Abnormal inhibitory processes in semantic networks in schizophrenia.

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Abstract.

Abnormal language in schizophrenia has been regarded as a hallmark of this disorder. Language abnormalities include loose and unusual associations, tangentiality, and inability to maintain a topic. Recent theories of language dysfunction have invoked working memory abnormalities, as well as abnormal processes within semantic memory in schizophrenia. Two views, often construed as opposing, have been offered to account for language peculiarities in schizophrenia: one holds that initial processes of activation are abnormal while the other holds that late processes of context utilization might be disturbed. We suggest that these views may be complementary rather than mutually exclusive. Given the relative paucity of data on the early processes within semantic networks, we present new evidence using ERP short SOA paradigm that these processes are abnormal in schizophrenia. Furthermore, reduced N400 in the unrelated condition found in this study suggests that the abnormality was related to inefficient early inhibitory processes.
Introduction.

Abnormal language function in schizophrenia has long been regarded as a hallmark of this disorder, dating back to the writings of Kraepelin (1919) and Bleuler (1911/50). Language dysfunction in schizophrenia is believed to be an important component of schizophrenia psychopathology and a contributing factor to formal thought disorder (e.g., Mitchell & Crow, 2005). The features commonly found in schizophrenia language include poverty of speech, derailment, loose associations, loss of goal, perseveration, distractibility, tangentiality, and an inability to adhere to a topic (e.g., Docherty et al., 2004). Existing research has highlighted attentional and working memory impairments as factors contributing to language abnormalities in schizophrenia (e.g., Cohen et al., 1999), as well as operations within semantic memory and their interactions with working memory. A number of studies, including those from our laboratory, support this line of theorizing (e.g., Niznikiewicz et al., 2004a, Niznikiewicz et al., 2004b, Salisbury et al., 2002; Mathalon et al., 2002).

The studies that explored semantic memory dysfunction in schizophrenia focused almost exclusively on processes that operate within semantic memory. Relatively recent memory models assume that memory is organized as a network (irrespective of how such a network might be instantiated in the brain) and that concepts close in meaning are activated proportionally to semantic and temporal distance from a word that has been activated (Neely, 1991; Hutchison, 2003). According to this model, if a person thinks/speaks/hears a word ‘dog’, concepts such as ‘cat’, ‘bone’ or ‘leash’ will also be activated proportionally to how close in meaning they are to the word ‘dog’. However, words such as ‘sky’ and ‘leaf’ will not be activated as they do not share any semantic features with the word ‘dog’. Thus, both activation of related items and inhibition of the unrelated items are taking place in the healthy functioning semantic system in the initial stages of word processing. It is often conceptualized that the initial
stages of a word analysis are dominated by processes of activation that last about 400-500 ms after the stimulus onset and that processes of inhibition are getting more dominant with the temporal distance from the onset of the stimulus (Neely, 1991). It is believed that after the first 400-500 ms processes of fitting the word into the context either via post-lexical matching strategy or via expectancy generation (Neely, 1991) come into play and that these are primarily inhibitory processes that narrow a set of word candidates that would fit a given word context. In behavioral research, one of the most common paradigms to probe processes in semantic memory is a word pair priming paradigm where the task is either lexical decision (deciding if a target is a word or non-word) or pronunciation (where the target word is read aloud). It is believed that when two words are presented sequentially, the first word activates its semantic neighbors such that if the next presented word is related to its ‘prime’ it will take less time to either make a decision about its lexical status or to pronounce it and this saving in time is called priming (e.g., Hutchison, 2003). It is further believed that designs using a short temporal distance between prime and target (stimulus onset asynchrony or SOA), i.e., SOA under 400-500 ms, probe primarily early processes of activation and inhibition, while designs using longer SOA over 500 ms probe processes of context use and contextually driven inhibition (e.g., Hutchison, 2003).

Most of the research on semantic dysfunction in schizophrenia has been dominated by two hypotheses, often described as opposing: 1) over-activation in semantic networks 2) dysfunction in late, controlled processes. The hypothesis of over-activation in semantic networks holds that in schizophrenia initial activation propagates too far and leaves a person with too many word choices thus producing characteristic schizophrenic utterances. Thus, in behavioral priming studies using short SOAs, faster RTs to related words in patients relative to normal control subjects are treated as evidence for over-activation in semantic networks (e.g., Frith 1979; Spitzer et al., 1993;
Manschreck et al., 1988; Maher et al., 1996; Henik et al., 1995; Kwapil et al., 1990; Moritz et al., 2003; Maher et al., 2005; Peled et al., 2005; Quelen et al., 2005; Gouzoulis-Mayfrank et al., 2005). In schizotypal personality disorder (SPD), increased automatic priming was found in individuals with high schizotypy scores (Moritz et al., 1999; Pizzagalli et al., 2001). Schizotypal individuals also show reduced negative priming, which has been interpreted as evidence of reduced inhibition, (Beech and Claridge, 1987; Beech et al., 1989; Claridge et al., 1992; Peters et al., 1994; Williams, 1995; Ferraro and Okerlund, 1996; Moritz and Mass, 1997).

The hypothesis of dysfunction in late processes of context use suggests that the inability to inhibit word choices by using context to guide the word selection process efficiently produces disturbances in language in schizophrenia (e.g., Vinogradov et al., 1992; Chapin et al., 1989; Blum and Freides, 1995; Passerieux et al., 1997; Barch et al., 1996; Cohen et al., 1999; Titone et al., 2000). In SPD, neuropsychological evidence of subtle, but significant, impairment in working memory was found in high schizotypy individuals (Tallent and Gooding, 1999; Gooding et al., 1999; Lenzenweger and Kortife, 1994; Park and McTigue, 1997). Thus, remarkably, both these hypotheses predict similar outcomes, i.e., features of language characteristic for schizophrenia sufferers such as loose associations, bizarre associations and inability to adhere to a topic, but they propose very different mechanisms to account for language abnormalities.

We believe that these hypotheses are not mutually exclusive and that both types of impairment operate in schizophrenia. In fact, the synergistic impact of these two impairment types might result in a particularly dysfunctional semantic system where both the initial processes of activation and inhibition, and later processes of context use and inhibition are abnormal. Some of the difficulties in constructing a detailed description of just how the processes within semantic system break down stem from the fact that many studies rely on behavioral data such as reaction times and errors rates. These, by
definition, reflect all processes that occurred before a button press, including response slowing which is related to the disease process but not to semantic dysfunction.

The exception are event related potential (ERP) studies that provide indices of cognitive processes as they happen in real time and thus can better assess both condition and group membership driven differences. ERP studies have significantly enriched our knowledge of cognitive processes in the brain, including our understanding of language processes. The ERP component most widely (but not exclusively) used to probe semantic processes is the N400, a negative, or negative going, component that has been recorded in several different paradigms and that is believed to reflect an ease of connecting two semantic concepts (e.g., Holcomb and Neville, 1990). The N400 has been used successfully as an index of priming, i.e., of the processes that operate within semantic memory. The N400 is less negative to items that are semantically related to preceding context and more negative to unrelated items. The N400 has been recorded at both long and short SOAs (e.g., Hill et al., 2002; Hill and Weisbrod, 2005), with masked and unmasked primes (e.g., Misra and Holcomb, 2003; Kiefer, 2002), for ambiguous words (Chwilla and Kolk, 2003), across visual and auditory presentations (Holcomb et al., 2005) and even for nonwords (Deacon et al., 2004) suggesting that N400 is also sensitive to lexical processes. In schizophrenia research, the N400 has been used as a useful tool in examining language dysfunction. Given its sensitivity to the ease of forming semantic connections between items, one can formulate specific predictions regarding semantic processes in schizophrenia. If it is easier for schizophrenia patients to make a semantic connection between items, the N400 amplitude should be reduced in the patient group relative to normal comparison subjects. Conversely, if it is more difficult to make such a connection, N400 amplitude should be more negative in the patient group. One should note that these somewhat mechanistic predictions are independent of theoretically motivated hypotheses. Thus,
given theoretical considerations outlined above, one can articulate the following predictions: at short SOAs, reduced, or less negative N400 in the patient group suggests 1) too strong or too broad initial activation within the semantic network 2) ineffective inhibition of unrelated items; and conversely, larger, or more negative N400 would suggest 1) too narrow range of activation of related items 2) too strong inhibition that might affect both related and unrelated items. At long SOAs, reduced N400 would suggest overly efficient processes of context integration and contextually guided inhibition, while more negative N400 would suggest that these processes are not sufficiently efficient.

To date, most ERP studies exploring language processes in schizophrenia have used either long SOA or sentence paradigms that tap into the processes of context use of contextually guided inhibition. These studies provide rather convincing evidence that indeed, late processes of context use are abnormal (e.g., Adams et al., 1993; Nestor et al., 1997; Niznikiewicz et al., 1997; Koyama et al., 1991; Grillon et al., 1991; Hokama et al., 2003; Salisbury et al., 2002; Sitnikova et al., 2002; Ruchso et al., 2003; Iakimova et al., 2005; Kostova et al., 2003; Kiang et al., 2008). Additional variables that may influence the results are the length of illness (Maher et al., 1996) and the degree of thought disorder (Aloia et al., 1998; Gouzoulis-Mayfrank et al., 2003). The association between N400 amplitude and severity of thought disorder was also reported (Kostova et al., 2005). The ERP studies suggest that integrative processes at long SOAs are intact in SPD (Niznikiewicz et al., 2002) but they become compromised with increased memory load (Niznikiewicz et al., 2004b). Also, Kiang and Kutas (2005), in a long SOA semantic category priming study in a college population, found reduced N400 to category exemplars and increased N400 amplitude to exemplars to be correlated with the Schizotypal Personality Questionnaire (SPQ), an index of schizotypy, concluding that decreased use of context characterized schizophrenia spectrum individuals. No
published studies of context processing in patients with first-episode schizophrenia (FES) exist.

There are many fewer ERP studies exploring initial processes within semantic networks. For example, Condray et al., (2003) reported reduced N400 effect in the patient group and a group difference between medicated patients and normal controls. Mathalon et al (2002) found reduced N400 amplitude to words from the same category, and Kreher et al. (2007) found increased priming effect to indirectly related primes (e.g., lion-stripes) in thought disordered patients but not in non-thought disordered individuals or normal comparison subjects. Kiang et al., (2008), who also used an indirect priming paradigm, found increased N400 amplitude to both directly and indirectly related primes at both the short and long SOAs. No published studies of priming at short SOAs have been reported in FES. The only published ERP study of DSM-IV defined SPD individuals that used a short SOA word-pair paradigm reported group differences in the related but not in the unrelated condition (Niznikiewicz et al., 2002).

In the face of a limited ERP evidence of abnormal early processes within semantic networks, we sought to gather evidence on electrophysiological indices of early priming processes using a short SOA paradigm in chronic schizophrenia patients and normal comparison individuals. Our hypothesis was that if such processes are abnormal, N400 amplitude will be reduced in the patient group. More specifically, we hypothesized that if dysfunction in the early processes is primarily characterized by too strong or too broad activation within semantic networks, the group difference will be observed in the related condition. If the early dysfunction is primarily characterized by inefficient inhibition of items as a function of semantic distance, then group differences will be observed in the unrelated condition. If both initial activation gradient and inhibition are abnormal, then group differences will be observed in both related and unrelated conditions.
Methods:

Subjects: Twenty chronic male schizophrenia patients and 20 normal male comparison subjects have been tested in the short SOA word pair priming, lexical decision paradigm. All subjects were right handed based on Edinburgh handedness scale with English as their first language, and had normal or corrected vision. The additional exclusion criteria for both groups were: illegal drug or alcohol dependence within the last 5 years and drug abuse within the last year; neurological disease, and electroconvulsive therapy (ECT). In addition, normal comparison subjects could not carry a DSM-IV- AXIS I diagnosis in themselves or first degree relatives. The diagnosis of schizophrenia was based on chart reviews and a SCID interview. Normal comparison subjects were screened for participation with non-patient SCID interview.

One schizophrenia subject and 3 normal comparison subjects have been excluded due to the low number of correct responses (over 50% errors). The statistical results are reported for the subjects that have been retained for the analyses. The two groups did not differ in age, or parental SES, but given the burden of the disease, they differed in SES (p < 0.003), education (p <0.02) and general IQ (p <0.02) (see Table 1). All patients were medicated (see Table 1 for antipsychotic CPZ medication levels); 17 patients were on atypical antipsychotic drugs, 1 was on a typical neuroleptic and 1 was both on typical and atypical antipsychotic medication. Fifteen patients carried a diagnosis of paranoid schizophrenia, 2 were schizoaffective and 2 were undifferentiated.

Stimuli: One hundred sixty stimuli were presented in a word pair priming paradigm with 40 word-pairs presented in the related condition (25%), 40 presented in unrelated condition (25%), 40 in a nonword condition where the target word was not a real word but followed English phonetic rules (25%), and 40 words presented in a non-word condition where target words were random letter strings (25%). All primes were real words. The task was lexical decision and the use of left and right hands to indicate
whether the target word was a word or non-word was counterbalanced across subjects. The target words were all nouns and adjectives and were one or two syllable long (1.2 syllables for related words and 1.3 syllables for unrelated words, no significant difference between the two word types). Using the Kucera norms, the average frequency of targets was 93.03 for related condition and 58.2 for unrelated condition (not significantly different). Concreteness for related words was 545.3 and for unrelated targets 534.7 (not significantly different). The words were placed in the middle of a computer screen one word at a time, subtended 4.5 visual angle, with the subjects seated 70 cm from the screen, white on black background. The prime stayed on the screen for 150 ms, and the interval between the offset of the prime to the onset of the target (ISI) was 50 ms. The target stayed on the screen until the response was made.

**ERP Procedure:**

EEG was recorded with 64 active silver-silver chloride electrodes, using a Neuroscience electrode cap, with the left earlobe used as a reference for all sites, and referenced off-line to average ears. EEG was recorded with Neuroscan SYNAMP amplifiers and software with a bandpass of DC to 100 Hz, at the sampling rate of 256 points. Vertical and horizontal eye movements were monitored with additional electrodes placed over the right and left canthi and over the left supra- and infra-orbital areas. EEG was continuously recorded and digitized for storage. The continuous EEG recording was epoched off line, with 100 ms baseline before the onset of the prime and for 1000 ms after the onset of the target. The EEG activity to the prime was included in the baseline to minimize the influence of the prime on the EEG recorded to the target. Single trials were corrected for eye movements using the Gratton and Coles algorithm, and single trials exceeding +/- 75 microvolts at any of the electrode sites were excluded from the analysis. Individual averages were constructed to related and unrelated word targets. On average, there were 34.4 (range: 18-40; SD: 7.3) for normal comparison and
34.8 (range: 19-40; SD: 5.8) for schizophrenia subjects single trials included in each individual average in the related condition and 34 (range: 19-40; SD: 7.3) single trials for normal comparison and 33.9 (range:18-40; SD: 6.6) for schizophrenia patients included in individual waveforms in the unrelated condition (no significant group differences). The single averages were filtered off line with the high pass filter at 16 Hz. The N400 amplitude was measured both as the most negative data point and as the mean area within the 420-530 ms latency window in normal comparison subjects and within the 490-600 ms latency window in schizophrenia patients, post-stimulus; and the N400 latency was measured within the same interval. The latency windows were selected based on inspection of individual averages and grand averages for each condition in each subjects group with a goal of including 95% of individual N400 peaks within the selected measuring windows. In addition, care was taken for the remaining 5% of N400 peaks not to fall more than 10 ms outside the chosen measuring windows.

**Statistical Analyses:**

**Behavioral analyses:** The differences in the demographics were assessed with one-way ANOVA. The priming effects were assessed with an ANOVA with RTs to correctly identified related and unrelated items as within subjects factors and group as a between subject factor. The error rates and the number of correct responses were assessed with independent t-tests and with one sample paired t-tests.

**N400 amplitude:** The N400 amplitude has been evaluated with an ANOVA with condition (related and unrelated) and electrode (Fz, Cz, Pz, Oz) as within-subjects variables and group (NC and SZ) as a between-subjects variable. We have chosen midline electrodes only as these were the sites where both the condition and group separation was maximal and also because we did not make predictions regarding laterality of the effects (none were observed in the inspection of the grand averages across conditions and groups. The overall ANOVA was followed by within-subjects
ANOVAs with the same number of electrodes (4) and two conditions, as well as two ANOVAs comparing groups in the related and unrelated conditions using the same electrode chain (4 electrodes).

N400 latency. Given a lack of latency differences across sites, N400 latency was assessed at Pz using an ANOVA model.

Exploratory Correlational analyses. In exploratory analyses, we analyzed the relationship between N400 amplitude and latency and clinical symptoms using Pearson product correlations (two-tailed) in order to assess the possible commonalities between processes involved in N400 generation and those related to schizophrenia symptomatology. We correlated N400 amplitude at midline (Fz, Cz, and Pz) in related and unrelated conditions with Positive and Negative Syndrome Scale (PANNS; Kay, Opler, Fiszbein, 1986) SANS (Andreasen, 1981) and SAPS (Andreasen, 1984) scores (both total scores and subscales of these tests). We also assessed the relationship between antipsychotic medication levels (CPZ equivalents), age of illness onset and illness duration and dependent variables (N400 amplitude and latency). Bonferroni correction was used to adjust for multiple correlations.

Results:

Behavioral data: Behavioral priming was observed in the normal comparison group (p <.01); (560.15 (35.9) ms for related and 702.07 (28.3) ms for unrelated targets) but not in the schizophrenia group; (790.2 (33.9) ms for related and 787.5 (28.3) ms for unrelated targets). In the ANOVA analysis, there was a main effect of condition (F (1,34) = 6.94 p < 0.01), the group by condition interaction (F (1,34) = 7.49) and a main effect of group (F (1,34) = 18.15 p < 0001). Longer RTs were observed in the unrelated (744.76 (20.58) ms than related condition (675.17 (24.7) ms and in the patient (788.84 (25.4) ms relative to comparison subject group (631.1 (26.8) ms. The error rates did not differ significantly between groups for related condition (.64 for NC and 1.78 for SZ) or for
unrelated condition (1.26 for NC and 2.31 for SZ). In within-group comparisons, more errors were made in the unrelated condition by the normal controls (p < 0.016) and, at a trend level, by the schizophrenia patients (p < 0.098).

**N400 amplitude:**

In the overall ANOVA, there was a main effect of condition ($F_{(1,34)} = 7.85, p < 0.008$) and a significant interaction between group and condition ($F_{(1,34)} = 4.28, p < 0.046$) but not the main group effect ($F_{(1,34)} = 2.21, p < 0.15$). Less negative N400 amplitude was observed in the schizophrenia group. When related and unrelated conditions were examined separately, the two groups differed in the unrelated condition ($F_{(1,36)} = 5.12, p < 0.03$) with a less negative N400 amplitude found in the schizophrenia group, but they did not differ significantly in the related condition ($F_{(1,37)} = 0.35, p < 0.56$) (see Figure 2 and Tables 2 and 3). When the effect of relatedness (priming) was analyzed separately within each group, the normal comparison subjects showed a priming effect (significantly reduced N400 amplitude to related targets) ($F_{(1,16)} = 13.552, p < 0.002$) while the schizophrenia subjects did not ($F_{(1,18)} = 0.25, p < 0.626$) (see Figure 1 and Tables 2 and 3).

**N400 latency.**

In the overall ANOVA, there was a main effect of group at Pz ($F_{(1,34)} = 46.44, p < 0.0001$) but there was not a main effect of condition or an interaction between condition and group. Longer N400 latency was found in the patient group relative to the comparison subjects. In the related condition, in the comparison subjects, the N400 latency peaked at 466.82 (38.35) ms and in the patient group at 533.68 (44.14) ms latency. In the unrelated condition, in the comparison subjects, the N400 latency peaked at 465.65 (42.35) ms and in the patient group, the N400 peaked at 536.74 (39.22) ms.

**Exploratory correlational analyses with clinical measures.** In the patient group, N400 amplitude at Cz in the related condition was significantly correlated with PANSS.
score ($r = 0.48$, $p < 0.021$), total SANS ($r = 0.44$, $p < 0.04$); alogia ($r = 62$, $p < 0.002$) and attention ($r = 46$, $p < 0.03$); in the unrelated condition Cz was correlated with avolition ($r = .51$, $p < .02$). For all these correlations, more positive N400 (i.e., more impaired) was associated with more impairment on a clinical scale. No significant correlations were found in the patient group for the N400 latency. No significant correlations were found with CPZ medication equivalents, age of onset or years of illness duration. None of the significant correlations survived Bonferroni correction.

Discussion.

In this study we examined semantic processes using ERP indices of priming in a short SOA (200 ms) paradigm and a relatively low number of related primes (25%). This design is believed to engage primarily early automatic semantic processes. Given the functional role of the N400, it has been hypothesized that the N400 amplitude will be reduced in the schizophrenia group. This effect has been observed only in the unrelated condition suggesting that in this study the processes that were statistically different between the two groups were processes of inhibition and not primarily the processes of activation (in spite of the visual impression of the N400 reduction in the grand averages to the related targets). This is one of the first studies to demonstrate an abnormality in the early semantic processes using a direct priming paradigm and documenting statistical differences both in within and between group comparisons: a reliable priming effect was found in the normal comparison group while no priming effect was found in the schizophrenia group in addition to the already mentioned group effect in the unrelated condition. Importantly, the N400 amplitude was found significantly reduced in the patient group in the unrelated condition which would suggest abnormal processes of inhibition and not the processes of activation. These results are in line with Lecardeur et al (2007) study who, using behavioral priming paradigm at both short (250 ms) and relatively long (500 ms) SOAs, sought to distinguish between facilitation and inhibition as
contributing factors to hyper-priming observed in several earlier studies. Unlike in the current study, neutral, in addition to related and unrelated, items were used allowing for the computation of facilitation and inhibition effects. At short SOA (identical to the one used in the current study) no significant inhibition effect was found in normal comparison subjects while a significant inhibition effect was found in the schizophrenia group.

Based on the behavioral measures, the schizophrenia patients did not show priming (paralleling the N400 results) while the normal comparison subjects did. In a fairly recent paper, Mitzenberg and colleagues (2002) reviewed results of existing behavioral priming studies in schizophrenia. There was a consistent finding of hypo-priming in schizophrenia at long SOAs while results from short SOA designs were more variable with some studies reporting hyper-priming, others reporting normal priming or a lack of priming effects in schizophrenia individuals. The authors suggested that the lack of priming effects, like the one observed in the current study, may be due to abnormal, post-lexical, controlled mechanisms. We think that this explanation is possible as the distinction between automatic and controlled processes is not categorical but rather is a matter of the dominance of one type of processes over others. However, we would like to point out that entertaining a possibility of the influence of controlled processes on RT data does not mean that we believe that the same mechanisms contributed to the lack of N400 priming effects. In fact, the N400 and the behavioral data provide two different temporal windows of analysis of cognitive mechanisms underlying priming with the N400 capturing temporally earlier events by about 200 ms.

Finally, the characteristics of the schizophrenia sample should be considered. The subjects in this study were somewhat older than those used in the previous studies. Also, fifteen out of twenty schizophrenia subjects were paranoid type suggesting the absence of disorganized thinking at the time of clinical evaluation. These subject features may have additionally contributed to the results observed in this study.
Overall, these results complement in interesting ways available evidence on early semantic processes in schizophrenia. First, this study used the shortest SOA of all reported ERP studies, which by itself may be an important variable in probing processes within semantic networks. Also, the study used a relatively low ratio of related primes (25%) further assuring that captured processes will be early automatic processes within semantic networks (Neely, 1991). The results of the study are closest to the results of Condray et al. (2003) who reported group differences between normal comparison and chronic medicated schizophrenia patients at the short SOA (350 ms) to directly related primes. The results are somewhat different from Kiang et al (2008) who used directly and indirectly related primes at 300 and 750 ms SOA and found group differences to both directly and indirectly related targets but not to unrelated targets irrespective of the SOA. Interestingly, the authors concluded that the affected processes were the processes of context use at both SOA. While we do not propose context involvement, we do propose ineffective mechanisms of inhibition related to suppressing unrelated items. In a way, these two proposals are related, as the use of context does imply the use of inhibition.

The results are different from Kreher et al (2007) study, who reported comparable priming effects between patients (both thought and non-thought disordered) and normal control subjects at 350 SOA but found group effects for the indirectly related primes in thought disordered patients. Importantly, this effect was significant only for 300-400 ms latency window but not for the 400-500 ms latency window, underscoring the importance of temporal factors in the comprehensive analysis of semantic abnormalities in schizophrenia. Finally, the results are also different from Mathalon et al (2002) who reported reduced N400 amplitude to related targets at the short SOA of 325 ms in chronic schizophrenia. Unrelated targets were not used in this experiment so it is impossible to predict what results would be obtained.
Overall, the ERP studies reviewed here as well as the new data presented in the paper provide important evidence for the disturbances in the processes within semantic networks. Moreover, this evidence relates directly to abnormal neural processes uncontaminated by complications of behavioral responses. What emerges is strong evidence for abnormal processes of context use in guiding a well-formed train of thought that emanates from studies using long SOA and sentence paradigms. A growing number of studies focusing experimentally on early semantic processes suggest that these processes are also abnormal. Both the results of the current study, as well as the results of Kiang at al. suggest that the early abnormality consists of ineffective inhibitory processes. There is also indication that processes of activation propagation throughout the network are abnormally fast (Kreher et al., 2007). It is worth noting that apparent differences between the studies are most likely related to exact methodologies employed. While this situation may create some interpretative difficulties, it has an important function of forming a detailed account of the type of processes that are affected by schizophrenia. It moves the field away from a simple dichotomy between abnormalities in the early as opposed to late semantic processes and closer to a full appreciation of the different ways in which the semantic system is broken in schizophrenia. Overall, it appears that abnormal inhibitory processes at different levels play a major role in language abnormality in schizophrenia, but that over-activation is also a factor.

References:


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4. Andreasen NC. (1984). Scale for the assessment of positive symptoms (SAPS). Iowa City, IA: Department of Psychiatry, University of Iowa College of Medicine


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Figure and table captions:

1. Figure 1: Grand average waveforms to related and unrelated target words for normal control and schizophrenia subjects –within group comparisons.

2. Figure 2: Grand average waveforms in 17 normal control and 19 schizophrenia subjects to related and unrelated target words – between group comparisons.

3. Table 1: Demographic data for normal control and schizophrenia subjects and clinical data for schizophrenia subjects.

4. Table 2: N400 mean amplitude to related and unrelated word targets in 17 normal control and 19 schizophrenia subjects.
Table 1: Demographic data for schizophrenia and normal comparison individuals.

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<th>SZ</th>
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<td>CPZ</td>
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* Two factor Index of Social Position, Hollingshead, 1957 was used to calculate educational score and (P)SES. For educational score the scale is from 1 to 7 with the lowest educational level scored as 1 (less than 7th grade) and for (P)SES the scale is 1-5 with the lowest level scored as 5.
Table 2: N400 amplitude to related and unrelated word targets

<table>
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<th>Electrode</th>
<th>Related word targets</th>
<th>Unrelated word targets</th>
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<td></td>
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<td>SZ</td>
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<td>Electrode</td>
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<td>Mean (SD)</td>
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<tr>
<td>Oz</td>
<td>-1.960 (6.072)</td>
<td>0.815 (3.431)</td>
</tr>
</tbody>
</table>
Figure 1

Grand average waveforms in normal control subjects to related and unrelated target words.

Fz

Grand average waveforms in schizophrenia subjects to related and unrelated target words.

Fz

Cz

N400

Pz

Related

Unrelated

Pz

Related

Unrelated
Figure 2
Grand Average waveforms in normal control and schizophrenia subjects.

Related target words

Fz

Cz

Pz

Unrelated target words

Fz

Cz

Pz

NC=17
SZ=19