Immediate *versus* sustained processing in schizophrenia

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Abstract

A Stroop negative priming (NP) task was used to assess immediate selective attention and priming in schizophrenia and schizoaffective disorder. Subject groups were comprised of 12 state hospital inpatients (41.8 ± 7.5 years of age), 11 outpatients (39.8 ± 7.5 years of age), and 16 controls (36.4 ± 11.7 years of age). Compared with the control group and the outpatients, inpatients failed to exhibit NP [F(2, 36) = 6.09, p < .01], despite exhibiting equivalent Stroop RT interference (p > .05). Error rates did not differ significantly between the 3 groups. Although medication types and dosages were similar between the 2 patient groups, length of illness was significantly longer in the inpatients (19.8 years) than in the outpatients (12.4 years; p < .05). Positive symptom ratings were also significantly higher in the inpatients. The finding of reduced NP in the state hospital patients appears to be related to severity of symptomatology and chronicity of illness. (*JINS*, 2002, 8, 794–803.)

Keywords: Schizophrenia, Selective attention, Stroop, Priming

INTRODUCTION

In the process of everyday functioning, human beings are confronted with a multitude of objects and events to which they must respond. Selection of relevant information is a critical element of successful human behavior. It has been proposed that as we select relevant events and objects, we inhibit those that are irrelevant (Tipper et al., 1991). If in the process of selection, an inhibitory tag for the irrelevant object or event is formed, subsequent influence of that perceptual event on behavior will be observed. It has been suggested that the sustained inhibition of a previously ignored object or event may serve as an “adaptive mechanism for sustaining selective attention” because in the natural environment, perceptual events that are irrelevant at the time of selection are likely to remain irrelevant over a period of time (Tipper et al., 1991). Thus, a mechanism of sustained inhibition may have evolved to ignore irrelevant actions and objects through inhibition over time. Because of its adaptive importance, the study of sustained attentional processes may yield valuable insight into the mechanisms underlying cognitive performance in both normal and patient populations.

There is a substantial body of evidence suggesting that the ability to sustain inhibition over time may be impaired in patients with schizophrenia (Neuchterlein & Dawson, 1984). Studies using different paradigms have reported that attentional processes appear to break down in schizophrenia patients when temporal gaps are introduced in the flow of information (Beech et al., 1989; Cohen & Servan-Schreiber, 1993; Salo et al., 1996). Patients with schizophrenia appear to be more distractible and exhibit more performance errors when time delays are introduced between events (Cohen & Servan Schreiber, 1993; Neuchterlein & Dawson, 1984). It may well be that the immediacy of information in the environment is a strong determinant of behavior in patients with schizophrenia (Salzinger et al., 1970). Recent evidence suggests that when interfering irrelevant information is immediate, the ability to inhibit distracting information improves (Carter et al., 1992; Elkins & Cromwell, 1994; Knight et al., 1985; Salo et al., 1996; Taylor et al., 1996). Because temporal distance appears to modulate attentional performance in schizophrenia patients, priming paradigms are well suited for measuring attentional performance in this population.

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Negative priming paradigms have been used extensively to understand the nature of inhibitory deficits in patient populations. Negative priming (NP) refers to a slowed reaction time or increase in errors that occurs when a previously ignored stimulus becomes the current relevant target (Neill, 1977; Tipper, 1985). Several views have evolved over the years regarding the mechanisms underlying negative priming. One of the earliest views is the inhibition account (Neill, 1977; Tipper, 1985), which proposes that in the process of selectively attending to a target, subjects actively inhibit the distractor. When the distractor then becomes a target on the subsequent trial, as it does in a NP sequence, residual inhibition slows the reaction time. Another proposed mechanism of NP is that of episodic retrieval (Neill, 1997; Neill et al., 1992). According to this theory, NP occurs because of a retrieval process that occurs when selecting the probe. On NP sequences, the response to be made conflicts with information from the previous trial. Yet another hypothesis regarding negative priming, the feature mismatch hypothesis, proposes that negative priming occurs because of a mismatch in features between the prime and probe (Lowe, 1979; Park & Kanwisher, 1994).

Deficits in NP have been reported in a number of schizophrenia studies (Beech et al., 1989; Fuller et al., 2000; LaPlante et al., 1992; Park et al., 1996; Salo et al., 1996, 1997), but not all (Moritz et al., 2000). Abnormal NP has also been reported in schizotypal disorder (Beech & Claridge, 1987; Park et al., 1996; Watson & Tipper, 1997), and obsessive compulsive disorder (Enright & Beech, 1990, 1993a, 1993b; MacDonald et al., 1999). Many of these studies have reported abnormal NP effects in these patient groups, with patients showing faster reaction times on NP sequences compared to the normal slowing displayed by healthy controls. Findings of abnormal NP in these patient groups suggest that either the irrelevant distractor information was not suppressed efficiently at the time of selection, or that the inhibitory tag formed at the time of selection faded during the interval between trials. Watson and Tipper (1997) suggest that abnormal NP effects in schizophrenia and schizotypy may be a result of both reduced inhibition and a deficit in the capacity to link perceptual events across time. The latter is consistent with other theories of episodic memory trace decay (Neill et al., 1992), theories that propose perceptual integration deficits in schizophrenia (Hemslley, 1987) as well as deficits in short-term visual memory functions (Rabinowitz et al., 1996). In all cases, reports of abnormal negative priming in these patient groups suggest that the ability to maintain efficient inhibitory processes across time may be deficient.

Although a large body of research has been devoted to the study of negative priming (see, e.g., Fox, 1995, for review), under similar experimental conditions positive priming effects have also been reported (Lowe, 1979; Neill, 1977; see Table 3). In most cases the positive priming effects were larger than the suppression effect (Lowe, 1979; Neill, 1977). Abnormal positive priming or hyper-priming in schizophrenia has been reported in some studies (Henik et al., 1995; Kwapil et al., 1990; Manschreck et al., 1988; Spitzer et al., 1993), but not all (Barch et al., 1996; Chapin et al., 1992; Henik et al., 1992; Ober et al., 1995; Vinogradov et al., 1992). Because of these conflicting findings on hyperpriming (i.e., positive priming), and our previous reports of abnormal NP processes in schizophrenia outpatients, it was of interest to examine both positive and negative priming effects within the same paradigm. In addition, because severity of illness and symptomatology have been shown to correlate with attentional processing in schizophrenia patients (Barch et al., 1996; Maher et al., 1996; Peters et al., 2000), it was of further interest to compare inhibitory function between long-term hospitalized schizophrenia patients and schizophrenia outpatients. Because of the heterogeneity of schizophrenia and the few studies that have examined medication as a variable (David, 1996; Salo et al., 1997) an important goal of this study was to test two groups of schizophrenia patients who were on a similar medication treatment regime, but differed in symptomatology and illness chronicity.

The present experiment was carried out in order to examine the possible relationship between within-trial attentional processes (Stroop effects) and sustained or between-trial attentional processes (priming effects) in two groups of clinically diverse schizophrenia patients. Within-trial Stroop effects refer to interference and facilitation. Stroop interference is measured as the difference in reaction time (RT) between incongruent and neutral stimuli. Facilitation is measured as the RT difference between the congruent and neutral stimuli. Negative priming using Stroop stimuli refers to the difference in RT to respond to the ink color when it is the same as the word of the preceding trial (which was presumably inhibited at the time of selection) compared to when the color has no relationship to the word of the preceding trial. Positive priming sequences using Stroop stimuli in this study refer to the facilitation of RT response to the ink color when it is the same as the color on the preceding trial compared to when it has no relationship to the word on the preceding trial (Neill, 1977). Positive and negative priming are believed to reflect the activation of the relevant dimension and the suppression of irrelevant dimensions of the stimulus on the previous trial (n − 1). At the same time, the Stroop effect itself is the result of the relative ability (or inability) to focus on the relevant color and ignore the irrelevant word at the time of response decision, and this ability, in turn, is partially dependent upon the strength or speed of processing of the two dimensions. We hypothesized that effects carried over from one trial to another would affect the magnitude of the Stroop effect.

In this experiment we orthogonally manipulated the congruency between the relevant and irrelevant dimensions of the Stroop stimuli and the sequential relationship between them on consecutive trials. Our hypotheses were (1) within-trial Stroop interference effects would not differ between either patient group and matched controls (consistent with our previous results); (2) differences in positive priming effects might emerge between groups (based on a subset of
studies that have reported hyperpriming in schizophrenia patients (Henik et al., 1995; Kwapil et al., 1990; Mischreck et al., 1996; Spitzer et al., 1993); and (3) both patient groups would exhibit negative priming equivalent to controls since both patient groups were medicated (Beech et al., 1990; Salo et al., 1997). These predictions are based on the hypothesis that there may be more than one mechanism responsible for within- and between-trial effects.

METHODS

Research Participants

Thirteen hospitalized psychiatric inpatients (11 with schizophrenia and 2 with schizoaffective disorder), 12 schizophrenia outpatients, and 16 controls participated in the experiment. The data from 2 patients (1 male outpatient and 1 male inpatient) were excluded from the analysis due to an excessive number of errors. The analyses were then carried out on 11 outpatients and 12 inpatients; see Table 1 for demographics. All patients were diagnosed according to DSM-IV criteria. The outpatients were interviewed by the psychiatrist associated with the study (T.E.N.) as well as undergoing an abbreviated version of the Structured Clinical Interview (SCID). The hospitalized patients all received a SCID (Spitzer & Williams, 1987) that was later reviewed by the same psychiatrist (T.E.N.). All subjects reported normal color vision and had normal or corrected to normal visual acuity. All patients were medicated and had continued use of the same neuroleptic medication for the past 2 months and a fixed dosage for the 2 weeks prior to participation in the study (see Table 2). Exclusionary criteria included the following: (1) history of head trauma or neurological injury; (2) history of psychiatric illness; (3) history of drug or alcohol abuse within the last year. The three groups did not differ significantly in age or parental level of education. There was, however, a significant difference in education levels (see Table 1). Age at first psychiatric hospitalization was significantly earlier in the hospitalized patients ($M = 20.5$ years) than in the outpatients ($M = 27.5$ years) and chronicity of illness (age minus age at first psychiatric hospitalization) was also significantly longer in the hospitalized patients (19.8 years) than in the outpatients (12.4 years). A review of the patient ratings on the Schedule of Assessment of Positive Symptoms (SAPS) and the Schedule of Assessment of Negative Symptoms (SANS; Andreasen, 1982) revealed that the hospitalized patients had significantly higher positive symptom ratings than the outpatients did. In contrast negative symptoms as measured by the SANS rating scale did not differ significantly between the two groups (see Table 1).

Sixteen control subjects were recruited from the hospital staff as well as from nearby communities. The control subjects were screened using the SCID and did not differ significantly from the schizophrenia subjects on age and years of parental education. All control participants reported normal color vision and had normal or corrected to normal acuity. Exclusionary criteria included the following: (1) history of head trauma or neurological injury; (2) history of psychiatric illness; (3) history of drug or alcohol abuse within the last year; and (4) family history of psychiatric illness. Both patients and controls were paid for their participation in the study and all gave informed consent.

Apparatus

Stimuli were presented on a 36 cm VGA color monitor. An IBM compatible computer controlled stimuli presentation and data collection. Voice responses were recorded via a voice-operated relay interfaced to the microcomputer. Response timing was to 1-ms resolution and was controlled by the 8253 chip. Stimulus timing was tied to the vertical sync pulse.

Table 1. Demographic and clinical characteristics of subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Outpatients</th>
<th>Inpatients</th>
<th>Controls</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$N$</td>
<td>12$^a$</td>
<td>13$^b$</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Age ($M \pm SD$)</td>
<td>39.8 ($\pm 7.5$)</td>
<td>41.8 ($\pm 7.5$)</td>
<td>36.4 ($\pm 11.7$)</td>
<td>$p &gt; .05$</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9</td>
<td>11</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
<td>2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Age at first psychiatric Hx</td>
<td>27.5 ($\pm 7.3$)</td>
<td>20.5 ($\pm 4.5$)</td>
<td></td>
<td>$p &lt; .05$</td>
</tr>
<tr>
<td>Chronicity (age − 1st Psych Hx)</td>
<td>12.4 ($\pm 7.5$)</td>
<td>19.8 ($\pm 8.2$)</td>
<td></td>
<td>$p &lt; .05$</td>
</tr>
<tr>
<td>Education (in years)</td>
<td>12.8 ($\pm 1.3$)</td>
<td>12.4 ($\pm 2.1$)</td>
<td>14.4 ($\pm 2.1$)</td>
<td>$p &lt; .05$</td>
</tr>
<tr>
<td>Parental level of education (in years)</td>
<td>12.2 ($\pm .4$)</td>
<td>12.8 ($\pm 1.8$)</td>
<td>13.8 ($\pm 2.9$)</td>
<td>$p &gt; .05$</td>
</tr>
<tr>
<td>SAPS rating ($M$)</td>
<td>9 ($\pm 5.6$)</td>
<td>26 ($\pm 17.3$)</td>
<td></td>
<td>$p &lt; .01$</td>
</tr>
<tr>
<td>SANS rating ($M$)</td>
<td>8 ($\pm 10.9$)</td>
<td>15 ($\pm 13.5$)</td>
<td></td>
<td>$p &gt; .05$</td>
</tr>
</tbody>
</table>

$^a$The data from 1 outpatient were excluded due to excessive errors.

$^b$The data from 1 inpatient were excluded due to excessive errors.
Stimuli (See Table 3)

Four colors were employed: red, green, blue, and yellow. The incongruent stimuli were created by printing each of the four color names in the three other ink colors. The congruent stimuli were created by printing each of the four color names in its own color. The neutral stimuli consisted of strings of XXXXs printed in one of the four colors of ink. Each letter within the stimulus words was upper case and subtended 1° vertically. The width of each word display varied as a function of the word presented (range 3–6 letters; approximately 2.4–5.4° visual angle). There were three sequential conditions: in the color–color sequence, the colors of the stimuli on trials n−2 and n were the same, but the levels on the irrelevant dimensions were different—the word RED in blue ink followed by the word GREEN in red ink; in the unrelated control sequence, the two stimuli were different on the levels of both relevant and irrelevant dimensions—the word GREEN in yellow ink followed by the word RED in blue ink; and in the word–color sequence, the irrelevant word on Trial n−1 was the same as the relevant color on Trial n—the word BLUE in red ink followed by the word GREEN in blue ink. For a given pair of stimuli, the leading stimulus (the one referred to as the stimulus on Trial n−1) was always an incongruent stimulus.

Procedure

Subjects were instructed to name the color of ink that the word was printed in while ignoring the word itself. They were given instructions to discourage a speed/accuracy trade-off. Each trial began with a blank screen followed by the stimulus at the center of the screen. The onset of the subject’s voice triggered the voice-operated relay switch (recorded by the computer to the nearest millisecond) and terminated the stimulus display on the screen. The experimenter then typed in the first letter to record the subject’s response. The response stimulus interval employed (RSI) was 494 ms.

There were two blocks of trials, each one composed of 162 stimuli: 58 neutrals, 54 congruent and 50 incongruent. The first trial (Trial n−1) was not analyzed for negative priming costs, thus served as a filler and was always an incongruent trial. In the critical pairs the leading stimulus was always incongruent and in the filler pairs it could be any one of the three congruency conditions. The trailing

<table>
<thead>
<tr>
<th>Medication</th>
<th>Outpatients** N = 12 Mean dose</th>
<th>Inpatients*** N = 13 Mean dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quietapine</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Sertindole</td>
<td>3</td>
<td>18.6 mg</td>
</tr>
<tr>
<td>Clozapine</td>
<td>2</td>
<td>350 mg</td>
</tr>
<tr>
<td>Respirodone</td>
<td>1</td>
<td>8 mg</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>1</td>
<td>5 mg</td>
</tr>
<tr>
<td>Valproic Acid</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>1</td>
<td>125 mg</td>
</tr>
<tr>
<td>Thoridazine</td>
<td>1</td>
<td>125 mg</td>
</tr>
<tr>
<td>Loxapine</td>
<td>1</td>
<td>25 mg</td>
</tr>
<tr>
<td>Thiothixene</td>
<td>1</td>
<td>20 mg</td>
</tr>
</tbody>
</table>

**2 of the outpatients were taking benzodiazepenes and 2 were taking anticholinergics.
***1 of the hospitalized patients was taking anticholinergic only, 2 were taking anticholinergics + depakote, 1 was taking depakote and 1 klonopin.

Note. Compared with an unrelated (control) condition (the word GREEN in yellow ink followed by the word RED in blue ink), Lowe (1979) found positive priming for the following conditions: (1) SAY-SAY condition; (2) SUP-SUP (SUP = suppress) condition; and (3) SAY-SUP condition. The effect was most pronounced for the first two conditions, when the stimuli on trials n−1 and n were identical or required the same naming response. Negative priming was found in the SUP-SAY condition.
stimulus in each critical pair was further analyzed and will be referred to here as a critical stimulus. The practice blocks were not included in the analysis.

Data Analysis

Median RTs for responses for every condition were computed for each subject. Only correct responses were included in the RT analyses. Medians were used instead of means to reduce the influence of outlier responses, which can exaggerate group differences, especially in patient studies. Analysis of variance procedures for repeated measures were used to analyze the data in a 3 × 3 × 3 mixed ANOVA with group as a between-subjects factor (hospitalized vs. outpatients vs. controls) and word type (congruent vs. incongruent vs. neutral) and priming (color–color: positive; word–color: negative; and unrelated) as within-subjects variables. Further analyses were planned to examine the effect of error responses on within- and between-trial effects. Although analyses were carried out across individual word types, planned comparisons of facilitation (neutral minus congruent RT), interference (incongruent minus neutral) negative priming (word–color minus unrelated), and positive priming (unrelated minus color–color) were also performed.

RESULTS

Analyses revealed main effects of group \(F(2,36) = 6.72, MSe = 148,139, p < .05\), word type \(F(2,72) = 124.4, MSe = 4,661, p < .001\) and priming \(F(2,72) = 36.65, MSe = 12,309, p < .001\) as well as an interaction between Word Type × Priming \(F(4,144) = 7.9, MSe = 3,840, p < .001\]. Controls had faster overall reaction times (663 ms) than either the hospitalized patients \(F(1,26) = 16.9, MSe = 11,639, p < .001\] or the outpatients \(F(1,25) = 6.5, MSe = 49,495, p < .05\]. The overall reaction times of the hospitalized patients and the outpatients did not differ significantly from each other \((F < 1)\). In addition, there was a three-way interaction between Group × Word Type × Priming \(F(8,144) = 2.58, MSe = 3,846, p < .05\]. The triple interaction led us to analyze the between-trial effects and the within-trial effects separately.

Between-Trial Effects

Analyses revealed that the groups differed significantly on negative priming \(F(2,36) = 6.09, MSe = 4,587, p = .006; +42 ms, −28 ms, and −22 ms, for the inpatients, outpatients, and controls, respectively\]. Negative priming effects differed significantly between inpatients and outpatients \(F(1,21) = 6.21, MSe = 6,980, p = .02\] as well as between inpatients and controls \(F(1,26) = 8.87, MSe = 1,566, p = .006\] in contrast, negative priming effects did not differ significantly between the outpatients and controls \((F < 1)\). Hospitalized patients showed no NP and in fact NP effects were reversed (see Figure 1). Although there was no interaction between Group × Positive Priming \(F(2,36) = 1.11, MSe = 15,789, p = .34\], further comparisons revealed that the differences in positive priming between the inpatients (+122 ms) and the controls (+77 ms) approached significance \(F(1,26) = 4.1, MSe = 5,003, p = .05\]. In contrast, the positive priming of the outpatients (+130 ms) did not differ from either the inpatients \((F < 1)\) or controls \(F(1,25) = 1.48, MSe = 19,098, p = .05\]; see Table 4].

To take into account the difference in RTs between the schizophrenia patients and controls, we also computed a percent negative prime score as follows: 

\[% \text{Negative Prime Score} = RT (\text{control trials}) \times 100\]

An analysis of variance showed that the three groups differed significantly on their percentage in negative prime scores \(F(2,36) = 4.727, MSe = 35,942, p < .02\]. The state hospital inpatients showed a 4.1% decrease in the NP reaction time score \((i.e., \text{absence of negative priming})\). In contrast, the outpatients showed 3.01% increase that did not differ statistically from the 1.51% increase shown by the matched control subjects. Hospitalized inpatients exhibited less percentage in negative priming compared to the outpatients \(F(1,21) = 6.08, MSe = 48.20, p = .02\] and controls \(F(1,26) = 6.41, MSe = 34.02, p = .01\]. Outpatients did not differ from the controls in percent negative priming \((F < 1);\] see Table 5].

Within-Trial Effects

Interference effects did not differ between groups when analyses were collapsed across Stroop sequences \((F < 1);\]
see Figure 2). Planned analyses revealed that interference effects were reduced across groups in color–color sequences (69 ms) relative to word–color sequences [112 ms; $F(1,36) = 6.62, MSe = 2,755, p < .05$] and unrelated sequences [164 ms; $F(1,36) = 18.5, MSe = 4,747, p < .001$]. We then examined interference effects as a function of sequence and group. Within-trial Stroop effects did not differ among the three groups in the word–color (negative priming) sequence [$F(2,72) = 1.72, p > .05$] and the color–color sequence ($F < 1$), but there was a significant Group × Word Type interaction in the unrelated sequence [$F(4,72) = 2.5, p < .05$]. Although facilitation effects did not differ between groups in the unrelated sequences [$F(2,36) = 1.95, p > .05$], the hospitalized patients exhibited significantly greater interference on unrelated sequences (201 ms) compared to controls [126 ms; $F(1,26) = 7.6, p < .05$].

### Error Analyses

Errors were analyzed within the same design. Analyses revealed a main effect of word type [$F(2,70) = 30.6, p < .05$] and priming [$F(2,70) = 38.94, p < .001$]. Outpatients with schizophrenia produced a larger number of errors (7%) compared to both inpatients (4%) and controls (5%), [$F(2,36) = 3.2, p = .05$], although the magnitude of the difference was

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### Table 4. Median reaction times for between-trial and within-trial conditions across groups (in milliseconds)

<table>
<thead>
<tr>
<th>Group</th>
<th>Word–color</th>
<th>Unrelated</th>
<th>Color–color</th>
<th>% errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>649 (±106)</td>
<td>656 (±99)</td>
<td>577 (±112)</td>
<td>.01</td>
</tr>
<tr>
<td>Incongruent</td>
<td>798 (±82)</td>
<td>758 (±94)</td>
<td>655 (±99)</td>
<td>.09</td>
</tr>
<tr>
<td>Neutral</td>
<td>662 (±98)</td>
<td>632 (±83)</td>
<td>584 (±97)</td>
<td>.03</td>
</tr>
<tr>
<td>Interference</td>
<td>136</td>
<td>126</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>Facilitation</td>
<td></td>
<td>−24</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Error data</td>
<td>.05</td>
<td>.04</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>Inpatients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>789 (±107)</td>
<td>795 (±123)</td>
<td>730 (±125)</td>
<td>.03</td>
</tr>
<tr>
<td>Incongruent</td>
<td>923 (±148)</td>
<td>1034 (±206)</td>
<td>812 (±107)</td>
<td>.08</td>
</tr>
<tr>
<td>Neutral</td>
<td>823 (±135)</td>
<td>833 (±176)</td>
<td>755 (±97)</td>
<td>.03</td>
</tr>
<tr>
<td>Interference</td>
<td>100</td>
<td>201</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Facilitation</td>
<td>34</td>
<td>38</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Error data</td>
<td>.06</td>
<td>.04</td>
<td>.06</td>
<td></td>
</tr>
<tr>
<td>Outpatients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent</td>
<td>765 (±171)</td>
<td>799 (±238)</td>
<td>669 (±105)</td>
<td>.05</td>
</tr>
<tr>
<td>Incongruent</td>
<td>944 (±269)</td>
<td>928 (±322)</td>
<td>748 (±122)</td>
<td>.12</td>
</tr>
<tr>
<td>Neutral</td>
<td>853 (±261)</td>
<td>751 (±124)</td>
<td>669 (±99)</td>
<td>.05</td>
</tr>
<tr>
<td>Interference</td>
<td>91</td>
<td>177*</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Facilitation</td>
<td>88</td>
<td>−48</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Error data</td>
<td>.08</td>
<td>.08</td>
<td>.06</td>
<td></td>
</tr>
</tbody>
</table>

*One outpatient exhibited Stroop interference in excess of 500 ms. When his data were removed from the analysis the interference score for the outpatients was 107 ms.

* $M$ (± SD).

### Table 5. Negative priming effects in schizophrenia patients and control subjects

<table>
<thead>
<tr>
<th>Reaction times (ms)</th>
<th>Inpatients (n = 12)</th>
<th>Outpatients (n = 11)</th>
<th>Controls (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrelated</td>
<td>888 (+198)</td>
<td>826 (+246)</td>
<td>682 (+106)</td>
</tr>
<tr>
<td>Word–color</td>
<td>846 (+139)</td>
<td>854 (+242)</td>
<td>704 (+116)</td>
</tr>
<tr>
<td>Negative priming</td>
<td>+42</td>
<td>−28</td>
<td>−22</td>
</tr>
<tr>
<td>Negative priming %</td>
<td>4.13 (7.40)</td>
<td>3.02 (6.39)</td>
<td>1.51 (4.33)</td>
</tr>
</tbody>
</table>

* One outpatient exhibited Stroop interference in excess of 500 ms. When his data were removed from the analysis the interference score for the outpatients was 107 ms.

### Fig. 2. Stroop interference was calculated by subtracting the RT of neutral trials from the RT of incongruent trials. Facilitation was calculated by subtracting the RT of congruent trials from the RT of neutral trials.
small. Additional comparisons revealed that all three groups made significantly more errors in the incongruent condition (9%) than in either the neutral condition (3%) or the congruent condition (3%). In addition, all groups made more errors on word–color sequences (6%) than on unrelated sequences [5%; \( F(1,36) = 5.8, p < .05 \)] and color–color sequences [4%; \( F(1,36) = 9.8, p < .01 \)]. Error rates also differed significantly between the color–color and unrelated sequences \([F(1,36) = 3.9, p = .05]\). Mean error rate for each group is reported in Table 3.

**Symptomatology**

Another variable that differed between the two patient groups was symptomatology. The hospitalized patients had a significantly higher rate of positive symptoms than the outpatients \([F(1,21) = 9.05, p < .01]\). Negative symptoms did not differ significantly between the two groups \([F(1,21) = 1.8, p > .05]\). Correlational analyses of symptomatology and NP effects between each group of patients were small (inpatients SAPS/NP = +.34; SANS/NP = −.19; outpatients SAPS/NP = −.11; SANS/NP = −.14). We performed paired t tests to test if the regression slopes for the two patient groups differed. The results showed that the correlations between SAPS ratings and negative priming for the two patient groups differed significantly \([t(19) = 4.02, p < .001]\). These findings suggest a stronger positive relationship between positive symptoms and negative priming for the inpatients compared to the outpatients. Given that the symptom ratings of the hospitalized inpatients are much higher than the outpatients, the findings might also suggest that medication affects both cognition and symptomatology to a lesser degree in the more chronically ill state hospital patients than in the outpatients. Negative priming differed significantly between the outpatients and inpatients \((p = .02)\), however, when the data were analyzed with chronicity as a covariate, group differences in negative priming disappeared \([F = 0.544, p = .47]\).

**DISCUSSION**

**Priming**

The hospitalized patients showed positive priming in NP sequences, which demonstrates that the irrelevant stimulus on Trial \(n − 1\) was processed, but the inhibitory tag attached to the irrelevant word faded across trials and turned into a positive prime for Trial \(n\). Our previous studies on negative priming and schizophrenia have shown that medication-withdrawn outpatient schizophrenia patients fail to exhibit negative priming, but the restoration of medication therapy normalizes negative priming (Salo et al., 1997). These current findings replicate our previous work in that the medicated outpatients in this study also exhibited normal NP priming. In contrast, 10 of the 12 more severely ill hospitalized patients failed to show normal NP and exhibited abnormal facilitation on negative priming sequences, much as the unmedicated outpatients in our previous studies (Salo et al., 1996, 1997). This abnormal pattern of inhibitory priming occurred in the hospitalized patients even though they were receiving similar doses of like antipsychotic medications as the outpatients and were matched on baseline processing speed. A similar finding was reported by Park et al. (1996) using a spatial negative priming paradigm. Park et al. found that a group of relatively stable schizophrenia outpatients showed significant spatial NP compared to a more acutely ill group of inpatients that failed to exhibit significant spatial inhibition. The priming results reported in the current study and the study by Park et al. support the importance of examining severity of illness and symptomatology when interpreting priming results in schizophrenia patients.

**Within–Trial Effects**

The design of this experiment allowed for the further analysis of between and within trial effects and the data revealed a significant interaction between Priming Sequences × Within-Trial Word Type effects. This interaction was produced by the positive priming and not by the negative priming across all groups. All groups exhibited reduced interference in the color–color positive priming sequence. The repetition of the color stimulus increased the ability to effectively inhibit the irrelevant word on the next trial in all subjects. The triple interaction between Group × Word Type × Priming Sequence is less clear. In most Stroop studies the interaction of sequences on Stroop effects is not examined. One strength of the orthogonal design employed in this study is that we were able to separately analyze Stroop interference and facilitation effects as a function of whether they are embedded in priming or neutral sequences. When sequential conditions were analyzed separately, different patterns of interference emerged for the three groups. Unrelated sequences (i.e., the word YELLOW in red following the word BLUE in green), created increased within-trial interference in the hospitalized schizophrenia patients \((inpatients = 201 \text{ ms}; \text{outpatients} = 177 \text{ ms})\) compared to controls \((126 \text{ ms})\). This may suggest that the appearance of a novel stimulus following sequences in which either the word color or word name was repeated causes the inpatients to slow their responses. The error rates, however, did not differ between the two groups on the same sequence of trials \((F < 1)\).

**Illness Severity**

Both groups of schizophrenia patients in this study were matched for age and educational level, but the hospitalized patients had nearly double the length of illness as the outpatients \((20 \text{ years} \text{ vs.} \ 12 \text{ years})\), earlier age of first hospitalization \((20 \text{ years of age} \ 27 \text{ years of age})\) and a higher rate of positive symptomatology as measured by the SAPS rating scale. Different patterns of priming have also been reported in schizophrenia patients as a function of length of illness (Maher et al., 1996). Patients with a shorter length
of illness showed normal priming on a lexical decision task compared to patients with a longer length of illness. Although the lexical decision paradigm used in the Maher et al. study differed from ours, a pattern of abnormal priming in the patients with longer duration of illness is consistent with the findings reported in this study. This convergence of findings across paradigms suggests that the processing of related stimuli across trial pairs appears to be abnormal in schizophrenia patients with a longer duration of illness.

Medication

One could argue that medication accounted for the group differences in our study. It is reasonable to expect that hospitalized schizophrenia patients would be receiving higher doses of antipsychotic medication than patients in an outpatient setting. A review of the medication records does not support this hypothesis as antipsychotic medication types and dosages are quite similar between the two groups (see Table 2). The main treatment difference was that 4 of the hospitalized patients were also receiving moderate dosages of valproic acid (an anticonvulsant) and none of the outpatients were receiving anticonvulsants. Although valproic acid has been shown to cause motor slowing (Vermeulen & Aldenkamp, 1995), no significant effects have been documented in relation to cognition (Aldenkamp et al., 2000). The NP pattern of the 4 patients on anticonvulsants in this study was similar to the pattern of the hospitalized patients not taking anticonvulsants. Thus a review of current pharmaceutical treatment in the schizophrenia patients does not suggest that medication differences separate the two patient groups. It is possible, however, that long-term medication intake might have a deleterious effect on attentional processing.

General Slowing

Importantly, baseline reaction times did not differ significantly between the two groups of schizophrenia patients ($F < 1$) demonstrating that overall slowing is not a contributing factor. Although the inpatients did not differ significantly from the outpatients on overall RT their priming patterns were distinctly different. The model of a general deficit does not contain any underlying mechanism for explaining better or faster performance in groups of schizophrenia patients who are matched on baseline RT.

CONCLUSION

Negative priming measures are sensitive measures of sustained inhibitory functioning, and abnormal NP effects have been reported in many patient groups (Beech & Claridge, 1987; Beech et al., 1989; Laplante et al., 1992; MacDonald et al., 1999; Park et al., 1996; Salo et al., 1996; Watson & Tipper, 1997). These findings are also consistent with those reported in the latent inhibition (LI) literature (see Lubow & Gewirtz, 1995, for review). In the LI paradigm previously exposed stimuli subsequently become the signal to which the subjects must respond, similar to NP tasks. Deficits in latent inhibition have been reported in high schizophrenic patients (Claridge & Brooks, 1984) as well as acutely ill schizophrenia patients (Baruch et al., 1988a; Gray et al., 1992). As the individuals in the Baruch et al. study were characterized as “very symptomatic” at the time of testing, those findings are consistent with the data reported in this current study and another recently published report linking abnormal NP effects to the level of symptomatology (Park et al., 1996; Peters et al., 2000).

Since both patient groups in this study were medicated on similar antipsychotic types and dosages, the effects of medication reported in earlier studies do not appear to have the same strengthening effect on inhibitory processes in chronic state hospital patients as they do in outpatient schizophrenia patients (Salo et al., 1997). Group differences in age at first hospitalization, chronicity and symptom severity however need further exploration. The continued study of cognitive processes that are normally sustained over time (e.g., priming processes) in schizophrenia patients is an important area to pursue and may lead to a better understanding of how attentional deficits are linked to underlying cognitive dysfunction in neuropsychiatric disorders.

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REFERENCES


