearm, and blood samples were taken for baseline levels of progesterone (women). To establish baseline, three sets of SEV measurements and visual analogue ratings of sedation and alcohol intoxication were made, with 5-min rests in between. Thereafter, a double-blinded randomized intravenous infusion of either placebo or alcohol was given for 30 min. The infusions were performed with a volume-directed infusion pump (IVAC 598) with a precision of 1 ml/h and a capacity of 999 ml/h. The experimental medications were prepared by the University Hospital Pharmacy. The alcohol solution contained 10% alcohol, dissolved in NaCl (9 mg/ml, Baxter Healthcare, IL, USA). Each patient received 0.2 g/kg alcohol. The infusion rate was adjusted according to the weight of the participant to allow infusion of the stipulated amount of alcohol within 30 min. The placebo preparation consisted of NaCl. To give a slight odor of alcohol, a small patch of cotton, wetted in alcohol, was placed near the participant's head. After the start of the alcohol infusion, SEV recordings and visual analogue ratings were made at 5,

15, 25, 35, 45, 55, 65 and 75 min. Blood samples for alcohol levels were taken at 5 and 25 min after the start of the infusion.

2.3. Measurements of eye movements

SEV was measured using electrooculography (EOG) with the CSGAAS5 system (Cardiff Clinical Trials, Cardiff, Great Britain), fully documented elsewhere (Marshall et al., 1985; Marshall and Richens, 1989). The test was performed in a quiet, semilighted room, with the patient sitting in a comfortable chair. Head movement was prevented by supporting the participant's head with a pillow. EEG cup electrodes (Synetics, Stockholm, Sweden) with a small amount of electrode gel (Elefix, Nihon Kohden) were used. After the skin had been scarified with Skinpure cream (Nihon Kohden), the electrodes were placed 1 cm lateral of the outer canthus of both eyes, with one common electrode in the center of the forehead. Electrode impedances were measured and confirmed to be less than 5 kohm.

The participant was instructed to watch an array of light-emitting diodes (LED) placed at eye-level, 67 cm from the glabella. The target for the eye movements was an illuminated LED. The participant was asked to look at the illuminated LED and to move her eyes to the next target (the next illuminated LED) as that LED was turned off and the next one in the array was lit. The target movements took place at 1.5-s intervals. A fixed, nonrandom sequence of 4×24 targets, producing target steps of 10°, 20°, 30°, and 40°, was displayed with a brief rest in between. The first 4 of these 24 target steps of each session were removed from the subsequent analyses to allow the participant to adjust to the procedure. The EOGs were DC amplified and low-pass filtered (-3 dB at 50 Hz) before being digitized to 12-bit resolution at a sampling frequency of 250 Hz. A personal computer controlled the target movements and digitized the waveform using an A-D converter. The 80 individual EOGs resulting from the 4×20 target steps were stored and analyzed off-line according to the method of Marshall and Richens (1989). First, the digitized data from each target displacement were processed to locate saccades. To avoid preemptive saccades and blinking artifacts, only saccades initiated between 50 and 400 ms after target movement were included. Also, to be considered a saccade, the recorded eye movement had to display a velocity of more than 100°/s. Second, each saccade was analyzed to determine the size of the saccade in degrees, the peak saccadic velocity, the peak saccade deceleration, the latency from target movement to onset of saccade and the saccade accuracy by comparing the actual eye position at the end of the saccade with the attempted target. Thereafter, a velocity–saccade size curve, known as the main sequence (Bahill et al., 1975), was plotted. The relationship between saccade size and peak velocity is important because it remains intact even when voluntary control of saccades is attempted. The main sequence was fitted by a quadratic equation to the peak velocity data using the calculated saccade angle as the independent variable. The influence of outliers in the data was minimized by carrying out the fitting procedure twice and weighing the second fit with the inverse of the square of the residuals from the first fit. From the main sequence, the velocity of an idealized saccade with 30° amplitude was chosen for further analyses because SEV reaches a maximum at approximately 30°–35° of angular movement (Bahill et al., 1975).

2.4. Visual analogue ratings

A visual analogue score (VAS) scale was used to rate sedation and subjective feelings of intoxication during the alcohol challenge. The scale measured from 0 to 100 mm, where 0 equaled complete absence of sleepiness/intoxication and 100 represented falling asleep/heavy intoxication. The patients were asked to rate their feelings of sedation and alcohol intoxication using the VAS scale after every set of SEV measurements.

2.5. Alcohol assays

Alcohol in serum was determined by gas–liquid chromatography on GLC 8600 (Perkin Elmer, USA) at the department of Clinical Chemistry. The between-day coefficient of variation (CV%) was 2.1% at the levels 10.5 and 31.0 mmol/l.

2.6. Statistics

The baseline saccade parameters and visual analogue ratings were calculated as mean baseline scores. Saccade parameters, self-ratings of sedation and intoxication were calculated as Δ scores (difference from baseline at every time point). Nine time points were available: one baseline mean, three measurements during and five measurements immediately after the alcohol/placebo infusion. Based on prior findings of no difference between cycle phases in saccadic eye movement sensitivity to alcohol among healthy women, data from follicular and luteal phase were combined in the female group (Nyberg et al., 2004; Holdstock and de Wit, 2000).

Baseline values of saccade parameters and visual analogue ratings were compared between male and female participants by Mann–Whitney U test. The alcohol-induced impairment in saccade parameters and visual analogue ratings were evaluated by three-way ANOVA with repeated measures. The independent factors were time (three time points during the alcohol/placebo infusion), drug (alcohol vs. placebo) and group (female vs. male participants). For menstrual cycle effects in the female participants, similar ANOVAs including cycle phase were performed. Blood alcohol concentrations were evaluated by two-way ANOVA with repeated measures, with time

and gender as independent variables. Significant changes at specific time points were extracted from the within-subject contrast derived from each significant ANOVA. Correlations between maximum alcohol effect on saccade parameters and visual analogue ratings (at the 25-min time point) and retrospective reports of alcohol use were made by Pearson's correlation. All values in the text and tables are displayed as mean ± S.E.M., unless otherwise stated. A P value $<.05$ was considered significant. The SPSS 10.0 statistical package was used for all analyses.

3. Results

The demographic data of the study group is given in Table 1. All participants were moderate alcohol consumers, reporting use of approximately 23–54 g alcohol/week during the month preceding the study. The reported use of alcohol among male participants was significantly greater than the reported use among women ($P<.05$).

With respect to progesterone levels >15 nmol/l in the late luteal phase, cycle length and onset of next menstrual bleeding, all female participants were considered to have had ovulatory cycles (mean luteal phase progesterone levels 22.3 ± 3.42 nmol/l). One male participant was unable to perform saccades at the 25-min time point during the alcohol infusion; otherwise, all participants had complete data. Missing values for this participant was substituted by interpolated values.

Baseline values for saccadic eye movement parameters and visual analogue ratings are given in Table 2. There were no gender-related differences at baseline for any of the studied parameters. No menstrual cycle effects on dependent variables were detected in the female participants [Drug × Cycle Phase—SEV: $F(1,11)=0.1$; latency: $F(1,11)=0.77$; accuracy: $F(1,11)=0.21$; peak deceleration: $F(1,11)$ 0.015; sedation: $F(1,11)=0.03$; and intoxication: $F(1,11)=0.18$].

3.1. Alcohol provocation

The alcohol-induced impairments in SEV, saccade latency, saccade accuracy, saccade deceleration and intoxication scores in male and female participants are depicted in Fig. 1. Sedation scores are not displayed because of limited space.

Table 1
Demographic data of the study group

	Female participants ($n=12$)	Male participants ($n=12$)
Age (S.D.) [years]	29.9 ± 5.6	30.0 ± 6.4
Weight (S.D.) [kg]	67.3 ± 17.8	77.2 ± 7.1
Married [n]	7 (58%)	7 (58%)
Employed [n]	12 (100%)	11 (92%)
Education university/college [n]	10 (83%)	8 (67%)
Psychiatric history [n]	1 (8%)	0
Alcohol consumption (S.D.) [g/week]	23.0 ± 14.3	54.1 ± 49.1 *

* Significantly different from female subjects, $P<.05$.

Table 2
Saccadic eye movement parameters and visual analogue ratings at baseline

	Female participants ($n=12$)	Male participants ($n=12$)
SEV (degrees/s)	466 ± 8	456 ± 8
Saccade deceleration (degrees/s^2)	− 46.1 ± 1.6	− 42.5 ± 1.6
Saccade accuracy (degrees)	− 3.1 ± 0.5	− 3.8 ± 0.6
Saccade latency (millisecond)	177 ± 4	173 ± 13
Alcohol intoxication scores (cm)	0	0
Sedation scores (cm)	1.7 ± 2	1.3 ± 0.2

Values are given as mean ± S.E.M. of four testing days in the female group and of two testing days in the male group.
There were no significant gender-related differences in baseline values by Mann–Whitney U test.

Compared with placebo, the alcohol infusion induced a marked increase in subjective alcohol intoxication scores in both male and female participants [main effect of drug: $F(1,22)=19.80$; $P<.001$; Fig. 1]. The alcohol infusion also induced a marked decrease in SEV [main effect of drug: $F(1,22)=10.36$; $P<.01$] and an increase in saccade deceleration [main effect of drug: $F(1,22)=9.30$; $P<.01$; Fig. 1]. Likewise, saccade accuracy was significantly deteriorated by alcohol [main effect of drug: $F(1,22)=7.80$; $P<.05$]. All other measures were unaffected by the alcohol infusion in both groups [saccade latency: $F(1,22)=0.37$; sedation scores: $F(1,22)=0.1$]. Alcohol concentrations at the 5- (T_5) and 25-min (T_{25}) time points were similar between groups (Table 3).

During the alcohol infusion, no difference between male and female participants in SEV, saccade deceleration, saccade latency or saccade accuracy response were detected [Drug × Gender interaction; SEV: $F(1,22)=0.88$; saccade deceleration: $F(1,22)=0.70$; saccade latency: $F(1,22)=0.22$; and saccade accuracy $F(1,22)=0.02$]. Likewise, no differences in self-rated levels of alcohol intoxication or sedation scores were found between groups [Drug × Gender interaction; alcohol intoxication: $F(1,22)=1.29$; sedation scores: $F(1,22)=0.40$]. Furthermore, there were no significant Drug × Gender × Time interactions for any of the saccade parameters or visual analogue ratings (Fig. 2).

The alcohol infusion induced a marked initial effect (at T_5) in SEV and saccade deceleration in both groups (Table 3). However, only women reported a significant increase in saccade accuracy and in self-rated intoxication scores already at 5 min of alcohol infusion (Table 3). During the following 20 min (between T_5 and T_{25}) of alcohol infusion, both groups displayed unaltered SEV and saccade deceleration responses between T_5 and T_{25}, despite a doubling of alcohol concentrations between these two time points (Table 3). However, saccade accuracy and intoxication were further deteriorated between T_5 and T_{25}. There was no difference between groups in any of

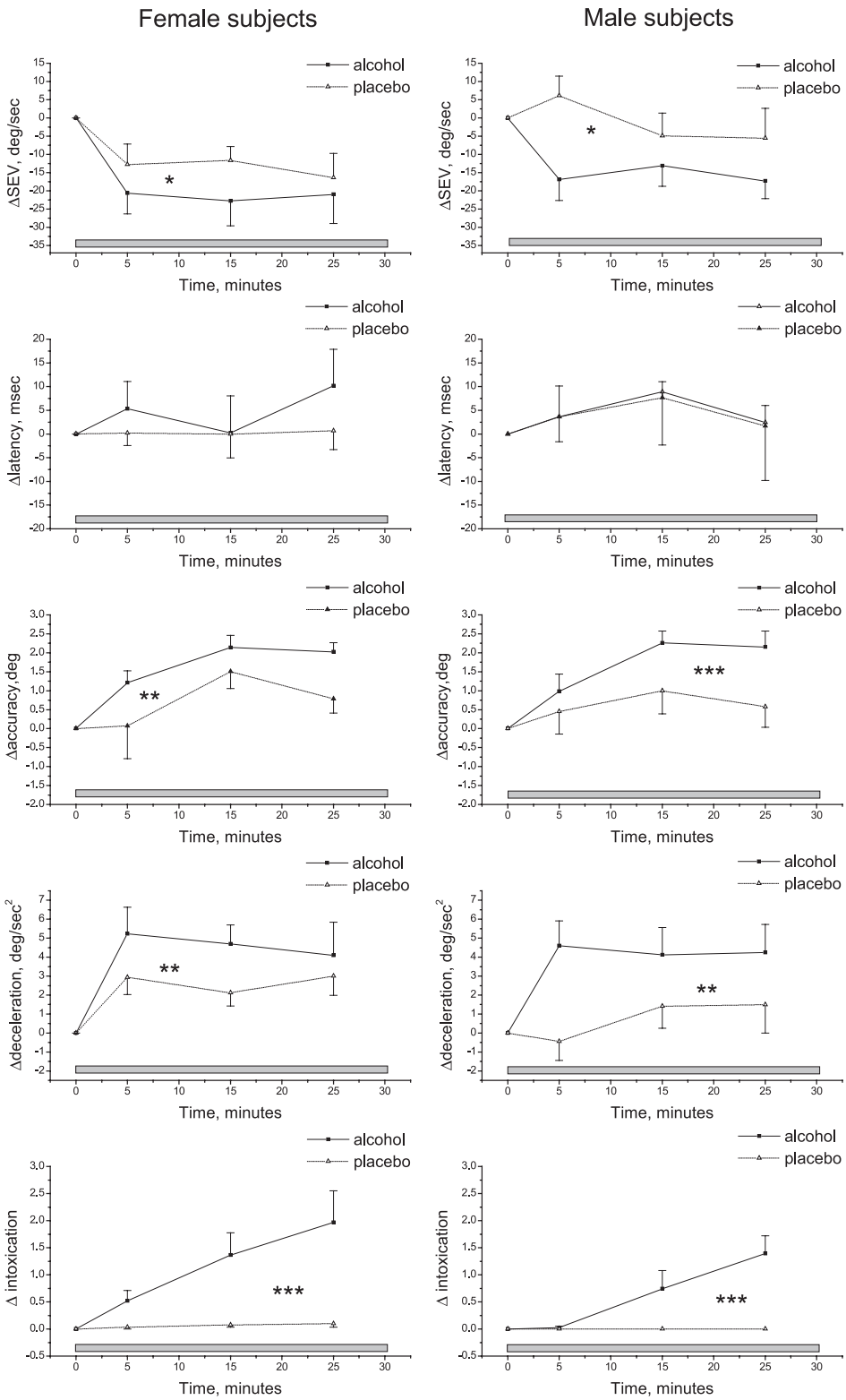

Fig. 1. Mean ± S.E.M. of change in SEV, saccade latency, saccade accuracy, saccade deceleration and alcohol intoxication scores from preinfusion baseline in response to alcohol or placebo infusion in healthy female ($n = 12$) and male subjects ($n = 12$). The alcohol infusion was 0.2 g/kg and lasted for 30 min, and the gray horizontal bars in the figures indicate its time course. Compared with placebo, the alcohol infusion induced a marked increase in subjective alcohol intoxication scores in male and female subjects. The alcohol infusion also induced a marked decrease in SEV and an increase in saccade deceleration and saccade accuracy. Saccade latency was unaffected by the alcohol infusion in both groups.

Table 3
Mean + S.E.M. of saccade parameters, subjective levels of alcohol intoxication and blood alcohol concentrations at 5 (T_5) and 25 (T_{25}) min of alcohol infusion

	Female participants ($n = 12$)		Male participants ($n = 12$)	
	T_5	T_{25}	T_5	T_{25}
SEV (degrees/s)	-21 ± 6 **	-21 ± 8 *	-17 ± 6 *	-17 ± 5 **
Saccade deceleration (degrees/s^2)	5.2 ± 1.4 **	4.1 ± 1.8 *	4.6 ± 1.3 **	4.2 ± 1.5 *
Saccade accuracy (degrees)	1.2 ± 0.3 **	2.0 ± 0.2 ***,†††	0.98 ± 0.5	2.2 ± 0.4 ***,††
Intoxication (cm)	0.5 ± 0.2 *	2.0 ± 0.6 **,††	0.03 ± 0	1.4 ± 0.3 ***,†
Blood alcohol concentration (mmol/l)	3.2 ± 0.2***	7.7 ± 0.5 ***,†	3.3 ± 0.4***	6.7 ± 0.8 ***,†

* Significantly different from baseline levels, $P < .05$.
** Significantly different from baseline levels, $P < .01$.
*** Significantly different from baseline levels, $P < .001$.
† Significantly different from T_5, $P < .05$.
†† Significantly different from T_5, $P < .01$.
††† Significantly different from T_5, $P < .001$.

the saccade parameters or visual analogue scores after the infusion was terminated (data not shown).

There was a significant, positive correlation between maximum change in self-rated sedation during the alcohol challenge and retrospective reports of alcohol use ($P < .05$). Otherwise, there were no correlations between maximum alcohol-induced effects on saccade parameters and prior alcohol use.

4. Discussion

Consistent with prior studies evaluating the effect of alcohol on saccadic eye movements, the low-dose alcohol infusion induced a significant decrease in SEV compared with placebo (Baloh et al., 1979; Jäntti et al., 1983; Stapleton et al., 1986; Steveninck von et al., 1993; Gale et al., 1996; Blekher et al., 1997; Moser et al., 1998). A

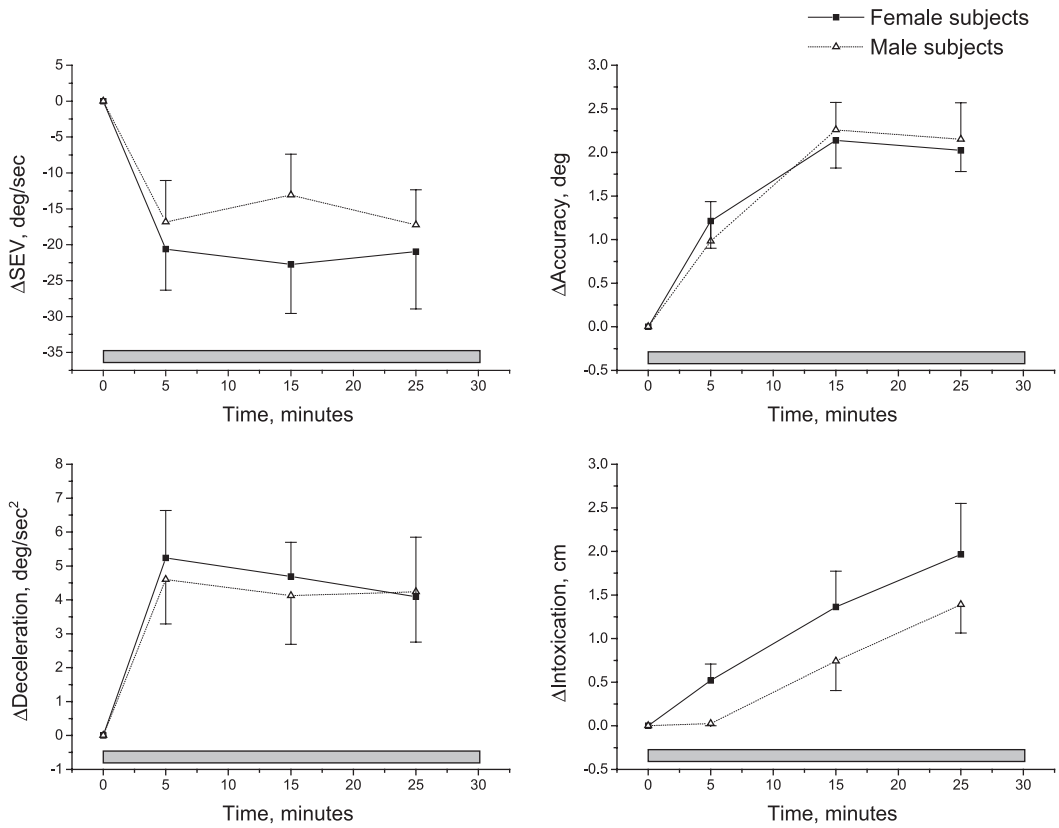

Fig. 2. Mean ± S.E.M. of change in SEV, saccade accuracy, saccade deceleration and alcohol intoxication scores from preinfusion baseline in response to alcohol infusion in healthy female ($n = 12$) and male subjects ($n = 12$). The alcohol infusion was 0.2 g/kg and lasted for 30 min, and gray horizontal bars in the figures indicate its time course. No difference between male and female subjects in alcohol-induced SEV, saccade deceleration or saccade accuracy response were detected [SEV: $F(1,21) = 0.83$; saccade deceleration: $F(1,21) = 0.11$; saccade accuracy: $F(1,22) = 0.01$]. Furthermore, no difference in self-rated level of alcohol intoxication between groups were found [$F(1,22) = 1.22$].

number of studies have not reported any alcohol-induced increase in saccade latency (Lehtinen et al., 1979; Holdstock and de Wit, 1999), which is in line with the findings in the present study. The alcohol infusion also affected the saccade accuracy and saccade deceleration response (Blekher et al., 1997; Gale et al., 1996), and there was also a marked increase in the subjective ratings of alcohol intoxication during the alcohol infusion in both groups. From previous studies, it is known that alcohol can produce both sedative-like effects and stimulant-like subjective effects (Downing et al., 2003). However, despite subjective reports of stimulatory effects, alcohol nevertheless reduces SEV (Holdstock and de Wit, 1999).

The main finding in the present study is the absence of gender-related differences in the saccadic eye movement sensitivity to low doses of alcohol. Our findings are in line with Blekher et al. (2002), who reported a decreased SEV after the ingestion of alcohol among African-American and non-Hispanic white college students. No gender differences were observed in their study in any of the studied saccade measurements (Blekher et al., 2002).

A number of studies (although not all) have identified impaired cognition and psychomotor performance after moderate doses of alcohol. Compared with male subjects, women recorded long-term functioning slower (Haut et al., 1989), had greater performance deficits on short-term memory tasks (Niaura et al., 1987; Jones and Jones, 1976a,b) and delayed recall tests (Jones and Jones, 1976a,b). Using a divided attention task, Mills and Bisgrove (1983), with two different alcohol doses, reported gender differences with the higher (0.76 g/kg) but not the lower dose (0.37 g/kg). Had a higher alcohol dose been used in the present study, it is possible that we might have surfaced a gender-related difference in the saccadic eye movement response to alcohol. In the current study, by using an intravenous route of administration, good control of blood alcohol concentration was achieved, as indicated by the absent gender difference in blood alcohol concentrations after 25 min of alcohol infusion. In addition, possible gender-related differences in absorption and first pass in metabolism were avoided. Gender differences in blood alcohol concentrations have been reported after oral intake of alcohol, whereas intravenous administration results in similar blood alcohol levels in men and women (Arthur et al., 1984; Goist and Sutker, 1985; Frezza et al., 1990).

In our study, alcohol response variables were combined for follicular and luteal phases in the female participants. The reason for using mean data across the entire menstrual cycle is that prior research has not indicated any differences in alcohol pharmacokinetics, cognitive or psychomotor performance, including effects on SEV, across the menstrual cycle in healthy female controls (Holdstock and de Wit, 2000; Nyberg et al., 2004; Lammers et al., 1995). By using data from both phases of the menstrual cycle, variability in examined parameters was reduced, and this procedure would hence have increased the possibility to detect differences in alcohol responsiveness between male and female participants.

A major weakness and limitation to the interpretation of the study is that baseline alcohol consumption was based on retrospective reports of alcohol use during the 4 weeks preceding the study. Retrospective reports of alcohol consumption are less valid than prospective, long-term data are and it can be assumed that the reported use of alcohol is underestimated. Based on the retrospective reports, it is therefore impossible to draw any conclusions about the actual alcohol consumption in these two groups of healthy participants, other than the fact that the study participants appeared to be light or moderate consumers. According to official Swedish alcohol statistics, women aged 20–24 consume approximately 61.5 g alcohol/week and men aged 20–24 consume 154 g alcohol/week (Centralförbundet för alkohol och narkotikaupplysning, 2002). There is no available statistics for the age group 30–34 other than a statement that alcohol consumption decreases with increasing age. Given the available data on alcohol consumption and the fact that the retrospective reports underestimated their actual alcohol consumption, we are confident that the participants in this study are representative of the healthy general population. Furthermore, according to the retrospective report of alcohol consumption, the male group consumed significantly more alcohol per week than the women did. Although this is not an unexpected finding, a larger consumption could result in tolerance to the effect of alcohol, which, in turn, might result in decreased alcohol responsiveness in men. We did find a significant, positive correlation between the maximum effect of alcohol on self-rated sedation scores and the retrospective reports of alcohol use; otherwise, there were no correlations between saccade parameters and alcohol use. As this correlation would indicate that participants who reported greater alcohol consumption would become more sedated during the alcohol challenge, we feel confident that the retrospective ratings are valid for ruling out participants with an alcohol consumption that would interfere with the interpretation of our results. In addition, as we failed to detect any gender-related differences in alcohol sensitivity, although the difference in baseline alcohol consumption could have worked in favor of the hypothesis that women would have been more sensitive to the alcohol infusion than men are, differences in baseline alcohol consumption were considered acceptable. Furthermore, another limitation to the study was that no standardized diagnostic instrument for the evaluation of history of alcohol and/or drug abuse and/or dependence was used to exclude participants with prior history of these disorders. It must be assumed that changes in sensitivity to alcohol remains even after a number of years of abstinence and that the lack of validated diagnostic procedures for prior alcohol abuse and dependence in our participants could result in the inclusion of such participants in the current study. However, although the validity of self-reporting of alcohol problems is low, it must be emphasized

that the included participants, in a semistructured study-specific interview, were asked about prior alcohol abuse and dependence prior to inclusion.

In conclusion, this study did not reveal any gender differences in saccadic eye movement responsiveness to a low dose of alcohol infusion or in self-rated scores of intoxication compared with placebo.

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