Nonconscious and conscious color priming in schizophrenia

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A B S T R A C T

Deficits in visual processing are well established in schizophrenia. However, there is conflicting evidence about whether these deficits start before the formation of percepts because visual processing studies in schizophrenia have typically examined the processing of consciously registered stimuli. In this study, we used nonconscious color priming to evaluate the very early visual processing stages in schizophrenia. Nonconscious and conscious color priming was assessed in 148 schizophrenia patients and 54 healthy control subjects. In both conditions, subjects identified the color of a ring preceded by a disk (prime) in the same color (congruent) or a different color (incongruent). The ring rendered the disk invisible in the nonconscious condition (SOA of 62.5 ms) or did not mask the disk (SOA of 200 ms) in the conscious condition. Schizophrenia patients exhibited a color priming effect (longer reaction times in the incongruent vs. congruent trials) that was similar to healthy controls in both the nonconscious and conscious priming conditions. Healthy controls had a significantly larger priming effect in the nonconscious vs. conscious condition, but patients did not show a significant difference in priming effects between the two conditions. Our results indicate that schizophrenia patients do not have deficits at the nonconscious, pre-perceptual stages of visual processing, suggesting that the feed forward sweep of information processing (from retina to V1) might be intact in schizophrenia. These results imply that the well-documented visual processing deficits in this illness likely occur at later, percept-dependent stages of processing.

1. Introduction

Patients with schizophrenia exhibit a wide range of cognitive and perceptual impairments, including deficits in basic visual processing, such as visual motion perception (e.g., Chen et al., 1999) and backward masking (e.g., Butler et al., 2002; Green et al., 1994; Rund et al., 2004). These early-stage sensory processing deficits have consequences for the downstream processing of higher-level social cognitive tasks and functioning (Brittain et al., 2010; Norton et al., 2009; Rassovsky et al., 2011; Sergi and Green, 2002). Studies of visual backward masking in schizophrenia have found highly replicable deficits at both early and late perceptual stages of processing (Green et al., 2011a). What remains unclear is how early in the visual processing stream these deficits commence.

Studies have been inconsistent regarding whether deficits exist at the earliest processing stages. There is some evidence of deficits occurring as early as input at the retina. For example, a study using electrorretinography (Balogh et al., 2008) reported that schizophrenia patients exhibited decreased a-wave amplitude (a measure of photoreceptor function) while symptomatic, but not when symptoms were controlled. Studies have found a reduction in contrast sensitivity in schizophrenia (Keri et al., 2002) and this reduction was related to backward masking dysfunction (Slaghuis, 2004).

On the other hand, other studies of visual processing in schizophrenia have demonstrated intact processing at the earliest visual stages. For example, patients and controls were comparable in the amount of contrast needed for target detection in a psychophysical procedure that was part of a masking task (Rassovsky et al., 2005). In addition, two recent studies have reported normal visible persistence in schizophrenia (Green et al., 2011b; Hahn et al., 2011).

The goal of the present study is to evaluate whether patients with schizophrenia exhibit impairments at the earliest, pre-perceptual stage of information processing. One way to assess
very early visual processing (i.e., before the initial formation of the percept) is through a color priming paradigm. In one version of this task, a disk serves as a prime, and a ring that surrounds the disk appears slightly later. Subjects are asked to identify the color of the later-occurring ring. The disk and ring can be the same or different color. When the colors of the disk and ring are incongruent, it takes longer to identify the color of the ring than if the colors are congruent; referred to as a color priming effect. When the interval between the disk and the ring is short, the ring effectively masks the disk so that it is not consciously perceived. Notably, color priming occurs even if the disk is not consciously registered and this form of nonconscious color priming is thought to be due to pre-perceptual, stimulus-dependent levels of visual processing (Breitmeyer et al., 2004a, 2004b). Specifically, it involves the early feed forward sweep of information processing starting at the retina through V1 (Lamme and Roelfsema, 2000) to higher levels in the cortical object recognition pathway (VanRullen, 2007; VanRullen and Thorpe, 2002). When the disk is visible (unmasked), it produces priming at multiple stages, including later, percept-dependent levels of cortical processing (Breitmeyer et al., 2007).

In the current study, we used color priming (Breitmeyer et al., 2004b) in a large sample of schizophrenia patients and healthy controls. We examined both conscious and nonconscious priming, and the focus was on nonconscious color priming because it provides a way to isolate the feed forward sweep. However, to our knowledge, this paradigm has not been used previously in schizophrenia research. If patients show a similar nonconscious priming effect (longer reaction times in the incongruent vs. congruent condition) to healthy controls, it would support the idea that they have intact visual processing at the very early feed forward stage before the formation of percepts.

2. Method

2.1. Participants

An initial sample of 181 patients with schizophrenia and 85 healthy comparison subjects participated in the study. Due to the exclusion criteria described below, data from 148 patients and 54 controls were used in the analyses. All participants were between the ages of 18 and 60, had an IQ over 70, were substance-free for any lifetime psychotic disorder, bipolar disorder, recurrent depression, substance dependence, paranoid, schizotypal, or schizoid personality disorder, or if they reported a history of psychotic disorder among their first-degree relatives. All participants had the capacity to give informed consent and provided written informed consent after all procedures were explained in accordance with procedures approved by the Institutional Review Boards at the University of California, Los Angeles and VAGLAHS.

2.2. Clinical ratings

Psychiatric symptoms during the month prior to testing were rated using the 24-item version of the Brief Psychiatric Rating Scale (BPRS; Lukoff et al., 1986) and the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984) by a trained rater. We report the “positive symptoms” and “depression/anxiety” factors, as well as the total score for the BPRS (Kopelowicz et al., 2008); for the SANS we report the global scores for affective flattening, alogia, anhedonia, and avolition (Table 1). All clinical assessments were conducted by interviewers trained to reliability through the Treatment Unit of the Department of Veterans Affairs VISN 22 Mental Illness Research, Education, and Clinical Center (MIRECC) based on previously reported procedures (Ventura et al., 1993, 1998).

2.3. Color priming task

The experiment was conducted on a cathode ray tube monitor with a refresh rate of 160 Hz (6.25 ms per screen sweep). Participants were seated 100 cm from the computer monitor in a dimly lit room. All stimuli were presented using E-Prime 1.1 (Psychological Software Tools, Pittsburgh, PA).

The procedure involved three different tasks, presented in separate blocks, in which the participant either identified the color of a disk or the color of a ring that surrounded the disk. The color of the disk and ring could be either green or blue. Participants were asked to quickly and accurately make their choice by using either the left or right button of a computer mouse for green or blue stimuli, respectively. The disk had a diameter of 8 mm (0.46 degrees of visual angle); the surrounding ring had an inner and outer diameter of 8 and 18 mm, respectively (0.46 and 1.03 degrees of visual angle). The disks and rings were either a desaturated green (red—blue—green [RGB] values = 202, 218, 254) or blue (RGB = 198, 254, 241) and were presented on a gray background (RGB = 127, 127, 127) within a fixation mark that consisted of four bars (2 cm for each bar) arranged in a notional cross (Breitmeyer et al., 2004b). The luminance of the gray background, green and blue stimuli was 12.6, 13.4, and 14.3 cd/m², respectively. The disks were presented for 12.5 ms and the rings for 25.0 ms, with different stimulus onset asynchronies (SOAs) depending on the task. Examples of the stimuli were shown until participants were comfortable discriminating between the two colors. Fig. 1 shows examples of the stimuli.

The first task was a validity task in which participants were asked to identify the color of the disk that preceded the ring. This task was given to determine if the ring effectively masked the disk for each participant. Twelve practice trials were given with

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic and clinical characteristics.</th>
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<tbody>
<tr>
<td></td>
<td>Healthy controls (N = 54)</td>
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<tr>
<td>Age (mean/SD)</td>
<td>41.31 (9.84)</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>72.22%</td>
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<tr>
<td>Personal education (mean/SD)</td>
<td>14.32 (1.74)</td>
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<tr>
<td>Parental education (mean/SD)</td>
<td>13.23 (2.39)</td>
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<tr>
<td>BPRS total for 24 items (mean/SD)</td>
<td>–</td>
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<tr>
<td>BPRS positive symptom (mean/SD)</td>
<td>–</td>
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<tr>
<td>BPRS depression/anxiety (mean/SD)</td>
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<tr>
<td>SANS affective flatening (mean/SD)</td>
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<td>SANS anhedonia (mean/SD)</td>
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BPRS = Brief Psychiatric Rating Scale; SANS = Scale for the Assessment of Negative Symptoms.

* Significant difference in age and personal education between healthy controls and patients, p < 0.001.
a relatively long SOA of 150 ms to familiarize participants with the task and to ensure they could differentiate between the colors of the disk at the duration they were shown. At this SOA, the ring did not mask the disk. After practice, 56 trials were given in which the ring followed the disk at an SOA of 62.5 ms, and participants were again asked to identify the color of the disk. The inter-trial interval varied with the participant’s reaction time, i.e., presentation of the next trial began 500 ms after the participant made a response. This validity task was used to exclude subjects who were not effectively masked at the 62.5 ms SOA. Specifically, we excluded participants who correctly identified the color of the disk in at least 37 of the 56 trials ($p < 0.01$ based on the binomial distribution). The SOA was selected based on pilot data that showed most subjects were masked at this interval.

Two other tasks, nonconscious and conscious priming, were administered in counterbalanced order across participants. For both tasks, the disk was presented before the ring, and participants identified the color of the ring and ignored the color of the disk. For nonconscious color priming, the SOA between the disk and the ring was 62.5 ms, which is suitable for masking. For conscious color priming, the SOA was 200 ms, which is too long for masking to occur. The color of the disk and ring were either congruent (both blue or both green) or incongruent (one blue and one green). There were 80 trials in each task (20 for each combination of disk-ring color: blue-blue, green-green, blue-green, green-blue). Only reaction times to correct responses to the color of the ring were analyzed.

For the nonconscious and conscious priming tasks, an incongruency score was calculated by subtracting the reaction time (RT) to the congruent from the RT to the incongruent condition. A score above 0 indicated a longer RT when the colors of the disk and ring were incongruent vs. congruent. As an additional check to make sure subjects could perform the task, we excluded from the analyses participants who had poor accuracy in the conscious color priming condition (i.e., scores < 48 out of 80 correct; $p < 0.01$ based on the binomial distribution). We considered performance at that level to be invalid.

2.4. Data analysis

For demographic variables, independent samples $t$-tests and chi-square tests were used to assess group differences for continuous and categorical variables, respectively. A $2 \times 2$ repeated measures analysis of variance (rmANOVA) with congruency (congruent vs. incongruent) as the within-subject factor and group as the between-subject factor was conducted to examine raw reaction time scores in the nonconscious condition. The same analysis was repeated for the conscious condition.

We also conducted a $2 \times 2$ rmANOVA with condition (conscious vs. nonconscious) as the within-subject factor and group as the between-subject factor to investigate group differences in priming (incongruency scores). Significant interactions were decomposed using paired samples $t$-tests within each group. Finally, we performed Pearson’s correlations between the incongruency scores and symptom ratings within the patient group.

3. Results

3.1. Exclusion for invalid performance

First, in the validity condition, we excluded 19 out of 181 (10.5%) patients and 30 out of 85 (35.3%) controls who scored above the cut off, reflecting a lack of masking.

Second, in the conscious priming condition, we excluded an additional 13 patients (7.2%) and no controls for poor performance as defined above. Lastly, we excluded one control and one patient who were outliers in terms of their incongruency scores (>3 SDs above the mean and >2 SDs relative to the next highest score). Therefore, the final sample sizes used in the analyses included 148 patients and 54 controls.

3.2. Demographic and clinical characteristics

Demographic and symptom ratings for the subjects in the final sample are shown in Table 1. There was a significant group difference in age ($t_{[199]} = 3.94, p < 0.001$), with healthy controls being significantly younger than patients. Due to this age difference, we examined the correlation between age and each dependent variable. Age was not significantly associated with any of the variables of interest in either group, and was not considered in the analyses below. Groups did not differ in gender or parental education. The groups differed on personal education ($t_{[198]} = 5.14, p < 0.001$), with patients having less education than healthy controls. We attempted to match the groups on parental, not personal, education. Patients exhibited mild to moderate levels of symptomatology.

3.3. Accuracy results

After excluding subjects who did not exhibit masking, the mean number of trials in which the disk color was identified (out of a possible 56 trials) was 30.93 (2.96) for the healthy control group and 29.91 (3.18) for the patient group, with a range of 24–36 for both groups. Although this difference was significant at this sample size ($t_{[200]} = -2.05, p = 0.04$), healthy controls correctly identified one more trial, on average, than patients. We also examined the number of correct responses to the color of the ring (out of a possible 80 trials per task) for each of the color priming tasks. Independent samples $t$-tests revealed no significant differences between patients and healthy controls in the nonconscious condition ($t_{[200]} = -1.67, p = 0.10$), 76.5 (4.2) and 77.6 (2.7), respectively. However, healthy controls had a significantly larger number of correct trials relative to patients in the conscious condition ($t_{[200]} = -3.05, p = 0.003$), 78.2 (1.7) and 75.7 (6.1), respectively.
3.4. Nonconscious color priming

The $2 \times 2$ ANOVA with the raw reaction time data revealed significant main effects of congruency ($F[1, 200] = 116.98, p < 0.001$) and group ($F[1, 200] = 13.19, p < 0.001$). The main effect of congruency was due to longer RTs in the incongruent vs. congruent condition, 653 (246) and 583 (256) ms, respectively. The main effect of group was due to longer RTs in the patients vs. controls, 681 (218) and 555 (218) ms, respectively. The congruency $\times$ group interaction was not significant ($F[1, 200] = 2.53, p = 0.11$). These results are shown in Fig. 2.

3.5. Conscious color priming

The $2 \times 2$ ANOVA with the raw reaction time data revealed significant main effects of congruency ($F[1, 200] = 65.38, p < 0.001$) and group ($F[1, 200] = 22.60, p < 0.001$). Similar to the results for the nonconscious condition, the main effect of congruency was due to longer RTs in the incongruent vs. congruent condition, 702 (260) and 642 (250) ms, respectively. The main effect of group was due to longer RTs in the patients vs. controls, 756 (221) and 589 (221) ms, respectively. The congruency $\times$ group interaction was not significant ($F[1, 200] = 2.21, p = 0.14$). These results are shown in Fig. 3.

3.6. Incongruency scores

The $2 \times 2$ ANOVA with the incongruency scores revealed no significant main effects of consciousness ($F[1, 200] = 1.07, p = 0.30$) or group ($F[1, 200] = 0.005, p = 0.94$). However, the consciousness $\times$ group interaction was significant ($F[1, 200] = 4.58, p = 0.03$). Follow-up paired $t$-tests revealed that the interaction was due to healthy controls having a significantly larger priming effect in the nonconscious vs. conscious condition, 81 (46) and 49 (71) ms, respectively ($t[53] = 2.72, p = 0.01$). Patients showed the opposite pattern: a non-significantly larger priming effect in the conscious vs. nonconscious condition, 71 (100) and 60 (91) ms, respectively ($t[147] = -0.98, p = 0.33$). These results are shown in Fig. 4.

3.7. Correlations between symptoms and behavioral performance

We did not find any significant correlations at the $p < 0.01$ level between the incongruency scores (for the conscious and nonconscious conditions) and the symptom ratings, specifically BPRS Total, BPRS positive symptoms, BPRS depression/anxiety, SANS affective flattening, SANS alogia, SANS anhedonia, and SANS avolition.

4. Discussion

In this paper, we examined early, pre-perceptual stages of visual information processing using a behavioral color priming paradigm in a large sample of patients with schizophrenia compared to healthy controls. We focused on assessing the very early feed forward visual processing stage before the formation of percepts. In nonconscious color priming, we found evidence of priming (i.e., longer reaction times in the incongruent vs. congruent trials) to roughly the same extent in both groups. Given this finding, our results suggest that the stimulus-dependent, feed forward sweep of information processing might be intact in schizophrenia. That is,
feed forward connections that convey information from the retina to lateral geniculate nucleus (LGN) to primary visual cortex (V1) do not seem to be disrupted in schizophrenia in this task. These results imply that the well-documented visual processing deficits in schizophrenia are likely due to abnormalities beyond the feed forward sweep. They may occur at later, percept-dependent, cortico-cortical stages of processing.

Regarding the conscious condition, results were similar to the nonconscious condition: Patients showed a conscious color priming effect similar to healthy controls. The neural processes underlying the intact priming effect in this condition is harder to interpret because conscious priming could involve multiple mechanisms, including feed forward, feedback or re-entrant activity from higher visual cortical areas (e.g., V4), as well as strategic influences.

Our findings also revealed that healthy controls had a significantly larger priming effect in the nonconscious vs. conscious condition; a reversed pattern (non-significantly larger priming in conscious vs. nonconscious condition) was observed in patients. Given that several prior studies in non-clinical samples (Tapia et al., 2010) showed stronger priming effects when primes were consciously than nonconsciously processed, the pattern in our controls was not expected. However, the finding is consistent with a previous report of non-clinical subjects showing no significant priming effects with consciously vs. nonconsciously processed stimuli (Ro et al., 2009). The absence or weakness of conscious priming effects may have been due to conscious control processes that conflict with and override automatic response tendencies (Morsella, 2005). It is possible that, in subjects who were visually aware of the prime, a conscious response strategy was adopted that produced somewhat faster responses in the incongruent conditions (Ro et al., 2009). Hence, the finding in patients of a greater priming in the conscious as compared to nonconscious condition, reflecting the more commonly-reported finding (Tapia and Breitmeyer, 2011; Tapia et al., 2010, 2011), might suggest that schizophrenia patients did not adopt conscious response strategies used by controls in this study to override automatic response tendencies.

Our results have implications in terms of visual pathways. Visual information is conveyed in two cortical processing streams; the ventral and dorsal cortical pathways that are dominated by parvocellular (P) and magnocellular (M) input, respectively. These pathways have differential properties; for example, M cells are not highly responsive to chromatic (color) contrast, while P cells are (Merigan and Maunsell, 1993). Because the primes and probes in the current study were luminance changes on an intermediate neutral background, they likely would have activated both M and P channels. However, because the color priming task relied specifically on the processing of chromatic information, the processing in the color-selective P channels was critically important. The color-blind M pathway is not relevant to the current task. Thus, our finding of normal nonconscious color priming in schizophrenia patients indicates intact P pathway function, consistent with a number of studies demonstrating M pathway dysfunction with relatively intact P processing in schizophrenia (Cadenhead et al., 1998; Green et al., 1994; Kim et al., 2006; Martinez et al., 2008; Schechter et al., 2003), although see others for exceptions (Keri et al., 2002; Slagman, 1998). In addition, two electrophysiological studies with schizophrenia patients specifically manipulated chromatic stimuli to differentially activate the M and P pathways (Butler et al., 2001; Schechter et al., 2005). In both studies, schizophrenia patients showed impairments in conditions that biased processing toward the M pathway (i.e., achromatic stimuli) but not in conditions emphasizing the P pathway (i.e., chromatic stimuli).

Finally, our findings can be viewed within a prominent theory on the pathophysiology of schizophrenia: abnormalities in the gamma amino butyric acid (GABA) system. GABA is involved in the modulation of visual processing and GABA interneuron abnormalities are present in the visual cortex in schizophrenia (Hashimoto et al., 2008). It has been proposed that these abnormalities might become more prominent as one moves up the processing hierarchy from V1 to the lateral occipital complex (Green et al., 2011a). That is, these abnormalities might not be very noticeable in the early feed forward processing stages (at the level of the LGN or V1) because GABA modulated lateral inhibition is not needed for the simple registration of brightness, color, line orientation, motion, and depth cues. However, the importance of GABA increases with higher-level visual processes where GABA inhibition is necessary for the processing of more complex visual stimuli, as well as contour integration. Hence, the GABA theory of schizophrenia could explain why a very early visual processing stage (i.e., the feed forward sweep) might be intact, even though later stages involved with object detection might be dysfunctional.

The study has several limitations. First, the majority of our patient sample was receiving antipsychotic medications at the time of testing which raises the question of medication effects. However, potential effects of medication on the present results are unlikely given the lack of group differences in priming effects. Moreover, previous studies of visual masking in schizophrenia found no effects of antipsychotic medications (Butler et al., 1996; Green et al., 1999). Second, our sample consisted of chronic patients and therefore would not be representative of recent-onset schizophrenia. Third, we did not formally test for color vision, which could have potentially affected our results. Nevertheless, both groups showed over 94% accuracy in identifying the color of the ring during the color priming tasks, suggesting that color vision dysfunction did not influence the results. Despite these limitations, results from this study are consistent with a growing literature on well-defined perceptual and cognitive processes that are intact in schizophrenia (Gold et al., 2009; Horan et al., 2012; Lee et al., 2012).

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Contributors

MFG, JKW, and BGB designed the study. CJ and JKW analyzed the data. All authors interpreted the findings. CJ, JKW, and MFG wrote the first draft of the manuscript with BGB providing feedback and edits. All authors have contributed to and approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest arising from this manuscript.

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