Absence of Visual and Auditory P300 Reduction in Nondepressed Male and Female Alcoholics

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Background: The P300 component of the event-related potential has been extensively studied as a possible neurobiological risk marker for the development of alcoholism. Although P300 amplitude reduction has frequently been documented in high-risk children, studies of adult alcoholics are inconsistent.

Methods: P300 amplitude from 121 adult alcoholics was compared to 68 controls utilizing event-related potential paradigms from the auditory and visual modalities. All participants were evaluated clinically with psychiatric interviews and administered the MMPI.

Results: Male alcoholics did not show a reduction in amplitude in either the auditory or visual modality. Female alcoholics showed reduced P300 amplitude, but only when a comorbid lifetime diagnosis of depression was present. Similar results were found using current depressed mood (Scale 2 from the MMPI).

Conclusions: No differences in P300 amplitude were found between alcoholics and controls unless comorbid depression was present. Therefore, P300 amplitude reduction seen in children at high-risk for developing alcoholism seems to represent a neurodevelopmental delay that normalizes by adulthood. Biol Psychiatry 1999;46:982–989 © 1999 Society of Biological Psychiatry

Key Words: ERP, P300 amplitude, adults, alcoholics, depression, MMPI

Introduction

The event-related potential (ERP) and the P300 component, in particular, has been studied for some time with respect to its possible utility as a marker for the development of psychiatric problems, including such diverse diseases as schizophrenia (Pfefferbaum et al 1989; Steinhauer et al 1991) and alcoholism. A number of laboratories have documented reduction in P300 amplitude in children determined to be at high risk for developing alcoholism compared to those who are at low risk, based on their familial loading for alcoholism (Begleiter et al 1984; Steinhauer and Hill 1993; Hill and Steinhauer 1993a; Whipple et al 1988; Berman et al 1993; Hill et al 1990). There are few longitudinal data sets available to test the validity of P300 amplitude in childhood as a risk marker in adulthood. In a preliminary 8-year follow-up study, P300 amplitude was determined to be associated with the presence of substance dependence in adolescence (Hill et al 1995b). Also, longitudinal assessments (n = 635) of children and adolescents followed for up to 7 years show that P300 reduction in high-risk children is linked to a developmental delay in P300 production (Hill et al, in press). These studies of young children and adolescents are intriguing in that there is potential to tap a neurocognitive deficit that precedes the regular use of alcohol and drugs.

In contrast to studies of high-risk children, results obtained for adult alcoholics are quite mixed. Reduction in the amplitude of the P300 component has been reported for abstinent male alcoholics when compared with control subjects using auditory stimuli (Patterson et al 1987; Pfefferbaum et al 1991; Ramachandran et al 1996), though negative reports are abundant (Lille et al 1987; Hermanutz et al 1981; Hill et al 1995a; Keenan et al 1987; Pfefferbaum et al 1979; Steinhauer et al 1987). Similarly, utilizing the visual modality, amplitude reduction has been reported for male alcoholics (Emmerson et al 1987; Glenn et al 1996; Parsons et al 1990; Patterson et al 1987; Pfefferbaum et al 1979; Porjesz et al 1987) though not uniformly (Biggins et al 1995; Cadaveira et al 1991).

Discrepancies between studies of alcoholics in our own laboratory are instructive with respect to the inconsistencies among studies of adult alcoholics. In a recent study utilizing an auditory paradigm involving 217 adult males, no differences were found between 98 young male alcoholics (average age 36 years) and 80 age-matched controls (Hill et al 1995a). We did find significantly reduced amplitudes in both the auditory and visual modality in women (Hill and Steinhauer 1993b).

The previously reported discrepancies between P300 amplitude in female and male alcoholics found in our laboratory suggested the need to further examine gender...
differences by modality. Because a greater prevalence of affective disorders has frequently been reported in women (see Hill, in press for review), a secondary purpose of this report was to investigate the effect of comorbid depression on the P300 component measured in alcoholics. Significant reductions in auditory P300 amplitude in patients diagnosed with major depressive disorder (DSM-III-R) have been seen (Blackwood et al 1987; Bruder et al 1995; Yanai et al 1997). In two of those reports, P300 amplitudes were reported to increase in patients who underwent treatment for depression, resulting in similar amplitude to controls (Blackwood et al 1987; Yanai et al 1997). Thus, an analysis of male and female alcoholics was undertaken utilizing data from both auditory and visual modalities and covarying the effects of comorbid depression.

Methods and Materials

Data for a total of 121 adult alcoholics and 68 low-risk controls who participated in one of two family studies of alcoholism (Cognitive and Personality Factors Family Study [CPFFS] and the Biological Risk Factors Family Study [BRFFS]) were analyzed. All subjects provided consent and were paid for their participation. The alcoholic subjects were from high-risk families selected for an especially high density of alcoholism and minimal other psychopathology. The high-risk families were selected through either a pair of alcoholic male siblings (CPFFS) or a pair of alcoholic female siblings (BRFFS). Therefore, these high-risk families have an exceptionally high loading for alcohol dependence. Parents of these adult siblings were also included in the clinical assessments. Identification of families occurred while one member of the pair was in treatment. The presence of alcoholism and other psychopathology was determined in the sibling pairs and their first-degree relatives through face-to-face interviews (Diagnostic Interview Schedule-DIS), allowing for DSM-III and Feighner criteria (Feighner et al 1972) to be applied. Individuals who were excluded from the family studies because of extensive psychopathology were nevertheless, retained for exploratory analyses and provided cases for testing our hypotheses concerning comorbid depression.

Low-risk families were selected for an absence of psychopathology from among volunteers answering an advertisement to participate in a research study. Each family consisted of a minimum of two same-sexed adult siblings and their parents. Later, children of these siblings were recruited as well for other initiatives. No criteria for acceptance was advertised. Thus, families were selected through a pair of normal male or female siblings so that the structural characteristics of the high and low-risk families would be similar. Control index cases and their first-degree relatives were also interviewed in-person to confirm the absence of alcoholism and Axis I psychopathology.

On the day of testing, all subjects were administered the DIS (RDC criteria) by a trained Masters-level clinician (each clinician was required to meet 90% reliability before test administration) to determine the lifetime presence of the following disorders: Major Depressive Disorder, Antisocial Personality, Anxiety (Panic Attack), Mania, Schizophrenia, and Drug and Alcohol Dependence. Additionally, a second clinician (M.A. or Ph.D. level) conducted an unstructured interview and a consensus diagnosis was obtained. Because the family studies required screening subjects for the absence of Axis-I psychopathology, comorbidity was minimal. The database included 18 cases that originally did not qualify for the family studies (CPFFS and BRFFS) because of primary depression (occurring at least 1 year before the onset of alcoholism) or simultaneous onset of depression or drug dependence. To enrich our sample for depression, these individuals were added to the data set. Therefore, among the 121 alcoholics in the present analysis, 24 met criteria for major depression and 50 met criteria for drug dependence. An approximately equal number of depressed and non-depressed alcoholics carried a diagnosis of drug dependence. Of the 24 depressed alcoholics, 54% had comorbid drug dependence, with 38% of the nondepressed alcoholics (n = 97) meeting criteria for drug dependence. Due to the larger family study design that excluded individuals with primary drug dependence, only 16% of the depressed alcoholics and 3% of the nondepressed group met criteria for primary drug dependence (onset of drug dependence preceded diagnosis of alcoholism). Drug dependence, tested as a covariate in an analysis of variance, was not significant and therefore, was not used in further analyses. Due to limited sample sizes, analyses were conducted using only comorbid depression in women. The demographic characteristics were comparable in the female alcoholic group with comorbid depression, the female alcoholic group without depression, and the female control group without depression. Similarly, the male alcoholic and control groups were well matched (Table 1).

In addition to lifetime history of psychopathology, subjects were also assessed using the MMPI. This provided the opportunity to measure current Depression Scale (Scale 2) elevations indicating presence of a depressed mood. Thus, the MMPI was administered on the same day the ERP assessment was completed. Specifically, Scale 2 T-scores above 65 were used to classify those with a current depressed mood.

Adult alcoholics from high density alcoholism families were compared to controls using both auditory and visual modalities. Three different paradigms were utilized to collect ERPs: an auditory Counting task, an auditory Choice Reaction task, and a Visual discrimination task.

Subjects were asked to refrain from using alcohol and illicit drugs for 48 hours before testing. To verify the report of recent abstinence, a blood sample was obtained to analyze liver enzymes (SGOT, SGPT, Y-glutamyltranspeptidase [GGTP]). Any indication that a liver enzyme value was out of the normal range would be the occasion for cross-checking alcohol use with self report and collateral informants. Presence of illicit drugs or psychoactive medications was determined by self report and by obtaining urine drug screens. The drug screen included cocaine, amphetamines, barbiturates, opiates, benzodiazepines, antidepressants, antihistamines, and analgesics. Out of the 185 available urine screens 11 were found to be positive (3 cocaine, 3 benzodiazepines, 1 barbiturate, and 4 antidepressants). The accuracy of self report was quite good with 7/11 individuals reporting use in the past 24 hours. All subjects with positive
screens were retained in the analysis. Self report data indicated that the illicit drugs had been used in small quantities and medications were being used as prescribed.

Subjects were asked to refrain from consuming any caffeinated beverage the morning of testing. A pre-protocol interview conducted immediately before testing confirmed that no caffeine had been consumed. Because of concerns about withdrawal from caffeine at the time of testing, an estimate of the usual amount of caffeine consumed was determined. Typical use of caffeine was determined in the interview by asking the subject to report on his/her usual consumption of coffee per day (no significant differences were seen). Analysis of the average amount of coffee drunk per day showed a similar amount being consumed in all of the subgroups (alcoholic males drank 3.5 cups/day whereas control men drank 2.1 typically). The alcoholic women with or without depression drank approximately 2 cups per day. Once at the laboratory, subjects were offered decaffeinated coffee until the afternoon, at which time ERP testing had been completed.

Procedure

Visual Task

The task employed in this study was a visual event-related potential task after the procedure of Begleiter et al (1984). An Atari 130 computer executed a BASIC program to present stimuli at 33 ms duration with intertrial intervals varying randomly from 2.25 to 4 sec. The subjects were seated in a darkened, sound-attenuated testing room. A Magnavox RGB color monitor, placed 132 cm from the subject, subtending and visual angle of 3.8°, was used to display the stimuli. One view, the non-target stimuli, was a simple circle to which the subject was asked not to respond (blank condition). Additionally, there were four possible views of target stimuli, a representation of a head with a nose and either a right or left ear. The subject was instructed to press the button (right or left) that corresponded to the depicted ear. The “easy” condition occurred when the nose was oriented upward and the button pressed was on the same side as the ear (the right ear was depicted on the right side of the head so that the correct response was to press the right button). In the “hard” condition, the nose was oriented downward and the subject needed to spatially rotate the head to respond correctly.

Thus, for the hard condition, the ear was depicted on the opposite side as the button pressed. Although the conditions have been termed “hard” and “easy” (Begleiter et al 1984), no significant differences in P300 amplitude have been found by condition (Begleiter et al 1984; Hill et al 1993a). Therefore, the present analysis was based on results obtained for the hard condition.

Standard instructions were read to each subject. If additional information was needed, it was provided by the experimenter. Practice trials were presented on the monitor using a long exposure duration. Once the subject was performing correctly (after approximately 10 trials), the visual display duration was decreased to the 33 msec exposure time of the main experiment for several additional practice trials. (The subjects were encouraged to respond quickly but more importantly, to respond accurately.) Two blocks of 120 trials were presented to the subjects. Of the 240 total trials, 160 were blank (nontargets), 40 were easy conditions targets (20 right and 20 left), and 40 were hard condition targets (20 right and 20 left). Previous studies (Begleiter et al 1984; Hill and Steinhauser 1993a) have indicated no differences in P300 amplitude in the hard and easy conditions. Therefore, data were analyzed for only the hard condition.

Auditory Task

The auditory procedure consisted of two tasks: Counting and Choice Reaction Task (RT). For both tasks, subjects sat in a sound-attenuated darkened room and were presented with either a high-pitched tone (1500 Hz) or a low-pitched (800 Hz) tone randomly generated by a computer every 3 sec (40 msec duration, 2 msec rise/fall time, intensity 70 dBA). The overall probability of a high (infrequent) tone was .25. Subjects were instructed that two high tones could not occur in succession.

Therefore, the following conditional probabilities applied: the totally predictable event of a low tone after a high (1.0 condition); two low tones in succession (.67 condition); and the rare event of an infrequent high tone after a low (.33 condition). P300 is typically maximal at the .33 probability condition (Steinhauer and Hill 1993). For the present report, only the .33 condition was analyzed.

For the Counting task, the subjects were asked to count the number of high tones they heard and report the number at the end

Table 1. Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
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<tbody>
<tr>
<td></td>
<td>Alcoholic with depression</td>
<td>Alcoholic without depression</td>
</tr>
<tr>
<td></td>
<td>(n = 54)</td>
<td>(n = 20)</td>
</tr>
<tr>
<td></td>
<td>Alcoholic without depression</td>
<td>(n = 47)</td>
</tr>
<tr>
<td>Age</td>
<td>37.9 (12.3)</td>
<td>36.5 (7.5)</td>
</tr>
<tr>
<td></td>
<td>44.0 (13.5)</td>
<td>35.4 (9.2)</td>
</tr>
<tr>
<td>Education</td>
<td>12.8 (1.6)</td>
<td>12.9 (2.2)</td>
</tr>
<tr>
<td></td>
<td>14.9 (3.5)</td>
<td>13.0 (1.8)</td>
</tr>
<tr>
<td>Age drank once/month</td>
<td>15.9 (2.7)</td>
<td>19.4 (5.8)</td>
</tr>
<tr>
<td></td>
<td>18.7 (4.5)</td>
<td>16.7 (7.1)</td>
</tr>
<tr>
<td>Number of years drank</td>
<td>21.0 (11.3)</td>
<td>17.0 (5.3)</td>
</tr>
<tr>
<td></td>
<td>23.5 (14.2)</td>
<td>17.8 (5.9)</td>
</tr>
<tr>
<td>Days since last drink</td>
<td>336.2 (993.5)</td>
<td>61.1 (74.5)</td>
</tr>
<tr>
<td></td>
<td>19.7 (35.6)</td>
<td>149.1 (351.9)</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td>70%</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>96%</td>
<td>64%</td>
</tr>
</tbody>
</table>

* Percentage of cases in professional, semiprofessional/technical and skilled categories. The SES was determined using Hollingshead’s Four Factor Index of Social Status (Hollingshead, 1975). A chi-square analysis did reveal significant differences between risk groups when individuals in the top three categories were compared to those in the semi-skilled and unskilled categories (χ² = 6.64, df = 1, p = .009 for the two male groups; χ² = 10.62, df = 2, p = .005 for the three female groups).
of the trial (two 80 trial blocks were completed). In the RT task, the subject was asked to press one button when a high tone was presented and press the opposite button for a low tone. Again two blocks of 80 trials were presented. Subjects could earn a small bonus for accurate performance ($0.25). Only trials with 5 or fewer errors were included in analyses.

**ERP Recordings**

Event-related potentials were recorded using Ag/AgCl electrodes placed over the midline frontal, vertex, parietal and occipital (Fz, Cz, Pz, Oz) locations, and left and right parietal locations (P3, P4), and referred to linked ears with forehead ground. Ocular artifacts were monitored with an electrode placed under the left eye, referred to linked ears. Data were monitored on-line by an oscilloscope, and all trials affected by eye artifact (those exceeding 75 μV) were excluded. Electrophysiological data were amplified by 20 K (10 K for eye channel) using a Grass Model 12 Neurodata system, set to a bandpass of 0.01 to 30 Hz. A Digital Equipment Corp. PDP 11/23 computer (slaved to coincide with the Atari) sampled each trial for a 1200 msec epoch, at 8 msec intervals, beginning with a 200 msec prestimulus baseline for the visual task. Data were digitized for 1200 msec at 125 Hz, beginning 200 msec before the stimulus onset, by the PDP 11/23. The subject’s response, reaction time and correctness of response were encoded into the data file. All data were stored on magnetic media.

Artifact free trials were averaged for condition and electrode. At least two raters, blind to the status of the family, identified the ERP components (N100, P200, N250, P300) off-line using an interactive peak detection algorithm that chose the maximal amplitude for a given component (Cz for N100, P200 and N250, and Pz for P300) within a predefined latency window (P300: 264–424 msec). Components found outside the latency range were identified by consensus among raters. Peak amplitude was computed as the deviation from the median voltage during the 200 msec baseline. Latency and amplitude data were extracted and stored in ASCII files for subsequent analysis. ERPs were collected in the morning so as to minimize diurnal variation. P300 amplitude was analyzed using a repeated-measures ANOVA (BMDP 2V) and the SPSS statistical package. Greenhouse-Geisser corrections for nonhomogeneity of variance were applied where appropriate.

**Results**

An ANOVA was performed to determine the effects of group (alcoholic vs. control), gender (male and female), and modality (Counting, Choice RT and Visual) on the amplitude of P300. All analyses utilized the P300 amplitude at the Pz electrode, the point of maximal deflection. No group differences were found overall. The main effect of modality ($F = 21.95; df = 2,352; p < .0001$) was due to an approximate 2 μV reduction seen in the visual task. Gender was also found to be significant ($F = 13.72; df = 1,185; p = .0003$), with females showing higher amplitudes than males. Further analyses, conducted separately by gender, revealed that although no differences were seen for males (Figure 1), P300 in alcoholic females was significantly lower than in control females ($F = 4.01; df = 1,108; p = .04$). Separate analyses by task revealed that this overall effect was due to group differences being seen in the Counting task only ($F = 6.44; df = 1,109; p = .013$).

The present analysis confirmed our previous auditory
P300 results for male alcoholics (Hill et al 1995a). Moreover, no amplitude differences were found in the visual modality for the male alcoholics. A tendency for P300 to be reduced in alcoholic women was seen, though only in the Counting task. Because women have a much greater likelihood of having a lifetime diagnosis of depression in association with alcoholism (Hill, in press), we reasoned that any differences in amplitude seen in women might be due to comorbid depression. To test this theory, further analyses were performed using a 3 group comparison: Female alcoholics with a lifetime clinical diagnosis of depression (AD), Female alcoholics without depression (A), and control females without depression (C).

All study participants had been diagnosed by DSM-III criteria for the presence of at least one major depressive episode by lifetime history. Additionally, the Research Diagnostic Criteria (RDC) were applied (one month duration of depressed mood). Using the lifetime presence or absence of depression based on RDC criteria to classify the subject groups (A, AD, and C), an analysis of P300 amplitude was performed revealing significant differences for the Counting task ($F = 5.07; \text{df} = 2.95; p = .008$) and for the RT task ($F = 4.31; \text{df} = 2.95; p = .016$) (Table 2). Further analyses comparing the Counting task means of any two groups showed that only the female alcoholics with depression differed significantly from the controls (Duncan Multiple Range tests: $p < .05$). Similar findings were noted for the RT task. Female alcoholics with depression had significantly lower amplitude than the alcoholics without depression. Therefore, it seems as if the presence of depression, not alcoholism alone, is contributing to the auditory P300 amplitude reduction seen in women alcoholics. Analyses were performed for the visual task, comparing female alcoholics and controls. No significant differences were found. Thus, when P300 reduction is seen in alcoholics, it seems to occur only in association with comorbid depression. Grand averaged EEG waveforms for females can be seen in Figure 2.

To determine whether current depressed mood influenced the reduction in P300 in female alcoholics, T-scores from the MMPI (Scale 2—depression scale) were used to classify the three groups. An analysis of variance using current depressed mood to classify the A and AD groups revealed similar results, providing evidence that comorbid depression was responsible for the reduction in P300 amplitude (Table 3). The only significant effects seen (2 group comparisons) were between alcoholics with depressed mood and controls (AD vs. C) and between alcoholics without depressed mood and alcoholics with depressed mood (A vs. AD).

Analyses of ERP performance measures were conducted to determine whether differences in P300 amplitude seen for the depressed female alcoholics might be due to differences in overall performance of the task. Specifically, depressed individuals might have more problems

<table>
<thead>
<tr>
<th>Task</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>$F$</th>
<th>$p$</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcoholic with depression (AD)</strong></td>
<td>$n = 20$</td>
<td>$n = 47$</td>
<td>$n = 31$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Counting task</td>
<td>11.04 (3.9)</td>
<td>13.82 (6.2)</td>
<td>16.12 (5.5)</td>
<td>5.07</td>
<td>.008</td>
<td>AD vs. C</td>
</tr>
<tr>
<td>Choice reaction task</td>
<td>10.98 (6.3)</td>
<td>15.45 (6.4)</td>
<td>15.94 (6.4)</td>
<td>4.31</td>
<td>.016</td>
<td>AD vs. C; A vs. AD</td>
</tr>
<tr>
<td>Visual discrimination task</td>
<td>11.69 (7.5)</td>
<td>11.57 (6.9)$^a$</td>
<td>13.44 (5.9)</td>
<td>0.79</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Alcoholic without depression group, $n = 46$.

Figure 2. Grand averaged EEG waveforms for females performing the two auditory tasks (Counting and RT—33 condition). Note that the only significant differences for females was in the auditory task (a downward deflection indicates a positive component).
performing accurately. Similar error rates were found for the female alcoholics with depression (AD) and for those without depression, the alcoholic only (A) group. Analysis of performance scores for the two groups revealed no significant differences (Table 4), suggesting that reduction of P300 in the depressed alcoholics was not due to their inability to perform the tasks.

**Discussion**

Considerable controversy continues to exist concerning whether P300 reduction is seen in adult alcoholics. If it is seen, the question remains whether it is a result of the alcoholic’s biological vulnerability to develop alcoholism or rather due to other concomitant factors (alcohol exposure, comorbid psychopathology). Pfefferbaum et al. (1991) found that lifetime exposure did not predict P300 reduction in middle-aged alcoholics. The combined effects of advanced age and alcohol exposure have not specifically been tested with respect to P300. It has been shown that neuropsychological deficits are greater in alcoholics with long term exposure and advanced age (Ryan and Butters 1980). Thus, it is possible that the reduced P300 previously seen in alcoholics might be due to alcohol exposure is still an open question. Secondly, reduced amplitude has been reported for schizophrenic patients (Steinhauer and Zubin 1982; Steinhauser et al 1991; Pfefferbaum et al 1989) and patients diagnosed with depression (Bruder et al 1995; Blackwood et al 1987; Yanai et al 1997), suggesting that comorbid disorders may influence the amplitude of P300 in alcoholics.

Patterson et al (1987), Pfefferbaum et al (1991), and Ramachandran et al (1996) have all reported that auditory P300 amplitude does not differentiate male alcoholics and controls, confirming an earlier negative report from this laboratory utilizing the auditory modality (Hill et al 1995a). Furthermore, the present analysis found no differences in visual P300 amplitude between male alcoholics and controls. Our previous findings of reduced auditory and visual P300 amplitude in female alcoholics (Hill and Steinhauer 1993b) were puzzling. This discrepancy between male and female alcoholics studied in our own laboratory, using the same paradigms and testing conditions, suggested that other factors (e.g., exposure to other drugs, comorbid psychiatric problems) might be responsible. The greater prevalence of affective disorders among women suggested that reduction of P300 in adult alcoholic women might be due to comorbid depression rather than the presence of an alcoholism diathesis marker (there were too few cases of depression diagnosed in males [n = 4] to undertake an analysis.) Therefore, analyses were conducted with females, classifying the alcoholic group into those with and without comorbid depression. The only significant mean differences found were between the group of alcoholics with depression and the controls. No differences were found for P300 obtained from either the auditory or visual

<table>
<thead>
<tr>
<th></th>
<th>Alcoholic with depressed mood (n = 37)</th>
<th>Alcoholic without depressed mood (n = 29)</th>
<th>Controls without depressed mood (n = 28)</th>
<th>F</th>
<th>p</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counting task</td>
<td>12.39 (5.1)</td>
<td>13.80 (6.5)</td>
<td>16.83 (6.0)</td>
<td>4.68</td>
<td>.012</td>
<td>AD vs. C</td>
</tr>
<tr>
<td>Choice reaction task</td>
<td>12.66 (5.4)</td>
<td>16.21 (7.6)</td>
<td>16.20 (7.8)</td>
<td>2.98</td>
<td>NS</td>
<td>AD vs. C; A vs. AD</td>
</tr>
<tr>
<td>Visual discrimination task</td>
<td>10.27 (6.2)</td>
<td>13.19 (7.6)</td>
<td>13.16 (7.2)</td>
<td>1.95</td>
<td>NS</td>
<td>AD vs. C; A vs. AD</td>
</tr>
</tbody>
</table>

Errors were analyzed using t tests. No significant differences were found. Percentages of the total number of trials.
modality when “pure” female alcoholics (no comorbid depression) and controls were compared. Thus, the present study demonstrates that the P300 reduction seen in adult women is most likely due to comorbid depression.

The present findings offer one explanation for the controversial results seen in adult P300 studies. Female alcoholics without comorbid depression did not differ from normal controls. We suspect that if we had a sufficient number of male alcoholics with depression, P300 reduction might also have been seen in males. A limitation of the present analysis was that too few male alcoholics with depression were available to test the effects of comorbid depression on P300 amplitude. This was due to the design of the larger study that systematically eliminated specific comorbidity including recurrent depression (Hill 1992; Hill and Smith 1991; Yuan et al 1996). In fact, to have sufficient cases for analyses in the female alcoholic groups, data were included from our files of “rejected” comorbid cases (e.g., recurrent depression present with alcohol dependence).

A number of laboratories have consistently documented lower amplitudes in minor children at high risk for developing alcoholism compared to controls (Begleiter et al 1984; Steinhauser and Hill 1993; Hill and Steinhauser 1993a; Whipple et al 1988; Berman et al 1993; Hill et al 1990). We have suggested that reduced amplitude may be a developmental delay marker in children that normalizes by adulthood (Hill et al 1990; Hill and Steinhauser 1993a). Results from a longitudinal study of children utilizing a latent growth curve of visual P300 amplitude for children at high risk for developing alcoholism and normal controls demonstrate the convergence of the groups by young adulthood (Hill et al, in press). Therefore, previous results with high and low-risk for alcoholism children and adolescents, coupled with the present results showing minimal P300 reduction in adult alcoholics (seen only when comorbid depression was present), suggest the neurodevelopmental delay hypothesis may have merit.

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