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Making Sense of Sentences in Schizophrenia: Electrophysiological Evidence for Abnormal Interactions Between Semantic and Syntactic Processing

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Event-related potentials to critical verbs were measured as patients with schizophrenia and healthy controls read sentences word by word. Relative to their preceding context, critical verbs were (a) congruous, (b) incongruous and semantically unrelated to individual preceding words (pragmatic–semantic violations), (c) incongruous but semantically related to individual preceding words (animacy–semantic violations), or (d) syntactically anomalous. The N400 was modulated normally in patients, suggesting that semantic integration between individual words within sentences was normal in schizophrenia. The amplitude of the P600 to both syntactic and animacy–semantic violations was reduced in patients relative to controls. The authors suggest that, in schizophrenia, an abnormality in combining semantic and syntactic information online to build up propositional meaning leaves sentence processing to be primarily driven by semantic relationships between individual words.

Keywords: language, schizophrenia, N400 event-related potential, semantics, syntax

Language dysfunction is a fundamental feature of schizophrenia. At least two major theories have been proposed to explain its pathogenesis. The first is that it arises from abnormalities in the structure and function of semantic memory (e.g., M. Spitzer, Braun, Hermle, & Maier, 1993). The second is that it arises from an impairment in the buildup and use of context (e.g., Kuperberg, McGuire, & David, 1998). Thus far, these two theories have been considered in relative isolation: There has been little attempt to examine how semantic processes interact with syntactic processes to build up linguistic context in schizophrenia. In the current study, we present evidence for abnormalities in the interaction between semantic and syntactic processing in schizophrenia and suggest that such abnormalities may explain some of the language abnormalities in this disorder.

Abnormalities in Semantic Memory Structure and Function

Evidence for abnormalities in the structure and function of semantic memory in schizophrenia comes from reports that the semantic priming effect—the faster reaction time to target words that are preceded by semantically related (relative to unrelated) words—is reduced, increased, or no different in patients with schizophrenia relative to healthy controls, depending on experimental conditions and on the semantic distance between prime and target (see Minzenberg, Ober, & Vinogradov, 2002, for a review).

Event-related potentials (ERPs), measured on the surface of the scalp, are a direct electrophysiological index of fast, online brain activity during language processing. Electrophysiologically, semantic priming is manifest by the attenuation of a negative-going wave, the N400, after the presentation of words that are preceded by semantically related, relative to unrelated words (Bentin, McCarthy, & Wood, 1985; Rugg, 1985). This difference in the amplitude of the N400 to target words preceded by related relative to unrelated primes is called the *N400 effect.* In schizophrenia, studies of the N400 effect in semantic priming paradigms have yielded conflicting findings. The N400 effect is sometimes normal (Koyama et al., 1994), sometimes abnormally reduced (Condray, Siegle, Cohen, van Kammen, & Steinhauer, 2003; Condray, Steinhauer, Cohen, van Kammen, & Kasparek, 1999; Mathalon, Faustman, & Ford, 2002; Strandburg et al., 1997), and sometimes variable between patients (Grillon, Rezvan, & Glazer, 1991).[1]

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[1] A second approach to studying the modulation of the N400 in schizophrenia has been to directly compare the absolute amplitude of the N400 elicited by primed or unprimed words between patients and controls. Some studies have failed to find significant effects in such direct group comparisons (Condray et al., 1999, 2003), whereas other studies have reported less negative N400s to unprimed words (Mathalon et al., 2002) and more negative N400s to primed words (Bobes, Lei Xiao, Ibanez, Yi, & Valdes-Sosa, 1996) under conditions that bias toward automatic and controlled processing, respectively.

Abnormalities in the Buildup and Use of Linguistic Context During Sentence Processing

Evidence that patients with schizophrenia show abnormalities in the buildup and use of context during sentence processing comes from a variety of behavioral studies that have reported abnormalities in patients' abilities to recall (Truscott, 1970), judge (Anand, Wales, Jackson, & Copolov, 1994; Kuperberg et al., 1998; Tamlyn et al., 1992), and monitor (Kuperberg et al., 1998; Kuperberg, McGuire, & David, 2000) words in contextually incongruous versus congruous sentences.

Electrophysiologically, studies examining the sentential N400 effect—the attenuation of the amplitude of the N400 to words that are preceded by congruous relative to incongruous sentence contexts—have been mixed. Just as in single word paradigms, the N400 effect in sentence paradigms is sometimes normal (Andrews et al., 1993; Nestor et al., 1997; Niznikiewicz et al., 1997; Ruchsow, Trippel, Groen, Spitzer, & Kiefer, 2003), sometimes abnormally reduced (Adams et al., 1993; Mitchell et al., 1991; Ohta, Uchiyama, Matsushima, & Toru, 1999; Sitnikova, Salisbury, Kuperberg, & Holcomb, 2002), and sometimes variable between patients (Olichney, Iragui, Kutas, Nowacki, & Jeste, 1997).[2]

There have also been several reports of a reduced late positivity following the N400 during sentence processing in schizophrenia (Adams et al., 1993; Andrews et al., 1993; Mitchell et al., 1991; Nestor et al., 1997). These findings have often been attributed to a reduction in the P300 component indexing general contextual updating processes (Donchin & Coles, 1988), but there have been few attempts to understand its attenuation within a theoretical framework of online sentence processing (although see Ruchsow et al., 2003).

Variable Electrophysiological Abnormalities During Language Comprehension in Schizophrenia

Although some discrepancies between studies may be due to differences in the types of patients studied (Andrews et al., 1993; Condray et al., 1999), these factors are unlikely to account for all of this variability. Taken together, these conflicting reports suggest that schizophrenia is not characterized by a fixed electrophysiological deficit. Rather, abnormalities appear to depend on whether experimental conditions bias toward automatic or more controlled processing (at the level of single words) and on the precise types of linguistic stimuli presented (at the level of whole sentences).

A clear illustration of the nonfixed nature of the electrophysiological abnormalities during sentence processing in patients with schizophrenia comes from our recent study (Sitnikova et al., 2002) of the effects of homographs (words with more than one meaning) within sentences. The study demonstrated that patients with schizophrenia showed an abnormally reduced N400 effect to contextually incongruous words in sentences when these incongruous words were semantically related to the dominant meaning of a preceding homograph. On the other hand, the modulation of the N400 to anomalous words that were not semantically related to the homograph in the same sentences was normal in patients with schizophrenia. In other words, the same patients showed both abnormal and normal modulation of the N400 in the same sentences depending on the precise relationship between lexicosemantic associations between individual words and the buildup of whole sentence context. This study suggested that the balance between the buildup of lexicosemantic relationships between individual words and the buildup of whole-sentence context is disturbed in schizophrenia and that abnormalities are maximal when semantic relationships between individual words bias toward one meaning, but the syntactic order of individual words dictate another sentence meaning. One explanation for such an imbalance is that semantic associations between individual words are "hyperactive" in patients with schizophrenia, leading to increased semantic priming between individual words (M. Spitzer, Braun, Maier, Hermle, & Maher, 1993) that overcomes the effects of sentential context. Another explanation is that patients fail to build up sentential context; that is, they fail to combine semantic information with syntactic structure online to derive a propositional representation of meaning, and that this, in turn, leaves them vulnerable to semantic associative effects between individual words.

In the current study, we aimed to distinguish between these two hypotheses using a different psycholinguistic paradigm that we have previously studied in healthy individuals (Kuperberg, Caplan, Sitnikova, Eddy, & Holcomb, in press; Kuperberg, Kreher, Sitnikova, Caplan, & Holcomb, in press; Kuperberg, Sitnikova, Caplan, & Holcomb, 2003) and in patients with schizophrenia (Kuperberg, Kreher, Gaff, McGuire, & David, in press). This paradigm manipulates not only semantic but also syntactic parameters. Below we discuss its logic.

Consider the sentence, "At breakfast the boys would bury every day" (see Table 1B). In this sentence, the verb "bury" elicits a robust N400 effect (Kuperberg, Caplan, et al., in press; Kuperberg, Kreher, Sitnikova, et al., in press; Kuperberg, Sitnikova, et al., 2003). The N400 ERP waveform is known to be modulated by lexicosemantic relationships between content words (Van Petten, 1993), by the structure of semantic memory (Federmeier & Kutas, 1999; Kutas & Federmeier, 2000), and by sentential (Kutas & Hillyard, 1984) and discourse (van Berkum, Hagoort, & Brown, 1999) context. It is thought to reflect the difficulty of integrating the *meaning* of a word into its preceding context (Holcomb, 1993). In this sentence, the verb "bury" is incongruous with its preceding content words ("breakfast," "boys"), as well as with its sentential context and world knowledge. We descriptively term such sentences pragmatic–semantic violations (see Table 1 for further explanation).

Now consider the sentence, "At breakfast the boys would eats every day" (see Table 1D). In this sentence, the verb "eats" is morphosyntactically violated, but its meaning is semantically congruous with its preceding context. This verb does not evoke an N400 effect but rather evokes a positive-going waveform that peaks at approximately 600 ms—the P600. The P600 effect describes the difference in amplitude between the P600 evoked by such anomalies ("eats") and the P600 evoked by nonviolated verbs ("eat"; Hagoort, Brown, & Groothusen, 1993; Osterhout & Holcomb, 1992). Several studies have established that the P600 effect

[2] As in studies of word pairs, some investigators have directly compared the absolute amplitude of the N400 between patients and controls and have reported a more negative N400 amplitude to congruous words (Mitchell et al., 1991; Nestor et al., 1997; Niznikiewicz et al., 1997; Ohta et al., 1999) and, in some studies, also to incongruous words in patients relative to controls (Nestor et al., 1997; Niznikiewicz et al., 1997). Other studies have reported less negative N400s to incongruous words in patients (Sitnikova et al., 2002) or have not reported differences in the absolute amplitude of the N400 between patients and controls (Ruchsow et al., 2003).

Table 1
Description and Examples of Sentence Types

Linguistic violation	Explanation	Example
(A) None	Baseline condition against which the other conditions are evaluated.	"For breakfast the boys would only eat toast and jam."
(B) Pragmatic–semantic violation[a]	The critical verb is replaced by another verb taken from another sentence scenario. This makes the sentence implausible.	"For breakfast the boys would only bury toast and jam."
(C) Animacy–semantic violation[b]	The animate noun that is assigned the role of Agent by the critical verb is replaced by an inanimate noun. This makes the sentence implausible.	"For breakfast the eggs would only eat toast and jam."
(D) Morphosyntactic violation	The verb is changed either to violate subject–verb agreement or by using a finite in place of an infinitival verb.	"For breakfast the boys would only eats toast and jam."

[a] We follow Marslen-Wilson, Brown, and Tyler (1988) in the use of the term *pragmatic* for these types of violations. We do not imply that real-world knowledge is not used in processing the animacy–semantically violated sentences. However, in the pragmatically violated sentences the anomaly could not be determined simply by considering the relationship between the subject noun and the verb: It could only be determined by considering the entire context of the sentence with respect to one's real-world pragmatic knowledge. We also use the term *semantic* to emphasize that these are violations of meaning. [b] Our use of the term *animacy violation* conveys the fact that, in all of these sentences, an inanimate subject noun was used together with verbs that assign the role of Agent (normally animate in nature) to their preceding subject noun in simple English sentences (Agent–Theme or Experiencer–Theme verbs). Again, we use the word *semantic* to emphasize that these are violations of meaning. Subject nouns and critical verbs (to which event-related potential responses were measured) in the examples are underlined.

is maximal when there is conflict between plausible semantic relationships and an unlicensed syntax (Gunter, Friederici, & Schriefers, 2000; Kuperberg, Caplan, et al., in press). Thus, although primarily sensitive to syntactic anomalies and ambiguities, the P600, under certain circumstances, is also modulated by semantic parameters.[3]

Now consider a sentence in which the semantic relationships between individual words are congruous but the meaning of the sentence, dictated by syntactic order of these words, is impossible. For example, in the sentence, "At breakfast, the eggs would *eat* every day" (see Table 1C), the combination of the individual words, "breakfast," "eggs," and "eat," biases toward a plausible meaning (it is plausible that eggs could be eaten), but the actual syntax dictates that this sentence is semantically anomalous: Eggs, being inanimate, cannot eat.[4] We use the descriptive term, animacy–semantic violations, to describe such anomalies. In such sentences, verbs such as "eat" evoke both an N400 effect and a P600 effect (Hoeks, Stowe, & Doedens, 2004; Kim & Osterhout, 2005; Kolk, Chwilla, van Herten, & Oor, 2003; Kuperberg, Caplan, et al., in press; Kuperberg, Kreher, Sitnikova, et al., in press; Kuperberg, Sitnikova, et al., 2003). The amplitude of the N400 to these animacy–semantic violations is smaller than the N400 evoked by the pragmatic–semantic violations (and sometimes does not reach significance at all), probably because it is easier to semantically integrate verbs that are congruous than incongruous with their preceding individual content words. The P600 effect in these sentences is thought to reflect the processing cost incurred because of the conflict between the potentially plausible semantic relationships between the content words and the impossible meaning dictated by the actual syntax. It is dependent on a word-by-word, online interaction between semantic and syntactic processing (MacDonald, Pearlmutter, & Seidenberg, 1994; Trueswell & Tanenhaus, 1994).

In the current study, we presented all four types of sentences described above to patients with schizophrenia and healthy controls. We focused on the modulation of both the N400 and the P600. If patients with schizophrenia are unable to semantically integrate words into their preceding context, this would predict a reduced N400 effect to the pragmatic–semantic violations (relative to the nonviolated verbs) in patients relative to controls. If patients with schizophrenia are unable to construct syntactic structure or use syntactic information at all, this would predict an absent P600 effect to both the morphosyntactic violations and the animacy–semantic violations (relative to the nonviolated verbs) in patients. On the basis of the studies discussed above, we predicted that abnormalities in schizophrenia would be most marked to the animacy–semantic violations where plausible lexicosemantic relationships contradicted the implausible meaning of the sentence. If patients show a hyperactivation of semantic associates, this would predict an abnormally increased attenuation of the N400 to verbs such as "eat," preceded by semantically related words ("breakfast," "eggs") in the animacy–semantically violated sentences, relative to verbs such as "bury" that are preceded by semantically

[3] There is debate about the precise neurocognitive process reflected by the P600: a general process of context updating (Coulson, King, & Kutas, 1998; Osterhout & Hagoort, 1999), syntactic integration after the activation of parallel semantic and syntactic structures (Kaan, Harris, Gibson, & Holcomb, 2000), syntactic reanalysis (Friederici, 1995), thematic reanalysis or integration costs (Kuperberg, Sitnikova, et al., 2003) or monitoring (Kolk et al., 2003; van Herten, Kolk, & Chwilla, 2005). In this article, we refer to the P600 as simply reflecting a processing cost that is incurred when semantic and syntactic information conflict and that is distinct from the cognitive process of semantic integration reflected by the N400.

[4] The syntax is said to assign the thematic role of Agent to the inanimate subject–noun phrase that is highly unlikely to act as an Agent and is more likely to act as a Patient or Theme. In a series of studies using these types of sentences in healthy individuals, we have termed such anomalies *animacy thematic role violations* (Kuperberg, Caplan, et al., in press; Kuperberg, Kreher, Sitnikova, et al., in press; Kuperberg, Sitnikova, et al., 2003). In the current study, we use the term *animacy* descriptively and the term *semantic* to emphasize that these violations are semantic in nature, allowing theoretical comparisons with previous sentence ERP studies in patients with schizophrenia.

unrelated words ("breakfast," "boys") in the pragmatic–semantic violations—that is, increased electrophysiological semantic priming. If patients are impaired in integrating semantic with syntactic information to build up sentence context, this would predict an absent P600 effect to animacy–semantic violations (relative to nonviolated verbs) and a reduced P600 to the morphosyntactic violations (relative to the nonviolated verbs).

Method

Participants

Twenty patients with schizophrenia were recruited from the Erich Lindemann Mental Health Center, Boston, and 20 healthy volunteers were recruited by advertisement. Selection criteria required all participants to be native speakers of English, to be right-handed (Oldfield, 1971; White & Ashton, 1976), and to have normal or corrected-to-normal vision. Exclusion criteria for all participants included neurological damage, head trauma with documented cognitive sequelae, medical disorders that can impair neurocognitive function, a history of substance dependence, and substance abuse within the previous 3 months. Written informed consent was obtained from all persons before participation according to the established guidelines of the Massachusetts General Hospital and Tufts Human Subjects Research Committees. All patients met *Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition* criteria for schizophrenia (R. L. Spitzer, Williams, Gibbon, & First, 1992). Healthy volunteers were not taking any medication and were screened (R. L. Spitzer et al., 1992) to exclude the presence of psychiatric disorders. Demographic characteristics of all participants and psychopathological details for the patient group are given in Table 2.

Construction and Classification of Stimuli

Stimuli are described in detail in previous research (Kuperberg, Caplan, et al., in press; Kuperberg, Kreher, Sitnikova, et al., in press; Kuperberg, Sitnikova, et al., 2003). In brief, 240 fairly highly constrained congruous sentences were constructed with animate nouns separated from critical verbs by one (and occasionally more than one) intermediate word (see Table 1). None of the critical verbs were sentence-final words. Animacy–semantically violated sentences were constructed by replacing the animate nouns with inanimate nouns that were congruous with the critical verbs and their preceding content words. Morphosyntactically violated sentences were constructed by introducing a morphosyntactic violation, either by violating subject–verb agreement or by using a finite in place of an infinitival verb. Pragmatically–semantically violated sentences were constructed by replacing the critical verbs in the congruous sentences with verbs chosen pseudorandomly from sentences of another list. Sentences were fully counterbalanced across four lists, each with 240 test sentences (60 in each experimental condition).

Table 2
Demographic and Psychopathological Data of Healthy Controls and Patients With Schizophrenia

Parameter	Control	Patient
Gender		
Male	16	15
Female	4	5
Age (years)	41 (12)	43 (10)
Education (years)	13.7 (2)	12 (2)
Hollingshead Index	2.6 (1)	3.3 (1)
Race		
African American	1	9
Caucasian	19	11
Premorbid IQ	116.44 (8.5)	104.38 (11.05)
CPZ equivalent		467 (344)
Duration of illness (years)		18 (9)
PANSS total		59.8 (9.7)

Note. Means are shown with standard deviation in parentheses. CPZ = chlorpromazine; PANSS = Positive and Negative Syndrome Scale (Kay, Fiszbein, & Opler, 1987). Patients and controls were matched closely on gender, and there was no significant difference between the groups in age ($p = .57$). Relative to controls, patients had 1 year less of education (significant at $p < .05$), a trend ($p = .06$) toward a slightly higher Hollingshead Index (reflecting a slightly lower parental socioeconomic status), and a slightly lower premorbid IQ (differing by 12 points, significant at $p < .001$), as assessed by the North American Adult Reading Test (Blair & Spreen, 1989). There were significant differences between the two groups in their race distribution ($p < .008$).

ERP Procedure

Sentences were presented word by word on a computer monitor. Each trial (one sentence) began with presentation of a fixation point at the center of the screen for 450 ms, followed by a 100-ms blank screen, followed by the first word. Each word appeared on the screen for 450 ms, with an interstimulus interval of 100 ms separating words. The final word of each sentence appeared with a period. A 750-ms blank-screen interval followed the final word in each sentence, followed by a . This cue remained on the screen until the participant made his or her response, at which point the next trial started. The participant's task was to decide whether each sentence was acceptable by pressing one of two buttons on a response box with either the left or right thumb (counterbalanced across participants). Participants were instructed to wait until the *?* cue before responding. This delayed response reduced contamination of the ERP waveform by response-sensitive components such as the P300 (Donchin & Coles, 1988).

Electrophysiological Recording

Twenty-nine active tin electrodes were held in place on the scalp by an elastic cap (Electro-Cap International, Eaton, OH). Several of these electrodes were placed in standard International 10–20 System locations. These included five sites along the midline (FPz, Fz, Cz, Pz, and Oz) and eight lateral (four over each hemisphere) sites (F3/F4, C3/C4, T3/T4, and P3/P4). Eight extended 10–20 system sites were also used (FC1/FC2, FC5/FC6, CP1/CP2, and CP5/CP6), and eight additional 10–20 sites were altered to form a circle around the perimeter of the scalp. These altered sites included FP1′/FP2′ (33% of the distance along the circle between T3/T4), F7′/F8′ (67% of the distance between FPz and T3/T4), T5′/T6′ (33% of the distance between T3/T4 and Oz), and O1′/O2′ (67% of the distance between T3/T4 and Oz). Electrodes were also placed below the left eye and at the outer canthus of the right eye to monitor vertical and horizontal eye movements, and on the left and right mastoids. The EEG signal was amplified by an Isolated Bioelectric Amplifier System Model H&W-32/BA (SA Instrumentation, San Diego, CA) with a bandpass of 0.01–40 Hz and was continuously sampled at 200 Hz by an analogue-to-digital converter. The stimuli were presented to participants, and their behavioral responses were simultaneously monitored by the digitizing computer.

ERP Data Analysis

Averaged ERPs were formed offline from trials free of ocular and muscular artifact. The mean of the right and left mastoids was subtracted from all electrode sites to produce algebraically linked mastoids as the reference. All ERPs were time-locked to the critical verb in each sentence. The averaged ERPs were quantified by calculating the mean amplitude values (relative to a 100-ms prestimulus baseline) for the voltage points in time windows that encompassed the N400 and P600 effects in patients and controls (see Results, below). The resulting data for each time window

were analyzed with analyses of variance (ANOVAs) for repeated measures. Four separate analyses were performed to examine parasagittal columns of scalp electrodes along the anterior–posterior axis of the head. The midline analysis had repeated measures on five levels of electrode site from anterior to posterior (FPz, Fz, Cz, Pz, Oz). The medial analysis had three levels of electrode site (FC1/FC2, C3/C4, CP1/CP2) and two levels of hemisphere. The lateral analysis had four levels of electrode site (F3/F4, FC5/FC6, CP5/CP6, P3/P4) and two levels of hemisphere. The peripheral analysis had five levels of electrode site (FP1′/FP2′, F7′F8′, T3/T4, T5′/T6′, O1′/O2′) and two levels of hemisphere. In all cases, sentence type (normal, pragmatically–semantically violated, animacy–semantically violated, and morphosyntactically violated) was a within-participants factor, and group (control, schizophrenic) was a between-participants factor.

In addition to these overall ANOVAs, we carried out planned simple effects ANOVAs that allowed comparisons between two sentence types. Group by sentence type interactions in these simple effects analyses were followed up in two ways: first, by directly comparing ERPs elicited by each type of critical verb between the two groups and then by examining the difference between the ERPs elicited by each type of violation and nonviolated verbs in each group separately. Finally, analyses at each electrode column that led to significant interactions involving topographical variables (electrode site and hemisphere) were repeated after amplitude values were normalized with the use of z scores for each sentence type (McCarthy & Wood, 1986). For all interactions involving electrode site and hemisphere, F and p values for z-normalized data are reported. Only interactions that remained significant after normalization are interpreted. The Geisser–Greenhouse correction (Greenhouse & Geisser, 1959) was applied to all repeated measures with more than one degree of freedom in the numerator. We used a standard significance level of $\alpha = .05$.

To eliminate the possibility that ERP differences in patients relative to controls were driven entirely by the trials in which patients made incorrect judgments, we report findings of ERPs elicited in the trials in which participants' responses were correct. However, as reported in the Results, patients made significantly more errors than controls. Thus, the exclusion of incorrectly answered trials could have potentially biased the between-groups comparison by selectively reducing power to detect responses in the patient group. We adopted two methods to determine whether this confounded our main findings. First, we repeated all analyses using all trials rather than just those trials that were correctly answered. Second, we repeated the analyses using the correctly answered trials with all 20 patients but only 14 controls, so that the total number of trials in each sentence type was either slightly less in the control than in the patient group or was comparable between the two groups.

Behavioral Analysis

Accuracy was computed as the percentage of correct responses. A correct response was a judgment of acceptable for the normal sentences and unacceptable for the anomalous sentences. We examined the effects of group (control, schizophrenic) and sentence type (normal, pragmatically–semantically violated, animacy–semantically violated, or syntactically anomalous) on decision accuracy with repeated measures ANOVAs. We also carried out correlational analyses at Pz to explore the relationship between (a) the percentage of errors to pragmatically–semantically, animacy–semantically, and morphosyntactically violated sentences and (b) the amplitudes of the N400 and P600 elicited by each of these violated verbs (relative to nonviolated verbs) in the patient and control groups. Of note, however, the exclusion of incorrectly answered trials from the ERP averages in these analyses would lead to noisier data and larger ERPs in participants who performed poorly behaviorally. This could, in turn, lead to positive correlations that are not interpretable. We therefore conducted these correlations using ERPs not only averaged across correctly answered trials but also averaged across all trials. We only interpreted correlations that were significant on both analyses.

Results

ERPs Elicited by Critical Verbs

Below we report results of analyses of correctly answered trials. The final number of trials included in these analyses (correctly answered trials minus trials rejected for artifact) was significantly less in the patient than the control group, $F(1, 38) = 13$, $p < .001$. However, these analyses and the analyses using a subset of controls such that the number of correctly answered trials was equated across patients and controls (see Method section) yielded essentially the same pattern of findings as those reported below.

Grand-average ERPs elicited by the critical verbs in trials that were answered correctly are shown in the control and patient groups in Figures 1, 2, and 3. In both groups, a clear negative–positive complex is seen in the first 300 ms following the onset of the critical verb (the N1–P2 complex). There appeared to be no differences in the waveforms elicited by the different types of verbs within this early time window. This was reflected by a failure to find significant main effects of sentence type or group (Fs < 2.42, ps $> .10$) or significant interactions between sentence type and electrode site and/or group (Fs < 1.30, ps $> .10$) in the 0–300-ms time window at any of the electrode columns.

The N400

The N1–P2 complex was followed by a negative-going component—the N400—in both patient and control groups. We report the results of statistical analyses comparing the mean amplitude values (relative to a 100-ms prestimulus baseline) for voltage points between 375 and 500 ms that encompassed the peak of the N400 response in patients and controls.

Of most theoretical interest were the effects and interactions involving sentence type. In the overall ANOVA comparing all four sentence types, there were significant main effects of sentence type at the midline, $F(3, 114) = 3.65$, $p < .05$; medial, $F(3, 114) = 4.47$, $p < .05$; and lateral, $F(3, 114) = 3.95$, $p < .05$, electrode columns and highly significant electrode site by sentence type interactions at all electrode columns (all Fs > 3.54, all ps $< .01$). There were no significant interactions between sentence type and group (all Fs < 1.31, all ps $> .10$). There were also no significant three-way interactions between group, sentence type, and electrode site (all Fs < 1.84, all ps $> .10$) and no significant main effects of group (all Fs < 0.42, all ps $> .10$). Planned simple effects analyses were carried out across all participants to determine how the amplitude of the N400 was modulated by the different types of violation.

Pragmatically–semantically violated versus nonviolated verbs. The N400 elicited by pragmatic–semantic violations was generally more negative-going than that elicited by nonviolated verbs in both patient and control groups (see Figure 1). This was reflected by significant main effects of sentence type at all electrode columns across all participants (all Fs > 5.73, all ps $< .05$). There were also significant interactions between sentence type and electrode site at the midline, $F(4, 152) = 9.72$, $p < .0001$; lateral, $F(3, 114) = 9.66$, $p < .001$; and peripheral, $F(4, 152) = 8.56$, $p < .01$, electrode columns, reflecting a larger N400 effect posteriorly than anteriorly. Although the interaction between sentence type and hemisphere approached significance at the peripheral electrode column, $F(1, 38) = 4.25$, $.05 < p < .10$; right > left, it was nonsignificant at all other electrode columns (Fs < 2.25, ps >

(*text continues on page 259*)

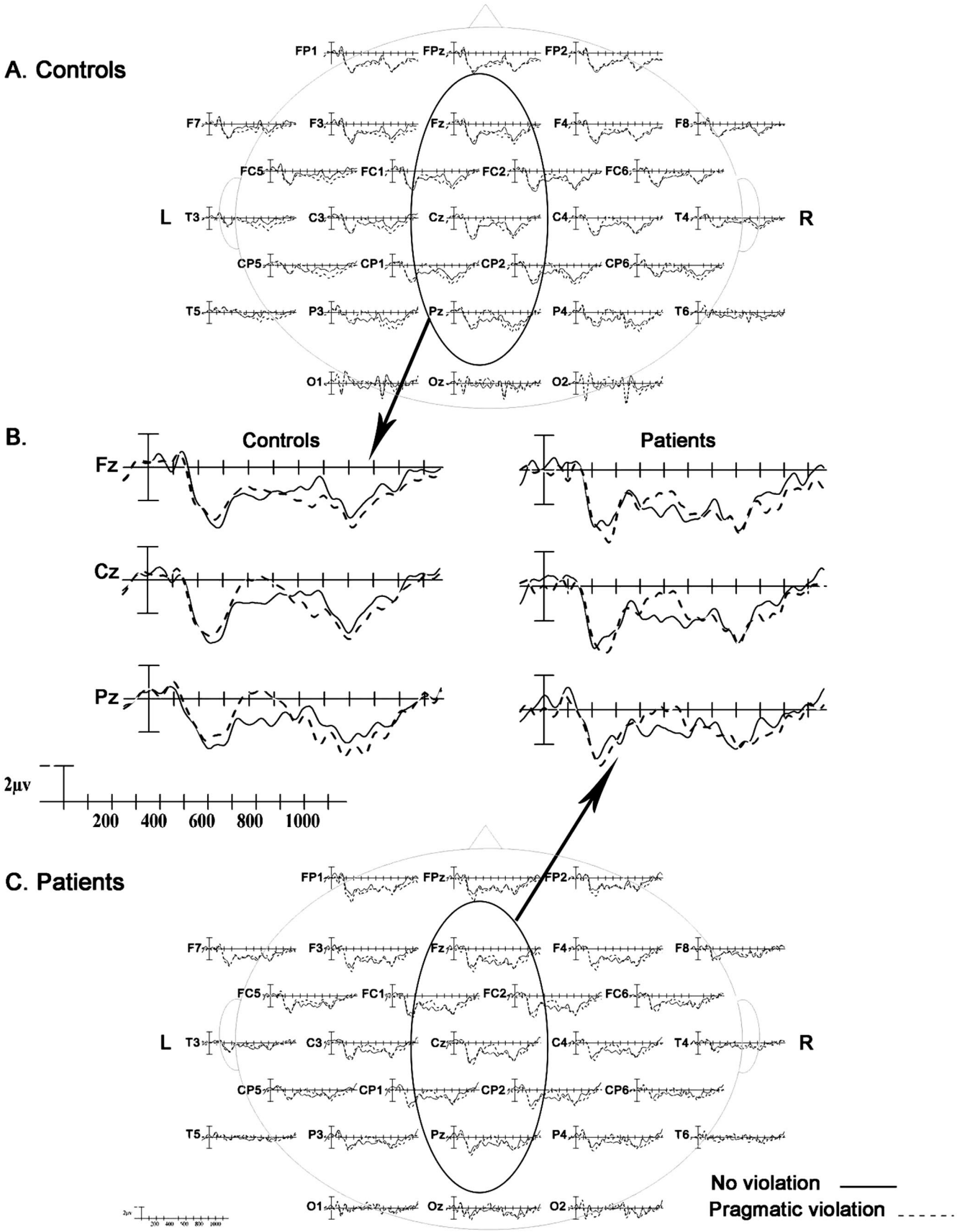

Figure 1. Averaged waveforms elicited by nonviolated verbs (solid) versus pragmatically–semantically violated verbs (dotted). Event-related potentials (ERPs) elicited by critical verbs are shown at all electrode sites in controls (A) and in patients (C). B: ERPs at Fz, Cz, and Pz are shown at higher magnification. L = left; R = right.

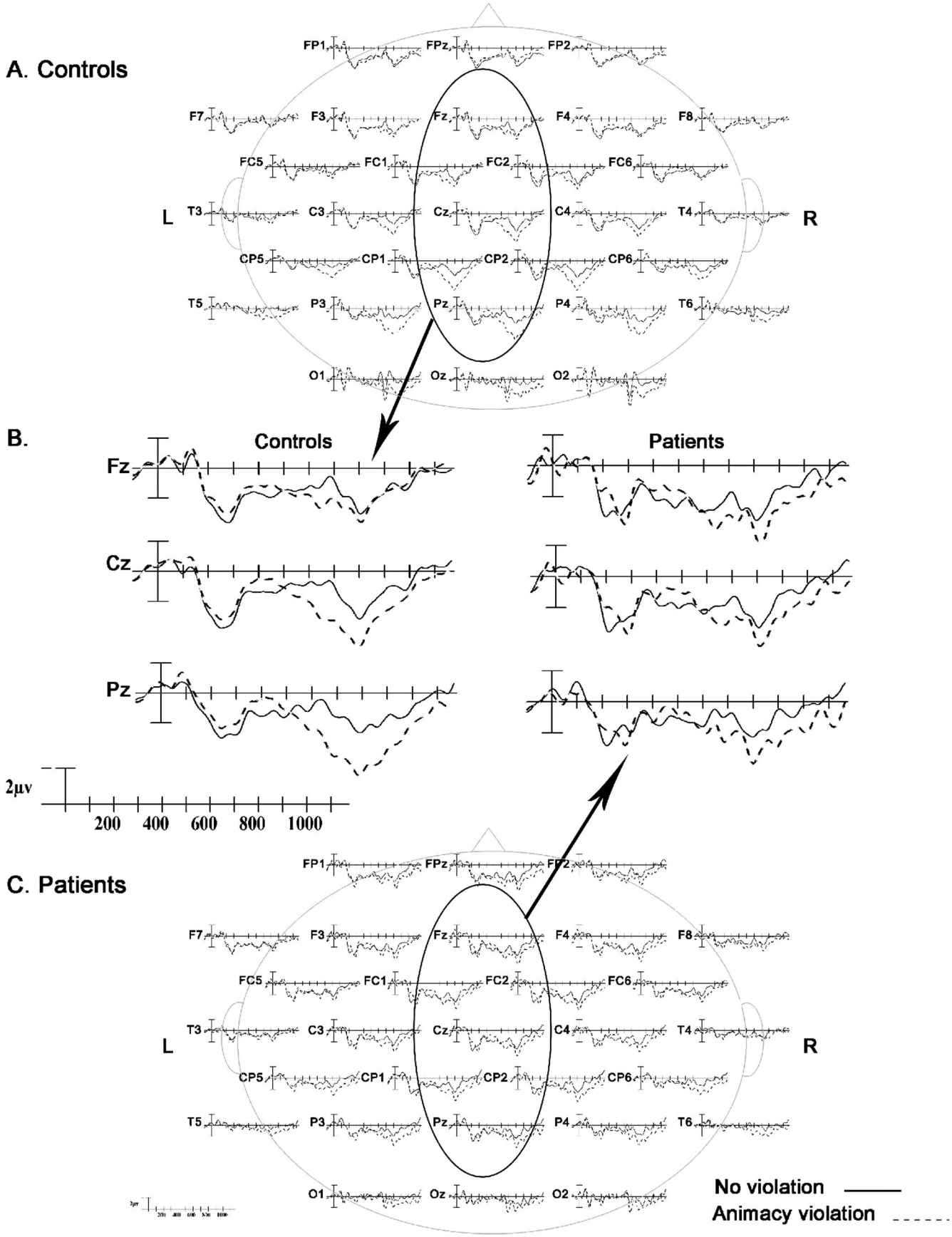

Figure 2. Averaged waveforms elicited by nonviolated verbs (solid) versus animacy–semantically violated verbs (dotted). Event-related potentials (ERPs) elicited by critical verbs are shown at all electrode sites in controls (A) and in patients (C). B: ERPs at Fz, Cz, and Pz are shown at higher magnification. L = left; R = right.

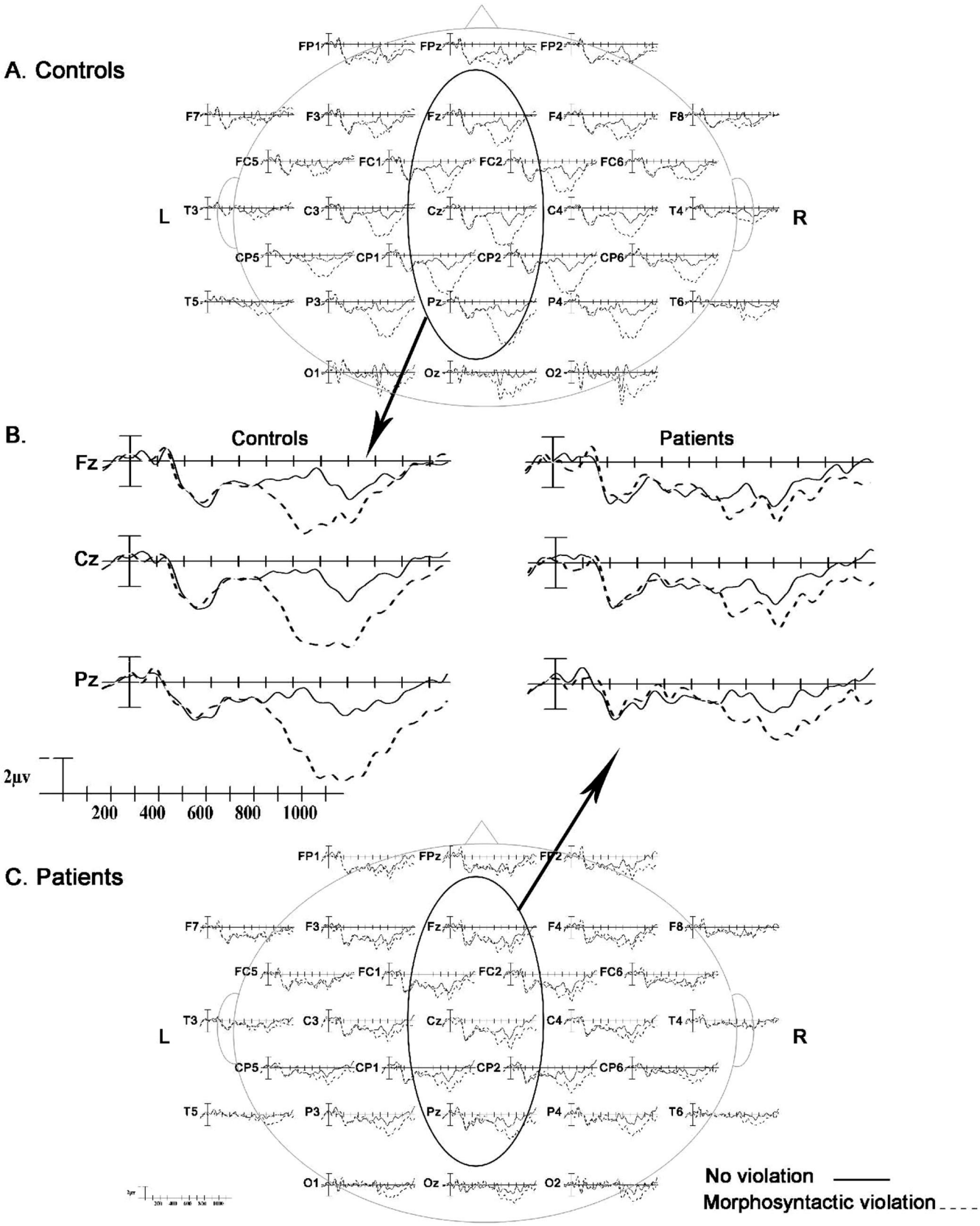

Figure 3. Averaged waveforms elicited by nonviolated verbs (solid) versus morphosyntactically violated verbs (dotted). Event-related potentials (ERPs) elicited by critical verbs are shown at all electrode sites in controls (A) and in patients (C). B: ERPs at Fz, Cz, and Pz are shown at higher magnification. L = left; R = right.

.10), reflecting the generally bilateral distribution of the N400 effect elicited by pragmatic–semantic anomalies. As can be seen in Figure 1, the absolute amplitude of the N400 elicited by both pragmatically–semantically violated and nonviolated verbs as well as the magnitude of the N400 effect elicited by pragmatically–semantically violated (relative to nonviolated) verbs were comparable in the patient and the control groups. This impression was supported by the failure to find significant main effects of group or group by sentence type interactions (all Fs < 0.43, all ps $> .10$).

Animacy–semantically violated versus nonviolated verbs. In both patient and control groups, the N400 elicited by the animacy–semantic violations was more negative-going than that elicited by nonviolated verbs (see Figure 2), with main effects of sentence type across all participants that reached significance at the medial, $F(1, 38) = 5.56$, $p < .05$, and lateral, $F(1, 38) = 4.79$, $p < .05$, electrode columns. Interactions between sentence type and electrode site were nonsignificant (all Fs < 0.36, all ps $> .10$). There were, however, significant interactions between sentence type and hemisphere: medial, $F(1, 38) = 7.51$, $p < .01$; lateral, $F(1, 38) = 7.50$, $p < .01$; and peripheral, $F(1, 38) = 6.56$, $p < .05$, reflecting a larger N400 effect on the right than on the left. The absolute magnitude of the N400 elicited by animacy–semantic violations as well as the magnitude of the N400 effect to animacy–semantic violations (relative to nonviolated verbs) were comparable in the patient and the control groups: There were no significant main effects of group (all Fs < 0.10, all ps $> .10$) or group by sentence type interactions (all Fs < 0.09, all ps $> .10$).

Morphosyntactically violated versus nonviolated verbs. At most electrode sites, the amplitude of the N400 elicited by morphosyntactically violated verbs was of similar magnitude to that elicited by nonviolated verbs, although a small N400 effect to morphosyntactic violations was seen at some sites, particularly in the patient group. This was reflected by a small but significant main effect of sentence type at the medial, $F(1, 38) = 4.74$, $p < .05$, and lateral, $F(1, 38) = 6.97$, $p < .05$, electrode columns; a small Sentence Type × Electrode Site interaction at the peripheral column, $F(1, 38) = 3.78$, $p < .05$; and a significant sentence type by group interaction at the midline column, $F(4, 152) = 0.78$, $p < .05$. Follow-up of this group by sentence type interaction, however, failed to reveal either significant main effects of sentence type in the patients or the control groups (Fs < 3.9, ps $> .07$) or to reveal significant main effects of group in comparing the amplitude of the N400 elicited by either the normal (Fs < 0.28, ps $> .10$) or the morphosyntactically violated verbs (Fs < 1.79, ps $> .10$).

Animacy–semantically violated versus pragmatically–semantically violated verbs. To examine how the N400 was modulated by semantic relationships between words within sentences, irrespective of overall sentence context, we directly compared the amplitude of the N400 elicited by the animacy–semantically violated verbs (that were semantically related to their preceding content words) and the pragmatically–semantically violated verbs (that were semantically unrelated to their preceding content words). The N400 effect elicited by the animacy–semantically violated verbs appeared to be smaller than that elicited by the pragmatically–semantically violated verbs in both patient and control groups (compare Figures 2 and 3). This was reflected by significant sentence type by electrode site interactions at all electrode columns (Fs > 6.40, ps $< .01$). The degree of attenuation of the N400 elicited by the animacy–semantic violations relative to the pragmatic–semantic violations was the same in patients and controls, as reflected by the absence of significant interactions involving sentence type and group at any of the electrode columns (Fs < 0.77, ps $> .10$).

The P600

Following the N400, there was a later positivity—the P600—that, in both control and patient groups, had a widespread distribution across the scalp. The P600 appeared to have a slightly later onset in the patients than in the controls; that is, the N400 appeared to be slightly prolonged in the patients relative to the controls. In the controls, the waveforms to the different types of linguistically violated verbs crossed the waveforms to the nonviolated verbs at approximately 500–550 ms. In the patients, however, the waveforms to the different types of linguistically violated verbs crossed the waveforms to the nonviolated verbs at approximately 600–650 ms. This relative prolongation of the N400 and consequent delay of late positivities in patients with schizophrenia relative to controls has been noted in previous studies (Andrews et al., 1993; Salisbury, O'Donnell, McCarley, Nestor, & Shenton, 2000). We report the results of statistical analyses comparing the mean amplitude values (relative to a 100-ms prestimulus baseline) for voltage points between 600 and 850 ms. This time window was chosen to avoid capturing the end of the N400 effect in patients and to encompass the peak of the P600 in both patients and controls.

Again, of most theoretical interest were the effects and interactions that involved sentence type and/or group. The overall ANOVA comparing all four sentence types revealed significant main effects of sentence type (all Fs > 10.58, all ps $< .0001$) and significant interactions between sentence type and electrode site (all Fs > 6.16, all ps $< .0001$) at all electrode columns. There were also significant interactions between sentence type and group at all electrode columns except the peripheral column, where the interaction approached significance: midline, $F(3, 114) = 6.75$, $p < .001$; medial, $F(3, 114) = 7.14$, $p < .001$; lateral, $F(3, 114) = 4.94$, $p < .01$; and peripheral, $F(3, 114) = 2.47$, $.05 < p < .10$. This suggested that the amplitude of the P600 was modulated differently by the different types of sentences in patients and controls. We carried out a series of planned simple effects analyses to follow up these interactions.

Pragmatically–semantically violated versus nonviolated verbs. In comparing the pragmatically–semantically violated sentences with the nonviolated sentences (see Figure 1), we found no significant main effects of sentence type (all Fs < 0.09, all ps $> .10$) and no significant sentence type by electrode site interactions (all Fs < 0.51, all ps $> .10$) at any of the electrode columns. There were, however, significant group by sentence type interactions at the midline, $F(4, 152) = 0.43$, $p < .05$, and peripheral, $F(4, 152) = 0.18$, $p < .05$, electrode columns. Follow-up ANOVAs comparing pragmatically–semantically violated verbs with nonviolated verbs separately in each group revealed significant main effects of sentence type at the midline, $F(1, 19) = 5.10$, $p < .05$, and peripheral, $F(1, 19) = 8.07$, $p < .01$, electrode columns in controls but not in patients (all Fs < 1.24, all ps $> .10$). Follow-up ANOVAs comparing the P600 elicited by pragmatic–semantic violations between the two groups at these electrode columns failed to reveal main effects of group or group by electrode site interactions (Fs < 1.67, ps $> .30$). There were also no main effects

of group or group by electrode site interactions in examining the P600 elicited by nonviolated verbs at these electrode columns ($Fs < 1.56$, $ps > .10$).

Animacy–semantically violated versus nonviolated verbs. In comparing animacy–semantically violated verbs with nonviolated verbs (see Figure 2), there were significant main effects of sentence type (all $Fs > 6.54$, all $ps < .05$), significant sentence type by electrode site interactions (all $Fs > 8.86$, all $ps < .001$), and significant group by sentence type by electrode site interactions (all $Fs > 3.7$, all $ps < .05$) at all electrode columns. Follow-up ANOVAs showed that animacy–semantically violated verbs elicited significantly larger P600s in controls than in patients, especially at posterior sites, as reflected by significant group by electrode site interactions at all electrode columns (all $Fs > 4.93$, all $ps < .05$). However, when the animacy–semantic violations and nonviolated verbs were compared in each group separately, the controls produced significant P600 effects (all $Fs > 17.58$, all $ps < .0001$), but the patients failed to produce P600 effects (all $Fs < 0.86$, all $ps > .10$).

Morphosyntactically violated versus nonviolated verbs. In comparing morphosyntactically violated verbs with nonviolated verbs (see Figure 3), there were significant main effects of sentence type (all $Fs > 28.08$, all $ps < .0001$), significant sentence type by electrode site interactions (all $Fs > 10.54$, all $ps < .0001$), and significant group by sentence type interactions (all $Fs > 7.01$, all $ps < .05$) at all electrode columns.

Direct comparisons between the two groups of the P600 elicited by morphosyntactic violations revealed main effects of group that reached significance at the midline, $F(1, 38) = 0.00$, $p < .05$; medial, $F(1, 38) = 0.12$, $p < .05$; and lateral, $F(1, 38) = 0.09$, $p < .05$, columns and significant group by electrode site interactions at all electrode columns (all $Fs > 4.50$, all $ps < .05$), reflecting a significantly larger and more widespread P600 to morphosyntactic violations in controls than in patients. Comparisons of the P600 elicited by morphosyntactic violations and nonviolated verbs in each group separately revealed a significant P600 effect in both control (all $Fs > 24.12$, all $ps < .001$) and patient (all $Fs > 1.87$, all $ps < .05$) groups.

Effects of Potential Confounds and Positive Thought Disorder

As reported in Table 2, the patient and control groups differed in their race distribution. In addition, there were small differences between groups in years of education, premorbid IQ, and parental socioeconomic status that reached or approached significance and that may have potentially confounded our findings. However, ANOVAs with 12 patients and 12 controls who were matched for race distribution (11 Caucasian and 1 African American participant included in both groups), years of education, premorbid IQ, and parental socioeconomic status, as well as for the other demographic variables reported in Table 2 (all $ps > .10$), revealed essentially the same pattern of findings as those described above: That is, in the N400 time window, there were significant main effects of sentence type ($Fs > 3.5$ and $ps < .05$ at all electrode columns except the peripheral column) but no interactions involving sentence type and group ($Fs < 1.08$ and $ps > .10$ at all electrode columns), and in the P600 time window, there were significant interactions involving sentence type and group ($Fs > 2.8$ and $ps < .05$ at all electrode columns except the peripheral column).

There were significant inverse correlations between severity of thought disorder (as indexed by the disorganization score on the Positive and Negative Syndrome Scale [PANSS]; Kay, Fiszbein, & Opler, 1987) and (a) the N400 effect to animacy–semantic violations at Pz (Spearman's $r = .55$, $p < .01$) and (b) the N400 effect to morphosyntactic violations at Pz (Spearman's $r = .52$, $p < .05$). There was also an inverse correlation between disorganization and the absolute N400 amplitude evoked by nonviolated verbs that approached significance (Spearman's $r = -0.44$, $p < .06$), but no correlations between disorganization and the N400 evoked by animacy–semantic or morphosyntactically violated verbs ($ps > .10$). In other words, the smaller N400 effects in the most severely thought-disordered patients arose because such patients tended to evoke the most negative N400 amplitudes to nonviolated verbs. There were no significant correlations between severity of thought disorder and the N400 or the P600 effects to any other type of violation at Pz (all $ps > .10$). There were also no significant correlations between PANSS measures of hallucinations, delusions, negative symptoms (total negative PANSS score) or overall psychopathology (total PANSS score) and the N400 or the P600 effects to any of the three violations at Pz (all $ps > .10$). There was a significant correlation between the N400 effect to pragmatic violations and positive symptoms (total positive PANSS score; Spearman's $r = .50$, $ps < .05$).

Behavioral Data: Acceptability Judgments

The percentages of errors made in judging the acceptability of each sentence type in the patient and control groups are shown in Table 3. There was marked variability and heterogeneity across individual schizophrenic patients in their response accuracies to each type of sentence—results that were consistent with our previous findings (Kuperberg et al., 1998, 2000). As expected, pa-

Table 3
Percentage of Errors for Nonviolated, Pragmatically–Semantically Violated, Animacy–Semantically Violated, and Morphosyntactically Violated Sentences in Patients and Controls

	Control			Patient		
Sentence type	*M*	*SD*	*Mdn*	*M*	*SD*	*Mdn*
Nonviolated	13.72	9.77	10.00	21.42	18.14	16.67
Pragmatic–semantic	14.96	14.81	8.33	32.25	25.17	23.33
Animacy–semantic	3.75	8.05	0.83	25.33	27.70	10.83
Morphosyntactic	10.61	19.13	3.33	42.67	35.61	25.83

tients performed significantly less accurately than did controls overall; see Table 3, main effect of group, $F(1, 38) = 14.49$, $p < .0001$. In addition, patients and controls showed different patterns of responses across the four sentence types; that is, there was a group by sentence type interaction, $F(3, 114) = 3.80$, $p < .05$.

Follow-up of this interaction showed that controls made fewer errors on the animacy–semantically violated sentences than on any of the other sentence types: animacy–semantically violated versus nonviolated, $t(19) = 4.17$, $p < .0001$; animacy–semantically violated versus pragmatically–semantically violated, $t(19) = 3.70$, $p < .001$; and animacy–semantically violated versus morphosyntactically violated, $t(19) = 2.33$, $p < .05$. Patients, however, did not make fewer errors on the animacy–semantically violated sentences than on the other types of sentences, but they made relatively more errors on the morphosyntactically violated sentences: morphosyntactically violated versus nonviolated, $t(19) = 2.61$, $p < .01$, and morphosyntactically violated versus animacy–semantically violated, $t(19) = 3.21$, $p < .01$. Behavioral analyses on 12 patients and 12 controls who were matched for all the demographic factors reported in Table 2 (all ps $> .10$) showed a similar pattern of findings.

Relationship Between ERP and Behavioral Data

Within the patient group, we carried out correlations between the percentage of errors to pragmatically–semantically, animacy–semantically, and morphosyntactically violated sentences and the amplitudes of the raw N400 and P600 waveforms and the N400 and P600 effects elicited by each of these violated verbs relative to nonviolated verbs. We calculated amplitudes of ERPs at Pz using both (a) trials that were correctly answered and (b) all trials (see Method section). There were no correlations that reached significance (at $p < .05$).

Discussion

In this study we explored the electrophysiological correlates of manipulating both semantic and syntactic relationships between words within sentences in patients with schizophrenia. There were two main ERP findings. First, the N400 effect (the difference in amplitude of the N400 to violated relative to nonviolated verbs) to pragmatically–semantically and animacy–semantically violated verbs was the same in patients and controls. Second, the amplitude of the P600 elicited by morphosyntactically violated and animacy–semantically violated verbs was attenuated in patients relative to controls: In patients, the P600 effect (the difference in amplitude of the P600 to violated relative to nonviolated verbs) was reduced to morphosyntactic violations and absent altogether to animacy–semantic violations. It is unlikely that demographic differences between the patients and controls confounded these findings, as analyses conducted on subgroups of patients and controls, matched for all demographic variables, yielded the same results as for the larger cohorts.

A second factor that could have confounded our findings was the inferior behavioral performance (in terms of overall accuracy) in patients relative to healthy controls—a finding that replicates several previous studies (Anand et al., 1994; Kuperberg et al., 1998, 2000; Tamlyn et al., 1992). There are many reasons why patients might arrive at different conclusions from controls about whether a sentence is acceptable, including an inability to engage in the task at all. This was unlikely in the current study. First, examination of the individual patients' accuracies did not suggest that they were responding at chance.[5] Second, it is unlikely that a normal N400 response would have been evoked in patients if they were not attempting to make sense of the sentences, as the N400 is known to attenuate when participants do not attend to the meaning of stimuli (Chwilla, Brown, & Hagoort, 1995). It is also unlikely that abnormalities in patients were driven by the trials that were answered inaccurately, as ERPs were generated from correctly answered trials only. Although the exclusion of more incorrectly answered trials in the patient than the control group might have selectively reduced power to detect significant electrophysiological differences between conditions within the patient group, this would have been unlikely to differentially affect the reduction of the P600 effect as opposed to both the P600 and N400 effects. Moreover, when we repeated analyses after matching the total number of trials across patient and control groups by including only a subset of control participants, the results were the same. We consider the theoretical relevance of the behavioral findings and their relationship with the ERP findings later in this Discussion.

The N400

The absolute amplitude of the N400 evoked by the different sentence types did not differ between patients and controls.[6] The

[5] Although accuracy was globally impaired across the entire schizophrenic group (see Behavioral Results), as in our previous studies (G. R. Kuperberg et al., 2000) there was marked variation in accuracy across different types of sentences across individual patients. Most individual patients responded with at least 75% accuracy to two or more of the different sentence types. Two patients, however, consistently responded that anomalous sentences made sense. Two additional patients responded with 80% accuracy to one type of sentence but with only 60% accuracy to the other types of sentences. Although subsequent debriefment of these 4 patients suggested that they were attending to the task (they were able to remember and talk about many of the sentences), we cannot exclude the possibility that they were not attending and were pressing the buttons randomly. We therefore repeated all ERP and behavioral analyses after excluding these 4 patients. The pattern of both ERP and behavioral results including and excluding these 4 patients was similar in their essential aspects.

[6] These findings are consistent with some but not all previous findings examining the absolute amplitude of the N400 (see footnotes 1 and 2). Although the examination of between-groups effects in the absolute amplitude of ERPs is an important complementary approach, there are some caveats to its interpretation. Differences between patients and controls in the absolute N400 amplitude could theoretically arise from differences between groups in the prestimulus baseline and/or components that overlap in time but that do not mediate semantic processes. For example, an overall more negative N400 in patients relative to controls might have nothing to do with semantic processing but might arise from a less positive overlapping late positivity or P600 component in patients. Examining the modulation of an ERP to one condition relative to another experimental condition allows the "isolation" of the specific feature of a waveform that mediates the cognitive process of interest, in this case, semantic processing (Coles & Rugg, 1995; Donders, 1868/1969). This is why we focus on the modulation of the N400 to each type of violation relative to nonviolated verbs, in which the assumption is that such nonsemantic prestimulus or poststimulus effects (with the exception of noise) subtract out.

N400 effect elicited by both pragmatic–semantic and animacy–semantic violations, relative to nonviolated verbs, was also the same in the patients and controls. Moreover, the degree of attenuation of the N400 elicited by the animacy–semantic violations relative to the pragmatic–semantic violations was the same in patients and controls. We have suggested that this attenuation of the N400 occurred because critical verbs were primed by their individual preceding content words in the animacy–semantically violated sentences ("eat" primed by "breakfast" and "eggs"), but not in the pragmatically–semantically violated sentences ("bury" not primed by "breakfast" and "boys"; Kuperberg, Caplan, et al., in press; Kuperberg, Sitnikova, et al., 2003). This observation therefore suggests that priming occurred to the same degree in the patients and controls and is inconsistent with the theory that lexical associates are hyperactivated (or disinhibited) in schizophrenia, at least during sentence comprehension under these experimental conditions.

The P600

The P600 elicited by all types of violations was significantly reduced in the patients with schizophrenia relative to the healthy controls. There has been extensive debate about the nature of the cognitive process indexed by the P600 waveform (Coulson et al., 1998; Osterhout & Hagoort, 1999). One aspect of this debate has focused on whether the P600 constitutes part of the P300 family of waveforms and, consequently, whether it indexes a general updating of contextual information within memory (Donchin & Coles, 1988) rather than processes that are specific to the language system. This debate is clearly of relevance for the findings in the current study because the reduction of the P300 is one of the most robust and consistent biological markers of schizophrenia (Ford, 1999), and there have also been several reports of a reduced late positivity during sentence processing paradigms in schizophrenia (Adams et al., 1993; Andrews et al., 1993; Mitchell et al., 1991; Nestor et al., 1997; Salisbury et al., 2000; Salisbury, Shenton, Nestor, & McCarley, 2002). In the current study we do not specifically address the question of whether the reduction of the P600 observed in patients with schizophrenia is related to the reduction of the P300 or the LPC observed in other paradigms. These components may reflect activity from common neural sources and/or more general contextual updating processes (although Frisch, Kotz, von Cramon, & Friederici, 2003, have argued against this explanation in another patient population). What the current study does shed light on are the psycholinguistic ramifications of the abnormally reduced P600 in schizophrenia.

Within the language system, the P600 is thought to be influenced by both semantic and syntactic information and to reflect a processing cost that occurs when potentially plausible semantic relationships conflict with a syntax that is either unlicensed or that dictates an implausible meaning of a sentence.[7] Thus, the reduction in the P600 in patients might have arisen from an impairment in detecting plausible semantic relationships, from an impairment in computing syntactic structure, or from an abnormal interaction between syntactic and semantic processing. As discussed above, the normal modulation of the N400 in patients suggests that their processing of lexicosemantic relationships in these sentences was normal. It is also unlikely that patients showed a pure syntactic deficit: They did retain sensitivity to the morphosyntactic violations—a finding that is consistent with classic behavioral studies suggesting that patients with schizophrenia are able to use some syntactic constraints during sentence processing (Carpenter, 1976; Grove & Andreasen, 1985; Rochester, Harris, & Seeman, 1973), and also with a more recent ERP study that reported a normal left anterior negativity to syntactic violations of word category in schizophrenia (Ruchsow et al., 2003).[8]

We therefore suggest that the P600 was reduced in schizophrenia because of abnormalities in the way in which semantic information interacted with syntactic information to build up context and meaning. This interpretation is consistent with findings of a recent behavioral study in which we asked patients and controls to read the same sentences word by word in a self-paced manner. In this self-paced reading study, patients showed less sensitivity (smaller reading time differences) than controls to the animacy–semantically violated and morphosyntactically violated sentences, relative to the pragmatically–semantically violated or nonviolated sentences, at sentence-final words and at acceptability decisions points in the sentence where semantic–syntactic integration demands are particularly high (Kuperberg, Kreher, Goff, McGuire, & David, in press).

Such abnormalities in the interaction between semantic and syntactic processing had their greatest impact on how patients treated animacy–semantic violations: The quantitative reduction in the P600 in patients led to a qualitative difference between patients and controls in their electrophysiological response to these violations; unlike controls, patients failed to show a significant difference in the amplitude of the P600 to these types of violations relative to nonviolated verbs, that is, no P600 effect. These animacy–semantically violated sentences were characterized by semantic relationships between nouns and verbs that biased toward a plausible interpretation, but a syntax that dictated an implausible interpretation. It is possible that an impairment in combining semantic and syntactic processes to effectively build up context in these sentences (indexed by the absent P600 effect) left patients vulnerable to computing the meaning of sentences according to semantic relationships between single words (indexed by the normal N400 effect).

Indirect evidence for this conclusion comes from the pattern of behavioral findings. Whereas healthy controls made significantly fewer errors to the animacy–semantically violated sentences than to the other types of sentences, patients did not perform relatively better on these types of sentences. In addition, whereas healthy controls had no trouble in judging the acceptability of the morphosyntactically violated sentences, patients tended to make more

[7] The online processing cost of combining syntactic and semantic information may be greater when participants are required to perform an acceptability judgment task. It will be interesting to determine whether the same pattern of ERP findings are observed if participants do not perform an overt judgment task.

[8] The left anterior negativity is a waveform that is thought to reflect the establishment of an initial syntactic structure that only later interfaces with semantic information (Friederici, 1995). In the current study, the morphosyntactic violations in the current study did not elicit an anterior negativity in either the patient or the control group. This failure to elicit a LAN to morphosyntactic violations is consistent with some (e.g., Hagoort et al., 1993) although not all (e.g., Hagoort & Brown, 2000) findings. It also replicates previous findings using these identical morphosyntactically violated sentences on a younger group of healthy individuals (Kuperberg, Holcomb, et al., 2003).

errors to these sentences than to the other types of sentences. In other words, in comparison with controls, patients tended to incorrectly interpret animacy–semantically and morphosyntactically violated sentences as acceptable: The plausible lexicosemantic relationships between individual words appeared to be driving their judgments.[9]

Positive thought disorder is characterized by a preoccupation with semantic relationships between individual words at the expense of whole sentence and discourse context. It is therefore tempting to infer a link between this phenomenon and the neurophysiological abnormalities described here. Although not all the patients sampled in the current study had positive thought disorder, it is possible that the P600 abnormalities described here characterize schizophrenia as a whole and that additional electrophysiological abnormalities must occur for positive thought disorder to manifest clinically. Some intriguing clues as to the nature of such additional abnormalities come from correlations within the patient group: Patients with the most severe thought disorder showed the smallest N400 effects to animacy–semantic and morphosyntactic violations because of more negative N400s to nonviolated verbs. There were no other correlations with any other individual symptoms, suggesting some degree of specificity to this finding. A more negative N400 to nonviolated verbs in schizophrenia has been noted in previous studies (Mitchell et al., 1991; Nestor et al., 1997; Niznikiewicz et al., 1997; Ohta et al., 1999) but has not been specifically linked to positive thought disorder. It is possible that schizophrenia, as a whole, is associated with electrophysiological abnormalities when there is increased demand to combine semantic and syntactic information, but that, for thought disorder to manifest, electrophysiological abnormalities must also occur even when processing demands are lower, such as in integrating contextually congruous words in normal sentences. In other words, clinical thought disorder may occur only when there is a complete breakdown in the effective use of linguistic context (see Kuperberg et al., 1998, 2000) that is apparent electrophysiologically within both the P600 and N400 time windows. It is, however, important to note that our patient sample was relatively small, and it will therefore be important to replicate these findings.

Interpretation of Previous ERP Studies of Sentence Comprehension

An account by which an impairment in building up sentence context arises because of abnormal interactions between semantic and syntactic processing may explain why some previous studies have reported a normal N400 effect in schizophrenia whereas others have reported it to be abnormally attenuated. We suggest that, as for the P600 in the current study, the N400 is abnormally attenuated in schizophrenia under circumstances in which, to correctly make sense of incoming discourse, there is a relatively high demand to integrate semantic and syntactic information. This might occur during wrap-up, evaluative processes (Friedman, Simson, Ritter, & Rapin, 1975) when anomalies fall on sentence-final words (Adams et al., 1993; Mitchell et al., 1991; Ohta et al., 1999). It might also occur when processing sentences containing homographs, as discussed in the introduction (Sitnikova et al., 2002).

Conclusions, Implications, and Future Directions

In summary, we have demonstrated a dissociation between the modulation of the N400 and P600 during sentence processing in schizophrenia. We suggest that this electrophysiological dissociation reflects an abnormal interaction between semantic and syntactic processing whereby patients are able to process semantic and syntactic information but have problems combining this information to build up a propositional representation of meaning. We suggest that this, in turn, leads to patients being relatively vulnerable to misinterpreting semantic relationships between individual words at the expense of building up sentence context.

[9] Although offline judgments may have been influenced by an impairment in combining syntactic with semantic information online, they were also influenced by strategic and reasoning processes specific to the task of deciding whether a sentence is acceptable that may have little to do with normal online language comprehension. This might explain the variability in behavioral findings across participants (see also G. R. Kuperberg et al., 2000) as well as the absence of any robust correlations between accuracy and raw ERPs or ERP effects to each type of violation across individuals in either the patient or the control group.

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