0145-6008/98/2204-0945$03.00/0
ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH

Vol. 22, No. 4
June 1998

Effects of Ethanol on Temporal Recovery of Auditory-Evoked Potentials in Individuals at Risk for Alcoholism

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The present investigation examined the effects of placebo (P), low dose (LD), and high dose (HD) ethanol on auditory event-related potential (AEP) recovery functions in a group of males at high risk to develop alcoholism (HR; n = 23, mean = 22.3 years) and a low risk (LR; n = 27, mean = 23.0 years) control group. Condition order was randomized, with one condition (P, LD, or HD) per day and a minimum 1-day interval between conditions. For each subject, both blood alcohol levels (BALs) measured via breathalyzer, and event-related potentials recorded with the entire 10/20 International System, were assessed prior to and at mean intervals of 20, 60, 90, and 130 min after P, LD, or HD administration. A series of binaural auditory stimuli with randomly interposed interstimulus intervals of 0.5, 1.0, and 10.0 sec were used to elicit the N100 and P200 components of the AEP. Between-groups comparisons indicated that ethanol elicited risk group differences in recovery functions not present at baseline. The differences were manifested in the HR group as larger decrements in P200 amplitude during the ascending blood alcohol curve (acute sensitivity) and more rapid returns of both N100 and P200 to baseline levels during the descending blood alcohol curve (acute tolerance). These findings support Newlin and Thomson's (1990) Differentiator Model, suggesting that LR and HR individuals are differentially sensitive to the effects of ethanol.

Key Words: Low Risk, High Risk, Alcohol, Recovery Function, Auditory-Evoked Potential.

STUDIES OF event-related potentials (ERPs) in individuals at high risk (HR) to develop alcoholism have sought to identify the components that can best discriminate between HR individuals and low risk (LR) controls. Most studies have focused on the P300 component and have documented that, in general, P300 amplitude is reduced in HR individuals without ethanol ingestion.[1,2] While investigations of other components (e.g., N100) have been more limited, they have also demonstrated decreased N100 amplitudes.[3,4] One study[3] used a bimodal paradigm (auditory and visual stimuli) to examine both abstinent alcoholics and controls, and the first degree, family history-positive (FHP) relatives of each. The results indicated that visual N100 amplitude was reduced in the alcoholics, whereas auditory N100 amplitude was reduced in the FHP individuals. Another study[4] recorded auditory ERPs in both alcoholics and their family members, and documented that, in alcoholic families, N100 amplitude was decreased in both the affected and unaffected relatives.

There is evidence that ethanol ingestion may elicit risk group differences that are not apparent with baseline measures. This effect has been observed in studies of EEG,[5–9] plasma hormones,[10,11] muscle tension,[12] cognitive and psychomotor performance,[13] as well as ERPs. In one investigation,[14] both N100 and P300 were recorded from LR and HR individuals performing a visual discrimination task. Although both groups manifested ethanol-related decreases in N100 amplitude, the magnitude and duration of the deficit was greater in the LR group. Furthermore, although both groups demonstrated reduced P300 amplitudes during the ascending blood alcohol curve (BAC), the decreases were larger in the HR group. Lastly, although both groups evidenced ethanol-related increases in P300 latency, the return to normal values was more rapid in the HR group, an observation also documented by other investigators.[15]

The aforementioned results suggest that HR individuals compared with LR individuals manifest both greater initial sensitivity and greater acute tolerance to the effects of alcohol. These findings support the Differentiator Model (DM)[16] that attempts to explain the fact that, by a variety of measures, LR and HR individuals are differentially sensitive to the effects of ethanol ingestion. The model proposes that HR individuals are more sensitive on the ascending phase of the BAC and recover more quickly during the descending phase. During the ascending phase when the slope of the BAC is positive, HR individuals manifest an enhanced response to ethanol (i.e., acute sensitivity). In contrast, during the descending phase when the slope of the BAC is negative, HR individuals demonstrate a faster recovery to baseline response levels (i.e., acute tolerance).

However, any attempt to define the relationship between ethanol ingestion and an electrophysiological response is complicated by numerous factors, including the: (1) rise and fall in BAC following ethanol ingestion that may reflect the volume and concentration of alcohol ingested and the time period over which ingestion occurs; (2) electrode locations analyzed; (3) time course over which the changes are examined; (4) individual's drinking history; and (5) family history of alcoholism. Even after controlling for these variables, both electrophysiological and subjective responses to acute ethanol ingestion may be highly variable

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Received for publication July 29, 1997; accepted February 3, 1998

This study was supported by Grants AA-05524 and AA-02686 (to H.B.).

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both across individuals and within the same individual on different occasions.[17,18]

In the previously described ERP studies, a wide variety of information processing paradigms were used to compare risk group differences in component morphology. However, one classical electrophysiological method that lends itself to measuring CNS excitability has almost never been used to evaluate alcohol-related phenomena. The recovery function[19] or excitability cycle[20–22] is generated by presenting paired adequate or electrical stimuli with varying interstimulus intervals (ISIs). The consequent changes in ERP morphology reflect the absolute or relative refractory states of the neurons comprising the activated populations.[21–24] Because recovery functions are valuable in assessing CNS excitability, they have been used to evaluate: (1) normal reflexes;[25,26] (2) the sequelae of pathological conditions known to alter CNS excitability, such as Parkinson's disease,[27] Huntington's chorea,[28] and multiple sclerosis;[29,30] and (3) the CNS effects of pharmacological agents.[24,31–33]

In general, analyses of recovery functions have revealed that the N100 and P200 components of auditory, visual, and somatosensory ERPs increase as a function of increasing ISI up to about 10 sec.[21–23,34,35] Evidence from one study[35] suggests that both N100 and P200 are independent components rather than the elements of a single response. The authors evaluated auditory-evoked potential (AEP) recovery functions generated with three randomly presented ISIs (0.75, 1.5, and 3.0 sec), two stimulus intensities [65 dB (soft) and 85 dB (loud)] and both an attention (button press to target tone) and inattention (read while tones are presented) condition. The results indicated that increases either in stimulus intensity or ISI generated larger increases in P200 amplitude than N100 amplitude. Moreover, the two components differed topographically such that P200 amplitudes were largest centrally and fell off quickly, both frontally and parietally, whereas N100 amplitudes were largest both frontally and centrally. In contrast to the observation that increasing either stimulus intensity or ISI differentially affected component amplitudes, attending to the stimuli had no such effects. Rather, attending to the stimuli affected both components similarly, resulting in significantly increased component latencies. The fact that component amplitudes were not augmented during the attention condition contrasts with the effects of attention documented in Nd (negative difference) studies.[36–38] Those investigations reported that Nd amplitude, which is related to the allocation of attentional resources, increased as a function of increasing attention.

Few studies have used recovery functions either to evaluate the effects of acute or chronic alcohol ingestion, or to assess risk group differences. One investigation[39] used somatosensory-evoked potential (SSEP) recovery functions to test the hypothesis that, in humans, withdrawal from alcohol is characterized by CNS hyperexcitability. The subjects were male alcoholics of 10 years duration who were first required to remain abstinent for 3 weeks prior to testing. Next, they participated in both a 3-week control session and a 3-week period of experimental alcoholization and withdrawal. During alcoholization, SSEP recovery functions increased with increasing alcohol ingestion, although peak excitability appeared to occur on the first day following alcohol withdrawal. Additionally, there was evidence that, with as little as 1 day of drinking, excitability in somatosensory cortex increased as early as 10 hr after withdrawal. The authors concluded that, as measured by recovery functions, periods of partial and total withdrawal following heavy alcoholization are characterized by cortical hyperexcitability. Another study[40] compared auditory recovery functions between boys at HR for alcoholism (HR; mean = 13.1 years) and matched LR (LR; mean = 12.9 years) controls. In each group, N100 and P200 amplitudes, but not latencies, increased as a function of increasing ISI. Although none of the risk group comparisons produced any statistically significant differences, the larger P200 amplitude at Cz in the LR group approached significance ($p < 0.06$). Lastly, one investigation[41] found that abstinent alcoholics manifested lower recovery functions and reduced N100 and P200 amplitudes, perhaps reflecting hypoexcitability that develops during prolonged abstinence.

The present investigation examined the effects of ethanol on AEP recovery functions in carefully defined populations of HR and LR males. Furthermore, to test the DM,[16] we assessed whether the recovery functions generated by the LR and HR groups were differentially sensitive to the ascending and descending phases of the BAC. In contrast to many previous ethanol challenge studies that used only a placebo and a single ethanol dose, our subjects received placebo (P), low dose (LD), and high dose (HD) ethanol in a randomized order, using a repeated-measures design.

METHODS

Subjects

The subjects were 50 males ranging from 18 to 30 years of age. LR (n = 27, mean = 23.0 years) subjects were recruited either through newspaper ads or via notices posted in the Health Science Center. In contrast, HR (n = 23, mean = 22.3 years) individuals each had a father undergoing treatment for alcohol dependency (DSM III-R criteria). The initial screening procedure required each prospective subject to fill out a questionnaire detailing alcohol and drug use, and the medical and psychiatric histories for both himself and his first- and second-degree relatives. Participation in the study depended on responses to the questionnaire. The requirement for an individual's inclusion in the HR group was that at least his father be classified as alcohol-dependent (DSM III-R); optimally, there would be multiple first- or second-degree alcoholic relatives. Inclusion in the LR group required that none of the candidate's first- or second-degree relatives be diagnosed as alcoholic. Exclusion criteria for either group included an alcoholic mother, major medical problems, a current requirement for medication that affected the CNS, or a self-reported history of psychiatric problems, and/or drug abuse in the subject or his first- and second-degree relatives. Upon meeting the aforementioned criteria, each subject was invited to the laboratory wherein he underwent a detailed psychiatric interview (H.B. and B.P.) that focused on questions of drug and alcohol use, and the medical and psychiatric history

Table 1. Subject Characteristics for the LR and HR groups

	LR (n = 27)	HR (n = 23)
Age (yr)	Mean: 23.0, SD: 2.99 Range: 19–30	Mean: 22.3, SD: 3.21 Range: 18–29
Education (yr)	Mean: 16.2, SD: 2.79 Range: 12–20	Mean: 13.8, SD: 1.65 Range: 12–17
Drinking days*/month	Mean: 4.01, SD: 3.35 Range: 0–14	Mean: 8.13, SD: 8.82 Range: 0–30
Drinks/occasion	Mean: 2.61, SD: 1.58 Range: 0–7	Mean: 3.74, SD: 3.15 Range: 0–10
Drink Index†	Mean: 11.6, SD: 12.2 Range: 0–42	Mean: 45.0, SD: 63.2 Range: 0–260
No. of alcoholic relatives	Individuals in this group could not have any first- or second-degree alcoholic relatives	Mean: 2.74, SD: 1.89 Range: 1–8

* $p < 0.04$.
† $p < 0.02$.

for himself and his first- and second-degree relatives. Table 1 summarizes the subject characteristics for each group. The two groups had similar ages and educational backgrounds, but differed significantly in two measures of drinking history: the number of drinking days per month (LR, mean = 4.01; HR, mean = 8.13; $p < 0.04$) and the Drink Index (the product of the number of drinking days per month by the number of drinks per occasion) (LR, mean = 11.6; HR, mean = 45.0; $p < 0.02$).

Experimental Design

The subject was seated comfortably in a dimly lighted, temperature-regulated, sound-attenuated chamber (Industrial Acoustics Corp.). Each subject wore a fitted electrode cap (Electro-Cap International, Inc.) using the entire 10/20 International System. The nasion served as reference and the forehead as ground. Both horizontal and vertical eye movements were monitored.

While the subject fixated on a target presented on a computer monitor, he received a series of brief binaural auditory clicks [70 dB, 1500 Hz, 40 msec duration (5 msec rise and fall time, 30 msec plateau)] generated by a click-tone control module (Grass Instruments) and presented through headphones (TDH). ISIs of 0.5, 1.0, and 10.0 sec were interposed randomly between the auditory stimuli. Data acquisition terminated when 30, artifact-free responses were acquired for each ISI.

ERP activity was amplified 20 K with a Neuro Data Acquisition System (Grass Instruments). Prestimulus activity (80 msec) and poststimulus activity (400 msec) were sampled continuously at a sampling rate of 250 data points per second (bandpass: 0.1 to 100 Hz). Data were then digitally filtered with a 30-Hz low-pass filter. Artifact rejection (electromyogram, electro-oculogram, and saturation artifact > 73.3 μV) was performed on-line.

Each subject was tested once under three different conditions: P, LD, and HD ethanol. Condition order was randomized, and there was a minimum 1-day interval between conditions. In the LD and HD conditions, the subject drank a volume (ml) of 100% ethanol equal to 0.5 times and 0.8 times his weight in kg, respectively, dissolved in a volume of ginger ale equal to 3 times that number. In the P condition, the subject drank a volume (ml) of ginger ale equal to twice his weight in kilograms, so that the total volume equaled that of the LD day. Under each condition, the subject ingested the drink over a 10-min period. A specially designed container[42] was used to provide an equally strong odor for both placebo and alcohol conditions. Within the container, a small trap held 3 ml of a solution consisting of 3 parts ethanol dissolved in 7 parts ginger ale; this ensured that, under each condition, the subject's first taste was ethanol. However, the small amount of ethanol ingested did not produce a measurable blood alcohol level (BAL).

Five recordings were made under the P, LD, and HD conditions: the first, approximately 2 min before the placebo or ethanol (LD or HD) was administered; the second through fifth at intervals of 20, 60, 90, and 130 min postingestion.

A breathalyzer (Alco-Sensor III, Intoximeters, Inc.) was used to monitor the subject's BAL, first upon arriving at the laboratory and then immediately preceding each recording subsequent to the placebo or drink.

Data Analysis

For both the LR and HR groups, an automatic peak detection program was used to measure both N100 and P200 components of the auditory recovery functions at each of the 19 electrodes. N100 was defined as the largest negativity between 60 to 160 msec, whereas P200 was defined as the maximum positivity between 160 to 290 msec. Each of the automatically selected peaks could also be edited manually. Separate assessments of N100 and P200 responses were made for the 0.5, 1.0, and 10.0 sec ISIs both at baseline and at the four postingestion intervals. This procedure was repeated on each of the P, LD, and HD days.

Data were recorded using the entire 10/20 International System, and analyses were performed on the responses at midline electrodes Fz, Cz and Pz, and lateral electrode pairs F3, F4, C3, C4 and P3, P4. The large magnitudes of the responses at these electrodes appeared to offer the best opportunity to obtain significant risk group differences.

However, before we could assess risk group differences in response to the ethanol challenge, we needed to be certain that a significant difference reflected the effects of ethanol, and not group difference in baseline N100 or P200 responses. To make this determination, we used within-group multivariate analyses of variance (MANOVAs; SAS, version 6.03)[43] to ascertain that neither group manifested significant differences in baseline responses across the P, LD, and HD days, and between-group MANOVAs to ensure that the two groups did not differ in baseline responses on corresponding test days.

Another concern was that the HR group drank significantly more than the LR group (Table 1). Thus, it was possible that risk group differences in recovery functions could reflect differences in drinking histories. To test this hypothesis, individuals in the HR group were assigned to either a "light" drinker or "heavy" drinker group based on their Drink Index scores. The "light" drinkers (n = 14) had a mean index of 5.07 (SD = 4.65), whereas the "heavy" drinkers (n = 9) had a mean index of 107.2 (SD = 61.8). Between-group MANOVAs, one for each test day, were then used to compare recovery functions for the two groups, both at baseline and following LD and HD ethanol. The results indicated no significant differences between the two HR groups. A similar analysis could not be performed with the LR individuals because the distribution of Drink Index scores did not allow creation of two, statistically meaningful groups.

Next, within-group MANOVAs were used in both the LR and HR groups to evaluate recovery functions for each combination of component and ISI. Separate analyses were performed for each of the four postingestion data runs. The entire procedure was repeated on the P, LD, and HD days.

Lastly, between-group MANOVAs were used to compare recovery functions for each combination of component and ISI on each of the four postingestion data runs. Again, these procedures were repeated on the P, LD, and HD days.

RESULTS

Blood Alcohol

Figure 1 presents the BACs (percent) as a function of time (min) postingestion, for both the LR and HR groups under LD and HD ethanol. Time 0 is the point immediately following ingestion of the drink. The results of independent groups t tests (significant at $p < 0.05$) revealed no statistically significant differences between the two groups at any time point under either the LD or HD conditions.

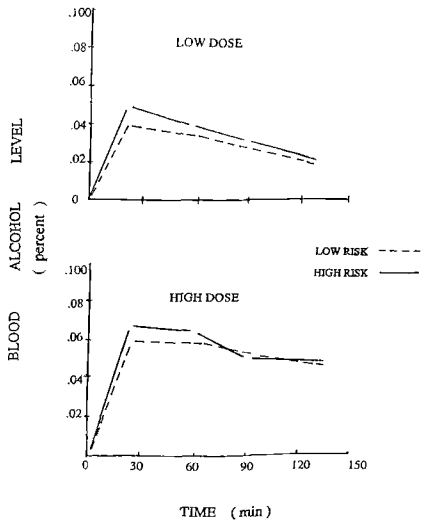

Fig. 1. Mean blood alcohol levels (percent) as a function of time (minutes) for both the LD (top) and HD (bottom) conditions. Broken line represents LR individuals. Solid line represents HR individuals.

Recovery Functions—Within-Group Comparisons

Initially, within each risk group, pairwise comparisons were made between the entire datasets (baseline plus four postingestion runs) for the P, LD, and HD conditions. For each comparison, separate analyses were performed on each combination of component (N100 and P200) and ISI (0.5, 1.0 and 10.0 sec). The results revealed that the HR group was generally more sensitive than the LR group to differences between conditions. This increased sensitivity was observed in the comparisons between placebo and both LD and HD ethanol. It presented as significant differences in N100 and P200 amplitudes at both the 1.0 and 10.0 sec ISIs. For example, at the 10.0 sec ISI, the HR group manifested significant differences in N100 amplitude between both P and LD ethanol ($F = 3.29, p < 0.01$) and P and HD ethanol ($F = 2.86, p < 0.02$); the LR group differed only between P and HD ethanol ($F = 3.11, p < 0.014$). Similarly, for the P200 component, the HR group again demonstrated significant differences between P and LD ethanol ($F = 4.98, p < 0.001$) and P and HD ethanol ($F = 4.29, p < 0.003$); the LR group evidenced no amplitude differences in any comparisons.

Next, within-group MANOVAs using the responses at all nine electrodes, were used to compare baseline recovery functions across the P, LD, and HD days. Neither group manifested a significant difference in any of the comparisons between each combination of component and ISI.

Lastly, for each group, we assessed the percent change from the baseline recovery functions that followed ingestion of the P, LD, and HD drinks. The results demonstrated that, during the ascending BAC (time 0 to 20 min postingestion), both the LR and HR groups were characterized by decreased N100 and P200 amplitudes without any latency changes. However, whereas the direction of the changes in both groups was similar, the magnitude of the changes often was significantly larger in the HR group (see next section). During the descending BAC (20 to 90 min postingestion and 20 to 130 min postingestion), the HR group generally evidenced large returns of component amplitudes to baseline levels. In the LR group, returns to baseline were often smaller and, at some electrodes, response amplitudes even continued to decrease.

Table 2. Summary of Risk Group Comparisons of % Change in N100 and P200 Amplitudes as a Function of the Ascending BAC (0 to 20 Min)

			ISI (sec)		
			0.5	1.0	10.0
Ascending BAC (time 0 to 20 min)	N100	LD	—	—	0.002
		HD	—	—	—
	P200	LD	—	0.0001	—
		HD	—	0.002	0.0001

—, not significant.

Recovery Functions—Between-Group Comparisons

Initially, between-groups comparisons of baseline recovery functions (each combination of component and ISI) were made for the P, LD, and HD conditions. None of the analyses revealed significant risk group differences.

Next, between-group comparisons of percent change in component amplitudes and latencies at all nine electrodes were made for each ISI under LD and HD ethanol. Analyses were made during the ascending BAC (time 0 to 20 min postingestion) and over two intervals on the descending BAC (20 to 90 min postingestion and 20 to 130 min postingestion).

As described previously, during the ascending BAC, both groups were characterized by N100 and P200 amplitude reductions without latency changes. However, between-group comparisons of the magnitudes of the changes (percent change from baseline across all nine electrodes) indicated that the decrease in component amplitudes typically was larger in the HR group. Table 2 presents the results of risk group comparisons for both N100 and P200 during the ascending BAC (time 0 to 20 min postingestion). Significance levels are shown for each combination of ethanol dose and ISI. The results demonstrate that, during the ascending BAC, the changes that most effectively discriminated between the two groups occurred under HD ethanol and consisted of reduced P200 amplitudes at the 1.0 and 10.0 sec ISIs. For example, at the 1.0 sec ISI, the amplitude decrease in the LR group was 17.3%; that in the HR group, 50.2% ($p < 0.002$). At the 10.0 sec ISI, the decrease in the LR group was 35.3%; that in the HR group, 53.0% ($p < 0.0001$).

In a similar manner, Table 3 presents the results of the risk group comparisons of percent change in component amplitudes over two intervals (20 to 90 min postingestion and 20 to 130 min postingestion) on the descending BAC. In general, the return of N100 and P200 amplitudes to

Table 3. Summary of Risk Group Comparisons of % Change in N100 and P200 Amplitudes as a Function of Two Intervals Over the Descending BAC

			ISI (sec)		
			0.5	1.0	10.0
			20 to 90 Min		
Descending BAC	N100	LD	—	0.041	0.004
		HD	—	—	—
	P200	LD	—	—	—
		HD	—	—	—
			20 to 130 Min		
	N100	LD	—	—	0.035
		HD	—	—	—
	P200	LD	—	0.0001	—
		HD	—	—	0.003

—, not significant.

baseline levels was more rapid and of greater magnitude in the HR group. For example, over the 20 to 90 min interval under LD ethanol, the HR group manifested significantly larger increases in N100 amplitude at both the 1.0 and 10.0 sec ISIs. At the 10.0 sec ISI, N100 amplitude increased 36.1% in the HR group, but continued to decrease (−3.2%, $p < 0.004$) in the LR group. Furthermore, over the 20 to 130 min interval, the HR group evidenced significantly larger increases in both N100 and P200 amplitudes under both LD and HD ethanol. Thus, at the 10.0 sec ISI under LD ethanol, N100 amplitude increased 55.5% in the HR group, but only 16.9% ($p < 0.035$) in the LR group. P200 amplitude increased 19.9% in the HR group, but continued to decrease (−12.6%; $p < 0.003$) in the LR group.

Figure 2 presents, for both LR and HR individuals, grand mean waveforms at Cz under HD ethanol. The ISI is 10.0 sec. The figure indicates that, for example, during the ascending BAC, P200 amplitude decreased 51.0% in the HR group, but only 38.6% in the LR group. Then, during the descending BAC, P200 amplitude returned to 64.8% of baseline in the HR group, but only 57.8% of baseline in the LR group.

Because the DM[16] posits that LR and HR individuals are differentially sensitive to both the ascending and descending phases of the BAC, we felt it was important to compare not only the magnitudes of the amplitude changes, but the slopes of the changes as well. Figure 3 presents the changes in P200 amplitude (μV) at the Cz electrode under both LD ethanol (left) and HD ethanol (right). Plots are presented for both the ascending BAC (time 0 to 20 min postingestion) and the two intervals on the descending BAC (20 to 90 min and 20 to 130 min postingestion). The ISI is 10.0 sec. The plots indicate that, on the ascending BAC under HD ethanol, both groups manifested a decrease in P200 amplitude, but the rate of change in the HR group (solid line) was significantly faster ($p < 0.05$). Moreover, as measured over the two intervals on the descending BAC under both

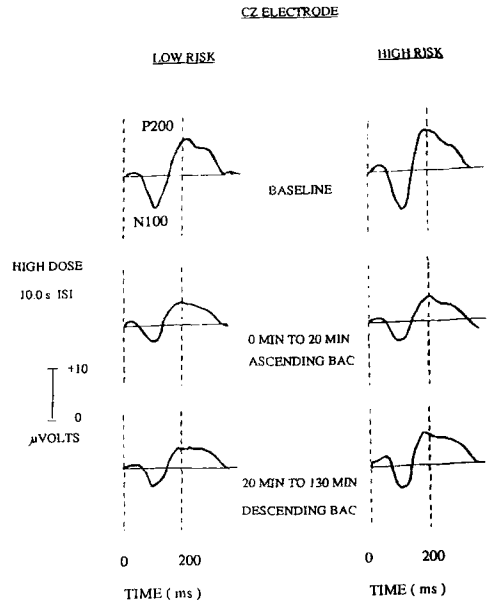

Fig. 2. AEP recovery functions at the Cz electrode for both the LR and HR groups. Grand mean waveforms are presented at baseline and during the ascending and descending BAC following HD ethanol. The ISI is 10.0 sec. The decrease in component amplitudes during the ascending BAC and the return to baseline levels during the descending BAC is greater in the HR group.

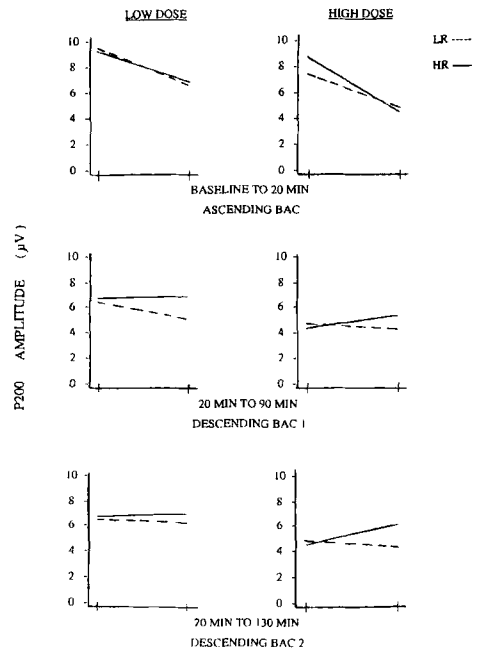

Fig. 3. Changes in P200 amplitude (μV) at the Cz electrode are indicated for both LR (broken line) and HR (solid line) individuals. Plots are presented as a function of the ascending and descending BAC under both LD and HD ethanol. The ISI is 10.0 sec.

LD and HD ethanol, the plots indicated that whereas P200 amplitude was returning to baseline in the HR group, it continued to decrease in the LR group.

DISCUSSION

The present investigation demonstrates that ethanol ingestion elicits risk group differences in AEP recovery func-

tions not present with baseline comparisons. In general, HR individuals, compared with LR individuals, had significantly larger response decrements during the ascending phase of the BAC (acute sensitivity) and larger returns to baseline values during the descending phase of the BAC (acute tolerance).

During the ascending BAC, these differences were most consistently documented in the P200 component, at the 1.0 and 10.0 sec ISIs, under HD ethanol. In contrast, during the descending BAC, there were significant differences in both N100 and P200 components under LD and HD ethanol, at the 1.0 and 10.0 sec ISIs. Furthermore, whereas there were significant risk group differences in recovery functions, there were no differences in the the blood alcohol curves of the two groups under either the LD or HD conditions. The pattern of greater acute sensitivity and tolerance in the HR group supports the DM[16] that suggests LR and HR individuals are differentially sensitive to the effects of ethanol.

Initially, we observed that following either LD or HD ethanol ingestion, there were no significant differences in the BACs generated by the two groups (Fig. 1). Often, there are large individual variations in the rate, latency, and peak of the BAC[44] that may reflect differences in ethanol metabolism, rate of tolerance, or the amount of food eaten prior to ethanol ingestion.[45] In contrast, most studies that have compared the BACs of LR and HR individuals typically have found no differences.[5,8,9,12,45–47]

To verify that any risk group differences we observed reflected differential ethanol effects rather than differences in baseline recovery functions, we first established that there were no statistically significant differences at baseline, either within groups across the P, LD, and HD days, or between groups on the P, LD, and HD test days. It was also necessary to examine the possibility that a risk group difference in recovery functions could reflect the fact that HR individuals drank significantly more than LR individuals. To address this possibility we compared the N100 and P200 responses of "light" and "heavy" drinkers in the HR group as determined by the Drink Index. Comparisons were made both at baseline, and following LD and HD ethanol. Because there were no differences in their recovery functions either at baseline or following ethanol ingestion, we have indirect evidence that the risk differences we documented did not reflect differences in drinking history.

The assessments of baseline recovery functions indicated that, in both groups, N100 and P200 amplitudes generally increased as the ISI increased from 0.5 to 10.0 sec, and from 1.0 to 10.0 sec. These findings agree with those of previous investigations that reported that the amplitudes of N100 and P200 components of AEPs, visual ERPs, and SSEPs increased as a function of increasing ISI up to about 10 sec.[21–23,34,35] Moreover, the largest response magnitudes were recorded primarily at the frontal and central electrodes and were the basis for selecting the group of electrodes whose responses were analyzed in the present investigation. The large magnitudes of the responses observed support the findings of one study[35] that reported that P200 was largest at Cz, whereas N100 was largest at Fz and Cz. The fact there were no baseline differences between the two groups confirms the generally accepted observation that with the exception of P300[1,2] and the limited findings regarding N100,[3,4] few baseline electrophysiological responses reliably discriminate between LR and HR individuals.

Our subsequent demonstration of significant risk group differences in recovery functions following an ethanol challenge replicates another well-documented phenomenon (i.e., that numerous baseline measures that do not discriminate between risk groups at baseline manifest significant differences following ethanol ingestion). For example, EEG studies have described ethanol-related differences in slow and fast α-energy and mean α-frequency,[5] both slow and fast α-energy,[6] the coefficient of variation in both slow and fast α,[7] β-activity,[8] and both acute sensitivity and acute tolerance in slow α.[9] A similar pattern has been shown in ERP studies. One investigation[15] demonstrated that, while ethanol ingestion increased P300 latencies in both groups, the HR individuals manifested a faster return to normal values. In another study,[14] P300 latencies in the HR group returned to normal values at 90 min postethanol ingestion, but those in the LR group did not return to normal values within the 130-min duration of the experiment. Moreover, although both groups displayed an ethanol-induced decrease in N100 amplitude, the return to normal amplitudes again occurred more rapidly in the HR group (90 min vs. >130 min). It should also be noted that ethanol-related risk group differences have been found not only in EEG and ERP studies, but in measures of plasma hormones,[10,11] muscle tension,[12] and cognitive and psychomotor performance.[13] Together, these findings suggest that while the underlying physiology of both LR and HR individuals is generally quite similar, the two groups are differentially sensitive to the effects of ethanol.

By controlling for the possibilities that baseline differences and/or differences in drinking histories accounted for the risk group differences in the recovery functions, our results suggest the possibility that these differences reflect a contribution from genetic factors. Evidence derived from both EEG and ERP studies supports this hypothesis. For example, one study[48] reported that both baseline EEG activity and the EEG response to an ethanol challenge were more similar in monozygotic than dizygotic twins, whereas another[49] described more similar EEG variants in alcoholics and their nonalcoholic first-degree relatives than in alcoholics and matched controls. In two studies using an auditory oddball paradigm,[50,51] the former[50] reported that both P300 amplitudes and latencies were significantly correlated in monozygotic twins, compared with control pairs, whereas the latter[51] demonstrated significant heritability of P300 amplitude, with responses of monozygotic twin pairs more similar than those of dizygotic twin pairs.

As indicated previously, our results confirm the widely

documented observations that ethanol ingestion may elicit risk group differences in measures whose baseline levels do not effectively discriminate between the two groups. More specifically, by describing a significant risk group difference in the relationship between ethanol-induced ERP changes and the ascending and descending phases of the BAC, our results support the DM.[16]

Tables 2 and 3 and Figs. 2 and 3 indicate that, in the HR group, there were larger and more rapid decreases in component amplitudes during the ascending BAC, and larger and more rapid returns to baseline levels during the descending BAC. These findings of greater acute sensitivity (an enhanced ethanol response when the slope of the BAC is positive) and greater acute tolerance (an attenuated ethanol response when the slope of the BAC is negative) in HR individuals are important to the DM in another respect, because they demonstrate both acute sensitivity and acute tolerance in the same experiment. Observations of larger response magnitudes in HR individuals during the ascending BAC (acute sensitivity) have been documented in measures of EEG activity (slow α),[9] electromyogram activity,[12] psychomotor performance,[52] subjective anxiety (lower anxiety levels in HR),[53] and autonomic function (e.g., skin temperature, skin conductance, and pulse amplitude).[16] Similarly, HR individuals have evidenced greater response decrements than LR individuals during the descending phase of the BAC (acute tolerance). This pattern has been demonstrated in the return of EEG (slow α),[9] P300 latencies,[14,15] and N100 amplitudes[15] to control levels.

Interestingly, baseline measures of some of the aforementioned autonomic functions have revealed a hyperreactivity in the HR group. These augmented responses effectively discriminated between the two groups and were often elicited during stressful experimental situations (e.g., where the subjects had to perform mental arithmetic[54] or when they received signaled electric shock).[55–61] The hyperreactivity in the HR group was manifested as increases in skin conductance,[57] cardiovascular activity [e.g., heart rate[55,57,58,62] and vasoconstriction (digital blood volume)[54,56,57]], and sensitivity to pain.[61] Moreover, when the experiments were repeated in both groups following ethanol ingestion, each evidenced a reduced magnitude in the autonomic stress responses, a phenomenon described as stress-dampening. However, because the magnitude of the decrease was typically greater in the HR group, ethanol ingestion (moderate to HDs but not P)[60] effectively reduced or eliminated risk group differences in pain responses,[61] skin conductance,[57] and in several measures of cardiovascular reactivity (e.g., heart rate[55,58,60,62] and digital blood volume[56]).

Lastly, we observed that ethanol consumption (as measured by the Drink Index) in the HR group was approximately four times that in the LR group. One explanation for the increased consumption comes from the previously described observations that HR individuals, compared with LR individuals, are more sensitive to the ascending BAC. Interestingly, several studies have documented that, during the ascending BAC, individuals have frequently described feelings of well-being (such as elation, vigor,[63] and euphoria[18]). In one study,[18] the feelings of euphoria were associated with transient increases in α-activity above already elevated α-levels. Consequently, if HR individuals are more sensitive to the reinforcing properties of alcohol on the ascending curve, alcohol ingestion is likely to be higher. Furthermore, it has been demonstrated that, during the descending BAC, individuals have often reported negative feelings, including anger, depression, fatigue, anxiety,[63,64] and dysphoria.[16] One investigation[64] observed that very strong negative feelings after HD alcohol was the best single independent discriminator between HR and LR men. However, if HR individuals manifest faster returns to baseline values during the descending BAC, their experience with the negative emotions associated with alcohol ingestion will be shorter. It then follows, that if HR individuals experience both more pleasurable feelings during the ascending BAC and decreased amounts of negative feelings during the descending BAC, their subjective experiences may act to reinforce increased ethanol consumption (both quantity and frequency measures) with subsequent increases in the risk to develop alcohol-related problems.

In conclusion, the present investigation demonstrates that ethanol ingestion elicits risk group differences in AEP recovery functions not otherwise observed with baseline measures. These differences are manifested in the HR group as larger decrements in component amplitudes during the ascending BAC (acute sensitivity) and larger returns to baseline magnitudes during the descending BAC (acute tolerance). This response pattern supports the DM[16] that suggests LR and HR individuals are differentially sensitive to the effects of ethanol.

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