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ORIGINAL PAPER

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Lower P300 amplitude in eight-year-old offspring of alcoholic fathers with a delinquent history

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Abstract The aim of the present study was to investigate the P300 amplitude as a possible vulnerability marker in children of alcoholic (COA) fathers with and without paternal delinquency. Event-related potentials (ERPs) of 122 children aged 8 years (63 boys, 59 girls) were compared depending on father's alcoholism subtype: 30 COAs without paternal delinquency, 10 COAs with paternal delinquency, and 82 children of non-alcoholic and non-delinquent fathers. ERPs were recorded from Fz, Cz, and Pz, using an auditory oddball paradigm. Sinus tones of 60 dB HL were presented binaurally at 1,000 Hz (standard stimulus) and 2,000 Hz (target stimulus), at a relative frequency ratio of 80:20. Two trial blocks of 250 stimuli each were collected. Results indicated that only COAs with paternal delinquency displayed significant differences from the control group, characterized by reduced P300 amplitude at frontal site and in the second trial block. Thus, the combination of fathers' alcoholism and delinquency was more likely to relate to attenuated P300 amplitude in the offspring than paternal alcoholism alone. Our results suggest that both alcoholic and delinquent family history appear to play a role in P300 amplitude reduction in the offspring.

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Introduction

Alcoholism represents a serious medico-social problem in modern society. The sequelae of father's alcoholism can be observed in the offspring. A growing body of research has identified children of alcoholics (COAs) as a group at risk for later alcohol use disorders (AUD) due to a combination of environmental and genetic factors [35]. Moreover, it has been well-documented that, compared to normative controls, COAs have significantly more psychiatric problems, such as more externalizing disorders (conduct problems, hyperactivity) as well as more internalizing disorders (depression, anxiety) [16].

A substantial body of research has established the comorbidity of alcohol dependence with antisocial personality disorder (ASPD) [3, 19, 30]. Recent data from a family study of alcoholism [9] confirmed that individuals with ASPD have a higher prevalence of alcohol and other substance dependence compared to their non-ASPD counterparts. Regarding the etiology, features of ASPD and of childhood conduct disorders are important elements in two subtypes of alcoholism: type II [11] and type B [2], both of which have common features and are considered more familial than non-ASPD alcoholism. Many studies have demonstrated that adolescents with higher scores on aggression and delinquency have alcoholic parents [17]. However, the comorbidity of ASPD in some alcoholic fathers should not be overlooked and might have exaggerated these findings [14, 42], making the relationship between COAs and ASPD an issue to be investigated in more detail.

Over the past two decades, neurophysiological markers in alcoholics and their offspring have been widely studied. Much attention has been focused on

the P300 component of the human event-related potential (ERP), a positive polarity brain wave occurring approximately 300–400 ms after the presentation of an infrequent but anticipated stimulus. The P300, which is of maximal amplitude over the midline central and parietal sites (Cz and Pz) can be considered as a manifestation of CNS activity involved with the processing of new information when attention is engaged to update memory representations [31, 34]. Numerous studies have demonstrated attenuated P300 amplitude in young people with a family history of alcoholism [8, 35]. Since the first reports by Elmasian et al. [15] of a reduced P300 amplitude in the offspring of alcoholics, many studies in COAs have been conducted in an attempt to replicate these findings and to search for a specific vulnerability to alcoholism. A lower voltage of the P300 component was observed in the sons of parents with the exclusive diagnosis of alcoholism, mainly type II. This effect was demonstrated before alcohol exposition, suggesting that COAs might have a subtle abnormality in their brains [7]. The same result was found in a group of male COAs, aged 7 to 16 years, from type II alcoholism fathers, using an auditory task [8]. Further studies have indicated that reduced P300 recorded in early adolescence predicted the development of alcoholism 4–8 years later [20]. These findings were corroborated by others demonstrating that the development of substance use disorders was associated with P300 amplitude reduction prior to their expression [18, 23]. Thus, the hypothesis was advanced that attenuated P300 amplitude may represent an endophenotype for alcoholism.

However, alcohol-related problems typically occur in the context of other psychopathological conditions. Recent evidence suggests a link between a reduced P300 amplitude in COAs and high sensation-seeking, particularly high disinhibition [40], and externalizing behavior, such as aggression and delinquency [44]. The Minnesota Twin Family Study [21] confirmed the relationship between low P300 amplitude and externalizing disorders, positing a continuum of risk that varies with P300 magnitude. Other authors, however, argued that a low P300 amplitude may be seen in young adult males manifesting externalizing disorders, especially ASPD, in the absence of alcohol or illicit drug problems and irrespective of a family history of alcoholism [6]. This suggestion was corroborated by evidence showing attenuated P300 amplitudes in adults with ASPD [32], and in youths with conduct disorder [5]. Unlike findings with COAs, revealing a lower P300 amplitude at posterior sites, in these studies a significant decrement was identified at frontal sites only [12].

A number of studies have demonstrated that the amplitude of the P300 may decline in response to repeated stimulation, with a greater attenuation of amplitude at frontal than at parietal electrode sites (e.g., [29]). It has been concluded that this reduction at least partly reflects a change in the amount of attentional resources invested in the task. Few studies have reported differences in the time-on-task effect between groups, indicating a higher decrement of P300 amplitude in individuals with an elevated risk for AUD [16]. However, the factors responsible for this effect have not been clearly defined.

The present study addressed the influence of parental alcoholism and ASPD on P300 amplitude evoked by auditory stimuli in the 8-year-old offspring. The primary aim was to investigate whether the combination of father's alcoholism and delinquency would display additional effects on P300 amplitude and topography. Furthermore, repeated trial blocks were introduced to uncover potential time-on-task effects interacting with these variables.

Methods

Subjects

Participants in this investigation were selected from the Mannheim Study of Risk Children, a prospective longitudinal study of the long-term outcome of early risk factors followed from birth onwards [27]. The initial sample consisted of a cohort of 384 mostly Caucasian infants born 1986–1988, who were recruited from two obstetric and six children's hospitals of the Rhine-Neckar region of Germany. To be included in the study, parents and children had to meet well-defined criteria intended to enrich and to control the risk status of the sample [27, 28]. Depending on pregnancy and birth history and on family background, children were assigned to one of nine groups of a two-factorial design, with factor I representing the degree of obstetric risk (perinatal complications such as preterm birth or neonatal asphyxia) and factor II the degree of psychosocial risk (family adversity such as parental psychiatric disorder or chronic difficulties). Each factor was scaled as no risk, moderate risk, or high risk. All groups were of about equal size with a slight oversampling in the high-risk combinations and with sex evenly distributed in all subgroups. To control for confounding effects of family environment and infant medical status, only firstborn children with singleton births and German-speaking parents were enrolled in the study. Additionally, children with severe physical handicaps, obvious genetic defects, or metabolic diseases were excluded. The participation rate at the time of recruitment was 64.5%, with a slightly lower rate in families from psychosocially disadvantaged backgrounds. Assessments were conducted at regular intervals from infancy into adolescence (3 months, 2, 4, 8, 11, and 15 years). At the 8-year-assessment a total of 370 children of the initial sample were followed up (i.e., retention rate = 96.4%), of the remaining 14 children four were untraceable, two were subsequently excluded because they did not meet the inclusion criteria, and the parents of eight refused to participate.

Here we included a subsample of 122 children (63 males, 59 females) of the 8-year-assessment for whom ERP data were available and who fulfilled the criteria of group definition described below. To assure a more rigorous control of confounding factors of the family environment, only biological fathers were included. The ethics committee of the University of Heidelberg approved the study and written informed consent was obtained from all participants.

Assessments

Paternal alcoholism

A positive family history of AUD, including the DSM main categories of alcohol dependence and abuse, was determined according

to the following procedure. At age 15 years, the SCID I (German version by Wittchen et al. [46]) was administered by trained clinical psychologists to obtain lifetime diagnoses of AUD in direct interviews with the fathers living with the family. Additional cases of paternal AUD in biological fathers not living with the family at the 15-year-assessment were provided by direct and indirect SCID interviews with the parents conducted during a visit to the household of the family at the 3-month- to the 11-year-assessment. In case of absent fathers, the evaluation of paternal psychopathology relied on maternal information. According to research analyzing the concordance between direct and indirect assessments, symptoms of the affective and anxiety disorder types were more likely to be underreported by indirect interviews, while more externalizing disorders, such as alcohol abuse and dependence, which are among the most frequent paternal diagnoses, may even be better reported by informants [13].

Paternal delinquency

At the 3-month-assessment, self-report of criminal offences of the fathers was obtained in a standardized interview with the father or, in case of his absence, with the mother. The interview assessed lifetime incidence of a number of illegal offences including property and violent crimes as well as traffic-related offences (e.g., driving without license). Fathers were designated as having a delinquent history if they had been convicted for at least one criminal offence.

Children were assigned to the COAs group if they had a positive family history of paternal AUD. This group was subdivided into those children having a father with a delinquent history (ALCDEL; delinquent COAs, n = 10: six males and four females) and without a delinquent history (ALC; non-delinquent COAs, n = 30: 14 males and 16 females). Children of the control group fulfilled the criteria of negative family history of AUD and no paternal delinquency (CONTR; n = 82: 43 males and 39 females).

Child psychological assessment

The German version of the Child Behavior Check List (CBCL/4-18) [1] was used to measure children's behavior problems as reported by parents at age eight. Intelligence was measured by the Culture Fair Intelligence Test, Scale 1 (CFT 1) [45]. Assessments of fine and gross motor skills were obtained using a short form of the KTK [25] and a standardized neurological examination according to Touwen and Prechtl [43]. Children with severe handicaps (MQ or IQ < 70 or neurological disorder) were excluded.

Event-related potentials

All children participated in an auditory oddball paradigm using an active task condition. Stimuli were sinus tones (60 dB HL, 10 ms rise/fall, 80 ms plateau) presented binaurally through earphones, at randomized 0.75–1.5 s inter-stimulus-intervals. The frequent or standard stimulus (1,000 Hz tone) and the rare or target stimulus (2,000 Hz tone) occurred at a relative frequency of 80:20. Two trial blocks of 250 stimuli each were collected. During the recording the subjects were instructed to respond to each target stimulus by pressing a button. Subjects did not receive any feedback on their performance. To ascertain subjects' understanding of the task, a short practice phase took place. ERPs were collected from three sites (Fz, Cz, and Pz). P300 was defined as the maximum positive peak that occurred 250–500 ms after stimulus onset. Baseline-to-peak amplitudes were computed by subtracting the baseline (average over 200 ms before the stimulus) from the peak amplitude of the P300 component.

EEG recording

During the EEG recording, the child sat in a comfortable reclining chair, in a dimly illuminated, sound-attenuated and partially electrically shielded chamber. The EEG activity was recorded according to the 10–20 System [24], using a Schwarzer amplifier at a rate of 256 Hz, with 19 Ag–AgCl scalp electrodes embedded in a lycra stretch cap. All electrodes were referred to linked mastoid electrodes. Data were digitally filtered (0.1–70 Hz band pass). Vertical and horizontal EOG was recorded with four electrodes placed above and below the left eye and in the outer canthi. After automatic artifact rejection of epochs with voltages exceeding ±75 mV, all epochs were visually inspected and those contaminated by eye or motor artifacts or slow drifts were excluded, as were all epochs with performance errors. A minimum of 15 artifact-free target trials was required for inclusion into the analysis. Groups did not significantly differ in mean number of artifact-free target trials.

Statistical analysis

Statistical analysis of P300 amplitudes was performed by repeated measures analysis of variance (SPSS 12.0), with the between-subject factor COA GROUP (ALC, ALCDEL, and CONTR) and the within-subject factors SITE (frontal, central, and parietal) and BLOCK (first, second), using the Greenhouse-Geisser correction. Where the analysis of variance yielded significant GROUP interactions, successive univariate and single comparisons were performed. To examine differences between groups on control variables (e.g., child and family environment measures), univariate comparisons of continuous variables were computed using t-tests and ANOVAs and of frequencies and ratios using χ^2 Tests and Fisher's Exact Tests.

Results

Sample characteristics

Demographic and clinical characteristics for the COA groups are presented in Table 1. Results indicated that groups did not differ significantly regarding paternal and maternal age at childbirth, obstetric risk score, and internalizing behavior problems at age 8. As expected, significant differences according to family adversity at childbirth were observed. COAs families showed a higher number of adverse living conditions such as low educational level of a parent or disharmonious partnership. Differences between groups according to IQ and CBCL externalizing problems (with lower IQ scores in COAs and more externalizing problems in the non-delinquent COA group) failed to reach statistical significance ($p < 0.10$).

Event-related potentials

Table 2 presents means and standard deviations of P300 amplitudes in groups of children of alcoholic fathers and controls as a function of electrode site and trial block. Analyses revealed no significant main effect of group (F (2,119) = 1.51, p = 0.225). However, the interaction group × block (F (2,238) = 3.54, p = 0.032) became significant, indicating that there was a differential group effect on P300 amplitudes according to trial block. Separate analyses for the first and the second trial block showed the group effect

Table 1 Demographic and clinical characteristics in groups of children of alcoholic fathers and controls

	CONTR (1) $n = 82$	ALC (2) $n = 30$	ALCDEL (3) $n = 10$	F (2, 119)	p
Father's age at child birth: mean (SD)	30.4 (5.1)	32.1 (6.6)	28.5 (4.3)	1.93	0.149
Mother's age at child birth: mean (SD)	27.7 (4.0)	27.8 (5.1)	25.5 (3.3)	0.96	0.385
Psychosocial risk score[a]: mean (SD)	1.20 (1.50)	2.40 (2.03)	4.6 (2.12)	19.88	< 0.001
Obstetric risk score[b]: mean (SD)	1.12 (1.17)	1.37 (0.85)	1.40 (1.51)	1.00	0.371
IQ: mean (SD)	105.1 (13.8)	100.0 (14.2)	97.0 (17.6)	2.68	0.073
CBCL externalizing problems: mean (SD)	51.4 (9.0)	55.6 (10.7)	51.3 (7.9)	2.46	0.090
CBCL internalizing problems: mean (SD)	51.8 (9.5)	54.9 (8.8)	50.4 (7.6)	1.69	0.190

COAs with (ALCDEL) and without paternal delinquency (ALC), controls (CONTR)

[a]"Enriched" family adversity index as proposed by Rutter and Quinton [41] measuring the presence of 11 adverse family factors covering characteristics of the parents, the partnership, and the family environment during a period of one year prior to birth

[b]Obstetric adversity score counting the presence of nine adverse conditions during pregnancy, delivery, and postnatal period such as preterm labor, asphyxia or seizures

Table 2 Means and SD (in parentheses) of P300 amplitudes (μV) in groups of children of alcoholic fathers and controls by electrode site and block

Electrode site	CONTR (1) $n = 82$	ALC (2) $n = 30$	ALCDEL (3) $n = 10$	F (2, 119)	p	Significant contrasts 1 vs. 3, $df = 90$	
						F	p
Block 1							
Fz	3.05 (5.98)	4.62 (6.45)	1.41 (4.77)	1.28	0.282		
Cz	8.25 (6.80)	9.54 (8.00)	6.60 (7.01)	0.72	0.489		
Pz	12.53 (6.42)	14.71 (7.90)	11.60 (4.95)	1.39	0.253		
Block 2							
Fz	4.71 (7.11)	2.80 (8.26)	−2.09 (7.41)	4.02	0.020	8.09	0.006
Cz	8.91 (8.21)	6.31 (8.81)	3.59 (6.36)	2.54	0.083	3.90	0.051
Pz	12.18 (7.27)	11.01 (6.98)	10.51 (8.68)	0.44	0.645		

COAs with (ALCDEL) and without paternal delinquency (ALC), controls (CONTR)

only for the second block, whereas no significant group differences were obtained for the first block. Single comparisons revealed that, in the second block, children of alcoholic and delinquent fathers displayed a significantly lower frontal P300 amplitude and a nearly significantly lower central P300 than children of the control group, while differences between children of non-delinquent alcoholic fathers and the control group were far from being statistically significant ($p > 0.138$). Furthermore, a main effect of electrode site (F (2,238) = 111.78, $p < 0.001$) emerged, with increasing amplitudes from frontal to parietal sites. In addition, a trend to smaller amplitudes in the second block was found (F (1,238) = 3.42, $p = 0.067$).

Discussion

The present study investigated event-related potentials in children of alcoholics and control children at elementary school age. Results indicated that eight-year-old COAs with delinquent fathers displayed significant differences from their same-age counterparts, characterized by reduced P300 amplitude. This finding relates to numerous studies indicating a smaller amplitude of P300 in non-alcoholic individuals at high risk for alcoholism than in low-risk controls [7, 20, 36]. A specific finding of this study is that this difference was linked to certain conditions: lower amplitudes were found only in COAs with paternal delinquency, in later trials, and at frontal area.

Others have also shown that impaired inhibitory regulation, such as conduct disorder and antisocial personality disorder, was characterized by diminished P300 amplitude [22]. Interestingly, it was suggested that P300 decrements, which were previously attributed to familial alcohol/substance dependence, might be due to a coincidental increase in the rate of conduct problems [5]. In agreement with this hypothesis, it has recently been shown that neurobehavioral disinhibition mediated the association between P300 amplitude in childhood and substance use disorders in early adulthood [18]. Severity of neurobehavioral disinhibition as assessed by measures of affect regulation, behavior control, and executive cognitive function was negatively related to P300 amplitude. However, the literature on ERPs in COAs from alcoholic and delinquent fathers is scanty. This study is among the first to compare COAs with and without paternal delinquency. Our results are consistent with the ones from Begleiter et al. [7], who demonstrated low P300 amplitude in COAs from type II alcoholics.

In contrast to the majority of studies investigating P300 in COAs, a significant P300 amplitude decrement was obtained at frontal site only. This finding

may point to a distinctive feature of COAs with delinquent fathers and may suggest a potential for impulsivity and aggressiveness in this group. One possible interpretation may relate to the differentiation of the P3a and P3b variants of P300. The former has a more anterior localization and has been interpreted as reflecting an initial orienting process, while the latter has a more parieto-central distribution which, may be indicative of the capacity to use attentional resources. Bauer and Hesselbrock [5] also demonstrated P300 decrements over the frontal region, but only among teenagers older than 16 years with conduct problems, whereas among those younger than this age, decrements on P300 amplitude were only detectable over the posterior region of the scalp. They concluded that the frontal and parieto-temporal generators of P300 were differently sensitive to the effects of conduct problems at different stages of brain development. These findings are in line with the assumption that the last area of the brain to mature is the frontal region. One could speculate that having a delinquent father would be related to frontal area dysfunction expressed by low P300 amplitude, which could be a precursor of conduct disorders and antisocial behavior. According to many studies, frontal brain dysfunction correlates with persistent conduct problems into adulthood [6, 38, 39]. Although in our study there were no significant behavioral differences among groups, as hypothesized by Barnow et al. [3], differences in P300 amplitude were observed, suggesting that COAs' family history may be a more important predictor than childhood psychopathology.

The finding that the reduction in P300 amplitude was more pronounced in later trials suggests a stronger habituation, i.e., decrement of the P300 amplitude over repeated stimulation, in COAs with paternal delinquency as compared to the other groups. Consistent with prior research, this effect appeared to be particularly marked in the frontal area. Several studies have demonstrated P300 habituation from auditory oddball paradigms [33], supporting a possible role for habituation in COAs' P300 reduction. Psychophysiological research has provided substantial evidence indicating that low autonomic arousal and orienting is related to antisocial behavior [37]. This hyporesponsiveness may be reflected, among others, in a more rapid habituation to orienting stimuli. However, for a thorough analysis of the effect of stimulus repetition on ERPs, a higher number of trial blocks is needed.

Several limitations of this study warrant consideration. Paternal AUD and delinquent history by direct assessment may have been underreported. Thus, it is possible that the results obtained, at least in part, reflect the fathers' own perception of their alcohol consumption and delinquent behavior. This is an important issue since the more marked P300 decrements were obtained in the ALCDEL group. Probably due to fathers' underreport, the group size of COAs with delinquent fathers was relatively small, which reduces the statistical power to detect differences among groups. Furthermore, the relatively young age of our children may have restricted the identification of conduct problems. Most studies in COAs have shown externalizing disorders in adolescents [3, 4, 17]. Kuperman et al. [26] also reported a lack of significant relationship between a parental diagnosis of ASPD and conduct disorder in their offspring, which they attributed to the relative young age of their children.

In conclusion, the results of this study suggest that COAs with delinquent fathers may have a deviation in brain maturation expressed by low P300 amplitude in the frontal area. According to our findings, the combination of fathers' delinquent behavior and alcoholism was more likely to relate to low P300 amplitude than paternal alcoholism alone. Therefore, our results stress the significance of fathers' antisocial psychopathology for P300 amplitude in children of alcoholics. Others, however, have hypothesized that a small P300 amplitude may be associated with a cognitive or neurophysiological dysfunction common to many types of psychopathology [10]. Further studies are required including a sample with externalizing psychopathology in the absence of a family history of alcoholism to better clarify this issue.

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