

## Do chronic alcoholics have intact implicit memory? An ERP study

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### Abstract

In order to investigate whether visual object priming differs from visual word priming and whether the visual repetition priming in chronic alcoholic patients is impaired, we performed an ERP study on 27 male control and 67 male alcoholic subjects. Sixty-one electrodes were employed to record ERPs that were elicited by random presentations of object pictures, words, and scrambles for both pictures and words. We also used an implicit task that required subjects to identify whether each stimulus was recognizable. The current experiment revealed that (1) the reaction times to both recognizable picture and word stimuli were significantly shortened by the prior exposures of the same stimuli, (2) control subjects reflected visual object and word priming in different ERP components with different topographic patterns, (3) alcoholic subjects manifested visual word priming in the same ERP component as controls, and (4) the differences in ERP components, both in amplitude and topographic distribution, between the two groups occurred mainly in the different stimuli. These data suggest that the visual object and word priming have distinctive neural processes. The visual object priming in alcoholic subjects may be impaired while the visual word priming seemed to be intact. © 1997 Elsevier Science Ireland Ltd.

**Keywords:** Alcoholics; Implicit memory; ERP; Priming; Picture; Word

### 1. Introduction

Memory studies have distinguished two ways in which memory for prior experiences can be expressed, most frequently referred to as explicit and implicit memory for different operating characteristics (Graf and Schacter, 1985; Schacter, 1987). Explicit memory reflects intentional or conscious recollection of facts or events, while implicit memory denotes a facilitation or change in test performance that is attributable to information or skills acquired during a prior study episode, i.e. implicit memory is expressed through performance rather than recollection (Squire et al., 1993). It has also been proposed that performance on explicit memory tasks and repetition priming procedures are manifestations of different memory systems (Tulving and Schacter, 1990).

However, new experimental findings have led investiga-

tors to reconsider the dichotomy between explicit and implicit measures of memory. It has been reported that experimental dissociations between explicit and implicit memory performance do not fully respect the traditional boundaries between repetition priming and measures of episodic memory (Blaxton, 1989; Weldon et al., 1989). Some recent results suggested that both perceptual and conceptual processes contribute in variable proportions to priming phenomena (Carlesimo, 1994). Indeed, the evidence for impaired priming in some conceptual tasks has been documented in amnesic populations (Cermak et al., 1988; Shimamura and Squire, 1989; Blaxton, 1992). McGlinchey-Berroth et al. (1995) further reported impairments of delayed eyeblink conditioning, one of the basic forms of implicit memory in amnesic Korsakoff patients and recovered alcoholics. However, the literature regarding repetition priming in amnesic patients is controversial and the experimental evidence suggesting normal priming seems to be prevalent (Shimamura and Squire, 1984; Graf et al., 1985; Schacter et al., 1991a; Carlesimo, 1994). Nevertheless, most of the studies have adopted a purely neuropsychological approach, using one or more overt measures of task perfor-

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mance, e.g. percentage of correct answers and/or response time as the dependent variable. These experimental methods merely delineate the information processing solutions in memory systems. A complementary approach is to study this interesting phenomenon with scalp-recorded event-related potentials (ERP).

Numerous investigations indicate that ERPs are sensitive to word and picture repetition priming (Rugg, 1987, 1988, 1990, 1994, 1995; Friedman et al., 1988; Smith and Halgren, 1989; Bentin and Peled, 1990; Friedman, 1990; Van Petten et al., 1991; Young and Rugg, 1992; Besson and Kutas, 1993; Otten et al., 1993; Smith, 1993; Zhang et al., 1995). ERPs to both repeated words and pictures are characterized by greater positive amplitude from approximately 300 to 600 ms poststimulus relative to their first presentation. The amplitude of the ERP priming effect is influenced by the level of processing induced by task demand (Rugg et al., 1988). Direct comparisons between word and picture repetition priming with ERP techniques have revealed different ERP patterns between these stimuli, respectively (Zhang et al., 1997). These ERP differences were reflected not only in the different ERP wave forms and topographic distribution patterns which were generated by word and picture repetitions, but also in the latencies of the components which exhibit the priming effects.

It is a widely accepted fact that chronic alcohol abuse has detrimental effects on both brain structures and its cognitive functions. Mild cognitive impairment can be demonstrated by neuropsychological testing in 50–70% of detoxified alcoholics (Martin et al., 1986). MRI studies confirmed large increases in subarachnoid cerebrospinal fluid (CSF) and mild ventricular enlargement in alcoholics, and revealed associated volume reductions of localized cortical and subcortical cerebral structures. Volume losses in the diencephalon, the caudate nucleus, dorso-lateral frontal and parietal cortex, and mesial temporal lobe structures were the most prominent (Jernigan et al., 1991; Pfefferbaum et al., 1992, 1993; Charness, 1993; Di Sclafani et al., 1995). In a recent MRI study on memory in a sample of various amnesic patients and control subjects, Jernigan and Ostergaard (1993) investigated the priming effects through a tachistoscopic word identification threshold task. These authors observed that temporo-limbic damage was associated with memory impairments and reduced priming, whereas caudate damage was associated with impaired lexical or perceptual processing and increased measured priming. They attributed priming to at least two factors, one related to memory and one related to processing efficiency; if the subject's processing is highly efficient, the actual priming may result in little facilitation of performance and thus relatively little measured priming, whereas if the subject's stimulus processing is inefficient, there may be more possibility for improvement. Thus, the same amount of actual priming of words may produce larger measured priming effects. These results may explain the contentious results of studies on implicit memory in amnesic alcoholics.

However, much of the memory literature focuses on Wernicke–Korsakoff patients, often at the exclusion of non-amnesic alcoholics. The investigation of chronic alcoholics who are not clinically amnesic and who manifest no neurological signs of Wernicke–Korsakoff syndrome may nevertheless provide some objective evidence of changes in brain function caused by long term alcohol abuse.

In the current experiment, we tested whether the repetition priming effects are influenced by long term alcohol abuse in a large group of chronic alcoholics without neurological signs of Wernicke–Korsakoff syndrome using ERP techniques. ERP techniques were used because they are extremely sensitive to the various aspects of acute and chronic alcohol administration on the brain, specifically alcoholization, tolerance, withdrawal and long-term brain effects (Porjesz and Begleiter, 1993). We hypothesized that long term alcohol abuse may affect implicit memory, as it inevitably causes a general degeneration of brain function. We tested this hypothesis on chronic alcoholics without clinical signs of amnesia in order to assess the independence of memory processes; correlations of implicit and explicit memory measures within samples of amnesic patients may not be optimal.

In a series of studies of ERPs on visual memory (Begleiter et al., 1993, 1995; Hertz et al., 1994; Zhang et al., 1995), an ERP component, named as the visual memory potential (VMP) by Begleiter et al. (1993), was demonstrated to correlate with visual working memory. This ERP component appears to be located in the occipito-temporal region. Both the spatial and temporal characteristics of the component parallel single cell studies in monkeys (Mikami and Kubota, 1980; Miller et al., 1991, 1993). However, because the VMP had been previously studied in explicit memory tasks, the current study was undertaken to determine whether the VMP can be elicited by repetition effects in an implicit memory task. We chose real words, object pictures, word scrambles and picture scrambles as stimuli to elicit the ERPs. It has been suggested that visual word and object priming are supported separately by different domain-specific subsystems of a cortically based, presemantic perceptual presentation system (PRS) (for review see Schacter, 1993a). Extrastriate cortex participates in mediating the visual word form system for word priming, while inferior temporal regions are involved in mediating the structural description system for object priming. Hence, we hypothesized that if the ERPs showed different patterns due to the two kinds of priming effects, we would be able to further examine the effects of long term alcohol abuse on implicit memory. In order to substantiate the priming effects shown by ERPs, scrambles were interspersed among stimuli to serve as a foil to the priming effects of words and object pictures on ERPs. We assumed that these scrambles would not produce any priming effects on ERPs, because it would be very difficult to establish representations in memory from these unidentifiable scrambles. The priming effects are likely to be supported by newly acquired memory repre-

sensation (Micco and Masson, 1991; Musen, 1991), and several experimental results demonstrated that impossible objects show little or no priming (Schacter et al., 1990b; Schacter et al., 1991b). In addition, we attempted to characterize the general regionalization of subprocesses and subsecond dynamics of repetition priming by using 61 electrodes and scalp current density to assess topographically the word and object picture priming effects on ERPs.

## 2. Materials and Methods

### 2.1. Subjects

Twenty-seven normal male subjects (mean age  $24.03 \pm 3.30$  years) participated in the experiment. These control subjects were recruited from the students and staff of the SUNY HSCB via notices posted on the campus. All the control subjects were right-handed and had no personal or family history of alcohol and drug abuse, or any personal history of neurological or psychiatric disease. The alcoholic group consisted of 67 male alcoholics (mean age  $35.98 \pm 6.45$  years). All the alcoholic subjects in the study had undergone detoxification for more than 4 weeks in the Short-Term Alcohol Treatment Unit of Kings County Hospital Center before the study. Most of the alcoholics involved in the current experiment had been drinking heavily for more than 15 years, and the majority of them started drinking before 20 years of age. The diagnosis of alcohol abuse or dependence was documented using DSM-III-R criteria by direct interview. Alcoholic individuals were excluded from the study if they had a history of overt liver (e.g. cirrhosis), metabolic (e.g. diabetes), vascular (e.g. coronary artery disease), or neurological (e.g. head injury, encephalitis, epilepsy) disorders. Patients with a history of drug dependence or of major psychiatric illness (e.g. schizophrenia, bipolar affective disorder) predating the onset of alcoholism were also screened from the study. All alcoholics received the Mini Mental Status examination which indicated that no individual manifested serious memory deficits. The alcoholics were significantly older than the controls ( $T(86.7) = 10.81$ ,  $P < 0.0001$ ). All subjects had normal vision or corrected normal vision. Each individual was required to give his informed consent and was paid for his services.

### 2.2. Experimental design

#### 2.2.1. Stimuli and stimulus presentation

The stimuli consisted of 120 images (pictures) of objects, 120 words, 120 picture scrambles, and 120 word scrambles. The total of 480 stimuli comprised 40 image same trials (by repeating each image once, 40 images needed), 40 image different trials (80 images needed), 40 word same trials (40 words needed), 40 word different trials (80 words needed), 40 image scramble same trials, 40 image scramble different

trials, 40 word scramble same trials and 40 word scramble different trials. These trials were intermingled and presented consecutively in a pseudorandom order. The inter-stimulus interval was fixed at 1.2 s and the duration of presentation for each stimulus was 312 ms. The images were selected from the Snodgrass and Vanderwart (1980) set of 260 pictures and the words were the nouns of the selected pictures. The presentation of a word on the CRT matched its corresponding picture in size. Scrambled words and images were centered in a square of  $260 \times 260$  pixels. Each square was divided into 169 smaller squares of  $20 \times 20$  pixels. The positions of the smaller squares were then randomly shuffled to make up a scrambled image. Therefore, the scrambled words or pictures were all matched to their original words or pictures in size and pixel. All the stimuli were presented in black on a white background square at the center of a CRT. All the stimuli were approximately 10 cm in height and 10 cm in width, thus subtending a visual angle of  $5-6^\circ$ .

#### 2.2.2. Subjects' task

The subjects' task was to decide whether each visual stimulus could be recognized or not. They were instructed to press a mouse key in one hand when they could recognize a stimulus, whether it was a picture or a word, or to press a mouse key in the other hand when they could not recognize the stimulus (scramble). The designation of the hand indicating recognizable or unrecognizable was alternated across subjects. Response accuracy and speed were equally stressed.

#### 2.2.3. Electrophysiological recording

The subject was seated in a reclining chair located in a sound-attenuated RF shielded room and fixated at a point in the center of a computer display located 1 m away from his or her eyes. Each subject was fitted with a 61-lead electrode cap (ECI, Electrocap International). We used the entire 10/20 International montage along with additional 41 sites as follows: Fpz, Afz, Af1, Af2, Af7, Af8, F1, F2, F5, F6, Fcz, Fc1, Fc2, Fc3, Fc4, Fc5, Fc6, Fc7, Fc8, C1, C2, C5, C6, Cpz, Cp1, Cp2, Cp3, Cp4, Cp5, Cp6, Tp7, Tp8, P1, P2, P5, P6, Poz, Po1, Po2, Po7 and Po8 (standard electrode position nomenclature, American Electroencephalographic Association, 1990). The nose electrode served as a reference and the forehead electrode served as ground. The electrode impedance was always below 5 k $\Omega$ . Two additional bipolar derivations were used to record the vertical and horizontal EOG. The signals were amplified with a gain of 10 000 by an Ep-A2 amplifier (Sensorium) with a bandpass between 0.02 and 50 Hz, and recorded on a Concurrent 5550 computer. The amplified signals were sampled at a rate of 256 Hz during an epoch of 190 ms of prestimulus baseline and 800 ms following each stimulus presentation. Trials with excessive eye and body movements ( $>73.3 \mu\text{V}$ ) were rejected on-line. At least 25 artifact-free ERPs were needed to generate an average ERP for each condition.

### 2.3. Data analysis

Only ERPs with artifact-free trials and correct responses (i.e. recognized or unrecognized) were averaged, yielding eight ERP categories according to the different stimulus conditions. Figs. 1 and 2 show the grand mean ERPs to recognizable stimuli (image same, image different, word same and word different) and unrecognizable stimuli (image scramble same, image scramble different, word scramble same and word scramble different) in control and alcoholic groups, respectively. As illustrated in Figs. 1 and 2, both in controls and alcoholics, the ERP patterns consisted of five components. Component 1 (c110) was

selected as the largest peak within a time window from 85 to 135 ms; component 2 (c180) was determined as the largest trough within a time window from 160 to 210 ms; component 3 (c240) was determined as the largest peak within a time window from 210 to 260 ms; component 4 (c300) was determined as the largest trough within a time window from 280 to 330 ms; and component 5 (c450) was determined as the largest peak within a time window between 400 and 500 ms. The first four components were most clearly discernible at posterior electrodes; however, the last component was ubiquitous over all scalp electrodes. The amplitudes of the ERP components to recognizable stimuli varied with the stimulus conditions; however, the

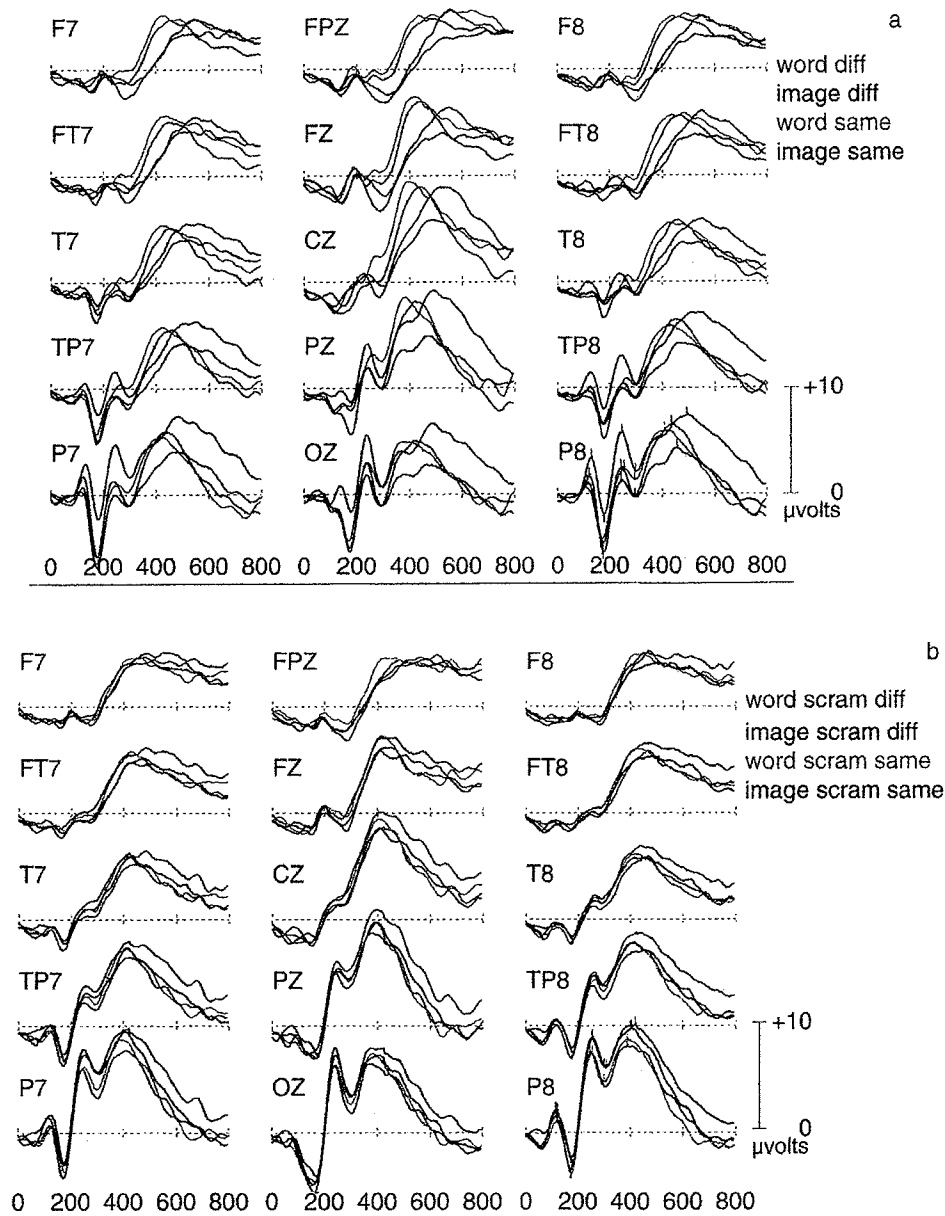


Fig. 1. (a) Grand mean ERPs to different recognizable stimuli in control subjects. For all of the ERP wave illustrations in the paper, the upgoing wave represents positivity. (b) Grand mean ERPs to different unrecognizable stimuli in control subjects.

unrecognizable stimuli (scrambles) seemed to elicit identical ERPs. Amplitudes were measured from baseline to peak, and latencies were recorded from the onset of stimuli to the peaks of each component.

The measurements of amplitudes of each component were organized into groups by region. The frontal region consisted of Fp1, Fp2, Fpz, Af7, Af8, Af1, Af2, Afz, F7, F8, F5, F6, F3, F4, F1, F2 and Fz, the central region consisted of Fc1, Fc2, Fc3, Fc4, Fc5, Fc6, Fcz, C1, C2, C3, C4, C5, C6 and Cz, the parietal region consisted of Cp1, Cp2, Cpz, Cp3, Cp4, Pz, P1, P2, P3 and P4, and the occipital region consisted of Po1, Po2, Poz, O1, O2 and Oz. The left temporal region consisted of T7, Tp7, Cp5, P5, P7 and Po7, and the right temporal region consisted of T8, Tp8, Cp6, P6, P8 and

Po8. A number of MANOVAs or MANCOVAs were carried out separately for the amplitude measurements at each regional electrode array as a dependent vector for comparisons among different stimulus conditions within and across groups. For the statistical analyses on latencies of each ERP component, we initially calculated the mean values according to each of the arbitrarily designated brain regions, then conducted within and across group comparisons with MANOVAs or MANCOVAs.

Because the scalp potentials may reflect the average activity of multiple neural sources recorded at a distance, they are neither reference-free nor independent of the volume conductor effects. These limitations mean that ERP components will be altered if the placement of the

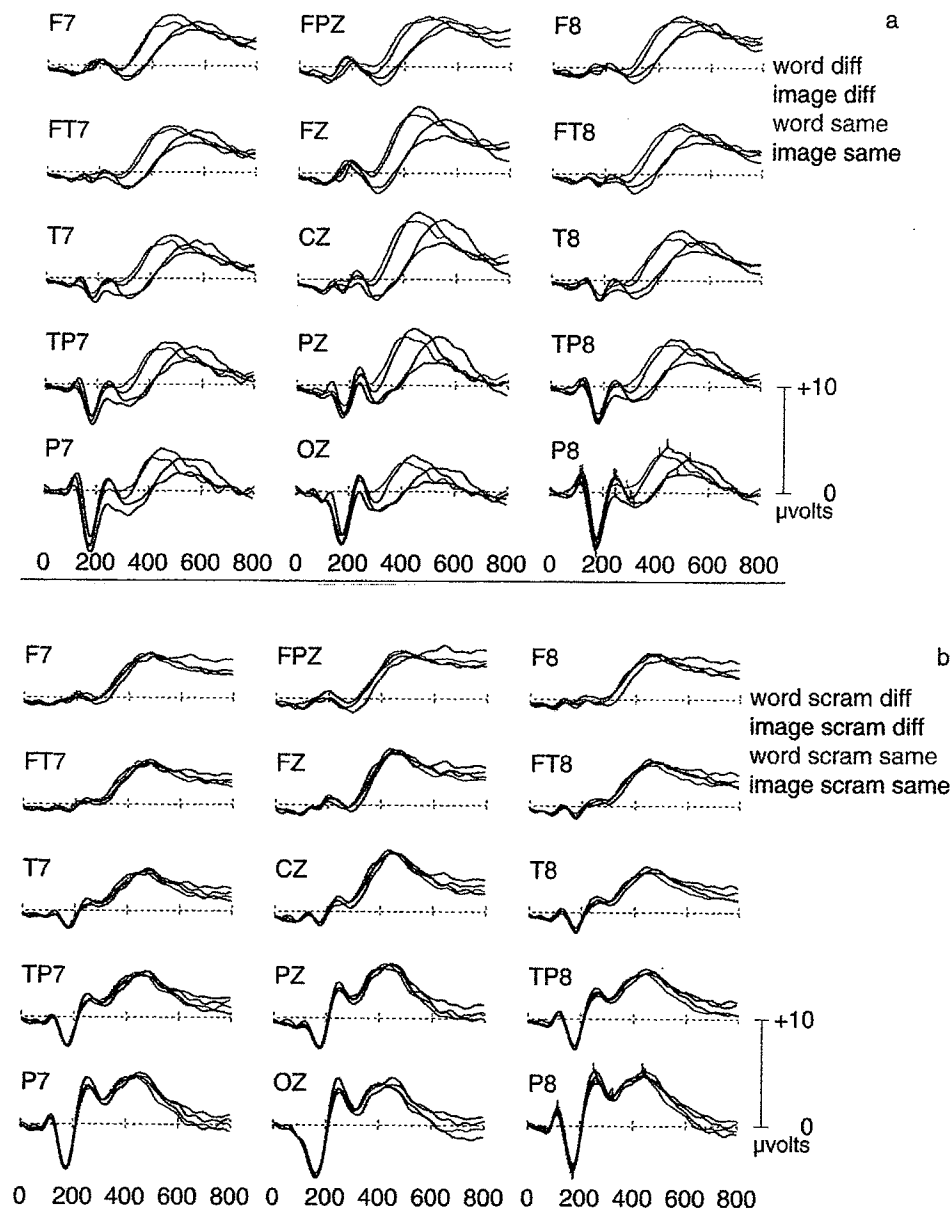


Fig. 2. (a) Grand mean ERPs to different recognizable stimuli in alcoholic subjects. (b) Grand mean ERPs to different unrecognizable stimuli in alcoholic subjects.

reference is changed or if it is not a 'quiet' reference (Nunez et al., 1991) and there may be spatial smearing of the potential record as a consequence of volume conductor effects. For further analysis of our electrophysiological data, we constructed topographic maps of SCD (source current density). The SCD represents both scalp sources and sinks of current, reflecting mainly neocortical activity; a scalp region having a positive current density corresponds to a source region where a local radial current is flowing through the skull into the scalp.

### 3. Results

As the *T*-test showed that the alcoholic subjects were significantly older than the control subjects in this study ( $T(86.7) = 10.81, P < 0.0001$ ), all the following statistical analyses regarding the comparisons between the two groups employed covariance analyses controlling for age.

#### 3.1. Behavioral data analyses

Both groups had a very low response error rate (less than 0.5%). Response times to the different stimulus conditions were analyzed by a two way ANCOVA using age as a covariate, with two between factors. This analysis revealed significant main effects for stimulus condition ( $F(7,735) = 7.69, P < 0.0001$ ) and group difference ( $F(1,735) = 44.16, P < 0.0001$ ). The interaction between stimulus condition and group proved to be non-significant ( $F(7,735) = 0.34$ ). The sample means are displayed in Fig. 3, which clearly indicates that alcoholics had longer response times than controls to all corresponding stimuli. Tukey's HSD showed that response time in the image different condition was significantly longer than in the image same condition. The response time to word different stimuli was also significantly longer than to word same stimuli. No significant differences in reaction times could be observed across different scramble stimulus conditions within and between groups.

#### 3.2. Statistical analyses of ERP amplitudes

Statistical analyses (MANOVAs) confirmed our initial impressions from Figs. 1b and 2b that stimulus condition had no significant effect on any of the ERP components elicited by the unrecognizable stimuli in both control and alcoholic groups. Stimulus condition had no robust effect on c110 to recognizable stimuli either.

##### 3.2.1. Comparisons between ERPs to image same and image different stimuli

In the control group, the ERPs to image different stimuli had a more positive shift, which occurred between 110 ms (c110) and 300 ms approximately after stimulus presentation, most clearly in posterior electrodes, than the ERPs to

image same stimuli (see Fig. 4a). However, the ERPs to image same and image different stimuli were almost identical within that time range in the alcoholic group (see Fig. 4b). MANOVAs demonstrated that the image different stimuli elicited significantly higher amplitudes of c180 than image same stimuli at the left temporal region, the right temporal region and the occipital region in the controls. On the contrary, no such effects on c180 could be revealed by MANOVAs in the alcoholics. With MANOVAs, widespread significant stimulus condition effects on c240 in the control group were demonstrated in the left temporal, right temporal, occipital, parietal, central and frontal regions of the brain. The results of MANOVAs also confirmed the observation that in alcoholic subjects, c240 did not reflect the amplitude differences that resulted from the image stimulus being preceded by the same or a different image stimulus. The effects of the image stimulus condition on c300 in the control group reached significance by MANOVAs at the left temporal, right temporal and frontal regions. Again, no significant effects of the image stimulus condition on c300 at any scalp region could be revealed by MANOVAs in the alcoholics. The results from MANOVAs indicated that the image stimulus conditions had no significant effects on c450 in both the controls and alcoholics.

MANCOVAs using age as a covariate were performed to make the group comparisons. In the image same stimulus condition, no significant group difference was documented. In the image different condition, however, the extensively robust group effects were demonstrated by MANCOVAs, i.e. the significant group effects on c240 at the left and right temporal regions, the occipital region and the frontal region, the significant group effects on c300 at the left temporal region and the frontal region, and the robust group effects on c450 at the left temporal region, the occipital region and the central region.

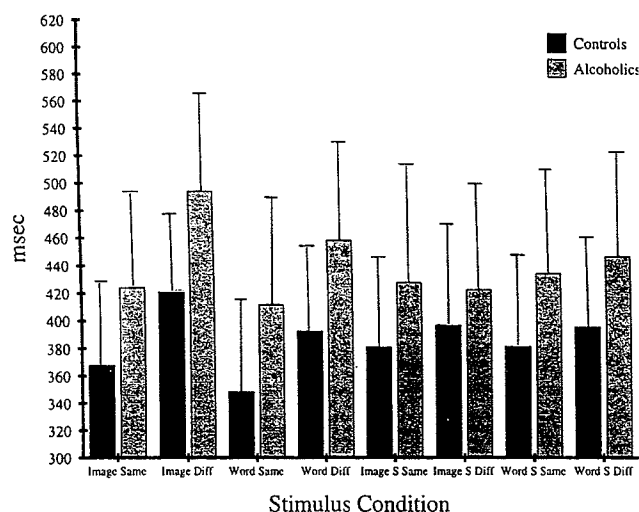


Fig. 3. Response time histogram for control and alcoholic subjects in each stimulus condition. The bars represent the means of response time in different stimulus conditions, and the whiskers represent the standard deviation in corresponding conditions.

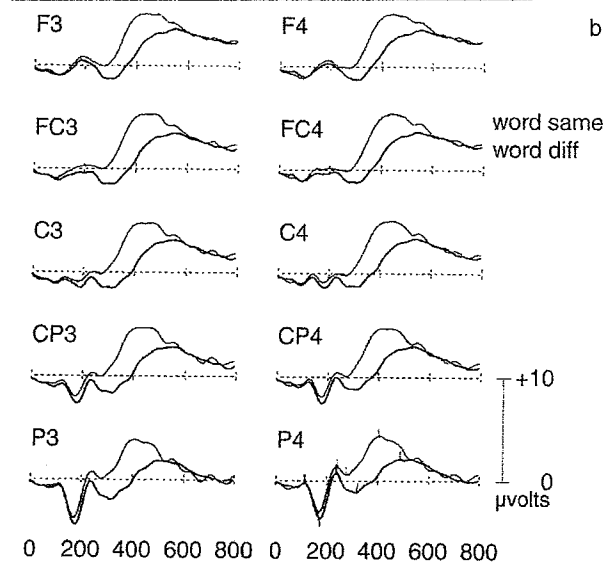
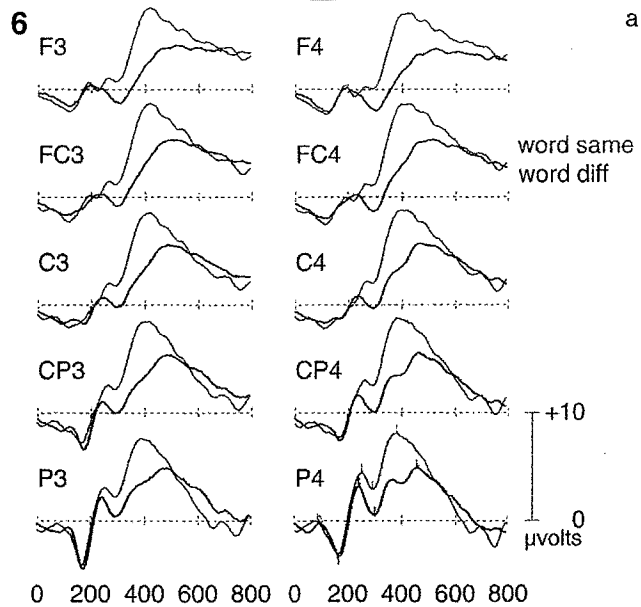
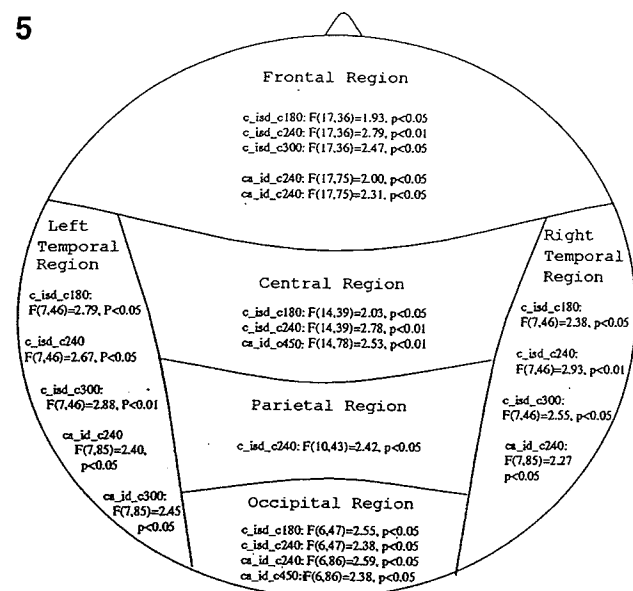
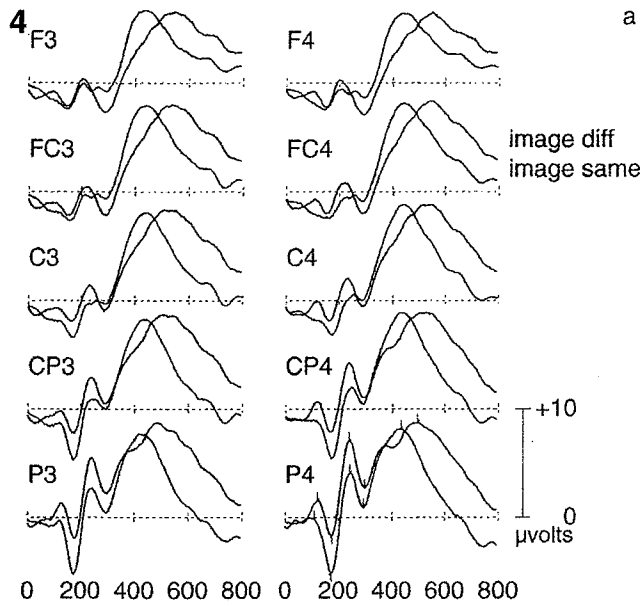


Fig. 4. (a) Grand mean ERPs to image same and image different stimuli in control subjects. (b) Grand mean ERPs to image same and image different stimuli in alcoholic subjects.

Fig. 5. Analyses of MANOVAs or MANCOVAs on ERP components to image stimuli. c180, c240, c300 and c450 represent the ERP components, respectively.  $c\_isd$  means MANOVA comparison between image same and different stimulus trials within control subjects.  $ca\_id$  means MANCOVA comparison between the control group and the alcoholic group within image different trials.

Fig. 6. (a) Grand mean ERPs to word same and word different stimuli in control subjects. (b) Grand mean ERPs to word same and word different stimuli in alcoholic subjects.

All the statistical results pertaining to the ERP components to image stimuli are presented in Fig. 5.

### 3.2.2. Comparisons between ERPs to word same and word different stimuli

Fig. 6a,b illustrates the ERPs to word same and word different stimuli in the controls and the alcoholics. Unlike the ERPs to image stimuli, the most prominent characteristic of the ERPs to word stimuli was the stronger positive deflection, taking place approximately between 300 and 600 ms poststimulus, in word same trials than in word different trials. The more positive shift in ERPs to word same stimuli, compared with the ERPs to word different stimuli, existed in both control and alcoholic groups. A number of MANOVAs were performed to test the word stimulus condition effects on the components of the ERPs. The results confirmed that no statistically significant word stimulus condition effects were found on c110, c180 and c240 in both control and alcoholic groups. As illustrated in Fig. 7, MANOVAs demonstrated significant effects of word stimulus condition on c300 at the left temporal, parietal and frontal regions in the control group. Similar results were found in the alcoholic group at the left temporal, parietal and central regions. The results of MANOVAs on c450 at the parietal, central and frontal regions in the controls demonstrated a strong word stimulus condition effect on the amplitude of c450 in the control group. MANOVAs also resulted in similar significant stimulus condition effects in alcoholic subjects at the parietal, central and frontal regions.

For the group comparisons, MANCOVAs were performed using age as a covariate. In word same stimulus trials, the significant group differences on c450 at the right temporal, occipital, central and frontal regions were demonstrated. In word different stimulus trials, the group factor had significant influence on c300 only at the frontal region. The significant group differences on c450 at occipital, parietal and frontal regions were also documented in the word different stimulus trials.

A general overview of the statistical results regarding the ERP components to word stimuli are presented in Fig. 7.

### 3.2.3. Comparisons between ERPs to image stimuli and corresponding word stimuli

Figs. 1a and 2a suggest that the patterns of the ERPs to image same stimuli are almost the same as the patterns of ERPs to word same stimuli. These impressions were confirmed by MANOVAs which showed that the stimulus condition had no significant effects on any components of the ERPs. Nevertheless, Fig. 8 illustrates that the ERPs to image different stimuli were more positive than those of the ERPs to word different stimuli. These trends which were most discernible within the time range between 110 and 700 ms poststimulus occurred mainly in posterior electrodes. These positive deflections were more evident in controls than in alcoholics. The MANOVAs demonstrated that the differences between ERPs to these two stimulus conditions on

c180 were mainly found at the posterior brain regions in the controls, namely the left temporal ( $F(7,46) = 4.42$ ,  $P < 0.001$ ), right temporal ( $F(7,46) = 2.40$ ,  $P < 0.05$ ) and parietal ( $F(10,43) = 2.18$ ,  $P < 0.05$ ) regions. The stimulus condition had robust effects on c240 at several brain regions in the controls as indicated by MANOVAs, namely the left temporal ( $F(7,46) = 3.83$ ,  $P < 0.01$ ), occipital ( $F(6,47) = 2.38$ ,  $P < 0.05$ ), parietal ( $F(10,43) = 2.34$ ,  $P < 0.05$ ) and central ( $F(14,39) = 2.21$ ,  $P < 0.05$ ) regions. The effect of stimulus condition on c300 in the control group also reached significance at the left temporal ( $F(7,46) = 2.81$ ,  $P < 0.05$ ), right temporal ( $F(7,46) = 2.46$ ,  $P < 0.05$ ) and parietal ( $F(10,43) = 2.32$ ,  $P < 0.05$ ) regions as revealed by MANOVAs. The MANOVAs further demonstrated the significant effect of stimulus condition on c450 at the left temporal ( $F(7,46) = 3.07$ ,  $P < 0.01$ ) and parietal ( $F(10,43) = 5.19$ ,  $P < 0.001$ ) regions in the controls. For the statistical analyses in the alcoholics, however, the significant effects of stimulus condition on c240 ( $F(10,123) = 2.17$ ,  $P < 0.05$ ), c300 ( $F(10,123) = 2.07$ ,  $P < 0.05$ ) and ( $F(10,123) = 2.01$ ,  $P < 0.05$ ) were found only at the parietal region.

### 3.3. Statistical analyses on ERP latencies

There was no significant difference between latencies of analogous components of ERPs to the four kinds of unrecognizable stimuli, nor were the differences in latencies of c110, c180, c240 and c300 between various kinds of recog-

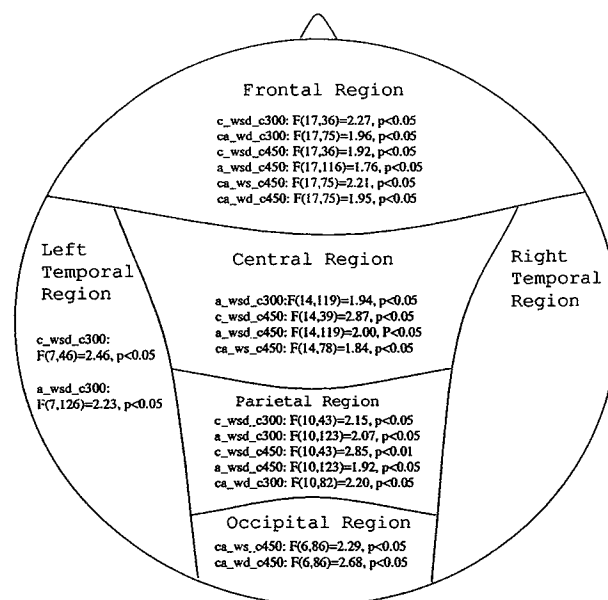


Fig. 7. Analyses of MANOVAs or MANCOVAs on ERP components to word stimuli. c\_wsd represents MANOVA comparison between word same and word different stimuli within controls; a\_wsd represents MANOVA comparison between word same and word different stimuli within alcoholics; ca\_ws represents MANCOVA comparison between controls and alcoholics on word same stimuli; ca\_wd represents MANCOVA comparison between controls and alcoholics on word different stimuli.

nizable stimuli significant. However, MANOVAs indicated that the significant latency differences occurred only on c450. As shown in Fig. 4, the latencies of c450 to image same stimuli were significantly shorter than to image different stimuli both in control ( $F(6,47) = 2.51$ ,  $P < 0.05$ ) and alcoholic ( $F(6,127) = 4.62$ ,  $P < 0.001$ ) groups. The latencies of c450 to word same stimuli were also significantly shorter than to word different stimuli in control ( $F(6,47) = 2.75$ ,  $P < 0.05$ ) and alcoholic ( $F(6,127) = 3.79$ ,  $P < 0.01$ ) groups. No significant differences between the latencies of c450 to image same and to word same stimuli were found by the MANOVAs in either group. However, the comparisons between the latencies of c450 to image different and to word different stimuli achieved significance only in the control group ( $F(6,47) = 2.71$ ,  $P < 0.05$ ). MANCOVAs showed no group difference in the latencies of c450.

### 3.4. SCD topographic results

Because the group difference on amplitude came mainly from the ERP to image different and word different trials, only four SCD maps were included in this paper. Fig. 9 represents the SCD map of c240 to image different stimuli. As suggested in this figure, the main current sources were located in the occipito-temporal regions. Moreover, the parietal region had a deep current sink, and smaller current sources were also found in frontal regions. This pattern suggests that while the occipito-temporal regions are the most active regions in processing the image stimuli, many other regions such as frontal, parietal, etc. participate in this process. In contrast, the pattern of c240 to image different stimuli in alcoholics was different from that in the controls. Fig. 9 also indicates that the current source activities were generally lower in the alcoholics than in the controls, though the main current sources were also located in the occipito-temporal regions. However, the current sources located in the occipito-temporal regions were asymmetrical, with the source on the left side being stronger than on the right. Furthermore, it was hard to locate the current sources and sinks at other regions in the alcoholics. Fig. 10 reflects the SCD maps of c450 to word different stimuli in the controls and the alcoholics. This figure reveals that the current sources can be found at many regions of the brain. In addition, the current sources and sinks at the temporal regions suggested that the neurons in these regions were active and involved in word processing. In control subjects, the frontal regions seemed to be activated equally or more than the posterior regions of the brain. This suggests that frontal regions play an important role in word processing. However, the topography in the alcoholic group is completely different. The most prominent differences between the two groups are the lack of current sources and sinks over the frontal regions in the alcoholics. This phenomenon may suggest that word processing in alcoholics might differ from controls.

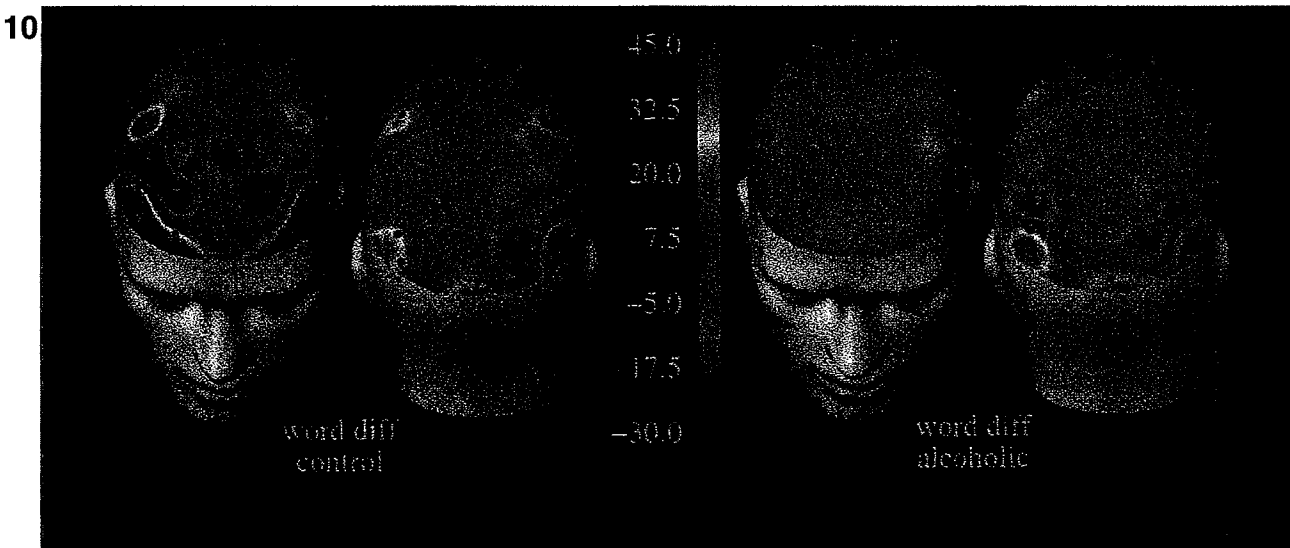
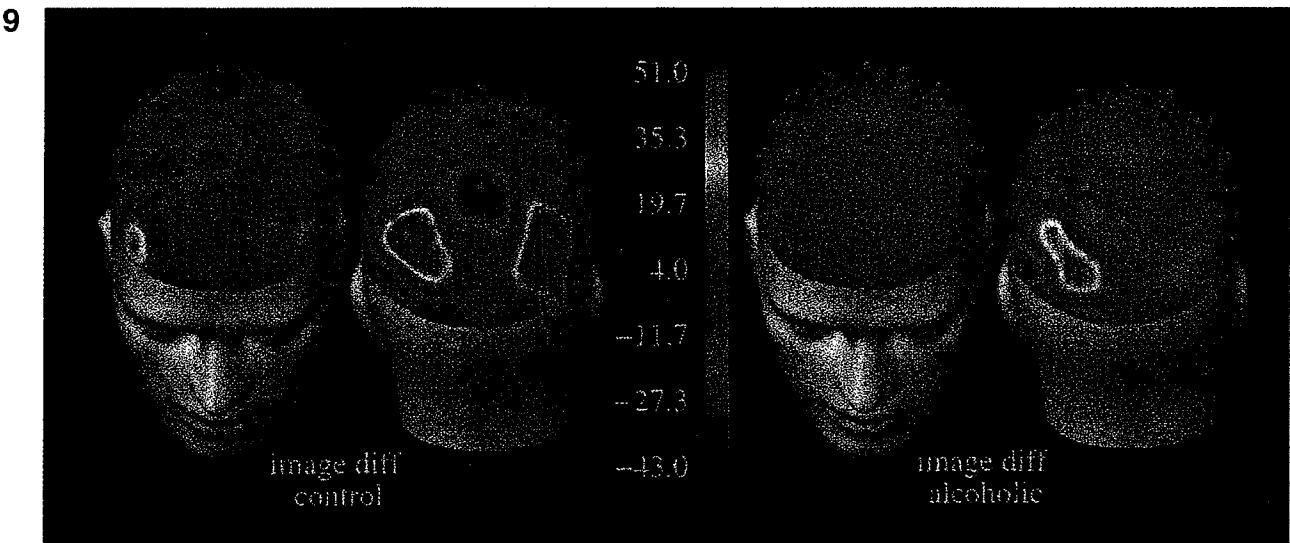
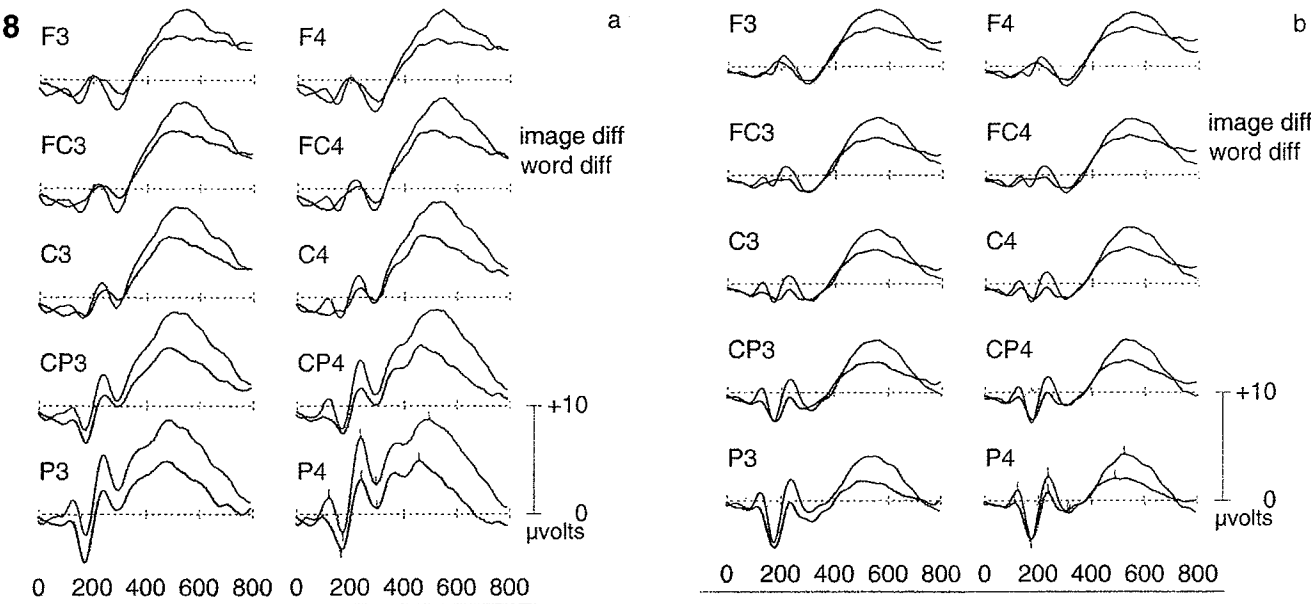
## 4. Discussion

In the current experiment, the subjects' task required them to make a categorical decision, i.e. recognizable or unrecognizable, not based on the specific features of the stimuli. The task was assumed to be an implicit repetition memory task, and the experiment was assumed to assess implicit memory electrophysiologically. The results of this experiment on implicit memory in chronic alcoholics both replicate previous findings and present new evidence regarding differences from controls in visual repetition priming.

### 4.1. Behavioral response times (RTs) to recognizable stimuli in the two groups

In this experiment, the RT patterns in the controls and the alcoholics were similar (Fig. 3), except that alcoholics generally had longer RTs than controls. The RTs in the two groups were faster both for repeated images and repeated words compared to the corresponding unrepeated images and unrepeated words. The significant facilitation in identification of repeated recognizable stimuli in this study is in agreement with the results of previous studies, in which subjects were shown drawings of real and nonsense objects (Kroll and Potter, 1984) or structurally possible and impossible objects (Schacter et al., 1991b). The shortened reaction time for repeated words in this experiment is also in accordance with the studies exploring word repetition effects (Bentin and Moscovitch, 1988; Bentin et al., 1992; Cave and Squire, 1992). As Fig. 3 indicates, the RTs in the image different trials compared to RTs to other recognizable trials were the longest in both groups. Because object decision tasks concerning pictures showed priming effects of the same magnitude without a naming response (Kroll and Potter, 1984), the name-retrieval was eliminated as a source of the priming effect. Furthermore, the word identification in this experiment was primarily guided by the physical properties of the test cues. Therefore, our longer RTs in object image compared to word identification may be due to the fact that the objects had more complex physical properties than words, thus requiring a longer time to be processed.

Many studies support our current RT results to repeated recognizable stimuli in alcoholic subjects. With a picture-naming paradigm, Cave and Squire (1992) found normal priming in a mixed group of amnesic patients and further demonstrated that the priming persisted over a 7-day retention interval. The intact priming of words in amnesics was also demonstrated in tests such as word identification or perceptual identification (Graf et al., 1984; Carlesimo, 1994). In the present experiment, however, we also noticed that the RTs to all kinds of stimuli in the alcoholics were generally longer than those in the controls though the absolute priming effects were almost equal in the two groups. In a combined study of MRI and neuropsychological test, Jerinigan and Ostergaard (1993) divided the priming variability



in their task into a significant memory related component and an independent perceptual or lexical processing component, and found that slower word identification predicted larger priming effects. Thus, it is important to take baseline values into account in order to assess the priming effect. Therefore, to assess our alcoholics' priming functions based solely on RT data is not the most optimal method.

#### *4.2. Repetition effects reflected by c240 to recognizable image stimuli exist in controls but not in alcoholics*

The ERPs were sensitive to recognizable stimuli in our implicit test of memory. In the control group, the significant repetition effects of object pictures on ERPs were initially found in c180 at most brain regions except for the parietal region. These effects became more obvious on c240 at all brain regions and lasted until c300 at most regions. Though the c240 could be documented at all brain regions, it was more prominent at the temporal region. These findings in the control group regarding object image processing are in agreement with the earlier studies on visual short term memory in which we identified an ERP component named visual memory potential (VMP) with a different recording montage using Cz as a reference (Begleiter et al., 1993, 1995; Hertz et al., 1994; Zhang et al., 1995). Though the electrical recording pattern in this experiment differed from previous studies which resulted in a clear VMP over the occipito-temporal region, the c240 to image stimuli in this study was not only in accordance with the characteristics of the VMP topographic locations confirmed by the SCD topographic map, but its latency was also in keeping with that of the VMP.

The most widely accepted proposal for the role of inferior temporal (IT) areas in object recognition is that IT provides perceptual constancy, that is, the ability to see that two inputs with different retinal positions, orientations and sizes arise from the same physical object (Desimone et al., 1985; Iwai, 1985). Plaut and Farah (1990) proposed that regions of IT play a major role in computing the global form and structure of visual objects. Therefore, the most ostensible difference between ERPs to repeated and non-repeated object image stimuli in this experiment occurred in occipital-temporal regions, not only reflecting the electrophysiological processing difference between repetition

priming and non-priming effects, but also suggesting that the IT or the analogous system in humans plays a significant role in object decision priming (Plaut and Farah, 1990; Schacter et al., 1990b, 1993b). The SCD map for image stimulus trials in the controls also showed strong current sources and sinks in the frontal and the parietal regions, suggesting the involvement of these brain regions in processing visual information. Recent functional imaging studies (Haxby et al., 1991; McIntosh et al., 1994) have put forward the existence of separate processing streams by having people perform object identity and spatial perceptual tasks analogous to the tasks that have been used in monkeys (for review, see Ungerleider and Haxby, 1994). These studies revealed regions activated in the dorsal occipito-parietal cortex in spatial perceptual tasks and regions activated in the ventral occipito-temporal cortex in object identity tasks. Aside of the visual cortex per se, functional imaging studies in humans have revealed additional zones in the prefrontal cortex that are activated during performance of object or spatial vision tasks (Jonides et al., 1993; Petrides et al., 1993; McCarthy et al., 1994). Thus, the results of the ERPs to recognizable image stimuli fit the previous investigations involving both non-human primates (Wilson et al., 1993) and human subjects.

In contrast to the results in the controls, statistical analyses did not reveal any significant difference between the amplitude of ERPs to image same and image different stimuli in the alcoholics, i.e. the distinctions between neuronal processing of images (repetition versus non-repetition) could not be manifested electrophysiologically. However, the fact that c240 in the alcoholics could be clearly identified and is mainly located in the occipito-temporal regions suggests that the information of object images is also mainly processed in these regions. In this experiment, the robust distinctions between the two groups were widespread on the amplitudes of c240 to image different stimuli. These deviations may indicate that the neurons in these regions are less activated to the formation of new pictorial representations in the brains of these alcoholic subjects. Compared to the controls, the pattern of SCD topographic map to image stimuli in the alcoholic group indicated that the frontal region was minimally involved in image processing. Furthermore, the weak current source at the right occipito-temporal region and weak current sink at the parietal region in the alcoholics

Fig. 8. (a) Grand mean ERPs to image different and word different stimuli in control subjects. (b) Grand mean ERPs to image different and word different stimuli in alcoholic subjects.

Fig. 9. Grand mean SCD topographic maps for c240 to image different stimuli in the control and the alcoholic groups. In control subjects, the strongest current sources are located in occipito-temporal regions, and the density seems higher in the right and in the left. There are also strong current sources and sinks over frontal and parietal regions in the control group. The current sources are weaker in alcoholic subjects than in control subjects. Moreover, the current source over the right occipito-temporal region in alcoholic subjects is even less active than its left counterpart. Almost no current sources and sinks can be found over the frontal region in alcoholic subjects.

Fig. 10. Grand mean SCD topographic maps for c450 to word different stimuli in the control and alcoholic groups. These two groups have similar topographic distributions of current sources and sinks over brain regions except for the frontal region, i.e. there are no obvious current sources and sinks over the frontal region in the alcoholic group.

also suggest discrepancies between the two groups in processing visual information in these brain regions. It has been suggested that occipito-temporal, prefrontal and parietal cortices are strongly involved in visual information encoding and processing. Therefore, our results may suggest that difficulty and/or deficiency in forming new pictorial representations in the alcoholics cause relatively weak memory traces which, in turn, may not be sufficient to produce measurable priming effects. In a study testing episodic effects on picture identification in alcoholic patients by using a delay between study and test, Cermak et al. (1993) documented a pattern of below normal facilitation in picture identification accompanied by poor recognition memory. This pattern of results was very similar to those obtained in Korsakoff amnesics. These authors attributed their findings to the delay between study and test which has the same effect as reducing the accessibility to memory of earlier stimuli for amnesics and alcoholic patients. Our results that alcoholics may have difficulties in forming new pictorial representations in the brain could be complementary to the above findings.

The c450, the biggest positive-going shift after c240, could be found in both groups. There was no difference in amplitudes in this component between image same and image different trials within each group. The most obvious positive statistical results come from the analyses of latencies of this component, i.e. the latencies of c450 to image same stimuli are shorter than those to image different stimuli within each group. We did not replicate the findings of Friedman et al. (1988) who documented two positive components, namely P400 and P500, in a picture matching ERP study; P400 was mainly influenced by N400 according to these authors' explanation. In our opinion, this is because the tasks for the subjects were completely different. We were testing the ERP repetition effects implicitly by asking subjects to identify whether each stimulus was recognizable, while Friedman et al. asked their subjects to compare each picture stimulus with the previous one. The latencies of the c450 to recognizable image stimuli in this experiment varied with the RTs between image same and image different trials. It might be an integrated component like P3b which occurs in response to task-relevant stimuli within the subject's awareness.

#### *4.3. ERPs may reflect word priming effects both in controls and alcoholics*

Relative to the ERPs to unrepeatd word stimuli, the ERPs to repeated word stimuli are characterized by a later, temporally sustained and topographically widespread positive-going shift in both groups. The higher positive-going shift in ERPs to repeated word stimuli than to unrepeatd stimuli is generally believed to be the reflection of ERP word repetition effects.

The later higher positive shift (significantly beginning at c300 and most prominently occurring at c450) in word

repeated trials compared to word unrepeatd trials in this experiment is in line with the results of ERP studies on word repetition priming effects (Rugg, 1985, 1987, 1988, 1990, 1995; Rugg and Nagy, 1987; Bentin and Moscovitch, 1988; Bentin and Peled, 1990; Petten et al., 1991; Young and Rugg, 1992; Otten et al., 1993). Most ERP studies on word repetition effects employ a paradigm in which the effects of repetition are studied in the absence of overt responses to the critical items. In these kinds of tasks, subjects are required to detect the occasional presence of a target item against a background of more frequent non-targets, some of which are repetitions of preceding items. The critical comparison is between the ERPs to the non-targets on their second as opposed to their first presentations. Though this kind of paradigm has the advantage of minimizing the contribution of the parietally-maximum P3 component to the ERPs, it inevitably makes subjects process each item semantically; subjects have to decide for each item whether it is a word or whether it belongs to a specific semantic category. In the current experiment, the word identification is primarily guided by the physical properties of each stimulus; no extra requirement for the subjects is made as to whether the item is a word or what the meaning of the item (word) is. The results on word repetition effects in this experiment indicate that the perception of a word mainly relies on memory for prior processing episodes (Jacoby and Hayman, 1987). It occurs independently of the level of semantic processing, and largely reflects experience-induced changes in a cortically based, presemantic perceptual representation system (PRS) (Schacter, 1990, 1990a).

Our results showed that the amplitudes of c300 and c450 to repeated word stimuli were significantly higher than the corresponding amplitudes to word different stimuli in alcoholic subjects. These results suggest that the alcoholics basically retain their word repetition priming function. Although there are few electrophysiological studies similar to ours for comparison, the results from neuropsychological studies offer support for our current observations. It has been indicated that even amnesic patients showed intact priming of familiar word and word pairs on data-driven implicit tests, such as stem completion, perceptual identification and lexical decision (Graf et al., 1984; Cermak et al., 1985). Haist et al. (1991) found entirely normal non-word priming on a modified version of the perceptual identification task in a mixed group of amnesic patients.

However, the ERPs still reveal some differences between the two groups in word repetition priming. The amplitude of c300 to word same stimuli was significantly lower in the alcoholics than in the controls at the parietal and frontal regions. The alcoholics had statistically lower amplitudes of c450 to word same stimuli at the central region and c450 to both word same and word different stimuli at the frontal regions than the controls. From a psychological point of view, the repetition effects, even over very short time intervals, can be understood solely in terms of the formation and retrieval of episodic memories of the item's prior occur-

rences (Jacoby, 1983; Salasoo et al., 1985). Identification of a word may establish and/or update a representation in memory, and the memory trace may be enhanced by the word repetition. The lower amplitudes of c300 and c450 to word same stimuli in the alcoholic subjects relative to those in the controls may suggest two possible interpretations: (1) physiologically, the neurons in the alcoholics' brains are less activated by the visual stimuli; (2) neuropsychologically, the alcoholic subjects are not able to enhance the memory trace of the previous representation by repeating the same visual stimuli as much as the controls do. The failure to enhance a sufficient memory trace may be perhaps attributable to the initial insufficient encoding of the information.

The SCD maps further demonstrated the differences between the two groups in word repetition priming. In the controls, the SCD maps suggested that the occipito-temporal, parietal and frontal regions are among the primary regions involved in the word repetition processing. This SCD pattern is in agreement with previous PET studies in which recognition of words showed activations on frontal, temporal and parietal regions, and these activations were most predominant in dorso-lateral frontal cortex and adjacent anterior cingulate cortex (Howard et al., 1992; Riddle et al., 1993). Studies of brain lesions (Damasio and Damasio, 1983; De Renzi et al., 1987) and cortical stimulation (Luders et al., 1991) in patients suggested that there is a specialized region for the processing of written words in the inferior temporal lobe. A mounting body of evidence also indicates that there are neurons sensitive to word stimuli in the anterior and posterior fusiform gyrus (Nobre et al., 1994), the anterior medial temporal lobe, the neocortex near the collateral sulcus and anterior fusiform gyrus (McCarthy et al., 1995; Nobre and McCarthy, 1995). Similarly, there are neurons sensitive to word stimuli in frontal regions (Bechtereva et al., 1991; Halgren et al., 1994a,b). However, compared to the controls, the current sources were mainly located over posterior regions, and the frontal regions manifested the absence of current sources in alcoholics. There has been evidence that the frontal regions are involved in visual information processing which modulates affect and attention (Oscar-Berman et al., 1992; Dupont et al., 1993; Jenkins et al., 1994). Thus, the alcoholic subjects might process words in a superficial way. The processing level influences the ERP manifestations (Rugg et al., 1988). Moreover, there are reasons to suspect that performance by the controls on the word identification task is with the use of explicit memory strategies (Haist et al., 1991). In two studies which reported impaired implicit memory in amnesic patients (Cermak et al., 1985; Squire et al., 1987), all positive results came from tasks which sometimes tended to make subjects use explicit memory strategies in priming tasks.

We suggest that the controls could differ from the alcoholic subjects by invoking declarative or elaborative strategies during word identification. That is, the control subjects

might sometimes process the word both orthographically and semantically, thus evidencing a more sophisticated level of processing than the alcoholic subjects.

#### *4.4. Visual object priming clearly differs from visual word priming in ERP manifestations*

The results of our experiment clearly support the view that visual word and object priming occur in different subsystems for implicit memory (Tulving and Schacter, 1990) by demonstrating that visual word and object priming manifest different ERP patterns, and that visual word and object priming effects shown on ERPs are unevenly affected by long term alcohol abuse.

In the current study, the ERPs to different unrecognizable stimuli were almost identical to each other. We believe that the duplicated ERP patterns in the different scramble conditions may be due to the null and void or meaningless internal representations in memory. The logic of implicit memory tests is that information related to previous experience must have been retained in memory since it affects performance. It has also been documented that impossible objects show little or no priming effects because it is difficult to form an internal representation of their three dimensional structure (Schacter et al., 1990b, 1991b). Thus, the phenomena of identical ERP patterns to different scramble stimuli in this experiment suggest that the initial encoding and/or formation of representation in memory play an important role in the following priming functions.

The statistical analyses of ERPs to recognizable stimuli indicated that the statistical differences between the ERPs to the image and word stimuli in each group, but especially in the control group, came from the comparisons between ERPs to image different and word different stimuli. In the controls, the differences could be seen through earlier ERP component (c180) to late component (c450). These results indicate not only that the controls could detect the stimulus as an image or a word within a short time, but also that the later processing of word and object perceptual identification in memory might involve different mechanisms electrophysiologically. Furthermore, the SCD distribution patterns of c450 to image different and word different stimuli distinguished the two modes of processing more empirically. The occipito-temporal regions were predominantly responsible for the current source during visual object processing, though there were sources over frontal regions, whereas the current sources were more widespread during word processing. The frontal region became one of the principal current sources during the recognition of words, though the occipito-temporal region also manifested major current sources. Tulving and Schacter (1990) suggested that priming and perceptual identification are expressions of a single perceptual representation system (PRS), which exists separately from but interacts closely with other memory systems. The facilitation (priming) process for both words and objects might be significantly different, as suggested

by the statistical comparisons between the ERPs to word same and image same stimuli in both control and alcoholic groups. However, the perceptual identification processes for the two types of stimuli would be different because access to representation that supported priming was very inflexible, or hyperspecific (Tulving and Schacter, 1990). Therefore, the different patterns between ERPs to word and object different stimuli might be a reflection of neuronal processes gaining access to different representations in memory.

The statistical analyses in the alcoholics generated similar results as in the controls only over the parietal region; however, the most conspicuous characteristics of SCD maps to both word and image different stimuli was the lack of the current sources in frontal regions, suggesting less neuronal activity in the frontal regions in the alcoholic subjects. This interpretation conforms to the SPECT results that the chronic alcoholic patients had significantly low cerebral blood flow in frontal regions, and decreased frontal/whole slice ratios in comparison with a normal group; thus, the frontal region was more affected by alcohol than other regions (Erbas et al., 1992). It is well documented that the frontal regions widely influence the mental activities such as attention and mnemonic processes. There is a body of evidence indicating the involvement of frontal regions during word and picture processing (Nenov et al., 1991; Salmelin et al., 1994; Guillem et al., 1995). Nevertheless, our results suggested that the frontal lobes in our alcoholic groups are adversely affected by the long term abuse of alcohol and the frontal lobes may not play a key role in repetition priming, considering the fact that the word repetition priming effects in the alcoholic group can be readily obtained. We hypothesize that both visual picture and visual word priming are generated by different neural systems. It has been long proposed that the left hemisphere (LH) is involved in verbal processing and the right hemisphere (RH) is involved in pictorial processing. Recent evidence also indicates that the verbal tasks activated LH more than RH and a visuo-spatial task (perceptual speed) led to a complementary higher activation in RH than LH (Gur et al., 1993; Gainotti et al., 1994; Hartje et al., 1994). In the current experiment, the SCD maps of the alcoholics indicate the asymmetry of the current sources to pictorial stimuli and the symmetry of current sources to word stimuli. The right hemisphere functions are depressed more by acute alcohol ingestion as suggested by the performance of visual-spatial tasks which is dominated mainly by the right hemisphere (Porjesz and Begleiter, 1985). Electrophysiological evidence also supports the view that hemisphere interaction is disturbed due to predominant deficiency of the visual-spatial function in the right hemisphere in chronic alcoholism (Tsagareli, 1995). Thus, we suggest that the deviant visual object priming in the alcoholics may be due to the damage to the RH by long-term alcohol abuse, and that visual word priming is basically intact owing to the LH which is less vulnerable to alcohol abuse. The different manifestations between visual word and visual object primings in the alcoholic

group further demonstrate that different neuronal mechanisms underlie visual word and object priming.

## 5. Conclusions

In the current study, the repetition priming effects of words and object pictures in the controls and the alcoholics were investigated with ERP techniques. Though the response times to both recognizable word and image stimuli in the two groups were significantly shortened by the prior exposures of the identical stimuli, the ERP patterns reflected differences between repetition priming to word and to object picture stimuli in both groups. The differences between the two groups in repetition priming effects were also demonstrated. In the control group, the priming effect to image stimuli occurred earlier than to word stimuli; the SCD maps of the ERP components at which the maximal priming effects to image and word stimuli were manifested also showed different patterns. In the alcoholic group, however, the priming effect could only be elicited by word repetitions. The distinctive SCD patterns of ERP components differed between the alcoholics and the controls with regard to both word and image stimuli. The differences between the two groups in ERP amplitude could also be documented. Therefore, the present study shows electrophysiological evidence that visual object priming differs from visual word priming, and that the two visual priming systems are affected unevenly by long-term alcohol abuse.

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