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Alcoholism risk, tobacco smoking, and P300 event-related potential

John Polich*, Christian J. Ochoa

Cognitive Electrophysiology Laboratory, Department of Neuropharmacology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA

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Abstract

Objective: The P300 event-related potential (ERP) is sometimes larger for individuals at low- compared to high-risk for alcoholism. These effects are inconsistent, and how P300 is affected by tobacco smoking in the context of alcoholism risk is unknown. The present study used P300 to examine the inter-relationship between alcoholism heritability and smoking status.

Methods: P300 was elicited with a visual discrimination task from young adults at low- and high-risk for alcoholism. Half of the subjects in each risk category reported that they did not smoke cigarettes, and the other half reported that they smoked regularly, with equal numbers of male and female subjects assessed. ERPs were recorded, and subjects were instructed to respond only to an infrequently presented target stimulus that occurred in a series of standard and distracter stimuli.

Results: P300 amplitude from the target stimuli was larger for the low-risk compared to high-risk subjects overall. However, smoking status demonstrated even stronger effects, with non-smokers producing consistently larger component amplitudes than smokers and accounting for more variance than alcoholism risk. These group factors also significantly affected P300 scalp topography. No reliable alcoholism risk or smoking group effects were obtained for the ERPs from the other stimuli.

Conclusions: The findings suggest that P300 measures of alcoholism risk in young adults are moderated by smoking status. Theoretical implications are discussed.

Keywords: Alcoholism heritability; Event-related potentials; P300; Tobacco; Smoking

1. Introduction

1.1. Alcoholism risk and P300

Children of alcoholic parents raised by non-alcoholic foster parents are at higher risk for developing alcoholism than are the biological children of non-alcoholic parents. As the P300 event-related brain potential (ERP) has been found to be smaller in long-term abstinent alcoholics relative to controls (Begleiter and Porjesz, 1995; Porjesz and Begleiter, 1996), ERP procedures have been used to study individuals at low- and high-risk (LR, HR) for alcoholism by virtue of their biological background (e.g. Begleiter et al., 1984; Elmasian et al., 1982; Polich, 1984). Neuroelectric measures are heritable (van Beijsterveldt and van Baal, 2002), and the P300 component is strikingly similar for pairs of monozygotic compared to dyzygotic twins and unrelated controls (Katsanis et al., 1997; O'Connor et al., 1994; Polich and Burns, 1987; van Beijsterveldt et al., 1996, 1998). Moreover, biologically related family members demonstrate significant inter-family member correlations for P300 measures (Eischen and Polich, 1994; Polich and Bloom, 1999), with loci on the human genome identified that appear related to ERP generation (Almasy et al., 1999; Begleiter et al., 1998). Given these genetic influences, the P300 may serve as a diagnostic marker of heritability and disease phenotypic etiology (cf. Carlson et al., 2002; Hill et al., 1999a, 2000; Iacono et al., 2002).

Meta-analysis was used to quantify this possibility by evaluating P300 findings from the sons of alcoholics compared to unaffected male controls (Polich et al., 1994). Analysis of the then 30 available studies indicated that 40% of the reports found statistically reliable P300 amplitude effects, such that LR subjects exhibited significantly larger components than HR subjects. However, considerable inter-study variation was evident, and P300 amplitude appeared related to how populations were defined, stimulus modality,

* Corresponding author. Tel.: +1-858-784-8176; fax: +1-858-784-9293.
E-mail address: polich@scripps.edu (J. Polich).

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and task difficulty. These factors have been found to affect P300 outcomes in subsequent alcoholism risk-group reports (cf. Benegal et al., 1995; Cohen et al., 1997; Ramachandran et al., 1996; Reese and Polich, 2003; Rodríguez-Holguín et al., 1998a). Additional influences include: (1) in particular, children and younger adolescents demonstrate stronger P300 risk-group effects than older adolescents or adults (Hill et al., 1999b; Rodríguez-Holguín et al., 1999b; van der Stelt et al., 1998a); (2) female LR and HR groups yield amplitude differences generally similar to those observed for males (Hill and Steinhauer, 1993; Hill et al., 1995a,b; Polich et al., 1988; Reese and Polich, 2003; van der Stelt et al., 1998b); (3) P300 variability from alcoholism risk is likely to stem from co-morbidity for conduct disorders, substance abuse, and disinhibited psychopathologies (Bauer and Hesselbrock, 1999a,b; Carlson et al., 1999; Costa et al., 2000; Finn et al., 1997; Hill et al., 2000; Iacono et al., 2002; Malone et al., 2001); and (4) the anatomical size of the right amygdala is significantly correlated with P300 amplitude in HR adolescents (Hill et al., 2001). Thus, at least some P300 variability for alcoholism-risk studies reflects subject age, population characteristics, and the neuroanatomy of ERP generation (Ford et al., 1994; Polich and Hoffman, 1998).

1.2. Tobacco smoking and P300

P300 variation across subjects has also been related to individual differences in propensity for tobacco use. It is noteworthy that adolescents who begin smoking are 3 times more likely to use alcohol, and smokers are 10 times more likely to develop alcoholism than non-smokers (Hughes, 1995; Hurt et al., 1994; Jarvik and Schneider, 1992). Further, 80–95% of alcoholics smoke cigarettes with 70% smoking more than one pack per day compared with 10% of the general population (Collins and Marks, 1995; Patten et al., 1996). When coupled with behavioral data that suggest a strong link between tobacco smoking and alcohol consumption (Friedman et al., 1991; Madden et al., 1995; Torabi et al., 1993), it is likely that smoking history contributes to P300 outcomes in alcoholism risk studies.

ERP data on smoking history effects are sparse. Knott et al. (1999) compared young and old non-smokers and smokers on several ERP tasks but found no reliable smoking history effects. Haarer and Polich (2000) assessed normal young adults who smoked daily with individuals who smoked infrequently using a visual task and found smaller P300 target amplitude for the regular compared to occasional smokers before and after tobacco smoking. A large-scale study by Anokhin et al. (2000) assessed smokers, former smokers, and never-smokers using a visual discrimination task. P300 amplitude was smaller for any subject who had smoked, with current smokers producing components about 5 μV smaller than never-smokers. More important, some subjects carried a diagnosis of alcoholism, but this factor contributed to P300 amplitude in a manner that was relatively weak and additive with smoking status. Enoch et al. (2001) used combined auditory/visual ERP tasks to assay subjects with diagnoses for alcoholism and anxiety disorders. A marginal P300 amplitude smoking effect for the easy auditory but not difficult visual task for a sub-sample of the unaffected subjects was obtained. In sum, ERPs may be affected by tobacco smoking history, but how this variable contributes to alcoholism risk and P300 is unclear.

1.3. Present study

Most ERP reports on tobacco have focused on the acute rather than chronic effects of smoking. P300 amplitude generally increases and latency decreases immediately after smoking (Hasenfratz et al., 1989; Houlihan et al., 1996a,b; Knott et al., 1995), although relative information processing task difficulty (Ilan and Polich, 1999, 2001; Knott, 1995; Le Houezec et al., 1994; Pritchard and Robinson, 1998; Pritchard et al., 1995) and amount smoked or nicotine level can affect P300 measures (Kodama et al., 1996; Lindgren et al., 1999). Given the variable findings from alcoholism-risk and smoking history P300 studies outlined above, both task and chronic factors are likely to affect ERP outcomes. The present study was conducted to compare LR and HR young adult subjects who either had never smoked tobacco or regularly smoked cigarettes in order to characterize these effects more directly.

2. Methods

2.1. Subjects

Subjects were young adults obtained as part of the Collaborative Study on the Genetics of Alcoholism (COGA) or related projects and recruited at The Scripps Research Institute laboratory. HR subjects had fathers and at least one first-degree or two second-degree relatives who met the criteria for both alcohol dependence as defined by DSM-III-R and definite alcoholism. No HR subject carried a diagnosis of alcoholism. LR subjects had no familial alcoholism or personal alcoholism. Each participating family member was interviewed with the Semi-Structured Assessment for the Genetics of Alcoholism, which uses both DSM-III-R alcohol dependence and Feighner criteria (Bucholz et al., 1994). All individuals were gainfully employed or engaged in educational pursuits. Exclusionary criteria for both groups included major medical problems, CNS medication, a history of psychiatric problems, or history of drug abuse. These procedures have been successfully used to evaluate alcoholism risk with ERPs (e.g. Hada et al., 2001; Polich and Bloom, 1999; Ramachandran et al., 1996; Rodríguez-Holguín et al., 1999a,b).

A total of $n = 80$ subjects were obtained, with equal numbers in each LR/HR risk and smoking category for $n = 20$ per group, as well as equal numbers of each gender, comparable age (21.9 ± 3.9, 18–32 years), education (12.7 ± 1.9 years), and number of drinks per week (3.5 ± 5.3) as obtained by random assignment. Participants reported normal visual acuity, handedness was distributed equitably across samples, and each subject was tested in a single 2-h session. Smoking was defined as daily cigarette smoking for 6 months or more. Smoking subjects smoked a mean of 12.4 ± 7.7 cigarettes per day for an average of 5.9 ± 3.3 years, with no differences obtained for the smoking history variables. Smoking subjects were instructed to smoke before they came to the laboratory and were assessed 1–3 h after smoking to ensure that acute nicotine effects were minimized (Domino et al., 1995; Pritchard, 1991). ERP smoking deprivation effects for this time duration are undetectable (cf. Bell et al., 1999; Haarer and Polich, 2000; Houlihan et al., 1996c; Knott et al., 1995). Each subject provided informed consent.

2.2. Recording conditions and procedure

EEG activity was recorded monopolarly using an electrode-cap with, 19 electrode sites (Fp1/2, F3/4, C3/4, P3/4, F7/8, T7/8, P7/8, O1/2, Fz, Cz, Pz) referred to the nose, with a forehead ground and impedances maintained at 5 kΩ or less. Electro-ocular (EOG) activity was assessed with two channels referred to the nose. One electrode was placed at the outer canthus of the left eye to measure vertical eye movement, and the second electrode was located on the forehead to monitor horizontal eye movement. The filter bandpass was 0.02–50 Hz (3 dB down, 6 dB octave/slope). The EEG was digitized at 3.9 ms per point for 1500 ms, with a 187 ms prestimulus baseline. ERP data were averaged on-line with the same computer also used to control the stimulus presentation and artifact rejection. Trials on which the EEG or EOG exceeded ± 73.3 μV were rejected automatically, with comparable numbers of artifact trials obtained among subject groups.

The same paradigm employed by Anokhin et al. (2000) was used. ERPs were elicited with 280 stimuli presented on a computer monitor for 60 ms, with an inter-stimulus interval of 1.6 s. The target stimulus was a white X-shape (4×4 cm^2, $2.9° \times 2.9°$), distracter stimuli (5×5 cm^2, $3.6° \times 3.6°$) consisted of non-repeating colored geometric shapes (e.g. blue hexagons, red pentagons, etc.) arranged in variegated patterns, and the standard stimulus was a white square (4×4 cm^2, $2.9° \times 2.9°$). All stimuli were viewed from a distance of 110 cm, with low level, diffuse ambient lighting provided by a ceiling fixture. The target and distracter stimuli each occurred with a probability of 0.125; the standard stimuli occurred with a probability of 0.75. Subjects were instructed to look at a dot in monitor's center, to press a keypad with their forefinger whenever a target stimulus was detected, and to refrain from responding when the distracter or standard stimuli occurred. Response hand was counterbalanced across subjects. Stimulus presentation ended when 25 target, 25 distracter, and 150 standard artifact-free trials were acquired.

3. Results

3.1. Task performance and trial number

Error rates were negligible (<1%) and did not differ among subject groups. Although LR responded somewhat more quickly compared to HR (468 vs. 505 ms) subjects, no significant group effects were obtained for the response time data.

3.2. ERP analyses

Fig. 1 illustrates the target stimulus ERP grand averages from the midline and EOG electrodes for each alcoholism risk and smoking group. Topographic representations of P300 amplitude from all scalp electrodes are illustrated below the grand averages. The P300 component was defined as the largest positive-going peak occurring within 300–800 ms at each electrode. Peak amplitude was measured relative to the pre-stimulus baseline, and peak latency was assessed from the time of stimulus onset. Extensive preliminary analyses revealed no gender-related risk-group or smoking-status effects. No group effects were obtained for the distracter or standard stimuli, which most likely reflect the minimal stimulus processing required for these stimuli. These data were not considered further.

Fig. 2 illustrates the mean target P300 amplitude as a function of coronal electrode for the frontal, central, and parietal recording locations for each alcoholism risk and smoking group. A 4-factor (2 risk groups [LR vs. HR] × 2 smoking status [non-smokers vs. smokers] × 3 anterior-to-posterior positions [frontal vs. central vs. parietal] × 5 coronal electrodes [F7, F3, Fz, F4, F8 vs. T7, C3, Cz, C4, T8 vs. P7, P3, Pz, P4, P8]) repeated measures ANOVA was applied to the P300 data from the target stimuli. Geisser–Greenhouse corrections to the df were employed as needed, with only the corrected probabilities reported. The η^2 statistic was computed for subject group effects or interactions to calculate the proportion of variance accounted for by each comparison.

3.2.1. Alcoholism risk and smoking groups

LR subjects produced significantly larger P300 amplitudes than HR subjects, $F(1, 76) = 4.19$, $P < 0.05$, $\eta^2 = 0.047$. Non-smokers yielded significantly larger P300 amplitudes overall than smokers, $F(1, 76) = 8.01$, $P < 0.01$, $\eta^2 = 0.089$, which accounted for twice the between-groups variance as the alcoholism risk-group factor. In addition, non-smokers demonstrated larger increases in P300 amplitude from the frontal to parietal

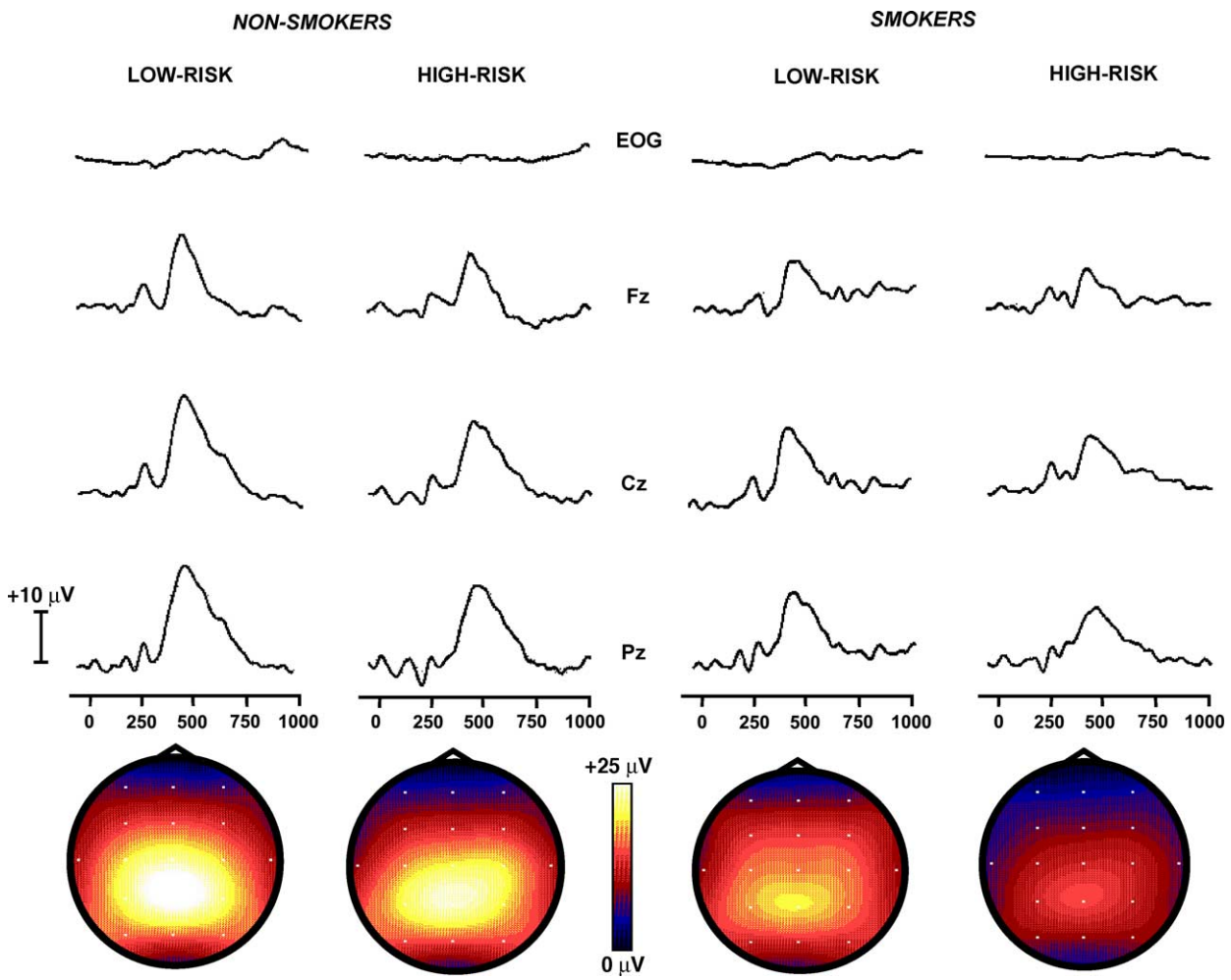

Fig. 1. Grand averaged EOG, midline electrode waveforms, and topographic head plots of P300 amplitude from a visual stimulus paradigm from non-smoking and smoking young adult subjects who were either at low- or high-risk for alcoholism ($n = 20$ per group). The topographic maps reflect peak P300 amplitude at each electrode.

recording sites compared to smokers. This outcome contributed to the significant interaction between the smoking status and anterior-to-posterior topography variables, $F(2, 152) = 6.50$, $P < 0.01$, $\eta^2 = 0.048$. Similarly, a significant interaction between smoking status and coronal electrode location was obtained, $F(4, 304) = 8.90$, $P < 0.0002$, $\eta^2 = 0.036$, such that non-smokers demonstrated larger midline amplitudes that decreased less toward the temporal sites compared to smoking subjects. No other effects or interactions involving the alcoholism risk group factor were obtained. P300 amplitude increased from the frontal to parietal recording sites, $F(2, 152) = 53.06$, $P < 0.0001$, was maximal over the midline and decreased over the lateral coronal sites, $F(4, 304) = 161.16$, $P < 0.0001$. The anterior-to-posterior and coronal factors yielded a significant interaction, $F(8, 608) = 20.74$, $P < 0.0001$, reflecting the usual pattern of less P300 amplitude coronal electrode differentiation at the frontal compared to central and parietal electrodes.

The same 4-factor analysis of variance was applied to the peak latency results. No risk-group or smoking status main effects or interactions were found. Peak latency increased from the frontal to parietal sites, $F(1, 76) = 11.19$, $P < 0.0001$, from the midline to lateral electrodes, $F(4, 304) = 9.02$, $P < 0.0001$, with a significant interaction between these factors obtained, $F(8, 608) = 4.49$, $P < 0.0001$.

3.2.2. Midline electrodes

To assess the interaction between smoking status and the frontal-to-central electrode position effects found in the overall analysis, P300 amplitude data from just the midline electrodes were assessed with a 3-factor (2 risk groups [LR vs. HR] × 2 smoking status [non-smokers vs. smokers] × 3 midline electrodes [Fz vs. Cz vs. Pz]) repeated measures ANOVA. P300 amplitude was larger for LR compared to HR subjects, $F(1, 76) = 5.38$, $P < 0.05$, $\eta^2 = 0.056$, and non-smokers again produced larger P300 components than smokers, $F(1, 76) = 14.06$, $P < 0.001$, $\eta^2 = 0.146$. More important, non-smokers demonstrated larger increases in P300 amplitude across the midline recording sites compared to smokers, $F(2, 152) = 9.93$,

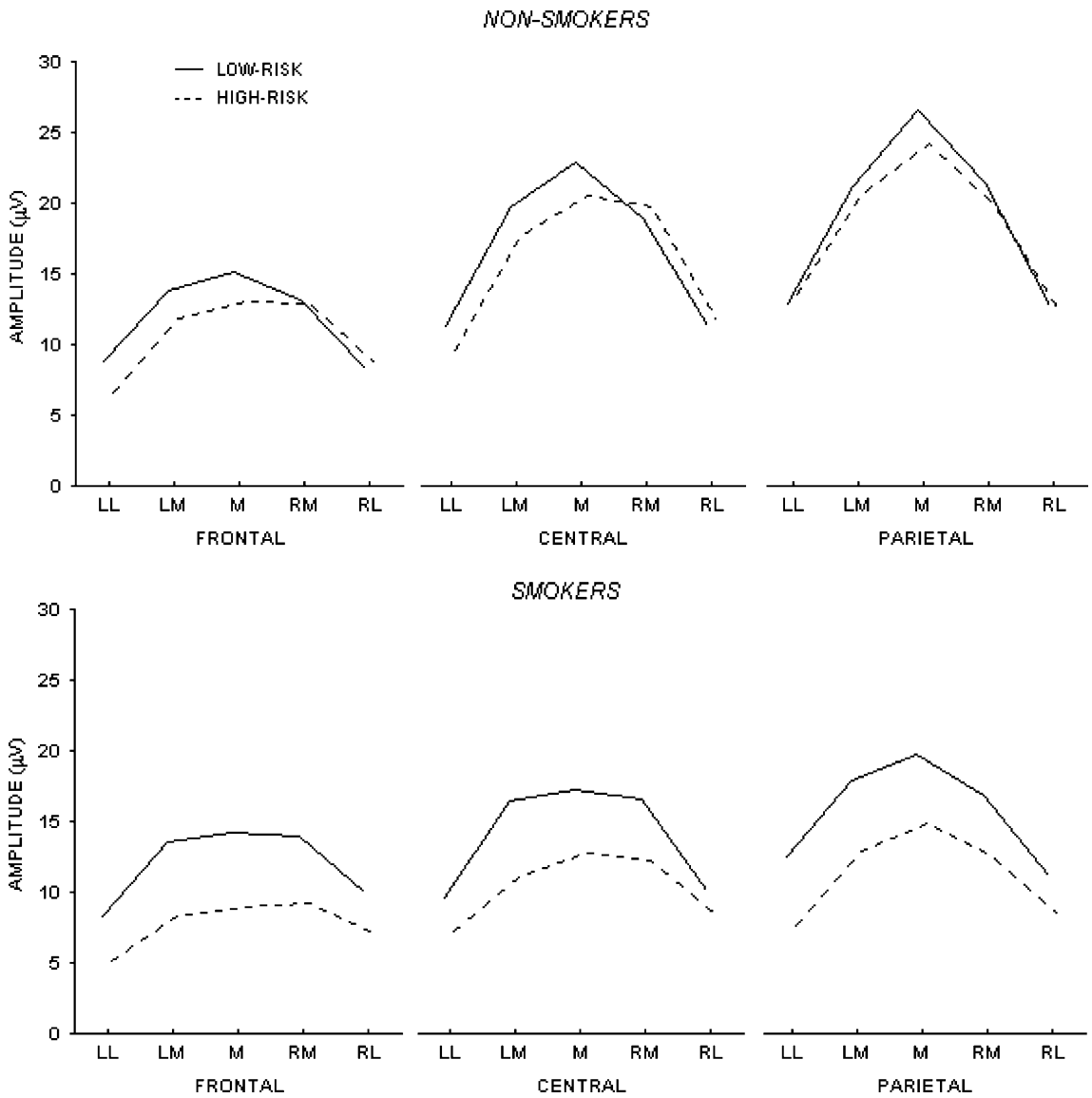

Fig. 2. Mean P300 amplitude as a function of coronal electrode placement for the frontal, central, and parietal arrays site from non-smokers and smokers who were either at low- and high-risk for alcoholism (LL, left lateral; LM, left medial; M, medial; RM, right medial; RL, right lateral).

$P < 0.0001$, $\eta^2 = 0.057$. No other main effects or interactions involving alcoholism risk group were obtained. Component amplitude increased from the frontal to central electrodes, $F(2, 152) = 88.39$, $P < 0.0001$.

3.2.3. Hemispheric P300 effects

Fig. 2 suggests that the alcoholism risk and smoking groups appear to differ with respect to the laterality patterns for P300 amplitude. This possibility was assessed with a 4-factor (2 risk groups [LR vs. HR] × 2 smoking status [non-smokers vs. smokers] × 2 hemispheres [left vs. right]) × 2 lateral electrode positions (medial vs. lateral) × 3 anterior-to-posterior electrode positions [frontal vs. central vs. parietal] repeated measures ANOVA. Only the outcomes involving subject groups will be described, as the other effects were similar to the overall analyses. P300 amplitude over the left hemisphere was smaller than that over the right hemisphere for the HR subjects with little hemispheric difference obtained for the LR subjects to produce a marginal interaction between these factors, $F(1, 76) = 2.95$, $P < 0.10$, $\eta^2 = 0.037$. In addition, smoking status contributed to these effects such that the difference between P300 left and right hemisphere amplitudes was smaller for the smoking HR subject compared to LR group and decreased more from the frontal to parietal electrodes to yield a significant 4-way interaction among these variables, $F(2, 152) = 3.64$, $P < 0.05$, $\eta^2 = 0.042$. Moreover, these P300 amplitude hemispheric differences were larger for non-smokers compared to smoking subjects over the medial compared to lateral electrodes to produce a strong two-way interaction between laterality electrode location and smoking group, $F(1, 76) = 10.9$, $P < 0.002$, $\eta^2 = 0.030$, which was also found in the 3-way interaction that included the frontal-to-parietal location factor,

$F(2, 152) = 3.47$, $P < 0.05$, $\eta^2 = 0.032$. In sum, HR subjects demonstrated smaller P300 amplitudes over the left compared to right hemisphere, and smoking decreased overall amplitudes and this hemispheric difference relative to LR subjects.

4. Discussion

4.1. Alcoholism risk and smoking

The present study employed the P300 ERP to assess genetic predisposition to alcoholism by comparing young adult low- and high-risk groups comprised of non-smoking and tobacco smoking subjects. P300 amplitude was larger for LR compared to HR subjects overall—a finding consistent with some reports using visual stimuli in young adult subjects (Benegal et al., 1995; Cohen et al., 1997; Ramachandran et al., 1996). However, P300 amplitude was also larger for non-smokers compared to smokers in agreement with some (Anokhin et al., 2000; Haarer and Polich, 2000; Kodama et al., 1996) but not all (Enoch et al., 2001; Knott et al., 1999) previous smoking ERP studies. The reasons for these discrepancies are unclear but may stem from task parameters that contribute to ERP smoking findings (cf. Domino, 2003; Houlihan et al., 1996b; Ilan and Polich, 1999; Knott, 1995; Pritchard and Robinson, 1998; Pritchard et al., 1995). For example, in the present study active attentional processing of the visual target stimulus reflected ERP smoking, whereas the passive processing of the distracter and standard stimuli produced no reliable effects of smoking history (Houlihan et al., 1996a; Ilan and Polich, 2001; Knott et al., 1995). Thus, P300 variability from at-risk for alcoholism and tobacco smoking individuals may index task parameters that interact with fundamental group differences.

In addition, it is possible that some of the non-smoking compared to smoking group differences could reflect initial tobacco deprivation effects (Bell et al., 1999; Domino et al., 1995; Sayette et al., 2003). Even though subjects smoked just before ERP testing so that the time since last their cigarette was short, behavioral and neuroelectric effects have been found for tobacco smokers when deprived conditions are compared to post-smoking (Herning et al., 1983; Hughes and Hatsukami, 1986; Pritchard and Robinson, 1998). However, the LR and non-smoking subjects consistently demonstrated larger and more robust P300 components than the HR and smoking subjects (cf. Anokhin et al., 2000; Carlson et al., 1999; Haarer and Polich, 2000; Rodríguez-Holguín et al., 1999b). Given the short pre-test deprivation time in conjunction with the relative strength and overall pattern of the effects, the P300 risk-group differences appear more likely to be associated with genetic variation rather than a situational factor (Begleiter et al., 1998; Hill et al., 2001; Iacono et al., 2002; Katsanis et al., 1997).

Although P300 and other neuroelectric measures are heritable (Eischen and Polich, 1994; Eischen et al., 1995; Katsanis et al., 1997; O'Connor et al., 1994; Polich and Burns, 1987; van Beijsterveldt and van Baal, 2002), considerable variability underlies ERP effects for LR and HR subjects with task difficulty, stimulus modality, and subject age differentially contributing to alcoholism-risk findings (cf. Hill et al., 1999a,b, 2001; Polich and Bloom, 1999; Polich et al., 1994; Reese and Polich, 2003; Rodríguez-Holguín et al., 1998b,c). Indeed, recent studies have suggested these effects could indicate that "reduced P3 may be associated with genetic risk for disinhibited psychiatric disorders generally" (Carlson et al., 2002, p. 756), and that this relative amplitude reduction may be an endophenotype associated with a broad spectrum of disorders (Iacono et al., 2002). The present results are consonant with the view that both alcoholism risk and tobacco smoking history can contribute to P300 group differences.

4.2. Neuropharmacological moderation of P300

Although a direct neuropharmacological connection between alcoholism risk and P300 has not yet been identified, the acute rewarding effects of ethanol on dopaminergic activity are clear from animal studies: "In general, enhancement of dopamine transmission in the nucleus accumbens increases ethanol-reinforced responding, whereas decreasing transmission decreases ethanol responding…These findings suggest the importance of dopaminergic activity in the acute rewarding effects of alcohol" (Hill et al., 1998, p. 47). Such ERP group variation also may be related to individual mesolimbic dopamine system differences for nicotine as a positive reinforcer (Reavill, 1990), since several lines of evidence link P300 and catecholaminergic mediation of the underlying generator system: (1) P300 measures are deficient in Parkinson patients who have decreased levels of dopamine (Hansch et al., 1982; Stanzione et al., 1991). (2) The dopamine antagonist sulpiride increases P300 in low-amplitude subjects and decreases it in high-amplitude subjects (Takeshita and Ogura, 1994). (3) Pharmacological studies have demonstrated dopaminergic mediation of P300 amplitude and latency (Hansenne et al., 1995; Wang et al., 2000). (4) Children at elevated risk for alcoholism evince dopamine-related genetic differences associated with P300 amplitude deficits (Hill et al., 1998). P300 amplitude from individuals at risk for alcoholism may therefore vary as a function of dopamine levels and contribute to an 'endophenotype of alcoholism' (Hesslebrock et al., 2001).

The attentional operations engaged during P300 generation have been hypothesized to reflect similar mechanisms in a manner that could vary systematically across individuals and risk-groups (Polich, 2003; Reese and Polich, 2003). Moreover, tobacco smoking is likely to stem from genetic influences (Carmelli et al., 1992; Comings et al., 2001; Hughes, 1986), with the propensity to use tobacco related to

alcohol consumption in HR subjects and alcoholism development (Drobes, 2002; Friedman et al., 1991; Madden et al., 1995; Torabi et al., 1993). These observations imply that individuals vary with respect to their responsiveness to nicotine, and that P300 amplitude reduction in smokers occurs regardless of alcoholism risk diagnosis (Anokhin et al., 2000; Carlson et al., 2002; Iacono et al., 2002). Given dopaminergic system activation with nicotine intake (Koob, 1992; Watkins et al., 2000), it is reasonable to suppose that P300 differences between low- and high-risk disorder groups may reflect a predisposition for dopamine deficits that encourages drug use stemming from underlying or concomitant psychopathology (Bauer and Hesselbrock, 1999a,b; Carlson et al., 1999; Costa et al., 2000; Finn et al., 1997; Hill et al., 2000). Although speculative, the present P300 findings point toward a fundamental deficit in dopaminergic brain mechanisms (Anokhin et al., 2000; Begleiter et al., 1998; Hill et al., 1998, 2001; Jeon and Polich, 2003).

4.3. Hemispheric P300 differences

Young adult HR subjects produced smaller P300 amplitudes than LR subjects over the left compared to right frontal and central electrodes. Smoking subjects demonstrated smaller P300 hemispheric differences relative to non-smokers across alcoholism risk categories. P300 amplitude right hemisphere superiority in normals has been reported previously (Alexander et al., 1995, 1996), with the implication that P300 generation may be initiated in right frontal areas (Polich et al., 1997). In addition, left-handers produce larger P300 components compared to right-handed individuals over the frontal and central electrodes—findings consistent with corpus callosal size differences between handedness groups (Alexander and Polich, 1997; Polich and Hoffman, 1998). How P300 amplitude hemispheric differences effects may be related to risk-for-alcoholism and tobacco smoking is uncertain, although reliable left hemisphere deficits in patients with schizophrenia are well documented (Jeon and Polich, 2001). A connection among these factors also has been suggested by a recent PET study that found left relative to right hemisphere blood flow decreased as nicotine dose level increased (Rose et al., 2003). Whether similar hemispheric effects can be related directly to alcoholism risk and smoking history has yet to be determined, but intriguing hints have emerged (cf. Haarer and Polich, 2000; Hill et al., 2001).

5. Conclusion

Young adults genetically at high-risk for alcoholism can demonstrate smaller P300 amplitudes compared to their low-risk counterparts. These effects appear to be moderated by tobacco smoking, such that non-smoking individuals are less likely to reflect P300 alcoholism risk-group differences than smoking subjects. The influence of smoking status on P300 may originate from genetic influences that govern ERP generation. Thus, the present results suggest that it is important to account for tobacco smoking history when assessing P300 across subject group categories.

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