

Spared and Impaired Spoken Discourse Processing in Schizophrenia: Effects of Local and Global Language Context

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Individuals with schizophrenia are impaired in a broad range of cognitive functions, including impairments in the controlled maintenance of context-relevant information. In this study, we used ERPs in human subjects to examine whether impairments in the controlled maintenance of spoken discourse context in schizophrenia lead to overreliance on local associations among the meanings of individual words. Healthy controls ($n = 22$) and patients ($n = 22$) listened to short stories in which we manipulated global discourse congruence and local priming. The target word in the last sentence of each story was globally congruent or incongruent and locally associated or unassociated. ERP local association effects did not significantly differ between control participants and schizophrenia patients. However, in contrast to controls, patients only showed effects of discourse congruence when targets were primed by a word in the local context. When patients had to use discourse context in the absence of local priming, they showed impaired brain responses to the target. Our findings indicate that schizophrenia patients are impaired during discourse comprehension when demands on controlled maintenance of context are high. We further found that ERP measures of increased reliance on local priming predicted reduced social functioning, suggesting that alterations in the neural mechanisms underlying discourse comprehension have functional consequences in the illness.

Introduction

Language abnormalities, including deficits in comprehension, are among the most salient cognitive deficits in schizophrenia. A fundamental question is whether these abnormalities mainly reflect deficits in relatively low-level linguistic functions (e.g., lexical access) or whether they reflect deficits in higher-level comprehension processes that rely on the controlled maintenance of context relevant information in working memory (Cohen et al., 1999). Language disorders in schizophrenia may be related to impairments in the buildup of context, especially when integration demands are high, as is the case during discourse comprehension (Kuperberg et al., 2008a). Indeed, communication deficits typically manifest at the level of discourse rather than at the level of individual words or sentences (Hoffmann et al., 1986; Docherty et al., 1998), yet very few studies have examined discourse processing in schizophrenia under controlled experimental conditions (Ditman and Kuperberg, 2007). Thus far, the results of these studies suggest that patients have deficits in their ability to benefit from language context (Gernsbacher et al., 1999; Kuperberg, 2010a,b; Boudewyn et al., 2012a).

In contrast to deficits in contextual processing, schizophrenia patients have shown intact or amplified effects of associative relations between words in a two-word priming paradigm (Manschreck et al., 1988; Spitzer et al., 1993; Barch et al., 1996), when priming does not depend on controlled strategic processes induced by task demands (Kreher et al., 2009). In addition, there is evidence for increased sensitivity to lexical associations when the demands of maintaining the language context are higher, as in discourse comprehension (Ditman et al., 2011).

In electrophysiological studies of healthy participants, sensitivity to global discourse coherence and local meaning associations is reflected by a modulation of the N400, an ERP that is sensitive to semantic aspects of linguistic input (Swaab et al., 2012). Specifically, in studies that have manipulated global coherence and local association in the same experiment, we have shown that the amplitude of the N400 is reduced to both words that are coherent with preceding discourse context compared with words that are not and words associated with meaning to a preceding word in the local context compared with words that are not (Boudewyn et al., 2012b,c).

In the current study, we used ERPs to measure the effects of manipulations of global discourse coherence and local associative relations between words within the same paradigm (see Table 2). We predicted that effects of discourse coherence would be attenuated in schizophrenia patients (relative to healthy controls), because discourse comprehension produces additional demands on the controlled maintenance of context-relevant information, which relies on prefrontally mediated cognitive control operations that are impaired in schizophrenia (MacDonald et al., 2005; Lesh et al., 2011). In contrast, we predicted that schizophrenia patients would show an increased reliance on local lexical associ-

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Table 1. A summary of demographic information for healthy control and patient participants, as well as clinical and functional characteristics for patients

	Healthy controls (<i>n</i> = 22) (mean ± SD)	Schizophrenia patients (<i>n</i> = 22) (mean ± SD)
Age	22.5 ± 4.4	24.3 ± 5.2
Participant education (years)	14.6 ± 1.4	13 ± 1.5
Parent education (years)	15.2 ± 2.4	15.4 ± 2.6
Symptom severity		
BPRS		41.4 ± 10.6
SAPS		13.9 ± 15.1
SANS		32.1 ± 14.4
Disorganization (maximum 36)		6.1 ± 2.8
Positive (maximum 38)		10.5 ± 6.8
Negative (maximum 41)		14 ± 5.6
Functional characteristics		
GAF (maximum 100)		49.1 ± 9.7
Social		5.4 ± 1.6
Role		4.2 ± 2.9

ations among words. We used naturally produced spoken discourse to make a link with real-world comprehension demands and daily functioning in schizophrenia. We further examined whether abnormal processing of global discourse context and local associative relations were correlated with impairments in social and occupational functioning in schizophrenia.

Materials and Methods

Participants. In this study, 22 schizophrenia patients (18 males) and 22 healthy control participants (16 males) were tested. Patients were recruited through the Early Diagnosis and Preventive Treatment of Psychosis clinic of the Department of Psychiatry at University of California, Davis School of Medicine. Healthy controls were recruited from the community through advertisements. All subjects provided informed consent, using a protocol approved by the Institutional Review Board at the University of California, Davis, and were compensated for participation at a rate of \$25.00/h.

All participants were native speakers of English who had not learned any other language before age 5 years, and all but three patients and two control participants were right-handed. The average age of the patient group was 24.27 years (range, 19–39 years) and 22.5 years for the control group (range, 18–37 years); the groups did not significantly differ in age ($p = 0.13$). Patients and controls were also matched on parental education (patient group average, 15.39 years; control group average, 15.2 years; $p = 0.77$) but, as expected because of the age of onset of the disease, differed in self-education level (patient group average, 13.02 years; control group average, 14.59 years; $p < 0.05$). All patients had a Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) diagnosis of schizophrenia or schizoaffective disorder and were on stable doses of antipsychotics at the time of testing. Control participants had no DSM-IV Axis I or Cluster A DSM-IV Axis II disorder, no first-degree relative with a psychotic disorder, and were not taking any psychotropic or cognition-enhancing medication. All participants had an estimated IQ >70 on the Wechsler Test of Adult Reading (Pearson Education, 2001). No participants had a head injury or neurological disease or a history of substance dependence in the past 6 months or substance abuse in the past month. All were negative on a comprehensive urine drug screen on the test day. A summary of demographic information for healthy control and patient participants, as well as clinical and functional characteristics for patients, are shown in Table 1.

Clinical and functional characteristics. Patients were assessed by clinicians using the Structured Clinical Interview for DSM-IV-TR, and the severity of clinical symptoms was rated using the 24-item Brief Psychiatric Rating Scale (BPRS) (Overall, 1974). Scales for the assessment of both positive symptoms (SAPs) and negative symptoms (SANs) (Andreasen, 1983a,b) were used to evaluate positive and negative symptom severity. A disorganization score was calculated as the sum of several measures from the BPRS (conceptual disorganization, mannerisms and posturing, dis-

orientation), SANS (total score for attention), and SAPS (total score for positive formal thought disorder and bizarre behavior), following from Barch et al. (2003). Likewise, a positive score was computed using measures from the BPRS (grandiosity, suspiciousness, hallucinations, unusual thought content) and SAPS (total scores for hallucinations and delusions) and a negative score from the BPRS (emotional withdrawal, motor retardation, and blunted affect) and SANs (total scores for anhedonia/asociality, avolition, apathy, alogia, and affective flattening) (Barch et al., 2003). Community and role functioning was assessed using the Global Functioning: Role scale, and social functioning was assessed using the Global Functioning: Social scale (Cornblatt et al., 2007). Both of these are scales from 1 to 10 measuring functioning in a role and functioning socially. Finally, the Global Assessment of Functioning (GAF), a scale ranging from 1 to 100, was additionally administered. High scores on the clinical measures (disorganization, positive, and negative) indicate greater severity of symptoms; high scores on the functional measures (role, social, and GAF) indicate higher functioning.

Stimuli. The stimuli were 72 experimental story sets, in which discourse congruence (congruent or incongruent) and lexical association (associated or unassociated) were orthogonally varied to produce four conditions (Table 2): (1) congruent–associated; (2) congruent–unassociated; (3) incongruent–associated; and (4) incongruent–unassociated. Story sets were matched across conditions for story coherence using latent semantic analysis values, which are a measure of similarity of meaning among words, sentences, or multi-sentence stories that do not necessarily pattern with propositional plausibility or coherence (Landauer et al., 1998). Congruent stories were also rated as significantly more congruent than incongruent stories, regardless of association condition. Overall story cloze probability (a measure of the predictability of the target word) was low (<33%) and did not affect the pattern of results in two previous studies (Camblin et al., 2007; Boudewyn et al., 2012b). The critical target words were matched for length and lexical frequency across conditions. For a more detailed description of the construction and pretesting of these stimuli, see Boudewyn et al. (2012b).

The first two sentences of each passage established a discourse context, and the third (final) sentence contained the associated or unassociated target (Table 2). For example, the first story set shown in Table 2 included the locally associated prime–target pair “tables and chairs” in the third sentence to create the associated conditions, whereas the locally unassociated prime–target pair “tables and lamps” is included in the third sentence to create the unassociated conditions. In addition, target words were either congruent or incongruent with the discourse context. Using the same example at the top of Table 2, both target words (tables/lamps) are congruent when the preceding global discourse context describes rearranging furniture and are incongruent when the preceding global discourse context specifies that there would be no furniture except chairs. All except 22 of the prime and target pairs were separated by one intervening word; the remaining stimuli had either two intervening words (8) or three (14). Target words were always congruent with the meaning of the final sentence. That is, target words made sense in context if the sentence were to be heard in isolation. Story sets were divided into four lists and counterbalanced such that the critical target words and the two sentences preceding the final sentence were not repeated within subjects. Each list contained 144 experimental stories, 36 in each condition. An additional 40 filler stories were included: 20 were congruent, and 20 ended with a word that was anomalous at both the discourse and sentence level.

Story sets and fillers were spoken by a female speaker, with natural inflection and at a natural speaking rate. The words were digitally recorded using a Schoeps Mikrofone MK2 microphone and Sound Devices USBPre A/D (44,100 Hz, 16 bit). Discourse context (first two sentences of the passage) and the critical sentences were recorded separately. The onset and offset of each critical word in all conditions was determined by visual inspection of the speech waveform and by listening to the words using speech-editing software (Audacity; Soundforge). The average duration of the stories was 8951 ms (ranging from 7917 to 9359 ms), and the average duration of the critical words was 568 ms (ranging from 293 to 861 ms). The duration of the critical words did not differ between conditions ($t < 1$). The duration between prime and target was the same for

Table 2. Example stimulus sets showing each of the four conditions described in text

Condition	Context	Target sentence
Associated congruent	Keith was arranging furniture in the lobby of the hotel. He wanted to make sure the room appeared comfortable but not overly cluttered.	Keith was very specific about the placement of the <i>chairs</i> and TABLES.
Unassociated congruent	Keith was arranging furniture in the lobby of the hotel. He wanted to make sure the room appeared comfortable but not overly cluttered.	Keith was very specific about the placement of the <i>chairs</i> and LAMPS.
Associated incongruent	Keith wanted the arrangements for his outdoor wedding to be very simple. There would only be seats for the guests and a simple archway.	Keith was very specific about the placement of the <i>chairs</i> and TABLES.
Unassociated incongruent	Keith wanted the arrangements for his outdoor wedding to be very simple. There would only be seats for the guests and a simple archway.	Keith was very specific about the placement of the <i>chairs</i> and LAMPS.
True/False	Keith was very specific about the arrangements.	
Associated congruent	Rick was unaware that his sister had submitted his poem in the prestigious contest. He was shocked when he won the award and the hefty cash prize.	He was not prepared for the <i>fame</i> and FORTUNE.
Unassociated congruent	Rick was unaware that his sister had submitted his poem in the prestigious contest. He was shocked when he won the award and the hefty cash prize.	He was not prepared for the <i>fame</i> and FORTUNE.
Associated incongruent	Rick was mortified when the videotape of his arrest was shown on the news. After the news show aired, he was ridiculed by the entire neighborhood.	He was not prepared for the <i>fame</i> and FORTUNE.
Unassociated incongruent	Rick was mortified when the videotape of his arrest was shown on the news. After the news show aired, he was ridiculed by the entire neighborhood.	He was not prepared for the <i>fame</i> and FORTUNE.
True/False	Rick was given a public service award.	

For clarification, the primes are shown in italics and target words are capitalized; during the experiment, these words were not specifically emphasized.

the congruent/incongruent-associated and congruent/incongruent-unassociated conditions because the same final sentence was used for the two associated conditions and the two unassociated conditions. This was accomplished by inserting a 1 s silence between the speech files that contained the first two context sentences and the speech files that contained the final sentences using Presentation software (Neurobehavioral Systems). (The duration of this pause was set to 1 s to match the average of the naturally produced pauses between sentences one and two.) There were no statistically significant differences in duration of the onset of the prime to the onset of the target between the associated and unassociated conditions ($p = 0.43$). The target sentences were the same in all conditions up to the sentence-final target word.

Comprehension questions did not focus on the prime or the target but rather on the context of the discourse (for examples, see Table 2). The same true/false question was asked in the congruent-associated/unassociated and incongruent-associated/unassociated conditions. Half of the questions required a true response, and half required a false response.

Procedure. Participants sat in a comfortable chair in an electrically shielded, sound-attenuating booth. The stimuli were presented through BeyerDynamic headphones using Presentation software. The discourse trials began with a white fixation cross at the center of the screen, ~100 cm in front of the participants. The fixation cross was present from 900 ms before onset of the stimuli and during presentation of the entire passage until the offset of the final word. The fixation cross was then replaced by a visually presented comprehension question about the preceding discourse, after 1000 ms. Subjects were asked to make a true/false response by pressing a yes or no button with the index and middle fingers of their right hand, respectively. The comprehension question remained on the screen until the subject made a response.

Each experimental session began with a practice block consisting of filler passages, after which two of the four counterbalanced lists were presented in random order, each containing both experimental trials and fillers in a pseudorandom order. Each list was divided into four blocks for presentation purposes such that each participant listened to eight blocks of stimuli (two lists). The order of blocks was counterbalanced.

ERP recording and data reduction. EEG was recorded from 29 tin electrodes, mounted in an elastic cap (ElectroCap International). The right mastoid electrode was used as the recording reference (except for electrodes used to measure blinks and eye movements: one electrode beneath the left eye was referenced to FP1 and two placed at the outer canthi of each eye were referenced to each other). The left mastoid was also recorded for later offline algebraic re-referencing. The EEG signal was digitized online at a sampling rate of 500 Hz, with bandpass half-amplitude cutoffs of 0.05–100 Hz (Neuroscan Synamp II). EEG was digitized con-

tinuously along with accompanying stimulus codes used for subsequent averaging. Impedances were kept below 5 k Ω .

Data processing and analysis were performed using the SCAN packages (Compumedics Neuroscan) and MATLAB (MathWorks) using EEGLAB toolbox (Delorme and Makeig, 2004) with the ERPLAB plugin (<http://erpinfo.org/erplab>), along with custom MATLAB and UNIX routines. ICA-based artifact correction was used to correct for eyeblinks. Single-trial waveforms were then screened for amplifier blocking, muscle artifacts, horizontal eye movements, and any remaining blinks over epochs of 1200 ms, starting 200 ms before the onset of the critical target words. Average ERPs were computed over artifact-free trials in the four conditions. There were no differences in the average number of trials in each condition between the healthy controls (average, 30.6) and the patients (average, 30.3; $p = 0.71$). All ERPs were filtered offline with a Gaussian low-pass filter with a 25 Hz half-amplitude cutoff. Statistical analyses were conducted on the filtered data.

Results

Behavior

Accuracy on the true/false comprehension showed a main effect of group. Patients, on average, scored 85% correct on the true/false comprehension questions, whereas controls were slightly but significantly more accurate on average (89%; $p < 0.05$). There were no effects of either global discourse congruence or local lexical association on performance, nor any interactions of these factors with group (p values > 0.12), with patients scoring 86, 85, 84, and 85% compared with 91, 90, 90, and 88% for the congruent/associated, incongruent/associated, congruent/unassociated, and incongruent/unassociated conditions, respectively. This pattern of a general deficit in performance but no differential deficits for the patients relative to controls was an expected outcome, because the questions in this study were always about the discourse that was heard before the critical manipulations occurred (i.e., before the prime and target words of the final sentence of the discourse). Nevertheless, we included these questions to encourage participants to engage in comprehension when they heard the stories.

ERPs

ERP waveforms comparing all four conditions are shown in Figure 1*a* for the control group and Figure 1*b* for the patient group.

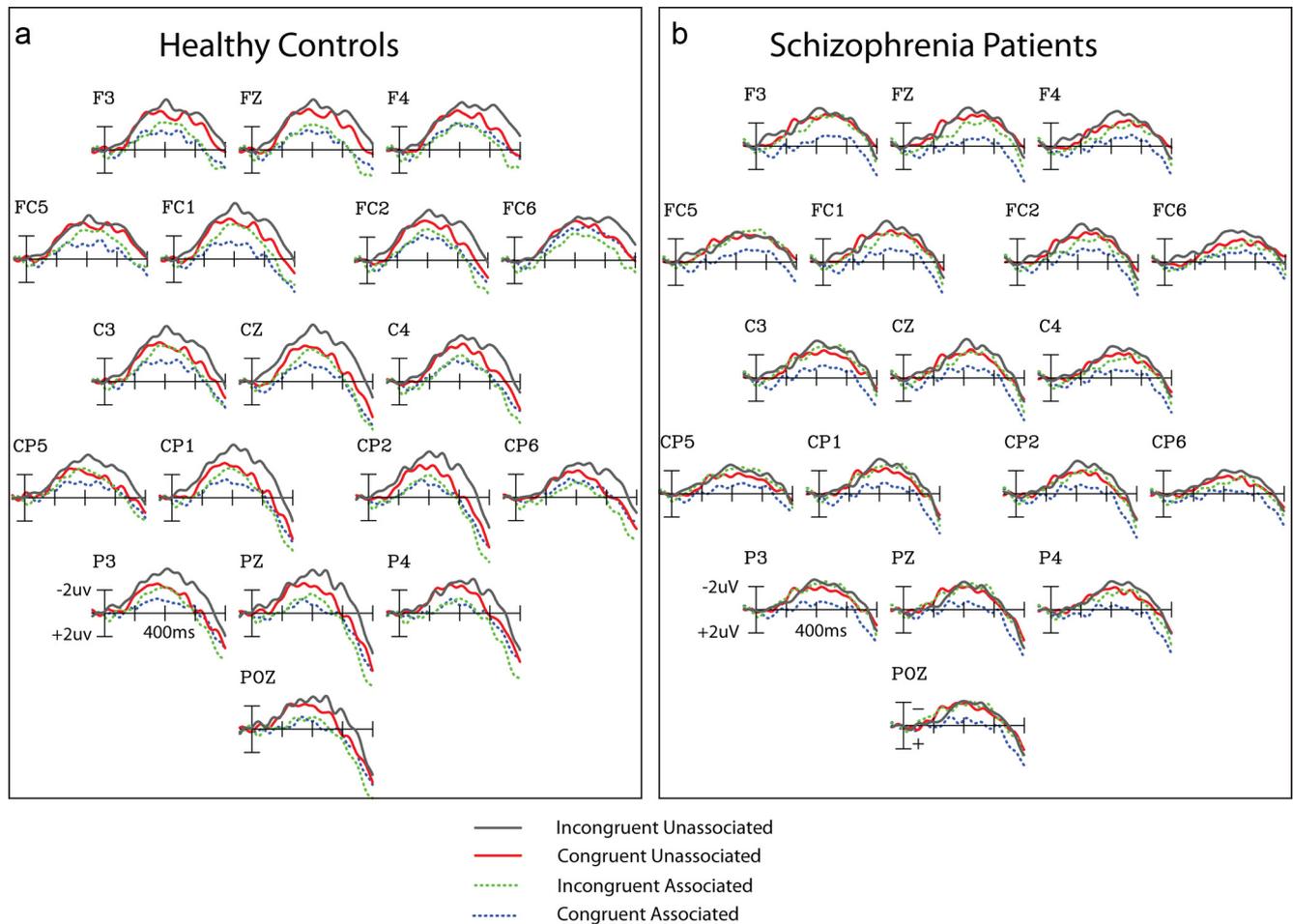


Figure 1. *a, b*, Displayed are ERP waveforms comparing the four conditions: (1) congruent associated (blue dotted); (2) congruent unassociated (red solid); (3) incongruent associated (green dotted); and (4) incongruent unassociated (gray solid). *a* shows the results for the control group, and *b* shows the results for the schizophrenia group. The vertical axis depicts the amplitude in microvolts (μV). Negative voltage is plotted up. The horizontal axis depicts the time in milliseconds (ms). Each tick mark is 200 ms.

Topographic maps showing the distribution of the effects across all four pairwise comparisons and time windows are shown in Figure 2 for the control group and in Figure 3 for the patient group.

The omnibus by-groups repeated-measures ANOVA (rANOVA) showed significant three-way interactions of group \times global discourse congruence \times local association. Follow-up analyses revealed interactions of global discourse congruence \times local association in both the patient and control groups; these were followed up with pairwise analyses that revealed distinct patterns of effects for the control group compared with the patient group. In short, the control group showed robust effects of local association as well as global discourse congruence; in contrast, the patient group showed significant effects of local association but only showed effects of global discourse congruence when target words were also locally associated. In other words, the global discourse effects in the patient group were dependent on the presence of the local prime word in the associated conditions. These results are described in more detail below and are interpreted in Discussion.

Group analyses

Main ANOVAs

Three rANOVAs were conducted on the mean amplitude of the N400 in the 350–650 ms epoch, at midline, medial, and lateral electrode sites (based on previous studies; Kuperberg et al., 2010, 2011). Discourse congruence (congruent, incongruent), local as-

sociation (associated, unassociated), and electrode site (Fz, Cz, Pz, POz) were included as within-subjects factors in the midline analysis, and group (schizophrenia patients, healthy controls) was included as a between-subjects factor. For the medial (electrodes FC1, FC2, C3, C4, CP1, CP2) and lateral (electrodes F3, F4, FC5, FC6, CP5, CP6, P3, P4) analyses, two within-subjects topographic factors were included instead of electrode site: (1) hemisphere (left, right); and (2) anteriority (medial: fronto-central, centro-parietal, parietal; lateral: frontal, fronto-central, centro-parietal, parietal). A Greenhouse–Geisser correction was applied to *F* tests with more than one degree of freedom in the numerator for all relevant analyses in this study. The results of these omnibus group-level analyses are reported in Table 3.

The ANOVA for midline sites revealed significant main effects of discourse congruence ($F_{(1,42)} = 13.68; p < 0.001$) and local association ($F_{(1,42)} = 23.93; p < 0.001$) and a significant group \times discourse congruence \times local association interaction ($F_{(1,42)} = 4.35; p < 0.05$). There were no significant interactions by electrode site in this analysis.

The medial analysis also showed significant main effects of discourse congruence ($F_{(1,42)} = 12.07; p < 0.01$) and local association ($F_{(1,42)} = 19.65; p < 0.001$) and a significant group \times discourse congruence \times local association interaction ($F_{(1,42)} = 4.25; p < 0.05$). There was also a trend toward an interaction of group \times congruence \times hemisphere \times anteriority ($F_{(2,84)} = 2.61$;

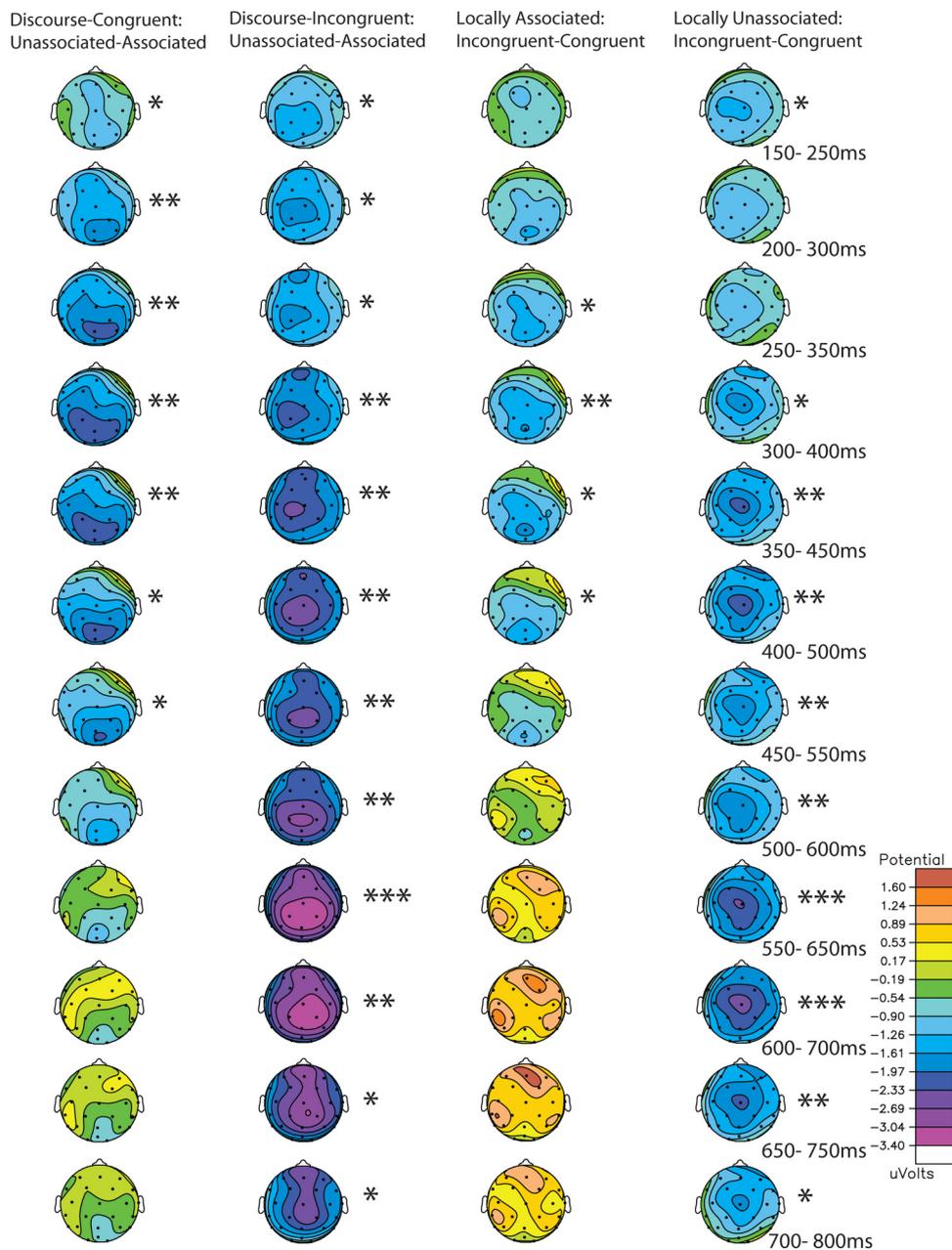


Figure 2. Topographic maps showing the scalp distribution of the N400 effects for the four pairwise comparisons in 100 ms epochs from 150 to 800 ms for the control group. * $p < 0.05$, ** $p < 0.001$, *** $p < 0.001$.

$p < 0.08$) and marginal interaction of local association \times hemisphere \times anteriority ($F_{(2,84)} = 3$; $p < 0.06$).

Finally, the lateral analysis also revealed significant main effects of discourse congruence ($F_{(1,42)} = 8.96$; $p < 0.01$) and local association ($F_{(1,42)} = 17.91$; $p < 0.001$) and a significant group \times discourse congruence \times local association interaction ($F_{(1,42)} = 4.56$; $p < 0.05$). Additionally, there were significant interactions of discourse congruence \times local association \times hemisphere ($F_{(2,84)} = 5.19$; $p < 0.05$), group \times hemisphere \times anteriority ($F_{(3,126)} = 5.32$; $p < 0.001$), local association \times hemisphere \times anteriority ($F_{(3,126)} = 3.33$; $p < 0.05$), and discourse congruence \times local association \times hemisphere \times anteriority ($F_{(3,126)} = 5.67$; $p < 0.01$).

Time course analyses

To determine the onset and duration of these effects (as in the study by Boudewyn et al., 2012b), we performed analyses in 100

ms epochs between 150 and 800 ms, with an overlap of 50 ms between consecutive windows (150–250, 200–300, 250–350, 300–400, 350–450, 400–500, 450–550, 500–600, 650–750, and 700–800 ms). These analyses revealed robust and long-lasting main effects of discourse congruence from ~250 to 750 ms ($p < 0.05$) and of local association throughout all time windows (150–800 ms; $p < 0.05$); these effects were further characterized by group \times discourse congruence \times local association interactions in all windows except between 250 and 500 ms.

Pairwise analyses

Motivated by our a priori predictions and the significant group-level interactions found in the analyses above involving group, discourse congruence, local association, and scalp distribution (electrode, hemisphere, and anteriority), we conducted pairwise comparisons for the two groups separately, across the same electrode configurations (midline, medial, lateral) and overlapping

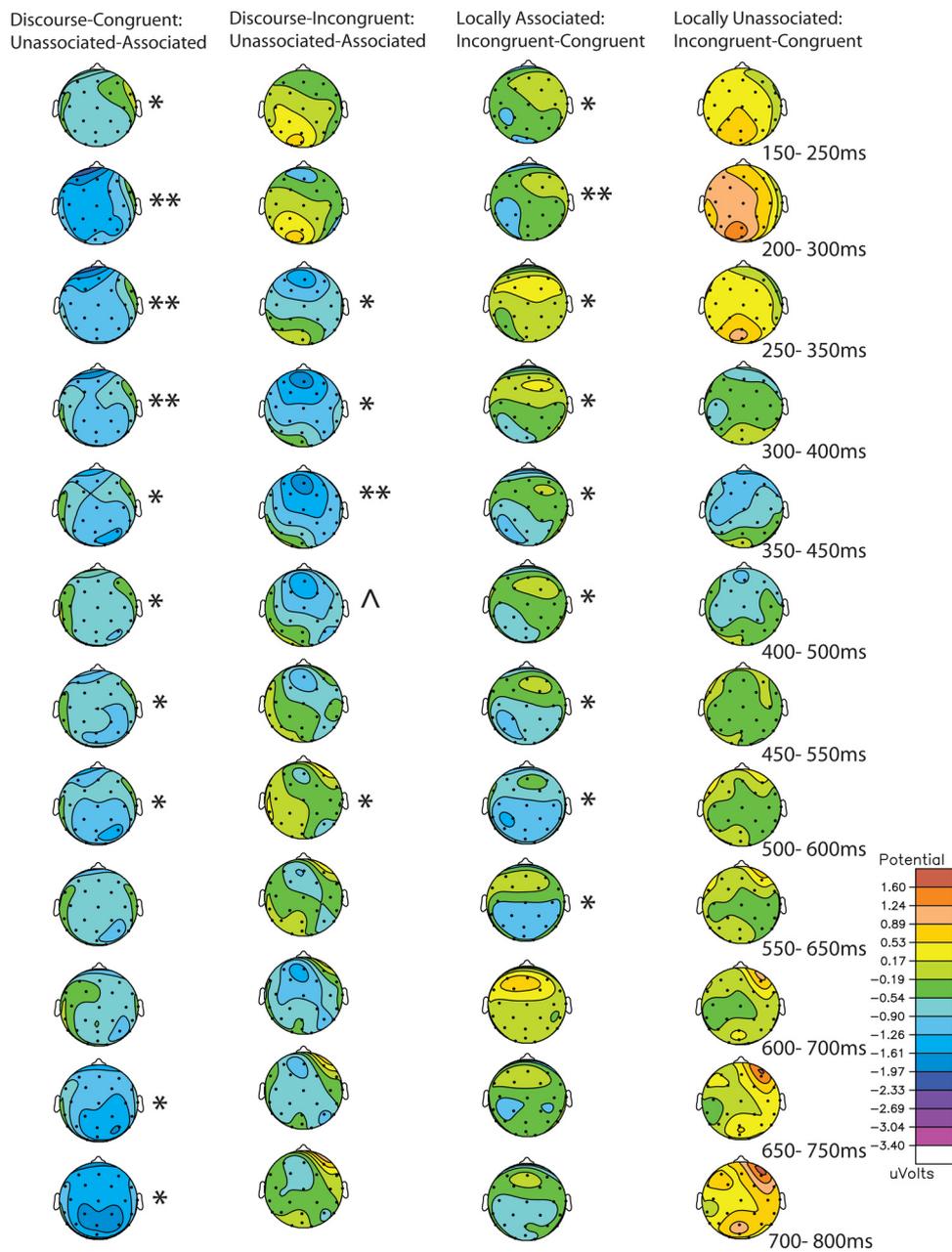


Figure 3. Topographic maps showing the scalp distribution of the N400 effects for the four pairwise comparisons in 100 ms epochs from 150 to 800 ms for the patient group. * $p < 0.05$, ** $p < 0.001$, *** $p < 0.001$, $\wedge p < 0.07$.

Table 3. Results of omnibus repeated-measures ANOVA in the N400 time window

Analysis	Global congruence	Global congruence \times group	Local association	Local association \times group	Global congruence \times local association	Global congruence \times local association \times group
Midline	13.68***	<1	23.93***	1.4	<1	4.35*
Medial	12.07**	<1	19.65***	<1	<1	4.25*
Lateral	8.96**	<1	17.91***	<1	<1	4.56*

Degrees of freedom for all F values were (1,42). Interactions with scalp distribution (electrode site, hemisphere, anteriority) are reported in Materials and Methods. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

100 ms time windows. These analyses enabled us to identify the source of the interactions and establish the pattern of results for each group; results are summarized in Figures 2 and 3 and described below.

For healthy controls, a significant effect of discourse congruence (reduced amplitude for congruent compared with incongruent targets) for locally associated words was found in all time

windows between 300 and 500 ms at midline sites and between 250 and 500 ms at medial sites but did not reach significance at lateral sites. For the schizophrenia patients, the effects of discourse congruence for locally associated words had an earlier onset and lasted longer: significant effects were found in all time windows between 200 and 300 ms, between 350 and 600 ms for midline sites, and between 150 and 550 ms for medial sites. In

contrast to controls, this effect was also significant at lateral electrode sites between 150 and 600 ms.

The control group showed a significant effect of discourse congruence (reduced amplitude for congruent compared with incongruent targets) for locally unassociated words in all time windows between 300 and 800 ms at midline sites, between 150 and 250 ms and 300 and 800 ms at medial sites, and between 350 and 750 ms at lateral sites. In contrast, schizophrenia patients showed no significant effect of discourse congruence for locally unassociated words for any of the analyses.

Significant effects of local association (reduced amplitude for associated compared with unassociated targets) for discourse-congruent words were found in the control group in all time windows between 150 and 550 ms at midline sites, between 150 and 500 ms at medial sites, and between 150 and 450 ms at lateral sites. For the schizophrenia group, significant effects of local association (reduced amplitude for associated compared with unassociated targets) for discourse-congruent words lasted longer and were found in all time windows between 150 and 600 ms and 700 and 800 ms for midline sites, between 150 and 550 ms and 700 and 800 ms for medial sites, and between 150 and 550 ms and 650 and 800 ms at lateral sites.

For healthy controls, significant effects of local association (reduced amplitude for associated compared with unassociated targets) for discourse-incongruent words were found in all time windows between 150 and 800 ms at midline sites, between 150 and 800 ms at medial sites, and between 150 and 800 ms at lateral sites. For the schizophrenia group, the effects of local association (reduced amplitude for associated compared with unassociated targets) for discourse-incongruent words were restricted to a more limited epoch: significant effects were found in all time windows between 250 and 350 ms and 350 and 450 ms for midline sites, between 300 and 450 ms for medial sites, and between 300 and 450 ms at lateral sites.

Correlations with clinical and functional measures

To test the hypothesis that the magnitude of ERP effects of lexical association and discourse congruence would be linked with clinical characteristics of schizophrenia patients, we conducted a series of correlation analyses. All the correlational analyses were planned comparisons, based on the approach adopted by previous studies (Yoon et al., 2008). We had two main predictions: (1) that our ERP results would correlate with functional measures (GAF) and (2) that they would correlate with disorganization. We found that ERP effects of local association (i.e., mean amplitude to associated targets subtracted from mean amplitude to unassociated targets) were significantly correlated with GAF, such that local association effects tended to be larger for individuals with lower GAF scores from 450 to 650 ms (Table 4).

In the pairwise comparisons (Tables 5, 6), increased ERP effects of local association for discourse-congruent words (unassociated/congruent minus associated/congruent) were associated with lower GAF scores from 450 to 800 ms. In addition, increased ERP effects of local association for discourse-incongruent words (i.e., unassociated/incongruent minus associated/incongruent) were associated with increased GAF scores from 300 to 400 ms. Finally, increased effects of discourse congruence for locally unassociated words (congruent/unassociated minus incongruent/unassociated) were associated with higher GAF scores in the 600–700 ms epoch.

Thus, our results showed a significant correlation with GAF but not with disorganization. This latter result may reflect the fact that the clinically stable outpatients in this sample had relatively

Table 4. Correlation values for GAF and main effects of association (left: unassociated–associated) and congruence (right: incongruent–congruent)

Duration (ms)	Correlations of clinical and functional characteristics with main ERP effects	
	Association	Discourse congruence
150–250	–0.059	0.182
200–300	–0.127	0.013
250–350	–0.256	–0.243
300–400	–0.129	–0.131
350–450	0.263	–0.118
400–500	0.328	–0.257
450–550	0.451*	–0.237
500–600	0.468*	–0.143
550–650	0.46*	–0.136
600–700	0.337	–0.189
650–750	0.273	–0.118
700–800	0.307	–0.17

n = 22. * indicates significant correlations. For interpretation, see Results.

Table 5. Correlation values for GAF and effects of association (left: unassociated–associated for congruent contexts only; right: unassociated–associated for incongruent contexts only)

Duration (ms)	Correlations of clinical and functional characteristics with effects of local association (priming: unassociated–associated)	
	Globally congruent	Globally incongruent
150–250	–0.099	0.024
200–300	0.033	–0.284
250–350	–0.062	–0.378
300–400	0.176	–0.429*
350–450	0.263	–0.278
400–500	0.328	0.245
450–550	0.426*	0.325
500–600	0.501*	0.066
550–650	0.566**	0.004
600–700	0.492*	–0.034
650–750	0.449*	–0.142
700–800	0.466*	–0.155

n = 22. * and ** indicate significant correlations. For interpretation, see Results.

Table 6. Correlation values for GAF and effects of congruence (left: incongruent–congruent for associated words only; right: incongruent–congruent for unassociated words only)

Duration (ms)	Correlations of clinical and functional characteristics with effects of global congruence (discourse: incongruent–congruent)	
	Locally associated	Locally unassociated
150–250	0.084	0.229
200–300	0.133	–0.114
250–350	–0.101	–0.305
300–400	–0.322	–0.322
350–450	0.123	–0.331
400–500	–0.133	–0.299
450–550	–0.084	–0.312
500–600	0.145	–0.366
550–650	0.176	–0.386
600–700	0.113	–0.424*
650–750	0.213	–0.376
700–800	0.168	–0.394

n = 22. * indicates significant correlations. For interpretation, see Results.

low levels of disorganization. To examine in more detail the effects of clinical and disorganization symptoms, we further examined correlations between our ERP results and positive and negative symptoms, and this did not lead to significant results.

Discussion

In the current study, we aimed to increase our understanding of the cognitive and neural systems underlying deficits in language comprehension in schizophrenia. We assessed the ability of schizophrenia patients to use global discourse context and local lexical context (associations) during the online comprehension of auditory discourse. We predicted that, in contrast to controls, deficits in the ability to maintain context-relevant information in schizophrenia would lead to deficits in global discourse comprehension. Importantly, we additionally predicted that the ability to benefit from local lexical context would be intact in schizophrenia. The presence of lexical association effects in the schizophrenia group coupled with a lack of discourse congruence effects indicates that the basic processing of words was intact, consistent with a specific deficit in higher-level cognitive control systems. The results revealed significant effects of both lexical associations and global discourse congruence in healthy control subjects. The pattern of results in the schizophrenia group was more complex: patients showed intact effects of lexical association regardless of whether the target words appeared in congruent or incongruent discourse contexts, but the patient group only showed discourse congruence effects for target words that were also associated. In other words, patients were always sensitive to the presence of local lexical associations and were additionally sensitive to whether or not incoming words fit well with the preceding global context, provided that local lexical associations were present. In contrast to healthy controls, when target words were locally unassociated, patients did not show effects of discourse congruence.

This pattern of results in the schizophrenia patients is particularly interesting given that we found sensitivity to discourse-level semantic fit in the associated condition, indicating that, under some circumstances, patients are able to benefit from global discourse context. This may appear to contradict results of previous studies that have shown deficits at the discourse level in schizophrenia (Levy and Maxwell, 1968; Maher et al., 1980; Manschreck et al., 1991; Ditman and Kuperberg, 2007; Ditman and Kuperberg, 2010). However, the schizophrenia patients in the present study may only have shown impaired discourse processing in one of the conditions for two reasons. First, previous studies have focused on relatively taxing manipulations (e.g., inference generation) compared with the condition in which patients showed intact discourse effects in the present study. Second, the main task of the participants was to listen for comprehension without imposing demands of a secondary task as they were processing the spoken input. Importantly, however, task demands were equally low for both congruent and incongruent conditions up to the point of the target word in the associated compared with the unassociated condition. In the associated condition, intact discourse effects were found in patients. In contrast, in the unassociated condition, when demands were higher, patients showed deficits compared with controls. Thus, the findings of the present study are not inconsistent with previous work in that we see discourse deficits when demands are relatively high, i.e., in our study, when the global discourse context is not cued by associated words in the local context.

Kuperberg et al. (2010b) have argued that differences in the N400 effects between schizophrenia patients and normal control participants are typically maximal at the sentence-final word position because of sentence final evaluation and wrap-up effects needed for sentence interpretation. The integration demands for discourse final words are typically greater than for sentences, because the overall meaning of the multi-sentence discourse has

to be activated and integrated. In the present study, these demands were further enhanced because of the fleeting nature of the speech signal, requiring listeners to distribute cognitive resources between attending to the final word and activating the discourse context. This process was maximally demanding when there was no local cue from an associated word that could boost the activation of the global discourse representation, and indeed the patients did not show any effects of discourse congruence in the unassociated condition. Thus, the results of this study indicate that discourse representations in schizophrenia needed a boost from a local cue to be able to fully integrate the discourse meaning at the discourse-final word. When this cue was missing, the patients did not immediately notice that a critical word was inconsistent with the meaning of the discourse. We suggest that this is attributable to a reduced ability to control the maintenance of discourse information, leading to a less stable representation of the discourse.

In addition, we found significant correlations between the size of the ERP effects of association and measures of social functioning (GAF) in schizophrenia patients, such that larger ERP effects of local association were correlated with reduced social functioning. This is consistent with our hypothesis that more severely impaired individuals rely to a greater extent on local word associations. The direction of the correlations for the two types of local association effects (for words that were also globally congruent vs incongruent) further characterized this relationship: increased ERP effects of local association for words that were also globally incongruent were associated with better functioning (as measured by GAF), whereas increased ERP effects of local association for words that were locally congruent were linked to poorer functioning (as measured by GAF). In other words, when comparing locally associated with unassociated words that were embedded in congruent discourse (i.e., under the least control-demanding circumstances), more impaired patients tended to show the largest local association effects. In contrast, when comparing locally associated with unassociated words that were also discourse incongruent (i.e., under more control-demanding circumstances), the better functioning patients tended to show the largest association effects. In addition, increased ERP effects of global congruence for words that were locally unassociated (i.e., the most control-demanding circumstances) were associated with better functioning in patients (as measured by GAF). Although this effect did not reach significance in the patient group as a whole, the significant correlation with GAF indicates that the higher functioning patients were more likely to be able to discriminate between globally congruent and incongruent discourse in the locally unassociated condition, indicating relatively higher levels of discourse comprehension and use of control. These findings suggest an intriguing and novel mechanism by which cognitive control deficits may have their widely demonstrated impact on social and role functioning in schizophrenia, mediated through their effects on language comprehension, which is such an essential element of human communication and social interactions.

The pattern of results in schizophrenia patients—spared local association effects but impaired discourse comprehension when not supported by local associations among meanings of words—cannot be explained by a generalized low-level deficit in basic auditory or language processing for several reasons. First, the patients in this study showed earlier effects of priming as a function of local association than did control participants. A perceptual processing deficit would predict later-than-normal effects of priming, because perceptual difficulties would most likely result

in reduced or later activation of word meanings. In addition, our findings are not consistent with generalized low-level cognitive deficits, because we show spared local language processing and intact global message comprehension when discourse comprehension was supported by local associations among words in the context.

Therefore, we propose that the very specific discourse comprehension deficit observed in the present study is mediated by deficits in prefrontal control in these patients. Several fMRI studies of language comprehension in unimpaired controls show increased activity in the dorsolateral prefrontal cortex (DLPFC) when contextual integration is especially demanding (Kaan and Swaab, 2002; Novais-Santos et al., 2007; Ferstl et al., 2008; Kuperberg et al., 2008a; Hoenig and Scheef, 2009), for example, when suppression of the contextually inappropriate dominant meaning of an ambiguous word is required (Novais-Santos et al., 2008; Hoenig and Scheef, 2009). This proposal of a deficit in prefrontal control in schizophrenia is also consistent with findings showing a direct relationship between hypofrontality in the DLPFC and impaired conflict control in schizophrenia (Minzenberg et al., 2009; Lesh et al., 2011). It is further supported by fMRI findings by Kuperberg et al. (2008a), who observed that impairments in sentence comprehension in schizophrenia patients may be directly related to abnormal functioning of the DLPFC. In this study, schizophrenia patients and controls showed relatively similar activation patterns during sentence processing in lateral temporal cortices and the inferior frontal gyrus (IFG), whereas increases in integration demands resulted in greater activation of DLPFC in healthy controls but not in patients with schizophrenia. In contrast, Kuperberg et al. (2007) observed increased temporal and IFG activations in response to semantic priming among individual words in schizophrenia patients.

In summary, these results suggest that patients with schizophrenia have difficulties with discourse comprehension, when control demands are increased in the absence of local associations that can cue the activation of the discourse representation. These results are consistent with a role for more general cognitive control problems in the language comprehension deficits in schizophrenia and implicate functional neural systems involving the prefrontal cortex in the socially disabling communication deficits that are present in this illness.

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