



Dysfunctional reward processing in male alcoholics: An ERP study during a gambling task

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ARTICLE INFO

Article history:

Received 10 June 2009

Received in revised form 21 November 2009

Accepted 26 November 2009

Keywords:

Outcome-related negativity

Outcome-related positivity

Error-related negativity

Medial frontal negativity

N2

P3

Impulsivity

Alcoholism

Reward deficiency syndrome

ABSTRACT

Objective: A dysfunctional neural reward system has been shown to be associated with alcoholism. The current study aims to examine reward processing in male alcoholics by using event-related potentials (ERPs) as well as behavioral measures of impulsivity and risk-taking.

Methods: Outcome-related negativity (ORN/N2) and positivity (ORP/P3) derived from a single outcome gambling task were analyzed using a mixed model procedure. Current density was compared across groups and outcomes using standardized low resolution electromagnetic tomography (sLORETA). Behavioral scores were also compared across groups. Correlations of ERP factors with behavioral and impulsivity factors were also analyzed.

Results: Alcoholics showed significantly lower amplitude than controls during all outcome conditions for the ORP component and decreased amplitude during the loss conditions for the ORN component. Within conditions, gain produced higher amplitudes than loss conditions. Topographically, both groups had an anterior focus during loss conditions and posterior maxima during gain conditions, especially for the ORN component. Decreased ORP current density at cingulate gyrus and less negative ORN current density at sensory and motor areas characterized the alcoholics. Alcoholics had higher levels of impulsivity and risk-taking features than controls.

Conclusions: Deficient outcome/reward processing and increased impulsivity and risk-taking observed in alcoholics may be at least partly due to reward deficiency and/or dysfunctional reward circuitry in the brain, suggesting that alcoholism can be considered as part of the cluster of the reward deficiency syndrome (RDS).

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1. Introduction

Alcoholism has been considered to be a complex neuropsychiatric condition with multifactorial etiology, and understanding of this disorder has warranted studies of diverse neurobiological methods. Event-related potentials (ERPs), derived from the scalp-recorded electroencephalogram (EEG) during a task condition, is considered to be one of the most effective and useful mea-

Abbreviations: ORN, outcome-related negativity; ORP, outcome-related positivity; ERN, error-related negativity; MFN, medial frontal negativity; SOG task, single outcome gambling task; BIS, Barratt impulsivity scale; TRB scores, task-related behavioral scores; sLORETA, standardized low resolution electromagnetic tomography.

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sure to understand the neurocognitive dysfunctions in alcoholism (Begleiter et al., 1980, 1984; Porjesz et al., 2005b). The amplitude reduction of the P3 component of the ERPs, a robust positivity around 300 ms, has been considered to be a marker for alcoholism and risk (Begleiter et al., 1984; Porjesz and Begleiter, 1990; Porjesz et al., 1998). Further, this 'P3-amplitude reduction' was also found to be common for a host of similar disorders called externalizing/disinhibitory disorders that often coexist with alcoholism (Patrick et al., 2006; Carlson et al., 2007).

Recent imaging studies have examined the brain reward system in alcoholics and suggested that alcoholism may be a part of a spectrum of disorders subsumed under a reward deficiency syndrome (RDS), as alcoholics showed abnormalities in the brain structures related to the reward network (Wrase et al., 2007; Makris et al., 2008; de Greck et al., 2009; Tanabe et al., 2009). ERP studies can further characterize the "millisecond-specific" brain dynamics of reward processing as well as deficiency in alcoholics. Although several ERP studies on reward processing (during monetary reward conditions) in healthy human subjects have been

previously documented since the early 1980s (e.g., Homberg et al., 1980, 1981; Begleiter et al., 1983; Otten et al., 1995; Ramsey and Finn, 1997; Gehring and Willoughby, 2002; Yeung and Sanfey, 2004; Hajcak et al., 2006; Kamarajan et al., 2009), there have been very few ERP studies on the reward/outcome processing in individuals diagnosed with alcohol dependence. To our knowledge, there have been only two ERP studies carried out on alcoholics during reward processing. Probably the first study of this kind was done by Porjesz et al. (1987a), who reported decreased P3 amplitude in response to incentive stimuli in abstinent alcoholics. More recently, using the balloon analogue risk task (BART) which measures risk-taking propensity, Fein and Chang (2008) reported smaller amplitude in feedback negativity in treatment-naïve alcoholics with a greater family history density of alcohol problems compared to controls. Although these findings lend support to the notion that alcoholics may have a specific deficiency in reward processing, the nature of these deficits are still not very clear due to the paucity of such studies in alcoholics. Further, there have been as yet no studies of reward processing in alcoholics using a gambling paradigm, and the present study is the first of its kind.

In recent years, a predominant electrophysiological task paradigm has been used to study reward processing, namely the “Gambling Paradigm” and the two ERP components that have been reported to occur during outcome processing are the negativity analogous to N2 (between 200 and 300 ms) and the positivity analogous to P3 (between 300 and 600 ms) as shown in Fig. 1 (Gehring and Willoughby, 2002; Luu et al., 2004; Nieuwenhuis et al., 2004, 2005b; Yeung and Sanfey, 2004; Cohen et al., 2007; Mennes et al., 2008; Kamarajan et al., 2009). While these components have been referred to by different names, we introduced and justified the terms ORN and ORP in our earlier works on outcome processing (Kamarajan et al., 2008, 2009), respectively, in the gambling task. In our earlier study, we analyzed the ERP waveforms, topography and functional significance of the ORN and ORP components in healthy individuals using a single outcome gambling (SOG) task that involved monetary losses and gains (Kamarajan et al., 2009). To our knowledge, only very few studies have examined the ERP components of monetary reward processing in alcoholics, and the current study is the first study on alcoholics using a typical “gambling paradigm”.

The main goal of the present study is to examine reward/outcome processing in alcohol dependent individuals as compared to healthy controls while they subjectively experience monetary loss and gain during the performance of a gambling task. Since

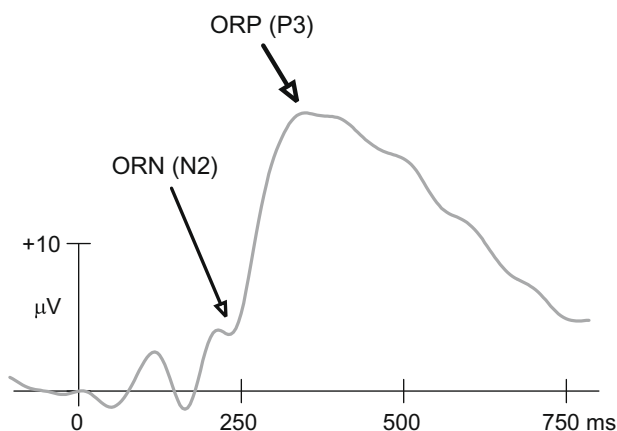


Fig. 1. Typical ERP waveform at the CZ electrode as produced by the single outcome gambling task. The ORN component that occurs approximately between 200 and 275 ms and the ORP component that lies approximately between 275 and 700 ms are considered to be important in the evaluative processes during loss and gain.

impulsivity is an important component of alcoholism as depicted both by models of disinhibition (Gorenstein and Newman, 1980; Begleiter and Porjesz, 1999; Krueger et al., 2002) as well as models of reward deficiency syndrome (Blum et al., 2000; Bowirrat and Oscar-Berman, 2005), we studied impulsivity in detail, both as a state measure (i.e., the task performance) and as a trait measure using Barratt impulsiveness scale (BIS) (Barratt, 1985; Patton et al., 1995). Although previous findings reported that ORN was localized to medial frontal areas (Gehring and Willoughby, 2002; Nieuwenhuis et al., 2004; Masaki et al., 2006), our earlier study using sLORETA (standardized low resolution electromagnetic tomography) (Pascual-Marqui, 2002) in healthy individuals showed that ORN during the loss conditions had a medial frontal source while the ORN for the gain conditions primarily had a medial posterior source (Kamarajan et al., 2009). Therefore, in the current study, we have used the sLORETA to further understand the possible alterations in the current density and/or source activities of ORN and ORP in alcoholic individuals. In addition, since there were distinct gender differences observed in the electrophysiological indices of reward processing (Kamarajan et al., 2008, 2009), it was decided to analyze each gender separately. Therefore, the present study has been designed to examine the ERP components only in male alcoholics (as there were too few female alcoholics to have a combined sample at the time of the study). Our hypotheses were the following: (1) alcoholics will show decreased amplitude in both ORN and ORP components; (2) the source activity of the reward processing will be localized (by the sLORETA) to regions of frontal lobes and reward circuitry, (3) alcoholics will have higher impulsivity, increased risk-taking and decreased cognitive control on the behavioral measures; and (4) lower amplitude in ORN and ORP components will be correlated with increased impulsivity and risk-taking. It is expected that alcoholics will demonstrate deficient reward processing in terms of decreased amplitude in both ORN and ORP components, apart from significant differences in topography, current density, and in behavioral measures of impulsivity and risk-taking.

2. Methods

2.1. Participants

A sample of 40 male alcoholics with an age range of 24–46 years (Mean = 38.28, SD = 6.44) and 40 healthy male controls aged between 18 and 35 years (Mean = 21.07, SD = 3.36) were selected. Control subjects were recruited through newspaper advertisements and notices. The alcoholic group consisted of alcohol dependent individuals who completed the de-addiction program in the treatment centers, and were abstinent from alcohol intake at least for 28 days before the EEG recording. The Bard/Porjesz adult alcoholism battery (BAAB), a semi-structured clinical assessment schedule based on DSM IV, was used to obtain the clinical data related to alcohol dependence and alcohol-related medical problems. The patients who were receiving treatment medication, such as antabuse and/or psychoactive drugs, were excluded from the study to avoid the possible interaction of drugs with the EEG profile. The participants did not have any other personal and/or family history of major medical or psychiatric disorders and substance-related addictive illnesses. Subjects who had positive findings (for their recent drug use within 48 h) in the urine screen and Breathalyzer test were excluded from the study. Subjects with hearing or visual impairment, liver disease, or head injury were also excluded from the study. The individuals who scored less than 21 on the mini mental state examination (MMSE) (Folstein et al., 1975) were excluded from the study in order to rule out possible cognitive deficits due to an organic pathology. The MMSE scores in the final

sample ranged from 21 to 30 with a mean of 27.77 for alcoholics while controls had a score range of 23–30 with a mean of 27.88. Experimental procedures and ethical guidelines were in accordance with approval of the institutional review board (IRB).

2.2. The gambling task

The single outcome gambling (SOG) task used in the study is illustrated in Fig. 2. At the start of each trial, a *choice stimulus* (CS) with two numbers 10 (left box) and 50 (right box), representing the monetary value in US cents, was displayed for 800 ms. The subject was instructed to select one number by pressing the left button for '10' or the right button for '50'. The *outcome stimulus* (OS) appeared 700 ms after the CS offset and lasted 800 ms. The OS comprised the selected number inside a green box (to indicate a gain) or a red box (to indicate a loss). Thus, there were four possible outcomes: gain 50 (+50), loss 50 (−50), gain 10 (+10), and loss 10 (−10). The subject had to respond by selecting either 10¢ or 50¢ within 1000 ms of CS onset. The OS would not appear if the subject did not respond/select within the specified time (1000 ms), and the next trial would commence. While the occurrence of loss (in red) or gain (in green) in the OS was maintained at equal probability (50%), the order of appearance was pseudo-randomized. Each subject had the identical presentation (i.e., there was no counter-balancing of trials). The subjects were not made aware of the probability of loss/gain or sequence of the task prior to the experiment. There were a total of 172 trials and the inter-trial interval was 3000 ms throughout the experiment. The task was presented in two blocks with each block (86 trials) lasting for 4 min; the procedure was identical in both blocks. At the end of each block, the status of overall 'loss' or 'gain' for the entire block was displayed on the monitor screen. The next block was started by the operator when the subject was ready. The instruction to the subject was as follows: "This task is a gambling type task in which you will be playing with 10 and 50 cents in each trial of the task. Two boxes with the numbers 10 and 50 will appear on the screen. Button #1 corresponds to the number 10 and button #4 corresponds to the number 50. When you see the numbers, select one of them quickly by pressing the appropriate button. Following your selection, the number you choose will reappear in a red box or a green box. If the number you selected is in a green box you gained that amount of money. If it is in a red box you lost that amount. The experiment is conducted in two blocks, and you will see a message telling you whether you're winning or losing money after each

block. Please try not to blink and sit as still as possible." At the end of the experiment, all the participants received the monetary reward of the total amount they had accrued during the gambling trials.

2.3. Measures of impulsivity

There were two types of impulsivity measures used in the study: (1) Barratt impulsiveness scale, version 11 (BIS-11) (Barratt, 1985; Patton et al., 1995), a self-rated measure that assesses trait-related impulsivity, and (2) task-related behavioral (TRB) scores as derived from the performance of the gambling task. The BIS-11 consists of thirty items yielding a total score, and additional scores for three subcategories: motor impulsivity (acting without thinking), cognitive impulsivity (making decisions quickly), and non-planning (lack of prior planning or of future orientation). The TRB scores were of three categories: (1) reaction time (RT) for the task conditions and responses, (2) selection frequency (SF) – number of times a particular amount (10 or 50) was chosen – following a single trial of loss and following two consecutive trials of loss (based on the absolute score), and (3) SF followed by a losing or gaining trend (based on the cumulative score) in the previous 2–4 trials. The gaining and losing trends were computed based on the resultant outcome of the cumulative account of the preceding outcomes. For example, if the previous three outcomes were −10, −10, and +50, then the trend was considered to be a *gain* (of 30¢), whereas if the previous three outcomes were +10, +10, and −50 then the trend would be considered as a *loss* (of 30¢).

2.4. EEG data acquisition and signal analysis

EEG was recorded on a Neuroscan system (Version 4.1) using a 61-channel electrode cap (see Fig. 3), referenced to the tip of the nose with a ground electrode at the forehead. A supraorbital vertical lead and a horizontal lead on the external canthus of the left eye recorded the electro-oculogram (EOG). Electrode impedance was maintained below 5 k Ω . The EEG signals were recorded continuously with a bandpass at 0.02–100 Hz and amplified 10,000 times using a set of amplifiers (Sensorium, Charlotte, VT). EEG segments that exceeded $\pm 75 \mu\text{V}$ threshold were rejected as artifacts. The grand averaged ERPs of each individual were also screened visually for further artifact rejection. Although the entire experiment consisted of two identical blocks, the analysis was done on all trials by combining the trials from both blocks. The statistical

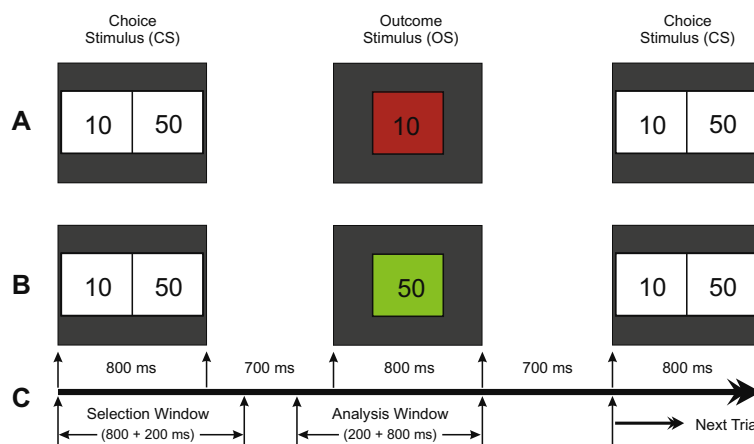


Fig. 2. Schematic illustration of the single outcome gambling task used in this experiment. One of the two numbers (10 or 50) in the choice stimulus (800 ms) is to be selected by the subject. The selected amount appears as the outcome stimulus (800 ms) either in red (to indicate a loss) or in green (to indicate a gain). (A) a typical trial showing a loss of 10 in red box; (B) another trial having a gain of 50 in green box; and (C) the time duration for the task events: the selection window (1000 ms) wherein the subject selects either of the numbers and the analysis window (200 ms pre-stimulus + 800 ms post-stimulus) represents the time segment that was used for the ERP analysis.

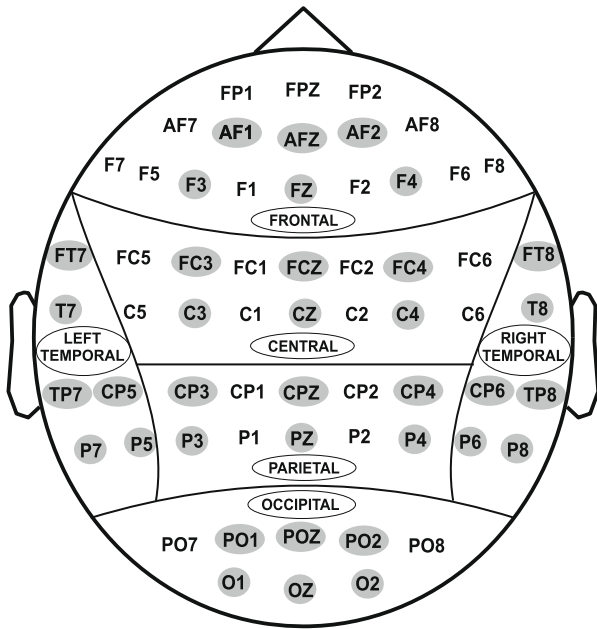


Fig. 3. Sixty-one electrodes as recorded from the surface of the scalp. For statistical analyses, 36 electrodes (as highlighted) were selected to represent six electrodes in six regions of the brain viz., frontal, central, parietal, occipital, left-temporal and right-temporal.

analyses were performed on the amplitude and latency data of ORN and ORP components.

The “outcome window” (1500 ms) began with the onset of OS, as the objective of the study was to analyze the outcome-related potentials of the ERPs (see Fig. 2). The ORP amplitude was measured as the voltage difference from the pre-stimulus baseline (200 ms) to the largest positive going peak in the waveforms filtered at 0.25–32.0 Hz in the latency window 275–700 ms after the stimulus onset, whereas the ORN was measured as a baseline-trough in the waveforms filtered at 2.0–16.0 Hz within post-stimulus 200–275 ms (Fig. 1). Since the ORP is very robust and prominent (compared to the ORN) and also involves slow wave activity (less than 2 Hz), the ORN component, which is often small and subtle, gets subsumed by the ORP component and is not apparent in the ERP signal. A filter setting of 2.0–16.0 Hz makes the ORN component relatively more prominent than with the regular filter setting of P3/ORP component. This approach of removing the slow wave activity has already been employed by several studies on error-related negativity (ERN) paradigms. For example, Luu et al. (2004) filtered the ERPs within a 4–12 Hz bandpass, while Trujillo and Allen (2007) used 3–13 Hz bandpass filter in order to optimize ERN component. In our previous study in healthy normals, we used a filter at 2.0–16.0 Hz for plotting the ORN topography (Kamarajan et al., 2009).

2.5. Current density analysis using sLORETA

Current density and source activity during reward processing were examined using sLORETA to identify brain regions involved and also to localize the brain deficits in alcoholics. The sLORETA is considered to be a successful solution to the inverse problem, i.e., the problem of localization of brain activity in the EEG and EMG data (Pascual-Marqui, 1999, 2002). Detailed description and technical information on sLORETA have been provided by its author, R.D. Pascual-Marqui, at: <http://www.unizh.ch/keyinst/NewLORETA/LORETA01.htm>. In the present study, the current den-

sity maps were created for the grand mean data of each condition in alcoholics and controls separately. Then, the time frames that represented the peak ORN and ORP activity were compared across groups and across conditions using the independent and paired *t*-tests, respectively. Statistical analyses involved a voxel-wise statistical non-parametric mapping (SnPM) with 5000 permutations. The *t*-values in all 2394 voxels were plotted and the *t*-values above the critical threshold (i.e., significance level) were highlighted (based on the color scale) to show the areas of significance. These values are calculated via a randomization method (Nichols and Holmes, 2002), and the SnPM approach controls for Type I error (Flor-Henry et al., 2004).

2.6. Statistical analysis of ERP data

Thirty-six electrodes, as indicated in Fig. 3, were grouped in to six scalp regions for the statistical analyses. The ERP data were analyzed by performing a linear mixed model of the Analysis of Variance (ANOVA) using the Statistical Analysis System (SAS, version 9.2) (SAS Institute Inc., NC 27513, USA). The application of mixed effects model of the Analysis of Variance (ANOVA) in our study is due to its several advantages over the traditional methods of ANOVA (Gueorguieva and Krystal, 2004), and has been successfully implemented by researchers to analyze EEG data (Bachman et al., 2008). The covariance structure used in the model was ‘Compound Symmetry’ which has a constant variance and constant covariance. The model included five factors as fixed effects: valence (loss and gain), amount (50¢ and 10¢), region (frontal, central, parietal, occipital, left-temporal, and right-temporal), electrode (six electrodes) as within-subjects factors, and group (control and alcoholic) as a between-subjects factor. In order to keep the number of electrodes equal across each region, only six electrodes from each region were selected (as some regions had only six electrodes). We treated electrodes as nested within region, as we were interested in the “region” effects but not in the individual “electrode” effects. Age was included as a covariate in the ANOVA model as age as a factor is known to have a significant influence on the ERP measures (Walhovd et al., 2008).

The BIS and TRB variables were compared across groups using *t*-tests. Based on the analyses done in our previous study (Kamarajan et al., 2009), the correlations between ERP variables and Behavioral measures were analyzed in a two-step procedure: (1) factor analysis was performed in order to reduce the ERP variables ($N = 144$) as well as the TRB variables ($N = 24$) into a few specific factors; and (2) Pearson (bivariate) correlations were performed to analyze the relationship between behavioral factors and ERP factors. ERP variables for the factor analysis comprised nine electrodes (F3, FZ, F4, C3, CZ, C4, P3, PZ, and P4), four outcomes (+50, +10, −50, and −10), two components (ORN, ORP), and two measures (amplitude and latency). For factor analysis, only nine electrodes were selected for two reasons: (1) we expected that factors comprising fewer but representative electrodes of maximum amplitude would facilitate the interpretation of the components and their correlation with other factors (due to data reduction), and (2) the topography of ORN and ORP components suggested three major regions, viz., frontal, central, and parietal areas. The factors were extracted using principal component analysis (PCA), and varimax rotation with Kaiser normalization was performed. The optimal number of factors was determined based on the shape of the scree plots (i.e., components lie on the steep slope). However, factor analysis was not done on BIS scores as they were already categorized into three distinct factors (Barratt, 1985; Patton et al., 1995).

3. Results

3.1. ERP waveforms and topography

The ERP waveforms of comparisons among conditions in each group and between groups in each condition have been illustrated in Fig. 4. The gain conditions (+50 and +10) had higher ORP amplitude than loss conditions in both groups. Alcoholics showed decreased ORP amplitude compared to controls in both loss and gain conditions. Although there were no significant condition differences, the ORN component showed a prominent group differences wherein the alcoholic group had a smaller ORN component than the control group.

On the other hand, the topographic maps of both ORN and ORP, derived from the waveforms filtered at 2.0–16.0 Hz and 0.25–16.0, respectively, showed significant group as well as condition differences. The loss conditions had anterior maxima while the gain conditions had posterior maxima, especially for the ORN component. Alcoholics showed decreased amplitude in both ORN and ORP components in all conditions. While the amplitude differences were robust, topographic differences were not prominent.

3.2. Current density across groups and conditions

The results of the voxel-by-voxel comparison of current density across groups and conditions are shown in Fig. 6 and Table 1. For the ORN component, alcoholics showed less negative current density compared to controls at postcentral gyrus, inferior frontal gyrus and precentral gyrus. In the ORP component, alcoholics showed decreased current density at anterior cingulate gyrus (BA-24). Differences between valences were significant only in the ORP component, wherein gain showed more activity than loss at posterior cingulate area (BA-23) in controls and at the insula region in alcoholics. However, current density differences were not significant for amount.

3.3. Mixed model ANOVA

Results of the mixed model ANOVA have been tabulated in Table 2. Group as a main effect was not significant. Main effects of valence, amount and region were significant. Gain condition as well as large amount (50) had higher amplitude and shorter latencies than loss condition and small amount (10), respectively. Frontal, central and parietal areas had higher amplitudes and shorter latencies.

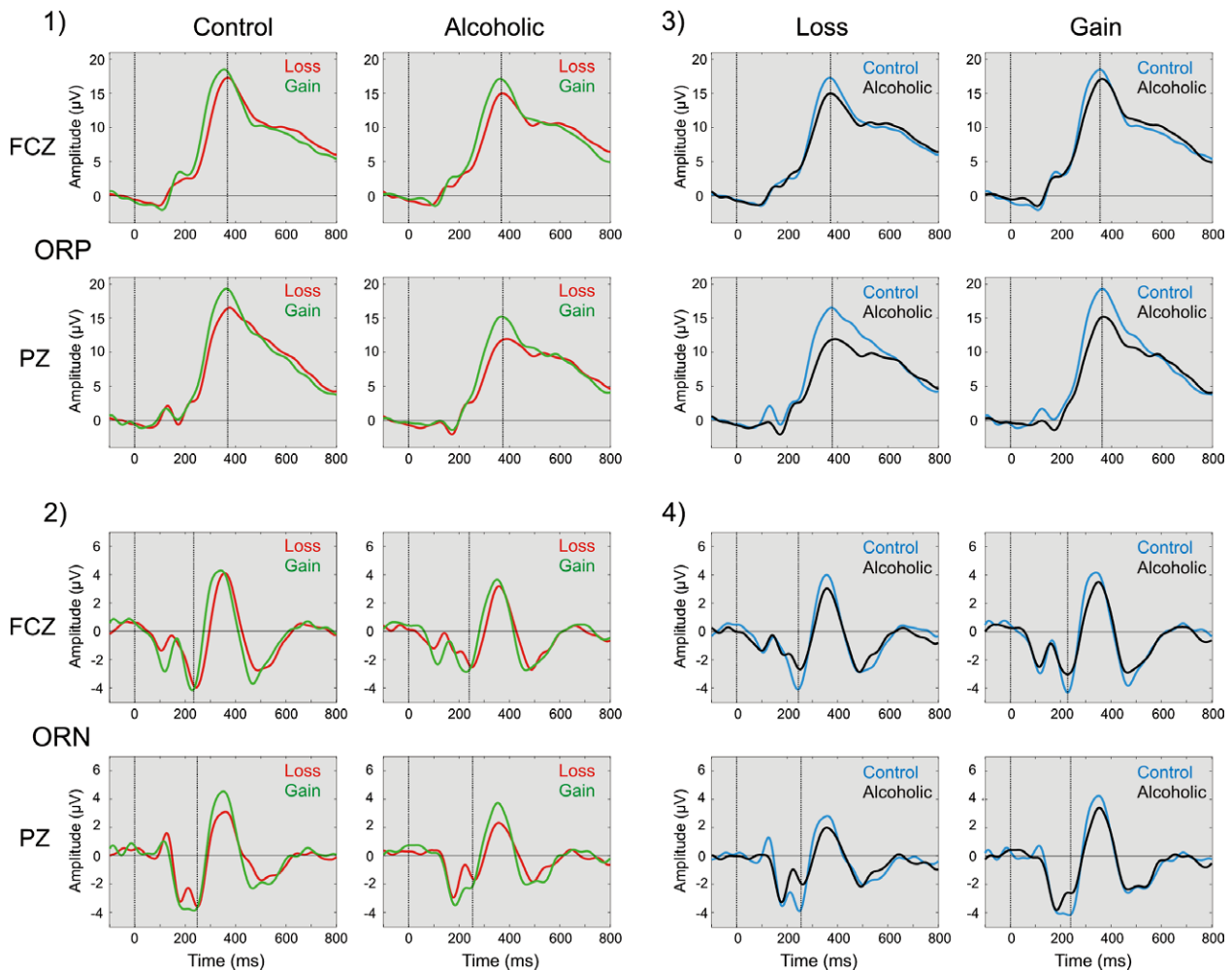


Fig. 4. The ERP waveforms compared across conditions (loss vs. gain) in each group (panels 1 and 2) and across groups (control vs. alcoholic) in each condition (panels 3 and 4) at FCZ and PZ electrodes at filter setting for ORP (0.25–16.0 Hz) shown in panels 1 and 3) and ORN (2.0–16.0 Hz) as shown in panels 2 and 4), respectively. ERPs during the gain condition (+50) have higher ORP amplitudes than the loss condition (–50) in both groups, more robust in the PZ electrode. Alcoholics have decreased ORP amplitude compared to controls in both loss and gain conditions, especially at PZ electrode. ORN component showed only a group difference wherein alcoholics had a smaller ORN component than controls.

Table 1

The voxel-by-voxel comparison of current density across groups and conditions. For ORN, alcoholics showed less negative current density than controls at postcentral gyrus, inferior frontal gyrus and precentral gyrus. For ORP, alcoholics showed decreased current density at cingulate gyrus. Differences between valences were significant only in the ORP component. Neither ORN nor ORP was significant between the amounts 50 and 10.

ERP component	Comparison between	Factor compared	Direction of significance	MNI coordinates [BA]	Brain area	Lobe	
ORN	Ctl × Alc	Loss	Ctl < Alc	−35, −30, 45 [2]	Postcentral gyrus	Parietal lobe	
		Gain	Ctl < Alc	−45, 5, 35 [9]	Inferior frontal gyrus	Frontal lobe	
		50	Ctl < Alc	−50, −5, 25 [6]	Precentral gyrus	Frontal lobe	
		10	Ctl < Alc	−45, 0, 40 [6]	Precentral gyrus	Frontal lobe	
	Loss × Gain	Ctl	None	–	–	–	
		Alc	None	–	–	–	
	50 × 10	Ctl	None	–	–	–	
		Alc	None	–	–	–	
	ORP	Ctl × Alc	Loss	Alc < Ctl	−5, −5, 35 [24]	Anterior Cingulate Gyrus	Limbic system
			Gain	Alc < Ctl	−5, −5, 30 [24]	Anterior Cingulate Gyrus	Limbic system
50			Alc < Ctl	−5, −5, 35 [24]	Anterior Cingulate Gyrus	Limbic system	
10			Alc < Ctl	−5, −10, 30 [24]	Anterior Cingulate Gyrus	Limbic system	
Loss × Gain		Ctl	Loss < Gain	−5, −35, 25 [23]	Posterior Cingulate Gyrus	Limbic system	
		Alc	Loss < Gain	−35, −25, 10 [13]	Insula	Sub-lobar	
50 × 10		Ctl	None	–	–	–	
		Alc	None	–	–	–	

Ctl, control; Alc, alcoholic; BA, brodmann area; None, not significant.

cies than occipital, left-temporal and right-temporal areas. Group × outcome interaction was significant in all four measures while group × amount interaction was significant only for the amplitudes of ORN and ORP. Group × valence × region was significant only for the ORN measures, and the group × amount × region was not significant in any of the ERP measures. Pair-wise comparisons were done to explain these findings (see Figs. 7 and 8). Comparisons of ORN and ORP amplitudes across groups in each outcome condition at different electrode sites are illustrated in Fig. 7 along with Bonferroni adjusted significance levels. Alcoholics showed significantly lower ORP amplitude during all outcome conditions and decreased ORN amplitude during loss conditions (−50 and −10). Latencies showed no group differences (not shown).

Comparisons across valences (loss vs. gain) and across amounts (50 vs. 10) are illustrated in Fig. 8 along with Bonferroni adjusted significance levels. For the ORP measures, both gain and large amount '50' conditions showed significantly higher amplitude and shorter latency than loss and small amount '10' conditions, respectively, in control as well as alcoholic groups. The findings in ORN measures are: (1) amplitude differences between valences (loss vs. gain) were obvious only in the alcoholic group (panel A-1),

whereas latency differences were explicit in both groups (panel B-1); and (2) alcoholics, in contrast to controls, showed more ORN amplitude for small amount '10' than for large amount '50' (panel A-3).

3.4. Group differences in behavioral variables

The statistical comparison of behavioral variables between controls and alcoholics is shown Table 3. Alcoholics scored significantly higher than controls in non-planning and total score of BIS. There was also a trend towards significance in motor impulsivity (i.e., loss of significance due to Bonferroni correction), and in selection frequency for '10' after a loss trend of previous two trials and for '50' after a loss trend of previous three trials.

3.5. Factor extraction and correlation among factors

The PCA-based factors obtained from TRB as well as ERP variables are explained in Table 4. Total variance accounted for the TRB and ERP factors were 77.34% and 52.49%, respectively. The three TRB factors were: (1) eight variables representing reaction

Table 2

Results of the mixed model ANOVA, showing the main and interaction effects (rows) in terms of *F*-values and *p*-values for ORN and ORP measures (columns). Group × valence interaction was significant in all four measures while group × amount interaction was significant only for the amplitudes of ORN and ORP.

	ORN amplitude		ORN latency		ORP amplitude		ORP latency	
	<i>F</i>	<i>p</i>	<i>F</i>	<i>p</i>	<i>F</i>	<i>p</i>	<i>F</i>	<i>p</i>
Group	3.83	0.0541	1.98	0.1636	0.19	0.6630	0.00	0.9731
Valence	87.60	<0.0001***	880.46	<0.0001***	599.67	<0.0001***	875.46	<0.0001***
Amount	1.11	0.2963	1.25	0.2661	380.42	<0.0001***	22.90	<0.0001***
Region	119.37	<0.0001***	61.67	<0.0001***	786.77	<0.0001***	164.43	<0.0001***
Group × valence	96.54	<0.0001***	13.51	0.0004***	23.90	<0.0001***	19.87	<0.0001***
Group × amount	44.93	<0.0001***	2.32	0.1316	18.15	<0.0001***	0.18	0.6766
Group × region	10.36	<0.0001***	1.36	0.2378	63.75	<0.0001***	6.13	<0.0001***
Valence × amount	14.58	0.0003***	39.06	<0.0001***	41.52	<0.0001***	36.96	<0.0001***
Valence × region	24.98	<0.0001***	3.05	0.0103*	6.56	<0.0001***	3.67	0.0029**
Amount × region	4.00	0.0015**	1.61	0.1558	3.94	0.0017**	0.80	0.5475
Group × valence × amount	12.48	0.0007***	9.44	0.0029**	7.21	0.0089**	0.09	0.7646
Group × valence × region	3.95	0.0017**	3.20	0.0076**	0.16	0.9781	0.94	0.4545
Group × amount × region	0.44	0.8212	1.35	0.2437	0.21	0.9580	1.63	0.1499
Valence × amount × region	0.66	0.6529	1.06	0.3833	0.68	0.6407	0.08	0.9952
Electrode (region)	11.59	<0.0001***	2.55	<0.0001***	49.57	<0.0001***	6.67	<0.0001***

* *p* < 0.05.

** *p* < 0.01.

*** *p* < 0.001.

Table 3

Comparison of impulsivity scores between control ($N = 40$) and alcoholic ($N = 40$) groups. Mean, standard deviation (SD), t -value and p -value are shown. Alcoholics had significantly higher scores than controls in non-planning and total score of BIS. There was also a trend towards significance in motor impulsivity and in two of the selection frequency scores.

Variable	Control		Alcoholic		t	p
	Mean	SD	Mean	SD		
BIS total score	60.67	9.75	68.26	9.36	−3.42	0.0010**
BIS non-planning	22.39	3.89	26.00	4.33	−3.77	0.0000***
BIS motor impulsivity	23.44	6.42	26.21	4.63	−2.14	0.0360^a
BIS cognitive impulsivity	14.83	3.53	16.08	3.68	−1.48	0.1420
SF for '50' after a single loss trial	38.62	3.08	38.58	3.63	0.05	0.9580
SF for '50' after two consecutive loss trials	19.79	4.00	21.10	4.92	−1.29	0.2000
SF for '50' after a loss trend of previous two trials	29.77	6.43	31.40	5.94	−1.17	0.2450
SF for '10' after a loss trend of previous two trials	28.59	5.92	25.22	7.70	2.17	0.0330^a
SF for '50' after a gain trend of previous two trials	53.54	9.34	56.25	9.45	−1.28	0.2040
SF for '10' after a gain trend of previous two trials	46.28	9.01	47.22	8.86	−0.47	0.6400
SF for '50' after a loss trend of previous three trials	38.59	8.04	43.02	9.51	−2.24	0.0280^a
SF for '10' after a loss trend of previous three trials	36.97	7.84	34.45	9.25	1.31	0.1950
SF for '50' after a gain trend of previous three trials	44.36	8.30	44.18	6.95	0.11	0.9150
SF for '10' after a gain trend of previous three trials	37.26	7.83	37.45	7.74	−0.11	0.9120
SF for '50' after a loss trend of previous four trials	33.36	7.98	35.95	7.58	−1.48	0.1430
SF for '10' after a loss trend of previous four trials	30.79	7.39	28.82	8.29	1.11	0.2690
SF for '50' after a gain trend of previous four trials	49.03	8.49	50.80	8.71	−0.92	0.3620
SF for '10' after a gain trend of previous four trials	43.00	9.67	42.52	9.25	0.22	0.8240
RT following −50 trials	340.40	90.37	341.48	76.81	−0.06	0.9540
RT following −10 trials	330.71	79.68	338.71	72.16	−0.47	0.6410
RT following +50 trials	340.56	83.78	351.05	82.72	−0.56	0.5770
RT following +10 trials	333.83	85.38	339.63	70.21	−0.33	0.7420
RT following loss trials (−50 and −10)	335.12	82.46	339.68	72.66	−0.26	0.7950
RT following gain trials (+50 and +10)	338.08	81.43	344.50	73.37	−0.37	0.7140
RT for trials of higher amount (−50 and +50)	332.23	81.00	339.18	70.22	−0.41	0.6850
RT for trials of lower amount (−10 and +10)	340.34	86.09	345.70	77.22	−0.29	0.7710

** $p < 0.01$.

*** $p < 0.001$.

^a The significance was lost after Bonferroni correction for multiple testing; BIS, Barratt impulsivity scale; IR-1, impulsive response-1 (selecting 50 after a single event of loss); IR-2, impulsive response-1 (selecting 50 after two consecutive events of loss); RT, reaction time; SF, selection frequency (refers to the number of times a particular amount was selected).

Table 4

Description of PCA-based factors that were extracted from the set of TRB and ERP variables. Eigen value, percentage of variance accounted for, and the detail and the number (N) of variables that had significantly high positive ($r \geq +0.5$) and negative ($r \leq -0.5$) loadings with the factor have been listed.

Factors	Eigen value	Accounted variance in %	Variables with significantly high positive loadings [N]	Variables with significantly high negative loadings [N]
ERP factor 1	34.92	24.25	ORN amplitudes during loss (−50 and −10) conditions [12]	None
ERP factor 2	19.09	13.26	ORP amplitudes during −10 condition [9]	None
ERP factor 3	12.23	8.49	ORP amplitudes during +10 condition [9]	None
ERP factor 4	9.34	6.49	ORN latencies during −10 condition [9]	None
TRB factor 1	7.98	36.25	All the RT variables [8]	None
TRB factor 2	5.98	27.18	SF for 50 after two consecutive loss trials; SF for 50 after a loss trend of previous two trials, three trials and four trials [4]	SF for 10 after a loss trend of previous two trials and three trials [2]
TRB factor 3	3.06	13.91	SF for 50 after a gain trend of previous two trials, three trials and four trials [3]	None

RT, reaction time; SF, selection frequency (refers to the number of times a particular amount was selected); N , number of variables; TRB, task-related behavioral variables.

times; (2) six variables of selection frequencies following loss trends/trials; and (3) three variables of selection frequencies following gain trends. The four ERP factors were: (1) twelve variables representing ORN amplitudes during loss (−50 and −10) conditions; (2) nine variables of ORP amplitudes during −10 condition; (3) nine variables of ORP amplitudes during +10 condition; and (4) nine variables of ORN latencies during −10 condition. Table 5 shows the correlation between ERP factors and behavioral (TRB and BIS) factors. In the total sample, non-planning and motor impulsivity of BIS showed significant correlations with ERP factors 3 and 4, respectively. There was no correlation between ERP and TRB factors. In the control group, TRB factor 1 (reaction times) correlated with ERP factor 4 (ORN latencies during −10) and non-planning (BIS) correlated with ERP factor 3 (ORP amplitudes during

+10). In the alcoholic group, TRB factor 1 (reaction times) correlated with ERP factor 1 (ORN amplitudes during loss conditions).

4. Discussion

The aim of the present study was to analyze the ERP as well as behavioral measures of reward/outcome processing in alcoholics (as compared to healthy controls) during the feedback of monetary outcomes (losses and gains) during a gambling task. The results revealed several key findings: (1) alcoholics had significantly lower ORP amplitudes than controls during both loss and gain conditions and decreased ORN amplitudes during loss conditions (Fig. 7); (2) in both alcoholic and control groups, gain (+50 and +10) conditions

Table 5

Correlation between ERP factors and impulsivity (TRB and BIS) factors in each group and in total sample. Correlation coefficient (r , top number within the cell) and the level of significance (p , bottom number within the cell) are shown. The significant correlations (highlighted in bold font) have been indicated with asterisks. The minus sign (–) indicates a negative correlation.

		TRB-1	TRB-2	TRB-3	BIS-NP	BIS-MI	BIS-CI
Control ($N = 40$)	ERP-1	0.214	0.038	–0.037	–0.159	0.030	–0.055
		0.1912	0.8190	0.8238	0.3532	0.8613	0.7496
	ERP-2	–0.225	0.026	0.080	–0.158	–0.125	0.168
		0.1677	0.8751	0.6294	0.3565	0.4690	0.3269
	ERP-3	–0.266	–0.089	–0.009	–0.400*	–0.113	–0.224
		0.1021	0.5897	0.9552	0.0157	0.5120	0.1899
	ERP-4	0.420**	0.038	0.023	0.042	–0.278	0.045
		0.0078	0.8180	0.8887	0.8086	0.1011	0.7929
Alcoholic ($N = 40$)	ERP-1	–0.339*	–0.131	–0.123	0.114	–0.016	0.115
		0.0321	0.4199	0.4512	0.4962	0.9242	0.4913
	ERP-2	0.027	0.128	0.169	–0.053	0.011	–0.016
		0.8663	0.4301	0.2965	0.7505	0.9457	0.9239
	ERP-3	0.038	–0.182	–0.004	–0.208	0.068	0.112
		0.8152	0.2613	0.9799	0.2104	0.6836	0.5019
	ERP-4	–0.231	–0.213	–0.277	–0.202	–0.271	0.084
		0.1520	0.1862	0.0839	0.2228	0.1005	0.6176
Total ($N = 80$)	ERP-1	–0.037	0.033	–0.050	0.173	0.114	0.109
		0.7468	0.7708	0.6623	0.1408	0.3315	0.3558
	ERP-2	–0.131	0.035	0.105	–0.168	–0.116	0.052
		0.2508	0.7601	0.3589	0.1516	0.3265	0.6621
	ERP-3	–0.137	–0.143	–0.010	–0.317**	–0.067	–0.080
		0.2275	0.2099	0.9277	0.0058	0.5704	0.5003
	ERP-4	0.027	–0.118	–0.159	–0.102	–0.240*	0.070
		0.8101	0.2999	0.1610	0.3886	0.0398	0.5529

* $p < 0.05$.

** $p < 0.01$.

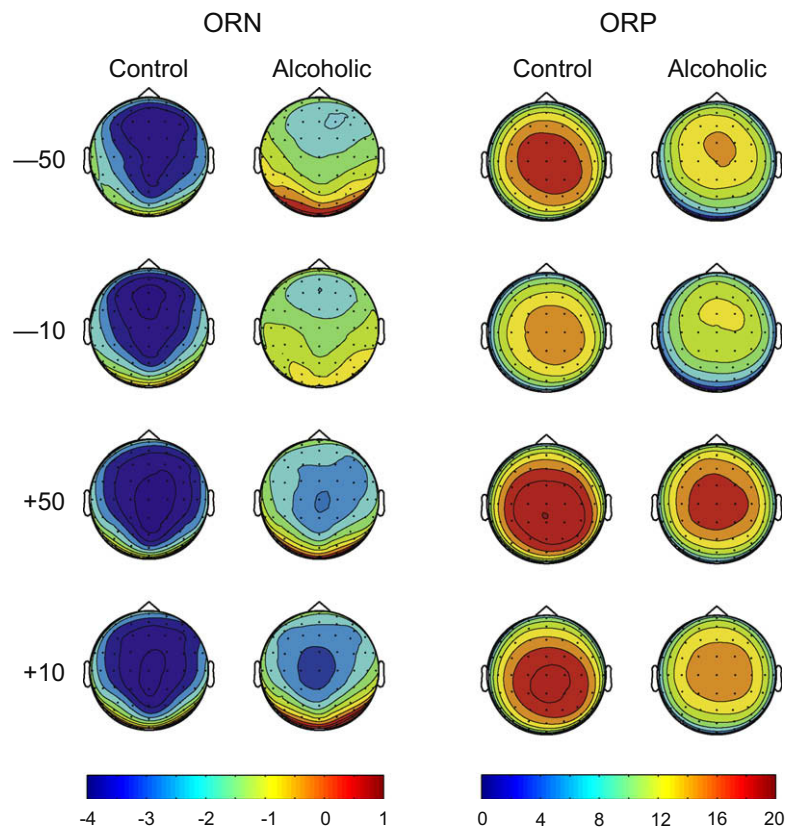


Fig. 5. The topographic maps of ORN (left-side plots) and ORP (right-side plots) in control and alcoholic groups at the peak/trough in the respective waveforms. Alcoholics show decreased amplitude (in μV) in both ORN and ORP components in all conditions. The loss conditions had anterior maxima while the gain conditions had posterior maxima in both groups, especially in the ORN component. The headplots of ORN and ORP were derived from waveforms filtered at 2.0–16.0 Hz and 0.25–16.0 Hz, respectively. While the amplitude differences are robust, topographic differences are not prominent.

had higher ORP amplitudes and shorter ORP latencies compared to loss (−50 and −10); similarly, the large amount (+50 and −50) had higher ORP amplitudes and shorter latencies compared to the small amount (+10 and −10) conditions (Fig. 8, right-side panels); (3) in terms of topography, in both groups, the loss conditions had anterior maxima while the gain conditions had posterior maxima, especially in the ORN component (Fig. 5); (4) sLORETA analysis showed that alcoholics, compared to controls, had a significantly decreased ORP current density at cingulate gyrus and less negative ORN current density at primary sensory and motor areas (Fig. 6); (5) comparison of behavioral measures indicated that alcoholics showed a significantly higher impulsivity non-planning category of BIS impulsivity, and there was also a tendency towards higher motor impulsivity and behavioral risk-taking features among alco-

holics; and (6) Some of the behavioral/impulsivity dimensions appeared to have high correlations with ERP measures, although alcoholics and controls differed in the nature of these correlations.

4.1. Deficient reward processing in alcoholics

The key finding is that alcoholics had significantly lower amplitudes during outcome processing characterized by: (i) markedly decreased ORP amplitude during all outcome conditions and (ii) suppressed ORN amplitude during loss conditions (see Fig. 7). This decrease in amplitudes could be suggestive of a dysfunctional reward processing (system) in alcoholics. Further, deficits in both earlier (ORN/N2) and later (ORP/P3) components may also indicate that cognitive resources necessary for different levels of reward

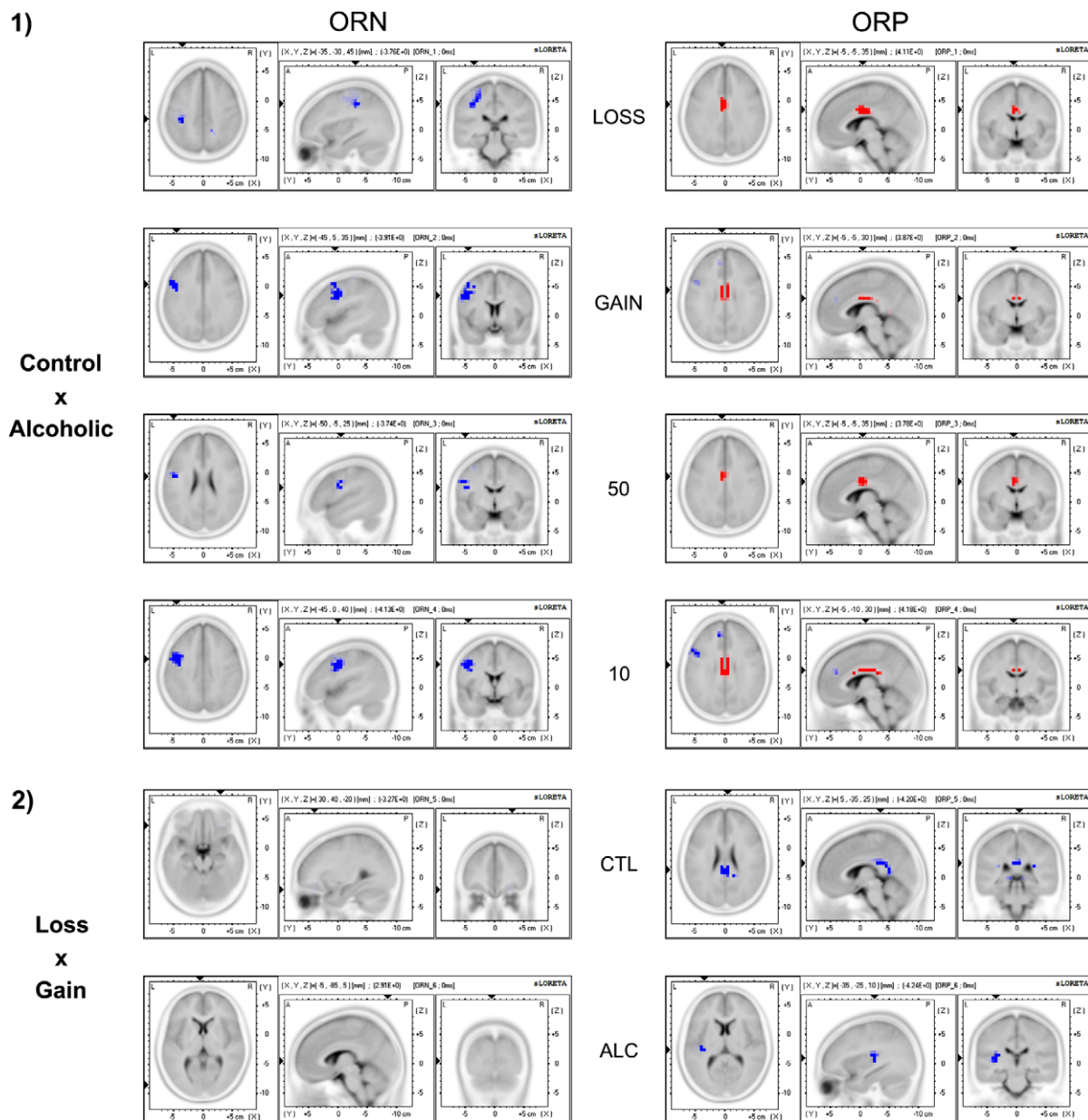


Fig. 6. The sLORETA (current density) images of voxel-by-voxel *t*-statistics comparisons of ORN (left-side panels) and ORP (right-side panels) between control and alcoholic groups (panel set 1), and between loss and gain conditions (panel set 2). Alcoholics showed decreased ORP activity at cingulate gyrus (as marked in red in top-right panels) and less negative ORN current density (as marked in blue in top-left panels) related activity at postcentral gyrus, inferior frontal gyrus and precentral gyrus. Gain showed more ORP activity than loss at posterior cingulate area in controls and at insula region in alcoholics (as marked in blue in bottom-right panels). Differences between valences were not significant in the ORN component. Neither ORN nor ORP was significant between the amounts 50 and 10 (not shown). The blue color in the images indicates significant negative *t*-values while the red color indicates significant positive *t*-values.

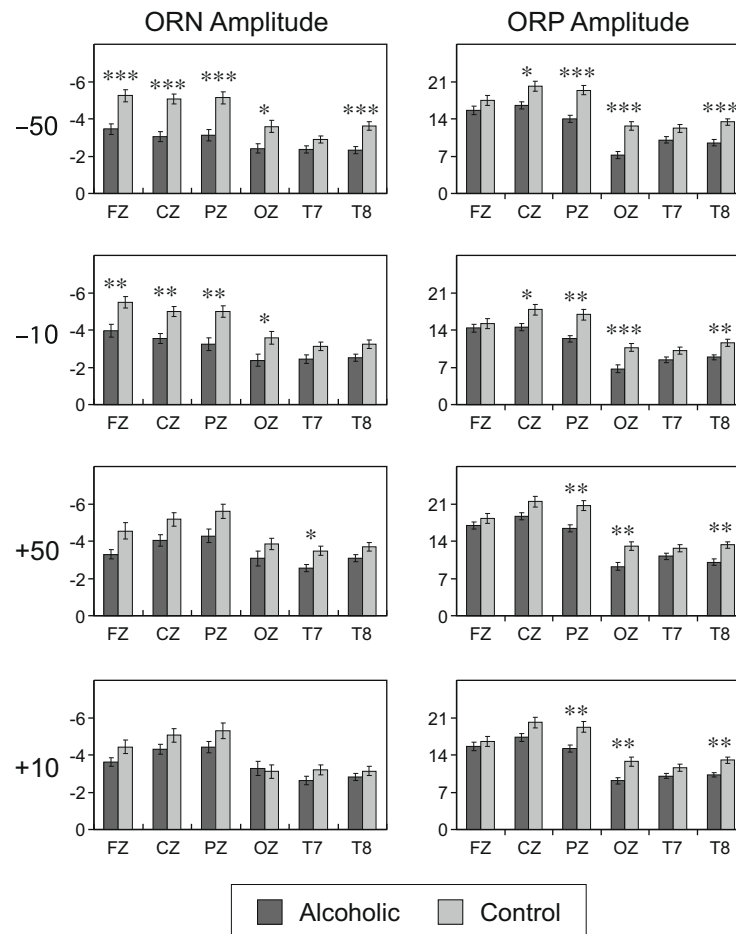


Fig. 7. The bar graphs show the comparison of ORN (left-side panels) and ORP (right-side panels) amplitudes between alcoholic and control groups during each of four outcomes. Six electrode sites are represented in the x-axis and the amplitude is scaled in the y-axis. Alcoholics showed significantly lower ORP amplitude during all outcome conditions and decreased ORN amplitude during loss conditions (−50 and −10). Latencies showed no group differences (not shown). Bonferroni adjusted significance level is marked with asterisks (* $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$). The error bars represent 1 standard error.

processing are impaired in alcoholics. It is well-known in the literature that alcoholics show deficits in N2 and P3 in a variety of cognitive tasks (Porjesz et al., 1987b, 1996, 2005a). However, it is still unclear whether the deficits observed in ORN and ORP components are reflective of generic cognitive deficits or a specific dysfunction in reward processing. Our previous findings from a single outcome gambling paradigm suggested that ORN and ORP could involve both evaluative/cognitive and emotional/affective processing (Kamarajan et al., 2009). Although it was argued that the ORN is functionally similar to the generic N2 component and does not have task-specific functions (Holroyd et al., 2008), our previous finding in a gambling paradigm indicated that ORN amplitude differed as a function of valence and amount (Kamarajan et al., 2009, 2008), suggesting that ORN is functionally distinct from the generic N2 component observed in signal processing. Several studies of gambling tasks showed that the amplitude of the negative component analogous to N2 reflects activity that codes the ongoing evaluation of events in terms of favorable (i.e., gain and correct) or unfavorable (i.e., loss and error) outcomes (Gehring and Willoughby, 2002; Holroyd and Coles, 2002; Hajcak et al., 2006). Thus, it may be stated that the ORN may indicate the detection of a particular outcome and the ORP may reflect the conscious recognition/awareness for the valence or magnitude of the outcome. In a similar vein, the positive component analogous to P3, was found to be sensitive to both the quality (loss/gain) and quantity (larger/smaller) of the outcomes (Toyomaki and Murohashi, 2005; Kamarajan

et al., 2009), which is very distinct from the generic P3 component observed in stimulus discrimination tasks. Although the ORN and ORP components may share common features of signal processing as indexed by N2 and P3, respectively, they indicate very specific levels of signal processing during outcome evaluation. Therefore, it is suggested that the dysfunctional outcome processing, as evidenced by decreased ORN and ORP amplitudes in alcoholics, could be due to a combination of generic signal processing deficits and a specific dysfunction in evaluative processing. Thus, the decreased amplitude observed in alcoholics in the earlier negative component (ORN) and in the later positive component (ORP) may indicate neurocognitive dysfunctions in both early detection of different outcomes and subsequent evaluation of quality (loss vs. gain) and quantity (10 vs. 50) of outcomes.

Despite these possible dysfunctions in alcoholics as compared to controls, a noteworthy inference is that the neural mechanisms for reward processing are similar in both alcoholic and control groups (as shown by the within-group analysis): (i) in both groups, gain (+50 and +10) conditions had higher ORP amplitudes and shorter ORP latencies compared to loss (−50 and −10) as did the large amount (+50 and −50) conditions compared to small amount (+10 and −10) conditions (Fig. 8, right-side panels); (ii) in terms of topography, in both groups, the loss conditions had anterior maxima while the gain conditions had posterior (central/parietal) maxima, especially in the ORN component. It should also be mentioned that an unusual finding in this study indicated that

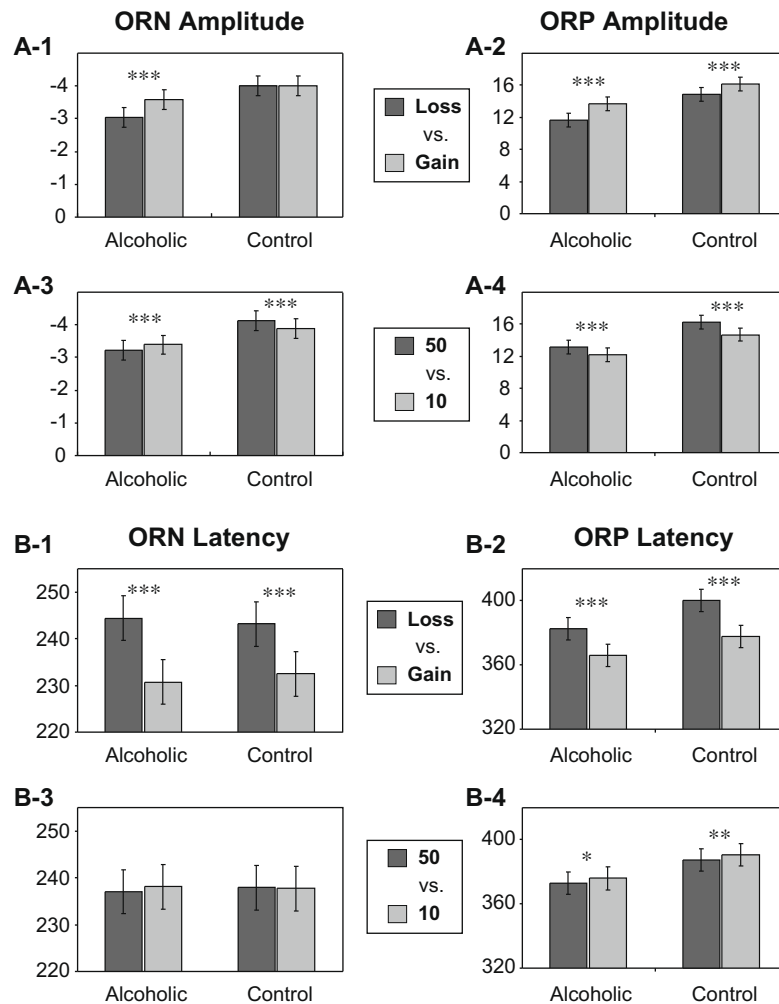


Fig. 8. The bar graphs showing pair-wise comparisons of least squares means of ORN (left-side panels) and ORP (right-side panels) between different outcomes in control and alcoholic groups. In the ORP measures, gain (compared to loss) conditions and large amount (compared to small amount) conditions showed significantly higher amplitude and shorter latency in control as well as alcoholic groups. The findings on the ORN measures are: (1) amplitude differences between valences (loss vs. gain) were obvious only in alcoholic group (panel A-1), whereas latency differences were explicit in both groups (panel B-1); and (2) alcoholics, in contrast to controls, showed more ORN amplitude for the small amount '10' than for the large amount '50' (panel A-3). Bonferroni adjusted significance level is marked with asterisks (* $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$). The error bars represent 1 standard error.

alcoholics showed more ORN amplitude for the small amount '10' than for the large amount '50' (Fig. 8, panel A-3). This finding of increased resource allocation for the small amount in alcoholics during the early processing (at ORN) is difficult to explain and poses an interesting question for further exploration.

4.2. Frontal network dysfunction in alcoholics as revealed by sLORETA

A noteworthy finding of sLORETA analysis in this study was that alcoholics, as compared to controls, showed significantly decreased current density in the ORP time frame at cingulate gyrus during each of the reward/outcome conditions. On the other hand, alcoholics demonstrated a significantly reduced negative ORN current density than controls at postcentral gyrus, inferior frontal gyrus and precentral gyrus. This finding is very much characteristic of the observation that alcoholics have a weaker and/or a dysfunctional activation in the cingulate cortex during the evaluative processing of monetary outcome, as evidenced by the decreased current density during the late processing of the ORP component. Further, alcoholics do show more activity during the early processing (of ORN component) associated with discrimination of outcomes at the sensory (postcentral area), motor (precentral area) and dorsolateral

prefrontal (brodmann area 9) areas of the brain. This differential effect of possible "hyper-excitability" during early processing at primary sensory and motor areas and prefrontal areas on the one hand, and diminished response to outcome evaluation during the later processing at anterior as well as posterior cingulate gyrus on the other, differentiate alcoholic individuals from healthy controls both in terms of intensity and time course of neural activity associated with ORN and ORP components during outcome processing.

In our earlier ERP study using the gambling task in controls (Kamarajan et al., 2009), we found that the maximum current density (i.e., the focus) involved specific brain regions: (i) the ORN activity involved medial frontal (including anterior cingulate) areas during the loss conditions and medial posterior (including posterior cingulate) areas for the gain conditions in both males and females; (ii) the ORP activity was concentrated at the medial frontal (including anterior cingulate) areas in females and at the medial posterior (including posterior cingulate) areas in males. This finding showed the importance of both anterior and posterior cingulate cortex for the processing of monetary outcomes. In this context, a weaker activation as indicated by decreased current density in the cingulate cortex in alcoholics during ORP processing (i.e., the awareness to loss/gain event) could either indicate a

localized dysfunction in the particular region of anterior cingulate cortex (ACC) or a generalized malfunction in the entire neural network of reward processing (due to the central and influential role of ACC in the reward network). Further, our findings also showed that the cingulate area and a related structure in the reward network (i.e., insula) showed prominence in the within-group differences between valences (i.e., loss vs. gain): in the ORP component, the gain conditions (+50 and +10) showed more current density activity (than the loss conditions) at the posterior cingulate area in controls and at the insula region in alcoholics. It is also to be noted that although amplitude of ERPs were different between the amounts (see Fig. 8), current density profiles could not differentiate between amounts. This finding suggests that differentiation in terms of current density of amount plays a less significant role than that of valence (loss vs. gain) in the reward network of the human brain.

Our finding that decreased current density in the ORP time frame at cingulate gyrus can be further supported and explained in the light of relevant findings in the literature. For example, neuroimaging studies of reward processing have identified a number of brain areas that are activated by the delivery of primary reinforcers such as appetitive stimuli (Berns et al., 2001; McClure et al., 2003; O'Doherty et al., 2001), as well as secondary reinforcement such as monetary gains and losses (Breiter et al., 2001; Delgado et al., 2004; Elliott et al., 2000; Holroyd et al., 2004; Thut et al., 1997, as cited from Nieuwenhuis et al., 2005a). Increasing evidence supports the integral role of the ACC in performance monitoring, especially involving predictability of an outcome (Paulus et al., 2002, 2003, 2004), which are critical in regulating various relevant social behaviors. Subdivisions within the ACC have specialized functions: (i) the dorsal (pregenual) region of the ACC may be involved in cognitive aspects of decision making, including reward-based decision making, error monitoring, anticipation, working memory, motor response, and novelty detection (Bush et al., 2000, 2002; Forman et al., 2004), and (ii) the rostral (infragenual) ACC has been implicated in emotional processing (Bush et al., 2000) and error monitoring (Forman et al., 2004), perhaps due to its interconnections with the orbitofrontal cortex, limbic structures, motor cortex and autonomic and endocrine systems (Bush et al., 2000). Thus, both regions of the ACC may play a role in risky decision making and also involve cognitive (probability) as well as emotive (reward/penalty) functions. These regions are all interconnected with each other and with the prefrontal cortex (Brutus et al., 1986; Bush et al., 2000; Elliott, 1992), and appear to play a role in modulation of disinhibitory behaviors, error monitoring, reward sensitivity, and emotional valence (cf. Fishbein et al., 2005). In essence, activity within this network functions to attach emotional context and valence to cognitive cues. Neurocognitive tasks such as the gambling task used in our study which, apart from the cognitive evaluation of outcomes, also include a feeling or emotional component (e.g., loss and gain) could invoke specific interconnected regions of the PFC, ACC, and limbic structures, suggesting that when task demands modify emotional responses, neural responses occur within this network (Elliott et al., 2000; Liberzon et al., 2000). Further, activity throughout this circuit has been implicated in behavioral dispositions/disorders involving addictive–impulsive–compulsive spectrum, including alcohol/drug abuse, gambling, and risk-taking (Bechara, 2001; Cavedini et al., 2002; Mitchell et al., 2002; Rogers et al., 1999; Harris et al., 2008).

4.3. Behavioral and trait impulsivity in alcoholism

Impulsivity is a complex multidimensional construct that has been frequently implicated in the pathogenesis of addictive disorders (Dom et al., 2007). The findings of the present study, which involved both trait impulsivity (using BIS) and behavioral impulsivity (derived from task performance) measures, showed that

alcoholics had higher levels of impulsivity in non-planning and total scores of BIS, while there was also a tendency towards higher risk-taking features (i.e., selecting '50' more often and '10' less often than controls following losing trends) among alcoholics. These findings on impulsivity in alcoholics tends to offer validity to the neurocognitive models of addiction disorders that implicate impulsivity as a major component. For example, Chambers et al. (2003) proposed that the primary motivation circuitry involving cortical–striatal–thalamic–cortical loops were putatively involved in impulsivity, decision making and the disorders of alcohol/drug addiction and pathological gambling. Goldstein and Volkow (2002) conceptualized alcohol/drug addiction as a syndrome of impaired response inhibition and salience attribution, and summarized the involvement of the frontosubcortical circuits in addiction disorders. Earlier studies done in our lab have consistently found that disinhibition and impulsivity were the key aspects in alcoholism (Cohen et al., 1997; Kamarajan et al., 2005a; Chen et al., 2007). Further, many researchers have considered impulsivity as the key vulnerability marker for substance-use disorders, especially alcoholism (see Verdejo-Garcia et al., 2008 for a review).

Further, since alcoholics do show anomalies in both neurophysiological and behavioral measures, the findings on the relationship between impulsivity and ERP factors suggest possible causal links: (1) both factors could be causally linked with each other, or (2) both could have been caused/linked by other common etiological factor(s). However, the claim for causal links may not be strong enough, considering the finding that no task-related performance variables showed a strong correlation with ERP factors, although the self-report measure (i.e., BIS) showed a high correlation with ERP factors. Although the lack of correlation between performance variables of impulsivity and ERP factors poses a difficult question, this can be possibly explained in two ways: (1) earlier studies on alcohol dependent individuals suggested that correlations between behavioral measures and self-report measures were weak, suggesting that they both tap into different aspects of impulsivity for detail, see Dom et al. (2007), and (2) age as a factor could have moderated the performance-related impulsivity (more than the trait impulsivity) resulting in a differential effect of younger controls with higher impulsivity as equated with relatively lower impulsivity in older alcoholics (i.e., higher the age lower the impulsivity). Future studies may address this issue of age effects on impulsivity. Finally, since the concepts of impulsivity, disinhibition and risk propensity forms the vulnerability not only for substance-use disorders but the entire rubric of disinhibitory or externalizing psychopathology (Krueger et al., 2002; Iacono et al., 2008), ERP studies on reward processing using a gambling paradigm on a wide spectrum of disorders may help integrate the relationship among these concepts and yield a comprehensive model for disease propensity.

4.4. Is alcoholism a reward deficiency syndrome?

Alcoholism has been described as part of the reward deficiency syndrome (RDS) (Bowirrat and Oscar-Berman, 2005). Recently, Makris et al. (2008) showed that there was a decrease in total reward-network volume in the brains of alcoholic subjects. Findings also supported the RDS model of alcoholism by identifying dysfunctions in the brain reward circuits of alcoholics (Wrase et al., 2007; Makris et al., 2008; de Greck et al., 2009; Tanabe et al., 2009). In this context, the present study is the first electrophysiological study to examine reward processing deficiencies in alcoholics using a gambling task, although several recent studies have examined the related concept of 'decision making' in gambling tasks in alcohol/drug dependent individuals (Bechara, 2005; Dom et al., 2006; Verdejo-Garcia et al., 2007; Cantrell et al., 2008). Since

the concept of RDS involves a cluster of impulsive–addictive–compulsive behaviors/disorders (Blum et al., 1995), our study has included several measures of impulsivity along with ERP measures. The findings of the current study indicate that alcoholics manifest deficient reward processing in neurocognitive measures (in terms of amplitude and current density of ORN and ORP) as well as in behavioral measures of impulsivity and risk-taking, as compared to healthy controls. These findings lend support to the notion that alcoholism can be construed as part of a reward deficiency syndrome.

According to the RDS model, a person with dysfunction in the brain reward cascade, especially in the dopaminergic system causing a hypodopaminergic trait, requires additional dopamine to feel good (Blum et al., 2000). This trait leads to multiple drug-seeking behaviors as the drugs, such as alcohol, cocaine, heroin, marijuana, nicotine, cause activation and neuronal release of dopamine, which could heal the abnormal cravings. The RDS model explains not just alcoholism but several common disorders such as pathological gambling, attention-deficit hyperactivity disorder (ADHD), Tourette's syndrome, PTSD, conduct disorder, and antisocial behavior (Blum et al., 2000; Comings and Blum, 2000; Bowirrat and Oscar-Berman, 2005).

Another dominant model to consider is the 'disinhibitory/externalizing spectrum' (DES) model (Gorenstein and Newman, 1980; Krueger et al., 2002; Iacono et al., 2003) which appears to have a similar cluster of disorders and similar etiological and neurocognitive explanations. Although, in many of our earlier studies, we have supported the DES model for alcoholism, especially to explain the neurocognitive disinhibition (Begleiter and Porjesz, 1999; Kamarajan et al., 2004, 2005a,b, 2006; Porjesz et al., 2005a; Porjesz and Rangaswamy, 2007; Chen et al., 2007; Rangaswamy et al., 2007), the scope of the present study appears to fit well with the RDS model, as it specifically deals with reward processing deficiency in alcoholism which is not explicitly part of the DES model. Interestingly, a common underlying aspect to both models is the ability to identify and integrate the spectrum of disorders that share a common etiology, pathophysiology, biological markers and brain circuitry. In this regard, these models may be complementary to each other in explaining different dimensions of the spectrum rather than assumed being competitive. As a final note, it should be mentioned that genetic vulnerability underlies these spectrum disorders including alcoholism, as both models illustrate (Blum et al., 1996; Porjesz and Begleiter, 1998; Comings and Blum, 2000; Hicks et al., 2004, 2007; Begleiter and Porjesz, 2006; Porjesz and Rangaswamy, 2007; Dick et al., 2008; Rangaswamy and Porjesz, 2008a,b), as many of these markers and dysfunctions related to these disorders are also present in their naïve offspring (Begleiter et al., 1984; Porjesz and Begleiter, 1997, 1998; Polich et al., 1994), and these specific dysfunctions in reward processing could be mainly due to certain inherited aspects of abnormal emotional traits in alcoholics (Oscar-Berman and Bowirrat, 2005).

In conclusion, our study has shown that alcoholics demonstrate dysfunctional outcome processing, high impulsivity and risk-taking (as observed in the behavioral scores), and possibly a compromised neural reward network. A possible limitation that could compromise the validity of the present study is that the alcoholic group is significantly older than the control group, although age has been treated as a covariate in the statistical analysis. Since age as a factor may have had an impact on the impulsivity variables, we suggest that future studies try to replicate our findings in an age-matched sample of controls and alcoholics. Converging evidence, including the 'reward deficiency' observed in the study, suggest that alcoholism and a host of externalizing and impulse control disorders may fall into the

rubric of RDS. Future studies should focus on the application of gambling paradigms to other clinical conditions of RDS in order to confirm and validate this model. Application of sophisticated methods of signal processing including event-related brain oscillations (EROs), synchrony, and componential analysis during outcome processing may further help understand the neurocognitive phenomena and the disorders, and these studies are underway. Since the present study has included only the male participants, further studies on clinical samples may be attempted to include both genders and analyze the effects in each gender separately. Further, imaging studies supplemented with simultaneous ERP recordings during the performance of a gambling task might shed more light on the exact source activity along with the time course of outcome processing.

Contributors

Chella Kamarajan participated in the study design and methods, interpreted the results and wrote the manuscript; Madhavi Rangaswamy helped in designing the task and interpreting the results, and offered expert comments for the manuscript preparation; Yongqiang Tang helped in statistical analysis, Niklas Manz helped with signal processing and manuscript preparation and editing, David B. Chorlian helped in computations and signal analyses, Ashwini K. Pandey and Bangalore N. Roopesh helped with expert suggestions in interpreting the results, Ramotse Saunders shared ideas to discuss the results; Arthur T. Stimus helped in the collection and management of EEG, clinical and behavioral data, and helped with manuscript preparation; Bernice Porjesz, as the director, supervisor and principal investigator, provided all-round expert help and support besides her expert guidance in designing the study and writing and editing the manuscript.

Role of the funding source

This study was funded by the National Institutes of Health (NIH) Grants #5 RO1 AA05524, AA02686 and AA005524 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The funding organization had no further role in study design (collection, analysis and interpretation of data), in the writing of the report, and in the decision to submit the paper for publication.

Conflict of interest statement

We, all the authors of this study (Chella Kamarajan, Madhavi Rangaswamy, Yongqiang Tang, David B. Chorlian, Ashwini K. Pandey, Bangalore N. Roopesh, Niklas Manz, Ramotse Saunders, Arthur T. Stimus, Bernice Porjesz), declare that we have no conflicts of interest.

Acknowledgments

In memory of Dr. Henri Begleiter, founder and longtime mentor of the Neurodynamics Laboratory, we acknowledge with great admiration his seminal scientific contributions to the field. We are indebted to his charismatic leadership and luminous guidance, and are truly inspired by his vision to carry forward the work he fondly cherished.

This study was supported by the National Institutes of Health (NIH) Grants #5 RO1 AA005524, AA02686 and AA008401 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA). We are grateful for the valuable technical assistance of Carlene Haynes, Joyce Alonzia, Chamion Thomas, Tracy Crippen, Glenn Murawski, Eric Talbert, Patrick Harvey, Cindy Lipper, Gabriel Wurzel, Irina Kushnir, and Aleksandr Razran.

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