ELSEVIER

INTERNATIONAL JOURNAL OF PSYCHOPHYSIOLOGY

International Journal of Psychophysiology 34 (1999) 249–265 www.elsevier.com/locate/physcho

Brain event-related potentials (ERPs) in schizophrenia during a word recognition memory task

Jürgen Kayser[a,b,*], Gerard E. Bruder[a,b], David Friedman[b,c], Craig E. Tenke[a], Xavier F. Amador[b,d], Scott C. Clark[b,d], Dolores Malaspina[b,d], Jack M. Gorman[b,d]

[a] *Department of Biopsychology, New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY 10032, USA*
[b] *Department of Psychiatry, Columbia University College of Physicians and Surgeons, New York, USA*
[c] *Department of Medical Genetics, New York State Psychiatric Institute, New York, USA*
[d] *Department of Clinical Psychobiology, New York State Psychiatric Institute, New York, USA*

Received 1 December 1997; received in revised form 4 August 1998; accepted 10 October 1998

Abstract

Impairments of recognition memory for words and attenuation of the ERP 'old–new' effect have been found in patients with left medial temporal lobe damage. If left temporal lobe dysfunction in schizophrenia involves medial structures (e.g. hippocampus), then schizophrenic patients might show similar abnormalities of verbal recognition memory. This study recorded ERPs from 30 electrode sites while subjects were engaged in a continuous word recognition memory task. Results are reported for 24 patients having a diagnosis of schizophrenia (n 16) or schizoaffective disorder (n 8) and 19 age-matched healthy controls. Both patients and controls showed the expected 'old–new' effect, with greater late positivity to correctly recognized old words at posterior sites, and there was also no significant difference between groups in P3 amplitude. However, accuracy of word recognition memory was poorer in patients than controls, and patients showed markedly smaller N2 amplitude. Reduced amplitudes of N2 and N2–P3 were associated with poorer performance, with highest correlations over the left inferior parietal (N2) and left medial parietal (N2–P3) region. Moreover, patients failed to show significantly greater left than right

* Corresponding author. Tel.: 1-212-543-5169; fax: 1-212-543-6540.
E-mail address: kayserj@pi.cpmc.columbia.edu (J. Kayser)

0167-8760 99 $ - see front matter
PII: S0167-8760(99)00082-3

hemisphere amplitude of N2–P3 at posterior sites, which was seen for healthy controls. These findings suggest that impaired word recognition in schizophrenia may arise from a left lateralized deficit at an early stage of processing, beginning at 200–300 ms after word onset.

Keywords: Schizophrenia; Word recognition memory; ERP repetition effect; ERP asymmetry; N2–P3 complex; Principal Components Analysis (PCA)

1. Introduction

Abnormalities of the temporal lobe, involving neocortical, e.g. the superior temporal gyrus (Barta et al., 1990, 1997; Shenton et al., 1992; Menon et al., 1995) and limbic structures, e.g. the hippocampus and amygdala (Bogerts et al., 1990, 1993; Arnold et al., 1991; Pearlson et al., 1997), have been reported in schizophrenia. These recent findings are in agreement with earlier psychophysiological (e.g. Gruzelier and Venables, 1972) and neuropsychological evidence (e.g. Gruzelier et al., 1988), and with theoretical accounts proposing temporal–limbic dysfunction in schizophrenia (e.g. Flor-Henry, 1976). Structural abnormalities of the temporal lobe may be directly linked to abnormalities of event-related brain potentials (ERPs) in schizophrenia, e.g. the reduction of N2 and P3 amplitude (McCarley et al., 1991, 1993; O'Donnell et al., 1993; Egan et al., 1994; Kawasaki et al., 1997). Several studies suggest that both structural and functional abnormalities in schizophrenia involve primarily the left side of the brain (e.g. Barta et al., 1990; Rossi et al., 1990, 1992; Shenton et al., 1992; Faux et al., 1993; Bilder et al., 1994; Salisbury et al., 1994a; Falkai et al., 1995; Vita et al., 1995; Pearlson et al., 1997), and support Crow's hypothesis of a left-sided deficit involving the supratemporal plane in schizophrenia (Crow, 1990, 1997). However, despite considerable converging evidence of temporal lobe abnormalities in schizophrenia, caution is advised before generalizing these findings since not all studies have reported abnormal structural (e.g. Weinberger et al., 1991; Flaum et al., 1995; Kulynych et al., 1996) or functional asymmetries (e.g. Pfefferbaum et al., 1989; Ford et al., 1994). This inconsistency may be related to the clinical heterogeneity of schizophrenic samples and other methodological issues.

For most healthy adults, structural asymmetries of the temporal lobe, in particular of the planum temporale, have been linked to a left-hemisphere language dominance (e.g. Geschwind and Levitsky, 1968; Witelson and Kigar, 1988). As a consequence, abnormal asymmetries might be associated with verbal deficits frequently reported for schizophrenia (e.g. Bull and Venables, 1974). However, unambiguous evidence of a direct correspondence between anomalous structural asymmetries and disturbed language processing capabilities in schizophrenia has not yet been presented (DeLisi et al., 1997).

Schizophrenic patients have been found to display moderate impairments of verbal learning and memory (Saykin et al., 1991; Colombo et al., 1993; Goldberg et al., 1993). An explicit memory deficit for verbal material was present in first-episode schizophrenic patients, indicating that this verbal memory impairment is not related to medication status or chronicity (Saykin et al., 1994). Moreover, neuroimaging studies have provided evidence linking the verbal memory deficits in schizophrenia to left medial temporal lobe structures (Gur et al., 1994; Mozley et al., 1996).

Several lines of evidence show that medial temporal lobe structures are crucial for mediating recognition memory. Patients with left medial temporal lobe damage are impaired in recognition memory for words (Smith and Halgren, 1989), medial temporal lobe neurons discharge differentially and selectively to recently displayed words or faces (Heit et al., 1988), scalp EEG theta power, possibly mirroring hippocampal activity, is increased during word recognition memory (Burgess and Gruzelier, 1997), and patients with left anterior temporal lobectomy show a reduced ERP 'repetition effect' to correctly recognized old words (Smith and Halgren, 1989; Rugg et al.,

1991). The ERP correlate of word recognition memory in healthy adults is a robust, replicable finding of greater positivity to 'old' as compared to 'new' words from approximately 250 to 800 ms post-stimulus (e.g. Rugg and Nagy, 1989; Smith and Halgren, 1989; Friedman, 1990; Rugg et al., 1991; Johnson, 1995).

If left temporal lobe dysfunction in schizophrenia involves damage to medial structures, then schizophrenic patients might also show abnormalities of word recognition memory and its electrophysiological correlates. We report findings from an ongoing study, which compares schizophrenic patients and age-matched controls in a continuous word recognition memory task. In this task, subjects view a series of words and respond by indicating whether the word is new (not previously presented in the series) or old (presented on a previous trial). This task was adapted from previous studies with healthy adults (e.g. Friedman, 1990; Friedman et al., 1993), but with modifications of several task parameters (e.g. stimulus exposure time and interstimulus interval) to ensure that most schizophrenic patients could perform adequately (i.e. above chance).

The sequence of ERP components reflect different aspects of information processing, ranging from early sensory attentional (e.g. as reflected in N1) to late cognitive processing (e.g. as reflected in P3). For this reason, ERP measures are uniquely suited to provide information about the temporal characteristics of the underlying recognition memory deficit in schizophrenia. Moreover, if ERP measures are recorded with adequate spatial resolution for displaying and analyzing topographic information, ERP scalp distribution can also help in inferring which cortical regions may contribute to abnormal word recognition memory.

2. Methods

2.1. Subjects

Twenty-four patients (15 male, 9 female) were recruited from the Schizophrenia Research Unit of New York State Psychiatric Institute and compared with 19 normal controls (9 male, 10 female). The patients met DSM-IV (American Psychiatric Association, 1994) criteria for schizophrenia (undifferentiated, *n* 8; paranoid, *n* 5; disorganized, *n* 3) or schizoaffective disorder (bipolar type, *n* 4; depressive type, *n* 4). The median age of the patients was 29 years (mean 32.8; S.D. 9.9; range 20–55) and median education level was 13 years (mean 12.9; S.D. 2.6; range 8–16). Research diagnoses were made on the basis of information provided from clinical interviews and from a semistructured interview by a trained and reliable rater using the Diagnostic Interview for Genetic Studies (Nurnberger et al., 1994). A consensus diagnosis was arrived at by the rater and a senior clinician (X.A.). In addition, ratings of symptoms of 21 patients were obtained using the Brief Psychiatric Rating Scale (BPRS) and the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1992). A mean BPRS score of 35.9 (S.D. 9.6; range 19–54) indicated that the patient group was mildly to moderately disturbed. At the time of testing, 21 patients were receiving antipsychotic medications: six patients were on risperidone (mean dosage 5.7 mg day; range 3–9), four patients were on haloperidol (mean dosage 14.4 mg day; range 7.5–20), four patients were on olanzapine (mean dosage 18.8 mg day; range 15–25), three patients were on thiothixine (mean dosage 18.3 mg day; range 15–20), two patients were on clozapine (mean dosage 625 mg day; range 450–800), one patient was on fluphenazine (30 mg day), and one patient was on trifluoperazine (40 mg day). The remaining three patients (one schizophrenic, undifferentiated, and two schizoaffective, bipolar type) did not receive antipsychotic medications for at least 14 days prior to testing.

The control subjects were screened using a modified version of the Schedule for Affective Disorders and Schizophrenia — Lifetime Version (Spitzer and Endicott, 1975) to exclude those with current or past psychopathology. The median age of the control group was 30 years (mean 32.2; S.D. 10.3; range 20–60) with a median education level of 16 years (mean 15.6; S.D. 1.9; range 12–21). There was no significant age difference between patients and controls, and no

significant Group × Gender interaction for age, both $F_{1,39}$ 1.0, but the patient group had significantly less education than the controls, $F_{1,39}$ 13.8, P 0.001. As indicated below in the results, however, education was not significantly associated with either performance in the word recognition memory task or with ERP measures in this study.

Only right-handed subjects were included in the study. As indicated by the laterality scores on the Edinburgh Inventory (Oldfield, 1971), there was no significant difference in the degree of right handedness between patients (mean 82.8; S.D. 13.8) and controls (mean 87.0, S.D. 20.4), $F_{1,39}$ 1.0. All subjects were screened to exclude those who had a history of neurological insult or illness, current substance abuse or a history of substance abuse that obscured diagnosis.

2.2. Word recognition memory task

The continuous word recognition memory paradigm was adapted from previous studies with healthy adults (e.g. Friedman, 1990; Friedman et al., 1993). In this task, subjects viewed a series of words and responded by indicating whether the word was new (never presented previously in the series) or old (presented on a previous trial), that is, subjects were instructed to press either a 'new' or 'old' hand-held button as quickly as possible after each stimulus. Response hand assignment (left thumb press to new items, right thumb press to old items, or vice versa) was counterbalanced across subjects. Responses were accepted from 200 ms post-stimulus onset until the next stimulus onset within a fixed 2.5-s interstimulus interval (ISI). Word stimuli were presented in foveal vision on a computer monitor (500 ms duration), subtending a vertical visual angle of 0.95°, and horizontal angles ranging from 3.3° to 8.7°. A small fixation cross in the center of the screen was visible between stimulus exposures to indicate stimulus location. All items were in black on a light grey background. Words were taken from the 925 nouns for which Paivio et al. (1968) had collected norms. From these stimuli, various sequences of 320 stimuli were constructed with the constraint that there be an equal number of words repeated after 4, 8, or 16 intervening items (i.e. lags) following their intial presentation, and that two-thirds of the words were new (see Friedman, 1990). No word was repeated more than once. This procedure resulted in various stimulus sequences consisting of 100–105 new old word pairs and 110–120 filler items. Each subject viewed a different stimulus sequence which was split into two blocks of 160 stimuli.

Although task parameters (i.e. exposure time, ISI, lags) had been selected to ensure that most schizophrenic patients could perform adequately (i.e. above chance), subjects who could not perform even under these conditions were not included in the sample. Out of 34 patients originally tested, two patients did not meet performance criteria, three patients did not meet diagnosis criteria (schizophrenia or schizoaffective disorder), and five patients had too few artifact-free trials (15 in any condition).

2.3. Data acquisition and recording procedures

Electroencephalograms (EEGs) were recorded from four midline (Fz, Cz, Pz, Oz) and 13 homologous sites from both hemispheres (Fp1 2, F3 4, F7 8, FT9 10, FC5 6, C3 4, T7 8, TP9 10, CP5 6, P3 4, P7 8, P9 10, O1 2) with a nose electrode serving as the reference and an Fpz ground, using an electrode cap (Electro Cap International, Inc.). Horizontal electrooculograms (EOGs) were recorded differentially from the outer canthi of each eye (horizontal bipolar) and from supra- and infraorbital sites (vertical bipolar). All impedances were maintained at 5 kΩ or less. EEG gain was 10 000 (5000 for eye channels), with a 0.01–30 Hz band pass (6 dB octave). Data were continuously sampled at 100 Hz. Recording epochs of 2000 ms (300 ms pre-stimulus baseline) were extracted off-line. The averaged ERP waveforms were spline-interpolated to 256 sample points (128 Hz) and digitally low pass filtered at 12.5 Hz (24 dB octave). Statistic analyses were based on an effective sampling epoch of 1700 ms (100 ms baseline).

2.4. Data reduction and analysis

Trials contaminated by artifacts were eliminated when EEG and horizontal EOG data exceeded 100 μV following vertical EOG reduction (linear regression; Semlitsch et al., 1986). Average ERP waveforms were computed for each subject and each condition (new old items) for artifact-free trials (correct responses only), resulting in an average of 74.5 (S.D. 16.4) and 49.5 (S.D. 22.5) trials per patient (range 15–101 trials), and 86.9 (S.D. 12.1) and 78.1 (S.D. 17.0) trials per control (range 29–103 trials) for new and old items, respectively.[1]

In order to determine the sources of variance in the ERP waveforms, the averaged ERP waveforms were submitted to a Principal Components Analysis (PCA) derived from the covariance matrix, followed by a Varimax rotation (Chapman and McCrary, 1995; Achim and Marcantoni, 1997; Kayser et al., 1997, 1998). The factor analysis was computed using BMDP statistical software (BMDP4M; Dixon, 1992). Columns of the data matrix represented time (218 sample points from 100 ms to 1600 ms), and rows consisted of subjects (43), conditions (2), and electrode sites (30). The number of orthogonal factors extracted by the PCA was limited by a criterion of Eigenvalues greater than 1.0.[2] Peak latencies of factor loadings and topographies of factor scores were used to identify four principal components extracted by the PCA, which together accounted for 89.5% of the ERP variance and corresponded to the following ERP components: slow wave (peak latency 1000 ms, broad central maximum, 26% explained variance), a late negativity (720–970 ms, midline occipital maximum, 25%), P3 (450–680 ms, broad parietal maximum, 25%), and a factor associated with the early negativities N1 and N2 (160–420 ms, peaking at 320 ms, left lateral inferior-parietal maximum, 13%; see Kayser et al., 1997, 1998, for detailed examples of this methodology). For theoretical reasons, this report will focus only on PCA factors associated with a late positivity (Factor P3) and the preceding negativity (Factor N2).

PCA factor scores were submitted to repeated measures ANOVA (BMDP4V; Dixon, 1992) with group (patients controls) as a between-subjects factor, and condition (old new), hemisphere (left right), and site (13 symmetric pairs of electrodes, excluding midline electrodes) as within-subjects factors.[3] Greenhouse–Geisser epsilon (ε) correction was used to evaluate F ratios for within-subject effects involving more than two degrees of freedom (Vasey and Thayer, 1987). Significant interactions involving site were examined through simple effects at each site and for each group to locate the source of the interaction.[4]

[1] Only overall averages across lags were calculated, because the small number of valid trials for some patients would have led to an insufficient number of trials for each lag. The analyses of the behavioral data for each lag did not indicate any significant performance differences between lags.

[2] The chosen cut-off criterion of Eigenvalue 1.0 with the covariance matrix factored resulted in an extraction of 37 factors explaining nearly the total variance (99.87%). Further restrictions in the number of factors to be extracted and rotated (e.g. applying a criterion equal or greater than the average variance of the original variables; see Chapman & McCrary, 1995) limited the capacity of the PCA to remove 'noise' or 'error' variance from meaningful components and resulted in less well-defined factor loadings.

[3] For all ERP components considered, similar ANOVA models were calculated including gender as an additional between-subject factor. Because no significant gender main effects or important interactions with the other factors were observed, and because of the uneven cell distribution of male and female subjects in the two groups, data analyses were collapsed across gender. Midline data were also submitted to repeated measures ANOVA. However, because these analyses revealed no additional information to the analyses of hemisphere sites, ANOVA results from the midline electrode sites will not be considered in this report.

[4] In order to confirm significant effects for PCA factor scores, N1, N2 and P3 components were also analyzed with a conventional technique for ERP component abstraction. Based on the time course of the respective factor loadings and the grand ERP averages for both groups, average ERP amplitudes were calculated with reference to the baseline (100 ms) between 100 and 229 ms (N1), 230 and 419 ms (N2), and 420 and 699 ms (P3), and submitted to repeated measures ANOVA as described above. Because ANOVA results for the window amplitudes were highly comparable to the ANOVA results of the PCA factor scores, but F ratios, effect sizes and significance levels were generally more robust for the latter method, only the results obtained for the PCA factor scores will be reported.

For the analysis of the behavioral data, response latency (mean reaction time of correct responses) and percentage of correct responses were submitted to repeated measures ANOVA with group (patients controls) and gender (female male) as between-subjects factors, and condition (old new) as a within-subjects factor. The d'-like sensitivity measure d_L was also calculated from the hit rate and false alarm rate (see Snodgrass and Corwin, 1988)[5] and submitted an ANOVA with group and gender as between-subjects factors.

For all analyses, response hand assignment (left hand to new items, right hand to old items, or vice versa) was entered as a control factor into the ANOVA design, but this variable will not be considered further in this report. No significant main effects or group- or condition-related topographic interactions for this variable were observed in any of the analyses.

An essential issue for clinical research, particularly with electrophysiological measures, is the possibility that differences in variance between groups and conditions may violate basic ANOVA assumptions of homogeneity of variance. However, inflated Type 1 error rates are the result of very small sample sizes and a large amount of heterogeneity of variance, and the effect of variance heterogeneity may be more serious when group sizes are unequal rather than equal (e.g. Lix et al., 1996). Moreover, when group sizes and variances are positively paired, that is, the group with the largest sample size (i.e. patients) have the largest degree of variability, the F test will be conservative (Lix et al., 1996). Still, to address the concern that the heterogeneity of cell variance in our data may have led to liberal F tests, a nonparametric analysis, the Approximate Degrees of Freedom (ADF) test (Lix and Keselman, 1995), was also applied to the data. The ADF test is a multivariate F statistic which does not pool across heterogeneous sources of variation (covariance matrices) and estimates the error df from the data (Keselman, 1998). Overall, effects of the ADF statistic were found to be comparable with the original univariate F test results for both behavioral data and ERP measures, and indicated that the traditional repeated measures ANOVA approach in combination with Greenhouse–Geisser ε correction (sphericity assumption) were

[5]The sensitivity measure d_L is a signal detection theory (SDT) discrimination index with a logistic distribution, d_L $\ln\{[H(1 FA)] [(1 H)FA]\}$, where *ln* is the natural logarithm, and H and FA indicate hit and false alarm rate, and can be interpreted analogously to the discrimination index d' with a normal distribution. However, the SDT logistic model allows one to observe bias differences among subjects even when performance approaches chance levels (see Snodgrass & Corwin, 1988, for a detailed comparison of SDT models in the context of measuring recognition memory).

Table 1
Behavioral data summary: grand means and ANOVA F ratios

Grand means[a]	Correct responses (%)		Sensitivity (d_L)		Latency (ms)	
	New	Old			New	Old
Controls	94.2	82.9	4.97		786	802
	(4.6)	(15.0)	(1.21)		(166)	(155)
Patients	91.0	57.4	3.44		753	823
	(9.4)	(22.8)	(1.40)		(228)	(231)
Effect[b]	F	P	F	P	F	P
Group	16.1	0.0003	14.6	0.0005		
Condition[c]	55.1	0.0001	–	–	12.3	0.001
Group × Condition[c]	12.9	0.001	–	–	5.1	0.03

[a]S.D. in parentheses.
[b]For all effects, df 1,35. Only F ratios with P 0.05 are reported.
[c]Not applicable to d_L sensitivity measure.

appropriate for this data set (Vasey and Thayer, 1987).

Non-parametric Spearman rank-order correlations were computed to examine the strength of the relationship between ERP measures and behavioral accuracy (the sensitivity measure d_L, see Snodgrass and Corwin, 1988; percentage of correct responses for old items). The relation of accuracy and ERP measures to symptom scores on the PANSS and BPRS and to age and education was also examined. Only ERP amplitudes for old items were used at sites where the ERP component was most robust so as to reduce the number of correlations. Correlations were compared with Pearson's correlations and are reported only if both correlational methods revealed a significance level of P 0.05 (two-tailed). Since a rank correlation may attain significance when a rank order is maintained for a subset of cases that vary below noise level, it would be misleading to report these relationships.

3. Results

3.1. Behavioral data

Table 1 summarizes the behavioral data for the two groups. The performance of both patients and controls was well above chance in distinguishing old from new items, although patients' accuracy was significantly poorer compared to controls, as can be seen both from the correct responses for old items and the measure of sensitivity (d_L). The latency data showed longer response times for old compared to new items, particularly for patients, which paralleled the findings for the accuracy measures. Overall, however, there was no significant group difference in response latency. No significant gender main effects or interactions of gender with group or condition were observed in any of the behavioral measures.

3.2. Grand average ERP waveforms

ERP waveforms averaged across levels of condition (i.e. new and old word items) for the control and the patient group are shown in Fig. 1. Distinctive ERP components were identified as N1 (peak latency 145 ms), N2 (330 ms), and P3 (600 ms). The N1, N2, and P3 components were present in both the patient and control groups, and peaked at approximately the same time in the two groups.

For controls, early negativities (i.e. N1 and N2) were maximal over inferior parietal sites (P9 10; see Fig. 1), and greater over the left than right hemisphere. For patients, however, these early negative components were markedly reduced at recording sites from the whole posterior scalp. Moreover, the patients failed to show the strong laterality effect for N2, which is evident for the control group (see sites P9 and P10 in Fig. 1).

The early negativities were followed by a late positivity (i.e. P3), which was most prominent over medial parietal sites and was equally present in both groups (see Pz in Fig. 1). The late positivity (i.e. P3) was increased between 400 and 700 ms for old items compared with new items, particularly over medial-posterior sites (see Fig. 2). This difference in P3 amplitude depicts the well-known ERP repetition or 'old–new' effect (e.g. Smith and Halgren, 1989; Friedman, 1990; Rugg et al., 1991; Berman and Friedman, 1993). As can be seen from Fig. 2, the 'old–new' effect for the patients was highly similar to that recorded in the controls, with late positivity being greater to 'old' than 'new' words at posterior sites.

3.3. ERP topographies

Fig. 3 depicts topographies derived from the PCA factor scores corresponding to factors N2 and P3. Dark blue colors correspond to scalp regions where N2 was most prominent, that is, over left inferior-parietal sites in controls. Patients showed relatively little negative N2 factor scores; however, the left inferior-parietal sites were less positive than other scalp regions (indicated by the yellow and orange colors). For both the control and patient groups, a typical P3-like distribution can be seen over medial-parietal sites for old items (indicated by purple and dark red colors in Fig. 3), which was also present but smaller for new items.

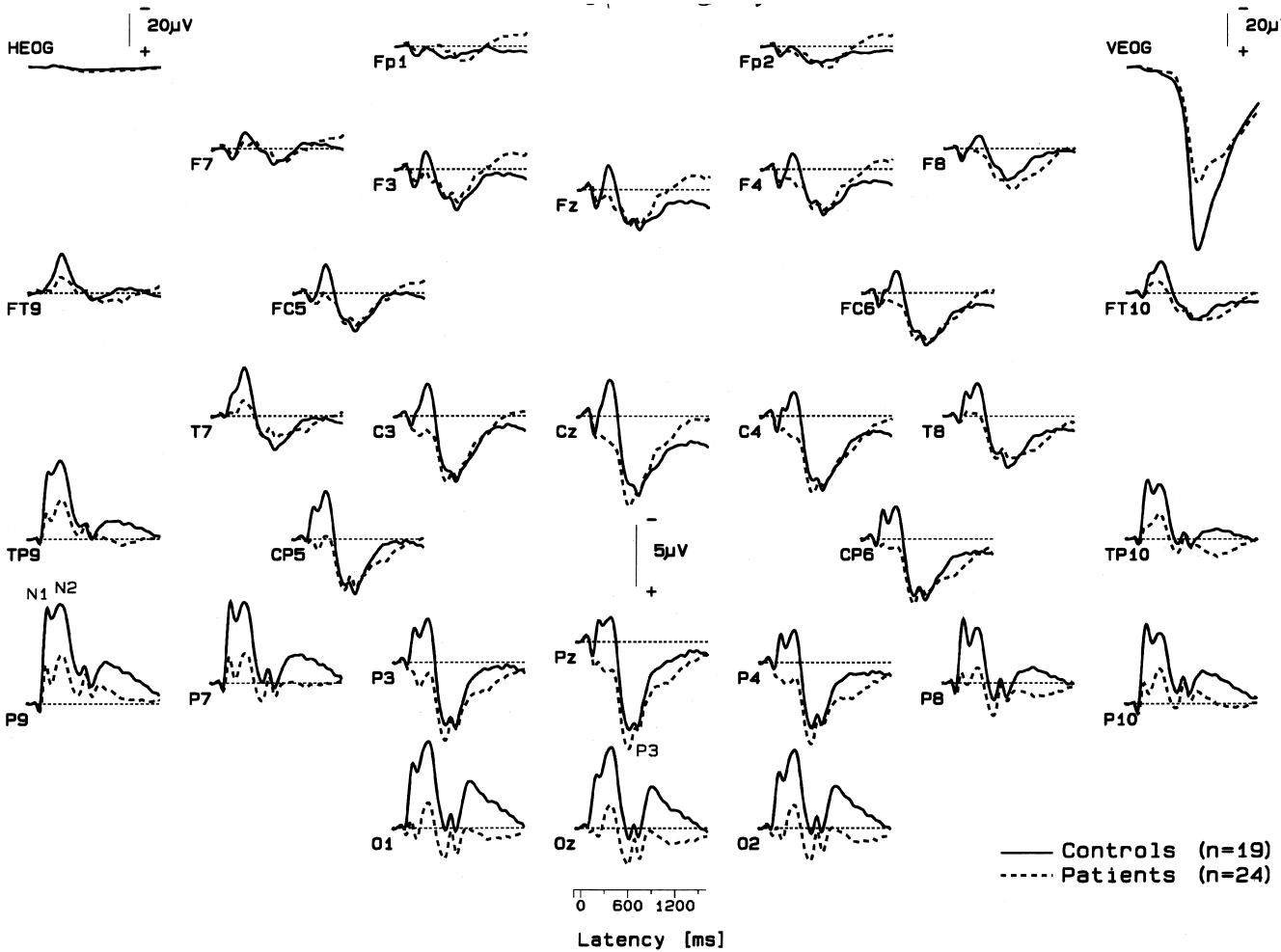

Fig. 1. Grand average event-related potentials (ERPs) for 19 control subjects (solid line) and 24 patients (dashed line) for all recording sites, averaged across condition (old new). ERP components are indicated at P9 and Pz. Note the different scale for electrooculogram (EOG) channels, showing horizontal (HEOG) and vertical (VEOG) EOG averages before eye blink correction.

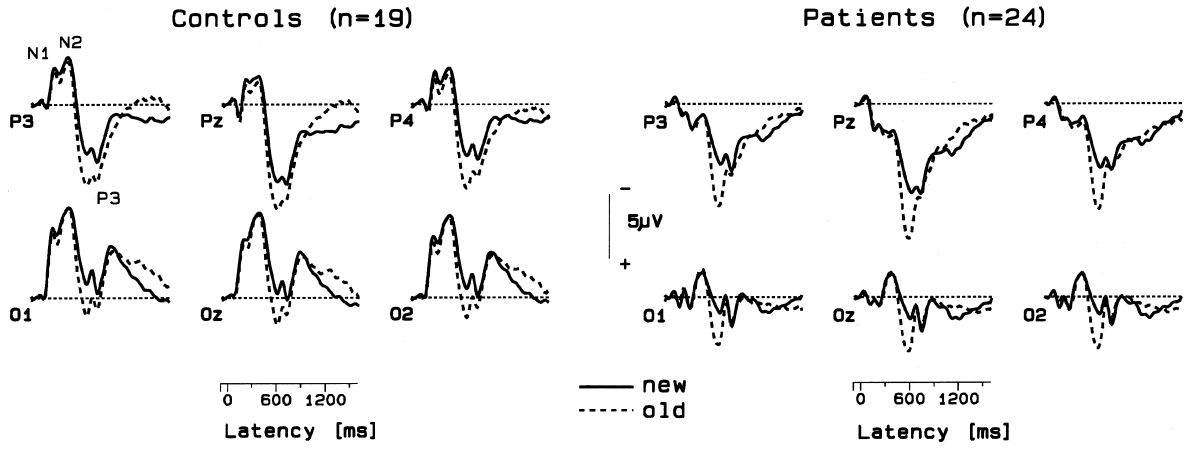

Fig. 2. Grand average event-related potentials (ERPs) for new (solid line) and old (dashed line) words for controls (left panel) and patients (right panel) at medial-parietal and occipital recording sites. ERP components are indicated at site P3 for controls.

3.3.1. N2 amplitude

N2 amplitude was markedly reduced in patients (see Fig. 3), which was statistically supported by a highly significant group main effect, $F_{1,39}$ 12.0, P 0.001, and a Group × Site interaction, $F_{12,468}$ 6.78, P 0.004, ε 0.13 (simple effects of

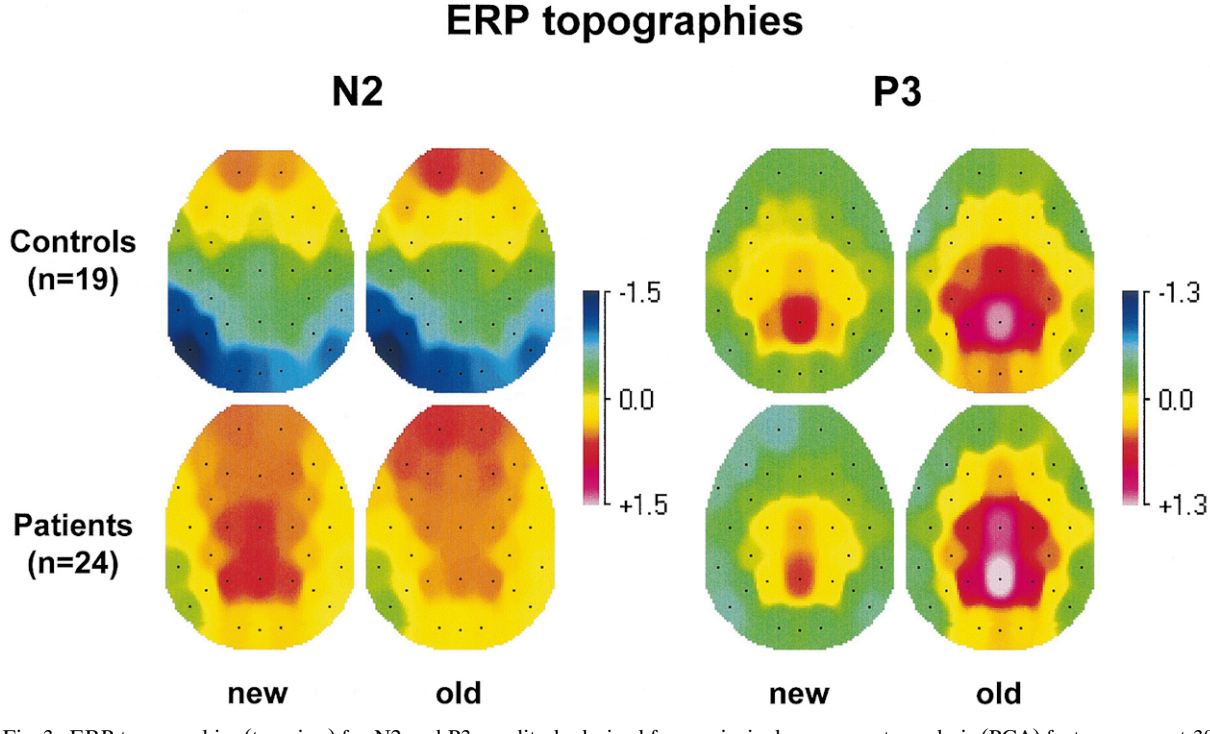

Fig. 3. ERP topographies (top view) for N2 and P3 amplitude derived from principal components analysis (PCA) factor scores at 30 electrode sites (left hemisphere sites on the left side of each map). Maps are shown for each ERP component for controls (top row) and patients (bottom row) for new (left columns) and old (right columns) items.

group were significant at all sites but Fp1 2 and F7 8; at all other sites, $F_{1,39} > 5.10$, P 0.03). A highly significant Hemisphere × Site interaction, $F_{12,468}$ 13.8, P 0.0001, ε 0.27, resulted primarily from a left-lateralized N2 amplitude at temporal-parietal sites (simple effects of hemisphere at TP9 10, P9 10, P7 8, all $F_{1,39} > 11.7$, all P 0.002). Although this effect, i.e. a greater N2 amplitude at left temporal-parietal sites, appeared to be more pronounced in controls than patients, the Group × Hemisphere interaction did not reach statistical significance, $F_{1,39}$ 1.93, P 0.17. A marginally significant Group × Hemisphere × Site interaction, $F_{12,468}$ 2.06, P 0.10, ε 0.27, stemmed from reduced left-lateralized N2 asymmetry in patients at occipital-parietal sites (simple interaction effects of Group × Hemisphere at O1 2, $F_{1,39}$ 4.37, P 0.04; at P9 10 and P3 4, both $F_{1,39} > 3.57$, P 0.07). Moreover, simple hemisphere main effects for each group, supportive of a larger N2 amplitude over the left hemisphere, were highly significant for controls at lateral and posterior sites (i.e. at TP9 10, P9 10, P7 8, O1 2, all $F_{1,39} > 9.11$, all P 0.005), and also significant at medial-parietal sites (i.e. at P3 4, $F_{1,39}$ 7.08, P 0.01, and at CP5 6, $F_{1,39}$ 4.51, P 0.04), but reached significance for patients only at P9 10, $F_{1,39}$ 4.27, P 0.05.

3.3.2. P3 amplitude

A parietal 'old–new' effect, that is, increased positivity to old compared with new items over parietal scalp regions (see Fig. 3), was statistically supported by significant main effects of condition, $F_{1,39}$ 7.82, P 0.008, and site, $F_{1,39}$ 19.5, P 0.0001, ε 0.18, and a Condition × Site interaction, $F_{12,468}$ 23.0, P 0.0001, ε 0.22. Simple effects of condition were most robust at medial and parietal sites (i.e. at F3 4, C3 4, CP5 6, P7 8, P3 4, O1 2, all $F_{1,39} > 9.28$, all P 0.005). However, this effect was equally present in schizophrenic patients and normal controls (all relevant ANOVA effects involving group revealed F values equal to or less than 1.0).

3.3.3. N2–P3 amplitude

Given the nature of the word recognition memory task using a fixed interstimulus interval, it is conceivable that some subjects developed task- or response-related slow wave activity, such as a contingent negative variation (CNV) or a postimperative negative variation (PINV; e.g. see Wagner et al., 1996). If, for instance, the CNV were smaller in schizophrenic patients than controls, this could result in less negativity in the N2 region and greater positivity in the P3 region in patients when compared to controls. However, such ERP potentials might be expected to have a similar (i.e. additive) effect on N2 and P3, leaving the difference between N2 and P3 relatively unaffected by any overlapping slow wave activity.

The difference between the N2 and P3 amplitude as measured by the PCA factor scores was computed (analogous to N2–P3 peak-to-peak differences) at posterior scalp locations where both ERP components were most prominent (i.e. at TP9 10, CP5 6, P9 10, P7 8, P3 4, and O1 2; see Fig. 1). N2–P3 difference scores were submitted to the same repeated measures ANOVA used for the individual components, but was confined to these six electrode placements. As can be seen in Fig. 4, the N2–P3 difference was consistently smaller in patients than in controls at these posterior sites, $F_{1,39}$ 8.51, P 0.006. This effect can also be seen from an inspection of the grand average ERP waveforms (see Fig. 1). There was also a Group × Hemisphere interaction, $F_{1,39}$ 5.79, P 0.02, which is evident in Fig. 4. Analyses of simple effects indicated that N2–P3 amplitude was larger over left than right posterior sites for controls, $F_{1,39}$ 10.8, P 0.002, but there was no hemisphere effect for patients, $F_{1,39}$ 1.0. The 'old–new' effect was also reflected in this measure, $F_{1,39}$ 9.31, P 0.004, but again, there was no Group × Condition interaction, $F_{1,39}$ 1.0.

3.4. Correlations between ERP and behavioral measures

The relationship between accuracy of word recognition memory and ERP component amplitudes was examined separately for patients and normal controls. For each ERP component, the most robust recording sites were selected, which

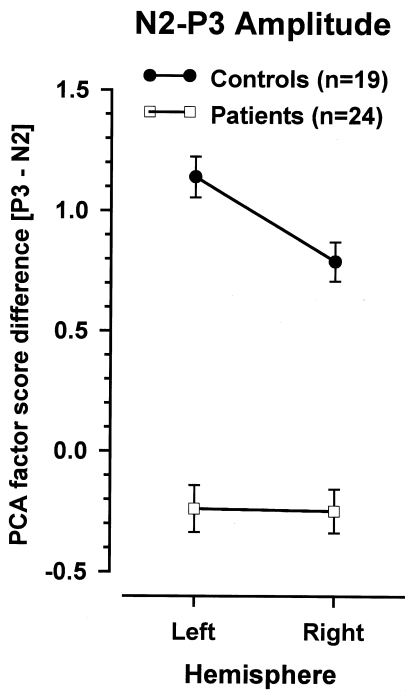

Fig. 4. Mean N2–P3 amplitudes (and standard error of the mean) at posterior sites of the left (TP9, CP5, P9, P7, P3, O1) and right hemisphere (TP10, CP6, P10, P8, P4, O2) for the control and patient groups. N2–P3 amplitude was calculated as the difference between principal components analysis (PCA) factor scores of factors P3 and N2. Note that the weights of each component (i.e. the factor scores) reflect the removal the grand mean ERP waveform for a covariance matrix based PCA (see Achim and Marcantoni, 1997).

were inferior-parietal sites (P9 10) for N2, the midline-parietal site (Pz) for P3, and medial-parietal sites (P3 4) for N2–P3 amplitude. The measures of sensitivity (d_L; see Snodgrass and Corwin, 1988) and percentages of correct responses to old items were highly correlated in both groups (r 0.79 for controls, r 0.83 for patients, both P 0.001). Table 2 summarizes the correlations between percentage of correct responses to old items and ERP amplitudes measures for the two groups.

Greater N2 amplitude was associated with better performance in both groups (i.e. negative correlations for N2; see Table 2). The highest correlations were found over the left inferior parietal region (P9) for both control and patient groups. N2 asymmetry at lateral inferior parietal sites (P9–P10) was also correlated with performance accuracy for controls, although this correlation was only marginally significant (r 0.40, P 0.09; a negative correlation indicates left-greater-than-right N2 amplitude was associated with higher accuracy).

N2–P3 amplitude revealed essentially the same relation to performance accuracy as N2 (i.e. positive correlations for N2–P3; see Table 2). For controls, the correlation was higher over the left medial site (P3), and the N2–P3 asymmetry was significantly correlated with performance accuracy (a positive correlation indicates left-greater-than-right N2-P3 amplitude was associated with higher accuracy).

P3 amplitude was associated with performance accuracy for both control and patient groups (see Table 2). Positive correlations indicated better word recognition memory with greater P3 amplitude. Likewise, the magnitude of the ERP recognition effect (i.e. the difference of P3 amplitude

Table 2
Spearman rank-order correlation coefficients between N2, N2–P3, and P3 amplitudes (PCA factor scores for old items) and accuracy of word recognition memory (percentage of correct responses to old items) at most prominent recording sites for each component

	N2 Amplitude			N2–P3 Amplitude			P3 Amplitude	
	P9	P10	P9–P10[a]	P3	P4	P3–P4[a]	Pz	$Pz_{old-new}$[a]
Controls (n 19)	0.46[b]	0.23	0.40	0.46[b]	0.23	0.56[b]	0.66[c]	0.66[c]
Patients (n 24)	0.44[b]	0.38	0.11	0.61[b]	0.60[b]	0.18	0.57[c]	0.47[b]

[a] Difference scores reflecting the ERP laterality effect or the magnitude of the ERP 'old–new' effect.
[b] P 0.05.
[c] P 0.01.

for old vs. new items) was also positively correlated with word recognition memory.

3.5. Relations to clinical status

Correlations were also computed to examine the relation of symptom ratings to behavioral performance and ERP measures. No significant correlations were found between ERP amplitudes or any behavioral measure and the total positive symptom, negative symptom or general psychopathology scores on the PANSS or the total BPRS scores. Education level was inversely related with the total positive symptom score on the PANSS (r 0.47, P 0.03). No significant correlation was found between age and clinical status.

3.6. Correlations between education level or age and ERP or behavioral measures

ERP amplitudes or accuracy of word recognition memory of patients were not significantly correlated with education level or age. ERP amplitudes of controls were also not significantly correlated with education level, but P3 amplitude at Pz for old items was inversely related to age (r 0.57, P 0.01). Likewise, accuracy (percentage of correct responses to old items) of word recognition memory among controls was also inversely correlated with age (r 0.51, P 0.03), but not with education level.

4. Discussion

Schizophrenic patients had poorer word recognition memory than normal controls, which is consistent with previous reports of impaired verbal learning and memory in schizophrenia (Saykin et al., 1991; Colombo et al., 1993; Goldberg et al., 1993; Gur et al., 1994; Mozley et al., 1996). The present study also confirmed the ERP 'old–new' repetition effect found previously for healthy adults (e.g. Friedman, 1990; Friedman et al., 1993). However, the ERP 'old–new' effect for word recognition was equally present in patients and controls. Assuming that the 'old–new' effect involves the medial temporal lobe, this finding provides little support for abnormalities of medial temporal lobe structures mediating word recognition memory deficits in schizophrenia.

The most striking group difference in the visual ERPs to word stimuli was a profound reduction of early negative potentials (N1, N2) and a marked attenuation of the N2–P3 complex in patients. This difference is similar to the reduction of early negativities in schizophrenia for visual discrimination tasks (Egan et al., 1994; Ford et al., 1994; Strandburg et al., 1994; Matsuoka et al., 1996; Bruder et al., 1998). Unlike these non-verbal visual tasks, the continuous word recognition paradigm used in this study revealed a distinct, left-lateralized scalp topography for these early negativities with largest N1 and N2 amplitudes over left inferior temporal-parietal sites. This same cortical region was activated in a positron emission tomography (PET) study of word perception (Petersen et al., 1990). Intracranial recordings from neurons of the human inferior temporal lobe revealed word-specific responses approximately 200 ms after word presentation (Nobre et al., 1994). Magnetoencephalography (MEG) recordings showed a localized activation of the left inferior temporal-occipital region at approximately 180 ms after word presentation for healthy controls, which was absent for dyslexic subjects (Salmelin et al., 1996). Similarly, the N2 asymmetry reported in this study was less evident among schizophrenic patients. N2 and N2–P3 reductions in patients were strongly related to poorer accuracy of performance, but N2–P3 asymmetry was associated with accuracy of word recognition memory only in controls. The associations of these components with accuracy of word recognition memory, their time frame (200–400 ms) and scalp topography (maximum at left lateral inferior temporal-parietal sites) suggests that the poorer performance of patients in this word recognition memory task arose from a left-lateralized deficit in an early stage of word processing. This conclusion is compatible with the notion of Bull and Venables (1974) that schizophrenic patients suffer from an impairment in the perception of individually spoken words, which would adversely affect information processing of verbal

material. The reduced N2–P3 asymmetry for schizophrenic patients may therefore stem from a deficit in the normal, left-lateralized phonological processing of words, comparable to that seen in dyslexia (Salmelin et al., 1996). This also suggests that impaired word recognition in schizophrenic patients may reflect a deficit in an early stage of processing, beginning at approximately 200–300 ms after word onset.

In this study, ERP components N1 and N2 were described by a common PCA factor that peaked at 320 ms. However, an additional low variance factor with a similar topography was also extracted by the PCA, which had a peak latency of 135 ms and captured the early phase of N1. Although the left-lateralized, inferior-parietal maximum of this early N1 was statistically supported in an ANOVA using the factor scores of this low variance factor, there were no significant group differences.[6] This is suggestive of an early sensory process, which is comparable in patients and controls. In contrast, the reductions of early negativities associated with factor N2 are more likely to arise from a deficit in the allocation of conceptual resources (e.g. Knight, 1984), as reflected by N2 (e.g. Deacon et al., 1991).

Group differences in slow wave activity prior to or following stimulus presentation, for example, an anticipatory CNV or a PINV, which are known to be abnormal in schizophrenia (e.g. Klein et al., 1996; Wagner et al., 1996), may have resulted in group differences of individual ERP components. However, such long-lasting ERP potentials can hardly account for the marked group differences of N2–P3 amplitude, as these consecutive ERP components should be similarly affected by slow potentials. Schizophrenic patients showed an overall reduction of N2–P3 amplitude, and also failed to show greater N2–P3 amplitude over the left than right hemisphere, which was seen in controls (see Fig. 4). Moreover, in controls, both N2–P3 amplitude and N2–P3 asymmetry was correlated with accuracy of word recognition memory, whereas in patients only reduced N2–P3 amplitude was associated with poorer performance. It is conceivable that the larger N2 in controls may indicate a benefit for automized word categorization and comparison processes, while patients may rely on more elaborate later cognitive processes, as reflected by the P3 component, to compensate for their early processing deficit. Consistent with the notion that the N2–P3 complex reflects the phonemic categorization of speech sounds (Maiste et al., 1995), we found during an oddball task requiring the discrimination of consonant–vowel syllables a left-lateralized temporal-parietal N2–P3 amplitude in healthy adults (Kayser et al., 1998). The findings presented here suggest that the psychological process reflected by the N2–P3 complex, that is, the categorization of speech stimuli, is impaired in schizophrenia.

The lack of any group difference in overall P3 amplitude is not a surprising finding, since several studies using visual discrimination tasks have not reported a difference in P3 amplitude between schizophrenic patients and normal controls (e.g. Egan et al., 1994; Ford et al., 1994; Matsuoka et al., 1996; Bruder et al., 1998). For the auditory modality, however, there is ample evidence of reduced N2 and P3 amplitudes in schizophrenia (e.g. McCarley et al., 1993; Egan et al., 1994; Ford et al., 1994; Salisbury et al., 1994b), which is consistent with the hypothesis that abnormalities of N2 and P3 in schizophrenia are related to pathophysiology of temporal lobe structures involved in the generation or modulation of auditory ERPs (McCarley et al., 1991; Salisbury et al., 1994a; Kawasaki et al., 1997). Studies reporting asymmetric ERP abnormalities in schizophrenia also used auditory stimuli (e.g. Faux et al., 1993; McCarley et al., 1993; Salisbury et al., 1994a), which provides additional support to the hypothesis that P3 abnormalities found in schizophrenia

[6] The topography of Factor 6 ('early N1') was very similar for controls and patients, showing a left-lateralized peak at P9 in both groups. Although mean factor scores were larger for controls (e.g. at P9, M 1.42, S.D. 1.56; at P10, M 0.87, S.D. 0.95) than for patients (at P9, M 1.00, S.D. 1.23; at P10, M 0.57, S.D. 0.99), this difference was not statistically significant (i.e. group main effect and all simple group main effects at posterior sites, all $F_{(1,39)}$ 1.33, $P > 0.25$).

are modality specific (Egan et al., 1994; Ford et al., 1994). Given that the P3 amplitude of schizophrenic patients in this visual word recognition task did not differ from normal controls, it would be important to ask whether the 'old–new' effect is impaired in schizophrenia during an *auditory* continuous word recognition task. To our knowledge, no study has measured ERPs during an auditory word recognition task. Group differences as a function of modality might be crucial for understanding cognitive deficits in schizophrenia.

The failure to find a difference in the ERP 'old–new' effect in this study does not necessarily rule out the possibility of medial temporal lobe dysfunction in schizophrenia. First, moderate impairments of medial temporal lobe structures may not affect the 'old–new' effect. Rugg et al. (1991) reported that the 'old–new' effect for temporal lobe epilepsy patients was of similar magnitude when compared to controls. Second, the ERP 'old–new' effect may not reflect processes necessary for discrimination between old and new items in recognition memory tasks (Rugg and Nagy, 1989). Third, the word recognition memory task may have been too easy for schizophrenia patients and normal controls, thus limiting our ability to find any group differences in the ERP 'old–new' effect. On the other hand, we did find reliable group differences in word recognition memory performance, and correlations of performance and the magnitude of the 'old–new' effect. Fourth, not all not schizophrenic patients are likely to suffer from structural temporal lobe abnormalities, and those with normal functioning of medial temporal structures (e.g. hippocampus and amygdala) should not show recognition memory abnormalities. It would be advantageous in future studies to have structural and functional neuroimaging data available for the subjects under investigation. Although these neuroimaging methods do not provide the high temporal resolution of ERPs, information critical to study cognitive processing in schizophrenia, concurrent recordings of ERP and functional magnetic resonance imaging (fMRI) could help in clarifying the role of medial temporal lobe contributions to word recognition memory in schizophrenia.

Acknowledgements

This research was supported by NIMH grant MH50715 to Gerard E. Bruder and by NIMH Senior Scientist Award MH01225 to David Friedman. We thank Jennifer Bunn-Watson, Regan Fong, Paul Leite, and Michelle Friedman for their help in testing, and Charles L. Brown for writing a flexible program to display ERP waveforms.

References

Achim, A., Marcantoni, W., 1997. Principal component analysis of event-related potentials: Misallocation of variance revisited. Psychophysiology 34 (5), 597–606.

American Psychiatric Association, 1994. Diagnostic and statistical manual of mental disorders, 4th ed. Author, Washington, DC.

Arnold, S.E., Hyman, B.T., Van Hoesen, G.W., Damasio, A.R., 1991. Some cytoarchitectural abnormalities of the entorhinal cortex in schizophrenia. Arch. Gen. Psychiatry 48 (7), 625–632.

Barta, P.E., Pearlson, G.D., Brill, L.B. et al., 1997. Planum temporale asymmetry reversal in schizophrenia: Replication and relationship to gray matter abnormalities. Am. J. Psychiatry 154 (5), 661–667.

Barta, P.E., Pearlson, G.D., Powers, R.E., Richards, S.S., Tune, L.E., 1990. Auditory hallucinations and smaller superior temporal gyral volume in schizophrenia. Am. J. Psychiatry 147 (11), 1457–1462.

Berman, S., Friedman, D., 1993. A developmental study of ERPs during recognition memory: Effects of picture familiarity, word frequency, and readability. J. Psychophysiol. 7, 97–114.

Bilder, R.M., Wu, H., Bogerts, B. et al., 1994. Absence of regional hemispheric volume asymmetries in first-episode schizophrenia. Am. J. Psychiatry 151 (10), 1437–1447.

Bogerts, B., Ashtari, M., Degreef, G., Alvir, J.M., Bilder, R.M., Lieberman, J.A., 1990. Reduced temporal limbic structure volumes on magnetic resonance images in first episode schizophrenia. Psychiatry Res. 35 (1), 1–13.

Bogerts, B., Lieberman, J.A., Ashtari, M. et al., 1993. Hippocampus-amygdala volumes and psychopathology in chronic schizophrenia. Biol. Psychiatry 33 (4), 236–246.

Bruder, G.E., Kayser, J., Tenke, C. et al., 1998. The time course of visuospatial processing deficits in schizophrenia: An event-related brain potential study. J. Abnorm. Psychol. 107 (3), 399–411.

Bull, H.C., Venables, P.H., 1974. Speech perception in schizophrenia. Br. J. Psychiatry 125 (0), 350–354.

Burgess, A.P., Gruzelier, J.H., 1997. Short duration synchronization of human theta rhythm during recognition memory. Neuroreport 8 (4), 1039–1042.

Chapman, R.M., McCrary, J.W., 1995. EP component identi-

fication and measurement by Principal Components Analysis. Brain Cogn. 27 (3), 288–310.

Colombo, C., Abbruzzese, M., Livian, S. et al., 1993. Memory functions and temporal-limbic morphology in schizophrenia. Psychiatry Res. 50 (1), 45–56.

Crow, T.J., 1990. Temporal lobe asymmetries as the key to the etiology of schizophrenia. Schizophr. Bull. 16 (3), 433–443.

Crow, T.J., 1997. Schizophrenia as failure of hemispheric dominance for language. Trends Neurosci. 20 (8), 339–343.

Deacon, D., Breton, F., Ritter, W., Vaughan Jr., H.G., 1991. The relationship between N2 and N400: Scalp distribution, stimulus probability, and task relevance. Psychophysiology 28 (2), 185–200.

DeLisi, L.E., Sakuma, M., Kushner, M., Finer, D.L., Hoff, A.L., Crow, T.J., 1997. Anomalous cerebral asymmetry and language processing in schizophrenia. Schizophr. Bull. 23 (2), 255–271.

Dixon, W.J. (Ed.), 1992. BMDP Statistical Software Manual: To accompany the 7.0 software release. University of California Press, Berkeley.

Egan, M.F., Duncan, C.C., Suddath, R.L., Kirch, D.G., Mirsky, A.F., Wyatt, R.J., 1994. Event-related potential abnormalities correlate with structural brain alterations and clinical features in patients with chronic schizophrenia. Schizophr. Res. 11 (3), 259–271.

Falkai, P., Bogerts, B., Schneider, T. et al., 1995. Disturbed planum temporale asymmetry in schizophrenia. A quantitative post-mortem study. Schizophr. Res. 14 (2), 161–176.

Faux, S.F., McCarley, R.W., Nestor, P.G. et al., 1993. P300 topographic asymmetries are present in unmedicated schizophrenics. Electroencephalogr. Clin. Neurophysiol. 88 (1), 32–41.

Flaum, M., Swayze, V.W., O'Leary, D.S. et al., 1995. Effects of diagnosis, laterality, and gender on brain morphology in schizophrenia. Am. J. Psychiatry 152 (5), 704–714.

Flor-Henry, P., 1976. Lateralized temporal-limbic dysfunction and psychopathology. Ann. N.Y. Acad. Sci. 280, 777–797.

Ford, J.M., White, P.M., Csernansky, J.G., Faustman, W.O., Roth, W.T., Pfefferbaum, A., 1994. ERPs in schizophrenia: Effects of antipsychotic medication. Biol. Psychiatry 36, 153–170.

Friedman, D., 1990. ERPs during continuous recognition memory for words. Biol. Psychol. 30 (1), 61–87.

Friedman, D., Berman, S., Hamberger, M., 1993. Recognition memory and ERPs: Age-related changes in young, middle-aged, and elderly adults. J. Psychophysiol. 7, 181–201.

Geschwind, N., Levitsky, W., 1968. Human brain: Left-right asymmetries in temporal speech region. Science 161 (837), 186–187.

Goldberg, T.E., Torrey, E.F., Gold, J.M., Ragland, J.D., Bigelow, L.B., Weinberger, D.R., 1993. Learning and memory in monozygotic twins discordant for schizophrenia. Psychol. Med. 23 (1), 71–85.

Gruzelier, J.H., Venables, P.H., 1972. Skin conductance orienting activity in a heterogeneous sample of schizophrenics. Possible evidence of limbic dysfunction. J. Nerv. Ment. Dis. 155 (4), 277–287.

Gruzelier, J., Seymour, K., Wilson, L., Jolley, A., Hirsch, S., 1988. Impairments on neuropsychologic tests of temporohippocampal and frontohippocampal functions and word fluency in remitting schizophrenia and affective disorders. Arch. Gen. Psychiatry 45 (7), 623–629.

Gur, R.E., Jaggi, J.L., Shtasel, D.L., Ragland, J.D., Gur, R.C., 1994. Cerebral blood flow in schizophrenia: Effects of memory processing on regional activation. Biol. Psychiatry 35 (1), 3–15.

Heit, G., Smith, M.E., Halgren, E., 1988. Neural encoding of individual words and faces by the human hippocampus and amygdala. Nature 333 (6175), 773–775.

Johnson Jr., R., 1995. Event-related potential insights into the neurobiology of memory systems. In: Boller, F., Grafman, J. (Eds.). Handbook of Neuropsychology, 10. Elsevier, Amsterdam, pp. 135–164.

Kawasaki, Y., Maeda, Y., Higashima, M. et al., 1997. Reduced auditory P300 amplitude, medial temporal volume reduction and psychopathology in schizophrenia. Schizophr. Res. 26 (2–3), 107–115.

Kay, S.R., Opler, L.A., Fishbein, A., 1992. Positive and negative syndrom scale (PANSS) rating manual. Multihealth System Inc, Toronto, Canada.

Kayser, J., Tenke, C., Bruder, G., 1998. Dissociation of brain ERP topographies for tonal and phonetic oddball tasks. Psychophysiology 35 (5), 576–590.

Kayser, J., Tenke, C., Nordby, H., Hammerborg, D., Hugdahl, K., Erdmann, G., 1997. Event-related potential (ERP) asymmetries to emotional stimuli in a visual half-field paradigm. Psychophysiology 34 (4), 414–426.

Keselman, H.J., 1998. Testing treatment effects in repeated measures designs: An update for psychopysiological researchers. Psychophysiology 35 (4), 470–478.

Klein, C., Rockstroh, B., Cohen, R., Berg, P., 1996. Contingent negative variation (CNV) and determinants of the post-imperative negative variation (PINV) in schizophrenic patients and healthy controls. Schizophr. Res. 21 (2), 97–110.

Knight, R.A., 1984. Converging models of cognitive deficit in schizophrenia. Nebr. Symp. Motiv. 31, 93–156.

Kulynych, J.J., Vladar, K., Jones, D.W., Weinberger, D.R., 1996. Superior temporal gyrus volume in schizophrenia: A study using MRI morphometry assisted by surface rendering. Am. J. Psychiatry 153 (1), 50–56.

Lix, L.M., Keselman, H.J., 1995. Approximate degrees of freedom tests: A unified perspective on testing for mean equality. Psychol. Bull. 117 (3), 547–560.

Lix, L.M., Keselman, J.C., Keselman, H.J., 1996. Consequences of assumption violations revisited: A quantitative review of alternatives to the one-way analysis of variance F test. Rev. Educ. Res. 66 (4), 579–619.

Maiste, A.C., Wiens, A.S., Hunt, M.J., Scherg, M., Picton, T.W., 1995. Event-related potentials and the categorical perception of speech sounds. Ear Hear. 16 (1), 68–90.

Matsuoka, H., Saito, H., Ueno, T., Sato, M., 1996. Altered endogenous negativities of the visual event-related potential in remitted schizophrenia. Electroencephalogr. Clin. Neurophysiol. 100 (1), 18–24.

McCarley, R.W., Faux, S.F., Shenton, M.E., Nestor, P.G., Adams, J., 1991. Event-related potentials in schizophrenia: Their biological and clinical correlates and a new model of schizophrenic pathophysiology. Schizophr. Res. 4 (2), 209–231.

McCarley, R.W., Shenton, M.E., O'Donnell, B.F. et al., 1993. Auditory P300 abnormalities and left posterior superior temporal gyrus volume reduction in schizophrenia. Arch. Gen. Psychiatry 50 (3), 190–197.

Menon, R.R., Barta, P.E., Aylward, E.H. et al., 1995. Posterior superior temporal gyrus in schizophrenia: Grey matter changes and clinical correlates. Schizophr. Res. 16 (2), 127–135.

Mozley, L.H., Gur, R.C., Gur, R.E., Mozley, P.D., Alavi, A., 1996. Relationships between verbal memory performance and the cerebral distribution of fluorodeoxyglucose in patients with schizophrenia. Biol. Psychiatry 40 (6), 443–451.

Nobre, A.C., Allison, T., McCarthy, G., 1994. Word recognition in the human inferior temporal lobe. Nature 372 (6503), 260–263.

Nurnberger Jr., J.I., Blehar, M.C., Kaufmann, C.A. et al., 1994. Diagnostic interview for genetic studies. Rationale, unique features, and training. NIMH Genetics Initiative. Arch. Gen. Psychiatry 51 (11), 849–1840.

O'Donnell, B.F., Shenton, M.E., McCarley, R.W. et al., 1993. The auditory N2 component in schizophrenia: Relationship to MRI temporal lobe gray matter and to other ERP abnormalities. Biol. Psychiatry 34 (1-2), 26–40.

Oldfield, R.C., 1971. The assessment and analysis of handedness: The Edinburgh Inventory. Neuropsychologia 9 (1), 97–113.

Paivio, A., Yuille, J.C., Madigan, S.A., 1968. Concreteness, imagery, and meaningfulness values for 925 nouns. J. Exp. Psychol. 76 (1), 1–25.

Pearlson, G.D., Barta, P.E., Powers, R.E. et al., 1997. Medial and superior temporal gyral volumes and cerebral asymmetry in schizophrenia versus bipolar disorder. Biol. Psychiatry 41 (1), 1–14.

Petersen, S.E., Fox, P.T., Snyder, A.Z., Raichle, M.E., 1990. Activation of extrastriate and frontal cortical areas by visual words and word-like stimuli. Science 249 (4972), 1041–1044.

Pfefferbaum, A., Ford, J.M., White, P.M., Roth, W.T., 1989. P3 in schizophrenia is affected by stimulus modality, response requirements, medication status, and negative symptoms. Arch. Gen. Psychiatry 46 (11), 1035–1044.

Rossi, A., Stratta, P., Mattei, P. et al., 1992. Planum temporale in schizophrenia: A magnetic resonance study. Schizophr. Res. 7 (1), 19–22.

Rossi, A., Stratta, P., D'Albenzio, L. et al., 1990. Reduced temporal lobe areas in schizophrenia: Preliminary evidences from a controlled multiplanar magnetic resonance imaging study. Biol. Psychiatry 27 (1), 61–68.

Rugg, M.D., Nagy, M.E., 1989. Event-related potentials and recognition memory for words. Electroencephalogr. Clin. Neurophysiol. 72 (5), 395–406.

Rugg, M.D., Roberts, R.C., Potter, D.D., Pickles, C.D., Nagy, M.E., 1991. Event-related potentials related to recognition memory. Effects of unilateral temporal lobectomy and temporal lobe epilepsy. Brain 114 (5), 2313–2332.

Salisbury, D.F., O'Donnell, B.F., McCarley, R.W., Nestor, P.G., Faux, S.F., Smith, R.S., 1994a. Parametric manipulations of auditory stimuli differentially affect P3 amplitude in schizophrenics and controls. Psychophysiology 31 (1), 29–36.

Salisbury, D.F., O'Donnell, B.F., McCarley, R.W., Shenton, M.E., Benavage, A., 1994b. The N2 event-related potential reflects attention deficit in schizophrenia. Biol. Psychol. 39 (1), 1–13.

Salmelin, R., Service, E., Kiesila, P., Uutela, K., Salonen, O., 1996. Impaired visual word processing in dyslexia revealed with magnetoencephalography. Ann. Neurol. 40 (2), 157–162.

Saykin, A.J., Gur, R.C., Gur, R.E. et al., 1991. Neuropsychological function in schizophrenia. Selective impairment in memory and learning. Arch. Gen. Psychiatry 48 (7), 618–624.

Saykin, A.J., Shtasel, D.L., Gur, R.E. et al., 1994. Neuropsychological deficits in neuroleptic naive patients with first-episode schizophrenia. Arch. Gen. Psychiatry 51 (2), 124–131.

Semlitsch, H.V., Anderer, P., Schuster, P., Presslich, O., 1986. A solution for reliable and valid reduction of ocular artifacts, applied to the P300 ERP. Psychophysiology 23 (6), 695–703.

Shenton, M.E., Kikinis, R., Jolesz, F.A. et al., 1992. Abnormalities of the left temporal lobe and thought disorder in schizophrenia: A quantitative magnetic resonance imaging study. N. Engl. J. Med. 327 (9), 604–612.

Smith, M.E., Halgren, E., 1989. Dissociation of recognition memory components following temporal lobe lesions. J. Exp. Psychol. Learn. Mem. Cogn. 15 (1), 50–60.

Snodgrass, J.G., Corwin, J., 1988. Pragmatics of measuring recognition memory: Applications to dementia and amnesia. J. Exp. Psychol. Gen. 117 (1), 34–50.

Spitzer, R.L., Endicott, J., 1975. Schedule for affective disorders and schizophrenia: Lifetime version. New York, Biometrics Research Division, New York State Psychiatric Institute.

Strandburg, R.J., Marsh, J.T., Brown, W.S. et al., 1994. Reduced attention-related negative potentials in schizophrenic adults. Psychophysiology 31 (3), 272–281.

Vasey, M.W., Thayer, J.F., 1987. The continuing problem of false positives in repeated measures ANOVA in psychophysiology: A multivariate resolution. Psychophysiology 24 (4), 479–486.

Vita, A., Dieci, M., Giobbio, G.M. et al., 1995. Language and thought disorder in schizophrenia: Brain morphological correlates. Schizophr. Res. 15 (3), 243–251.

Wagner, M., Rendtorff, N., Kathmann, N., Engel, R.R., 1996. CNV, PINV and probe-evoked potentials in schizophrenics. Electroencephalogr. Clin. Neurophysiol. 98 (2), 130–143.

Weinberger, D.R., Suddath, R.L., Casanova, M.F., Torrey, E.F., Kleinman, J.E., 1991. Crow's 'lateralization hypothesis' for schizophrenia. Arch. Gen. Psychiatry 48 (1), 85–87.

Witelson, S.F., Kigar, D.L., 1988. Asymmetry in brain function follows asymmetry in anatomical form: Gross, microscopic, postmortem and imaging studies. In: Boller, F., Grafman, J. (Eds.), Handbook of Neuropsychology, 1. Elsevier, Amsterdam, pp. 111–142.