EVENT-RELATED POTENTIAL RESPONSES TO ALCOHOL-RELATED STIMULI
IN AFRICAN–AMERICAN YOUNG ADULTS: RELATION TO FAMILY HISTORY
OF ALCOHOLISM AND DRUG USAGE

CINDY L. EHLERS*, EVELYN PHILLIPS, ANTONIO SWEENY and CRAIG J. SLawecki

Department of Neuropharmacology, The Scripps Research Institute, La Jolla, CA, USA

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Abstract — Aims: To use event-related potentials (ERPs) to investigate the response to alcohol-related stimuli in African–American young adults. Methods: ERPs to an object recognition task, that included pictures of objects, food and alcohol-related and non-alcohol-related drinks as stimuli, were obtained in 81 African–American young adult men and women (18–25 years old) without a personal history of alcohol dependence. Information on: psychiatric diagnoses, personal drinking and drug use history, and familial history of alcoholism was also obtained. Results: Family history was found to be associated with lowered P3 components and higher N1 components in response to the non-alcohol-related drinks. Additionally, an exploratory analyses revealed that lower amplitude N1 components were generated in response to alcohol-related stimuli in regular marijuana users compared with non-regular users. No associations of N1 or P3 amplitudes with conduct disorder symptoms or current drinking status were found in this population. Conclusions: These studies demonstrated that family history is significantly and selectively associated with lower P3 amplitudes in this group of young adult men and women of African–American heritage. Additionally, current usage of marijuana and alcohol do not modify P3 amplitudes. However, regular marijuana use may diminish N1 response to alcohol-related stimuli, whereas, family history of alcoholism may augment N1 responses. Taken together these studies further suggest that ERPs can provide specific information on alcoholism risk as well as use of other misused drugs.

INTRODUCTION

In a large national survey it was documented that Black adults, as compared with White and Hispanic adults, have the highest volume of alcohol intake and frequency of heavy drinking (Dawson, 1998). However, in several studies, African–American young adults were found to be more likely to abstain from alcohol, not engage in heavy drinking, and have lower rates of alcohol use disorders, when compared with EuroAmericans and some other ethnic groups (Herd, 1988, 1990; Johnston et al., 1991; Group for the Advancement of Psychiatry, 1996). Risk and protective factors, particularly in the biological realm, that may explain differences in drinking patterns in the African–American community are yet to be completely identified. However, within the psychosocial realm, family factors, peer involvement (Barnes and Farrell, 1992) and academic performance (Rodney et al., 1997) appear to be more important than poverty or psychosocial status in predicting drug and alcohol involvement.

One measure that has received considerable attention as a possible marker for alcoholism risk is the P3 component of the event-related potential (ERP). ERPs are time-locked electric fields generated by synchronous neural activity within specific brain areas engaged in neurosensory and cognitive processing. In human subjects, a series of waves of differing polarity and amplitude designated ‘components’ of ERPs are generally obtained from the averaged EEG when a subject is asked to attend to and/or discriminate a target stimulus from a series of background stimuli (see Roth, 1973; Squires et al., 1975; Polish and Bloom, 1987). The P3 component is positive in polarity, occurs at approximately 300 ms, and has been suggested to reflect stimulus evaluation and memory function (see Donchin et al., 1986; Donchin and Coles, 1988). Many studies have demonstrated that the amplitude of the P3 is reduced in individuals who have a family history of alcoholism but who have not yet developed the disorder (see Elmasian et al., 1982; Begleiter et al., 1984; O’Connor et al., 1986, 1987; Hill et al., 1987, 1988, 1990, 1995, 1999a,b; Whipple et al., 1988; Porjesz and Begleiter, 1990, 1998; Berman et al., 1993a,b; Hill and Steinhauer, 1993; Steinhauer and Hill, 1993; Ramachandran et al., 1996; Ramsey and Finn, 1997; Van der Stelt et al., 1998a,b; Begleiter and Porjesz, 1999; Ratsma et al., 2001). Other studies are less convincing or do not support this hypothesis (see Baribeau et al., 1987; Polish and Bloom, 1987, 1988; Hill et al., 1988; Bauer, 1994a,b; 1997; Rodriguez-Holg Quinn et al., 1998a,b; 1999a,b; Bauer and Hesselbrock, 1999a,b). However, a meta-analysis of the literature up to 1993 concluded that the P3 ’may be useful as an index for predicting alcoholism vulnerability’ (Polich et al., 1994).

It has been suggested that differences in ERP findings between studies may relate to heterogeneity in samples based on such factors as co-morbidity (Bauer et al., 1999; Hill et al., 1999a,b; Hill and Shen, 2002), alcoholism phenotypes in the parents, and the presence of other drug use disorders. Bauer, Hesselbrock, and colleagues have made a cogent case for the hypothesis that P3 reduction in individuals with a family history of alcoholism is primarily related to conduct disorder and its subtypes. In adults diagnosed with antisocial personality disorder (ASPD) (Bauer, 1994a,b, 1997; O’Connor et al., 1994; Costa et al., 2000) or in youths with elevated numbers of conduct disorder behaviours or externalizing disorders (Bauer and Hesselbrock, 1999a,b, 2001; Iacono et al., 2002), decrements in P3 amplitude were observed. P3 decrements have also
been correlated with level of subsequent substance use (Berman et al., 1993a,b; Iacono et al., 2002).

Another difference between studies is related to the tasks used to generate ERPs. Tasks utilized to generate ERPs in studies of high- and low-risk individuals have varied. The meta-analysis conducted by Polich et al. (1994) indicated that results were stronger when ERPs are generated by ‘difficult’ visual tasks. Generally the tasks used in high/low-risk studies employ ‘neutral’ stimuli such as: lines or words or feature orientation to generate ERPs. However, in one recent study (Ehlers et al., 2001a) high- and low-risk subjects of Native American Heritage were required to discriminate between photographs of faces with different affective expressions. This task was found to be particularly sensitive to a family history of alcoholism, when compared with a visual line orientation task, even though the latter task was a more difficult discrimination than the facial recognition task.

Two recent studies have introduced the use of paradigms that elicit ERPs with alcohol-related stimuli. In both studies, the stimuli were words presented on a computer screen that were either alcohol-related (bottle, tin, brandy, booze) or ‘neutral’ (coffee, water, apple, chips). Using these stimuli, it was found that alcoholics had higher P3 amplitude responses to the alcohol-related, vs non alcohol-related, stimuli, whereas controls did not (Herrmann et al., 2000), and that heavy social drinkers had higher P300s to the alcohol-related stimuli when compared with light social drinkers (Herrmann et al., 2001).

The present report is part of a larger study exploring risk factors for alcoholism among African–American young adults (see Ehlers et al., 2001b; Ehlers and Phillips, 2003). The present study was designed to explore the relationships between visual P3 and N1 amplitudes generated to alcohol- and non-alcohol-related beverage stimuli and potential vulnerability factors associated with risk for alcohol dependence in African–American young adults. While most studies have focused on the relationship between P3 and family history of alcoholism, recent studies have reported augmented N1 amplitudes in alcoholics that correlated with memory function (Ahveninen et al., 2000). A comparison of N1 and P3 amplitudes allows for determination of the specificity of an effect on late positive components vs earlier potentials. Thus, the specific aims of this study were (1) to evaluate whether visual P3 and N1 amplitudes to alcohol- and non-alcohol-related stimuli were associated with family history of alcoholism in African–American young adults; (2) in an exploratory analysis, to test whether symptoms of conduct disorder and/or personal drinking and drug use history were also associated with changes in the amplitude of the P3 or N1 components.

**Materials and Methods**

**Participants**

Participants were recruited by fliers placed on local college and university campuses, and by word of mouth within the African–American community. The fliers stated the participation requirements as being: African–American and between 18 and 25 years of age. One hundred and thirty individuals inquired, by phone, about participation in the study. Ninety-eight participants eventually elected to participate. After complete description of the study to the subjects, written informed consent was obtained using a protocol approved by The Internal Review Board of The Scripps Research Institute. Information on demography, personal medical and psychiatric history, and family history of alcohol and other substance dependence was obtained using two family history questionnaires (Schuckit, 1985) and the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA). The SSAGA is a poly-diagnostic psychiatric interview that has undergone both reliability and validity testing (Bucholz et al., 1994; Hesselbrock et al., 1999). Interviewers were all trained by personnel from the collaborative study on the genetics of alcoholism (COGA). All best final diagnoses were made by a board-certified psychiatrist. Participants were excluded from further inclusion if they were taking any prescribed medication or had any major medical condition (i.e. organ system disease, neurological disorder, head injury, endocrine disorder, etc.).

A participant was classified as family history-positive (FHP) if s/he had a biological parent (mother or father) who met DSM-III-R criteria for alcohol dependence (American Psychiatric Association, 1987). Family history-negative (FHN) participants lacked a history of alcohol dependence in all their first-degree relatives. Participants were further classified with respect to their drinking status, marijuana use and conduct disorder symptoms. Regular drinkers were defined as individuals who drank at least one drink a month over the preceding 6 months. They were compared with individuals who were not regular drinkers by this definition from the SSAGA. Marijuana users were defined by criteria specified in the SSAGA, namely, having used marijuana over 21 times in a single year. Their data were compared with participants who did not meet criteria for marijuana use. Additionally, the numbers of symptoms reported by the subjects for conduct disorder were tallied and those subjects with three or more symptoms were compared with those with two or less, as previously described by Bauer and Hesselbrock (1999a).

**ERP Collection and Analyses**

Seven channels of ERP data (Fz, Cz, Pz, F3, F4, F7, F8) referenced to linked ear lobes with a forehead ground, international 10–20 system) were obtained using gold-plated electrodes with impedance held below 5 KΩ. An electrode placed left lateral infraorbitally and referenced to the left earlobe was used to monitor both horizontal and vertical eye movement. ERP recording signals were amplified at a sensitivity of 7 μV/mm (time constant 0.3 s, 35 Hz low pass) using a Nihon Kohden EEG machine and were transferred online to a Macintosh computer for digitization. Visual stimuli were presented on a video screen and consisted of three classes of pictures of objects. The first class was pictures of ‘non-food or drink objects’ (camera, chair, phone, scissors, tennis shoe),...
the second was ‘foods’ (corn, banana, apple, canned green beans, white bread) and the third was ‘drinks’. The participant was instructed to press one button for food and another button for drink objects. Individual ERP trials were averaged separately for the categories of objects (non-food objects, food objects, drinks). However, the drink category was further separated into non-alcoholic drinks (milk carton, Perrier water bottle, Arrowhead water bottle, tall water glass, short water glass) and alcoholic drinks (Jack Daniels bottle, beer in mug. Budweiser can, King Cobra can, wine in glass) for averaging. Fifty trials of each class of stimuli (non-food objects, food objects, non-alcoholic drinks, alcoholic drinks) were presented randomly for a total number of 200 trials. Thus each class had equivalent probability. The stimuli were presented for 1000 ms, the inter-stimulus interval was 1000 ms, with a 100 ms pre-trial baseline, the total trial length was 2000 ms.

The ERP trials were digitized at a rate of 256 Hz. Individual trials containing excessive eye movement artifact as well as trials where the EEG exceeded ±250 µV (<5% of the trials) were eliminated before averaging. The N1 was defined as the occurrence of a negative peak 75–150 ms after stimulus presentation. The P3 was defined as the occurrence of a peak after the N1–P2–N2 complex within 250–600 ms after stimulus presentation. The amplitude was determined as baseline to that peak (µV). The baseline was determined by averaging the 100 ms of pre-stimulus activity obtained for each trial. The routine is user-driven and each peak detection must be verified by the user. All peaks were initially identified by one investigator (E.P.), and verified by a second investigator (C.L.E.) both of whom were blind to participant characteristics.

The first aim was to describe the relationship between N1 and P3 amplitude and a participant’s parental history of alcohol dependence. To investigate this aim, N1 and P3 amplitudes generated by the alcohol/non-alcohol-related stimuli from three leads across the head (Fz, Cz, Pz), were used as dependent variables for comparison to previous studies and as suggested by Polich and Bloom (1999). Using ANOVA, FH and gender were treated as between subjects variables. Post-hocs (Tukeys HSD) of whom were blind to participant characteristics.

RESULTS

The young adults who participated in the study had a mean age (±SD) of 19.6 years (±2.0), with roughly equal numbers of men (40%) and women (60%). Demographic data, including age, gender, number of years of education, current drinking and drug use history, and number of conduct disorder symptoms in relation to parental history of alcoholism are presented in Table 1. FHP participants had a mean of 1.2 first-degree alcoholic relatives. In this group of 81 young adults, 32 reported never drinking regularly (regular drinking = one or more drinks a month over a 6 month period). In those individuals who were currently drinking regularly, the average quantity per occasion was three drinks and the average frequency was 3 times/month. There were no significant differences between the groups (FHP vs FHN) on any of these variables, except age, where FHP participants were found to be 1 year older than FHNs (F = 7.9; df = 1, 96; P < 0.005).

Figure 1 displays ERP responses to the four stimuli categories (objects, food, alcohol-related drinks, non-alcohol-related drinks) over the three electrode sites (Fz, Cz, Pz) evaluated in the entire sample (n = 81). P3 amplitudes appeared to be larger to objects as compared with food or drinks in the Fz lead.

To address the first major research question, P3 and N1 amplitudes were compared between FHPs and FHNs for the alcohol- and non-alcohol-related beverage stimuli. Those participants with at least one alcoholic parent were found to have smaller P3 amplitudes, which were significant in the central lead (Cz), in response to the non-alcohol-related beverage stimuli (main effect of FH: F = 4.3; df = 1, 80; P < 0.04) as seen in Fig. 2. Gender and family history were also found to be associated with P3 amplitudes generated by the non-alcohol-related beverage stimuli in the frontal lead (Fz) [main effect of Gender: F = 4.3 df = 1, 80; P < 0.04, Gender × Family History interaction (F = 5.4; df = 1, 80; P < 0.02)]. Post-hoc analyses revealed that the differences were contributed by a lowered P3 amplitude in the FHP young men (Tukey’s HSD: P < 0.04) [FHP males: 0.6 ± 1.5; FHN males: 4.9 ± 1.2; FHP females: 5.8 ± 1.1; FHN females: 4.5 ± 0.7 (mean ± SE µV)].

N1 amplitudes were also influenced by a family history of alcoholism. Those participants who were FHP had larger N1 amplitudes when compared with FHNs in posterior leads (main effect of FH: F = 5.6; df = 1, 80; P < 0.02) [FHP = 3.3 ± 0.6; FHN = 1.5 ± 0.5 (mean ± SE µV)] to the non-alcohol-related stimuli. No gender differences were found in those analyses.

Our second hypothesis was to test for associations, in an exploratory analysis, between N1 and P3 amplitudes and

Table 1. Demographic characteristics of study subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FHP (n = 18)</th>
<th>FHN (n = 63)</th>
<th>Total (n = 81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>20.83 ± 2.31</td>
<td>19.34 ± 1.75</td>
<td>19.69 ± 1.97</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6</td>
<td>27</td>
<td>33</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>36</td>
<td>48</td>
</tr>
<tr>
<td>Years of education</td>
<td>13.44 ± 1.46</td>
<td>12.83 ± 1.55</td>
<td>12.96 ± 1.55</td>
</tr>
<tr>
<td>Alcohol usage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>11</td>
<td>38</td>
<td>49</td>
</tr>
<tr>
<td>Not regular</td>
<td>7</td>
<td>25</td>
<td>32</td>
</tr>
<tr>
<td>CD symptoms</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;3 = 15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3 = 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijuana usage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>6</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>Not regular</td>
<td>12</td>
<td>42</td>
<td>54</td>
</tr>
</tbody>
</table>

Values are means ± SD or numbers.

FHP, family history-positive; FHN, family history-negative; CD, conduct disorder.

*P < 0.005.
current drinking and marijuana use history, and conduct disorder symptoms. No significant associations were found between those participants who were current drinkers and those not currently drinking, or between those participants with three or more conduct disorder symptoms and those with two or less for any variables. However, a significant association was found between marijuana users and those who did not meet criteria for regular marijuana use in N1 amplitudes. Thus, as seen in Fig. 3, those individuals identified as regular marijuana users had significantly lower N1 amplitudes in the frontal (main effect of marijuana usage: Fz: $F = 5.6; \ df = 1, 80; P < 0.02$) leads, but not in the posterior lead (Pz: $F = 2.8; \ df = 1, 80; P < 0.09$). No gender effects were significant in these analyses.

**DISCUSSION**

Findings on the importance of genetics in the aetiology of alcohol dependence have stimulated a number of investigators to search for familial-based factors that might mediate increased risk for the disorder (Schuckit, 1985; Devor and Cloninger, 1989; Goldman, 1993). A positive family history of alcoholism is one of the most consistent and powerful predictors of a person’s risk for the development of the disorder. First-degree relatives of alcoholics are up to 7 times more likely than the general population to develop problems associated with alcohol at some time during their life (Cotton, 1979; Schuckit and Smith, 1996; Merikangas et al., 1998). This study assessed the amplitude of the N1 and P3 components of the ERP using alcohol- and non-alcohol-related stimuli. The study was designed to explore N1 and P3 amplitudes in African–American young adults in relation to parental history of alcoholism.

P3 amplitude is perhaps the most studied electrophysiological ‘marker’ of potential vulnerability to alcohol dependence. A meta-analysis in which P3 amplitude from 30 separate studies were analysed found that smaller P3 amplitudes were obtained from males with family histories of alcoholism compared with controls (Polich et al., 1994). However, a moderator analysis accomplished in the above study also indicated the ERP paradigms that used difficult visual tasks in younger participants, particularly in males, yielded the most reliable effects. Ethnicity was not evaluated in the meta-analysis. The present study confirms the findings of the meta-analysis and extends the studies to an African–American young adult population. In the present study, FHPs, particularly males, were found to have lower P3 amplitudes when compared with FHNs using a visual task. Approximately twice as many studies have used visual tasks to generate late positive components, as compared with auditory tasks, which may partly explain some discrepancies in the literature.

In the present study, both alcohol- and non-alcohol-related stimuli were employed to elicit ERPs. Both sets of stimuli elicited a late positive component occurring between 400 and 600 ms after presentation of the stimuli. The few ERP studies that have used alcohol-related stimuli have reported that the differences in the amplitudes of the late positive components elicited by alcohol-related stimuli, as compared with non-alcohol-related stimuli, are larger in male alcoholics and heavy social drinkers as compared with non-alcoholics and light social drinkers, respectively (Herrmann et al., 2000, 2001). The effect of family history was not assessed in these studies. A significant relationship between parental history of alcoholism and the amplitude of the P3 late positive component elicited by alcohol-related stimuli, as compared with non-alcohol-related stimuli, are larger in male alcoholics and heavy social drinkers as compared with non-alcoholics and light social drinkers, respectively (Herrmann et al., 2000, 2001). The effect of family history was not assessed in these studies. A significant relationship between parental history of alcoholism and the amplitude of the P3 late positive component elicited by alcohol-related stimuli, as compared with non-alcohol-related stimuli, are larger in male alcoholics and heavy social drinkers as compared with non-alcoholics and light social drinkers, respectively (Herrmann et al., 2000, 2001). A significant relationship between parental history of alcoholism and the amplitude of the P3 late positive component elicited by alcohol-related stimuli, as compared with non-alcohol-related stimuli, are larger in male alcoholics and heavy social drinkers as compared with non-alcoholics and light social drinkers, respectively (Herrmann et al., 2000, 2001).
Marijuana use, but not alcohol use or conduct disorder symptoms, was also found to modify ERP component amplitudes in the present study. Reduced N1 amplitudes were found in regular marijuana users, as compared with non-regular users. Previous studies have also found that the 'frontal processing negativity to irrelevant stimuli' was impaired in long-term marijuana users using an auditory paradigm (Solowij et al., 1995). However, other studies have stressed that auditory and visual P300s are not impaired in medically and psychiatrically normal chronic marijuana users (Patrick et al., 1995), which was also the case in the present study. In contrast to the findings of decreased N1 amplitudes in regular marijuana users, FHPs were found to have increases in N1 amplitudes. Increased N1 amplitudes have been reported previously in alcoholics (Ahveninen et al., 2000). Taken together, these studies suggest that risk for alcoholism and marijuana misuse may have different neurophysiological substrates.

The lack of a significant association between drinking history and ERPs is also consistent with other studies of younger alcoholic and non-alcoholic subjects, where P300 amplitudes were not found to be affected either by sobriety length or drinking history (Keenan et al., 1997). Finally, the present study did not find a relationship between ERP amplitudes and conduct disorder symptoms. One possible explanation is that the current population was recruited from the community and not treatment or detention facilities; thus, the severity of the...
conducted disorder was more likely to be milder, as compared with previous studies (Bauer and Hesselbrock, 1999a). Alternatively, it is possible that the particular ERP task employed in the present study may not be sensitive to brain processes affected by conduct disorder. However, it can be tentatively concluded that parental history of alcoholism significantly affects P3 amplitudes in these young adult African–American study participants, and this variable appears more selectively to modify P3 amplitudes than conduct disorder symptoms, or current alcohol or drug usage.

It is important to consider some of this study’s limitations. First, a modest, non-randomly selected sample was assessed. Thus, the findings may not generalize to all African–Americans. Second, the study was limited to young adults between the ages of 18 and 25 years. This allowed an investigation of the association between parental alcohol dependence and ERP components. However, since the participants in the study had not passed through the age of risk, associations with misuse and dependence were limited. Further studies employing a longitudinal design will be required to test the relationship of component amplitudes and eventual alcohol-related morbidity and mortality. Despite these limitations, this report represents an important first step in an ongoing investigation to determine risk and protective factors associated with the development of substance use disorders in this ethnic group.

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