Effects of Alcohol on Verbal Processing: An Event-Related Potential Study

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Background: Behavioral studies suggest that alcohol intoxication impairs the speed and accuracy of word recognition and categorization, but alcohol's effects on the brain during verbal cognitive processing are not adequately understood. Using event-related potentials (ERP) and a word-recognition paradigm, this study investigated the effects of alcohol intoxication on prelexical, semantic, and mnemonic aspects of verbal processing.

Methods: Concurrent measures of ERPs and skin conductance responses were obtained in a word-repetition priming task and permitted a comparison of the effects of alcohol on the central and autonomic physiologic systems. Social drinkers participated in all four cells of the within-subjects balanced placebo design, in which the effects of alcohol and information as to the beverage content (expectancy) were manipulated. The average peak blood alcohol level peaked at 0.045%.

Results: None of the manipulations affected behavioral performance, and expectancy had no effect on any of the measures. In contrast, alcohol ingestion attenuated the temporoparietal N180, suggesting an impairment in prelexical pattern-recognition processes. Alcohol significantly increased the amplitude of N450 and the latency of P580, particularly on trials evoking sympathetic arousal as measured with skin conductance responses.

Conclusions: Although behavioral measures were unaffected, ERPs showed that a moderately low alcohol dose affected verbal processing during both early, prelexical and late, semantic stages. Alcohol significantly increased the difficulty of semantic access and integration, as reflected in larger N450 amplitude and longer P580 latency. This effect was particularly prominent on arousal-related trials, suggesting that alcohol impairs processes that modulate cognitive functioning. The lack of an interaction between the factors of repetition and beverage suggests that a moderately low alcohol dose exerts these effects via the semantic and integration systems rather than via memory processes.

Key Words: Alcohol, Verbal Processing, Event-Related Potentials, N400, Electrodermal Activity.

IT HAS BEEN established that alcohol intoxication affects multiple cognitive and psychomotor functions, including verbal processing and memory. Intoxication impairs reaction speed and accuracy in word categorization, recall, and recognition tasks (Erblich and Earleywine, 1995; Haut et al., 1989; Maylor et al., 1987; Miller et al., 1978; Mungas et al., 1994; Williams and Rundell, 1984). Furthermore, paired-associates learning and verbal fluency are decreased by acute alcohol intake (Hartcollis and Johnson, 1956; Peterson et al., 1990). However, despite this behavioral evidence, the effects of alcohol on the brain during verbal processing and memory have not been adequately studied. On the basis of their capacity to reflect synaptic current flows that perform cortical information processing with millisecond accuracy, event-related potentials (ERPs) could offer important insights into the effects of alcohol on neurophysiological stages of verbal processing.

Most of the studies investigating changes in ERPs after acute intoxication or chronic abuse have used different versions of an oddball paradigm requiring detection of a rarely presented target among the standard stimuli in auditory, visual, and somatosensory modalities. Chronic alcohol use affects late endogenous potentials (primarily reflected in a smaller P3 amplitude) across sensory modalities and under different experimental conditions, possibly indicating abnormalities in multiple functional systems in the brain. Irreversibility of these effects even after long abstinence (Porjesz and Begleiter, 1987), in conjunction with evidence obtained from high-risk individuals (Rodriguez Holguin et al., 1999), has given rise to a vulnerability marker hypothesis whereby attenuated P3 amplitude may suggest a genetic susceptibility to alcohol dependence (Begleiter and Porjesz, 1999; Monteiro and Schuckit, 1988; Pfefferbaum et al., 1991). The most common finding of the studies investigating the effects of alcohol intoxication on healthy social drinkers is also attenuated P3

deflection (Jääskeläinen et al., 1996; Marinkovic et al., 2001; Porjesz and Begleiter, 1981, 1985, 1996). This effect is inversely related to the alcohol dose (Rohrbaugh et al., 1987; Teo and Ferguson, 1986) and is modulated by task difficulty (Campbell et al., 1984). However, such simple, nonsemantic paradigms may engage different brain processes than the cognitively more challenging tasks involving verbal material, which rely on semantic and memory networks (Halgren, 1990a; Halgren et al., 1998). Consequently, although the effects of acute alcohol intoxication on ERPs during simple discrimination tasks under various conditions have been described, evidence on the effects of alcohol on stages of verbal memory processing is still lacking. Of particular interest is a negativity peaking at approximately 400 msec (N400), which has been studied extensively in language studies. The N400 is evoked by potentially meaningful material, such as words (written, spoken, or signed) and pictures, and is thought to reflect access to a semantic network and the ease of semantic contextual integration (Brown and Hagoort, 1993; Halgren, 1990b; Holcomb, 1993; Kutas and Van Petten, 1988).

In addition to its deleterious effects on ERPs, a central measure of stimulus processing, alcohol affects autonomic functioning as well (Lyvers and Maltzman, 1991; Richter et al., 1977). Skin conductance responses (SCRs) are a good indicator of orienting response (OR) and sympathetic arousal (Boucsein, 1992) and can offer a good complement to the ERP indices of central activity. Indeed, concurrent measures of ERPs and SCRs revealed that alcohol selectively attenuated the P3a to novel sounds only on trials that also evoked SCR (Marinkovic et al., 2001). Thus, use of ERP measures in conjunction with autonomic measures may help discern the selective effects of alcohol on central word processing and sympathetic arousal, as well as the interplay between the two physiologic systems. It may provide insight into modulatory brain processes (e.g., arousal circuits) that aid and moderate cognition.

A repetition priming paradigm that probes verbal recognition memory was used in this study because it yields a robust effect on the ERPs (Rugg, 1985; Smith and Halgren, 1987). Furthermore, neural generators of the elicited ERP deflections have been studied extensively (Halgren et al., 1994a,b; Nobre et al., 1994). This approach allowed an investigation of selective effects of a moderately low alcohol dose on early prelexical and late semantic verbal processing stages, as well as its effects on memory processes. A within-subject placebo design permitted an examination of the pharmacological effects of alcohol versus the information regarding the beverage content (expectancy). The subjects served as their own controls.

METHODS AND MATERIALS

Subjects

Participants in this study were screened for their past and present alcohol, tobacco, and drug use habits; alcohol or drug-related treatment; medical problems; handedness; and age. The subjects were recruited from

an advertisement in the campus newspaper and from another study. They were all healthy, nonsmoking, right-handed men and native English speakers with no alcohol- or drug-related problems. Their answers on the adapted Alcohol Use Questionnaire (Mills et al., 1983) indicated that they drank alcohol occasionally (2 times per week on average) and in low to moderate amounts (3.4 drinks per occasion). The MAST (Selzer, 1971) indicated no alcoholism-related symptoms, and the subjects reported no family history of alcoholism or drug abuse. In addition, their responses on the Childhood Hyperactivity Questionnaire (Tarter et al., 1977), Eysenck Personality Questionnaire (Eysenck and Eysenck, 1975), and Socialization Scale of the California Psychological Inventory (Gough, 1994) were within normal range.

Out of 15 participants, 12 (mean age, 23.6 years; SD, 2.6 years) completed all 4 experimental sessions, yielding a total of 48 recording sessions. Before the experiment, they all participated in an introductory recording session to become familiarized with the laboratory setting and experimental procedures. No drinks were administered at this time, but the subjects underwent a brief recording and filled out questionnaires. All individuals gave their written consent (approved by the human subject protection review board) to participate in the study and were paid.

Experimental Design and Procedure

A within-subject design was used in this study so that subjects could serve as their own controls in physiologic measurements and intoxication manipulations. A balanced placebo design was used in an attempt to assess the effects of beverage content and the effects of information as to the beverage content (expectancy). The factors of beverage and expectancy were fully crossed, and the participants were tested under all four experimental conditions. The consumed beverage and information concerning the alcohol content varied across sessions, but otherwise the same procedure was used in all four randomly ordered sessions. To maximize the credibility of deception conditions (e.g., subjects were sometimes told that they would receive placebo when in fact they consumed alcohol), a low to moderate alcohol dose significantly below the legal intoxication level was used.

The recording sessions were scheduled at least 48 hr apart and started between 3:00 and 4:00 PM to minimize the potential variability in alcohol metabolism and circadian rhythms. Participants were asked to abstain from alcohol for 24 hr and from food for 3 hr before the experiment. After taking a breathalyzer reading, the experimenter informed the participants about the designated drink for that session and brought in a tray with the appropriate cues (e.g., a vodka bottle). The subjects finished drinking in 10 to 15 min. After the drink consumption, the participants were fitted with the recording electrodes. During the task, they reclined comfortably in an armchair in an electrically shielded room and indicated their responses with a handheld microswitch. In addition to this task, the protocol included a mood-rating questionnaire and a simple tone-discrimination task (Marinkovic et al., 2001). The blood alcohol concentration (BAC) was monitored throughout the experiment with an Alco-Sensor III breathalyzer (Intoximeters, Inc., St. Louis, MO). The task was administered between 72 and 90 min after the subjects were presented with their drinks. The average BAC reached a peak (0.0453%) immediately before the task and remained almost the same (0.045%) when measured immediately after the task (Fig. 1). However, because of the interindividual variability in metabolic rate (Reed, 1985), some of the subjects were already on the descending limb of the BAC when others were reaching the peak BAC. Even though the average peak BAC was reached quite late in this study, Fig. 1 illustrates its protracted nature, suggesting that near-peak BAC was maintained for an extended period of time on average. Subjects filled out a short version of the Profile of Mood States (McNair et al., 1981) that contained questions about their feelings of "high." At the end of each experimental session, the participants filled out a detailed questionnaire consisting of Likert scales (1–5) querying them about the type and content of the beverage they were given, about their feeling of intoxication, about the task difficulty, and so on. They were offered warm sandwiches and
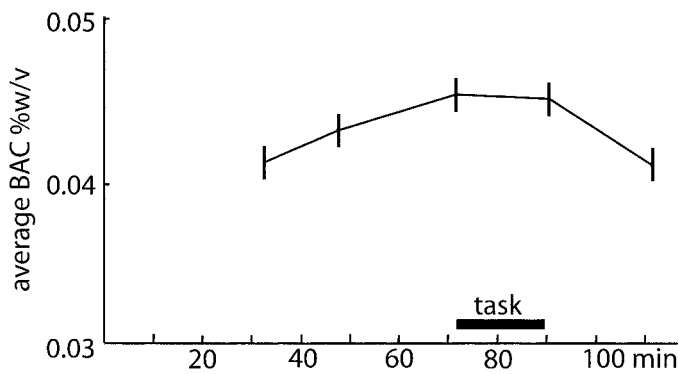
Fig. 1. Average blood alcohol concentrations (BAC; ±SEM) are presented for each measurement point in minutes after the start of drinking. The task was performed at near-peak levels on average; the BAC levels were 0.04527% w/v immediately before and 0.045% w/v immediately after the task.

were invited to read or play computer games. They remained in the laboratory until their BAC diminished to negligible (i.e., 0.01%) levels.

Beverage Administration

Smirnoff 80-proof vodka (40% alcohol by volume) was administered at a dosage of 0.4 g/kg of body weight mixed with chilled grapefruit juice and pineapple/orange/guava frozen concentrate in a 1:5.5 ratio based on a previously conducted pilot study. The beverage administration included the cues (e.g., vodka bottle) appropriate to the instructional expectancy condition procedure (Rohsenow and Marlatt, 1981). In the given juice/told alcohol condition, strong olfactory cues were provided by a small piece of vodka-saturated gauze placed in the cap of the bottle, unbeknownst to the participants.

Task

Subjects were instructed to memorize a list of 20 words presented individually on a computer screen for 300 msec every 4 sec, subtending a visual angle of 3° to 5°. At all other times, a fixation target consisting of five star characters was shown at the same screen location. Immediately afterward, a series of 200 words was presented within the recognition task. Ten words from the initially memorized list were randomly chosen as target words requiring a button press and were shown on half of the trials mixed in among the new, unlearned words. A 100-msec feedback tone occurred 1500 msec after word onset and informed the participants whether their response was correct (high pitch; 500 Hz) or not (low pitch; 100 Hz). All the words were four to six letters long and were equated across lists on their imagery, concreteness, and frequency of occurrence on the basis of published norms (Francis and Kucera, 1982; Paivio et al., 1968). The words had a low frequency of occurrence (one to seven per million) and were presented in a random order. A different set of words was used in each session in a randomized manner.

Recording of ERPs

The electroencephalogram was recorded with a Lycra (DuPont, Wilmington, DE) fitted electrode cap (Electro-Cap International, Inc., Eaton, OH) from 13 scalp sites (Fz, Cz, Pz, F3, F4, F7, F8, C3, C4, P3, P4, T5, T6) of the 10-20 international system; the electrode on the tip of the nose served as a reference, and the right earlobe served as a ground. The electrooculogram was recorded with bipolarly referred electrodes placed at the outer canthus of the right eye and just above the nasion. The electrode impedance was kept below 5 kΩ. The electroencephalogram and electrooculogram were recorded with a Grass-Telefactor (Quincy, MA) 16-channel polygraph with a bandpass of 0.05 to 75 Hz (half amplitude) and were digitized at 200 Hz (12-bit accuracy).

Only the trials with correct responses and without eyeblinks or other artifacts were included in the analyses, yielding 90.8 (SD, 5.1) and 91.2 (SD, 6.9) trials in averages of new and repeated words, respectively. Average voltages were quantified with an automatic algorithm within the following latency windows (corresponding peak latencies): 135 to 265 msec (P180), 270 to 370 msec (N310), 420 to 480 msec (N450), and 510 to 610 msec (P580). In addition, peak amplitude and the latency of the late positivity were measured within a 450- to 700-msec window. All measures were expressed in microvolts (amplitudes) and milliseconds (latencies) with respect to a baseline period of 100 msec before stimulus onset.

SCRs were recorded from Beckman Coulter, Inc. (Fullerton, CA) Ag-AgCl electrodes filled with lubricating jelly placed with adhesive collars (1 cm in diameter) on the volar surface of the first and third fingertips of one hand. Participants were pressing the microswitch with the other hand. The left hand/right hand order was counterbalanced across the four sessions. The SCRs were recorded with a Coulbourn Instruments (Allentown, PA) skin conductance amplifier through a constant 0.5 V bridge circuit. The SCR signal was digitized at 20 Hz for 100 msec before each word onset and continued for 3600 msec.

SCRs were measured on each trial with a semiautomatic computer algorithm and were defined as a maximum response within a latency window from 0.5 to 3.5 sec after stimulus onset. To ameliorate their skewed distribution, the SCRs were transformed with a square root function. Only the SCRs measured on trials with correct responses were accepted in the analyses that included the following measures: average SCR (response magnitudes averaged across all trials for new and repeated words) and block SCR (response magnitude averages of 5 consecutive trials for each stimulus type), resulting in 20 blocks across the course of the experiment, allowing an insight into response dynamics across the task. Because of equipment failure, SCR data of two participants (each during one experimental session) were not recorded.

Data Analysis

Repeated-measures ANOVAs with the factors beverage (alcohol or placebo), instructions (told alcohol or placebo), and repetition (new versus repeated) were performed on all measures. Additionally, a factor of electrode sites was included in the ERP analyses. Each of the five ERP time windows was analyzed separately with a repeated-measures ANOVA. To provide a conservative protection against sphericity assumption violations in the repeated-measures ANOVA, the p values were adjusted with the Huynh-Feldt procedure (Huynh and Feldt, 1980). When simple main effects were investigated, the Tukey post hoc procedure (Woodward et al., 1990) was used as protection against inflated probability values. These methods were applied to all analyses and for all response systems.

RESULTS

A nearly perfect recognition performance (mean, 98.3%; SD, 1.8%) and reaction time (mean, 641.45 msec; SD, 68.5 msec) were unaffected by any of the experimental factors. The subjects reported being more "high" when given alcohol than when given juice regardless of the instruction they were given [$F(1,11) = 11.56$; $p < 0.01$]. Similarly, the subjects' self-ratings of intoxication on a Likert scale (1–5) indicated that they felt moderately intoxicated (mean, 2.67; SD, 0.9). They felt equally inebriated whether they were told that the drink contained alcohol or placebo.

ERPs

Figure 2 depicts superimposed waveforms obtained in alcohol and placebo conditions averaged across all participants, sessions, and repetition conditions for all electrode
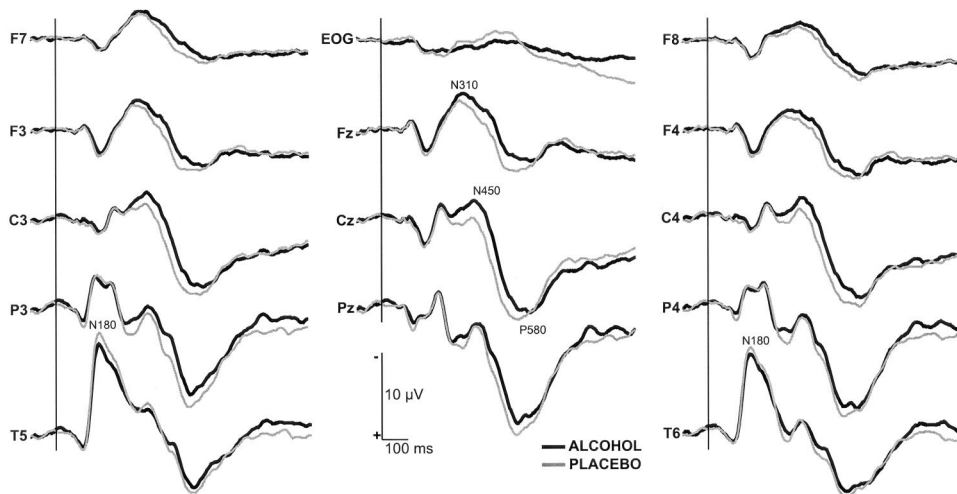
Fig. 2. Grand average waveforms obtained in alcohol and placebo conditions. The waveforms were averaged for both new and repeated words across all participants and sessions. Alcohol intoxication resulted in a selective attenuation of N180 at lateral temporal sites, a widespread increase of N450 amplitude, and an increased latency of P580. Word duration was 300 msec. Negative is up. EOG, electrooculogram.

sites. Visual inspection of the waveforms reveals a large, sharp-onset deflection 180 msec after stimulus onset that is negative at posterior temporal sites (T5 and T6) and inverts in polarity over central and frontal sites. It is followed by a series of superimposed broad negative deflections that could be observed at most sites, especially frontocentrally, between approximately 230 and 450 msec.

Effects of Beverage

None of the measures was affected by information about the beverage content (expectancy). A significant beverage × site interaction [$F(12,132) = 3.26; p < 0.01$] was observed for the earliest measured time window (135 to 265 msec after stimulus onset). The only scalp sites where ERPs were differentially affected by alcohol and placebo were T5 and T6 [$F(1,11) = 12.21; p < 0.05$]. At this latency, the overall event-related activity recorded over the posterior temporal sites (T5 and T6) was by far the largest, as compared with other sites within the montage. A closer look at the main effect of sites [$F(12,132) = 15.2; p < 0.001$] revealed a laterality difference, with larger potentials recorded over left parietotemporal sites [$F(1,11) = 7.74; p < 0.05$].

Whereas there was no significant effect of beverage on N310 (270- to 370-msec latency window), the overall laterality effect persisted: waveforms recorded on the left side were more negative than those on the right [$F(1,11) = 11.11; p < 0.05$]. This effect was particularly prominent at temporal sites because potentials recorded at T5 were more negative than at T6 [$F(1,11) = 16.23; p < 0.05$].
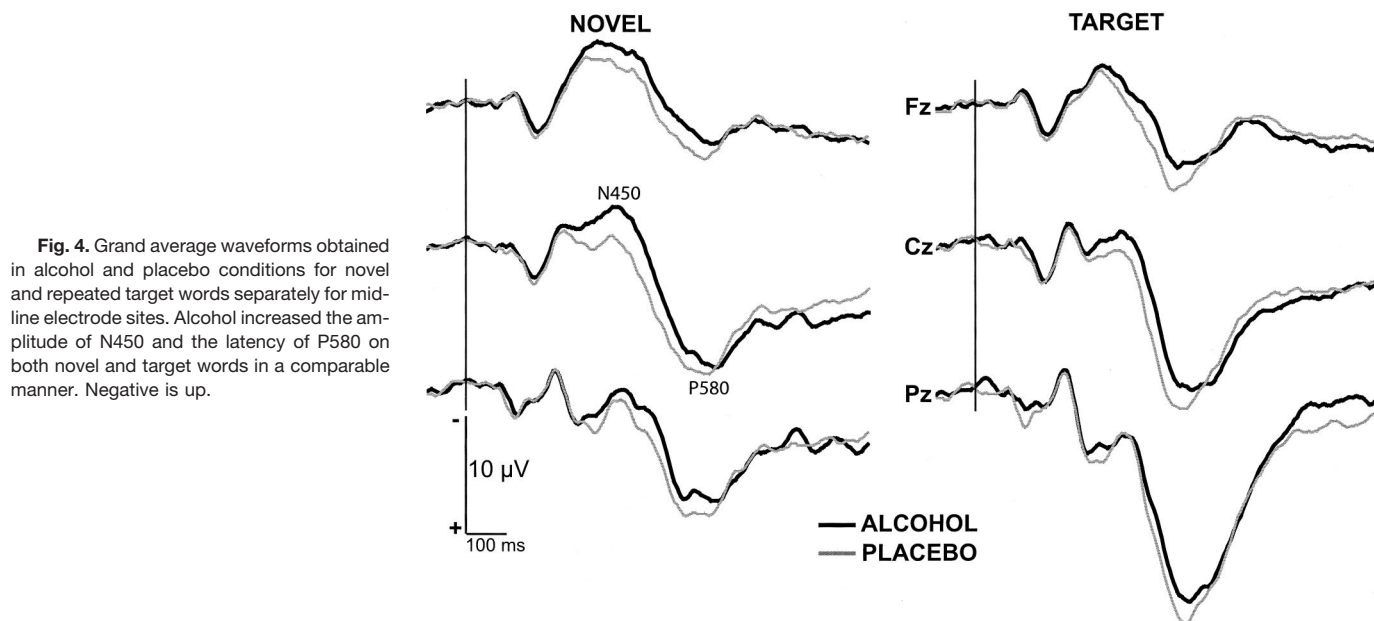
The waveforms obtained in alcohol and placebo conditions clearly begin to diverge in most sites at approximately 330 msec after word onset. A significant beverage × site interaction was obtained for the N450 area [420–480 msec; $F(12,132) = 2.59; p < 0.05$], with alcohol increasing the amplitude of N450. As can be observed in Fig. 2 by this latency, the waveform difference is quite pronounced over most scalp regions, although it is negligible over posterior temporal sites.

Effects of Repetition

As illustrated in Fig. 3, the main effect of repetition, with novel words evoking a more negative amplitude, was significant within all three measured time windows between 270 and 610 msec after stimulus onset: N310 [$F(1,11) = 10.4; p < 0.01$], N450 [$F(1,11) = 37.8; p < 0.0001$], and P580 [$F(1,11) = 19.3; p < 0.001$]. Similarly, the repetition × site interaction was very robust for these three latency windows (270–610 msec) as well, with the new/repeated difference increasing in the posterior sites: N310 [$F(12,132) = 6.9; p < 0.001$], N450 [$F(12,132) = 13.9; p < 0.0001$], and P580 [$F(12,132) = 12.0; p < 0.0001$]. Finally, the P580 peak
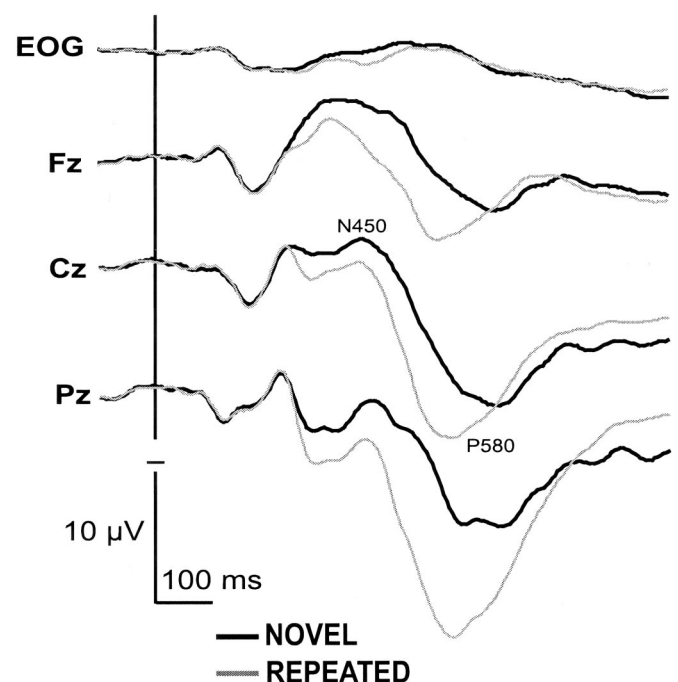
Fig. 3. Grand average ERP waveforms to novel and repeated words at midline electrode sites, averaged for both beverage and information conditions and across all participants. Repetition resulted in a sustained attenuated negativity and increased positivity after 270 msec. Word duration was 300 msec. Negative is up. EOG, electrooculogram.

NOVEL

TARGET

N450

P580

Fz

Cz

Pz

10 µV

100 ms

— **ALCOHOL**
— **PLACEBO**

Fig. 4. Grand average waveforms obtained in alcohol and placebo conditions for novel and repeated target words separately for midline electrode sites. Alcohol increased the amplitude of N450 and the latency of P580 on both novel and target words in a comparable manner. Negative is up.

latency was shorter for the repeated target (549 msec) than for the novel words [605 msec; $F(1,11) = 53.4; p < 0.0001$].

Waveforms recorded from the three midline sites in alcohol and placebo conditions are presented separately for the novel and repeated target words in Fig. 4. There was no interaction between the factors of beverage and repetition, indicating that although novel words evoked a larger negativity overall, alcohol intoxication affected the novel and target words in a comparable manner. Alcohol affected the series of superimposed negative components without exerting a significant influence on the peak amplitude of P580. However, it significantly prolonged its peak latency [$F(1,11) = 8.84; p < 0.05$; alcohol, 583 msec; placebo, 571 msec).

Electrodermal Activity

The main effect of stimulus type [$F(1,9) = 56.3; p < 0.0001$] reflected larger average SCRs evoked by target than nontarget words, with means of 0.22 µSiemens (µS) and 0.16 µS, respectively. Investigation of the dynamics across trials (Fig. 5) revealed that the SCRs habituated markedly within the first 10 trials, resulting in the main effect of block [$F(19,171) = 7.2; p < 0.0001$]. Even though the dose used in this study may not have been sufficient to significantly alter skin conductance, alcohol exhibited a trend to depress SCR amplitude in the last 16 blocks of the task [$F(1,9) = 4.6; p = 0.06$], in agreement with other studies using higher doses (Carpenter, 1957; Kilpatrick et al., 1980).

*ERPs as a Function of Electrodermal Responsivity*

In addition to the analyses performed on ERPs and peripheral autonomic (i.e., electrodermal) responses separately, their concurrent recording during this task afforded

an opportunity to directly compare the activity of the two physiologic systems (Lyytinen et al., 1992; Marinkovic et al., 2001). The SCRs were used as a grouping criterion during ERP averaging for each participant and for the repeated and novel words separately. The SCR^+ ERP averages contained only those trials for which a measurable phasic SCR was elicited. Conversely, no phasic SCRs were recorded on trials forming the SCR^- average waveform. Because SCRs were evoked on fewer trials than not, care was taken to balance the averages with respect to the total number of trials and the ordinal trial number. Averaged ERPs were based on 17.6 and 19 trials for new and repeated words on average. Data of four participants were eliminated from the analyses because of an insufficient number of trials. The waveforms were quantified by obtaining an average voltage within a 300- to 650-msec latency window, as well as the peak amplitude and latency for the P580 component.

As shown in Fig. 6, the SCR^+ and SCR^- waveforms

Skin conductance responses

Placebo

Alcohol

sqrt µSiemens
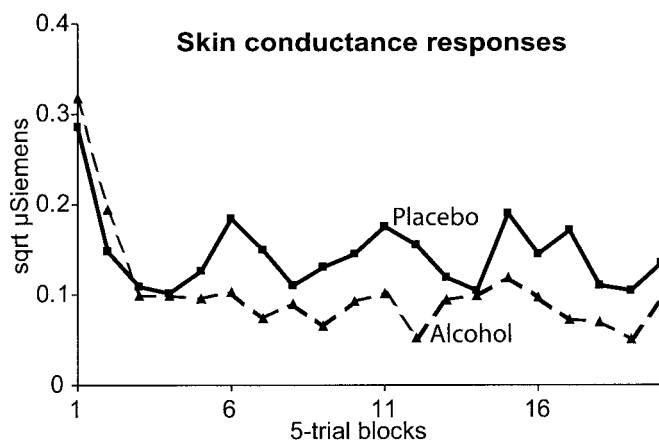
5-trial blocks

Fig. 5. Average SCRs (in $\sqrt{\mu}$Siemens) measured across five-trial blocks in alcohol and placebo conditions for the entire duration of the task. Alcohol tended to depress SCR amplitude in the last 16 blocks of the task.
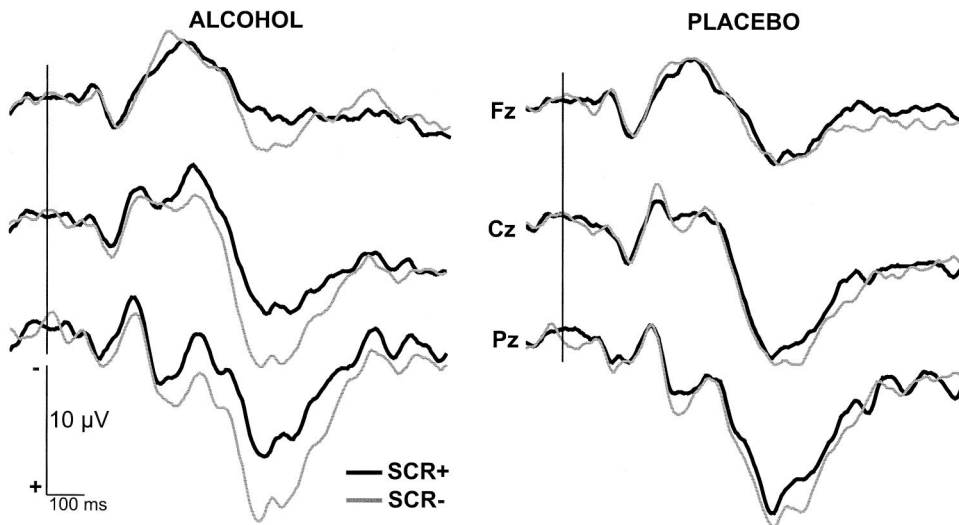
Fig. 6. Grand average waveforms obtained on trials with (SCR$^+$) and without (SCR$^-$) accompanying electrodermal reactions recorded from midline electrode sites in alcohol (left) and placebo (right) conditions. Alcohol increased the negativity in trials with sympathetic arousal 300 to 650 msec after stimulus onset. Negative is up.

begin to diverge significantly at approximately 300 msec after word onset, especially in the alcohol condition, with a large long-lasting negativity evoked on SCR$^+$ trials. Interaction between the factors of SCR and site [$F(12,84) = 4.3$; $p < 0.001$] was significant for the entire measured time window (300–650 msec).

Analysis of the peak amplitude and latency of the late positivity revealed that a smaller P580 was evoked on SCR$^+$ trials [$F(1,7) = 5.69$; $p < 0.05$]. This effect was primarily observed in the alcohol condition at centroposterior sites [$F(1,7) = 16.1$; $p < 0.05$]. Finally, the P580 peak latency was longer on SCR$^+$ as compared with SCR$^-$ trials under the alcohol condition only, as suggested by a beverage and SCR interaction [$F(1,7) = 5.61$; $p < 0.05$].

DISCUSSION

This study investigated the effects of alcohol on central measures of brain activity and on peripheral autonomic measures during a task of verbal recognition. Factors of beverage and repetition affected the overall ERPs independently from each other. Lack of an interaction between these two factors indicates that a moderately low alcohol dose does not impair recent verbal memory in normal participants. Instead, these results suggest that low-level alcohol intoxication exerts its influence on early (prelexical pattern analysis) and late (semantic and contextual integration) processing stages, but not on mnemonic aspects of word processing. Furthermore, the low to moderate alcohol dose was found to affect ERP deflections without impairing behavioral accuracy or speed on this verbal recognition task, suggesting the superiority of the physiologic measures in assessing the adverse effects of alcohol intoxication on verbal processing.

Alcohol Effects on Prelexical Pattern Analysis

A series of processes that are unrelated to the semantic significance of a word need to take place before the actual understanding of a word within its context. Some of those earlier stages (before 220 msec) embody a prelexical pattern-recognition process (Gros et al., 2002; Ritter et al., 1982), because they are unaffected by contextual constraints or word-processing task demands (Lovrich et al., 1986; Smith and Halgren, 1987). Neuronal ensembles in the ventral visual stream are selectively activated by wordlike visual stimuli and subserve processing of their morphological characteristics (Cohen et al., 2002; Dehaene et al., 2002; Nobre et al., 1994). The activation then proceeds anteriorly, encompassing the middle and superior temporal areas and the inferior prefrontal cortex, predominantly on the left (Dale and Halgren, 2001; Fiez and Petersen, 1998; Halgren et al., 1994a).

In this study, a large, left-dominant N180 was recorded over the posterior temporal areas. This corresponds to word-specific focal peaks observed in the left inferotemporal cortex at a similar latency with intracranial recordings (Halgren et al., 1994a), magnetoencephalography (Dhond et al., 2001; Marinkovic et al., 2003), and current source–estimated ERPs (Curran et al., 1993) during word-processing tasks. Alcohol significantly attenuated this large negative deflection at posterior temporal sites only. Thus, the effects of alcohol on this relatively early stage of verbal processing may reflect its influences on feature identification and prelexical pattern analysis subserved by the ventrotemporal area.

Alcohol Effects on Semantic and Contextual Integration

A negative deflection peaking at approximately 400 msec of latency (N400) is commonly evoked by potentially meaningful stimuli, including spoken, written, or signed words and pictures (Kutas and Federmeier, 2000). The N400 is modulated by priming and is commonly viewed as reflecting attempts to access and integrate a semantic representation into a current context (Brown and Hagoort, 1993; Halgren, 1990b; Holcomb, 1993; Rugg and Doyle, 1994). The N400 amplitude is attenuated by sentence-terminal words that

are congruent with the overall meaning of a sentence (Halgren et al., 2002; Kutas and Hillyard, 1980), as well as individually presented words that are repeated, semantically primed, or have a higher frequency (Osterhout and Holcomb, 1995; Otten et al., 1993; Smith and Halgren, 1987). Multimodal imaging studies sensitive to both spatial and temporal aspects suggest that the N400 to words in the sentential or single-word paradigm may be generated in the same brain region or highly overlapping brain regions (Halgren et al., 2002; Marinkovic et al., 2003).

In this study, the amplitude of N450 and the latency of P580 were significantly increased by alcohol. At this latency, it is likely that different informational aspects (e.g., semantic, mnemonic, contextual, and emotional) contribute modulatory influences to the amplitude of the N450. Understanding of a word then results from the process of their integration. A robust effect of repetition with repeated target words evoking a smaller negativity and larger positivity after approximately 270 msec has been reported in numerous studies, and this may reflect an easier access to the lexicon and the semantic store because of priming (Forster and Davis, 1984; Joyce et al., 1999; Nagy and Rugg, 1989; Otten et al., 1993; Rugg, 1985, 1990; Rugg and Doyle, 1994; Rugg and Nieto-Vegas, 1999; Smith and Halgren, 1987; Van Petten et al., 1991). The rather low alcohol dose used in this study did not affect priming per se, because there was no significant interaction between alcohol and word repetition. However, this result has to be viewed cautiously in light of other evidence suggesting that alcohol affects memory (Acheson et al., 1998; Mungas et al., 1994). Subsequent studies are needed to assess the dose-related effects of alcohol on priming under conditions of immediate and delayed repetition priming and with less well learned stimuli than was the case in this study.

A comparable increase in the N450 negativity to both repeated and novel words indicates that a sensitivity to repetition was preserved. This suggests that alcohol exerts its effect on at least partially different neural processes than those that underlie the effect of repetition itself. It is possible that mild intoxication increased the level of difficulty in semantic integration and prolonged the duration of word evaluation. This may have resulted from decreasing the inhibiting effects of the semantic context and increasing the difficulty of semantic and contextual integration. These results are in accord with other evidence (Zhang et al., 1997) that showed that chronic alcoholics preserved normal priming to words but exhibited increased negativity at this latency. Increased negativity of the N400 to sentence-terminal words has also been observed in schizophrenic patients, suggesting a weakening of the constraints provided by the semantic context (Nestor et al., 1997; Salisbury et al., 2000). Future work should determine whether the alcohol-induced N450 abnormality derives from the semantic or contextual aspects of verbal processing.

Recordings obtained with intracerebral electrodes in human subjects indicate multiple N400 generators, including the medial and ventral temporal and ventrolateral prefrontal areas (Halgren et al., 1994a,b; Nobre and McCarthy, 1995). Corroborating evidence comes from recent functional magnetic resonance imaging and magnetoencephalography studies suggesting that semantic processing is mediated by ventrolateral prefrontal and ventral temporal regions, especially on the left (Buckner et al., 2000; Halgren et al., 2002; Marinkovic et al., 2003). Thus, a low dose of alcohol may affect semantic word processing stage via its influence on the distributed circuits that primarily encompass the left prefrontal and temporal regions.

Alcohol, ERPs, and Arousal

A possibility that the effects of alcohol on cognitive ERPs were related to its effects on a more global sympathetic activation was explored by using concurrent electrodermal measures of the OR. An OR is usually evoked by a stimulus whose characteristics set it apart from other stimuli in the current context, such as its importance for the task performance, emotional significance (all the words used in this task had a neutral emotional valence), difficulty in processing, incertitude about stimulus categorization, or any other parameter that makes it different from the stream of other stimuli (Maltzman, 1979; Sokolov, 1963). The OR may have an adaptive value in pooling of activation across broad cortical, limbic, and subcortical circuits, increasing the likelihood of an appropriate and comprehensive stimulus evaluation and response selection (Halgren and Marinkovic, 1995). Alcohol may affect higher cognitive processes through its effects on the association cortices but also through its effects on the autonomic functioning and the relevant modulatory processes, such as sympathetic arousal. In this study, intoxication tended to decrease SCRs, although this change did not reach significance.

Concurrent recording of the ERPs and SCRs during this task indicated that only under the alcohol condition was a larger ERP negativity in the 300- to 650-msec latency range recorded on those trials that also evoked an arousal response. Consequently, these alcohol effects on the N450 and P580 were mainly due to an increased negativity confined to those trials that also evoked autonomic arousal. It is possible that this reflects increased difficulty in semantic integration, because the sympathetic arousal system may have been activated on trials that were somewhat more difficult to process because of alcohol intoxication or on which participants felt uncertain about their classification, resulting in a larger late negativity (Stuss et al., 1988). Furthermore, it is possible that engagement of the arousal system facilitated performance to counteract the effects of alcohol administration. Differences in temporal resolution between the measures of central (ERPs) and peripheral autonomic (SCR) activity obscure the nature of their interaction. That is, it is not clear whether alcohol primarily affected verbal processing or primarily resulted in aberrant

SCR elicitation. Nevertheless, even moderately low alcohol dose seems to alter central activation processes and may selectively impair modulatory brain processes, such as arousal, that moderate cognition and behavior. In a related study (Marinkovic et al., 2001) that used an auditory oddball task, a large P3a was evoked by novel, distracting tones on the SCR$^+$ trials. Alcohol intoxication abolished the P3a, indicating its interference with orienting to novel, unexpected, and potentially important events.

CONCLUSION

In summary, without impairing behavioral measures of verbal recognition, mild alcohol intoxication resulted in an attenuated P180, indexing the prelexical stage of verbal processing. Alcohol also affected the late widespread N450 and P580 potentials, potentially indicating an increased difficulty in semantic and contextual integration. The effects of alcohol on the late potentials mainly occurred on those relatively rare trials that also evoked sympathetic arousal, suggesting that alcohol may selectively impair processes that modulate cognitive processing.

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