THE EFFECTS OF FAMILY HISTORY, SOBRIETY LENGTH, AND DRINKING HISTORY IN YOUNGER ALCOHOLICS ON P300 AUDITORY-EVOKED POTENTIALS

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Abstract — Event-related potentials (ERPs) have been shown to be different between alcoholics and non-alcoholics. Of particular interest to investigators has been the P300 wave. Because it has been shown that alcohol-induced neural damage can alter P300 waves, particularly amplitude, we attempted to examine alcoholics who most likely suffered little damage because they drank heavily for relatively few years (mean = 6.9 years). The effects of long-term sobriety (mean = 5.0 years) were also investigated to determine if cognitive functioning, as measured by auditory-evoked P300 waves, varies with increased abstinence. Because family history for alcoholism has also been shown to influence P300 amplitude and latency, alcoholics and controls with and without family history were examined. The alcoholic group had significantly longer latencies in P300 measures in both the family history positive and negative groups; P300 amplitudes between alcoholics and non-alcoholics did not vary, regardless of family history. P300 waves were unaffected by sobriety length or drinking history. The results support the hypothesis that P300 differences can be seen between alcoholics and those at risk for alcoholism.

INTRODUCTION

Alcoholics appear to have different P300 event-related potential (ERP) waves when compared to non-alcoholic subjects (Porjesz and Begleiter, 1982; St Clair et al., 1985; Porjesz et al., 1987a; Miyazato and Ogura, 1993). These data, as well as P300 alcohol research focused on family history positive (FH +) against family history negative (FH −) subjects (e.g. Brigham et al., 1993; Steinhauer and Hill, 1993; Polich et al., 1994), have implicated the P300 as a possible biological marker for alcoholism (Begleiter et al., 1984; Noble et al., 1994). ERPs appear to be sensitive to neurological damage (Brown et al., 1982; O'Donnell et al., 1987). Patients with cognitive dysfunctions (Hansch et al., 1982; Hall, 1992) and elderly subjects (Barrett et al., 1987; Patterson et al., 1987) show decreased P300 amplitudes and increased P300 latencies. Increased P300 latency and decreased amplitude are also typically found in alcoholics (e.g. Pfefferbaum et al., 1979; Cloninger, 1987; Miyazato and Ogura, 1993); it has been hypothesized that these findings in alcoholics may reflect neural damage caused by alcohol, rather than an innate marker for alcoholism (Porjesz et al., 1987b; Hall, 1992). Recent findings may have verified this hypothesis. By combining ERP measurements with magnetic resonance imaging, Kaseda et al. (1994) reported that the lowered ERP amplitudes observed in male alcoholics with long drinking histories (28.6 years) correlated with severe neural deficits in areas including the ventricles, sulci, anterior fissure, and anterior and posterior horns. P300 latency measures did not differ between groups and were uncorrelated with neural deficits. Alcoholics tested on ERP measures usually report long drinking histories (≥15 years; Pfefferbaum et al., 1979; Porjesz et al., 1987a Miyazato and Ogura, 1993). It is thus reasonable to assume that at least part of the variance reflected by abnormal ERP amplitudes is related to alcohol-inflicted neural damage.

As well as testing alcoholics with long drinking histories, P300 studies typically examine newly abstinent alcoholics (<1 year, e.g. St Clair et al., 1985; Porjesz et al., 1987a; Cohen et al., 1995).
Because reliable ERP measures are dependent on a subject's ability to maintain attention and discriminate stimuli (Sommer et al., 1990; Strayer and Kramer, 1990; Hall, 1992; Polich et al., 1994), it is possible that in newly abstinent alcoholics there are deficits of these abilities, even if they can return the correct counting total (Hill et al., 1988). The effects of sobriety in alcoholics abstinent for >1 year have not been fully investigated, although preliminary data suggest that amplitudes may remain low years after alcoholics stop drinking (Porjesz and Begleiter, 1985). If amplitude is a measure of neural damage, which usually does not recover (Kandel and Schwartz, 1985), increases in sobriety length would not correlate with an increase in P300 amplitude. Because it has been shown that brain-stem auditory-evoked potentials (BAER) return to normal with abstinence (Porjesz and Begleiter, 1985), it is possible that brain-stem functions recover while mid-level areas, such as the hippocampus (Hall, 1992) remain altered in alcoholics.

P300 latency appears to measure the time needed to process novel stimuli (see Hall, 1992). While it is possible that latency is unrelated to neural damage in alcoholics (Miyazato and Ogura, 1993), many studies have reported that alcoholics show significantly increased latencies (Pfefferbaum et al., 1979; Porjesz et al., 1987a; Kaseda et al., 1994) as well as those at risk for alcoholism (Polich et al., 1994). It is thus possible that the neuronal transmission mechanism indicated by latency is altered in alcoholics prior to the commencement of drinking. Longer alcoholic latencies are almost exclusively found when amplitudes are abnormal (Miyazato and Ogura, 1993), though longer latencies in alcoholics are sometimes reported with an increased early sobriety (8 months; Frank et al., 1994).

In an attempt to determine if alcohol damage and/or family history is reflected in P300 measures, we examined FH+ alcoholics with short drinking histories and long sobriety length. We predict that P300 latencies may differ between alcoholics and non-alcoholics, but that latencies will not correlate with drinking or abstinence length. If alcohol-induced neural damage is the cause of abnormal alcoholic P300 amplitudes, then we expect to observe no difference between alcoholics with short drinking histories and non-alcoholics on amplitude. If family history is one causal agent then we predict that the non-alcoholic FH+ controls will have abnormal P300 measures, while the alcoholic FH- group will have normal P300 waves. By testing alcoholics with short drinking histories, we assume that the neural damage will be minimized and that the group differences will reflect characteristics other than alcohol-induced neural damage.

SUBJECTS AND METHODS

Subjects

The alcoholic group consisted of 13 (six male) FH+ alcoholics and 13 (six male) FH- alcoholics recruited from New Paltz, New York Alcoholics Anonymous meetings. The 10 FH- non-alcoholic (four male) and 10 non-alcoholic FH+ (four male) subjects were recruited from the college student SUNY New Paltz population. All alcoholics met the DSM-III-R (American Psychiatric Association, 1987) criteria for alcohol dependence, as well as the criteria put forth by the National Council on Alcoholism. All alcoholics were also previously diagnosed for alcoholism, either by a treatment centre professional or a licensed psychiatrist or psychologist. No subject (alcoholic or control) was permitted in the study if he: (a) was currently on any mood-altering medication; (b) had received a previous neurological or psychological diagnosis other than alcoholism (including drug addiction as a primary diagnosis); (c) had admitted to ingesting any alcohol in the previous 96 h to testing; (d) was unable to perceive tones <15 db in a pre-screening hearing examination.

A structured interview based upon the DSM-III-R criteria for alcohol dependence was administered to each subject. Assessment of the subjects' drinking behaviour was based upon this interview, as well as previous diagnoses (see above). Family history was obtained via DSM-III-R criteria as reported by the subject. Each relative was mentioned, and the criteria were given for that given relative. The subject then reported the number of criteria that the particular relative met for that criterion. To be included in the FH+ group, it was necessary that the biological father of the subject be diagnosed alcoholic by the structured DSM-III-R criteria as well as having a history of seeking professional treatment. All FH+
Table 1. Family history positive (FH+) alcoholics and family history negative (FH−) non-alcoholics: subject demographics

<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>M/F ratio</th>
<th>Age (years) mean (SD)</th>
<th>Education (years) mean (SD)</th>
<th>Abstinence (years) mean (SD)</th>
<th>Drinking length (years) mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic FH+</td>
<td>13</td>
<td>6/7</td>
<td>25.9 (2.3)</td>
<td>15 (1.1)</td>
<td>5.2 (1.0)</td>
<td>7.0 (2.5)</td>
</tr>
<tr>
<td>Alcoholic FH−</td>
<td>10</td>
<td>4/6</td>
<td>26.1 (3.1)</td>
<td>14.8 (1.3)</td>
<td>4.9 (1.1)</td>
<td>6.8 (3.2)</td>
</tr>
<tr>
<td>Non-alcoholic FH+</td>
<td>10</td>
<td>4/6</td>
<td>25.9 (2.7)</td>
<td>15.9 (1.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-alcoholic FH−</td>
<td></td>
<td></td>
<td>24.9 (3.2)</td>
<td>15.2 (1.3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No significant differences were found between groups on any demographic variable.

subjects reported at least one additional first- or second-degree relative as having met the criteria for alcoholism. FH− was defined as having no first- or second-degree relatives meeting the criteria for alcoholism based on the DSM-III-R interview. All subjects assigned in the non-alcoholic group reported alcohol intake frequency <1 drink per week.

The determination of abstinence length was based on self-reports. Drinking length was reported from the age of the first drink taken (excluding 'sips' or medication in childhood). All subjects reported that their first drinking bout was memorable, at least in part because heavy drinking soon commenced after. Abstinence was defined as not having ingested any quantity of alcohol or any other mood-altering drug, including prescribed medications. All subjects reported drinking at least 5 ounces of alcohol per occasion, and all subjects reported at least eight bouts per month almost immediately from the commencement of drinking to the commencement of sobriety.

Subjects were matched on demographics (gender, age, and education) considered pertinent for P300 testing (Hall, 1992; Table 1). All subjects received a free hearing examination as an inducement to participate in the study.

Materials and parameters

Testing was achieved via Biological Software and Hardware, Northbrook, Illinois, USA. The CPU was a Biologic Traveler ZFA-161-52, rated at 115 V, 3 A. The TDH-39P Telephonics headphones were connected via a Biologic Stimulus Connection Module Auditory output to TEAC HP: Model 'Breakout box'. The pre-amplifier was a Biologic electronically isolated patient connection unit. Gold plated, Nicolet electrodes were used at the following sites: Pz, Cz, Fz and A1 (linked reference).

An 'oddball paradigm' consisting of non-target (80%: 1000 Hz) and target (20%: 2000 Hz) tones was employed. The tones were presented at a rate of 1.5 s, with a 10 ms rise and a 50 ms plateau at 60 db. A total of 500 tones were presented (in a computer-generated random order), comprised of four hundred 1000 Hz tones and one hundred 2000 Hz tones (not including artefact rejected tones). The analogue filter was set at one-half down, at 0.3 Hz and 100 Hz. Impedance was at 3 kΩ, the rejection limit was ±45 mV.

Prior to stimulus presentation, each electrode was sampled 250 times over a 500 ms interval to provide a baseline for that particular electrode on each trial. If the sample exceeded 75% of the output of the amplifier for that trial (or 75 mV peak to peak), the trial was dismissed and the baseline sampling was reinstated. The same 75 mV screening was utilized for the post-stimulus presentation; again, excess of this limit led to the trial being reset. These are common parameters employed to eliminate eye-blink, eye movement, or other artefacts that might skew results (e.g. Glenn et al., 1993).

Analysis of ERP data

All physiological ERP recording was computed directly via the Biologic software (target and non-
target stimuli, electrode location, amplitudes and latencies). For each of the two active electrode sites (Pz and Cz), two trained ERP experts, blind to the subject's group, rated: P200, N250, P300 and N3 as they deviated from the 500 ms baseline. Inter-rater reliability was +1 for the Pz site, and 0.98 for the Cz site.

Procedure

All subjects were given a hearing screening/examination to ensure adequate hearing (15 db) prior to ERP testing. All subjects were prepared using standard ERP testing and electrode procedures (Hall, 1992). Testing occurred in a dimly lit room while subjects sat in a relaxed chair facing a 1 inch black on white dot (at eye level), 1 m from their forehead. The subjects were instructed to listen for, and silently count, the number of 'High' tones (2000 Hz) and to ignore the 'low' tones (1000 Hz) while maintaining eye-contact with the dot. The instructions, given twice, did not vary between groups. After the instructions were given, pre-testing of 100 trials was performed to: (a) ensure that the subjects could discriminate the tones; (b) confirm that the subjects understood which tones to count; (c) relax the subjects; (d) test the apparatus (e.g. electrode impedance consistency, artefact count) and electrode connections.

The 500 tones were presented in two 250-tone blocks. Between the trials, the subjects were asked the number of tones that they had counted and they were given a 1 min break. At the end of the second trial, the subjects were again asked the number of tones that they had counted. Artefact rejections and counting accuracy did not vary between the groups.

All statistical results were computed utilizing SPSS on a Gateway 2000 486 microprocessor. The data were computed by the principal investigator and a second analysis expert. There were no inter-rater differences.

RESULTS

A significant difference was found between the groups on P300 latency \[F(3, 42) = 3.73, P < 0.01\]. A Student–Newman–Keuls test revealed that the FH– non-alcoholic group (mean = 291.95, SD = 29.77) differed significantly from the FH+ non-alcoholics (mean = 318.5, SD = 36.81), FH– alcoholics (mean = 329.23, SD = 23.54) and FH+ alcoholics (mean = 325.42, SD = 25.13) on P300 latency (Fig. 1). The strength of the relationship, as indexed by $\eta^2$, was 0.21, which is considered a small effect. No difference was found between any of the groups on P300 amplitude measures [alcoholic FH+, mean = 14.57; alcoholic FH–, mean = 14.32; non-alcoholic FH+, mean = 13.99; non-alcoholic FH–, mean = 14.62; \( F(3, 42) = 1.21, P > 0.05 \)] (Fig. 2). There were no
Table 2. Inter-correlations between various measures in FH+ and FH— alcoholics

<table>
<thead>
<tr>
<th>Measures</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>FH+ alcoholics</td>
<td>(n = 26)</td>
<td>1. Age</td>
<td>-0.13</td>
<td>0.87***</td>
<td>-0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Sobriety length</td>
<td>-0.36</td>
<td>-0.04</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Drinking length</td>
<td>-0.05</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Latency</td>
<td>-0.49*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Amplitude</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FH— alcoholics</td>
<td>(n = 20)</td>
<td>1. Age</td>
<td>-0.01</td>
<td>0.46</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Sobriety length</td>
<td>-0.02</td>
<td>0.13</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Drinking length</td>
<td>-0.09</td>
<td>-0.10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Latency</td>
<td>-0.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Amplitude</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* P < 0.05; *** P < 0.001.

significant electrode difference site recordings for amplitude or latency within either group (F<1, P > 0.05), therefore an average of the Pz and Cz sites was used.

Drinking length correlated significantly with age in FH+ alcoholics [r(11) = 0.87, P < 0.001] as did amplitude with latency [r(11) = -0.49, P<0.05] (Table 2). Hierarchical regressions revealed that when the effects of age and/or sobriety were removed, Δr was statistically non-significant on both amplitude and latency measures. We conclude that drinking length and sobriety durations did not affect P300 latencies or amplitudes. However, extreme caution should be taken when interpreting these results due to the small size of the sample. It should also be noted that the range of the alcoholics (FH+ and FH—) measured between 285 and 389 ms on latency, and between 9.47 and 16.83 μV on amplitude. The non-alcoholics (FH+ and FH—) ranged from 238 to 347 ms, and from 11.80 to 16.91 μV. With subjects matched on age, ethnic background, education and examined per gender, the ranges found are extensive. Though statistically significant, latency measures overlap in the 285–347 ms range.

DISCUSSION

There was a significant difference found between the FH— non-alcoholics when compared to the FH+ and FH— alcoholics and the FH+ non-alcoholics on P300 latencies, while P300 amplitudes did not differ between these four groups. These results support the hypothesis that either alcoholism or family history for alcoholism will result in different P300 waves.

Because it has been argued convincingly that amplitude is an excellent indicator of P300 abnormalities (Hall, 1992), it is of interest that our results showed only latency differences. It is possible that subject selection resulted in more similar amplitudes than one might expect. Polich et al. (1994) reported that FH+ and FH— subjects tend to have more similar amplitudes after the age of 18; most amplitude differences reported are seen prior to age 18. Polich hypothesized that it is possible that FH+ amplitudes catch up to FH— amplitudes after the age of 18. Because our subjects were an average of 25 years old, Polich’s hypothesis should be considered when interpreting these data. Polich also reported that the sampling of FH+ college students may be an unfair representation of FH+ persons, and that this sampling may influence P300 amplitude. However, Pfefferbaum et al. (1979) and Cohen et al. (1995) found significant amplitude differences in subjects >18 years as a result of family history, contradicting Polich’s theory. Further investigations in non-college FH+ persons are necessary to determine this relationship.

Because the effects of long-term sobriety are not fully understood in terms of P300 amplitude, it is possible that an increase in sobriety length normalizes amplitudes. One possibility is that, with increased abstinence, there may be an improvement in P300 amplitude. Further investigations into abstinence are needed to confirm or reject this theory. Though the acute effects of alcohol can alter P300 waves (Hall, 1992), it is of great interest that even in long-term sober alcoholics, latency differences were still apparent. Because subjects were matched on college level and counting errors did not differ, it is unlikely that this is an indication of cognitive ability differences; instead it seems likely that P300 abnormalities as measured by either amplitude or latency may reflect a marker for alcoholism or a risk of developing alcoholism (Polich et al., 1994).

The difference between the alcoholic (FH+ and FH—) and FH+ non-alcoholic groups and FH— non-alcoholics on P3 latency supports the hypo-
thesis that P300 waves are altered by both alcoholism and family history for alcoholism. This result is also interesting because latency and amplitude did not correlate with either drinking history or sobriety length. These results support the hypothesis that alcohol-induced damage is not responsible for the abnormal waves often seen in alcoholics (Frank et al., 1994). Because it was found that the FH+ non-alcoholics also had prolonged latencies, it seems reasonable to conclude that family history is a factor in P300 differences (e.g. Begleiter et al., 1984).

Because younger subjects were tested, we assume that the possibility of alcohol-induced neural damage has been minimized (Kaseda et al., 1994). It is possible that different P300 waves indicate that a person has an increased chance of becoming an alcoholic (St Clair et al., 1985; Cloninger, 1987; Polich et al., 1988). Our results support this hypothesis as evidenced by our alcoholic groups and those at risk (FH+) for alcoholism having increased P300 latencies. By observing these results in younger alcoholics, we are reasonably confident that neural damage is not the sole cause for the differences observed.

Because nicotine and caffeine consumption were not controlled for in this study, it is possible that the effects of these drugs could be the cause of the differences. We believe this is unlikely because in the groups that were questioned [alcoholic (FH−), non-alcoholic (FH+)], there were equal numbers of smokers and coffee drinkers in each group. However, the effects of these drugs possibly could have altered our results (Hall, 1992). It is suggested that further studies should control for these effects. Because our sample was not representative of all alcoholics and/or all college students, caution should be exercised when extrapolating these results to other populations. We further recognize that this sample may be unique, thereby limiting interpretation of our data.

In conclusion, although we found no group differences in P300 amplitude, we did find that younger, long-term sober alcoholics (FH− and FH+) and those at risk for alcoholism (FH+) have prolonged P300 latencies.

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