Semantic Priming in Schizophrenia: An Examination of Spreading Activation Using Word Pronunciation and Multiple SOAs

Deanna M. Barch
Western Psychiatric Institute and Clinic

Jonathan D. Cohen
Western Psychiatric Institute and Clinic
and Carnegie Mellon University

David Servan-Schreiber and Sandra Steingard
Western Psychiatric Institute and Clinic

Stuart S. Steinhauer and Daniel P. van Kammen
Department of Veterans Affairs Medical Center,
Highland Drive

Semantic priming in word pronunciation was examined at 5 stimulus onset asynchronies (SOAs) in 75 medicated and 25 unmedicated people with schizophrenia (SCZ) and in 10 depressed and 28 normal controls. At SOAs <950 ms, SCZ displayed priming similar to that of normal and depressed controls. At the 950-ms SOA, SCZ displayed less priming than controls. Medication dosage, but not conceptual disorganization scores, was positively associated with priming at SOAs <950 ms. These results suggest that prior reports of enhanced priming in schizophrenia may have been confounded by methodological problems and that automatic priming processes operate normally in SCZ. The failure of SCZ to display significant priming at the 950-ms SOA is consistent with a hypothesized disturbance in higher level processes.

Since the seminal works of Kraepelin (1919/1971) and Bleuler (1911/1950), psychopathologists have considered disturbed language to be a primary symptom of schizophrenia. The most noticeable form of these disturbances is a disruption or "loosening" of semantic associations (Bleuler, 1911/1950). Theories of normal language processing typically postulate that such associations are mediated by a network that stores information about the semantic relationships between concepts or between lexical items (e.g., Collins & Loftus, 1975). Higher level language processes are assumed to draw upon this associative network for both language comprehension and production. Most recent theories of schizophrenic language disturbances have been formulated within this framework and fall roughly into two broad classes: (a) those that postulate a disturbance in the associative network itself (e.g., Manschreck et al., 1988; Spitzer, Braun, Maier, Hermle, & Maher, 1993), and (b) those that postulate disturbances in the higher level processes that make use of this network (e.g., Cohen, Targ, Servan-Schreiber,

& Spiegel, 1992; Maher, 1983; Manschreck et al., 1988; Vinogradov, Ober, & Shenaut, 1992). As yet, however, there has been neither a systematic examination of this question nor a convincing demonstration that one mechanism or the other is responsible for the abnormalities of language processing observed in schizophrenia. As we discuss below, we believe that one obstacle to progress in this area has been a set of methodological problems in previous research involving issues of (a) experimental design, (b) data analytic techniques, and (c) medication effects.

The method most commonly used in cognitive research for examining the functioning of the associative network has been semantic priming techniques. These techniques use simple linguistic tasks, such as word pronunciation (WP) or lexical decision (LD), to study the effects of semantic relationships on the processing of single words. Typically, participants are presented with two words, a prime and a target, usually in close succession. In WP participants pronounce the target word, whereas in LD they decide whether or not the target is a valid English word. In both cases, response time is consistently faster if the prime and target are semantically or associatively related than if they are not (e.g., Meyer & Schvaneveldt, 1971), an effect termed *semantic priming*. Several mechanisms are thought to be involved in producing this priming effect. One mechanism is an intralexical process of spreading activation. *Intralexical* refers to processes originating within the semantic store. Presentation of the prime activates its node within the network, following which activation spreads to associated nodes, facilitating the processing of these associates if they appear as targets. This mechanism is thought to be automatic, and to begin immediately upon presentation of a stimulus (Neely, 1991). In addition to spreading activation, extralexical language processes are also hypothesized to produce priming effects (e.g., Onifer & Swin-

---

ney. 1981). *Extralexical* refers to processes originating outside of the semantic store. These mechanisms include strategic processes such as expectancy effects and semantic matching (e.g.. Neely. 1991) as well as higher level language processes involved in comprehension (e.g.. Foss & Ross. 1983).

Priming studies with schizophrenic participants have demonstrated a range of results. Recently. several studies have reported findings of increased semantic priming among schizophrenic patients. particularly at short stimulus onset asynchronies (SOAs). As discussed further below. priming at short SOAs is thought to primarily reflect the operation of automatic spreading activation (Neely. 1991). Kwapil. Hegley. Chapman. and Chapman (1990) found increased facilitation in schizophrenic patients at a short SOA. as measured by accuracy in WP. In addition. Manschreck et al. (1988). Spitzer. Braun. Hermle. and Maier (1993). and Spitzer. et al. (1994) found that thought-disordered (TD) schizophrenic participants displayed larger priming effects than normal participants at a 240-ms SOA. Further. Spitzer. Braun. Hermle. et al. (1993) and Spitzer. et al. (1994) also found increased priming effects among TD schizophrenics at a 700-msec SOA. although Spitzer. Braun. Hermle. et al. (1993) found that the differences at both SOAs were not significant if overall longer reaction times (RTs) were taken into account. Spitzer also examined indirect priming effects in schizophrenia. in which the prime is related to the target by way of an associate (i.e.. lemon–sour–sweet). He found that schizophrenics as a group (Spitzer. Braun. Maier. et al.. 1993). and TD schizophrenics in particular (Spitzer. Braun. Hermle. et al.. 1993). displayed more indirect priming than normal participants at a 240-ms SOA. The results of other studies. however. have not indicated increased semantic priming in schizophrenic participants. Vinogradov et al. (1992) and Henik. Priel. and Umansky (1992) both found that schizophrenic participants displayed less semantic priming at short SOAs in an LD paradigm when compared with normal participants. In addition. several other studies have found no differences between schizophrenic and normal participants in semantic priming (Vinogradov et al.. 1992. using WP; Ober. Vinogradov. & Shenaut. 1995. using both WP and LD; and Chapin. McCown. Vann. Kenney. & Youssef. 1992. and Chapin. Vann. Lycaki. Josef. & Meyendorff. 1989. using LD).

Those studies that have found increased priming have been interpreted as evidence for stronger or farther-reaching spreading activation within the associative networks of schizophrenics. This. in turn. has been used to explain the inappropriate intrusion of associations into schizophrenic speech (e.g.. Spitzer. Braun. Maier. et al.. 1993). According to this account. the deficit in schizophrenia would be in a process (spreading activation) that is believed to be automatic and to operate within the semantic store. This would be an interesting and unusual finding. because reviews of the literature have typically concluded that schizophrenics suffer from primary abnormalities in strategic processes (e.g.. Braff. 1993; Callaway & Naghdi. 1982; Nuechterlein & Dawson. 1984). Unfortunately. however. most studies of lexical priming have suffered from a number of major methodological problems that make it difficult to conclude that schizophrenic patients display reliable increases in priming and that this is due to a deficit in automatic. intralexi-

cal processes as opposed to extralexical. potentially strategic. processes.

A first problem is that the majority of research in schizophrenia has not used methodology designed to clearly distinguish between different sources of priming. Such distinctions can be made along two dimensions: automatic versus strategic processes and intralexical versus extralexical processes. We distinguish between these dimensions to clarify that not all extralexical processes may be strategic (e.g.. sentence context effects). In the literature on normal language processing. researchers use manipulations of SOA and the proportion of related words to tease apart automatic and strategic components of priming. SOAs shorter than 500 ms. combined with short RTs. are thought to preclude the influence of trial-specific strategic processes (Neely. 1991). In addition. a high proportion of related words (e.g.. 70% or greater) is thought to increase the salience of the prime–target relationship and to elicit the use of strategic processes (den Heyer. 1985; Tweedy. Lapinski. & Schvaneveldt. 1977). In the schizophrenia literature. only a few studies have directly compared performance at short and long SOAs. and no studies have explicitly manipulated the proportion of related word pairs.

A similar problem arises with regard to the distinction between intralexical and extralexical processes. Most research on semantic priming in schizophrenia has used LD and not WP. This may be due in part to the fact that LD typically produces larger effects than WP. although WP priming effects are consistently robust and reliable (e.g.. Neely. 1991). The findings from studies that have used LD have been interpreted as evidence for intralexical disturbances (e.g.. Spitzer. Braun. Hermle. et al.. 1993). However. LD appears to be more influenced than WP by extralexical mechanisms. which may operate even at short SOAs (e.g.. Neely. 1991). For example. semantic matching (an extralexical strategic process) is thought to play a role in LD. even at short SOAs. but not in WP (e.g.. Seidenberg. Waters. Sanders. & Langer. 1984). Thus. with the use of the LD paradigm. it is difficult to be sure that priming abnormalities. even at short SOAs. are attributable to disturbances in intralexical processes such as automatic spreading activation. In contrast. the use of WP. particularly with short SOAs. may provide a cleaner measure of the operation of such processes.

A second major problem is that the majority of semantic priming studies of schizophrenic patients have been confounded by schizophrenics' longer overall RTs. As pointed out by Chapman. Chapman. Curran. and Miller (1994). difference scores can be spuriously inflated in participants who exhibit overall worse or more variable performance. Larger semantic priming scores in schizophrenics participants (usually measured as a difference between RTs to related versus unrelated targets) could reflect a psychometric artifact. rather than disturbances that are specific to semantic processing. Spitzer (e.g.. Spitzer. Braun. Hermle et al.. 1993) suggested that the use of percentage gain scores $[1-(\text{related}/\text{unrelated RTs})*100]$ addresses the confounding effects of longer RTs on semantic priming. However. no psychometric research has systematically examined whether percentage gain scores do address the effects of longer RTs. We are currently conducting simulation studies to examine this issue (Barch. Cohen. & Braver. 1996). Chapman et al. (1994) recently suggested an alternative post hoc RT data

analytic technique that helps remove the effects of overall performance levels. The use of such an analysis would help clarify the magnitude of priming effects in schizophrenia independent of overall slowing, an issue discussed further below. There is one study that demonstrated an abnormal increase in priming among schizophrenia patients after prospectively addressing psychometric issues concerning a differential deficit. Kwapil et al. (1990), using error rates instead of RTs and a target degradation procedure designed to equate mean performance between patients and controls, still found that schizophrenic patients appeared to display enhanced priming at a short SOA. However, it is possible that by using a stimulus degradation procedure, Kwapil et al. (1990) may have introduced a confound in their design. Specifically, it is well established that normal participants show a greater reliance on context, and a concomitant increase in priming effects, when target stimuli are degraded (e.g., Meyer, Schvaneveldt, & Ruddy, 1975). Thus, the variable Kwapil et al. used to equate performance between normal and schizophrenic participants was not independent of the measure they used (priming). Manipulating a variable that affects priming introduces the possibility that the schizophrenic patients were more influenced by target degradation than the controls were, which is an alternative interpretation of the observed increases in priming. In summary, research has yet to convincingly demonstrate, either through the use of post hoc correction procedures with established validity or through prospective designs, that schizophrenic patients display increases in priming at short SOAs that are not the result of psychometric artifacts or other confounds.

A third major problem is that all of the studies that have examined semantic priming effects in schizophrenia either have involved only medicated schizophrenic participants or have not separately analyzed the data of unmedicated schizophrenic participants if they were included. Several studies have shown that acute administration of antipsychotic medication is associated with longer RTs among schizophrenic patients on both cognitive and motor tasks (e.g., Bilder et al., 1991; Kornetsky, Pettit, Wynne, & Evarts, 1959; Spohn, Coyne, LaCoursiere, Mazur, & Hayes, 1985). If longer RTs are associated with the artifactual appearance of enhanced priming (Chapman et al., 1994), it is possible that the use of only medicated schizophrenic patients has confounded previous findings of enhanced priming among schizophrenic patients. Spitzer (e.g., Spitzer, et al., 1994) reported larger priming effects in TD than in non-TD (NTD) schizophrenics, irrespective of medication, which thus suggests that this is not a relevant variable. However, it is still possible that the presence of thought disorder in schizophrenic participants is correlated with higher doses of antipsychotic medication, which could lead to the appearance of increased priming in TD compared with NTD participants. This hypothesis is plausible given the common clinical practice of prescribing higher medication doses for individuals with more overt psychotic symptoms. Furthermore, medications may also obscure the interpretation of findings regarding the source of the observed abnormalities. As noted above, the finding of "hyperpriming" at short SOAs has been taken as evidence of a deficit in automatic spreading activation. However, long-term administration of antipsychotic medications may help ameliorate deficits in higher level or strategic processes (Cassens, In-

glis, Appelbaum, & Gutheil, 1990; Spohn & Strauss, 1989), thus masking any deficits in higher level or strategic components of priming that may be associated with schizophrenia and that would be apparent in unmedicated participants.

Our primary goal in the present study was to examine the hypothesis that schizophrenic patients suffer from a disturbance in automatic, intralexical processes (e.g., abnormally strong, or far-reaching, spreading activation) that results in enhanced semantic priming. We set out to address methodological problems in previous studies by (a) using WP as our priming paradigm instead of LD, (b) examining performance at a variety of both short and long SOAs, (c) using data analytic techniques known to account for the longer RTs generally found among schizophrenic participants, and (d) studying both medicated and unmedicated patients. The examination of medication effects in the present study should be considered exploratory. Medication status was not experimentally controlled and is thus open to a number of confounds. For example, it is possible that medication dosage is serving as a proxy for other relevant clinical variables, such as severity or symptomatology. However, no previous research has examined the issue of medication effects on semantic priming, and thus the present study may help shed light on whether more experimentally controlled investigations of this issue are warranted. Our specific hypotheses were (a) that schizophrenic patients would display normal semantic priming at short SOAs in WP, the conditions specifically thought to tap the functioning of automatic spreading activation, and (b) that if schizophrenic patients did display any priming disturbances, they would take the form of reduced priming at longer SOAs, the conditions most likely to tap the functioning of extralexical, higher level processes.

Method

Participants

Four groups were studied: unmedicated schizophrenic patients (N = 25), medicated schizophrenic patients (N = 75), patient controls with a diagnosis of major depression (N = 10), and normal controls (N = 28). All schizophrenic participants were inpatients at the Western Psychiatric Institute and Clinic (WPIC) or at the Department of Veterans Affairs Medical Center Highland Drive (DVAMC). All depressed participants were inpatients at the WPIC. Diagnoses were made by a staff psychiatrist in accordance with the revised third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-III-R*; American Psychiatric Association, 1987) and confirmed by trained research personnel using the Structured Clinical Interview for DSM-III-R Psychotic Disorders for schizophrenic patients and the Schedule for Affective Disorders and Schizophrenia for mood disorder patients. The unmedicated patients were either (a) first-episode schizophrenic participants (N = 16), without any prior history of antipsychotic medication, whose diagnoses had been confirmed 6 months later; (b) multi-episode schizophrenic participants who had a documented history of noncompliance with medication for 1 month or more prior to admission (N = 7); or (c) inpatients at the DVAMC participating in a medication withdrawal study who had previously been stabilized on haloperidol and had been receiving a placebo for at least 2 weeks in a double-blind design at the time of testing (N = 2). We attempted to test 3 additional unmedicated patients who were unable to complete the task. The medicated schizophrenic participants were either (a) first-episode schizophrenic participants whose diagnoses had been confirmed 6 months later and who were receiving medication at the time of testing (N = 2); (b) multi-

episode patients who were receiving standard doses of antipsychotic medication at the time of admission and who were tested while continuing to receive the same medication ($N = 21$); or (c) inpatients in the DVAMC medication withdrawal program who had been stabilized on haloperidol ($N = 52$; van Kammen et al., 1995).

Potential participants were excluded for the following reasons: (a) concurrent diagnosis of alcoholism, substance abuse, or any psychoactive substance use within 2 weeks prior to the study; (b) neurological illness or history of head trauma with loss of consciousness; and (c) mental retardation. The Brief Psychiatric Rating Scale (BPRS) was used to evaluate clinical state. Ratings were completed by trained members of research terms at both the WPIC and the DVAMC who regularly participated in training sessions to ensure reliability of ratings. All BPRS ratings were made within 1 week of admission to the study, and all raters were blind to the performance of participants in the task. To examine the potential association between thought disorder and semantic priming, we collapsed the schizophrenic participants across medication status and divided them into NTD and TD groups using the same method as Spitzer, Braun, Maier, et al. (1993). Schizophrenic participants with a 1 or 2 on the "conceptual disorganization" item from the BPRS were categorized as NTD ($N = 66$: 17 unmedicated, 49 medicated), whereas those with a 3 or above on this item were categorized as TD ($N = 34$: 8 unmedicated, 26 medicated). The minimum interrater reliability (intraclass correlation) of the conceptual disorganization scores was .70 at the DVAMC and .61 at the WPIC.

The clinical and demographic characteristics of each of the participant groups are shown in Table 1. The groups differed in age, education, and sex distribution, as shown in the table. The main effects of age and education were followed up with post hoc analyses that used Tukey-Kramer comparisons for unequal sample sizes. We investigated the overall group differences in sex distribution with chi-square analyses using the continuity correction. The results of these follow-up analyses are also shown in Table 1. As discussed later, none of these demographic differences between groups appeared to have any effect on priming performance. The NTD and TD schizophrenic patients differed only in severity of positive symptoms. The unmedicated and medicated schizophrenic patients differed on both negative symptom severity and length of illness. For the purposes of analysis, daily oral doses of antipsychotics were converted to chlorpromazine equivalents according to guidelines suggested by Davis, Janicak, Linden, Moloney, and Pavkovic (1983). We converted depot doses to average daily dosages using the guidelines suggested by Baldessarini (1985). All participants signed informed consent forms in accordance with the University of Pittsburgh and the DVAMC institutional review boards. All participants recruited from the WPIC were tested within 10 days of their admission to the hospital. Those participants at the DVAMC were tested prior to haloperidol withdrawal or after a minimum of 2 weeks on placebo.

Materials

A list of 200 target words was created. For each target word, we constructed a related and an unrelated prime from lists of published norms (e.g., Deese, 1964; Postman & Keppel, 1970). For an individual participant, a target was presented in only one condition (related or unrelated prime) and one SOA. Similarly, no prime was used more than once for a given participant. Condition of presentation and SOA for each target were counterbalanced so that within every 10 participants, a target appeared once in each condition (related or unrelated prime) at each of the five SOAs. Every participant was presented with 200 prime–target pairs, which included 100 related and 100 unrelated prime–target pairs, 20 of each at the five different SOAs. SOAs were randomly intermixed across trials with the constraint that 20 related and 20 unrelated pairs be presented at each SOA and that all conditions be sampled once in every 20 trials.

Table 1
Demographic Characteristics of Each Group

Variable	Depressed controls (n = 10)		Normal controls (n = 28)		NTD schizophrenics (n = 66)		TD schizophrenics (n = 34)		p(TD)[a]	Unmedicated schizophrenics (n = 25)		Medicated schizophrenics (n = 75)		p(MED)[b]
	M	SD	M	SD	M	SD	M	SD		M	SD	M	SD	
Age (in years)	36.8	10.7	22.1	7.4	33.4	8.5	33.7	8.9	.001 (N < D, NTD, TD)	29.1	10.3	34.9	7.5	.001 (N < D, UM, M; M: UM < M)
Education (in years)	15.9	4.0	13.8	1.3	12.9	1.8	12.8	1.7	.001 (D > N, NTD, TD)	13.4	2.0	12.7	1.6	.001 (D > N, UM, M; N > M)
Sex (% male)	30		46		83		85		.01 (NTD, TD > N, D)	50		93		.001 (M > N, D, UM)
BPRS conceptual disorganization score					1.4	0.5	3.7	0.8	.001	1.8	1.1	2.2	1.3	ns
BPRS positive symptoms score					8.6	3.9	14.2	4.1	.001	10.7	5.2	10.5	4.7	ns
BPRS negative symptoms score					4.2	2.1	4.7	2.1	ns	3.6	2.1	4.6	2.0	.06
Length of illness (in years)					9.4	8.0	8.9	7.6	ns	3.8	6.8	11.0	7.4	.001
Chlorpromazine equivalents (mg)					391.0	480.5	433.5	455.5	ns	0		589.1	460.6	

Note. NTD = non-thought-disordered; TD = thought-disordered; BPRS = Brief Psychiatric Rating Scale.
[a] This column shows the results, for schizophrenic participants categorized by thought-disorder status, of one-factor analyses of variance (ANOVAs), a chi-square analysis (sex), or two-tailed *t* tests between the NTD and TD groups (D = depressed controls, N = normal controls).
[b] This column shows the results, for schizophrenic participants categorized by medication (MED) status, of one-factor ANOVAs, a chi-square analysis (sex), or two-tailed *t* tests between the nonmedicated (UM) and medicated (M) groups (D = depressed controls, N = normal controls).

Apparatus and Procedure

Each participant was tested individually in an isolated room. Participants were told that they would be presented with pairs of words. Their task was to read the first word silently and then to say the second word aloud as fast as they could. Stimuli were presented on an Apple Macintosh computer with PsyScope software (Cohen. MacWhinney, Flatt, & Provost. 1993). Each word was centered in a fixation box measuring approximately 2 cm × 1 cm, was presented in a nondegraded, lowercase, Helvetica font, white against a black background, and subtended a visual angle of approximately 3°. RT for onset of word pronunciation was automatically recorded by the computer by means of a microphone and a voice-activated relay. The prime appeared for 100 ms and then the screen went blank (without masking) for either 100, 200, 350, 600, or 850 ms depending on the SOA condition. The target word was then presented and the participant had a total of 2 s from its onset in which to respond. Following either the participant's response or 2 s, the screen went blank. Regardless of RT, a new trial started 3 s after onset of the previous target, fixing the task pace for all participants. Feedback was provided by a buzzer for failures to respond and by no sound at all for pronunciation of the target within 2 s. Mispronunciations, of which there were very few, or any type of computer error were coded by the experimenter. We included a short practice period before testing to ensure that participants understood the instructions, were comfortable with the apparatus, and were performing the task appropriately.

Data Analysis

RTs have a non-normal distribution, which makes it difficult to detect outlier RTs in the upper tail of the distribution. This issue is particularly problematic with schizophrenic participants, whose longer RTs and more variable performance make it extremely difficult to determine outlier responses. To address this issue, we (a) eliminated RTs below 200 ms; (b) did not eliminate any long, potentially outlier, RTs from the data; and (c) used an inverse transformation (1/RT) of the data. Ratcliff (1993) demonstrated that the inverse transformation has the highest power, among a variety of methods tested. to minimize the effects of outliers on analyses of variance (ANOVAs). Only analyses in which we used the transformed data are reported below, and the results were almost identical to those we obtained using the untransformed data. As reported earlier, the groups differed in age, education, and sex distribution. Multiple regressions indicated that none of these demographic variables accounted for a significant amount of variance in priming (unrelated RT minus related RT) at any of the five SOAs. Further, all ANOVA analyses reported below were also conducted as analyses of covariance, with the demographic variables as covariates, with no change in the results.

Results

The means and standard deviations of RTs for each SOA and condition among each group are shown in Table 2. Error rates are not presented because they were less than 1% for all groups, which eliminated the likelihood of a speed–accuracy trade-off. In all ANOVAs. prime type (related or unrelated) and SOA (200, 300, 450, 700, or 950 ms) were both within-subject factors. When necessary, the degrees of freedom were adjusted according to the Greenhouse–Geisser procedure. First, we examined whether schizophrenic participants, either TD or NTD, displayed any evidence of increased semantic priming. To do so, we conducted a three-way ANOVA involving four groups (NTD schizophrenics. TD schizophrenics. depressed controls. and normal controls). two prime types, five SOAs, and RT as

the dependent variable. This analysis revealed main effects of group. $F(3, 134) = 17.01$. $p < .0001$: prime type. $F(1, 134) = 24.51$, $p < .0001$: and SOA, $F(4, 536) = 35.26$. $p < .0001$. Post hoc analyses examining the main effect of group. with Tukey–Kramer comparisons for unequal sample sizes. indicated that both NTD and TD schizophrenic participants were slower than normal controls ($p < .05$). In addition, TD schizophrenic participants were slower than the depressed controls ($p < .05$). The main effect of prime type indicates that all groups displayed significant priming effects. The main effect of SOA was modified by a marginal interaction between SOA and group. $F(12, 536) = 1.67$, $p = .08$. No other interactions were significant. We used post hoc comparisons. with Tukey's honestly significant difference test for repeated measures. to investigate the Group × SOA interaction. These analyses indicated that RTs at the 200-ms SOA were slower than RTs at all other SOAs among all groups but the depressed controls. In addition. RTs at the 300-ms SOA were slower than RTs at the 450- and 950-ms SOAs only among the TD schizophrenics. RTs at the 300-ms SOA were slower than RTs at the 700-ms SOA only among the NTD and TD schizophrenics. As can be seen in Table 3. neither the TD nor the NTD schizophrenics displayed evidence of a significant increase in priming (unrelated RT − related RT) at any of the SOAs.[1]

As discussed in the introduction, priming studies with schizophrenic patients are confounded by the effects of longer RTs because difference scores can be spuriously inflated in participants who exhibit overall worse or more variable performance (Chapman et al., 1994). This is illustrated in our data by the fact that even among the normal participants only, there was a strong positive correlation between overall RT and priming ($r = .40, p < .05$). Chapman et al. (1994) recently suggested a regression method that allows one to examine and account for the influence of longer RTs on observed priming scores. In accordance with this procedure. we computed the regression equation predicting the priming score at each SOA from a measure of overall RT (unrelated + related RTs) at that SOA, using only the data from the normal control participants.[2] We used this equation to compute predicted priming scores for each participant in all groups. and we calculated the difference between the observed and predicted priming scores for each participant. According to Chapman et al. (1994), this difference score measures the extent to which a participant displays more or less priming than would be expected given his or her overall level of performance. A two-way ANOVA involving four groups (NTD schizophrenics. TD schizophrenics. depressed controls. and

---

[1] Previous studies of priming in schizophrenia used only medicated patients. Thus. to ensure that the inclusion of unmedicated patients did not obscure a relationship between thought disorder and priming. we conducted these analyses using only medicated patients. with identical results.

[2] We also conducted these analyses using a regression equation derived from the data of both normal and depressed controls. with identical results. The depressed controls were slower than the normal controls and thus closer to the range of RTs displayed by schizophrenic patients. Therefore. using the data from both groups may provide a better estimate of the relationship between priming and overall RT in the latency range displayed by schizophrenia patients.

Table 2

Reaction Times (in Milliseconds) for Related and Unrelated Targets at the Five SOAs

| | | Schizophrenia group | | | | | | | | Control group | | | |
| | | NTD | | TD | | Unmedicated | | Medicated | | Depressed | | Normal | |
SOA (ms)	Target	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
200	Related	696.4	127.8	753.7	160.0	671.3	98.7	730.7	150.6	602.1	57.7	532.2	62.8
	Unrelated	716.3	139.2	765.5	181.2	679.3	111.9	750.9	164.4	612.5	62.3	546.0	72.9
300	Related	662.3	135.7	721.3	141.7	649.8	116.2	693.2	146.0	582.2	61.2	503.1	65.7
	Unrelated	684.3	136.6	736.5	152.2	666.6	110.1	713.9	151.8	593.5	79.4	508.1	63.8
450	Related	652.5	140.6	685.9	141.5	625.4	96.9	676.7	151.4	570.7	65.4	498.3	61.6
	Unrelated	678.0	158.4	708.3	153.6	659.5	124.3	697.9	165.7	578.3	69.3	516.5	81.5
700	Related	636.9	128.5	686.5	140.0	623.4	93.7	663.9	143.9	554.6	50.2	494.5	61.7
	Unrelated	659.1	138.8	699.5	141.1	638.3	90.9	684.4	151.9	578.1	58.9	512.1	65.8
950	Related	656.9	161.0	688.6	141.3	620.7	105.5	683.3	165.4	553.0	42.4	493.2	57.7
	Unrelated	657.8	130.6	694.2	140.1	635.4	96.2	681.8	143.5	589.4	56.7	512.5	66.6
Mean RT		670.0	133.1	714.0	142.2	647.0	98.3	697.7	146.2	581.4	55.7	511.7	60.2

Note. SOA = stimulus onset asynchrony; RT = reaction time; NTD = non-thought-disordered; TD = thought-disordered.

normal controls) and five SOAs, with the difference score (observed − predicted priming) as the dependent variable, revealed a significant main effect of SOA. $F(4, 536) = 3.85$, $p < .01$, and a significant interaction between group and SOA, $F(12, 536) = 2.10$, $p < .05$. Planned contrasts indicated that the NTD ($p < .01$) and the TD ($p < .01$) schizophrenics differed from the depressed and normal controls only at the 950-ms SOA, where they displayed significantly less priming.

To explore the potential effects of medication on priming (see Table 3), we used a three-way ANOVA with four groups (medicated schizophrenics, unmedicated schizophrenics, depressed controls, and normal controls), two prime types, five SOAs, and RT as the dependent variable. This ANOVA revealed significant main effects of group, $F(3, 134) = 17.16$, $p < .0001$, prime type, $F(1, 134) = 24.90$, $p < .0001$, and SOA, $F(4, 536) = 28.81$, $p < .0001$, but no significant interactions. Post hoc analyses with Tukey–Kramer comparisons for unequal sample sizes indicated that medicated and unmedicated schizophrenics were slower than the normal controls ($p < .01$) and that medicated schizophrenics were slower than the depressed controls ($p < .05$).

Analysis of the data for participants grouped by medication

status using the Chapman et al. (1994) procedure indicated results identical to those with the data grouped by thought disorder status. A two-way ANOVA involving four groups (unmedicated schizophrenics, medicated schizophrenics, depressed controls, and normal controls) and five SOAs, with the difference score (observed − predicted priming) as the dependent variable, revealed a significant main effect of SOA, $F(4, 536) = 3.44$, $p < .01$, and a Group × SOA interaction, $F(12, 536) = 2.2$, $p < .05$. Planned contrasts indicated that both the unmedicated ($p < .05$) and medicated ($p < .001$) schizophrenics differed from the depressed and normal controls only at the 950-ms SOA, where they displayed significantly less priming.

The ANOVAs did not indicate any significant effects of either thought disorder or medication on priming. However, given that these are likely to be continuous effects, it is possible that grouping participants categorically reduced our power to detect significant associations between semantic priming and either thought disorder or medication. To examine this possibility, we conducted hierarchical regression analyses using the conceptual disorganization scores and medication dosage (in chlorpromazine equivalents) to predict priming scores at each of the five SOAs. These analyses used only orally medicated patients (73

Table 3

Priming at the Five SOAs

| | Schizophrenia group | | | | | | | | Control group | | | |
| | NTD | | TD | | Unmedicated | | Medicated | | Depressed | | Normal | |
SOA (ms)	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
200	19.8	6.2	11.8	9.3	8.0	8.7	20.2	6.2	10.3	8.9	13.8	8.2
300	22.0	6.7	15.2	13.1	16.8	11.2	20.7	7.5	11.3	9.9	5.0	6.3
450	25.4	8.2	22.4	14.2	34.1	11.6	21.2	8.8	7.6	15.6	18.2	7.5
700	22.3	7.2	13.0	9.9	14.9	9.9	20.5	7.0	23.6	11.6	17.6	5.2
950	00.9	8.2	5.7	12.9	14.7	8.9	−1.5	8.7	36.4	10.2	19.3	6.6

Note. SOA = stimulus onset asynchrony; NTD = non-thought-disordered; TD = thought-disordered.

out of the 75 medicated patients) because of the questionable assumptions in converting depot into oral dosages. Thought disorder did not account for a significant amount of variance in priming scores at any of the five SOAs, whether entered before or after medication dosage. In contrast, medication dosage was positively associated with priming at the 200-ms ($R = .20, p = .08$), 300-ms ($R = .30, p < .01$), 450-ms ($R = .24, p < .05$), and 700-ms ($R = .40, p < .001$) SOAs. Medication dosage was negatively associated with priming at the 950-ms SOA ($R = .40, p < .001$). It is possible that thought disorder influences semantic priming differently in medicated and unmedicated schizophrenics and that medication is obscuring an important effect of thought disorder on priming. However, the addition of an interaction term between thought disorder and medication dosage to the previous analyses did not account for any additional variance in priming scores.

It is possible that higher doses of medication are related to priming at SOAs less than 950 ms because medication contributes to the general slowing shown by schizophrenic patients. In turn, such general slowing may lead to the appearance of more priming (Chapman et al., 1994). To examine this possibility, we conducted two additional sets of regression analyses. First, we examined the association between medication dosage and overall RT at each of the five SOAs. Higher doses of medication were strongly associated with longer RTs at all SOAs ($R > .38, p < .0001$). Second, we examined the relationship between medication dosage and the Chapman-corrected scores. If medication leads to the appearance of enhanced priming because of effects on RT latency, and if the Chapman et al. correction eliminates artifactual relationships between longer RTs and priming, then medication dosage should be unassociated with the Chapman-corrected scores. Consistent with this hypothesis, medication dosage was not significantly associated with the Chapman-corrected scores at any of the SOAs ($p > .10$).

Although the regression analyses indicated an association between medication dosage and priming, there are problems with its interpretation (e.g., Blanchard & Neale, 1992), particularly when dosages are clinically and not randomly determined. It is possible that medication dosage is serving as a proxy for other relevant clinical variables, such as severity, symptomatology, or length of illness. As discussed previously, the medicated schizophrenics had been ill longer and had more negative symptoms than the unmedicated schizophrenics. Further, the fact that the medicated schizophrenics were at least as symptomatic as the unmedicated schizophrenics suggests that the two groups may differ in severity. To explore this possibility, we conducted hierarchical regression analyses to determine whether medication dosage still accounted for a significant proportion of variance in priming scores beyond what was accounted for by negative symptom scores and length of illness. It should be noted that such analyses are post hoc and exploratory and do not eliminate confounds inherent in such data, particularly because negative symptoms and length of illness represent only a subset of variables potentially associated with medication dosage. Nevertheless, at each of the five SOAs, the clinical variables did not account for any significant variance in priming. In contrast, the increase in R^2 with the addition of dosage to the equation was either significant or near significant at the 200-ms ($R^2_{change} = .04, p = .09$), 300-ms ($R^2_{change} = .07, p < .05$), 450-ms ($R^2_{change}$

= .04, $p = .08$). 700-ms ($R^2_{change} = .17, p < .001$) and 950-ms ($R^2_{change} = .19, p < .001$) SOAs, consistent with the possibility that the effects of medications are independent of the severity and duration of illness.

Discussion

The results of this study support both of our primary hypotheses: (a) Schizophrenic participants have intact automatic, intralexical semantic priming but may suffer from deficits in higher level, extralexical processes that influence priming, and (b) previous findings of enhanced priming among schizophrenic patients at short SOAs and normal priming at longer SOAs may have been confounded by the use of inappropriate experimental designs, the effects of longer RTs, and potentially the effects of medication. First, there was no evidence of increased priming in schizophrenic participants at either short or long SOAs. Further, thought disorder was not associated with increased priming at any of the SOAs. As discussed in the introduction, WP with short SOAs is the experimental paradigm thought to most clearly tap the functioning of intralexical, automatic spreading activation. Thus, the present findings provide no evidence for a disturbance in such a mechanism among schizophrenic patients, whether TD or NTD.

Second, the results of the present study emphasize the importance of taking into account the effects of overall performance differences among schizophrenic participants (Chapman et al., 1994). We found a relationship between longer RTs and increased priming in our data, even among just the normal control participants. When overall RTs were taken into account, the schizophrenic participants, regardless of thought disorder or medication status, consistently displayed priming similar to that of the normal and patient controls at SOAs less than 950 ms but displayed significantly less priming at the 950-ms SOA.

Third, higher does of antipsychotic medications were associated with greater priming at SOAs less than 950 ms. These analyses should be considered exploratory given that medication status was not experimentally controlled and thus may have been confounded with other factors. For example, as discussed previously, higher doses of medication may have been associated with more severe symptomatology, which is actually associated with increased priming. Post hoc analyses cannot completely rule out the possibility of such confounds and address only a subset of potential confounds. However, the results of the regression analyses do not support the interpretation that factors such as severity or duration of illness are associated with increased priming. Instead, the analyses examining overall RTs suggest that if medication is associated with increased priming, it may be through a contribution to the general slowing shown by schizophrenic patients (e.g., Bilder et al., 1991). In turn, such overall slowing may lead to the appearance of increased priming (Chapman et al., 1994). Such an interpretation is consistent with our findings that (a) medication dosage was strongly associated with overall slowing; (b) at SOAs of 700 ms or less, neither the medicated nor unmedicated schizophrenics displayed more priming than would be expected by their overall RTs; and (c) medicated dosage was not associated with the Chapman-corrected scores (which account for the relationship between slowing and priming). Thus, at a minimum, our find-

ings suggest that additional experimentally controlled investigations of medication effects on priming are warranted. Most important, they call for a more careful examination of the hypothesis that observations of increased priming in schizophrenic patients are due to abnormally enhanced automatic spreading activation.

A related question is why some previous research has found enhanced priming at short SOAs among medicated TD patients, but not medicated NTD patients (e.g., Spitzer, Braun, Hermle, et al., 1993, Spitzer, et al., 1994). Presumably, both groups would have long RTs and be equally affected by medication. There are several possible answers to this question. First, in previous studies, the TD schizophrenics had longer (e.g., 1.045 vs. 870 ms, Spitzer, Braun, Hermle, et al., 1993; 1.187 vs. 1.050 ms, Spitzer, et al., 1994) or more variable (SDs of 176 vs. 82 ms, Manschreck et al., 1988; 452 vs. 335 ms, Spitzer, et al., 1994) RTs than the NTD schizophrenics, which may have led to the appearance of increased priming. In the present study, the average RTs of our TD schizophrenics were only 44 ms longer than the RTs of the NTD schizophrenics, and the variance in RTs was equal across these groups. It is also possible that in previous studies, the TD schizophrenics were on higher doses of antipsychotic medication than the NTD schizophrenics, which may potentially have contributed to longer RTs among the TD schizophrenics. Spitzer, Braun, Hermle, et al. (1993) and Spitzer, et al. (1994) did not report antipsychotic levels for their participants. However, in the study by Manschreck et al. (1988), the TD schizophrenics were on higher doses of antipsychotic medication than the NTD participants, although the difference was not statistically significant. In the present study, the TD and NTD schizophrenics were on equal doses of antipsychotic medication. It is also possible that thought disorder does influence priming in some way but that for some reason this influence was not apparent in our study. In particular, the assessment of thought disorder, in both the present study and the majority of previous studies on priming in schizophrenia, was based on a single item with less than ideal reliability. It is possible that more extensive and reliable assessments of thought disorder would help clarify its relationship to semantic priming in schizophrenia. Further work is clearly needed to tease apart the causal relationships among thought disorder, medication, RTs, and priming.

If, as our study suggests, schizophrenic patients do in fact have intact automatic, intralexical components of semantic processing, then higher level extralexical processes are more strongly implicated as a source of language disturbances in schizophrenia. We believe that our results provide some evidence consistent with this hypothesis. On first inspection, the magnitudes of the group priming scores at the 950-ms SOA among the schizophrenic participants do not appear decreased. However, the analyses accounting for overall RTs indicated that compared with the control groups, both medicated and unmedicated and NTD and TD schizophrenics displayed less priming at the 950-ms SOA than would have been expected from their overall RTs. Given that the influence of higher level, potentially strategic, mechanisms are thought to require SOAs greater than 500 ms, this pattern of results suggests that schizophrenic patients have normal automatic processing but may have deficits in higher level mechanisms mediating priming within this SOA

range. Among the medicated patients, dosage was negatively associated with semantic priming at the longest SOA, which suggests that the lack of significant priming may also have been due to medication effects. However, the fact that the unmedicated schizophrenics displayed the same priming pattern argues against this possibility.

Although these results are suggestive, they do not clarify the specific mechanisms that may lead to disturbances in extralexical components of priming among schizophrenic participants, nor do they establish how such deficits could contribute to language disturbances shown by those with schizophrenia in naturally occurring speech. Several possible extralexical processes may contribute to priming at longer SOAs (Neely, 1991). The primary extralexical process thought to operate in WP is strategic expectancy, a pretarget onset mechanism through which participants generate a set of potential targets related to the prime (Neely, 1991). Although expectancy is usually referred to as a single process, it actually involves several components: (a) detecting a semantic relationship between some primes and targets, (b) maintaining and using this contextual information throughout the task to generate expected sets of targets after seeing each prime, and (c) maintaining the set of expected targets for a given prime until the target occurs.

Elsewhere (Cohen & Servan-Schreiber, 1992), we have described a specific information-processing mechanism that may be deficient in schizophrenia and that could clarify the relationship between priming deficits and naturally occurring language disturbances. We argued that schizophrenic patients have a disturbance in the ability to construct and maintain representations of contextual information, particularly over time delays. In a priming paradigm such as WP, contextual information may include an enduring representation that semantic associations exist between the primes and targets. A deficit in the representation of this information could disturb the ability to represent or maintain information about the existence of semantic relationships between individual primes and targets. The ability to use contextual representations may also play a role in naturally occurring speech. In normal individuals, expectancies generated from representations of the current language context may serve to focus processing on relevant semantic concepts and to inhibit the intrusion of related semantic information that is not appropriate to the current speech context. If contextual representations and thus the ability to generate expectancies from these representations are disturbed in schizophrenia, it may allow inappropriate items to intrude into speech. Thus, it is possible that in schizophrenia, the same deficit in the ability to construct and maintain contextual representations impairs both strategic components of semantic priming and the processing of appropriate semantic concepts in language production (e.g., Maher, 1983).

The finding that schizophrenic participants failed to show significant priming at the 950-ms SOA is consistent with such a deficit in the use of contextual representations. As discussed previously, normal participants generally display increases in priming as SOAs increase from 500 ms and as the proportion of related prime–target pairs increases, presumably because such manipulations encourage the use of strategic processes such as expectancy (e.g., De Groot, 1984, den Heyer, 1985; den Heyer, Briand, & Dannenbring, 1983; Keefe & Neely, 1990; Tweedy,

Lapinski, & Schvaneveldt, 1977). The schizophrenic participants may fail to show significant priming at the 950-ms SOA because they are unable to apply strategies such as expectancy, possibly because of disturbance in the ability to represent or maintain task-relevant information. This hypothesis predicts that manipulating factors such as SOA and the opportunity or need to maintain contextual representations in priming paradigms should have different effects in schizophrenic patients than in normal participants or other patient groups. If schizophrenic patients, particularly those with thought disorder, have a deficit in the ability to represent or maintain contextual representations, they should not demonstrate an increase in priming as the time available to apply strategic processes increases or as the proportion of related prime–target pairs increases. In the present study, we did not find an association between thought disorder and reduced priming at the longest SOA. However, the longest SOA was still relatively short, and the proportion of related prime–target pairs was only 50%. The use of still longer SOAs (e.g., > 1,000 ms) and of an even higher proportion of related prime–target pairs, manipulations that clearly encourage the use of and allow adequate time to apply strategies such as expectancy, may provide more sensitive tests of the ability to construct and maintain contextual representations in schizophrenia.

In sum, our findings suggest several important avenues for future research. First, our results highlight the importance of paying careful attention to the choice of methodology when trying to selectively characterize the contributions of different cognitive processes to semantic priming among schizophrenic patients. Factors such as choice of paradigm (LD vs. WP), SOA (short vs. long), and proportion of related prime–target pairs are all important when examining automatic versus strategic or intralexical versus extralexical components of priming. Second, our results underscore the importance of accounting for longer RTs among schizophrenic patients. Third, our findings highlight the importance of examining the influence of medication on cognitive processes in schizophrenia by using both medicated and unmedicated samples of schizophrenics. Review of antipsychotic treatment suggest both beneficial and harmful effects of acute and chronic treatment on cognitive functioning (e.g., Blanchard & Neale, 1992; Spohn & Strauss, 1989). In addition, recent research with the Continuous Performance Test, another task commonly used to study attentional functioning in schizophrenia, has demonstrated that medicated and unmedicated groups display different patterns of performance (e.g., Servan-Schreiber, Cohen, & Steingard, in press). More systematic research is needed on this issue, particularly with tasks commonly used to investigate theories about cognitive deficits in schizophrenia. Finally, if the effects of longer RTs are taken into account, schizophrenic patients show normal automatic, intralexical priming but some evidence consistent with disturbed higher level processes that contribute to priming effects. These findings suggest the need for additional research focusing on the role that higher level deficits play in schizophrenic language disturbances and suggest that we can use the intralexical aspects of priming in other paradigms (e.g., ambiguity resolution) to examine such higher level deficits, as long as medication status and overall RTs are controlled. Following these avenues of research should lead to significant advances in our understanding of the

cognitive mechanisms underlying schizophrenic disturbances of language.

References

American Psychiatric Association (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., rev.). Washington, DC: Author.

Baldessarini, R. J. (1985). *Chemotherapy in psychiatry.* Cambridge, MA: Harvard University Press.

Barch, D. M., Cohen, J. D., & Braver, S. (1996). *Analytic techniques for examining the influences of overall performance on difference scores.* Manuscript in preparation.

Bilder, R. M., Lipschutz-Broch, L., Reiter, G., Mayerhoff, D. I., Loebel, A., Degreef, G., Ashtari, M., & Lieberman, J. (1991). Neuropsychological studies of first episode schizophrenia. *Schizophrenia Research, 4,* 381–382.

Blanchard, J. J., & Neale, J. M. (1992). Medication effects: Conceptual and methodological issues in schizophrenia research. *Clinical Psychology Review, 12,* 345–361.

Bleuler, E. (1950). *Dementia praecox or the group of schizophrenias* (J. Zinker, Trans.). New York: International Universities Press. (Original work published 1911).

Braff, D. (1993). Information processing and attention dysfunctions in schizophrenia. *Schizophrenia Bulletin, 19,* 233–259.

Callaway, E., & Naghdi, S. (1982). An information processing model of schizophrenia. *Archives of General Psychiatry, 39,* 339–347.

Cassens, G., Inglis, A. K., Appelbaum, P. S., Gutheil, T. G. (1990). Neuroleptics: Effects on neuropsychological function in chronic schizophrenic patients. *Schizophrenia Bulletin, 16,* 477–499.

Chapin, K., McCown, J., Vann, L., Kenney, D., & Youssef, I. (1992). Activation and facilitation in the lexicon of schizophrenics. *Schizophrenia Research, 6,* 251–255.

Chapin, K., Vann, L. E., Lycaki, N., Josef, N., & Meyendorff, E. (1989). Investigation of the associative network in schizophrenia using the semantic priming paradigm. *Schizophrenia Research, 2,* 355–360.

Chapman, L. J., Chapman, J. P., Curran, T. E., & Miller, M. B. (1994). Do children and the elderly show heightened semantic priming? How to answer the question. *Developmental Review, 14,* 159–185.

Cohen, J. D., MacWhinney, B., Flatt, M., & Provost, J. (1993). PsyScope: An interactive graphic system for designing and controlling experiments in the psychology laboratory using Macintosh computers. *Behavior Research Methods, Instruments, and Computers, 25,* 257–271.

Cohen, J. D., & Servan-Schreiber, D. (1992). Context, cortex, and dopamine: A connectionist approach to behavior and biology in schizophrenia. *Psychological Review, 99,* 45–77.

Cohen, J. D., Targ, E., Servan-Schreiber, D., & Spiegel, D. (1992). The fabric of thought disorder: A cognitive neuroscience approach to disturbances in the processing of context in schizophrenia. In D. J. Stein and J. E. Young (Eds.), *Cognitive science and clinical disorders* (pp. 99–127). New York: Academic Press.

Collins, A. M., & Loftus, E. F. (1975). A spreading-activation theory of semantic processing. *Psychological Review, 82,* 407–428.

Davis, J., Janicak, P., Linden, R., Moloney, J., & Pavkovic, I. (1983). Neuroleptics and psychotic disorders. In J. T. Coyle & S. J. Enna (Eds.), *Neuroleptics: Neurochemical, behavioral, and clinical perspectives* (pp. 15–64). New York: Raven Press.

Deese, J. (1964). The associative structure of some common English adjectives. *Journal of Verbal Learning and Verbal Behavior, 3,* 347–357.

De Groot, A. M. B. (1984). Primed lexical decision: Combined effects of the proportion of related prime–target pairs and the stimulus onset asynchrony of prime and target. *Quarterly Journal of Experimental Psychology, 36A,* 253–280.