Event-Related Potential Correlates of Linguistic Information Processing in Schizophrenics

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Event-related potentials (ERPs) were recorded from adult schizophrenics and age- and education-matched normal controls during performance of an idiom recognition task involving judgments of the meaningfulness of idiomatic, literal, and nonsense phrases. Schizophrenics produced more errors and had prolonged reaction times while attempting to correctly differentiate meaningful from meaningless phrases. An ERP correlate of that deficit was a larger than normal N400 to idioms and literals, with no difference in N400 amplitude to nonsense phrases. This result was interpreted as evidence that the influence of the linguistic context provided by the first word of two-word idiomatic and literal phrases is reduced in schizophrenia. Schizophrenics also showed reduced amplitude P300.

Key Words: Event-related potentials, schizophrenia, language, N400

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Introduction

Cognitive deficits have long been considered to be a central feature of schizophrenia. Both Bleuler (1950) and Kraepelin (1919), for example, emphasized that a loss of "associational threads" is a key symptom of schizophrenia. More recently, numerous behavioral studies (Nuechterlein and Dawson 1984; Asarnow and MacCrimmon 1982) have detected the presence of cognitive deficits in schizophrenic individuals across prodromal, acute, chronic, and remitted phases of this disorder. The persistence of cognitive deficits in schizophrenic individuals across variations in clinical state, as well as the presence of these deficits in unaffected first-degree relatives, is consistent with the hypothesis that these cognitive deficits reflect a trait that is a central feature of schizophrenia (Asarnow and MacCrimmon 1982; Braff 1993; Cromwell et al 1994; Nuechterline et al 1994).

Bleuler and Kraepelin both noted that cognitive deficits are often most readily apparent in the speech of schizophrenic individuals. Much subsequent research has focused on impairments of speech and language in schizophrenics. For example, Chapman et al (1964) used a lexical disambiguation task with schizophrenics, and numerous other investigators have examined priming in lexical decision and word relatedness tasks (Butler and Hemsley 1987; Chapin et al 1989; Grillon et al 1991; Henik et al 1992; Koyama et al 1991; Kwapil et al 1990; Manschreck et al 1988; Mitchell et al 1991; Vinogradov et

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al 1992). In these studies, schizophrenics typically showed less accurate and slower recognition of target words than normals, suggesting that they were less able to benefit from contextual or priming cues. With the exception of Henik et al (1992), normal priming was observed in schizophrenics only when prime and target words were presented together or in immediate temporal contiguity (Chapin et al 1989; Kwapil et al 1990; Manschreck et al 1988). It appears then that schizophrenics are unable to take full advantage of contextual information in determining the meaning of target words, and that this deficit is most apparent when the contextual cues and target stimuli are separated in time.

Cohen and Servan-Schreiber (1992) have suggested that a core deficit underlying cognitive and linguistic impairments in schizophrenia is an "inability to construct and maintain an internal representation of context for the control of action" (p 52). Using neural network simulations of performance on three disparate behavioral paradigms (the Stroop color interference task, the double target continuous performance task, and a lexical disambiguation task), these authors were able to duplicate the selective deficits seen in schizophrenics performing these tasks. The schizophrenialike performance of the neural network model was accomplished by reducing the gain of units in a processing module (common to all three simulations) that maintained contextual information such as the previous stimulus digit in the continuous performance task. In fact, decreased gain in this context module during simulation of Chapman et al's lexical disambiguation task produced performance deficits that were greatest when the disambiguating phrase was temporally remote from the target word.

Context effects in language processing can be studied using the N400 component of event-related potentials (ERPs). Initial studies by Kutas and Hillyard (1980a, 1980b, 1980c, 1982, 1983) showed that a large N400 is elicited when the terminal word in a sentence is incongruous with the expected meaning of the sentence. Subsequent studies have shown that N400 amplitude is inversely proportional to cloze probability of the final word (Hillyard and Kutas 1983; Kutas and Hillyard 1984). For words presented out of sentence context (as in the cited priming studies), N400 varies inversely with the degree of semantic relatedness of the prime to the target word. The closer the semantic relationship, the greater the priming, and the smaller the N400 amplitude (Rugg 1985, 1987; Rugg et al 1988).

Among the studies of language processing in schizophrenics cited above, three also examined the N400. Koyama et al (1991) found that overall N400 amplitude did not differ significantly in normals and schizophrenics; however, when the effect of incongruity on N400 was examined, the difference between related (congruous) and unrelated (incongruous) word pairs was much smaller in schizophrenics than in normals. For schizophrenics it appeared that the first word did not provide sufficient context to reduce N400 amplitude to the second word of congruous pairs.

Similar effects on N400 in schizophrenics were also reported by Mitchell et al (1991) and Grillon et al (1991). In both studies the incongruous-minus-congruous ERP difference potentials of schizophrenics were smaller in the N400 region. Absolute levels of N400 activity in the Grillon et al and Mitchell et al studies could not be determined due to overlapping P300 activity, but examination of the unsubtracted group mean ERP waveforms in both studies suggests that N400 amplitude to unrelated words was similar in schizophrenics and normals. Thus, the smaller difference potential (diminished incongruity effect) in the schizophrenics seems to be a result of a larger N400 to related words in these subjects. This suggests that the schizophrenics were less sensitive to the context provided by the first word in the related pairs.

We have recently completed an N400 study of high-functioning autistic adults utilizing an idiom recognition task in which subjects judged the meaningfulness of idiomatic, literal, and nonsense word pairs (Strandburg et al 1993). Idioms were of particular interest in autistics because of their difficulty with the comprehension of figurative language and their tendency to make literal interpretations (Prior 1979). Indeed, autistics in our study did not judge idioms to be meaningful expressions as rapidly or as accurately as normal individuals; however, N400 amplitude in ERPs to the last word of correctly identified idioms was markedly diminished or absent in autistics, whereas normals showed a small but recognizable N400 to these stimuli. Since N400 amplitude to nonsense word pairs was as large in autistics as normals, the nonsense-minus-idiom difference was significantly larger in autistics. Absence of an N400 to the second word of an idiomatic pair in autistics thus suggests rote, stereotyped retrieval of the idiomatic meaning. Thus, whereas the literature suggests that schizophrenics produce more N400 activity than normals to the second of two related words, these autistic subjects produced significantly less.

Use of this idiom recognition paradigm with schizophrenic subjects provides an opportunity to examine N400 activity in both schizophrenics and autistics performing the same language processing task, and to examine N400 activity in schizophrenics to idiomatic word pairs that have a stronger contextual link due to familiarity and frequent use. Swinney and Cutler (1979) have shown that in normal subjects semantic access to an idiomatic completion of a phrase is faster and more efficient than to other semantically meaningful completions. Thus, we might expect an even greater difference in N400 activity between normals and schizophrenic subjects when processing idioms if Cohen and Servan-Schreiber's hypothesis of diminished context effects in schizophrenics is correct.

P300 and contingent negative variation (CNV) were also measured and analyzed in this research largely for consistency and interstudy comparison with our study of semantic processing in autism (Strandburg et al 1993). CNV provides an index of anticipatory preparedness and, thus, task engagement. P300 has consistently been shown to be smaller in schizophrenics (Pritchard 1986). Since N400 and P300 can overlap somewhat in time, it is important to analyze both to assess component interactions.

Methods

Subjects

Seventeen schizophrenic adults and 19 normal controls participated in this study. These groups were matched for age (26.0 ± 6.3 and 26.1 ± 4.0 years, respectively), gender (1 woman each), and education level (12.4 ± 1.6 years and 13.4 ± 1.6 years, respectively). Two of the schizophrenics were left-handed, as were 4 of the normals; 1 of the normals was ambidextrous (assessed by the Edinburgh Handedness Inventory, Oldfield 1971). Full-scale IQ (FSIQ), as estimated from the information, similarities, and vocabulary subscales of the Wechsler Adult Intelligence Scale (WAIS) (correlations of the subscales with FSIQ: .84, .80, and .83, respectively) was significantly lower in the schizophrenics than in normals (102.2 ± 12.1 vs. 121.2 ± 12.0; $t = 4.70$, 1/34, $p < .001$); however, as Chapman and Chapman (1973) point out, equating schizophrenics with normals on the basis of current IQ measurements is problematic due to the effect of schizophrenic disorder on IQ test performance. In line with their recommendation, we have equated groups using education level as an estimator of premorbid intellectual functioning.

All but 1 of the schizophrenics had been previously hospitalized. At the time of testing all were outpatients receiving medications. Fourteen patients were receiving 12.5 mg of prolixin decanoate, and 3 patients, 6.25 mg every 2 weeks. If patients were receiving anticholinergic medications to control side effects, these were discontinued 24 hours prior to testing, except for those cases in which discontinuance resulted in tremors or uncontrollable movements that would produce unacceptable recording artifact (3 subjects). The majority (10) were living with family, 2 were in board-and-care facilities, and the remainder were independent or semi-independent. Mean duration of illness (since first psychotic episode) was 34 ± 31.4 months (range: 9–117 months).

Subjects were participants in an ongoing longitudinal study of schizophrenia. At the time of testing, all patients were being evaluated biweekly using the brief psychiatric rating scale (BPRS; Overall and Gorham 1962; Guy 1976) and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen 1982). Scale scores from the administration date closest to recording were used to assess the relationship of clinical variables with ERP measures. Positive symptoms were relatively mild at time of testing, with mean BPRS total score of 24.8 ± 4.8 (BPRS subscales: Anxiety–Depression = 1.4 ± 0.5, Anergia = 1.8 ± 1.1, Thought Disturbance = 1.1 ± 0.3, and Activation = 1.2 ± 0.2). Negative symptoms, in contrast, tended to be more prevalent, as indicated by the SANS (global ratings: Affective Flattening = 1.6 ± 1.6, Alogia = 1.0 ± 1.4, Avolition–Apathy = 3.1 ± 1.0, Anhedonia–Associability = 2.9 ± 1.6, and Attention = 1.4 ± 1.2).

Diagnostic Procedures

All patients met DSM-III-R (American Psychiatric Association 1987) criteria and research diagnostic criteria (RDC) (Spitzer et al 1977) for schizophrenia ($n = 14$), or RDC criteria for schizoaffective disorder, mainly schizophrenia ($n = 3$) based on the patient's response on an expanded version of the Present State Examination (PSE; Wing et al 1974), and consideration of information provided by family members. For inclusion in the longitudinal study, patients were required to have had their first psychotic episode within 2 years of intake evaluation. Subjects were excluded if there was any evidence of a) organic central nervous system disorder, b) significant and habitual substance abuse in the 6 months prior to project intake or a history of substance abuse that introduced ambiguity into the diagnostic procedure, or c) mental retardation.

Control subjects were recruited through a newspaper advertisement and matched as closely as possible to patients with regard to age, sex, and education. Controls were excluded from the study if there was evidence of a) major psychopathology based on an expanded PSE and the Minnesota Multiphasic Personality Inventory (MMPI), b) any prior treatment for a psychiatric disorder, c) organic central nervous system impairment, d) significant and habitual substance abuse, or e) a major psychiatric disorder in a first-degree relative. All subjects provided written informed consent for participation in the current study.

Procedure

One hundred and sixty common words were used to construct 40 literal (L), 40 idiomatic (I), and 80 nonsensical (N) two-word phrases. Thus, there were 80 phrases that were meaningful and 80 that were uninterpretable. Since the subjects were asked to respond to meaningful phrases, probabilities of occurrence on the task-relevant dimension were equal. Idioms were selected to have no literal interpretation (e.g., "pot luck," "dead beat," "fat chance," "point blank," "cop out"). Thirty-six of the 40 idioms are listed in *A Dictionary of American Idioms* (Boatner and Gates 1975), *Idiom Structure in English* (Makkai 1972), or *Webster's New World Dictionary* (Guralink 1982). The other four: "bum rap," "old flame," "tall order," and "high five" were judged to be sufficiently common for incorporation in the stimulus set. None of the literal phrases were found in the dictionary of idioms, but 19 of 40 were sufficiently common to be found in *Webster's New World Dictionary*. Mean word-frequencies were not significantly different for the three types of phrases (Kucera and Francis 1967). In pilot studies with individuals in the same age range as subjects of this research, 80–90% of the 40 idioms were recognized as meaningful. Each of the 40 first words in the idiomatic phrases was also a first word in either a literal phrase (20) or a nonsensical phrase (20). Thus, "vicious" was paired with "circle" (I) and "dog" (L), while "square" was paired with "deal" (I) and "wind" (N).

Words were between three and eight characters long and were presented individually on a computer graphic monitor for 100 msec with an interstimulus interval (ISI) of 500 msec. At the viewing distance, letters subtended 20 min of visual angle. I, L, and N phrases were presented in random order with an interphrase interval of approximately 4.0 sec. Subjects indicated whether each phrase was meaningful or not by pressing one of two buttons (right hand for meaningful, left hand for nonmeaningful). Stimuli were presented when the subject was still and fixating the center of the screen, and electroencephalogram (EEG) amplitude fell within $\pm$ 100 μV. EEG activity was recorded (2.5-sec epoch) on each trial beginning 500 msec before presentation of the first word of each pair.

Electrophysiological Methods

EEG was recorded from 17 International 10/20 System leads referenced to linked earlobes (Pz, Cz, and Fz on the midline; O1, P3, T5, C3, T3, F3, and F7 over the left hemisphere; and homologous locations over the right hemisphere) with Grass E5GH gold disk electrodes. Eye movements were recorded bipolarly from electrodes placed beside and below the left eye (for all electrodes, impedance < 5 kΩ at 30 Hz). The EEG was amplified 14,000$\times$ and filtered (0.1–30 Hz, 3 dB down). Data from all leads were digitized (256 points/sec) and stored on-line. All tasks were performed in an electrically shielded, sound-attenuating chamber, and a member of the research team was with the subject throughout the run to instruct and monitor performance.

Data Analysis

EDITING AND AVERAGING. ERPs obtained on correct response trials were averaged off-line from digitally stored single trials calibrated to equate amplifier gain and DC offset across all channels. As performance levels were high in both groups in all three paradigms, there were insufficient error trials to obtain ERP averages for incorrect responses.

Each subject's data were edited to exclude artifacts while retaining a sufficient number of trials to achieve an adequate signal-to-noise ratio when averaged. This was accomplished by an iterative procedure of reducing the artifact rejection threshold and comparing resulting ERPs until there was no further improvement in the signal-to-noise ratio by the application of more stringent criteria. Particular attention was paid to eliminating large voltages in the eye-monitor average. In this way, individualized editing produced ERPs in which the maximum number of trials were included while artifact was minimized. Number of trials remaining after editing did not differ between groups [normals = 145.3 $\pm$ 14.6; schizophrenics = 140.5 $\pm$ 20.1; $t(34) = 0.817$, ns].

COMPONENT MEASUREMENT. Components were identified by visually examining group mean ERP traces at each lead as well as topographic maps. Measurements were then made on individual subject data at those leads and within the latency range where components were at a maximum as determined from topographic maps of the group mean data from the control subjects. This strategy was chosen to avoid proliferating statistical comparisons given the multiple electrodes, conditions, and ERP components. Peak measures were made relative to a 300-msec baseline preceding the first word of the pairs. For CNV, P3, and N400 measurement, ERPs were further digitally filtered (15 dB per octave, down 40 dB at 15 Hz). Filtering characteristics were empirically chosen, after applying a number of trial filters, at the level that provided the greatest noise reduction with no visible waveform distortion in the component of interest.

CNV. For measurement of this slow component, the data were filtered (15 dB per octave, down 40 dB at 15 Hz), and the mean amplitude values were calculated for the midline electrodes (Pz, Cz, and Fz). Mean amplitude values were obtained over two successive epochs, the 100 msec immediately preceding, and the 100 msec immediately following the onset of the second word. These leads and epochs were chosen to obtain amplitude measures that include the time and region of maximum CNV development.

P300. Individual subject data were filtered (15 dB per octave, down 40 dB at 15 Hz), and peak P300 amplitude and latency for second-word ERPs were identified (between 450 and 850 msec) and measured at Pz, Cz, and Fz to include the electrode where this component was maximal (Pz), and detect potential anterior–posterior shifts in P300 amplitude between groups and conditions.

N400. This component was apparent as a large negativity peaking between 320 and 580 msec after the onset of the second word of two-word phrases. To measure the N400 within this window, the data were filtered (15 dB per octave, down 40 dB at 15 Hz), and peak amplitude and latency were measured at the three midline leads, where N400 could be readily identified in all subjects (Pz, Cz, and Fz).

PRINCIPAL COMPONENTS ANALYSIS. As a check on results from amplitude and latency measures made on the basis of decisions about peaks in displays of ERP waveforms, ERPs were also partitioned into components and measured using principal components analysis (PCA). PCA has the advantage of defining components on statistical criteria applied across multiple electrodes and conditions, and of making measurements over statistically defined epochs rather than single time points. PCAs were calculated using varimax rotation of covariance matrices of second-word ERP data from the nine midfield electrodes (P3, Pz, P4, C3, Cz, C4, F3, Fz, F4) and three stimulus conditions. Similarity of factor structures for the normal and schizophrenic groups was tested using a method proposed by Guthrie (1990). This method computes R, the cosine of the angle between the eigenspaces from two groups. To test similarity of factor structures, the computed R is compared with a set of sample Rs derived from assigning subjects to groups randomly. Perfect coincidence of factor structures yields $R = 1$; observed values of R that are smaller than those obtained from random assignment of ERPs to groups suggest that factor structures may differ due to group membership. By this method the factor structure for the normal and schizophrenic groups was found to be highly similar ($R = .934$), this similarity value falling well within the random assignment distribution. Thus, the data from the two groups were combined and a single PCA used to partition the ERPs into components. Effects of groups, condition, and electrode on different principal components were tested by analysis of variance (ANOVA) of factor scores from PCA analysis.

STATISTICAL METHODS. Group, electrode, and condition effects on ERP component amplitude, latency, or PCA factor scores were assessed using repeated-measures ANOVAs; post hoc tests were made for significant interactions (SAS PROC GLM, and SYSTAT MGLH), using Bonferroni significance levels to protect against type I errors. Repeated-measures ANOVAs were used for analysis of response accuracy and reaction time data. Greenhouse–Geisser corrections were made for significance levels of all repeated-measure effects.

Results

Behavioral Performance

Mean percent correct identification of word pairs as meaningful or nonmeaningful, as well as mean reaction times for correct responses, for the three word-pair types and two groups can be seen in Figure 1. As is evident in this figure, normal subjects correctly identified a larger percentage of word pairs as meaningful or nonmeaningful than did schizophrenics. A group-by-condition ANOVA of percent correct revealed significant group ($F = 18.06$, 1/34, $p < .001$) and condition effects ($F = 17.60$, 2/68, $p < .001$), whereas the interaction was not significant. Across both groups, idioms were judged less accurately than literal word pairs ($F = 26.06$, 1/34, $p < .0001$), and literals were judged only somewhat less accurately than nonsense ($F = 3.86$, 1/34, $p < .06$).

A similar picture was obtained for reaction times (RTs), with schizophrenics having longer RTs than normals. A group-by-condition ANOVA of RTs revealed significant group ($F = 17.84$, 1/34, $p < .001$) and conditions effects ($F = 16.00$, 2/68, $p < .001$), but the interaction was not significant. Across groups, meaningful word pairs were responded to faster than nonsense word pairs (L vs. N: $F = 20.78$, 1/34, $p < .0001$; I vs. N: $F = 13.92$, 1/23, $p < .001$), whereas idioms and literals did not differ from each other.

N400

Figures 2 and 3 present the grand mean ERPs from all 17 leads to the word pairs for the idiom, literal, and nonsense conditions for both normals (Figure 2) and schizophrenics (Figure 3). A clear N400 component can be seen in response to the second word of nonsense word pairs that has very similar latency and scalp topography in the ERPs of both groups. Mean N400 amplitudes over Fz, Cz, and Pz recordings for the two groups and three conditions can be seen in Figure 4A.

A group-by-condition-by-electrode (Pz, Cz, Fz) ANOVA of peak N400 amplitude was calculated. Although there was no main effect for group, there was a

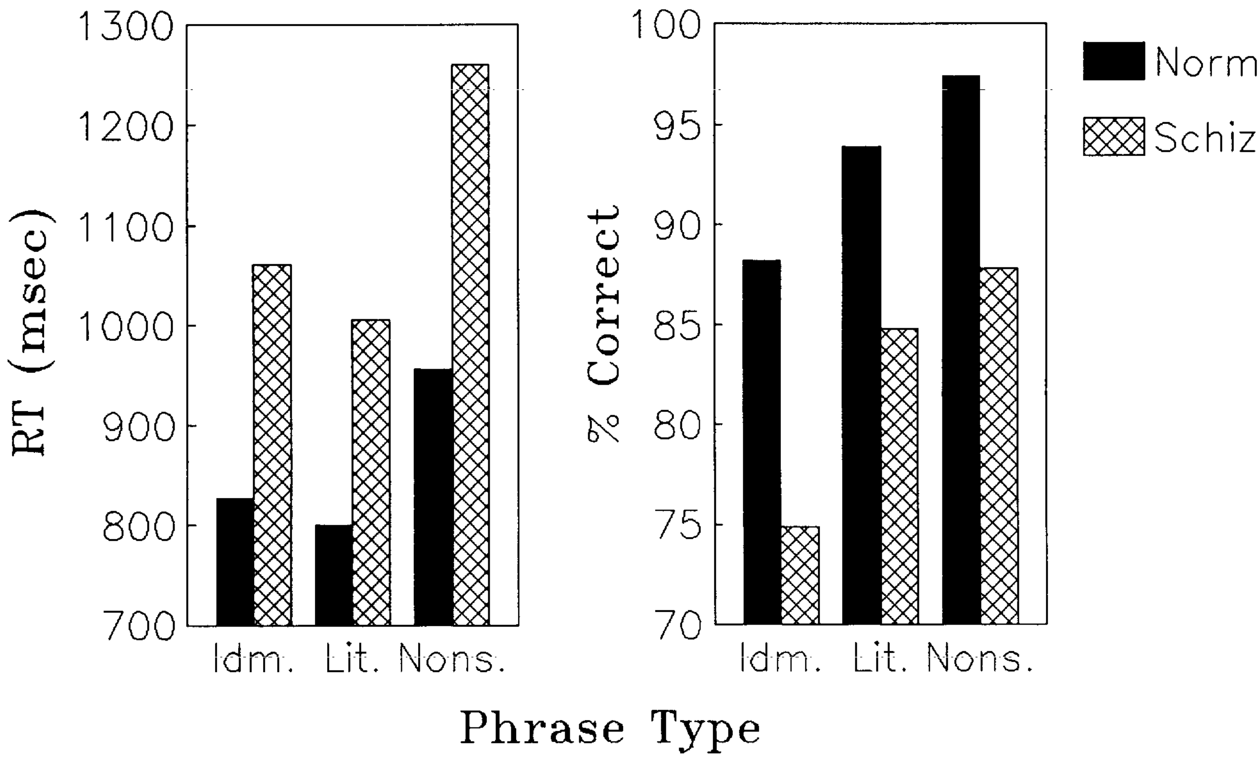

Figure 1. Mean reaction times (left) and percent correct response (right) for the normal subjects (dark bars) and schizophrenics (hatched bars) to judgments of the meaningfulness of idiomatic (Idm.), literal (Lit.), and nonsense (Nons.) two-word phrases.

highly significant condition effect ($F = 27.30$, 2/68, $p < .001$) and a significant group-by-condition interaction ($F = 8.65$, 2/68, $p < .001$). Normals and schizophrenics differed significantly for idioms ($F = 5.25$, 1/34, $p < .028$), but not for literals ($F = 1.87$, ns) or nonsense word pairs ($F = 0.252$, ns). The main effect of electrode only reflects a trend ($F = 2.76$, 2/68, $p < .07$; Fz > Cz > Pz), and there were no other significant effects.

Separate ANOVAs by group indicated a significant condition effect for normals ($F = 38.64$, 2/36, $p < .001$), but a nonsignificant trend for condition in schizophrenics ($F = 2.36$, 2/32, $p = .111$). Figure 4A makes it clear that for normals the peak amplitude of N400 increased (became more negative) across phrase type from idiom to nonsense (I vs. L: $F = 8.79$, 1/18, $p < .008$; L vs. N: $F = 19.74$, 1/18, $p < .001$). In schizophrenics, however, the N400 was equally large for idioms and literals (I vs. L: $F = 0.023$, ns), and the increase for nonsense pairs was not significant (L vs. N: $F = 3.67$, 1/16, $p < .073$).

PCA utilizing the nine electrodes in the middle of the scalp field for both groups identified a component (factor 2) with a peak factor weighting at 420 msec. A group-by-condition-by-electrode ANOVA of factors scores for this factor yielded results very similar to the analysis of peak N400 amplitudes. There were significant effects of group ($F = 16.53$, 2/68, $p < .034$), electrode ($F = 12.45$, 8/272, $p < .001$), and condition ($F = 16.53$, 2/68, $p < .001$), and a group-by-condition interaction ($F = 8.29$, 2/68, $p < .001$). As can be seen in Figure 4C, the mean factors scores over Pz, Cz, and Fz for the normals increase sharply (more negative) across conditions from idiom to nonsense, whereas those for schizophrenics are large and fairly uniform across the three word-pair types.

P300

As Figure 4B indicates, P300 amplitude was reduced in schizophrenics. A group-by-condition-by-electrode (Pz, Cz, Fz) ANOVA revealed that this difference was statistically significant ($F = 4.67$, 1/34, $p < .038$). Condition did not have a significant main effect ($F = 0.193$, ns), but there was a significant interaction with group ($F = 3.12$, 2/68, $p < .050$) that resulted from the fact that normals and schizophrenics differed significantly for the nonsense pairs only ($F = 7.20$, 1/34, $p < .011$). There was a significant electrode effect ($F = 6.72$, 2/68, $p < .002$) reflecting the typical midline distribution of P300 amplitude, and a group-by-electrode interaction ($F = 3.49$, 2/68, $p < .036$) with group differences significant at Cz ($t =$

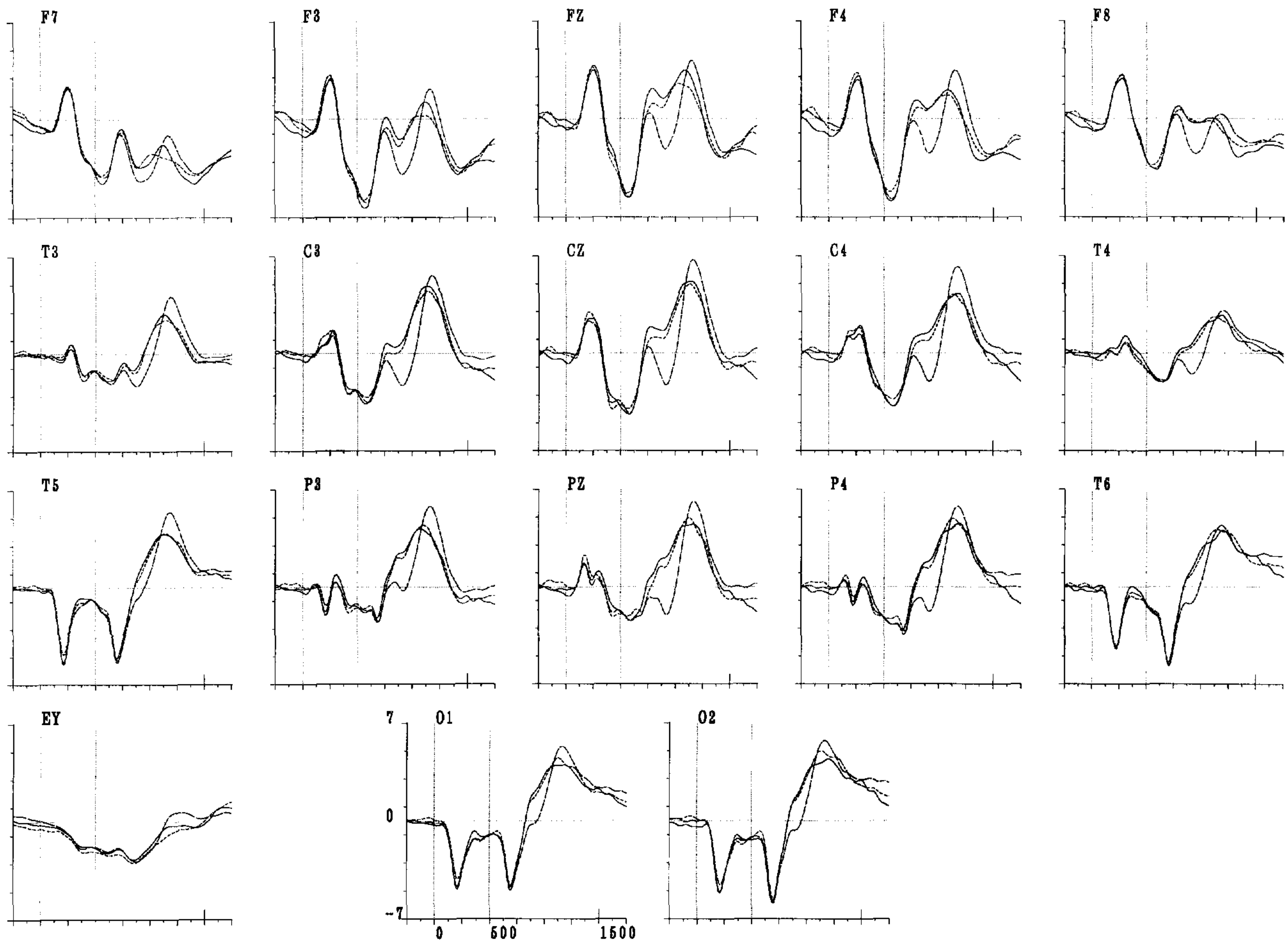

Figure 2. Grand mean ERP traces for the 17 scalp leads and the eye channel for the 19 normal subjects, arranged in approximate topographic scalp distribution. Over plotted waveforms are responses to idiomatic (solid lines), literal (short-dashed lines), and nonsense (long-dashed lines) two-word phrases. The zero point on the time scale represents the onset of the first word of the word pairs, the second word occurring at 500 msec. The amplitude scale is in microvolts.

2.61, $p < .014$) and Pz ($t = 2.64$, $p < .013$). Other interactions were not significant.

P300 latency, measured at the point of Pz peak amplitude, was analyzed in a group-by-condition-by-electrode ANOVA. There was a main effect of group ($F = 10.31$, 1/34, $p < .003$), with mean latency for normals (642 msec) shorter than that for schizophrenics (713 msec). There was also a significant condition effect ($F = 6.13$, 2/68, $p < .004$), with P300 latency increasing from idiom and literal to nonsense (I = 663, L = 669, and N = 700). There was a significant difference in P300 between electrodes (Pz = 690, Cz = 680, Fz = 662; $F = 6.10$, 2/68, $p < .004$). None of the other interactions were significant.

The PCA of the second-word ERP from the nine midfield electrodes revealed a factor at 600 msec (factor 1) that appeared to be a P300. Figure 4D presents factor scores averaged over Pz, Cz, and Fz for groups and conditions for this factor. A group-by-condition-by-electrode ANOVA of factor scores indicated significant group (normal > schizophrenic; $F = 4.48$, 1/34, $p < .042$) and electrode (Pz > Cz > Fz; $F = 12.64$, 8/272, $p < .001$) main effects, as well as an electrode-by-group interaction ($F = 6.02$, 2/272, $p < .003$). The interaction was attributable to a P300 peak amplitude at Cz in normals, and at Pz for schizophrenics.

CNV

As can be seen in Figures 2 and 3, particularly at Fz, an interword CNV was elicited by this task that reached its maximum in both groups at the point of the occurrence of the second word. This component is larger for normals than schizophrenics. A group-by-condition-by-electrode (Pz, Cz, Fz) ANOVA of the mean amplitude from the 100

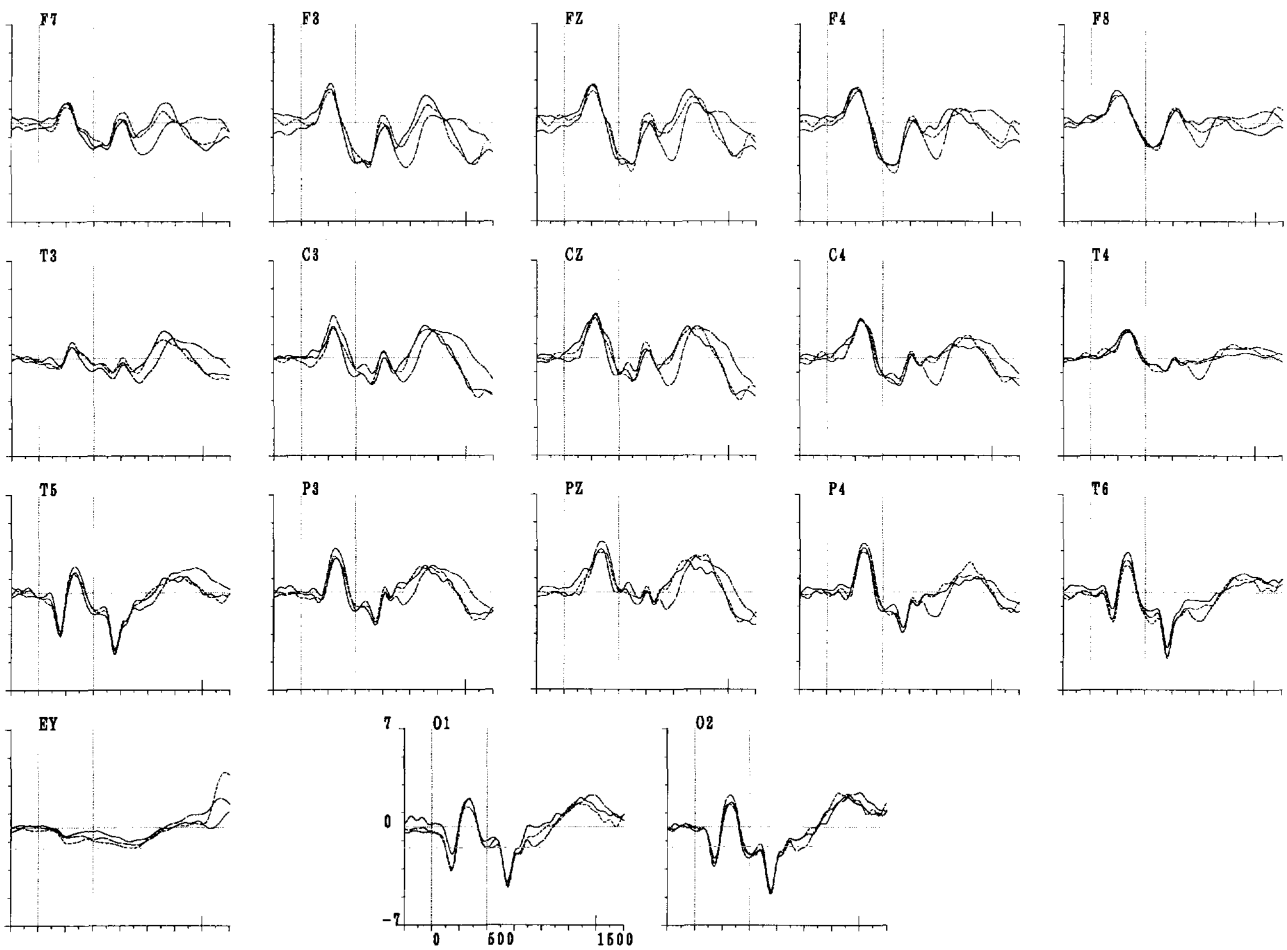

Figure 3. Grand mean ERP traces for the 17 scalp leads and the eye channel for the 17 schizophrenic subjects, arranged in approximate topographic scalp distribution. Over plotted waveforms are responses to idiomatic (solid lines), literal (short-dashed lines), and nonsense (long-dashed lines) two-word phrases. The zero point on the time scale represents the onset of the first word of the word pairs, the second word occurring at 500 msec. The amplitude scale is in microvolts.

msec immediately preceding the onset of the second word revealed significant group (F = 16.02, 1/34, $p < .001$), and electrode (F = 24.72, 2/68, $p < .001$) effects, and a group-by-electrode interaction (F = 3.88, 2/68, $p < .025$), with no effects of condition. Similarly, ANOVA of the mean amplitude for the 100 msec immediately after second-word onset revealed significant group (F = 14.02, 1/34, $p < .001$) and electrode (F = 70.10, 2/68, $p < .001$) effects, with no other main effects or interactions.

Discussion

The primary findings of this study are: 1) schizophrenics are slower and less accurate than normals in evaluating the meaningfulness of idiomatic, literal, and nonsense word pairs; 2) normals and schizophrenics had a clearly identifiable N400 to nonsense pairs with similar latency and topography; 3) normals show an increase in N400 amplitude across conditions from idiom to literal to nonsense; 4) N400 amplitude did not vary significantly across conditions in schizophrenics; and 5) the P300 of schizophrenics was smaller than that for controls, and P300 amplitude did not vary across conditions for either group.

The N400 results for normals are predictable on the basis of a number of studies investigating the effects of priming and cloze probability on N400 amplitude (Kutas and Hillyard 1980a, 1980b, 1980c, 1982, 1983, 1984; Rugg 1985, 1987; Rugg et al 1988). These studies demonstrate that high semantic predictability or priming is associated with low N400 amplitude. Conversely, maximum N400 amplitude is observed with semantically unexpected and unprimed stimuli. Since idiomatic pairs are learned and processed as a unit (Swinney and Cutler 1979), cloze probability is high and priming of the second

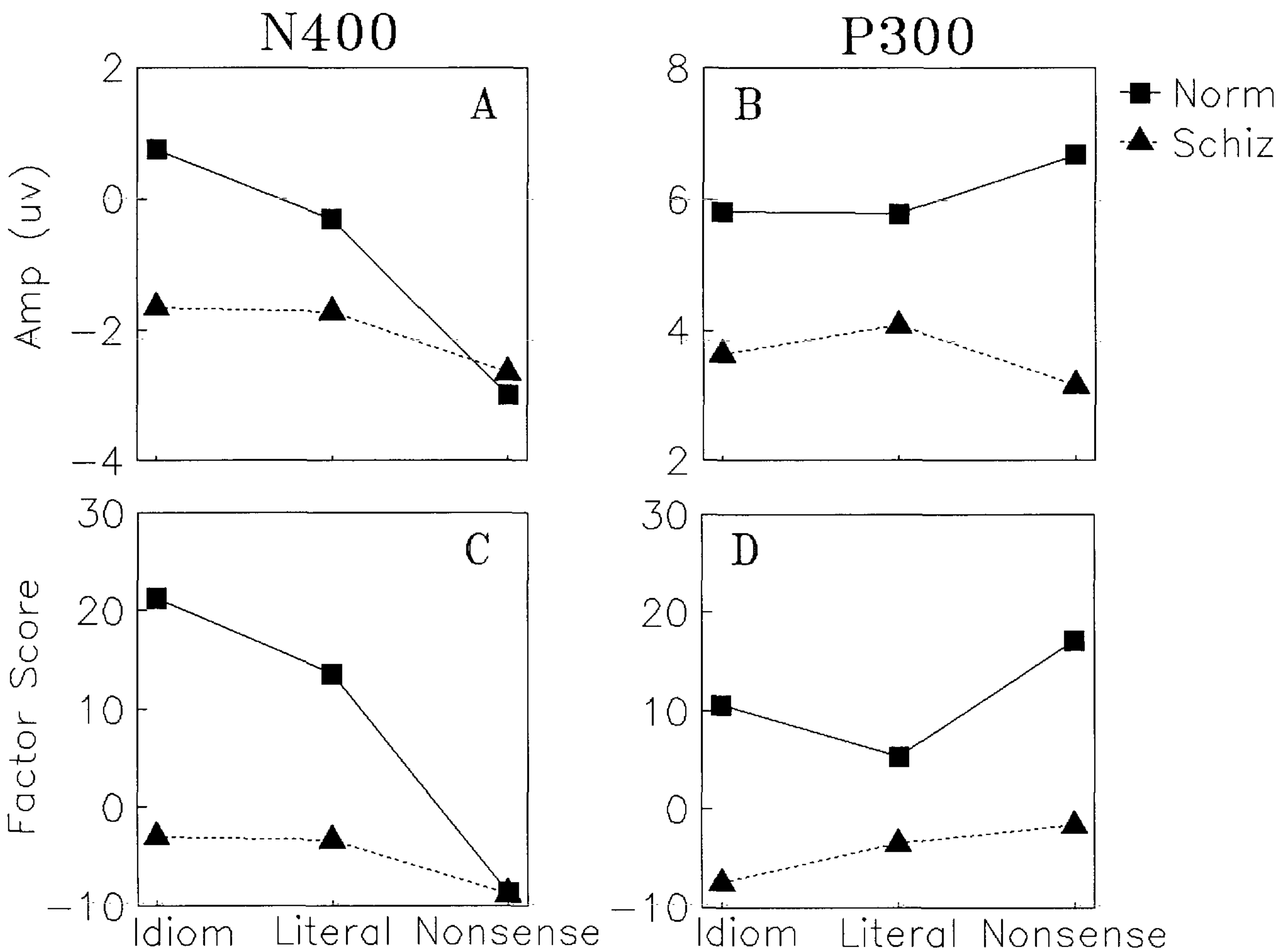

Figure 4. Mean peak ERP component amplitudes (**A** and **B**) and mean factor scores (**C** and **D**) for the N400 (**A** and **C**) and P300 (**B** and **D**) ERP components averaged across Fz, Cz, and Pz for the idiom, literal, and nonsense two-word phrases. Solid lines with square markers represent the mean values for normals, dashed lines with triangular markers, the mean values for schizophrenics.

word by the first is maximal. Literal word pairs produce less priming, and nonsense phrases, being semantically incongruent, produce no priming. Thus, normals show a relatively small N400 for idioms, a somewhat larger N400 for literal word pairs, and a large N400 for nonsense word pairs.

Comparing group mean ERPs, it is apparent that schizophrenics generate normal levels of N400 activity when processing nonsense pairs; however, they do not exhibit the significantly smaller N400 amplitudes for idioms and literals seen in normals, suggesting an absence or reduction of priming effects for these phrase types. Schizophrenics seem to find the second word of a literal or idiomatic two-word expression less semantically predictable than do normals, and thus, the N400 for idioms and literals is nearly as large as for nonsense word pairs.

These N400 results are consistent with the concept, proposed by Cohen and Servan-Schreiber (1992), that a disturbance in the internal representation of context is a core deficit in schizophrenia. Using neural networks, they modeled schizophrenic performance deficits on three critical cognitive tasks. Cohen and Servan-Schreiber define the internal representation of context as anything that is held in mind and used to mediate responses, for example task instructions and the content of previous stimuli. The equivalent operation in our task would be holding in mind the semantic constraints of the first word in a two-word phrase for use in the interpretation of the second. To the degree that context is lost in schizophrenics, the words of literal or idiomatic pairs would approach the level of unrelatedness that is found in a meaningless pair and thus would elicit a relatively large N400.

A deficit in the internal representation of context is modeled by Cohen and Servan-Schreiber in terms of reduced "gain" in the neural network module that maintained contextual information. The gain reduction need not be absolute, but rather needs only to produce sufficient uncertainty to affect performance and N400 amplitude, while still allowing an average of 80% correct responses to idioms and literals. Cohen and Servan-Schreiber speculate that the deficit in the maintenance of the internal representation of context reflects an abnormality in the neural modulatory effects of dopamine within the prefrontal cortex.

In our data posthoc tests of N400 amplitude revealed that idioms judged as meaningful by controls elicited significantly less N400 than did meaningful literal phrases. Thus, the ERP data from the idiom condition extend the continuum of N400 amplitudes to a point even less negative than the literal condition, suggesting that the idioms provide a degree of context significantly greater than that afforded by two-word literal phrases. It could be argued that familiar metaphors, colloquialisms, and other forms of figurative speech, when they are familiar and overlearned, also provide a degree of context and cloze probability significantly beyond that of literal statements and, therefore, would also elicit less N400 than literal statements.

In contrast, schizophrenics show no significant difference in N400 amplitude between meaningful idiomatic and literal phrases. The post hoc tests also demonstrated that the largest N400 amplitude separation between schizophrenics and controls was elicited by idiomatic phrases judged as meaningful. It is thus reasonable to assume that, for schizophrenics, the first words of known, meaningful idioms provide no more context than the first word of a literal pair.

The performance deficits evident in both the percent error and RT indicate that recognizing the meaningfulness of word pairs is a task that elicits a cognitive processing deficit in schizophrenics. It should be emphasized that the larger than normal N400 observed in schizophrenics was elicited by idioms and literals that they identified correctly as meaningful (75% and 85%, respectively). These data suggest a degree of semantic uncertainty even in those instances in which the meaningfulness of a phrase is correctly appreciated.

Sharply contrasting N400 results were found with high-functioning adult autistics on this same task (Strandburg et al 1993). Autistics appeared to be highly context dependent as indicated by little detectable N400 to idioms despite a large N400 to nonsense phrases. Thus, whereas autistics, schizophrenics, and normals all produce large N400 amplitudes to nonsense word pairs, the two patient groups differed in opposite directions from normals for idiomatic word pairs, i.e., a large N400 for schizophrenics and a small (or absent) N400 for autistics. These results suggest a difference between schizophrenics and autistics in the capacity to maintain internal context.

This difference was also evident in the performance of these groups on the Continuous Performance Task (CPT), another task for which schizophrenic deficits were accurately modeled by Cohen and Servan-Schreiber (1992). Context in the case of the CPT involves the holding in mind of an instructional set for the single-target version, or the stimulus digit from the previous trial for the repeating-number version. Schizophrenics have been shown in a number of studies to have a significant performance impairment on the CPT (Nuechterlein and Dawson 1984; Strandburg et al 1994b; and unpublished CPT results on the schizophrenic and normal subjects of the current experiment). We previously reported the absence of behavioral impairment on the CPT in adult high-functioning autistics (Strandburg et al 1993). Thus, these CPT data further support the hypothesis that schizophrenics have a general impairment in the maintenance of the internal representation of context, whereas autistics do not.

Of the previously published studies of N400 amplitude in schizophrenics, that conducted by Grillon et al (1991) is closest to the work reported here in both methodology and results. Grillon et al used semantically related or unrelated word pairs. The subject's task was to indicate whether the two words were related or unrelated. Schizophrenics made these discriminations more slowly and less accurately than did controls. N400 amplitude analysis revealed that controls had a significantly larger difference potential (unrelated-minus-related) than schizophrenics. They interpret this as a deficit in the generation of N400 in schizophrenics; however, the data suggest a different interpretation if absolute amplitude measures are used. Inspection of the ERP figures reveals that N400 amplitude elicited in the unrelated condition is about equal in the two groups, whereas it appears larger in schizophrenics than controls for the related condition. Thus, the smaller difference potential for schizophrenics results from the subtraction of a larger than normal N400 in the related condition from a normally large N400 in the unrelated condition. Viewed in this context, the results are very similar to those of the present study.

Koyama et al (1991) utilized word pairs in a lexical decision paradigm involving three conditions: related words (antonyms), unrelated words, and nonwords. The task was to decide whether the second word of a pair was a word or nonword. Reaction times were longer for schizophrenics than controls in all conditions, and accuracy was less in the nonword condition. Again, the N400 was equally large for both groups in the unrelated condition, but schizophrenics had larger N400s in the related word condition; however, due to a nonsignificant N400 amplitude group effect, Koyama et al concluded that overall N400 amplitude remains unchanged in schizophrenia.

Mitchell et al (1991) utilized a visual sentence-processing paradigm with congruous and incongruous final words. Because of a large overriding P300, the N400 could not be independently measured. Results were expressed as an incongruous-minus-congruous difference potential, which was significantly smaller in schizophrenics than controls. Again, inspection of their figures suggests a more negative N400 deflection in the congruous final word grand mean ERPs in schizophrenics than controls, whereas amplitudes appeared to be equal for incongruous sentence endings. Thus, the smaller difference potential in schizophrenics is likely a product of a larger N400 in the congruous condition.

While N400 amplitudes were measured in unsubtracted waveforms in our research, the usual procedure for isolating and measuring N400 involves creation of a incongruous-minus-congruous difference potential. This is an effective and appropriate procedure when assessing the effects of experimental conditions in a single group; however, when N400 amplitude in two clinical groups is being compared, use of a difference potential can obscure the source of group differences. Difference potentials can only be compared when it can be unambiguously demonstrated that the baseline condition (in this case the congruous word ERP) elicits the same amplitude response in both groups. With respect to the cited studies of N400 in schizophrenics, the mean waveforms suggest that the congruous ERPs contained a larger N400 in schizophrenics than in normals. From this perspective, despite a variety of methods and conclusions presented in these studies, a consistent pattern can be seen in terms of absolute (unsubtracted) N400 amplitudes. That is, schizophrenics tend to have N400 amplitudes similar to normals in unrelated or incongruous conditions, but larger than normal N400 amplitudes in related or congruous conditions.

The significantly reduced amplitude P300 found in schizophrenics in this study has been seen in most studies of schizophrenia. A reduced P300 amplitude could be understood in the framework of the Cohen and Servan-Schreiber hypothesis to be a result of reduced certainty due to loss of context and, therefore, reduced closure. Again, this P300 result is in marked contrast to the findings obtained with high-functioning adult autistics, who produce a larger than normal P300 in this task (Strandburg et al 1993). The delayed P300 in schizophrenics suggests that their prolonged RT may be largely a function of increased decision time (Kutas et al 1977). Similarly, condition effects on RT (see Figure 1) may be partially attributable to condition-related changes in decision time reflected in P300 latency.

It might be argued that these N400 results are the product of an interaction between overlapping N400 and P300 components, i.e., a smaller P300 in schizophrenics increases the apparent negativity of the adjacent N400 component. Given the changes in N400 amplitude across conditions seen in normals but not in schizophrenics, it is important to recognize that P300 amplitude did not vary across conditions in either group. In addition, for the nonsense condition the amplitude, latency, and topography of N400 is very similar for the two groups, but P300 amplitude differs significantly.

At the present state of knowledge, the interaction of adjacent components cannot be eliminated or completely assessed; however, we employed PCA with varimax rotation to create component measures that were statistically uncorrelated and minimally overlapping. Since N400 and P300 have differing topographic distributions, use of a larger number of electrodes in the PCA allowed spatial distribution to aid in the definition and measurement of independent components. As can be seen in Figure 4, the results for the factor scores parallel in detail the results from peak measures. Wood and McCarthy (1984) have cautioned that PCA does not entirely eliminate contamination between adjacent components and can result in misallocation of variance. Nevertheless, the PCA analysis provides increased confidence in the independence of the N400 results of this study from contamination by the adjacent P300. As with peak amplitude measures, it is clear from the PCA that N400 varies across conditions in normals, and does not vary across conditions in schizophrenics.

With respect to the reduced-amplitude CNV component in schizophrenics, many studies report similar results (for a review see Pritchard 1986); however, our CNV results in studies of schizophrenia (using paradigms not necessarily designed to elicit a large CNV) are not consistent. We have observed a reduced CNV in some studies (Strandburg et al 1984), whereas in others the CNV appears to be normal (Strandburg et al 1990, 1991, 1994b) or larger (Strandburg et al 1994a).

In summary, schizophrenics are slower and less accurate in their judgments of the meaningfulness of two-word phrases. N400 results suggest that idiomatic and literal phrases that are judged correctly by schizophrenics are more weakly primed by semantic context (indicated by relatively large N400 amplitudes). This N400 result for schizophrenics stands in sharp contrast to results from high-functioning adult autistics, whose N400 amplitudes suggest stronger than normal priming for idiomatic word pairs.

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