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ORIGINAL INVESTIGATION

Specific visuomotor deficits due to alcohol intoxication: Evidence from the pro- and antisaccade paradigms

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Abstract
Rationale Alcohol affects a variety of human behaviors, including visual perception and motor control. Although recent research has begun to explore mechanisms that mediate these changes, their exact nature is still not well understood.
Objectives The present study used two basic oculomotor tasks to examine the effect of alcohol on different levels of visual processing within the same individuals. A theoretical framework is offered to integrate findings across multiple levels of oculomotor control.
Materials and methods Twenty-four healthy participants were asked to perform eye movements in reflexive (pro-) and voluntary (anti-) saccade tasks. In one of two counterbalanced sessions, performance was measured after alcohol administration (mean BrAC = 69 mg%); the other served as a within-subjects no-alcohol comparison condition.
Results Error rates were not influenced by alcohol intoxication in either task. However, there were significant effects of alcohol on saccade latency and peak velocity in both tasks. Critically, a specific alcohol-induced impairment (hypermetria) in saccade amplitudes was observed exclusively in the anti-saccade task.
Conclusions The saccade latency data strongly suggest that alcohol intoxication impairs temporal aspects of saccade generation, irrespective of the level of processing triggering the saccade. The absence of effects on anti-saccade errors calls for further research into the notion of alcohol-induced impairment of the ability to inhibit prepotent responses. Furthermore, the specific impairment of saccade amplitude in the anti-saccade task under alcohol suggests that higher level processes involved in the spatial remapping of target location in the absence of a visually specified saccade goal are specifically affected by alcohol intoxication.

Keywords Alcohol · Pro-saccade · Anti-saccade · Intoxication · Inhibition

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Introduction

Within the context of a longstanding acknowledgment of alcohol's impact on general cognitive processing, relevant recent research has focused more specifically on how the substance impacts voluntary control and executive functioning (see Fillmore 2003 for a recent review). This emphasis emanates from appreciation of the fact that a basic feature of adaptive human functioning that appears to be compromised by alcohol intoxication is the ability to exhibit flexibility in response to dynamic environmental demands. In particular, a critical component of adaptive capacity that alcohol might impair is the ability to suppress reflexive impulses and to execute voluntarily controlled actions when effective performance in a situation calls for it. Examination of the effects of alcohol on basic visuomotor behavior provides a very promising method for evaluation of these phenomena because of the variety of oculomotor paradigms that can be linked to specific levels of information processing and their pertinent brain substrates. These paradigms yield considerably richer data sets than those available from more typical reaction time measures.

The key indices yielded by such paradigms are temporal and spatial parameters of saccades and fixations. Saccades are rapid eye movements that serve to bring the point of highest visual acuity to an area of interest, whereas fixations

represent phases of relatively stable visual axes during which information acquisition occurs. Two paradigms that are especially well suited to the study of reflexive and voluntary cognitive processing are the pro- and anti-saccade tasks. The former requires a reflexive saccade to an appearing target, whereas the latter involves voluntary inhibition of exactly this response and the execution of a saccade to the mirror position of the displayed target (cf. Hallet 1978; Everling and Fischer 1998; Massen 2004). Since their introduction, considerable knowledge has been accumulated regarding the physiological underpinnings of saccade tasks, thereby offering an opportunity to link alcohol's influences on performance to underlying brain systems (see Munoz and Everling 2004 for a review).

The impact of alcohol in the reflexive, pro-saccade task has been studied fairly extensively (Baloh et al. 1979; Lehtinen et al. 1979; Jantti et al. 1983; Gale et al. 1996; Moser et al. 1998; Wegner and Fahle 1999; Blekher et al. 2002; Vassallo and Abel 2002), but studies using anti-saccade tasks are still relatively rare. Moreover, the results of research on pro-saccade task performance have consistently demonstrated prolonged latencies under alcohol intoxication, without any effect on saccade accuracy. In contrast, the results from the few alcohol experiments that have included an anti-saccade task have been considerably more equivocal. Of the four such studies we could find, two found error rates were decreased by alcohol (Khan et al. 2003; Vassallo and Abel 2002), one found no alcohol effect (Blekher et al. 2002), and one found that alcohol increased error rates (Crevits et al. 2000). Results for saccade latencies were equally unclear. Although Khan et al. and Blekher et al. found increased latencies under alcohol, no significant differences were observed in either the Vassallo and Abel or the Crevits et al. studies.

Besides these inconsistencies, measures for saccade accuracy were reported in only two of these studies, with Blekher et al. finding significant overshoots under alcohol, whereas Vassallo et al. noted no differences between alcohol conditions for this parameter. The Blekher et al. study was the only one to report saccade velocity and it appeared to be decreased by alcohol. Other potentially informative parameters such as error correction rate and response variability have not been studied at all in previous work. In addition, the relevant pioneering work published so far has rarely included *both* reflexive *and* voluntary saccade tasks in the same study, making their direct comparison impossible. Moreover, of the two studies that did use both tasks, one involved different visual setups across tasks so that different saccade amplitudes were required for pro- versus anti-saccades, thereby clouding interpretation of the comparability of alcohol effects on them. This rather unsatisfying state of affairs has been compounded by the fact that most of the pertinent studies have been mainly descriptive rather than theory-driven.

The present experiment sought to improve upon the methodological precision and the conceptual framework of earlier research on alcohol and pro- vs anti-saccade task performance. The effort was designed to resolve existing equivocation and advance understanding of the impact that alcohol has on the cognitive processes being tapped by these two tasks. To help achieve this, both pro- and anti-saccades were examined in a single, unified procedure using the same participants, methods matched for consistency, and a wider array of parameters than has been incorporated in any analysis to date. Further, the study was integrated into the conceptualization framework for visual processing and saccade control suggested by Findlay and Walker (1999; see also Findlay and Gilchrist 2003) to provide a firmer theoretical grounding than has been evident in prior work.

This approach incorporates the common delineation of two parallel pathways—one responsible for the temporal aspect of the eye movement (when), the other responsible for the spatial parameters of the saccade (where). Both pathways are hierarchically organized on several processing levels. A fixate center is located in the when-pathway and competes with a move center in the where-pathway in a sort of push–pull interaction. Each center receives input from different control levels within its pathway. In this context, the pro-saccade task is ideally suited to probe the reflexive (automatic) level of control, whereas the anti-saccade task provides a useful tool to study the voluntary (cognitive) level (see also Leigh and Kennard 2004 for a recent review of research using oculomotor tasks in clinical research).

Peripheral targets in the pro-saccade task trigger saccades automatically, whereas in the anti-saccade task this reflex has to be inhibited by intentional input from a higher cortical level to cancel the reflexive movement (when pathway). In addition, a spatial transformation of the visual target information has to take place to enable a cognitive representation and parameter specification for redirection to a new saccade target. Recent analyses of anti-saccade performance suggest a 'race' between two parallel saccade programs (Massen 2004; Munoz and Everling 2004; Reuter and Kathmann 2004; Walker and McSorley 2006). Within the Findlay and Walker model this can be thought of in terms of two conflicts. The first of these is in the when-pathway, determining whether the current fixation on the central fixation cross is to be maintained or not. The second is between two simultaneously activated saccade targets, one exogenously triggered by the onset appearance of a peripheral target and the other endogenously generated in voluntary processing modules to direct the saccade to the desired location.

Generally, moderate alcohol intoxication is assumed to impair deliberate and voluntary functioning to a larger extent than automatic behaviors. Unfortunately, ethanol, unlike most other psychoactive substances, is not linked to any particular

receptors in specific brain areas, thus making it more difficult to determine which brain mechanisms are most likely to be vulnerable to alcohol intoxication. Indeed, studies in humans and rodents have mainly shown a general reduction in cortical activity due to ethanol (Davies and Alkana 2001; Wang et al. 1999; Krull et al. 1994; Liu et al. 2000). However, the underlying physiological structures that are relevant to our study can be linked to different modules of the theoretical framework introduced above. For instance, the intermediate layers of the superior colliculus (SC) are thought to mediate reflexive saccades in the pro-saccade task (Wurtz and Goldberg 1989; Munoz and Everling 2004).

Other cells in the rostral pole of the SC are tonically active during fixations and pause before saccades. The activity of the fixation related neurons in the SC is increased before anti-saccade trials (Everling et al. 1999) and there is evidence that this modulation in activity is mediated by frontal cortical projections from the frontal eye fields (FEF), supplementary eye fields (SEF), and the dorsolateral prefrontal cortex (DLPFC) (Guitton et al. 1985; Munoz and Everling 2004; Schlag-Rey et al. 1997). In the Findlay and Walker (1999) framework, the SC can be thought of as part of the fixate center and the frontal areas act as the substrate for top–down modulation from the voluntary level. In this context, the pro- and anti-saccade tasks allow for examination of the influence of alcohol intoxication at different levels of processing, specifically the automatic level via the pro-saccade task and the voluntary level via the anti-saccade task. To the extent that particular deficits are found in these tasks, inferences can be drawn about which brain functions and areas are likely to be sensitive to alcohol intoxication and these hypotheses could later be evaluated using appropriate measures of brain activity.

Given these theoretical considerations and the results of previously published studies, we predicted that alcohol intoxication would influence saccades in several specific ways. Although automatic processing in the pro-saccade task should be somewhat slowed by alcohol, it should remain metrically intact (i.e., saccade amplitudes and error rates might well remain unaffected). In contrast, higher levels of processing, especially those involving inhibition, can generally be expected to be significantly impaired by alcohol intoxication (cf. Abroms et al. 2006; Fillmore 2003). Consequently, performance on the anti-saccade task was hypothesized to be impaired by alcohol. It might be noted here that this hypothesis appears to be at odds with earlier findings by Khan et al. (2003), who reported an alcohol-induced *reduction* in anti-saccade error rate.

Given this apparent contradiction, we speculated that a to-be-expected impairment of performance by alcohol based on the voluntary level of processing might materialize, not in terms of direction errors, but rather as reduced spatial accuracy of saccades in the anti-saccade task. In other words, rather than the suppression of the reflexive movement, the spatial transformation processes necessary to perform in the anti-saccade task successfully may be specifically impaired by alcohol intoxication. Our design provides an opportunity to explore this possibility.

Materials and methods

Participants

Participants had to be of legal U.S. drinking age (21+) and have recent experience with alcohol doses comparable to those administered in our study. To ensure eligibility, participants were administered a face-valid Drinking Behavior Survey and Medical Screening Questionnaire, as well as the Short Michigan Alcoholism Screening Test (SMAST; Selzer et al. 1975). Grounds for exclusion were reports of an average of more than five drinks per day for men (or more than four for women), any medical condition reported on the Medical Screening Questionnaire that might contraindicate alcohol consumption, or a score of >3 on the SMAST. In addition, female participants had to have a negative result on a urine sample pregnancy test (Quick Vue One-Step hCG: Quidel, San Diego, CA). Twenty-four eligible participants (12 male, 12 female) gave informed consent to participate in two sessions, separated by 3 to 7 days and were instructed to abstain from alcohol for at least 24 h and all other drugs for at least 72 h before each session.

Participants received credit toward a course research participation requirement, a payment of $5 per hour, or a prorated combination of the two. Mean age of participants was 22.9 years (range=21–31 years). Self-reported drinking behaviors for the past year indicated a mean of 1.8 (SD=1.0) drinking episodes per week and an average of 3.5 (SD=1.6) drinks per episode. All participants had normal or corrected to normal visual acuity and intact color vision as determined by a test with a standard Snellen Chart. All procedures of the study were approved by the Florida State University Institutional Review Board.

Alcohol administration

The target breath-alcohol concentration (BrAC) in this study was 70 mg%, a level just below that constituting prima facie evidence of alcohol intoxication for driving purposes and one that is well above the minimum shown to impair a wide range of complex psychomotor tasks (Holloway 1994). In the alcohol session, participants received a beverage containing chilled tonic water mixed with 100-proof vodka in a 5:1 ratio. The amount of alcohol administered to reach the target was calculated for each participant based on height, weight,

age, gender, and the length of the drinking period (see Curtin et al. 1998 for details of the algorithm used). The beverage was equally distributed into four containers, each of which had to be consumed by the subject in consecutive 5-min periods. After this 20-min drinking period was a 20-min absorption period.

Accurate information was given about the approximate equivalence for the total beverage content in terms of standard alcohol drinks. BrAC was measured before the drinking period (to insure a zero baseline), at the end of the absorption period, immediately before, and immediately after the saccade tasks using an Alcosensor IV (Intoximeters, Inc, St. Louis, MO, USA). Mean BrAC during the saccade tasks was estimated to be 69 mg% based on averaging of before and after measures. In no-alcohol sessions, participants received the same total amount of liquid, consisting of tonic water only. They were also given accurate information about beverage content in this condition.

The decision to use a simple no-alcohol control rather than a placebo control condition in this study was a reasoned one. First, we wanted to implement the simplest possible design that still included the critical contrast. Second, in this connection, it is widely acknowledged among alcohol researchers that at least when using oral administrations of alcohol, it is quite difficult to achieve even nearly equivalent levels of either alcohol expectancy or subjective intoxication across alcohol and placebo conditions, thereby rendering suspect any comparative inferences based on them. Third, there is mounting evidence (see Testa et al. 2006 for a review) that when dealing with drugs like alcohol, whose effects are very familiar to subjects and which may therefore be subject to efforts to minimize them, placebos can invite misleading effects and might actually yield performances that exceed those obtained in simple no-alcohol conditions due to compensatory efforts. Obviously, we wanted to avoid such an artificially driven effect. Of course, future research might do well to include all three conditions, but that seemed premature before simple effects were documented.

Eye movement recordings

Eye movements were recorded using an EyeLink2 head-mounted video-based pupil tracking system (SR Research, http://www.eyelinkinfo.com), sampling at 250 Hz. This recording system includes a high-speed video camera positioned below the monitored eye and held in place by head-mounted gear. It has a relative spatial resolution in the order of a few minutes of arc and its absolute accuracy is better than 1/3°, depending on calibration. Viewing was binocular, but eye movements were recorded from the right eye only. Subjects were seated in a comfortable chair with a viewing distance of 60 cm in front of a nominal 22-in. CRT monitor. Calibration trials with three horizontal targets were performed before each block of trials. Mean average position error in an accuracy validation routine was not to exceed 0.33°. The on-line saccade detector of the eye tracking system was set to detect saccades with an amplitude of 0.15° or greater, using an acceleration threshold of 8,000°/s^2 and a velocity threshold of 30°/s.

Design

In each saccade task, a trial started with a light gray fixation cross of 1° diameter on a black background presented in the center of a black screen. After 1,000 ms the color of the fixation cross changed, indicating whether a pro-saccade trial (green) or anti-saccade trial (red) was to be executed. This fixation marker remained visible during the entire duration of each trial (overlap). At 300 ms after the color change, a light gray circle with a diameter of 0.5° visual angle appeared at 6° either to the right or left of the central fixation cross. For the pro-saccade trials, participants were asked to look at the peripheral target as quickly and accurately as possible as soon as it appeared. In anti-saccade trials, the task was to look to the mirror position of the appearing peripheral target as rapidly and accurately as possible.

The peripheral target stayed visible for 800 ms before the next trial started with a new light gray central fixation cross. If a participant moved back to the colored fixation cross while the peripheral target was still visible, an eye movement contingent display change was implemented during the return saccade to switch the display back to the neutral light gray centered fixation cross. At the same time, the peripheral saccade target was erased and a new trial started 50 ms later. There were a total of 280 trials divided into eight blocks. Within blocks pro- and anti-saccade trials were mixed and presented in a fixed random order. The completion of each trial block took about 90 s, resulting in a total duration of about 15 min for the experiment, including calibration of the eye tracking system at the beginning of each block. This, together with the timing and dosing of alcohol permitted performance assessment during peak, plateau BrAC, rather than on ascending or descending limbs.

Procedure

After eligibility screening and consent, participants were seated and the eye tracking equipment was set up for training. During an initial training block, instructions were given and eight self-paced sample trials were executed. Participants were then familiarized with the calibration routine and the saccade task in real time (20 trials). Following this second training block, participants were weighed to determine the amounts of beverage to be administered and either alcoholic or non-alcoholic beverages were prepared depending on

condition assignments made randomly at the first session. During the drinking and absorption periods, participants answered a battery of individual difference questionnaires on alcohol and other drug use, as well as some pertinent to personality, emotional, and behavioral attributes.

These data were collected for later exploratory analysis of possible moderators and/or mediators of observed effects. At the end of the absorption period, after BrAC was assessed, the experiment started with a calibration routine. Apart from the type of beverage administered, sessions 1 and 2 were identical. After alcohol sessions, participants completed additional BrAC tests until two consecutive readings were below established criteria for release (<20 mg%), at which time they were driven or escorted home. After the second session, participants were fully debriefed.

Data analysis

Saccades were classified online using EyeLink software. Following standard practice, the first two trials in each block were discarded for all subjects to reduce noise resulting from varying levels of attention to block beginnings. In addition, trials with primary saccade latencies shorter than 60 ms or longer than 800 ms and primary saccades with amplitudes <2° were excluded from analysis. These restrictions resulted in 94% valid primary saccades across all trials, corresponding to a total of 11,924 primary responses. Data were analyzed using 2×2 repeated measures analysis of variance (ANOVA) with the factors task and beverage condition.

Results

Table 1 presents an overview of results for all cells of the experimental design, including error rates, latencies for correct responses, and saccade amplitudes for both tasks. For the anti-saccade task error latencies, amplitudes of erroneous saccades and the frequency of executing corrective saccades are also reported. All analyses were based on individual mean values (n=24).

Error rates

The analysis of error rates revealed significant differences only for task ($F_{(1,\ 23)}$=28.71, p<0.001). Error rates in the pro-saccade task were very small (2.4%), but errors were made more frequently in the anti-saccade task (17.6%), as is typical (Fig. 1). However, there was no significant main effect of beverage condition ($F_{(1,\ 23)}$ <1, *ns*) on error rate and no Task X Beverage interaction ($F_{(1,\ 23)}$<1, *ns*).

Latencies

For saccadic latencies during trials in which participants responded correctly, we found significant effects of task ($F_{(1,\ 23)}$=135.54, p<0.001) and alcohol condition ($F_{(1,\ 23)}$= 16.36, p=0.001). Participants had shorter latencies in the pro-saccade task and showed longer saccadic latencies in the alcohol condition (Fig. 2). No interaction was found between task and alcohol condition ($F_{(1,\ 23)}$<1, *ns*). Looking at latencies in anti-saccade trials when erroneous reflexive saccades were made, there were no differences due to beverage condition ($F_{(1,\ 23)}$=2.44, *ns*).

Amplitudes

Saccade amplitudes in trials with correct saccade directions were affected by task ($F_{(1,\ 23)}$=4.38, p<0.05) as well as beverage condition ($F_{(1,\ 23)}$=6.15, p<0.05). There was also a significant interaction ($F_{(1,\ 23)}$=5.22, p<0.05) showing a

Table 1 Mean error rates, correct latencies, saccade amplitudes and saccade amplitude variability for pro and anti saccade tasks

For the anti-saccade task error latencies, amplitudes of erroneous saccades and the frequency of executing a corrective saccade. Means are based on the 24 subject means; standard deviations are indicated in parentheses.

	Pro saccade task		Anti saccade task	
	No alcohol	Alcohol	No alcohol	Alcohol
Error rate (%)	2.2 (2.3)	2.6 (1.8)	17.8 (14.3)	17.4 (15.1)
Correct latencies (ms)	197 (31)	219 (45)	240 (38)	266 (44)
Correct amplitudes (deg)	5.97 (0.25)	6.09 (0.37)	5.49 (0.91)	5.88 (1.09)
Correct amplitudes variability (deg)	0.65 (0.18)	0.70 (0.17)	1.38 (0.35)	1.38 (0.29)
Error latencies (ms)	–	–	154 (36)	175 (60)
Error amplitudes (deg)	–	–	4.95 (0.53)	5.25 (0.67)
% error correction	–	–	87 (14)	81 (25)

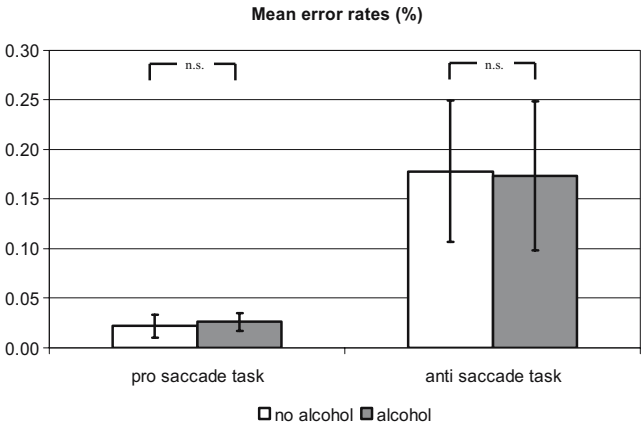

Fig. 1 Mean error rates for the pro- and anti-saccade task between no-alcohol and alcohol sessions

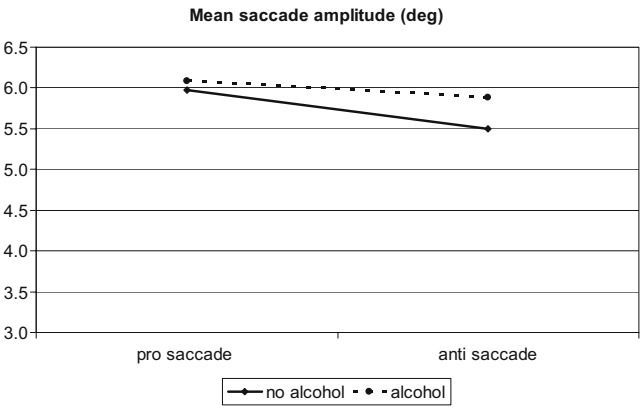

Fig. 3 Mean saccade amplitudes for correct primary saccades in the pro- and anti-saccade task between no-alcohol and alcohol sessions

greater influence of beverage condition on saccade amplitudes for the anti-saccade task than for the pro-saccade task. Participants executed very accurate primary saccades in the pro-saccade task under both alcohol and no-alcohol conditions, whereas saccade amplitudes were significantly enlarged (hypermetric) under alcohol in the anti-saccade task (Fig. 3). Analysis of standard deviations in a separate ANOVA revealed that saccade amplitudes were significantly more variable in the anti-saccade than the pro-saccade task ($F_{(1,\ 23)}$=4.81, p<0.05), but there was only a trend toward greater variability in the alcohol than in the no-alcohol condition ($F_{(1,\ 23)}$=3.67, p=0.07). Saccade amplitudes for erroneous primary saccade directions in the anti-saccade task also showed significantly larger saccade amplitudes under alcohol ($F_{(1,\ 23)}$=7.11, p<0.01).

Peak velocity

Peak velocity is a function of saccade amplitude. Because we found significant differences in saccade amplitude due to alcohol intoxication, we used an algorithm suggested by Collewijn et al. (1988) to determine peak velocity deviations from expected values for given saccade amplitudes. Results showed that there was no effect of task on peak velocity ($F_{(1,\ 23)}$=0.52, *ns*) for correct responses, but a significant effect of beverage condition ($F_{(1,\ 23)}$=8.68, p< 0.01). Under alcohol, saccadic peak velocities were slower than in the no-alcohol condition. In addition, the Task X Beverage interaction suggested a trend ($F_{(1,23)}$=3.37, p=.08), perhaps indicating that the effect might be more pronounced in the anti-saccade task. Figure 4 depicts the differences in deviation from expected saccade peak velocity, with the deviation of the pro-saccade task in the no-alcohol condition set to zero.

Error correction

The properties of corrective saccades for erroneous primary responses were also examined. Due to the very low error rate in the pro-saccade task, this analysis was confined to the anti-saccade task (see Table 1) using a simple repeated measures ANOVA. We found that in the no-alcohol condition, 87% of

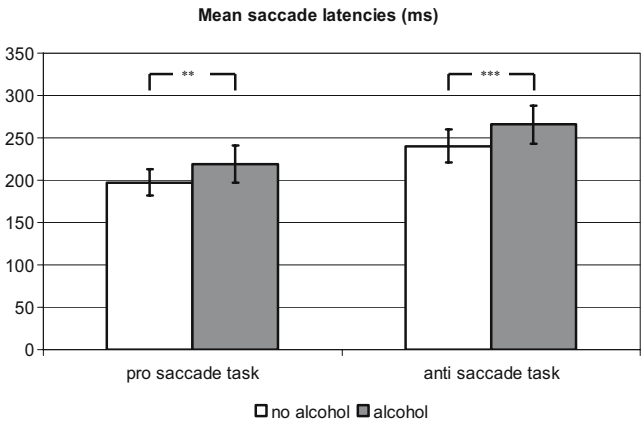

Fig. 2 Mean saccade latencies for correct primary saccades in the pro- and anti-saccade task between no-alcohol and alcohol sessions. **p<.01; ***p<.001

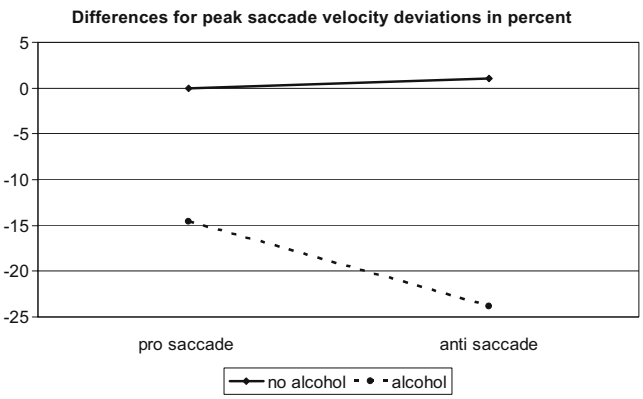

Fig. 4 Differences for peak saccade velocity deviations in percent for the pro- and anti-saccade tasks between the no-alcohol and alcohol conditions. Negative numbers reflect slower peak velocities

direction errors were immediately corrected with a secondary saccade. Unexpectedly, the error correction rate under alcohol was nearly 81%, a difference that was not significant ($F_{(1,\ 23)}$=1.62, *ns*). Moreover, neither the latencies nor the amplitudes of the corrective saccades differed significantly across beverage conditions (all *p*s>0.10).

Discussion

The present study examined the influence of moderate alcohol intoxication on performance in two visuomotor tasks (pro-saccade and anti-saccade) selected to represent different types of information processing. We structured the tasks to be identical in terms of the visual information presented and differ only in terms of required response. This permitted a clear determination of the effects of alcohol on different levels of visual processing and visuomotor control. Performance on the pro-saccade task involves reflexive processing, whereas anti-saccade performance reflects voluntary processing and includes inhibition of a reflexive response and reprogramming of the saccadic system to a new target location.

Results from the pro-saccade task indicated that processing on the reflexive level was altered by alcohol in terms of a general slowing of saccade preparation, apparent in the prolonged saccade latencies. However, neither the error rate nor the accuracy of saccades was influenced by moderate alcohol intoxication. These results replicated those of other studies that used variations of the pro-saccade task to study effects of alcohol intoxication (e.g., Baloh et al. 1979; Lehtinen et al. 1979; Jantti et al. 1983; Gale et al. 1996; Moser et al. 1998; Wegner and Fahle 1999; Blekher et al. 2002; Vassallo and Abel 2002).

Looking at the pattern of performances on the anti-saccade task, there were several findings that clarify, elaborate, and extend previous research results. First, we found that the error rate in the anti-saccade task was not affected by moderate alcohol intoxication. Although this is in line with the minority results of Blekher et al. (2002), it appears to contradict findings from studies by Vassallo and Abel (2002) and Khan et al. (2003), both reporting a decrease in error rate under alcohol, and also from Crevits et al. (2000), who found increased error rates. Although the results of Vassallo and Abel could be attributed to a learning effect due to the unbalanced sequence of non-alcohol and alcohol sessions they used, Khan et al. accounted for this factor.

The equivocal results for error rate across studies could be the result of at least two other factors. First, alcohol intoxication in the study of Crevits et al. (2000) study ranged up to very high levels, which could have impaired additional processes not affected by moderate intoxication as used in the present study. Second, in Khan et al., pro- and anti-saccade trials were presented in separate blocks and a gap condition was used throughout the experiment. The gap condition involves a blank screen introduced for a short time interval between the presentation of the central fixation point and the peripheral target (cf. Saslow 1967; Kingstone and Klein 1993; Walker et al. 1995). This typically leads to decreased saccadic response times and higher error rates. Such an outcome is likely based on two components: a non-specific warning signal effect (Ross and Ross 1980, 1981), which can also be induced using stimulation in non-visual modalities, and a specific oculomotor effect that is assumed to be the result of reduced activity in fixation related cells (Forbes and Klein 1996; Dorris and Munoz 1995).

It is quite possible that the decreased error rate in the Kahn et al. study is related to one of these additional gap-related factors not present in our study. This difference in results is interesting and warrants further research. However, because we were primarily interested in a comparison of reflexive vs voluntary processing mechanisms, we chose the more basic overlap condition paradigm as the more appropriate one to address this contrast.

The second finding for our anti-saccade task was that saccade latencies were significantly prolonged by alcohol. This is in line with earlier work (Khan et al. 2003; Blekher et al. 2002) and can be accounted for by an attenuation of motor preparation due to alcohol intoxication. Using single neuron recordings, Everling et al. (1999) demonstrated that saccadic reaction time is negatively correlated with the level of pre-stimulus activity in the saccade-related neurons in the SC ipsilateral to the stimulus. In addition to results consistent with these earlier findings, our design enabled us to directly compare this detrimental effect of alcohol at both reflexive and voluntary levels of processing. This was not possible in earlier studies because they either used only one task (Khan et al. 2003) or used substantially different versions of pro- and anti-saccade tasks (e.g., Blekher et al. 2002). Our present data indicate that the extent of prolonged latency in the anti-saccade task (10.5%) was almost identical to that in the pro-saccade task (about 11%). Given that both tasks can be directly compared in our study, this presents a strong case for the conclusion that alcohol intoxication impairs the temporal aspects of saccade generation, irrespective of the level of processing triggering the saccade. Apparently, this effect can be observed regardless of whether the saccade is generated via a reflexive or via a voluntary response. Furthermore, the results for erroneous anti-saccade trials showed no significant difference in saccade latencies as a function of beverage condition, which suggests that this type of saccade action is functionally different from reflexive saccades in the pro-saccade task.

Regarding the peak velocities of saccades, there was no significant effect of task, but alcohol intoxication led to decreased peak velocities, while leaving the main sequence intact. This finding replicates results from Blekher et al. (2002),

the only other study reporting velocity data for the anti-saccade task under alcohol. Results so far indicate that brain stem processes (indicated by an intact main sequence) and DLPFC functioning (indicated by stable error rates) are not specifically affected by moderate alcohol intoxication. However, increased latencies in the absence of any effect on error rates point to an alcohol-related impairment of FEF functioning (Pierrot-Deseilligny et al. 2003).

In contrast to findings for error rates, latencies and peak velocities, our results for saccade amplitude parameters indicate specific impairments in the anti-saccade task under alcohol. During no-alcohol anti-saccade trials, we found the typical undershoot in saccade extent (Bell et al. 2000; Edelman et al. 2006). Under alcohol, however, saccade amplitudes were significantly elongated in correct trials, thus appearing to be more "accurate." In reality, however, this pattern represents a substantial deviation from the normal hypometric saccades found in anti-saccade performance under no-alcohol conditions. Earlier studies did not report results on saccade amplitudes (Khan et al. 2003) or found no significant differences (Vassallo and Abel 2002).

However, despite using only a very small number of trials per subject, the authors of the latter study noted that *some* subjects showed improved accuracy when under alcohol, suggesting low power or low reliability of measurement might have masked a significant effect. In the only other study reporting saccade accuracy, Blekher et al. (2002) found a significant overshoot for saccades under alcohol for the anti-saccade task, but not the pro-saccade task. In our experiment, we also observed alcohol-induced overshoots in the anti-saccade task, but not in the pro-saccade task when the procedures were identical except for instructions. As suggested above, any apparently improved "accuracy" observed in the alcohol condition might be better interpreted as a deviation from the "normal" saccadic undershoot.

In this connection, we found that the variability of saccade amplitudes was *not* significantly affected by alcohol intoxication in either task. This suggests that alcohol intoxication does not have a global effect on saccade accuracy which, in turn, implies that cerebellar processes involved in the saccade control (Scudder et al. 2002; Enderle 2002) did not appear to be affected by alcohol, least not at the dose used here. However, whether the specific deficit in saccade programming we observed was due to impairment of higher level processes involved in the spatial remapping process or the generation of endogenous saccade targets—both are necessary in the anti-saccade task only—cannot be determined using the data available from the present study and will have to await further research.

It is perhaps interesting to note that somewhat parallel results were recently obtained in studies on *Cannabis* intoxication by Ploner et al. (2002). They found increased amplitudes for memory-guided saccades under THC intoxication. Unfortunately, they did not report saccade amplitudes for the anti-saccade task. More recently, Huestegge, Radach and Kunert (under review) found a very similar pattern of prolonged latencies and elongated amplitudes in chronic *cannabis* users tested when sober and compared to a *cannabis*-naive control group.

Further research on the effects of alcohol on visual processing is needed not only to establish the specific involvement and mechanisms of visuo-spatial remapping processes, but also to identify which specific inhibitory mechanisms are influenced by alcohol intoxication. Although our study found that there was no effect of alcohol on the inhibition of reflexive saccades in the anti-saccade task, a line of research using go/no-go paradigms has noted alcohol-induced impairment of inhibition (Mulvihill et al. 1997; Fillmore and Vogel-Sprott 1999, 2000; Easdon and Vogel-Sprott 2000). More recently, Abroms, Gottlob and Fillmore suggested that alcohol reduces intentional inhibitory control on selective attention, but has no effect on automatic inhibitory influences (Abroms et al. 2006). This assertion was based on their finding of impaired performance under alcohol in a delayed ocular response task, but not in a saccadic interference task, a conclusion that appears to contradict findings of the present study because reaction times in our reflexive pro-saccade task were significantly prolonged under alcohol.

However, looking closely at the performance data in the saccadic interference task used by Abroms et al. (2006), it seemed alcohol appeared to have a delaying effect of about 20 ms on saccade latency that fell just short of statistical significance ($p=0.07$). This effect might have proved to be significant with a sample size larger than the 12 and/or a number of test trials greater than the 40 they used. Future research is needed to explore this possibility.

In conclusion, the present analysis of alcohol effects on human performance using oculomotor control and visual processing as key dependent variables illustrates the potential of this approach to be as useful to alcohol researchers as it has been to those studying effects relevant to other clinical problems (see Leigh and Kennard 2004, for a recent comprehensive review). A variety of oculomotor paradigms are available and can be used to advance understanding of the modulating effects of alcohol on human behavior at various levels of visual processing and oculomotor control. In the present paper, we presented an initial study using the pro- and anti-saccade tasks in an integrated experimental design to evaluate alcohol effects at the levels of reflexive (automatic) and controlled (voluntary) processing.

Future research should include other tasks and incorporate attention to the intermediate level of "automated control" (Findlay and Walker 1999), which is critical for

many routine tasks, and should address additional facets of executive functioning and inhibition (cf. Fillmore 2003). Such systematic and theory-guided visuomotor research promises to contribute to a better understanding of the behavioral, cognitive, and neurobiological consequences of alcohol intoxication.

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