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Is the P300 deficit in alcoholism associated with early visual impairments (P100, N170)? An oddball paradigm

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Abstract

Objective: Studies exploring chronic alcoholism with event-related potentials (ERPs) have shown delayed latency and reduced amplitude of the P300, a long-lasting positive potential reflecting decisional processing. This P300 deficit in alcoholism is generally interpreted as a disturbance in central nervous system inhibition or in memory/attention. The present study aimed at identifying if this electrophysiological deficit is already present on earlier components, and advances a new hypothesis concerning the interpretation of the P300 alteration.
Methods: Patients suffering from alcoholism and matched healthy controls had to detect, in an oddball paradigm, emotional faces among a succession of neutral faces. Behavioral performance and ERP data (recorded from 32 electrodes) were analyzed.
Results: In line with previous studies, data showed that alcoholism led to a P300 deficit. Moreover, we observed for the first time that this deficit begins at earlier visual (P100) and face-processing (N170) stages, and we found high positive correlations between P100, N170 and P300 for amplitude and latency values, suggesting cumulative deficits on the cognitive continuum.
Conclusions: We suggest that the P300 deficit observed in chronic alcoholism could be linked to earlier visuo-spatial deficits rather than being an impairment of the specific processes linked to the P300.
Significance: These results call for reconsidering the interpretation of P300 impairments at a fundamental and clinical level, and shows that earlier ERP components must be taken into account in future studies.

Keywords: Alcoholism; ERPs; P3b; P300; Visuo-spatial abilities; Oddball paradigm

1. Introduction

It is now well established that, because of alcohol neurotoxicity, chronic alcoholism leads to deleterious effects on the central nervous system, i.e., brain atrophy and/or dysfunction (e.g. George et al., 1999; Sullivan and Pfefferbaum, 2005). This cerebral impairment has consequences at a behavioral level. Alcoholic individuals have impaired performance in a large range of cognitive, social and neuropsychological functions (Wegner et al., 2001). Although connections have been established between the cerebral and behavioral dysfunctions in alcoholism, i.e., anterior thalamic nuclei lesions leading to anterograde memory loss in the Korsakoff syndrome (Harding et al., 2000), many links between these two levels are still to be explored. A central question is still under debate. At which stage of cognitive processing does the deficit observed in alcoholism (particularly for the processing of complex and social stimuli) originate?

Event-related potentials (ERPs) represent an interesting tool to relate behavioral performance and cerebral activity as they monitor brain electrical activity during cognitive tasks with a high temporal resolution. More precisely, during a cognitive task, ERPs allow one to identify the electrophysiological component representing the onset of a

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dysfunction, and then to infer the impaired cognitive stages (Rugg and Coles, 1995).

Electrophysiological techniques, and particularly ERPs, have been used for decades to explore cerebral functioning in alcoholism. The majority of studies have focused on the P300, a long-lasting positive deflection appearing around 300 ms after stimulus onset. At a functional level, the P300 complex is not unitary but can be divided into at least two subcomponents. The P3a is linked to stimulus novelty and indexes the involuntary orientation of attention towards salient events; it has a more frontal scalp distribution (Knight, 1991). The P3b is linked to the closure of cognitive processing before starting the motor response and is maximally distributed over parietal sites (Polich, 2004). In studies on alcoholism, measurement of the P300 is generally centered on the P3b and elicited via an auditory or visual oddball paradigm (based on the detection of infrequent stimuli among a train of regular stimuli). Overall, alcoholic individuals have a reduced amplitude and a delayed latency for the P300 in comparison with non-alcoholic individuals (see Hansenne, 2006 for a review). The P300, maximal at centro-parietal sites among control participants, generally has the same amplitude across all sites among alcoholic individuals. In summary, the P300 is impaired (in amplitude and latency) in chronic alcoholism (Porjesz and Begleiter, 2003).

Other electrophysiological components have been explored only marginally, and this focus on the P300 may be explained by the fact that this very large component (5–20 μV) is easily elicited (with the oddball paradigm) and easily detected. Moreover, the P300 has proved its clinical and predictive usefulness in alcoholism and in many other pathologies, i.e. as a risk factor in psychopathologies (see Hansenne, 2006 for a review), as a tool for the differential diagnosis in dementia (Jimenez-Escrig et al., 2002), or as a tool to estimate the treatment efficacy in the syndrome of attention deficit and hyperactivity (Smeyers, 1999). Surprisingly, the other ERP components have received little attention. Indeed, it has been shown, for example in schizophrenia (Contreras et al., 1990; Foxe et al., 2001; Javitt et al., 1993; Javitt, 2000) and depression (Fotiou et al., 2003), that earlier components, and particularly those associated with perceptual processing (P100 and N100), could be affected by psychopathological states.

The aim of the present study was to explore two of the electrophysiological components that appear before the P300. The first component investigated was the P100, a positive deflection which appears around 100 ms after stimulus onset and is maximal at occipito-temporal sites. The P100 is classically associated with the primary visual processing of the stimulus (Heinze and Mangun, 1995), yet it has been shown (e.g. Debruille et al., 1998; Seeck et al., 1997) that it may also be linked to the processing of more complex aspects of the stimulus. The second component investigated was the N170, which is a negative component maximal around 170 ms at occipito-parietal sites, and associated with the specific processing of human faces (Bentin et al., 1996). P100 and N170 were chosen for two main reasons. First, exploring these components will offer some insight into visual abilities in alcoholism. Indeed, alcoholic individuals often have impaired performance in visual and spatial neuropsychological tests (Beatty et al., 1997; Schandler et al., 1995; Sullivan et al., 2002; Wegner et al., 2001); nevertheless, little is known concerning the cerebral correlates of this deficit. The investigation of P100 and N170, as they reflect visual processing, will clarify the ERP correlates of the deficit in basic visual abilities among alcoholic individuals. If there is a general visual deficit in alcoholism, the P100 (particularly if the deficit affects basic perceptual processing) and N170 (particularly if the deficit is linked to face processing) should be impaired (in amplitude and/or latency) among alcoholic individuals, in comparison with non-alcoholic individuals. Thus, one aim of this study was to specify the ERP correlates of the visual deficit often described in alcoholism.

Second, and importantly, assessing the P100 and N170 also allows the origin of the cognitive processing deficit to be determined. Indeed, as shown by Foxe et al. (2005) in schizophrenia, deficient early processes may underlie the failure of later "higher-level" processing. The processing of a stimulus can be roughly separated into different stages, each having electrophysiological correlates. Perception level with P100 and N170, attention level with N200 (Halgren and Marinkovic, 1995), and decision level with P300 (Donchin and Coles, 1988). Even though the impairment in the P300 among alcoholic individuals is well established, it does not necessarily mean that the deficit in alcoholism is exclusively due to a decision impairment, because a deficit at the earlier stages cannot be excluded. Indeed, it seems that chronic alcoholism leads to delayed latency (Cadaveira et al., 1991; Nicolas et al., 1997), reduced amplitude (Chan et al., 1986; Ogura and Miyazato, 1991) and abnormal topography (Miyazato and Ogura, 1993) of the P100. Alcoholism is also associated with abnormalities in other components, for example delayed latency and reduced amplitude of the N200 (Baguley et al., 1997; Kathmann et al., 1996) and contingent negative variation (van den Bosch, 1984). Thus, electrophysiological disruptions anterior to the P300 are potentially observable among alcoholic individuals. The present study investigated these early deficits, and attempted to confirm previous studies and to determine the source of the impairment observed in alcoholism.

In addition, the P300, and particularly the P3b, is considered as the reflection of the decisional processes and may mark the "closure" of the processes linked to the stimulus, just before the motor response (Desmedt, 1980; Verleger, 1997). Besides, some authors consider that the P300 latency indexes the end of stimulus evaluation and could be used as an alternative to response times (McCarthy and Donchin, 1981). The P300, linked to the cognitive stage of decision, seems to be the end of a continuum in cognitive processing. Consequently, a discrepancy at the earlier stages may last for the whole processing event and

still affect the later stages. In other words, if the visual processing of the stimulus is impaired (as indexed by the P100 and N170), decisional processing will also deteriorate. The decision stage could be delayed (delayed latency) and less definite (reduced amplitude) if the perceptual level is deficient. We evaluated the presence of an early time-lag in processing between controls and alcoholic individuals (time-lag linked to the retardation in visual processing among alcoholic individuals), and observed how this potential time-lag may influence the later stages.

Finally, this study explored the electrophysiological correlates of the processing of complex social stimuli in alcoholism. The studies using ERPs in alcoholism have more often been based on paradigms (particularly the oddball paradigm) using very basic visual or auditory stimuli, i.e., flashes, bursts, ... (e.g., Porjesz et al., 2005). Although some studies in alcoholism already used complex emotional paradigms (Herrmann et al., 2000; Hansenne et al., 2003), our study is to our knowledge the first using complex visual and social stimuli (namely emotional faces) in an oddball paradigm. Alcoholism leads to various social and interpersonal dysfunctions, notably for the decoding of emotional facial expressions (EFE) (Philippot et al., 1999; Townshend and Duka, 2003), and the appropriate processing of EFE is a major skill for the development and maintenance of satisfactory interpersonal relations (Feldman et al., 1991). The failure of this skill in alcoholic individuals might, therefore, have deleterious consequences on their social integration (Nixon et al., 1992), leading to a vicious circle. A deficit in the decoding of the EFE, provoked by the alcoholism, worsens interpersonal problems (Kornreich et al., 2002), which in turn could increase alcohol consumption used as a coping strategy (Kornreich et al., 2001). In view of the importance of EFE decoding in everyday life, this study explored the causes of the deficit observed for this ability in alcoholism. Moreover, EFE reflecting several emotions were used to allow assessment of variations in the deficit according to the emotion imbedded in the stimulus.

2. Methods

2.1. Participants

Ten inpatients (nine men), diagnosed with alcohol dependence according to DSM-IV criteria, were recruited during the third week of their treatment in a detoxification center (Brugmann Hospital, Brussels, Belgium). They had all abstained from alcohol for at least two weeks, were free of any other psychiatric diagnosis (the presence of a comorbidity with any other psychiatric disease constituted an exclusion criterion), and were all right-handed. Patients were matched for age, gender and education with a control group composed of 10 volunteers who were free of any history of psychiatric disorder or drug/substance abuse. Exclusion criteria for both groups included major medical problems, central nervous system disease (including epilepsy), visual impairment and polysubstance abuse. Education level was assessed according to the number of years of education completed since starting primary school. Patients and control participants were assessed for several psychological measures. State and trait anxiety (STAI A and B, Spielberger et al., 1983), depression (BDI, Beck and Steer, 1987), interpersonal problems (Horowitz et al. (1988), evaluating the quantity and quality of the social interactions, and the integration in the family and relationship background) and alexithymia (Bagby et al., 1994). Although all the participants in the control group were free of any medication, alcoholic individuals received doses of benzodiazepines (mean: 54.5 mg/day, s.d. 41.9). Participants were provided with full details regarding the aims of the study and the procedure to be followed. After receiving this information, all participants gave their informed consent.

2.2. Task and procedure

We used a visual and emotional oddball paradigm based on a face-detection task, in which participants were confronted with one regularly repeated standard stimulus (a neutral face) and four deviant stimuli (e.g. Campanella et al., 2005). Deviant faces differed from the standard faces either in identity (different identity, neutral expression), or in emotion (same identity, happy, fearful or sad expression).

Six faces (three males) with neutral, happy, sad and fearful expressions were selected from the standardized set of Ekman and Friesen pictures (1976). Participants were confronted with a total of 16 blocks each defined by 100 stimuli (76 regularly repeated stimuli and 24 infrequent stimuli. For example, 76 face A neutral, 6 deviant face A happy, 6 deviant face A fear, 6 deviant face A sad, and 6 deviant face B neutral). The order of the 16 blocks varied across participants. During the ERP recordings, participants sat in a dark room on a chair placed at 1 m from the screen with their head restrained in a chin rest. Stimuli subtended a visual angle of $3 \times 4°$. Each face was presented for 500 ms. A black screen was displayed between faces, for a random duration of between 1300 and 1600 ms. From the stimulus onset, participants had 1500 ms to answer. They had to indicate as quickly as possible the occurrence of a deviant stimulus by pressing a button with their right forefinger. Response time and error rate were recorded. There were two categories of error. Omission (i.e., forgot to press the answer key when a deviant stimulus appeared) and false recognition (i.e., pressed the answer key when a standard stimulus appeared). Participants were told that speed was important but not at the cost of accuracy. Only correct answers (i.e., deviant stimuli for which the subject pressed the answer key) were considered for analysis of reaction times and ERP.

2.3. EEG recording and analysis

The EEG was recorded by 32 electrodes mounted in an electrode Quick-Cap. Electrode positions included the

standard 10–20 system locations and intermediate positions. Recordings were taken with a linked mastoid physical reference but re-referenced using a common average. The EEG was amplified by battery-operated A.N.T.® amplifiers with a gain of 30,000 and a band-pass of 0.01–100 Hz. The impedance of all electrodes was kept below 10 kΩ. The EEG was recorded continuously (sampling rate 500 Hz, A.N.T. Eeprobe software) and the vertical electro-oculogram (VEOG) was recorded bipolarly from electrodes placed on the supraorbital and infraorbital ridges of the left and right eyes. Trials contaminated by EOG artifacts (mean of 10%) were eliminated off-line. Epochs were created starting 200 ms prior to stimulus onset and lasting for 800 ms. In order to compute different averages of ERP target stimuli for each subject individually, two parameters were coded for each stimulus: (1) the stimulus type (rare Happy, rare Fear, rare Sad, rare Different Identity or Standard); and (2) the response type (keypress for deviant stimulus, no keypress for standard stimulus). Data were filtered using a 30-Hz low-pass filter.

For each subject and each component of interest (namely P100, N170 and P300), individual peak amplitudes and maximum peak latencies were obtained from several electrodes separately for the ERPs evoked in response to deviant stimuli (see Tables 1 and 2 for complete electrophysiological results). Oz, O1, O2, T5 and T6 for P100 and N170 (Bentin et al., 1996), Fz and Cz for P3a, Pz and Oz for P3b (Polich, 2004). These values were tested using repeated measures of analysis of variance (ANOVA – Greenhouse–Geisser correction was applied when appropriate) and two-tailed Pearson correlations.

3. Results

3.1. Control measures

As shown in Table 3, alcoholic individuals and controls were similar in terms of age ($F(1,19) = 0.41$, NS), gender and education ($F(1,19) = 0.08$, NS). Moreover, the two groups did not differ significantly for anxiety state ($F(1,19) = 1.86$, NS), anxiety trait ($F(1,19) = 4.04$, NS), interpersonal problems ($F(1,19) = 2.41$, NS) or alexithymia ($F(1,19) = 0.40$, NS). Indeed, the only difference observed between the two groups for these control measures concerned the depression scale. Alcoholic individuals had a significantly higher level of depression than the controls ($F(1,19) = 5.44$, $p = 0.03$). However, this difference is unlikely to have influenced the experimental results, as no significant Pearson's correlations were shown between BDI scores and any behavioral and electrophysiological

Table 1
Electrophysiological results: mean amplitudes (μv (s.d.)) for each component on each emotion, among controls and alcoholics

Group	Emotion[a]	O1	Oz	O2	T5	T6
P100 (O1, Oz, O2, T5, T6)						
Alcoholics ($N = 10$)	S	2.87 (2.02)	2.49 (2.44)	3.41 (3.21)	2.35 (1.67)	2.66 (2.11)
	I	2.88 (1.40)	2.90 (1.54)	3.36 (2.55)	2.35 (1.71)	2.37 (1.56)
	H	3.06 (1.77)	2.40 (1.4)	3.54 (2.21)	2.64 (1.94)	2.46 (1.74)
	F	3.34 (1.52)	2.45 (2.24)	3.98 (2.22)	2.77 (1.74)	2.43 (1.62)
Controls ($N = 10$)	S	4.44 (2.37)	2.91 (2.07)	3.54 (1.91)	3.77 (1.64)	5.52 (2.68)
	I	3.38 (2.20)	2.38 (2.24)	3.30 (2.02)	3.53 (2.04)	5.53 (2.54)
	H	4.07 (2.12)	2.83 (2.07)	3.55 (1.79)	3.60 (1.54)	5.56 (2.39)
	F	4.05 (1.73)	2.72 (2.24)	3.54 (1.98)	3.60 (1.91)	5.47 (2.65)
N170 (O1, Oz, O2, T5, T6)						
Alcoholics ($N = 10$)	S	−2.26 (2.92)	−2.19 (2.49)	−2.41 (1.41)	−2.95 (1.45)	−3.32 (2.15)
	I	−2.36 (2.79)	−1.96 (2.51)	−2.61 (2.47)	−3.66 (4.60)	−3.92 (1.67)
	H	−1.88 (3.05)	−2.19 (2.18)	−2.52 (2.18)	−3.27 (3.86)	−3.95 (1.83)
	F	−2.50 (3.39)	−2.56 (3.12)	−2.55 (2.75)	−3.71 (1.37)	−3.89 (1.55)
Controls ($N = 10$)	S	−5.57 (5.62)	−5.72 (5.52)	−6.13 (5.65)	−6.44 (2.85)	−7.45 (5.55)
	I	−7.26 (5.56)	−5.11 (7.88)	−7.50 (5.34)	−7.66 (3.35)	−9.01 (5.70)
	H	−6.39 (5.54)	−6.43 (5.78)	−6.53 (5.53)	−6.61 (3.15)	−7.40 (5.09)
	F	−7.17 (5.11)	−7.21 (5.63)	−7.30 (5.60)	−7.13 (3.04)	−8.19 (5.10)

Group	Emotion[a]	Fz	Cz	Pz	Oz
P3a (Fz, Cz) and P3b (Pz, Oz)					
Alcoholics ($N = 10$)	S	3.09 (1.56)	4.70 (1.57)	6.21 (2.57)	2.42 (2.43)
	I	2.80 (2.26)	4.15 (0.89)	6.90 (2.92)	3.70 (2.54)
	H	2.83 (1.65)	4.00 (1.73)	6.12 (3.32)	3.25 (2.80)
	F	2.56 (1.25)	4.71 (2.62)	6.14 (3.13)	3.01 (2.67)
Controls ($N = 10$)	S	3.45 (2.19)	6.29 (4.56)	9.90 (4.28)	5.10 (3.99)
	I	3.52 (2.80)	6.93 (5.25)	10.64 (4.69)	6.27 (3.79)
	H	3.24 (2.23)	6.05 (4.49)	8.79 (4.30)	4.07 (4.03)
	F	4.05 (2.60)	7.45 (4.51)	9.78 (3.87)	4.53 (4.27)

[a] The emotions are: S, Sadness; I, Identity; H, Happiness; F, Fear.

Table 2
Electrophysiological results: mean latencies (ms (s.d.)) for each component on each emotion among controls and alcoholics

Group	Emotion[a]	O1	Oz	O2	T5	T6
P100 (O1, Oz, O2, T5, T6)						
Alcoholics ($N = 10$)	S	136 (20.6)	135 (19.7)	136 (18.4)	141 (13.1)	140 (10.3)
	I	135 (23.3)	135 (23.3)	137 (17.2)	145 (14.5)	140 (7.2)
	H	138 (9.8)	134 (18.4)	133 (17.2)	139 (15.1)	140 (11.6)
	F	122 (15.2)	138 (16)	137 (18.2)	139 (11.1)	141 (8.7)
Controls ($N = 10$)	S	130 (9.4)	129 (10.8)	128 (11)	131 (14.6)	136 (12.9)
	I	123 (14.3)	120 (21.5)	121 (17.3)	130 (15.8)	127 (11.1)
	H	120 (14.9)	121 (17)	120 (16)	130 (11.7)	124 (11.8)
	F	122 (18.1)	123 (17.7)	120 (17.7)	129 (11.8)	128 (11.4)
N170 (O1, Oz, O2, T5, T6)						
Alcoholics ($N = 10$)	S	199 (14.6)	205 (18.6)	197 (18.2)	204 (15.8)	200 (14.7)
	I	202 (16.8)	196 (12.9)	191 (13.9)	192 (16)	190 (15.6)
	H	198 (14.4)	195 (9.3)	194 (16.1)	194 (15)	193 (12.1)
	F	199 (13.3)	201 (12.2)	197 (12)	198 (15.2)	196 (14.7)
Controls ($N = 10$)	S	183 (8.1)	178 (10.2)	177 (8.2)	173 (12.3)	175 (10)
	I	189 (13.8)	182 (9.2)	179 (15)	175 (13.8)	176 (11.8)
	H	186 (8.1)	180 (9)	177 (7.2)	173 (13.7)	172 (11.5)
	F	185 (11.6)	180 (11.9)	176 (13)	174 (13.9)	174 (11.2)

Group	Emotion[a]	Fz	Cz	Pz	Oz
P3a (Fz, Cz) and P3b (Pz, Oz)					
Alcoholics ($N = 10$)	S	396 (59.9)	479 (81.2)	558 (75.4)	554 (90.9)
	I	412 (92.8)	472 (78.8)	524 (73)	539 (74.6)
	H	472 (84.6)	393 (64.4)	529 (78.6)	537 (79.3)
	F	407 (77.7)	471 (82.7)	532 (88.4)	537 (83.6)
Controls ($N = 10$)	S	472 (122.1)	505 (82)	497 (75.3)	442 (106.7)
	I	461 (131.7)	496 (61)	485 (70.6)	423 (114.4)
	H	457 (114.8)	500 (56.7)	478 (57.8)	420 (112.6)
	F	450 (121.7)	507 (64.2)	482 (69.6)	429 (107.4)

[a] The emotions are: S, Sadness; I, Identity; H, Happiness; F, Fear.

data ($p > 0.05$ for each correlation). This lack of influence may be explained by the fact that the scores observed among alcoholic individuals were all below the clinical level; none of these patients was diagnosed as depressed according to the DSM-IV criteria.

Although the study took place at the end of the detoxification treatment, low doses of benzodiazepines were still administered to the alcoholic individuals. As benzodiazepines are known to have sedative effects (e.g. Stewart, 2005), and despite the fact that the doses administered to the subjects were low, the influence of benzodiazepine treatment on cognitive abilities was taken into account. In the alcoholic group, there were no significant correlations between the doses of benzodiazepine and any behavioral or electrophysiological result ($p > 0.05$ for every correlation).

On the basis of these results, it seems unlikely that our behavioral and ERP data were significantly biased by interfering factors like medication, depression, anxiety, interpersonal problems or alexithymia.

3.2. Behavioral data

3.2.1. Performance

The mean level of error was 0.1% for omission and 0.7% for false recognition. There was no significant group difference concerning the performance ($F(1,18) = 1.57$, NS).

3.2.2. Reaction times

These results are illustrated in Fig. 1 and Table 4. A 4×2 ANOVA with deviant faces (sadness, fear, happiness, identity) as within-factor and group (alcoholic individuals,

Table 3
Patient and control characteristics: mean (s.d.)

Group	Age	BDI[a]	EL[b]	Stai[c] A	Stai[c] B	IIP[d]	TTAS II[e]
Controls ($N = 10$)	43.90 (9.48)	2.50 (3.86)	13.5 (2.12)	30.40 (14.17)	36.30 (10.57)	0.98 (0.57)	47.12 (12.55)
Alcoholics ($N = 10$)	46.90 (11.36)	8.80 (7.61)	13.4 (2.71)	41.00 (20.06)	48.20 (15.44)	1.38 (0.58)	51.00 (11.84)

[a] BDI, Beck Depression Inventory (Beck and Steer, 1987).
[b] EL, Education Level.
[c] STAI, State and Trait Anxiety Inventory (Spielberger et al., 1983).
[d] IIP, Inventory of Interpersonal Problems (Horowitz et al., 1988).
[e] TTAS, Twenty-item Toronto Alexithymia Scale – II (Bagby et al., 1994).

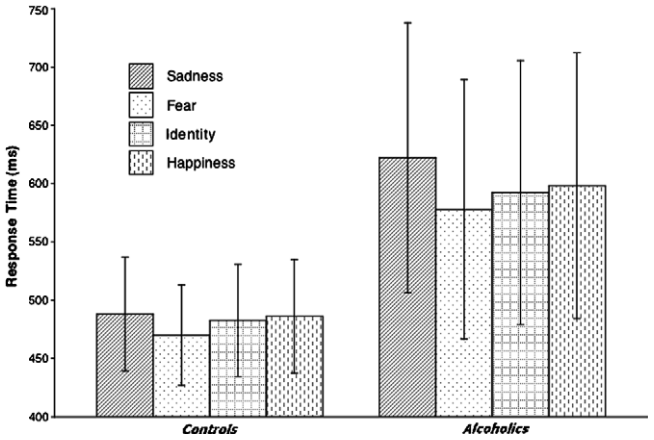

Fig. 1. Reaction times (ms) for each group on each rare stimulus category. This figure presents the three significant effects described for the behavioral results: – main effect of group: controls are faster than alcoholics at detecting infrequent stimuli; – main effect of deviant faces: fearful deviant faces are detected fastest in both groups; – interaction effect: sad faces are the most difficult to detect for the alcoholic group, this difference is not significant among controls.

controls) as between-factor was carried out. A main group effect was found ($F(1,18) = 9.07$, $p = 0.007$). The alcoholic individuals were significantly slower than the controls at detecting deviant faces. There was also a main effect of deviant faces ($F(3,54) = 15.28$, $p < 0.001$). Fearful deviant faces were the fastest to be detected ($p < 0.01$). Conversely, sad faces were the slowest to be detected ($p < 0.05$). These two main effects were qualified by a significant interaction ($F(3,54) = 3.41$, $p = 0.035$), and post-hoc paired-sample t-tests showed that. For the control group, reaction times were significantly shorter for fearful faces than for the three other categories of deviant face (sadness: $t(9) = -2.82$, $p < 0.05$; identity: $t(9) = 3.092$, $p < 0.05$; happiness: $t(9) = -4.35$, $p < 0.01$), which did not differ significantly. In the alcoholic group, fearful faces were also the fastest to be detected (sadness: $t(9) = -5.75$, $p < 0.001$; identity: $t(9) = -2.47$, $p < 0.05$; happiness: $t(9) = -3.56$, $p < 0.01$). Moreover, sad faces led to significantly longer reaction times than happy ($t(9) = 2.84$, $p < 0.05$) and different identity faces ($t(9) = 4.14$, $p < 0.01$). Thus, sad faces were the most difficult to detect for the alcoholic group, whereas there was no difference for the controls.

3.3. ERP data

For each component of interest (P100, N170, P3a and P3b), $2 \times 4 \times 5$ (2) ANOVAs were computed separately for latencies and amplitudes, with group (alcoholic individuals, controls) as between-factor, emotion category (sadness, fear, happiness, different identity) and localization (Oz, O1, 02, T5 and T6 for the P100 and N170 components; Fz and Cz for the P3a component, Pz and Oz for the P3b component) as within-factors. The electrophysiological results are illustrated in Fig. 2.

3.3.1. P100

Latencies. No main effect of emotion ($F(3,54) = 0.98$, NS) or localization ($F(4,72) = 2.69$, NS) were observed. There was no significant interaction. The only significant effect was a main effect of group ($F(1,18) = 6.00$, $p = 0.025$). The P100 latency was shorter for the control group, regardless of the emotion or localization.

Amplitudes. No main effect of emotion ($F(3,54) = 0.60$, NS) or group ($F(1,18) = 2.26$, NS) was found. There was a main effect of localization ($F(4,72) = 3.15$, $p = 0.03$). The P100 amplitude was maximal for T6 and minimal for Oz. The only significant interaction effect was between group and localization ($F(4,72) = 4.49$, $p = 0.006$). In the control group, the P100 had a higher amplitude for T6 than for other electrodes ($t(9) > 3.13$, $p < 0.05$), and this effect was not observed among alcoholic individuals.

3.3.2. N170

Latencies. No main effect of emotion ($F(3,54) = 1.72$, NS) was observed, but main effects were found for localization ($F(4,72) = 10.46$, $p < 0.001$) and for group ($F(1,18) = 14.42$, $p = 0.01$). Indeed, the N170 latency was significantly shorter at occipital sites (Oz, O1, O2) than at temporal sites (T5, T6) and was significantly shorter for controls than for alcoholic individuals. Moreover, the only significant interaction was between emotion and group ($F(3,54) = 4.03$, $p = 0.027$). In the control group, the latencies did not differ with emotion category, whereas in the alcoholic group, happy and different identity faces led to shorter latencies than fearful ($t(9) = 2.39$, $p < 0.05$) and sad faces ($t(9) = 2.67$, $p < 0.05$).

Amplitudes. There was no main effect of emotion ($F(3,54) = 3.08$, NS) or localization ($F(4,72) = 2.84$, NS), and there was no significant interaction. The only significant effect was a main effect of group ($F(1,18) = 5.87$, $p = 0.026$). Controls had a significantly higher N170 amplitude than alcoholic individuals.

3.3.3. P3a

Latencies. No main effect (emotion ($F(3,42) = 1.13$, NS), group ($F(1,14) = 1.72$, NS), localization ($F(1,14) = 3.10$, NS)) and no interaction reached significance.

Table 4
Behavioral results: reaction times (ms) (s.d.)

Group	Rare sad faces	Rare fearful faces	Rare identity faces	Rare happy faces
Controls ($N = 10$)	488.2 (48.7)	470 (43)	482.6 (48.1)	486.3 (48.6)
Alcoholics ($N = 10$)	622.2 (115.8)	577.8 (111.2)	592.3 (113.1)	598.2 (113.9)

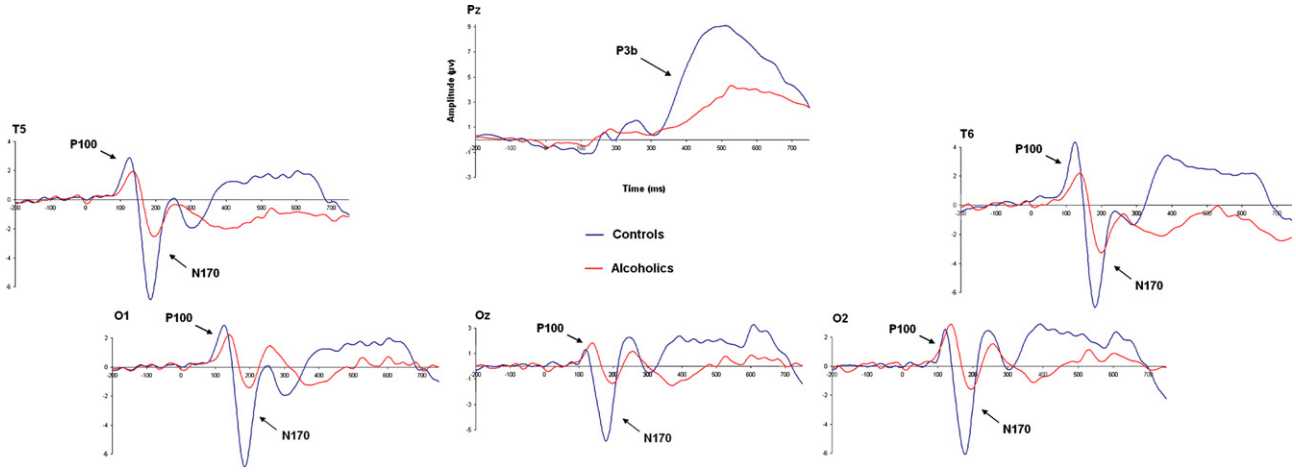

Fig. 2. Electroencephalographic results for both groups on O1, Oz, O2, T5, T6 (P100 and N170) and Pz (P3b). This figure shows the deficits observed among alcoholic subjects for the three ERP components: – delayed latency for P100, N170 and P3b; – reduced amplitude for N170 and P3b.

Amplitudes. The only significant effect was a main effect of localization ($F(1,14) = 11.59$, $p = 0.04$). The amplitudes were significantly higher for Cz than Pz. Other main effects (emotion ($F(3,42) = 1.65$, NS) and group ($F(1,14) = 1.04$, NS)) and interactions were not significant.

3.3.4. P3b

Latencies. Three main effects but no interaction was observed. The main effect of emotion ($F(3,51) = 4.53$, $p = 0.03$) showed that the P3b latency was significantly longer for the sad faces than for the other deviant stimuli, which did not differ significantly from each other. The main effect of group ($F(1,17) = 5.78$, $p = 0.028$) showed that controls had a significantly shorter latency for P3b than the alcoholic individuals. Finally, the localization main effect ($F(1,17) = 4.59$, $p = 0.047$) demonstrated that the P3b latencies were shorter at Oz than at Pz.

Amplitudes. Three main effects were observed but no interaction reached significance. First, the P3b amplitude was significantly higher for the different identity deviant faces than for the other deviant stimuli, which did not differ significantly ($F(3,51) = 4.97$, $p = 0.01$). Second, controls had a significantly higher amplitude for P3b than alcoholic individuals ($F(1,17) = 4.60$, $p = 0.047$). Third, the amplitudes were higher at Pz than at Oz ($F(1,17) = 24.32$, $p < 0.001$).

3.3.5. Overall

To test whether P100, N170 and P3b are the successive steps of a continuum in cognitive processing (and thus whether the deficit in P3b may be a consequence of earlier ERP impairments), Pearson's correlations were performed between these three components, for amplitude and latency. The results, shown in Table 5, clearly confirm that the latencies and amplitudes of P100, N170 and P3b are linked: the greater the delay in latency and the reduction in amplitude for P100, the greater the delay in latency and reduction in amplitude for N170, and for P3b.

Table 5
Pearson's correlations (r (p-value)) in amplitude and latency between P100, N170 and P3b

	Latency	Amplitude
P100 – N170	$r = 0.718$ ($p < 0.001$)	$r = -0.654$ ($p = 0.002$)
P100 – P3b	$r = 0.489$ ($p = 0.029$)	$r = 0.719$ ($p < 0.001$)
N170 – P3b	$r = 0.566$ ($p = 0.009$)	$r = -0.557$ ($p = 0.011$)

4. Discussion

The main results of this study can be summarized as follows. At a behavioral level, compared to control participants, alcoholic individuals were slower to detect deviant faces. This delay, independent of depression and medication levels, was also indexed in the electrophysiological data. The latency of earlier (P100, N170) as well as later (P3b) ERP components was longer for alcoholic individuals than for controls. Moreover, alcoholic individuals displayed reduced amplitude of N170 and P3b. There was no difference between groups for the P3a, and the different categories of deviant faces only influenced the late components (P3b and reaction times).

4.1. P100 and N170 as electrophysiological correlates of a visual deficit in alcoholism

Recently detoxified alcoholic individuals present deficits in a wide range of neuropsychological and cognitive abilities (Zinn et al., 2003), and are particularly deficient in visual processing. Visual acuity (Roquelaure et al., 1995), visual attention (Beatty et al., 1996), visual short- and long-term memory (Sullivan et al., 2002), perceptual learning (Fama et al., 2004) but also basic visual perception (Wegner et al., 2001) appear impaired in alcoholism. As the P100 and N170 reflect early visual processing, a deficit (in latency or amplitude) of these components may be the electrophysiological marker of the basic visual processing

deficit in alcoholism. Our behavioral data clearly confirm previous results, showing that alcoholic individuals are slower than controls in the processing of complex visual stimuli (namely emotional and neutral faces), and this deficit has electrophysiological correlates.

First, the latencies of P100 and N170 were longer in alcoholic individuals. This delay may constitute an electrophysiological marker of the early visual deficit in alcoholism. Indeed, longer response latencies observed among alcoholic individuals seem to originate at the visual stages (P100), and this early delay is maintained for the later, face-specific processing (N170).

Second, a significant interaction was observed between group and localization for the P100 amplitude. Controls exhibited the classical right-hemispheric dominance for emotional face processing (Balconi and Lucchiari, 2005; Esslen et al., 2004; Moreno et al., 1990), shown here by a higher P100 amplitude in T6 than in other electrodes. This right dominance was not present in alcoholic participants, where the P100 amplitude did not differ significantly across electrodes. The impairment in hemispheric dominance among alcoholic individuals, already described elsewhere (Gegeshidze and Tsagareli, 2004; McNamara et al., 1994), suggests that the disturbed processing of complex stimuli observed in chronic alcoholism may be linked to a dysfunction in hemispheric specialization. This may constitute a second electrophysiological marker for the visual deficit seen in alcoholism.

Third, the amplitude of N170 was significantly reduced among the alcoholic individuals, indicating that the underlying cognitive process (here, face processing) is impaired in alcoholism. Alcoholism seems to generate a shallower processing of faces; these stimuli are less deeply processed than among control individuals. The deficits observed for the P100 (latency and amplitude) may account, at least partly, for this deficit in N170, as the specialized processing of faces could be hampered by an earlier deficit. If basic visual processing is damaged, the inputs received by the face-processing areas will be biased. This reduced amplitude of N170 could represent a third ERP correlate of the visual dysfunction seen among alcoholic individuals.

In conclusion, our results indicate that the visual deficits observed in chronic alcoholism have early electrophysiological markers, and suggest three potential electrophysiological correlates for these deficits in recently detoxified alcoholic individuals. Delayed latencies for P100 and N170, absence of right-hemispheric dominance for P100 during the processing of faces, and reduced amplitude of N170. These proposals must be confirmed and extended by further studies, as the deficit in alcoholism may involve other forms of complex stimuli and not only human faces.

4.2. Initial level of impairment during the cognitive processing of complex stimuli in alcoholism

As most previous studies have focused on the P3b, little is known about the initial level of impairment during the processing of stimuli. Indeed, as described above, only few studies found an impairment on earlier components like P100 (Cadaveira et al., 1991; Ogura and Miyazato, 1991) and N200 (Baguley et al., 1997; Kathmann et al., 1996). And other studies have failed to detect any difference between alcoholic individuals and controls for some components, for example mismatch negativity (Fein et al., 2004) or N100 (Kathmann et al., 1996). Moreover, to our knowledge, the N170 component has not yet been investigated in chronic alcoholism.

Our data confirm that the impairment in alcoholism appears early in the cognitive processing. As described above, our results confirm the deterioration in P100, mainly for latency, but abnormalities were also found for the amplitude.

Moreover, as complex stimuli (namely emotional and neutral faces) were used, the results provide a generalization of the conclusions obtained in former studies, where only simple stimuli were used; the P100 deficit is also present with faces, which are more complex and ecological stimuli.

Finally, our study gives some insights into the N170, which had not been studied previously in chronic alcoholism. The N170 is clearly altered in alcoholism, for latency and amplitude. As this is, to our knowledge, the first observation of a modulation in N170 in chronic alcoholism, and as the N170 is influenced by many aspects of the stimuli (familiarity, emotion), these results must be confirmed. Nevertheless, these data are promising because the study of N170 has already given interesting results in the field of psychopathology over recent years, for example in schizophrenia (Herrmann et al., 2004) and autism (Dawson et al., 2005), and because this component is linked to a crucial social ability, which could be impaired in alcoholism, i.e., the processing of faces, and especially emotional faces (Philippot et al., 1999; Townshend and Duka, 2003).

To summarize, our data confirm and generalize previous results by showing that the electrophysiological deficit in alcoholism begins at a much earlier level of cognitive processing than the P300. The deficit is already present for the early visual components (P100), also appears when the stimuli are complex (faces), and has been shown, for the first time, to affect the specific face-processing component (N170).

4.3. The P3b deficit in alcoholism as a possible consequence of earlier damage

Many studies have focused on this component, and their conclusions are clear. Alcoholic individuals have a delayed latency and a reduced amplitude of the P300 (Cohen et al., 1995; Pfefferbaum et al., 1979; Porjesz and Begleiter, 1981; Steinhauer et al., 1987). As described below, our data confirm these results (with a distinction between P3a and P3b), but our main objective was to test a novel hypothesis to interpret this P300 deficit (and particularly the P3b deficit).

First, as the P300 is not a unitary component but is separated into different components according to task requirements (Johnson, 1986), we distinguished P3a and P3b. The absence of any notable effect on P3a was expected in our study. Indeed, the P3a component is maximally elicited in frontal areas when a novel event is introduced in the oddball task. As this was not the case in our paradigm, the P3a had a very weak amplitude for both groups, and it is not surprising that no difference was found between groups. The distinction between P3a and P3b, nevertheless, seems crucial in the field of alcoholism, as these two components may be affected differently by chronic alcoholism (Rodriguez Holguin et al., 1999).

The results obtained for P3b clearly confirm the results of previous studies. The alcoholic group showed significantly delayed latencies and smaller amplitudes than the control group. As for P100 and N170, these data extend the results of previous studies to complex and social stimuli (faces). Our behavioral, as well as electrophysiological, results clearly show that alcoholic individuals have a deficit during all stages of face processing, and this shortfall could have deleterious consequences, as faces are one of the more frequent social stimuli in everyday life.

However, while our results are totally in line with previous ones, showing a damaged P3b in alcoholism, the interpretation usually given to these data, namely a deficit in central nervous system inhibition (e.g. Porjesz and Begleiter, 2003) or in memory/attention (Polich, 2004), does not take into account the earlier ERP components and the fact that a deficit in these components may provoke the defect in P3b. In addition, the main interest of our results lies in the link between the commonly observed P3b deficit and the deficit in earlier processing stages. We hypothesize that the P3b damage may be explained as a consequence of perceptual disturbances rather than as a deficit in this late ERP component per se. This view is strengthened by the highly significant correlations in latency and amplitude among P100, N170 and P3b (see Table 5).

As described above, our study and others have clearly shown that alcoholism leads to deficits in early perceptual processing, as indicated by delayed latencies and reduced amplitudes of P100 and N170. Thus, if we subscribe to a cascade-processing view (Bentin et al., 1999), and if we consider the P3b as the end of a continuum in cognitive processing, the perceptual deficits (P100 and N170) may explain, at least partly, the problems at the decisional stages (P3b).

On the one hand, in an oddball paradigm, the amplitude of the P300 depends on the amount of information extracted from the event (Rugg and Coles, 1995). This assumption clarifies the reduced amplitude observed in alcoholism. As the perceptual processing (indexed by P100 and N170) is damaged, the extraction of the visual information from the stimuli appears deficient, and the perceptual representation of these stimuli is biased. This difficulty will hamper subsequent stages, explaining the reduced P3b amplitude. Thus, we assume that, in alcoholism, the ineffectiveness of the perceptual level provokes a lack of information for further stages, leading to a weaker decisional processing (indexed by a reduction in P3b amplitude).

On the other hand, it is known that the P300 latency can be used as a measure of the stimulus evaluation time (Donchin and Coles, 1988) or as an alternative to response times (McCarthy and Donchin, 1981). Moreover, according to the additive factors method in electroencephalography, if mental processing proceeds in a series of successive parallel and/or sequential stages, then behavioral performance (reflected by reaction times) should be the sum of the durations of each stage (Donders, 1969; Dehaene, 1995), and the P300 latency, considered as the outcome of a continuous process, will sum up all the delays provoked in early stages. This proposal may offer a new explanation of the delayed P300 latency in alcoholism. The discrepancy in the early stages, and particularly at perceptual stage, may create a time-lag that lasts for the whole processing and still affects the decisional stage. In this view, the longer latency of P300 in alcoholism could be, at least partially, the effect of earlier delays and not only a marker of damage to the cognitive processing and abilities associated with the P300.

To summarize, our main suggestion is that the deficit observed for P3b in alcoholism might not be due only to difficulties in the decisional stages. The deficit in latency and amplitude could rather be the consequence of the fact that the P3b, being the end of cognitive processing, accumulates all the delays and discrepancies generated in earlier processing stages. This assumption is in accordance with the results obtained by Foxe et al. (2005) in schizophrenia. Inefficient early processes may explain the failure of later processing, as it has been confirmed in our study by the highly significant correlations between successive ERP components. Nevertheless, these correlations do not allow concluding that there is a causal link between the successive electrophysiological deficits, and it cannot be excluded that another process is affecting early and late ERP components, thus explaining the high correlations observed. Moreover, some studies (i.e. Chan et al., 1986) suggested that earlier components, and particularly P100, could be a "state marker" in alcoholism, while the P300 is considered as a "trait marker". This distinction in the stability of the ERP components as regards the clinical status could invalidate our suggestions. Further studies (using larger groups) are thus needed to confirm our hypothesis, and notably to extend it to other stimulations (particularly to emotional auditory stimuli, which seem impaired in alcoholism (Monnot et al., 2001)).

4.4. Exploring the electrophysiological pattern during the perception of complex social stimuli (human emotional faces) in alcoholism

To the best of our knowledge, this study is the first attempt to explore the processing of complex social stimuli in alcoholism on the basis of an ERP paradigm. Indeed, our stimuli were happy, fearful, sad or neutral faces, while

previous oddball studies in alcoholism used non-social and simple stimuli. It seems well established that recently detoxified alcoholic individuals have a deficit in the decoding of EFE (Kornreich et al., 2002, 2003; Philippot et al., 1999); they overestimate the intensity of the EFE, whatever the actual intensity (even for neutral faces), and they misinterpret these EFE (except for fearful faces). What is more, these individuals are not aware of this deficit. In view of the deleterious effect of this deficit on social life, it appears crucial to define this problem further, by determining the exact differences between alcoholic individuals and control subjects.

As described above, our results show that alcoholic individuals are significantly slower than controls in the processing of faces, at a behavioral (longer response times) and electrophysiological level (delayed P100, N170 and P3b latency). However, we have to define whether this delay is general (i.e., identical for emotional and neutral faces) or specific to emotional faces, or even to some specific emotional categories. Indeed, only limited differences were observed between the two groups on the emotion factor in our results. At a behavioral level, as described in previous studies (Campanella et al., 2004), fearful faces were, for adaptive purposes, the fastest to be detected in both groups. The only difference between alcoholic individuals and controls was the fact that sad faces were detected significantly more slowly than other faces in the alcoholic group, while this effect was not present among controls. This increased difficulty to identify sad faces is in line with previous results (Frigerio et al., 2002) indicating that sadness is frequently misinterpreted in chronic alcoholism and mixed up with other emotions like disgust and anger. Our results underline an electrophysiological correlate of this difficulty to process sadness. The P3b latency is significantly higher for sadness than for other deviant stimuli. Moreover, N170 latency (which was, as shown above, significantly longer for alcoholic individuals than for controls) showed an interaction effect between group and emotion (alcoholic individuals had longer N170 latency for fearful and sad faces than for happy and neutral ones, and this difference was not found among controls). As the N170 is associated with perceptual processing of faces, this result may confirm the assumption (Frigerio et al., 2002) that alcoholic individuals have greater difficulty in detecting negative emotions in comparison with positive ones in the early processing stages. This initial difficulty for negative emotions would persist in later processing stages for sadness but would be compensated for fear as seen in our behavioral results, probably for adaptive reasons. Nevertheless, the differences in N170 latency between emotions were very small (<8 ms) and these results must be confirmed. We detected no other significant electrophysiological differences between groups according to emotional category.

Overall, our data confirm previous results. Alcoholic individuals have no deficit for identification of fearful faces (Philippot et al., 1999), but are significantly slower in the processing of sad faces (Frigerio et al., 2002). It should be noted that our procedure differed from that usually used in behavioral studies; indeed, these studies used explicit emotional judgments (with a qualitative measure of emotion evaluation), while our paradigm elicited implicit emotional processing (the participant did not have to determine which emotion was expressed in the faces but only to detect deviant ones). Moreover, our task was based on speed (with a measure of response time), was quite easy (very low error rate) and used only three emotional categories. Further studies, based on a more difficult task with explicit processing of emotions and using a bigger range of emotions (e.g., anger, disgust), are needed to explore the electrophysiological correlates of the EFE processing deficit in alcoholism.

In conclusion, this study confirms and expands previous results concerning the electrophysiological markers of perceptual deficit in alcoholism; the deficit in the early visual stages (P100) was observed and extended to complex stimuli (namely faces). Moreover, this study described, for the first time, a damage to the ERP component associated with face processing (N170) among alcoholic individuals. Our results also give some preliminary insight into the electrophysiological correlates of the deficit in emotional face processing observed in alcoholism. But the main finding of our study concerns the P300, which constitutes without doubt the most studied ERP component in alcoholism. We hypothesized that the P3b deficit (in amplitude and latency) generally observed in chronic alcoholism may be associated with earlier deficits (and particularly with deficits in perceptual processing) rather than reflecting a problem in the specific processing associated with the P3b. This assumption may influence the interpretation given to the impairment in P300 and encourages future studies to take into account earlier ERP components.

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References

Bagby RM, Taylor GJ, Parker JD. The Twenty-item Toronto Alexithymia Scale–II. Convergent discriminant and concurrent validity. J Psychosom Res 1994;38:33–40.

Baguley IJ, Felmingham KL, Lahz S, Gordan E, Lazzaro I, Schotte DE. Alcohol abuse and traumatic brain injury: effect on event-related potentials. Arch Phys Med Rehabil 1997;78:1248–53.

Balconi M, Lucchiari C. Event-related potentials related to normal and morphed emotional faces. J Psychol 2005;139:176–92.

Beatty WW, Hames KA, Blanco CR, Nixon SJ, Tivis LJ. Visuospatial perception construction and memory in alcoholism. J Stud Alcohol 1996;57:136–43.

Beatty WW, Blanco CR, Hames KA, Nixon SJ. Spatial cognition in alcoholics: influence of concurrent abuse of other drugs. Drug Alcohol Depend 1997;44:167–74.

Beck AT, Steer RA, editors. Beck depression inventory manual. San Antonio, TX: Psychological Corporation; 1987.

Bentin S, Allison T, Puce A, Perez E, McCarthy G. Electrophysiological studies of face perception in humans. J Cogn Neurosci 1996;8:551–65.

Bentin S, Mouchetant-Rostaing Y, Giard MH, Echallier JF, Pernier J. ERP manifestations of processing printed words at different psycholinguistic levels: time course and scalp distribution. J Cogn Neurosci 1999;11:235–60.

Cadaveira F, Grau C, Roso M, Sanchez-Turet M. Multimodality exploration of event-related potentials in chronic alcoholics. Alcohol Clin Exp Res 1991;15:607–11.

Campanella S, Rossignol M, Mejias S, Joassin F, Maurage P, Debatisse D, et al. Human gender differences in an emotional visual oddball task: an event-related potentials study. Neurosci Lett 2004;367:14–8.

Campanella S, Vanhoolandt ME, Philippot P. Emotional deficit in subjects with psychopathic tendencies as assessed by the Minnesota Multiphasic Personality Inventory-2: an event-related potentials study. Neurosci Lett 2005;373:26–31.

Chan YW, McLeod JG, Tuck RR, Walsh JC, Feary PA. Visual evoked responses in chronic alcoholics. J Neurol Neurosurg Psychiatry 1986;49:945–50.

Cohen HL, Wang W, Porjesz B, Begleiter H. Auditory P300 in young alcoholics: regional response characteristics. Alcohol Clin Exp Res 1995;19:469–75.

Contreras CM, Garnica R, Torres-Ruiz A, Arenas C, Marvan ML, Lara H, et al. Visual evoked potentials in a sample of schizophrenic patients. Bol Estud Med Biol 1990;38:22–8.

Dawson G, Webb SJ, McPartland J. Understanding the nature of face processing impairment in autism: insights from behavioral and electrophysiological studies. Dev Neuropsychol 2005;27:403–24.

Debruille JB, Guillem F, Renault B. ERPs and chronometry of face recognition: following-up Seeck et al. and George et al. Neuroreport 1998;9:3349–53.

Dehaene S. Electrophysiological evidence for category-specific word processing in the normal human brain. Neuroreport 1995;6:2153–7.

Desmedt JE. P300 in serial tasks: an essential post-decision closure mechanism. Prog Brain Res 1980;54:682–6.

Donchin E, Coles MGH. Is the P300 component a manifestation of context updating. Behav Brain Sci 1988;11:355–72.

Donders FC. Over de snelheid van psychische processen. Onderzoekingen gedaan in het Physiologisch Laboratorium der Utrechtsche Hoogeschool, 1868-1869. Tweede reeks 1868; II: 92–120. Translated by Koster WG. On the speed of mental processes. Acta Psychol 1969;30:412–31.

Ekman P, Friesen WV, editors. Pictures of facial affect. Palo Alto, CA: Consulting Psychologists Press; 1976.

Esslen M, Pascual-Marqui RD, Hell D, Kochi K, Lehmann D. Brain areas and time course of emotional processing. Neuroimage 2004;21:1189–203.

Fama R, Pfefferbaum A, Sullivan EV. Perceptual learning in detoxified alcoholic men: contributions from explicit memory executive function and age. Alcohol Clin Exp Res 2004;28:1657–65.

Fein G, McGillivray S, Finn P. Mismatch negativity: no difference between treatment-naive alcoholics and controls. Alcohol Clin Exp Res 2004;28:1861–6.

Feldman RS, Philippot P, Custrini RJ. Social competence and non-verbal behaviour. In: Feldman RS, editor. Fundamentals of non-verbal behavior. New York: Cambridge University Press; 1991. p. 329–50.

Fotiou F, Fountoulakis KN, Iacovides A, Kaprinis G. Pattern-reversed visual evoked potentials in subtypes of major depression. Psychiatry Res 2003;118:259–71.

Foxe JJ, Doniger GM, Javitt DC. Early visual processing deficits in schizophrenia: impaired P1 generation revealed by high-density electrical mapping. Neuroreport 2001;12:3815–20.

Foxe JJ, Murray MM, Javitt DC. Filling-in in schizophrenia: a high-density electrical mapping and source-analysis investigation of illusory contour processing. Cereb Cortex 2005;15:1914–27.

Frigerio E, Burt DM, Montagne B, Murray LK, Perrett DI. Facial affect perception in alcoholics. Psychiatry Res 2002;113:161–71.

Gegeshidze K, Tsagareli MG. Influence of emotional words on human visual recognition and brain asymmetry. World J Biol Psychiatry 2004;5:26–32.

George MS, Teneback CC, Malcolm RJ, Moore J, Stallings LE, Spicer KM, et al. Multiple previous alcohol detoxifications are associated with decreased medial temporal and paralimbic function in the postwithdrawal period. Alcohol Clin Exp Res 1999;23:1077–84.

Halgren E, Marinkovic K. Neurophysiological networks integrating human emotions. In: Gazzaniga MS, editor. The cognitive neurosciences. Cambridge: MIT Press; 1995. p. 137–1151.

Hansenne M. Event-related brain potentials in psychopathology: clinical and cognitive perspectives. Psychol Belg 2006;46:5–36.

Hansenne M, Olin C, Pinto E, Pitchot W, Ansseau M. Event-related potentials to emotional and neutral stimuli in alcoholism. Neuropsychobiology 2003;48:77–81.

Harding A, Halliday G, Caine D, Kril J. Degeneration of anterior thalamic nuclei differentiates alcoholics with amnesia. Brain 2000;123:141–54.

Heinze HJ, Mangun GR. Electrophysiological signs of sustained and transient attention to spatial locations. Neuropsychologia 1995;33:889–908.

Herrmann MJ, Weijers HG, Wiesbeck GA, Aranda D, Boning J, Fallgatter AJ. Event-related potentials and cue-reactivity in alcoholism. Alcohol Clin Exp Res 2000;24:1724–9.

Herrmann MJ, Ellgring H, Fallgatter AJ. Early-stage face processing dysfunction in patients with schizophrenia. Am J Psychiatry 2004;161:915–7.

Horowitz LM, Rosenberg SE, Baer BA, Ureno G, Villasenor VS. Inventory of interpersonal problems: psychometric properties and clinical applications. J Consult Clin Psychol 1988;56:885–92.

Javitt DC. Intracortical mechanisms of mismatch negativity dysfunction in schizophrenia. Audiol Neurootol 2000;5:207–15.

Javitt DC, Doneshka P, Zylberman I, Ritter W, Vaughan Jr HG. Impairment of early cortical processing in schizophrenia: an event-related potential confirmation study. Biol Psychiatry 1993;33:513–9.

Jimenez-Escrig A, Fernandez-Lorente J, Herrero A, Baron M, Lousa M, de Blas G, et al. Event-related evoked potential P300 in frontotemporal dementia. Dement Geriatr Cogn Disord 2002;13:27–32.

Johnson R. A triarchic model of P300 amplitude. Psychophysiology 1986;23:367–84.

Kathmann N, Soyka M, Bickel R, Engel RR. ERP changes in alcoholics with and without alcohol psychosis. Biol Psychiatry 1996;39:873–81.

Knight RT. Evoked potential studies of attention capacity in human frontal lobe lesions. In: Levin HS, Eisenberg HM, Benton AL, editors. Frontal lobe function and dysfunction. New York: Oxford University Press; 1991. p. 39–153.

Kornreich C, Blairy S, Philippot P, Dan B, Foisy ML, Hess U, et al. Impaired emotional facial expression recognition in alcoholism compared with obsessive-compulsive disorder and normal controls. Psychiatry Res 2001;102:235–48.

Kornreich C, Philippot P, Foisy ML, Blairy S, Raynaud E, Dan B, et al. Impaired emotional facial expression recognition is associated with interpersonal problems in alcoholism. Alcohol Alcohol 2002;37:394–400.

Kornreich C, Foisy ML, Philippot P, Dan B, Tecco J, Noël X, et al. Impaired emotional facial expression recognition in alcoholics opiate dependence subjects methadone maintained subjects and mixed alcohol-opiate antecedents subjects compared with normal controls. Psychiatry Res 2003;119:251–60.

McCarthy G, Donchin EA. Metric for thought: a comparison of P300 latency and reaction time. Science 1981;211:77–80.

McNamara P, Blum D, O'Quin K, Schachter S. Markers of cerebral lateralization and alcoholism. Percept Mot Skills 1994;79:1435–40.

Miyazato Y, Ogura C. Abnormalities in event-related potentials: N100 N200 and P300 topography in alcoholics. Jpn J Psychiatry Neurol 1993;47:853–62.

Monnot M, Nixon S, Lovallo W, Ross E. Altered emotional perception in alcoholics: deficits in affective prosody comprehension. Alcohol Clin Exp Res 2001;25:362–9.

Moreno CR, Borod JC, Welkowitz J, Alpert M. Lateralization for the expression and perception of facial emotion as a function of age. Neuropsychologia 1990;28:199–209.

Nicolas JM, Estruch R, Salamero M, Orteu N, Fernandez-Sola J, Sacanella E, et al. Brain impairment in well-nourished chronic alcoholics is related to ethanol intake. Ann Neurol 1997;41:590–8.

Nixon SJ, Tivis R, Parsons OA. Interpersonal problem-solving in male and female alcoholics. Alcohol Clin Exp Res 1992;16:684–7.

Ogura C, Miyazato Y. Cognitive dysfunctions of alcohol dependence using event related potentials. Arukoru Kenkyuto Yakubutsu Ison 1991;26:331–40.

Pfefferbaum A, Horvath TB, Roth WT, Kopell BS. Event-related potential changes in chronic alcoholics. Electroencephalogr Clin Neurophysiol 1979;47:637–47.

Philippot P, Kornreich C, Blairy S, Baerts I, Den Dulk A, Le Bon O, et al. Alcoholics' deficits in the decoding of emotional facial expression. Alcohol Clin Exp Res 1999;23:1031–8.

Polich J. Clinical application of the P300 event-related brain potential. Phys Med Rehabil Clin N Am 2004;15:133–61.

Porjesz B, Begleiter H. Human evoked brain potentials and alcohol. Alcohol Clin Exp Res 1981;5:304–17.

Porjesz B, Begleiter H. Alcoholism and human electrophysiology. Alcohol Res Health 2003;27:153–60.

Porjesz B, Rangaswamy M, Kamarajan C, Jones KA, Padmanabhapillai A, Begleiter H. The utility of neurophysiological markers in the study of alcoholism. Clin Neurophysiol 2005;116:993–1018.

Rodriguez Holguin S, Porjesz B, Chorlian DB, Polich J, Begleiter H. Visual P3a in male alcoholics and controls. Alcohol Clin Exp Res 1999;23:582–91.

Roquelaure Y, Le Gargasson JF, Kupper S, Girre C, Hispard E, Dally S. Alcohol consumption and visual contrast sensitivity. Alcohol Alcohol 1995;30:681–5.

Rugg MD, Coles MGH, editors. Electrophysiology of mind. Oxford: Oxford University Press; 1995.

Schandler SL, Thomas CS, Cohen MJ. Spatial learning deficits in preschool children of alcoholics. Alcohol Clin Exp Res 1995;19:1067–72.

Seeck M, Michel CM, Mainwaring N, Cosgrove R, Blume H, Ives J, et al. Evidence for rapid face recognition from human scalp and intracranial electrodes. Neuroreport 1997;8:2749–54.

Smeyers P. Studies of evoked potentials in children with the syndrome of attention deficit and hyperactivity. Rev Neurol 1999;28:173–6.

Spielberger DC, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA, editors. Manual for the state-trait anxiety inventory. Palo Alto, CA: Consulting Psychology Press; 1983.

Steinhauer SR, Hill SY, Zubin J. Event-related potentials in alcoholics and their first-degree relatives. Alcohol 1987;4:307–14.

Stewart SA. The effects of benzodiazepines on cognition. J Clin Psychiatry 2005;66:9–13.

Sullivan EV, Pfefferbaum A. Neurocircuitry in alcoholism: a substrate of disruption and repair. Psychopharmacology (Berl) 2005;180:583–94.

Sullivan EV, Fama R, Rosenbloom MJ, Pfefferbaum A. A profile of neuropsychological deficits in alcoholic women. Neuropsychology 2002;16:74–83.

Townshend JM, Duka T. Mixed emotions: alcoholics' impairments in the recognition of specific emotional facial expressions. Neuropsychologia 2003;41:773–82.

van den Bosch RJ. Contingent negative variation: components and scalp distribution in psychiatric patients. Biol Psychiatry 1984;19:963–72.

Verleger R. On the utility of P3 latency as an index of mental chronometry. Psychophysiology 1997;34:131–56.

Wegner AJ, Gunthner A, Fahle M. Visual performance and recovery in recently detoxified alcoholics. Alcohol Alcohol 2001;36:171–9.

Zinn S, Bosworth HB, Edwards CL, Logue PE, Swartzwelder HS. Performance of recently detoxified patients with alcoholism on a neuropsychological screening test. Addict Behav 2003;28:837–49.