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The effects of ethanol on EEG activity in males at risk for alcoholism

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Summary The present investigation examined the effects of placebo (P), low dose (LD) and high dose (HD) ethanol on EEG activity in two groups of males. One group consisted of individuals at high risk for the development of alcoholism (HR, N = 21) while the other consisted of matched, low risk (LR, N = 21) controls. Only one condition (P, LD or HD) was presented each day and condition order was randomized. For each subject, both blood alcohol level(s) (BAL) measured via breathalyzer and EEG activity, using the entire 10/20 international system, were recorded prior to and at intervals of 35, 70, 105 and 140 min after P, LD or HD administration. The Fast Fourier Transform (FFT) was used to calculate power spectral densities (PSD). Measures of relative area under the power spectral curve were obtained for each of the following frequency bands: slow alpha (SA, 7.5–10 Hz), fast alpha (FA, 10.5–13.0 Hz), slow beta (SB, 13.5–19.5 Hz) and fast beta (FB, 20–26 Hz) at electrodes: F3, F4, C3, C4, P3, P4, O1 and O2. The results of repeated measures MANOVA conducted on the normalized values of relative areas revealed that at each electrode examined, ethanol elicited significant changes only in SA activity. Risk group differences in SA activity were observed only at electrodes F3, F4 and P4. These differences were the consequence of differential ethanol effects rather than differences in baseline SA levels. Further analyses indicated that across all 8 electrodes there were significant risk group differences in the magnitude of change in SA activity as a function of the ascending and descending phases of the blood alcohol curve (BAC). HR individuals manifested significantly greater increases in SA activity on the ascending curve (acute sensitization) and significantly faster recovery to baseline SA levels during the descending phase (acute tolerance). Evidence is also presented that genetic factors, rather than differences in drinking history, may account for risk group differences in the ethanol-induced EEG response.

Key words: EEG; Alpha; Risk; Ethanol; Sensitization; Tolerance

Investigations into the electroencephalographic differences between individuals at risk for the development of alcoholism (high risk = HR) and matched controls (low risk = LR) have generally proceeded by comparing baseline EEG activity and/or observing the EEG response to an ethanol challenge. Studies of baseline EEG activity have generally concluded that these measures do not effectively discriminate between HR and LR individuals. Studies by Pollock et al. (1983), Volavka et al. (1985), Kaplan et al. (1988), Ehlers and Schuckit (1990) and Cohen et al. (1991), failed to find significant group differences at any of the locations or frequency bands investigated. However, in contrast, studies by Ehlers and Schuckit (1991) and Gabrielli et al. (1982) reported significant differences in the fast alpha and fast beta frequency bands, respectively. The former study (Ehlers and Schuckit 1991) demonstrated that HR individuals had significantly more energy in the fast alpha (9–12 Hz) frequency band than did LR individuals. In the latter study (Gabrielli et al. 1982), HR individuals manifested significantly more activity in the 18–26 Hz and greater than 26 Hz frequency bands than did LR individuals. While the authors argued for the heritability of this pattern, they neither controlled for the psychiatric classification of either or both parents, nor for the possible consequences of the pharmacologic treatment of the parent on the EEG in the offspring.

Ethanol challenge studies have sought to examine whether the response to acute ethanol ingestion, i.e., slowing of the predominant baseline frequency and increased energy in that frequency band (Davis et al. 1941; Engel and Rosenbaum 1945; Holmberg and Martens 1955; Begleiter and Platz 1972; Lehtinen et al.

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1981; Lukas et al. 1986; Michel and Battig 1989; Cohen et al. 1992), differs in HR and LR individuals. The number of such studies has been limited and the results have been inconsistent. For example, two studies (Pollock et al. 1983; Volavka et al. 1985) observed that following ethanol ingestion, HR individuals had significantly greater increases in slow alpha energy than did LR individuals. In the former study (Pollock et al. 1983), these differences occurred at both 30 and 120 min post ingestion, however, in the latter (Volavka et al. 1985), while there was an overall risk group difference, no differences were observed at the intervals examined. In contrast, another study (Ehlers and Schuckit 1991) reported no group differences in slow alpha activity. Two studies comparing risk group differences in the fast alpha frequency band (Pollock et al. 1983; Volavka et al. 1985) found that HR individuals had significantly greater decreases in fast alpha energy at 120 min post ethanol ingestion. Another study (Ehlers and Schuckit 1988) reported that EEG variability as measured by the coefficient of variation was significantly smaller in HR individuals. However, in contrast to these studies is one (Ehlers and Schuckit 1991) reporting that at 90 min post ingestion, LR subjects had larger decreases in fast alpha energy than did HR subjects.

Comparisons of ethanol-induced changes in the predominant baseline frequency have also been conducted. For example, Pollock et al. (1983) reported that HR individuals manifested significantly greater decreases in mean alpha frequency at 30, 60 and 120 min post ingestion at bilateral central and parietal sites and at right occipital cortex, and at 120 min at left occipital cortex. While previous studies (Engel and Rosenbaum 1945; Begleiter and Platz 1972; Lukas et al. 1986) have demonstrated that the magnitude of the ethanol-induced frequency decrease varies as a function of the baseline frequency, i.e., the magnitude of the decrease will be greater if the baseline frequency is higher, Pollock et al. (1983) reported no risk group differences in baseline frequency.

Similarly, risk group differences in both fast and slow wave activity have been examined. While one study (Ehlers and Schuckit 1990) demonstrated that HR individuals had significantly greater increases in beta energy than did LR individuals, two studies (Ehlers and Schuckit 1988; Kaplan et al. 1988) reported no such differences. Kaplan et al. (1988) found that while both HR and LR individuals manifested significant decreases in slow wave (2–4 Hz) activity and corresponding increases in alpha (9–12 Hz) activity, risk group differences were not significant.

Lastly, a limited number of studies have directly examined regional differences in risk group responses. Pollock et al. (1983) reported that the changes in both slow and fast alpha that most dramatically distinguished between LR and HR individuals tended to be localized to posterior scalp regions, while the changes in mean alpha frequency that most distinguished the two groups also occurred posteriorly, lateralized to the right hemisphere. Ehlers and Schuckit (1988) observed that, as measured by the the coefficient of variation (CV), spectral power in both the slow alpha and fast alpha frequency bands was more destabilized in LR than HR individuals. This effect was observed at P4-O2 but not at F4-C4. While Volavka et al. (1985) reported significant risk group differences in slow alpha activity in each of central, parietal and occipital regions, the largest risk group differences, derived from the statistical significance levels of their results, were in the parietal and occipital regions ($P < 0.01$ vs. $P < 0.05$ for the central regions). Lukas et al. (1989), using a topographic mapping procedure, reported that at baseline, the areal extent of both slow and fast alpha was greater in HR than LR individuals; following ethanol ingestion this relationship was reversed. However, this study used only 6 subjects, 5 LR and 1 HR. In contrast to the aforementioned studies, Kaplan et al. (1988) examined EEG activity within 4 frequency bands over 4 cortical regions and observed no regional differences between risk groups.

Recently, Newlin and Thomson (1990) proposed a model that attempts to explain the possible differential sensitivity of LR and HR individuals to the effects of ethanol ingestion. This differentiator model (DM) not only addresses the risk group differences observed in EEG activity, but in measures such as serum biochemistry, autonomic function, motor responses and subjective responses. It proposes that HR individuals are more sensitive to the ascending phase of the blood alcohol curve (BAC) and recover more quickly during the descending phase. During the ascending phase, when the slope of the BAC is positive, HR individuals manifest acute sensitization, that is, an enhanced response to ethanol. In contrast, during the descending BAC, when the slope of the BAC is negative, HR individuals demonstrate acute tolerance, a more rapid recovery to baseline response levels.

The present investigation examined ethanol-induced changes in EEG activity in both the alpha and beta frequency bands, in a carefully defined population of both high risk (HR) males and low risk (LR) controls. Furthermore, as a test of the DM, we assessed whether the ethanol-induced EEG responses in the LR and HR groups were differentially sensitive to the ascending and descending phases of the blood alcohol curve (BAC). Each of the above relationships was assessed at 8 electrodes. Additionally, while most previous investigations have typically used a placebo and a single ethanol dose, the subjects in this investigation received placebo, low dose and high dose ethanol in a randomized order using a repeated measures design.

Methods

Subjects

The subjects were 42 males ranging from 19 to 39 years of age. Low risk (LR, N = 21, $\overline{X}$ = 22.7) subjects were recruited either through newspaper ads or via notices posted in the Health Science Center. In contrast, high risk (HR, N = 21, $\overline{X}$ = 22.8) individuals 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 upon the responses to the questionnaire. The requirement for an individual's inclusion in the HR group was that his father be classified as alcohol-dependent (DSM III-R) and a high incidence of alcoholism in the first and second degree relatives of these individuals. 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 history of psychiatric problems and/or drug abuse in himself and 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 (BP and HB) that focused on questions of drug and alcohol use, and the medical and psychiatric history for both himself and his first and second degree relatives. Table I summarizes the subject characteristics for each group. They were matched on the basis of age, weight, education, smoking history and marijuana use. The two groups were almost identical in mean age (LR = 22.7; HR = 22.8) and had similar educational backgrounds (LR = 15.8 years; HR = 13.8 years) but they differed significantly in their drinking histories. Each measure of drinking habit as well as the Drink Index (the product of the number of drinking days per month by the number of drinks per occasion) was significantly higher in the HR group than in the LR group (days/month, $t = 2.30$, $P < 0.03$; drinks per occasion, $t = 2.87$, $P < 0.009$; Drink Index, $t = 2.71$, $P < 0.01$).

TABLE I

Characteristics of the individuals in the low risk and high risk groups (N = 21 per group).

	Low risk	High risk
Age (years)	Mean 22.7, S.D. 4.51 Range 19–39	Mean 22.8, S.D. 2.94 Range 19–29
Education (years)	Mean 15.8, S.D. 2.43 Range 12–20	Mean 13.8, S.D. 1.48 Range 12–16
Drinks per occasion	Mean 2.38, S.D. 1.20 Range 1–5	Mean 4.56, S.D. 3.0 Range 1–10
Days per month	Mean 4.05, S.D. 3.32 Range 1–14	Mean 9.11, S.D. 8.82 Range 1–30
Drink Index	Mean 9.62, S.D. 9.19 Range 1–40	Mean 53.1, S.D. 67.55 Range 2–260
Number of alcoholic relatives	Individuals in this group could not have any alcoholic relatives	Mean 4.10, S.D. 2.05 Range 1–8

Experimental design

Each subject was tested once under each of 3 conditions: placebo (P), low dose (LD) ethanol and high dose (HD) ethanol. Condition order was randomized and there was a minimum interval of 1 day between conditions. In the LD and HD conditions the subject received 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 kg 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 (Mendelson et al. 1984) 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 insured 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 EEG recordings were made under each of the 3 conditions; the first, approximately 2 min before the placebo or ethanol (LD or HD) was administered, the second through fifth at intervals of 35, 70, 105 and 140 min post ingestion.

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

Recording methods and parameters

The subject was seated comfortably in a dimly lit, temperature regulated, sound-attenuated chamber (Industrial Acoustics Corp.). He was told to close his eyes and relax but not fall asleep. 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 vertical and horizontal eye movements were monitored.

EEG activity was amplified 20 k (bandpass 0.1–100 Hz) with a Grass Neurodata Acquisition System. The data were sampled continuously for 2 min, at a sampling rate of 128 Hz, with a buffer size of 128 data points. Artifact rejection (EMG, EOG, and saturation

artifact) was performed off-line by both the first author and a highly trained technician.

Data analysis

A program was written to display continuous, 4 sec epochs of 21-channel EEG activity. Each epoch was examined for the presence of the aforementioned artifacts. Following inspection of the entire recording, the program was run a second time, and the 12, most artifact-free, epochs were selected for summation, averaging and analysis by Fast Fourier Transform (FFT). This procedure was repeated for each of the 5 EEG recordings made under the P, LD and HD conditions. A second program was written both to measure the area under the power spectral curve and to determine the relative area (area under the curve/bandwidth) within 4 frequency bands: slow alpha (SA, 7.5–10.0 Hz), fast alpha (FA, 10.5–13.0 Hz), slow beta (SB, 13.5–19.5 Hz) and fast beta (FB, 20–26 Hz). Determination of relative areas within these frequency bands was made at electrodes: F3, F4, C3, C4, P3, P4, O1 and O2. Statistical analyses consisted of repeated measures MANOVA (SAS/STAT, v. 6) performed on normalized, relative area values. Group differences were assessed at each electrode, for each combination of the aforementioned electrodes and frequency bands, across the P, LD and HD conditions.

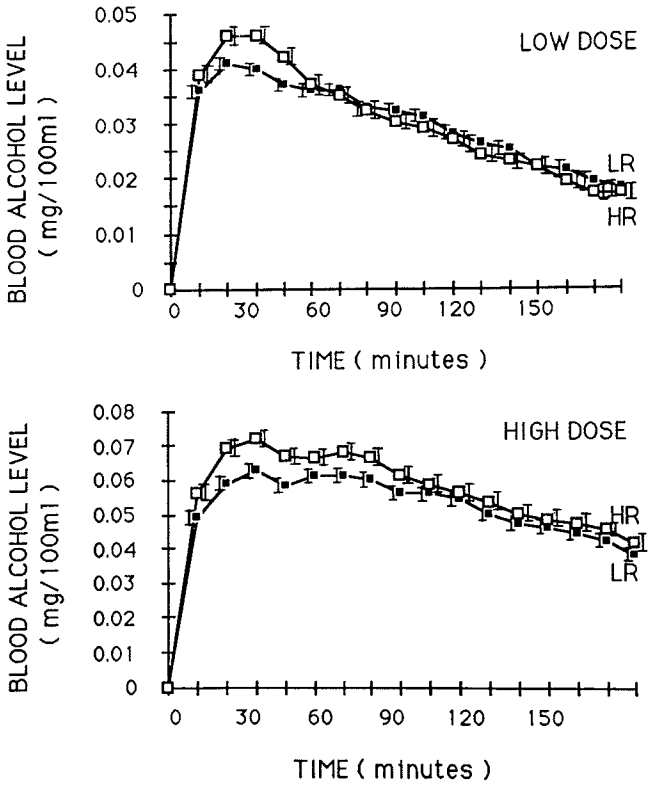

Fig. 1. Mean blood alcohol level (mg/100 ml) as a function of time (min) for both LR (black squares) and HR (white squares) groups. The data points are mean values; the error bars, standard errors (S.E.M.). The upper panel presents the low dose condition; the lower panel, the high dose condition.

Results

Fig. 1 presents the blood alcohol curves (BAC) for both the LR and HR groups under the LD and HD conditions, as a function of time (min) post ingestion. [1] Time zero is the point immediately following ingestion of the drink. The results of independent group t tests (significant at $P < 0.05$) under both the LD and HD conditions, revealed no statistically significant differences between the two groups at any time point.

Next, we observed that at each of the 8 electrodes examined, acute ethanol ingestion elicited significant changes only in the slow alpha (SA, 7.5–10 Hz) frequency band. In contrast, significant risk group differences in SA activity were observed only at electrodes F3 ($F = 31.03$, $df = 1$, $P < 0.0001$), F4 ($F = 24.89$, df 1, $P < 0.0001$) and P4 ($F = 5.40$, df 1, $P < 0.025$). To determine whether the differences observed at these electrodes were induced by ethanol or were due to risk group differences in baseline SA levels, an individual repeated measures ANOVA was conducted at each electrode (F3, F4 and P4) on baseline SA activity measured on the P, LD and HD days. The results revealed no statistically significant risk group differences in baseline SA activity. Individual repeated measures ANOVA at electrodes F3, F4, and P4 were also performed within each risk group in order to assess the stability of baseline SA activity across the P, LD and HD days. No statistically significant differences in SA activity were found for either the LR or HR groups. Because the risk group differences in SA activity at these electrodes were attributable to the effects of ethanol, t tests were then used to determine at which post-ingestion time intervals, under both the LD and HD conditions, these differences existed. At electrode F3, differences were found at 140 min under the LD condition and at 70 and 140 min under the HD condition; at electrode F4, at 70, 105 and 140 min under the LD condition and at 70 and 105 min under the HD condition. At P4, while there was an overall risk group difference, there was no significant difference at individual time points under either the LD or HD condi-

[1] Some individuals in each group, under both the low dose and high dose conditions, were excluded from the calculations of the mean blood alcohol levels. These subjects had a blood alcohol concentration that reflected a problem with the intoxicometer. Thus, under the low dose condition, LR = 17 and HR = 16. Under the high dose condition, LR = 15 and HR = 15.

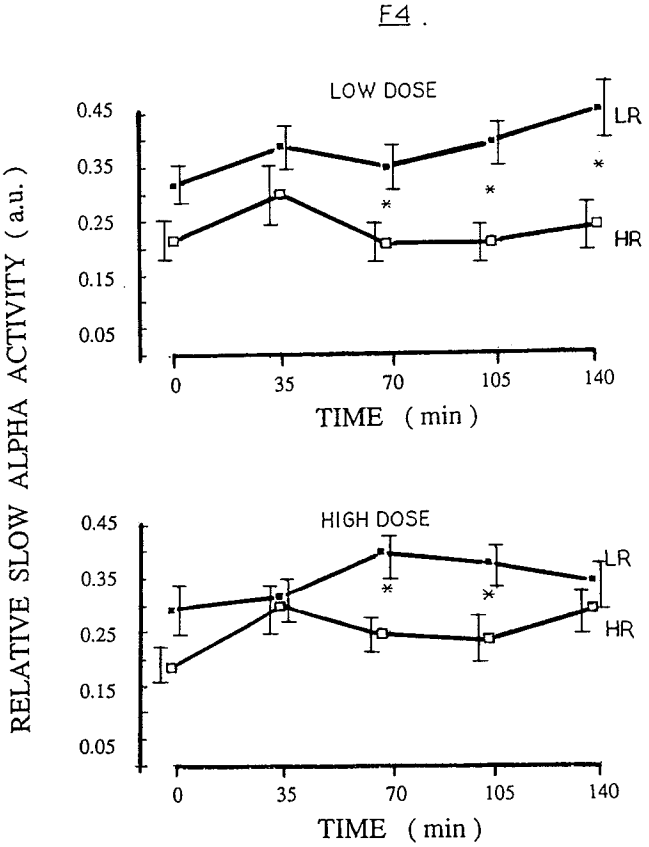

Fig. 2. Risk group differences in relative slow alpha (SA, 7.5–10.0 Hz) activity in arbitrary units (a.u.) as a function of time (min) at electrode F4. The upper panel compares low risk (LR, black squares) and high risk (HR, white squares) individuals under the low dose condition; the lower panel under the high dose condition. The data points are mean values; the error bars, standard errors (S.E.M). The asterisks indicate significant ($P < 0.05$) risk group differences in relative SA activity at those time intervals.

tion. Fig. 2 presents the changes in SA activity at electrode F4.

In addition to the aforementioned results were several significant main effects and interactions which tended to occur more frequently at anterior rather than posterior locations. For example, a significant Dose effect was observed at electrodes F4 ($F = 7.69$, $df = 2, 39$, $P < 0.002$) and C4 ($F = 3.29$, df 2, 39, $P < 0.048$); a significant Trial effect at electrode F3 ($F = 3.69$, df 3, 29, $P < 0.012$). Significant Trial × Group interactions occurred at electrodes F3 ($F = 2.85$, df 4, 37, $P < 0.037$), C3 ($F = 3.677$, df 4, 37, $P < 0.013$), C4 ($F = 3.94$, df 4, 37, $P < 0.009$) and O1 ($F = 3.11$, df 4, 37, $P < 0.026$); Frequency × Group interactions at electrodes F3 ($F = 7.86$, df 3, 38, $P < 0.0003$) and F4 ($F = 4.91$, df 3, 38, $P < 0.006$).

As can be observed in Table I, the Drink Index indicates that the HR group ingested significantly more ethanol than did the LR group. Thus, it was possible that any risk group difference in the ethanol-induced EEG response reflected 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 upon their Drink Index scores. The "light drinkers" (N = 11) had a mean index of 6.54, S.D. 3.93. In contrast, the "heavy drinkers" (N = 8) had a mean index of 110.6, S.D. 65.2. Two individuals who had abstained from drinking over the 6 months prior to the study were excluded from the calculations. Repeated measures ANOVA, one for each of the 8 electrodes, were used to compare EEG differences between the two groups. The results indicated that in the HR group, drinking history had no significant effect on the ethanol-induced EEG response. Additionally, analyses of covariance (SAS/STAT, v. 6), using the Drink Index as a covariate, were performed at each electrode in order to examine the relationship between current levels of ethanol consumption and the ethanol-induced EEG responses of the HR and LR groups. Again, there were no statistically significant effects.

Next, we tested the hypothesis that risk group differences in the SA response would reflect the ascending and descending phases of the blood alcohol curve. The percent change in SA activity was calculated from 0 to 35 min post ingestion (which corresponds to the ascending BAC) and from 35 to 70 min post ingestion (which corresponds to the descending BAC) under both LD and HD conditions. These percentages were calculated at electrodes F3, F4, and P4, where risk group differences in SA activity had been observed, as well as at electrodes C3, C4, P3, O1 and O2, where no differences existed. Independent group t tests were then used to determine the presence of significant risk group differences. Fig. 3 presents the results of these analyses. During the ascending phase of the BAC, under both the LD and HD conditions, increases in SA activity were observed in both the HR and LR groups. These increases, under both conditions, were significantly greater in HR than LR individuals (LD, $t = 3.18$, df 14, $P < 0.007$; HD, $t = 4.74$, df 14, $P < 0.0003$). During the descending phase of the BAC, changes in SA activity reflected dose differences as well as risk group differences. Under the LD condition, SA activity decreased in both groups; the decrease was significantly greater in the HR group ($t = 7.72$, df 14, $P < 0.0001$). In contrast, under the HD condition, SA activity continued to increase in the LR group but decreased in the HR group. This difference in the direction of change in SA activity was significant at $t = 6.24$, df 14, $P < 0.0001$.

Discussion

Initially, we observed that following acute ethanol ingestion the BACs generated by both the HR and LR

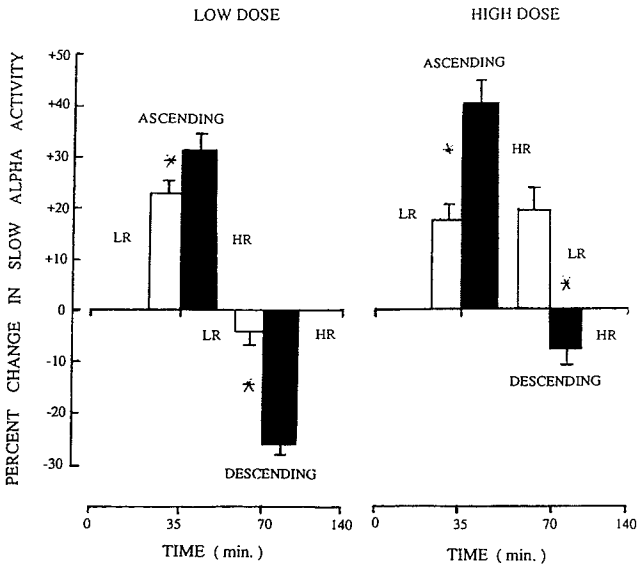

Fig. 3. Mean percent change in slow alpha activity as a function of time (min) for low risk (LR, empty bars) and high risk (HR, filled bars) individuals across all 8 electrodes. The left panel presents the low dose condition; the right panel, the high dose condition. Under each condition, the interval from 0 to 35 min corresponds to the ascending phase of the blood alcohol curve; the interval from 35 to 70 min to the descending phase. The data are mean values; the error bars, standard errors (S.E.M.). The asterisks indicate significant risk group differences at $P < 0.05$.

groups, under both the LD and HD conditions, manifested no statistically significant differences. Typically, there are large individual variations in both the rate, latency and peak of the BAC (Porjesz and Begleiter 1985) that may reflect differences in factors such as ethanol metabolism, rate of tolerance, or the amount of food eaten prior to ethanol ingestion (Schuckit 1981). However, most studies comparing the BACs of HR and LR individuals have typically found no differences (Schuckit 1981; Pollock et al. 1983; Kaplan et al. 1988; Schuckit et al. 1987; Schuckit and Gold 1988; Ehlers and Schuckit 1990, 1991).

Next, we demonstrated that acute ethanol ingestion elicits EEG changes in the slow alpha (7.5–10.0 Hz) frequency band that effectively discriminate between high risk (HR) and low risk (LR) individuals. In our study, acute ethanol ingestion was followed by an increase in SA activity in both the LR and HR groups. This effect has often been described as the primary EEG response to ethanol and has been reported in previous investigations (Davis et al. 1941; Engel and Rosenbaum 1945; Begleiter and Platz 1972; Lehtinen et al. 1981; Lukas et al. 1986; Cohen et al. 1992). In general, those studies which compared the responses of LR and HR individuals reported that HR individuals had significantly greater increases in both SA (Pollock et al. 1983; Volavka et al. 1985) and beta activity (12–20 Hz) (Ehlers and Schuckit 1990), as well as a significantly more stable EEG post-ethanol ingestion than did LR individuals (Ehlers and Schuckit 1988, 1991).

Furthermore, we observed significant risk group differences in SA activity at electrodes F3, F4 and P4. The difference obtained at P4 is in accord with those studies reporting that risk group differences in ethanol-induced EEG responses are more common in posterior regions (Pollock et al. 1983; Volavka et al. 1985; Ehlers and Schuckit 1988). Our novel findings of risk group differences at anterior electrodes F3 and F4 may reflect the fact that cortical recordings at a specific locus may represent afferent volleys originating in distant cortical and/or subcortical sites. Further, there is evidence from studies of event-related potentials (Salamy and Williams 1973; Porjesz and Begleiter 1985) that association cortex, possibly because of its complex, polysynaptic structure (Himwich and Callison 1972; Kalant 1975), may be more sensitive to the effects of ethanol than sensory cortex; F3, F4 and P4 each overlies association cortex (Homan et al. 1987).

In order to verify that the risk group differences we observed reflected differential ethanol effects rather than baseline EEG differences, we first established that there were no statistically significant differences in baseline EEG activity between HR and LR individuals. This finding confirms a previous report from our laboratory (Cohen et al. 1991) and has been documented by others (Pollock et al. 1983; Kaplan et al. 1988; Ehlers and Schuckit 1990). It indicates that baseline EEG measures do not reliably discriminate between LR and HR individuals.

The aforementioned discussion indicates that in general, our results confirm many previously documented observations concerning risk group differences in the ethanol-induced EEG response. However, most uniquely, our results give strong evidence for a significant risk group difference in the relationship between ethanol-induced EEG changes and the ascending and descending phases of the BAC, thus supporting Newlin and Thomson's (1990) differentiator model (DM). As can be observed in Fig. 3, during the ascending phase of the BAC, SA activity increased in both the LR and HR groups under both the LD and HD conditions; the increases in the HR group were significantly greater. During the descending phase of the BAC, changes in SA activity reflected both dose differences as well as risk group differences. Under the LD condition, SA activity decreased in both groups; the decrease was significantly greater in the HR group. In contrast, under the HD condition, between 35 and 70 min after ethanol ingestion, while SA activity decreased in the HR group it increased in the LR group. These findings of greater acute sensitization (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, demonstrate that the ethanol-induced EEG responses of HR and LR individuals are differentially sensitive to the ascending and descending phases of the BAC. Furthermore, these findings are important to the differentiator model in another respect, the ability to demonstrate both acute sensitization and acute tolerance in the same experiment.

Evidence that the phenomena of acute sensitization and acute tolerance are enhanced in HR individuals comes from numerous observations. That the responses of HR individuals are greater during the ascending phase of the BAC (acute sensitization) has been obtained from measures of EMG activity (Schuckit et al. 1981), psychomotor performance (O'Malley and Maisto 1985), autonomic function, i.e., skin temperature, skin conductance and pulse amplitude (Newlin and Thomson 1990) and from subjective measures (lower anxiety levels in HR) (Savoie et al. 1988). Similarly, HR individuals have reportedly shown greater decrements in response than LR individuals during the descending phase of the BAC (acute tolerance) in, for example, the return of P300 latencies to control levels (Schuckit et al. 1988; Porjesz and Begleiter 1990) and N1 amplitudes (Porjesz and Begleiter 1990). Acute tolerance has also been documented in rats genetically bred to prefer (P) or not prefer (NP) ethanol (Li et al. 1987; Lumeng et al. 1989; McBride et al. 1991). It has presented as more rapid recovery in both behavioral measures (foot shock avoidance, Lumeng et al. 1982; Waller et al. 1983; and reacquisition of the righting reflex, Kurtz et al. 1990, 1991) and autonomic responses, e.g., hypothermia (Froehlich et al. 1989), following a single sedative hypnotic dose of ethanol (Lumeng et al. 1992). In P rats, the tolerance following a single ethanol dose may persist for 10 days, compared with 3 days in NP rats (Gatto et al. 1987). Murphy et al. (1990) reported that in rats with a high voluntary ethanol consumption rate there is an increased likelihood of developing acute tolerance. Interestingly, our HR group had an ethanol consumption rate (as measured by the Drink Index) approximately 5 times that of the LR group. One possible explanation for the heightened level of ethanol consumption comes from the observations of Lukas et al. (1986, 1988) who reported that acute ethanol ingestion produced increased alpha activity in conjunction with episodes of subjective euphoria, usually within 10–15 min post ingestion (Lukas et al. 1988). These episodes of subjective euphoria were associated with transient increases in alpha activity above the already elevated alpha activity; increases in all of the aforementioned measures paralleled the ascending BAC. Lukas et al. (1986, 1988) as well as others, e.g., Propping (1977), reported that the early, abrupt increases in alpha activity were associated with pleasant sensations and the feelings of comfortable relaxation that may act to positively reinforce increased ethanol ingestion.

One might argue that the electroencephalographic differences we observed between the LR and HR groups may, in fact, reflect differences in their drinking histories. However, by dividing the HR group into "light" and "heavy" drinkers and demonstrating that there were neither baseline, nor ethanol-induced EEG differences between the groups, we have indirect evidence that the risk group differences in EEG activity were not due to differences in drinking history, but may reflect the contribution of genetic factors. Evidence derived from both twin studies and from comparisons of EEG patterns in alcoholics and their non-alcoholic relatives (Propping 1977; Propping et al. 1981) supports the possibility of a genetic contribution to the EEG. In the former study (Propping 1977), both baseline EEG activity and the EEG response to an ethanol challenge were found to be more similar in MZ than in DZ twins. In the latter study (Propping et al. 1981), more similar EEG variants were observed both in alcoholics and their non-alcoholic first degree relatives than between the alcoholics and matched controls. Additional evidence for a genetic contribution to the EEG, as well as to event-related potentials, comes from studies (Morzorati et al. 1988; Ehlers et al. 1991) demonstrating that both at baseline and under a variety of experimental conditions, there may be significant differences in the responses of P and NP rats.

Thus, in conclusion, our findings demonstrate the presence of significant differences in the ethanol-induced EEG responses of LR and HR individuals. These differences stand in contrast to baseline EEG measures which do not effectively discriminate between the two groups. The observed ethanol-induced EEG changes parallel the ascending and descending phases of the BAC and demonstrate that HR individuals manifest significantly greater response increments during the ascending phase (acute sensitization) and significantly faster recovery to baseline levels during the descending phase (acute tolerance). These risk group differences do not appear to reflect differences in drinking history, but rather the influence of genetic factors in the response to ethanol. This influence may manifest itself as an electrophysiological response that is an index of the reinforcing properties of ethanol, which may be higher in HR individuals and may act to positively reinforce a high frequency of ethanol ingestion.

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References

Begleiter, H. and Platz, A. The effects of alcohol on the central nervous system. In: B. Kissin and H. Begleiter (Eds.), The Biology

of Alcoholism. Vol. 2. Physiology and Behavior. Plenum Press, New York, 1972: 293–343.

Cohen, H.L., Porjesz, B. and Begleiter, H. EEG characteristics in males at risk for alcoholism. Alcohol. Clin. Exp. Res., 1991, 15: 858–861.

Cohen, H.L., Porjesz, B. and Begleiter, H. Ethanol induced alterations in EEG activity in adult males. Neuropsychopharmacology, 1992, in press.

Davis, P.A., Gibbs, F.A., Davis, H., Jetter, W.W. and Trowbridge, L.S. The effects of alcohol upon the electroencephalogram (brain waves). Quart. J. Stud. Alc., 1941, 1: 626–637.

Ehlers, C.L. and Schuckit, M.A. EEG response to ethanol in sons of alcoholics. Psychopharmacol. Bull., 1988, 24: 434–437.

Ehlers, C.L. and Schuckit, M.A. EEG fast frequency activity in the sons of alcoholics. Biol. Psychiat., 1990, 27: 631–641.

Ehlers, C.L. and Schuckit, M.A. Evaluation of EEG alpha activity in sons of alcoholics. Neuropsychopharmacology, 1991, 4: 199–205.

Ehlers, C.L., Chaplin, R.I., Lumeng, L. and Li, T.-K. Electrophysiological response to ethanol in P and NP rats. Alcohol. Clin. Exp. Res., 1991, 15: 739–744.

Engel, G.L. and Rosenbaum, M. Delirium III. Electroencephalographic changes associated with acute alcohol intoxication. Arch. Neurol. Psychiat., 1945, 53: 44–50.

Froehlich, J.C., Stewart, R., Kurtz, D., Zweifel, M., Lumeng, L. and Li, T.-K. Genetic differences in hypothermic effects of ethanol. Alcohol. Clin. Exp. Res., 1989, 13: 306.

Gabrielli, Jr., W.F., Mednick, S.A., Volavka, J., Pollock, V.E., Schulsinger, F. and Itil, T.M. Electroencephalograms in children of alcoholic fathers. Psychophysiology, 1982, 19: 404–407.

Gatto, G.J., Murphy, J.M., Waller, M.D., McBride, W.J., Lumeng, L. and Li, T.-K. Persistence of tolerance to a single dose of ethanol in the selectively bred alcohol preferrring P rat. Pharmacol. Biochem. Behav., 1987, 28: 105–110.

Himwich, H.E. and Callison, D.A. The effect of alcohol on evoked potentials of various parts of the central nervous system of the cat. In: B. Kissin and H. Begleiter (Eds.), The Biology of Alcoholism, Vol. 2. Plenum Press, New York, 1972: 67–84.

Holmberg, G. and Martens, S. Electroencephalographic changes in man correlated with blood alcohol concentration and some other conditions following standardized ingestion of alcohol. Quart. J. Stud. Alc., 1955, 16: 411–424.

Homan, R.W., Herman, J. and Purdy, P. Cerebral location of international 10–20 system electrode placement. Electroenceph. clin. Neurophysiol., 1987, 66: 376–382.

Kalant, H. Direct effects of ethanol on the nervous system. Fed. Proc., 1975, 34: 1930–1941.

Kaplan, R.F., Hesselbrock, V.M., O'Connor, S. and De Palma, N. Behavioral and EEG responses to alcohol in nonalcoholic men with a family history of alcoholism. Prog. Neuropsychopharmacol. Biol. Psychiat., 1988, 12: 873–885.

Kurtz, D., Stewart, R.B., Zweifel, M., Li, T.-K. and Froehlich, J.C. Genetic differences in tolerance and sensitization to the sedative/hypnotic effects of ethanol. Alcohol. Clin. Exp. Res., 1990, 14: 307.

Kurtz, D., Stewart, R.B., Zweifel, M., Li, T.-K. and Froehlich, J.C. Genetic differences in response to the sedative/hypnotic effects of ethanol. Psychopharmacology, 1992, in press.

Lehtinen, I., Lang, A.H., Jantii, V., Pakkanen, A., Keskinen, E., Nyrke, T. and Lempiainen, M. Ethanol-induced disturbance in human arousal mechanism. Psychopharmacology, 1981, 73: 223–229.

Li, T.-K., Lumeng, L., McBride, W.J. and Murphy, J.M. Alcoholism: is it a model for the study of disorders of mood and consummatory behavior. Ann. NY Acad. Sci., 1987, 499: 239–249.

Lukas, S.E. and Mendelson, J.H. Electroencephalographic activity and plasma ACTH during ethanol-induced euphoria. Biol. Psychiat., 1988, 23: 141–148.

Lukas, S.E., Mendelson, J.H., Benedikt, R.A. and Jones, B. EEG alpha activity increases during transient episodes of ethanol-induced euphoria. Pharmacol. Biochem. Behav., 1986, 25: 889–895.

Lumeng, L., Waller, M.B., McBride, W.J. and Li, T.-K. Different sensitivities to ethanol in alcohol-preferring and nonpreferring rats. Pharmacol. Biochem. Behav., 1982, 16: 125–130.

Lumeng, L., Li, T.-K., McBride, W.J., Murphy, S.L., Morzorati, S.L. and Froehlich, J.C. Mechanism(s) of modulation of alcohol consumption: studies on the P and NP rats. In: G.Y. Sun (Ed.), Molecular Mechanisms of Alcohol. Humana Press, New York; 1989: 359–370.

Lumeng, L., Murphy, J.M., McBride, W.J. and Li, T.-K. Genetic influences on alcohol preference in rodents. In: H. Begleiter and B. Kissin (Eds.), Alcohol and Alcoholism, Vol. 1. Oxford University Press, New York, 1992: in press.

McBride, W.J., Murphy, J.M., Gatto, G.J., Levy, A.D., Lumeng, L. and Li, T.-K. Serotonin and dopamine systems regulating alcohol intake. Alcohol Alcohol., 1991, Suppl. 1: 411–416.

Mendelson, J.H., McGuire, M. and Mello, N.K. A new device for administering placebo alcohol. Alcohol, 1984, 1: 417–419.

Michel, Ch. and Battig, K. Separate and combined psychophysiological effects of cigarette smoking and alcohol consumption. Psychopharmacology, 1989, 97: 65–73.

Morzorati, S., Lamishaw, B., Lumeng, L., Li, T.-K., Bemis, K. and Clemens, J. Effects of low dose ethanol on the EEG of alcohol-preferring and nonpreferring rats. Brain Res. Bull., 1988, 21: 101–104.

Murphree, H.B., Schultz, R.E. and Jusko, A.G. Effects of high congener intake by human subjects on the EEG. Quart. J. Stud. Alc., 1970, Suppl. 5: 50–61.

Murphy, J.M., Gatto, G.J., McBride, W.J., Lumeng, L. and Li, T.-K. Persistence of tolerance in the P line of alcohol-preferring rats does not require performance while intoxicated. Alcohol, 1990, 7: 367–369.

Newlin, D.B and Thomson, J.B. Alcohol challenge with sons of alcoholics: a critical review and analysis. Psychol. Bull., 1990, 108: 383–402.

Newlin, D.B and Thomson, J.B. Chronic tolerance and sensitization to alcohol in sons of alcoholics. Alcohol. Clin. Exp. Res., 1992, in press.

O'Malley, S.S. and Maisto, S.A., Effects of family drinking history and expectancies on responses to alcohol in men. J. Stud. Alcohol, 1985, 46: 289–297.

Pollock, V.E., Volavka, J., Goodwin, D.W., Mednick, S.A., Gabrielli, W.F., Knop, J. and Schulsinger, F. The EEG after alcohol administration in men at risk for alcoholism. Arch. Gen. Psychiat., 1983, 40: 857–861.

Porjesz, B. and Begleiter, H. Human brain electrophysiology and alcoholism. In: R.E. Tarter and D.H. Thiel (Eds.), Alcohol and the Brain. Plenum, New York, 1985: 139–182.

Porjesz, B. and Begleiter, H. Individuals at risk for alcoholism: neurophysiologic processes. In: C.R. Cloninger and H. Begleiter (Eds.), Banbury Report 33: Genetics and Biology of Alcoholism. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1990: 137–157.

Propping, P. Genetic control of ethanol action on the central nervous system. Hum. Genet., 1977, 35: 309–334.

Propping, P., Kruger, J. and Mark, N. Genetic disposition to alcoholism. An EEG study in alcoholics and their relatives. Hum. Genet., 1981, 59: 51–59.

Salamy, A. and Williams, H.L. The effects of alcohol on sensory evoked and spontaneous cerebral potentials in man. Electroenceph. clin. Neurophysiol., 1973, 35: 3–11.

SAS Institute Inc., SAS/STAT User's Guide, Version 6, Fourth Edition, Vol. 2. SAS Institute, Cary, NC, 1990: 891–996.

Savoie, T.M., Emory, E.K. and Moody-Thomas, S. Acute alcohol intoxication in socially drinking female and male offspring of alcoholic fathers. J. Stud. Alcohol, 1988, 49: 430–435.

Schuckit, M.A. Peak blood alcohol levels in men at risk for the future development of alcoholism. Alcohol. Clin. Exp. Res., 1981, 5: 64–66.

Schuckit, M.A. and Gold, E.O. A simultaneous evaluation of multiple markers of ethanol/placebo challenges in sons of alcoholics and controls. Arch. Gen. Psychiat., 1988, 45: 211–216.

Schuckit, M.A., Engstom, D., Alpert, R. and Duby, J. Differences in muscle-tension response to ethanol in men with and without family histories of alcoholism. J. Stud. Alcohol, 1981, 42: 918–924.

Schuckit, M.A., Gold, E.O. and Risch, S.C. Plasma cortisol levels following ethanol in sons of alcoholics and controls. Arch. Gen. Psychiat., 1987, 44: 942–945.

Schuckit, M.A., Gold, E.O., Croot, K., Finn, P. and Polich, J. P300 latency after ethanol in sons of alcoholics. Biol. Psychiat., 1988, 24: 310–315.

Volavka, J., Pollock, V., Gabrielli, Jr., W.F. and Mednick, S.A. The EEG in persons at risk for alcoholism. In: M. Galanter (Ed.), Recent Developments in Alcoholism. Plenum Press, New York, 1985: 21–36.

Waller, M.B., McBride, W.J., Lumeng, L. and Li, T.-K. Initial sensitivity and acute tolerance to ethanol in P and NP lines of rats. Pharmacol. Biochem. Behav., 1983, 19: 683–686.