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Title

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Permalink

https://escholarship.org/uc/item/1z95m731

Journal

Journal of Psychopathology and Clinical Science, 130(6)

ISSN

2769-7541

Authors

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Publication Date

2021-08-01

DOI

10.1037/abn0000683

Peer reviewed



HHS Public Access

J Abnorm Psychol. Author manuscript; available in PMC 2022 August 01.

Published in final edited form as:

Author manuscript

J Abnorm Psychol. 2021 August; 130(6): 651–664. doi:10.1037/abn0000683.

Oculomotor Inhibition and Location Priming in Schizophrenia

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Abstract

Schizophrenia is widely thought to involve elevated distractibility, which may reflect a general impairment in top-down inhibitory processes. Schizophrenia also appears to involve increased priming of previously performed actions. Here, we used a highly refined eye tracking paradigm that makes it possible to concurrently assess distractibility, inhibition, and priming. In both healthy control subjects (HCS, N=41) and people with schizophrenia (PSZ, N=46), we found that initial saccades were actually *less* likely to be directed toward a salient "singleton" distractor than toward less salient distractors, reflecting top-down suppression of the singleton. Remarkably, this oculomotor suppression effect was as strong or stronger in PSZ than in HCS, indicating intact inhibitory control. In addition, saccades were frequently directed to the location of the previous-trial target in both groups, but this priming effect was much stronger in PSZ than in HCS. Indeed, PSZ directed gaze towards the location of the previous-trial target as often as they directed gaze to the location of the current-trial target. These results demonstrate that—at least in the context of visual search—PSZ are no more distractable than HCS and are fully capable of inhibiting salient-but-irrelevant stimuli. However, PSZ do exhibit exaggerated priming, focusing on recently attended locations even when this is not beneficial for goal attainment.

GENERAL SCIENTIFIC SUMMARY

Impaired selective attention has been long recognized as a fundamental aspect of cognitive dysfunction in schizophrenia. In this study, we used sensitive measures of eye position to demonstrate that people with schizophrenia exhibit intact attentional control during visual search and can avoid distraction by salient irrelevant stimuli. However, we did find an increased influence of selection history in people with schizophrenia, and the magnitude of this effect was associated with individual differences in working memory and cognitive control.

DISCLOSURES

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The authors declare no competing financial interests.

Keywords

Oculomotor inhibition; priming; inhibitory control; selective attention; cognitive impairment; schizophrenia

1. INTRODUCTION

Many aspects of daily life require the use of selective attention to prioritize processing of task-relevant information while minimizing interference from irrelevant information. Impairments in selective attention have been considered fundamental to schizophrenia from its first description (Kraepelin,1971; Nuechterlein & Dawson, 1984), and the degree of impairment in attention has wide-ranging consequences for occupational and functional outcomes (Green et al., 2004). However, attention is a complex construct (Luck & Vecera, 2002), and it has been difficult to isolate the specific attentional processes that are intact and impaired in schizophrenia (Luck & Gold, 2008).

Previous studies of selective attention in people with schizophrenia (PSZ) have yielded mixed results. Some evidence is consistent with impaired top-down attentional control in PSZ (e.g. Fuller et al., 2006; Gold et al., 2007; Dima et al., 2010). For example, PSZ exhibited impaired performance when task-irrelevant distractors were more salient than task-relevant, to-be-remembered items in a spatial memory task (Hahn et al., 2010). We recently reported similar effects using eye tracking, showing that control mechanisms failed when searching for low contrast targets amongst high contrast distractors, as PSZ made more saccades to the salient distractors than did healthy control subjects (HCS) (Bansal et al., 2019). A recent large-N study (126 PSZ, 122 HCS) also found that PSZ were impaired when top-down control was needed to guide visual search but performed normally when guided by highly salient bottom-up inputs (Gold et al., 2018). These studies suggest that PSZ exhibit an unusually strong attraction of attention to physically salient stimuli.

However, there are a number of studies that suggest intact top-down control of attention in PSZ. For example, PSZ can efficiently encode task-relevant visual stimuli into working memory (WM) and suppress the encoding of equally salient distractors (Gold, et al.,2006). Erickson and colleagues (2015) documented intact selection for WM storage even in the face of highly salient distractors. Further, Leonard et al. (2014) found that PSZ were no more distracted by task-irrelevant color singleton (pop-out) stimuli than were HCS, with greater distractibility in PSZ only for stimuli that were biased towards the magnocellular system.

These diverging results can potentially be explained by variations in the presence of goalrelevant features in the distractors (Luck et al., 2019a). That is, distractors are most likely to capture attention in PSZ if they share a goal-relevant feature with the target stimulus. For example, Mayer et al. (2012) found that PSZ exhibited exaggerated distraction by non-target flanker objects that matched the color of a visual search target. Similarly, we have obtained both behavioral and electrophysiological evidence that PSZ exhibit exaggerated distraction by non-target objects that match the color of a task-relevant object (Leonard et al., 2017; Luck et al., 2014; Sawaki et al., 2017).

Considering these and other findings, we have proposed that PSZ tend to focus their processing resources in an overly narrow but intense fashion, which we have termed *hyperfocusing* (Luck et al., 2014, 2019b). This hypothesis accounts for the aforementioned results by proposing that the memory representation of the target's features (i.e., color) is abnormally intense and therefore biases attention towards that feature even if the stimulus lacks another feature that defines the target (e.g., the correct shape or location). In the absence of a distractor that shares a target-relevant feature, PSZ often demonstrate intact selective attention (e.g. Gold et al., 2009; Erickson et al., 2014; Elshaikh et al., 2015). In some cases, PSZ actually exhibit supranormal attention effects, consistent with the hypothesis of more intense focusing of processing resources (Leonard et al., 2013, 2017; Kreither et al., 2017).

A contrasting idea is that attentional impairments in schizophrenia are a consequence of deficits in prefrontally mediated inhibitory control processes, which are particularly important for the suppression of prepotent responses (e.g. Cohen et al., 1992, Barch et al., 2001; Perlstein et al., 2003; Cho et al., 2006; Lesh et al., 2011). In the antisaccade task, for example, individuals must inhibit the prepotent response of fixating the target stimulus so that they direct gaze to the opposite side of the display. PSZ exhibit robust deficits in this task (e.g. Fukushima et al., 1990; Everling & Fischer, 1998; McDowell & Clementz, 2001) and in several other tasks that require inhibition of prepotent responses (e.g. Badcock et al., 2002; Lipszyc & Schachar, 2010; Schaefer et al., 2013; Ettinger et al., 2018). A broad impairment in inhibitory control could readily explain some of the deficits exhibited by PSZ in selective attention tasks, such as their poor suppression of high-contrast distractors when searching for a low-contrast target (Bansal et al., 2019). However, this hypothesis has difficulty explaining cases of intact or even supranormal attention effects in PSZ (see Luck et al., 2019b for a review).

The present study contrasted the hyperfocusing hypothesis with the hypothesis of impaired inhibitory control of attention in schizophrenia using an attentional capture paradigm in which participants searched for a target shape while ignoring irrelevant but highly salient color singletons (see Figure 1). Participants were required to direct gaze to the target so that they could report the orientation of a small tilted line inside the target. Previous experiments with healthy young adults have found that color singletons are ordinarily very potent distractors, capturing both covert and overt attention (e.g., Theeuwes, 1991, 1992, 2010). However, people rapidly and automatically learn to suppress the singleton if its color remains the same from trial to trial (e.g., Andrews et al., 2011; Vatterott & Vecera, 2012; Gaspelin et al., 2015, 2017). The singleton still produces an automatic "attend-to-me" signal, but inhibitory mechanisms are used to suppress the singleton. As a result, gaze is actually *less* likely to be drawn to the singleton than to the nonsingleton distractors (e.g. Gaspelin et al., 2015, 2017, 2019), and the singleton elicits an inhibition-related ERP component (the *distractor positivity*; Hickey et al., 2009) that is correlated with behavioral measures of singleton suppression (Weaver et al., 2017; Gaspelin & Luck, 2018).

In the present eye-tracking study, the singleton color remained constant over trials, and we predicted that HCS would be able to suppress the singleton, fixating it less often than they fixated the nonsingleton distractors. If schizophrenia involves a general impairment in

top-down inhibition, then PSZ should fixate the singleton more often than HCS. However, if the inhibitory processes needed to avoid distraction by salient stimuli are not impaired, then PSZ should be able to avoid shifting gaze to the singleton just as well as HCS. Such a result would not indicate that *all* inhibitory processes are intact in PSZ; some inhibitory processes might still be impaired. However, a finding of intact inhibition in this paradigm would indicate that schizophrenia does not involve a generalized, domain-independent impairment in inhibition. It would further provide additional evidence for our hypothesis that PSZ do not exhibit exaggerated distractibility in the visual modality unless the distractors either create a strong magnocellular signal or share task-relevant features with the target.

Our paradigm also provides an opportunity to explore an additional aspect of attentional control that may be abnormal in PSZ, namely automatic priming effects. Previous research suggests that attention may be automatically attracted to the location that contained the target on previous trials (e.g., Kristjánsson & Campana, 2010; Geng & Behrmann, 2005; Talcott & Gaspelin, 2020). Typically, priming effects in visual search are unconscious, rely on implicit memory, and are independent of top-down guidance (Maljkovic & Nakayama, 1996; Leonard & Egeth, 2008; Jiang et al., 2016).

These priming effects are a consequence of focusing attention onto the target during previous trials (Goolsby & Suzuki, 2001; Kristjánsson et al., 2013). Because the hyperfocusing hypothesis proposes that this focusing of attention will be exaggerated in PSZ, it predicts that priming of that location will be greater in PSZ than in HCS. We found previous support for this prediction in a *priming-of-popout* paradigm, in which the target color varied randomly from trial to trial. Both PSZ and HCS exhibited faster response times (RTs) when the color of the current-trial target matched the color of the previous-trial target (compared to when the color changed), but this effect was greater in PSZ than in HCS (Leonard et al., 2020). In other words, when the target was drawn in a particular color on one trial, PSZ exhibited an exaggerated benefit when the target was drawn in that color on the next trial. The present study will examine whether this finding extends to location-based priming, using more sensitive eye-tracking methods.

2. METHODS

2.1. Participants

We tested 46 outpatients from the Maryland Psychiatric Research Center and other outpatient clinics meeting DSM-IV criteria for schizophrenia (N= 38) or schizoaffective disorder (N= 8), and 41 matched HCS with no lifetime or family history of psychosis, who were free or a substance abuse diagnosis for at least 6 months and did not currently meet diagnostic criteria for a mood or anxiety disorder. We recruited HCS through advertisements posted on the Internet and in local libraries and businesses. Demographic information is summarized in Table 1, and additional neurocognitive measures are described in supplemental materials.

2.2 Stimuli and procedure

Details of the stimuli and procedure are described in supplemental materials; here we provide a brief summary. The stimuli and task were based on those used by Gaspelin et al. (2017) and are illustrated in Figure 1. Each search display contained six items distributed at equal distances around an invisible circle. Each array contained one diamond, one circle, two triangles and two hexagons. The stimuli were drawn in pink or green. One item (the singleton) was drawn in one of these colors, and the other items were drawn in the other color. The singleton was pink among green for half the participants and green among pink for the other half. Each shape contained a tiny black line (much smaller than shown in Figure 1) that was tilted 45° to the left or right. The tilt of the line inside each shape varied randomly on each trial.

The target was the circle for half the participants and the diamond for the other half. Participants searched for the target shape and reported the tilt of the enclosed line by pressing one of two buttons on a gamepad. The locations of the target and singleton varied randomly from trial to trial, with the constraint that the singleton was never the target item. We did not explicitly require an eye movement to the target, but the line within the target was too small to be accurately perceived without fixating the target.

Trials began with a blank intertrial interval screen for 500 ms, followed by a screen containing the fixation cross; this screen remained visible until the participant maintained fixation for 500 ms. The search array then appeared and remained visible until the buttonpress response. The location of the target shape was selected at random on each trial (see Figure 1C). Thus, the location of the target on the previous trial (trial n - 1) was completely uninformative about the target location on the current trial (trial n). This yielded two types of trials: *repeat-location* trials (1/6th of trials), on which the current-trial target appeared at the same location as the previous-trial target, and *change-location* trials (5/6th of trials), on which the current-trial target location was different from the previous-trial target location (see also Talcott & Gaspelin, 2020). Participants first practiced the search task for two blocks of 32 trials, which were excluded from analysis. The main experiment consisted of eight blocks of 32 trials, yielding 256 trials. Participants received feedback about their mean manual RTs and accuracy following each block.

2.3. Analysis

Details of the eye-tracking analysis are provided in supplemental materials. As in previous studies (Gaspelin et al., 2017, 2019), we focused on the first eye movement on each trial. Saccade landing position was classified by defining interest areas surrounding each item in the display, and saccadic latency was measured as the start time of the first saccade that landed in one of these areas. We excluded trials with abnormal manual response times (<200 ms or >2000 ms), trials in which participants made no eye movement, and trials with abnormal saccade latencies (<50 ms or >1000 ms). This led to the exclusion of a modest percentage of trials, which did not differ across groups (PSZ: M=10.57%, SD=10.15%; HCS: M=9.86%, SD=6.92%; t(85)=0.38, p=0.71). Additionally, we excluded trials with manual response errors from all analyses except manual response error analyses.

First, to examine suppression of the color singleton, we compared the percentage of first saccades that landed on a given stimulus type (target, nonsingleton distractor, or singleton). Second, to examine location priming effects, we broke down the percentage of first saccades that were directed to the current target, the primed distractor (i.e., the location of the previous-trial target), and the average unprimed distractor (the average of the distractor locations that were not the same as the location of the previous-trial target).

We used a series of planned *t* tests to compare pairs of saccade destinations. This approach avoids issues of nonindependence; as the proportion of fixations of the target increases, this necessarily decreases the proportion of fixations to the singleton and nonsingleton distractors (see supplemental materials). Independent-samples t tests were used for comparisons of PSZ and HCS; paired *t* tests were used for within-group comparisons of different trial types. For analyses that did not suffer from nonindependence issue (e.g., RT analyses), we used ANOVAs. We report Greenhouse-Geisser-corrected *p* values (p_{GG}) for factors with more than two levels. The two different target shapes and the two different color combinations did not meaningfully impact performance, so the data were aggregated across these variables.

To examine associations between task performance, neurocognitive measures, and clinical symptoms, we computed Spearman rho correlations. Cohen's *d* was used as a measure of effect size in this study. All statistical analyses were performed using MATLAB and JASP (JASP v. 0.8.5; jasp262 stats.org).

3. RESULTS

3.1. Overall manual response performance

Overall accuracy in reporting the tilt of the line within the target stimulus was slightly but significantly lower in PSZ than in HCS (PSZ Mean=91.53, SD=11.02; HCS Mean=96.51, SD=2.75; t(85)= 3.03,p=0.003). Manual RTs were significantly higher in PSZ than in HCS (PSZ Mean=1159.07, SD=278.59; HCS Mean=897.38, SD=162.35; t(85)= 5.27,p<0.001).

3.2. Singleton Suppression

3.2.2 Initial saccade destination—As shown in Figure 2A, the first saccade was less likely to be directed to the target in PSZ than in HCS (t(85)=5.11,p<0.001, d=1.10) and more likely to be directed to the nonsingleton distractor in PSZ than in HCS [t(85)=5.38,p<0.001, d=1.16]. However, both groups directed the first saccade to the singleton less often than to the average nonsingleton distractor (singleton suppression), with nearly identical proportions of fixations of the singleton in the two groups (t(85)=0.80,p=0.43, d=0.17). Paired t tests indicated that the difference in fixation rates between the singleton and nonsingleton distractors was significant in both groups (HCS: t(40)=10.04,p<0.001, d=1.89; PSZ: t(45)=18.15,p<0.001, d=3.71)

Because frequentist statistics do not ordinarily make it possible to draw conclusions about a lack of difference, we also computed Bayes factors, which quantify the relative evidence for the null and alternative hypotheses. We used the approach of Rouder et al. (2009) with the default scale factor of 0.707. For first saccades to the singleton distractor, the

Bayes factor indicated that the data were 3.37 times more likely to be obtained under the null hypothesis of no difference between groups than under the alternative hypothesis of a difference between groups. This provides positive evidence that PSZ were able to suppress the singleton as well as HCS.

We also used difference scores to quantify the extent to which gaze was directed toward the singleton when it was not directed toward the target. Specifically, for trials on which the first fixation was not directed toward the target, we computed the percentage of trials on which the first fixation was directed to the singleton rather than to one of the nonsingleton distractors. As shown in Figure 2B, PSZ had a smaller percentage of first saccades directed to the singleton relative to HCS (t(85) = 2.33, p = 0.02, d = 0.5)¹. However, this could be an artifact of the smaller number of fixations directed to the target in PSZ than in HCS, which led more saccades to be directed to the nonsingleton distractor in PSZ than in HCS. Nonetheless, the results shown in Figure 2B are consistent with the conclusion that PSZ suppressed shifts of gaze to the singleton at least as well as HCS.

For completeness, we also examined saccadic latencies. Table 2A shows mean saccadic latencies as a function of saccade landing position. Overall, saccadic latencies were slower for PSZ than for HCS (significant main effect of group, $F_{1,85}=5.01$, p=0.03, $\eta^2_p=0.06$). For both groups, latencies were longest when gaze first landed on the target, shorter when gaze first landed on a nonsingleton distractor, and shortest when gaze first landed on the singleton distractor (significant main effect of Stimulus Type, $F_{1,85}=114.79$, $p_{GG}<0.001$, $\eta^2_p=0.58$). This replicates the pattern observed in healthy young adults (Gaspelin et al., 2017), and it may indicate that gaze errors are more likely when participants are in a less controlled state. This pattern was similar in PSZ and HCS, and we observed no hint of a Group X Stimulus type interaction ($F_{1,85}=1.11$, $p_{GG}=0.33$, $\eta^2_p=0.01$).

3.3. Location Priming

3.3.1. Priming of Manual Responses—To examine location priming, we first compared manual responses when the current-trial target was at the same location as the previous-trial target (repeat-location trials) versus when the current-trial target was at a different location from the previous-trial target (change-location trials). Figure 3A shows that manual response accuracy in both groups was significantly higher on repeat-location trials than on change-location trials (main effect of Target Location Repetition F_{1,85}=29.58, p<0.001, η^2_p =0.26). PSZ were less accurate overall than HCS (main effect of group, F_{1,85}=7.25, p=0.01, η^2_p =0.08), but target location repetition had a similar effect for both groups, leading to no significant Group X Target Location Repetition interaction effect (F_{1,85}=0.85, p=0.36, η^2_p =0.01). However, because accuracy is bounded at 100% and HCS were near ceiling, and there were several outliers, caution is needed in comparing the effects of priming on accuracy across HCS and PSZ².

¹This effect was partly driven by an outlier in the HCS group, who showed a strongly negative suppression effect. However, the group difference remained significant even when we removed this outlier (t(84)=1.73, p =0.043) ²When outliers within each group were removed(NC, N=36; PSZ N=42), we observed that the pattern of results was the same:

²When outliers within each group were removed(NC, N=36; PSZ N=42),, we observed that the pattern of results was the same: manual response accuracy in both groups was significantly higher on repeat-location trials than on change-location trials (main effect of Target Location Repetition $F_{1,76}=19.51$, p<0.001, $\eta^2 p=0.20$). PSZ were less accurate overall than HCS (main effect of group,

J Abnorm Psychol. Author manuscript; available in PMC 2022 August 01.

Figure 3B shows the effects of target location repetition on RT. Because the RTs were far from the fastest possible values, whereas accuracy was near ceiling in many participants, the RT results were easier to interpret than the accuracy results. As usual, RTs were slower overall in PSZ than in HCS (main effect of group, $F_{1,85}=12.71$, p<0.001, $\eta^2_p=0.13$). In addition, RTs in both groups were faster on repeat-location trials than on change-location trials (main effect of trial type, $F_{1,85} = 337.50$, p<0.001, $\eta^2_p=0.80$), replicating previous studies of location priming (e.g., Maljkovic & Nakayama, 1996; Tanaka & Shimojo, 1996; 2000; Talcott & Gaspelin, 2020). Notably, the effects of target location repetition were stronger in PSZ than HCS, such that PSZ benefited from repetition more than did HCS (significant group X trial type interaction effect, $F_{1,85} = 8.98$, p=0.004, $\eta^2_p = 0.10$). The mean benefit of target location repetition (change minus repeat) was 183.23 ms (SE=14.42) in PSZ and 131.82 ms (SE=8.25) in HCS.

3.3.2. Initial saccade landing position—Effects of location priming on RT are typically assumed to reflect greater allocation of attention to the location of the previous-trial target, but they can also be caused by postperceptual processes (Hilchey et al., 2018; Huang et al., 2004). To determine whether the RT priming effects shown in Figure 3B reflected greater allocation of attention to the location primed by the previous-trial target, we examined the landing position of the first saccades, which provide a direct measure of the allocation of overt attention (see Talcott & Gaspelin, 2020, for a detailed justification of this approach).

Figure 4A displays the effects of priming on eye movements using heatmaps of the location of the first saccade landing position, aggregated across all trials and all participants within each group. The plots show every possible location of the primed location relative to the target location, with the data being rotated so that the target appears at the 12 o'clock position (marked with a 'T') in each heat map. The arrow points to the primed location (which was also the target location on repeat-location trials). The high intensity at 12 o'clock in these heat maps indicates that many first saccades were directed to the location of the current-trial target, but the high intensity at the locations indicated by the arrow indicates that a large number of first saccades were instead directed to the location of the previous-trial target (location priming). Very few first saccades were directed at the other locations.

Although both groups showed strong location priming, the heatmaps indicate that the priming was stronger in PSZ than in HCS. In PSZ, the first eye movement was as likely or even more likely to be directed to the location of the previous-trial target as to the location of the current-trial target.

To provide a straightforward statistical analysis of these effects, we quantified the percentage of first saccades directed to each search item, pooled across all angular distances between the current target and the primed location (Figure 4B). We excluded trials in which the current-trial and previous-trial targets were at the same location, because these trials are

 $F_{1,76}=10.30$, p=0.002, $\eta^2 p=0.12$), but target location repetition had a similar effect for both groups, leading to no significant Group X Target Location Repetition interaction effect ($F_{1,76}=1.14$, p=0.29, $\eta^2 p=0.02$).

J Abnorm Psychol. Author manuscript; available in PMC 2022 August 01.

ambiguous with respect to whether gaze was driven by the current-trial target or by the previous-trial target. We collapsed the data into three first saccade landing locations: the target location; the primed location (the location of the previous-trial target); and the average of the unprimed locations (i.e., locations where the neither the current-trial target nor the previous-trial target appeared). The location of the color singleton distractor was disregarded in these analyses (because the joint analysis of primed location and singleton location yields too many combinations to be realistically analyzed).

We examined whether first saccades were more likely to be directed to the primed distractor location compared to the average of the unprimed distractor locations. As can be seen in Figure 4B, first saccades in both PSZ and HCS were much more likely to be directed toward the distractor at the primed location than toward the average of the distractors at the unprimed locations. Moreover, whereas HCS were more likely to direct the first saccade to the target location than to the primed nontarget location, PSZ were approximately equally likely to fixate these two locations.

We compared the two groups using three different approaches. First, we performed an independent samples t test to compare the two groups in terms of fixations of the primed distractor location. PSZ were significantly more likely than HCS to direct their first saccade to the primed distractor location (t(85) =4.02, p<0.001, d=0.86). Second, we used difference scores to quantify the extent to which gaze was more likely to be directed to the primed location than to the average unprimed location (percentage at primed location minus unprimed location, computed separately for each participant). As shown in Figure 4C, this difference score was higher in PSZ (46%) than in HCS (38.5%) [t(85)=2.997, p=0.004, d=0.64]. Finally, we compared the percentage of first saccades directed to the primed distractor relative to the target by computing a target-minus-primed difference score. This difference score was higher in HCS (Mean=13.39, SE=3.28) than in PSZ (Mean=2.37, SE=2.44; t(85)= 2.73, p=0.008, d=0.59). In PSZ, this difference score was not significantly different from zero in a one-sample t test (t(45)=0.98, p=0.33), indicating that PSZ were approximately equally likely to direct gaze towards the previous target and the current target. In HCS, by contrast, the difference score was significantly greater than zero (t(40)=4.088, p=0.0002), indicating that HCS directed gaze to the target more often than to the primed location. Altogether, these results indicate that overt attention was strongly attracted to the location primed by the previous target and that this priming effect was so strong in PSZ that the primed location attracted attention as strongly as the location containing the actual target.

We also examined location priming by analyzing saccadic latencies for eye movements directed to the primed and unprimed distractor locations (excluding repeat-location trials). Group means for each saccade destination are shown in Table 2B. In both groups, saccadic latencies were faster when the saccade was directed toward a primed distractor location than toward an unprimed distractor location. This observation was supported by an ANOVA on mean saccadic latencies, with factors of saccade destination (primed distractor versus unprimed distractor) and diagnostic group. The shorter latencies for the primed versus the unprimed distractors led to a significant main effect of saccade destination ($F_{1,85}$ =134.75, p<0.001, η^2_p =0.61). Latencies were slower overall for PSZ than for HCS ($F_{1,85}$ =6.16, p=0.015, η^2_p =0.07), but we did not obtain a significant Group X saccade destination

interaction effect (F_{1,85}=1.41, p=0.24, η^2_p =0.02). Thus, the effects of priming on saccadic latencies were similar for PSZ and HCS.

As a secondary analysis that is more directly analogous to the RT analysis, we compared the latencies of saccades directed to the target location on repeat-location trials versus change-location trials. If first saccades are automatically biased toward the previous-trial target location, then first saccades would have shorter latencies to the target on repeat-location trials than on change-location trials. As can be seen in Figure 5A, in both groups, saccadic latencies were faster when the saccade was directed toward a repeat-location target than toward a change-location target. (main effect of Target Location Repetition, $F_{1,85}$ =179.25, p<0.001, η^2_p =0.68). PSZ had longer latencies overall (main effect of Group, $F_{1,85}$ =6.5, p=0.013, η^2_p =0.07). Notably, as with manual RTs, the effects of target location repetition were stronger in PSZ than HCS—PSZ benefited from repetition more than did HCS such that their initial saccades to the repeated target location were faster than saccades to the target on change trials to a greater degree than in HCS (significant Group X Target Location Repetition interaction effect (F1,85=8.42, p=0.005, $\eta^2 p$ =0.09).

With regards to oculomotor response accuracy (initial saccade destination, Figure 5B), first saccades in both groups were more likely to be directed to the target on repeat-location trials than on change-location trials (main effect of trial type, $F_{1,85} = 689.15$, p<0.001, $\eta^2_p=0.89$). However, PSZ were less accurate overall in directing initial gaze to the target (main effect of group, $F_{1,85}=18.79$,p<0.001, $\eta^2_p=0.18$). This lower accuracy led to the difference in priming effects for the two trial types being greater in HCS than in PSZ, as evidenced by a significant Group X Trial type interaction effect, $F_{1,85}=32.35$, p<0.001, $\eta^2_p=0.28$). A potential explanation for this result is described in the online supplementary materials.

3.4. Correlations with clinical symptoms and neurocognitive measures.

We examined associations between our experimental measures of suppression and priming and the working memory and attention domain scores from the MATRICS battery. We also examined correlations with symptom scores and medication dosage in PSZ. The Spearman rho correlation coefficients and corresponding p values are provided in Table 3. In PSZ, we found that location priming (percentage of saccades to primed location minus unprimed location) was significantly associated with reduced working memory and with attention-vigilance from the MATRICS battery. An independent measure of working memory capacity, change localization K, showed the same direction of correlation but did not reach statistical significance. PSZ also exhibited a significant negative correlation between location priming and a measure of executive control (overall d') from a 12-AX-CPT task (see Gold et al., 2017 for detailed description), indicating that poorer control was associated with a greater priming by the previous trial's target location. We did not observe any significant correlations between priming and symptom measures (no correlations were found with BPRS Total or any BPRS factor scores).

We did not observe any significant correlations between priming and the neurocognitive measures in HCS (which may reflect a restriction of range in HCS). Singleton suppression (quantified as percentage of trials on which the first fixation was directed to the singleton rather than to one of the nonsingleton distractors) was not associated with any

neurocognitive measures in PSZ. However, in HCS, we did observe a correlation between suppression and working memory from the MATRICS battery such that HCS with higher working memory scores were better able to suppress covert shifts of attention to salient-but-irrelevant color singletons. This is consistent with other studies suggesting a relationship between WM capacity and the control of attention (Engle 2002;2018). Neither priming nor singleton suppression was significantly correlated with medication dose in PSZ.

4. DISCUSSION

The idea that attentional dysfunction in schizophrenia is a consequence of a general deficit in inhibitory control predicts that PSZ will be especially vulnerable to distraction by taskirrelevant stimuli that are physically salient and therefore elicit a prepotent orienting of attention. The hyperfocusing hypothesis, by contrast, posits that attention is allocated more narrowly but more intensely in PSZ, which can lead to normal or even supranormal attention effects (e.g., exaggerated priming by previously attended stimuli; see review by Luck et al., 2019b).

Singleton suppression in PSZ

In the present study, we used an attentional capture paradigm (Theeuwes, 1992; Theeuwes et al., 1998, Gaspelin et al., 2017) to investigate these two accounts of attentional deficits in PSZ. Specifically, we sought to determine whether PSZ would be unable to suppress a salient singleton distractor due to a generalized deficit in inhibitory control.

Previous research using this paradigm has found that healthy young adults can suppress eye movements to the salient singleton relative to the nonsingleton distractors (Gaspelin et al. 2017, 2019; Gaspelin & Luck, 2018). Additional evidence of singleton suppression can be found in both behavioral studies (Andrews et al., 2011; Vatterott & Vecera, 2012; Gaspelin et al., 2015, 2017) and electrophysiological studies (Gaspar & McDonald, 2014; Sawaki & Luck, 2010; Gaspelin & Luck, 2018). This ability to suppress salient items appears to be the result of implicit learning from previous attempts to ignore that feature (i.e., selection history) and not conscious intentions (Gaspelin & Luck, 2018, 2019; Stilwell & Vecera, 2019, see also Adams & Gaspelin(in press); Adams & Gaspelin(2020)).

In the present study, we replicated the finding of singleton suppression using eye tracking: In both HCS and PSZ, overt attention was less likely to be directed toward the salient distractors than toward nonsalient distractors. Surprisingly, PSZ suppressed the singleton distractor at least as effectively as HCS, indicating intact top-down inhibitory control of overt attentional orienting in PSZ. Thus, PSZ were no more distractible than HCS and were fully capable of implicitly inhibiting salient-but-irrelevant stimuli. Because the singleton suppression effect appears to be an automatic consequence of implicit learning, the present results do not rule out the possibility that PSZ have a deficit in intentional inhibition based on explicit task goals. However, our results provide evidence against a general deficit in inhibitory processing in schizophrenia that impacts both implicit and explicit control.

Location Priming: Greater Facilitation in PSZ

We also examined the effects of *selection history* (Awh et al., 2012; Kristjánsson & Campana, 2010; Lamy & Kristjansson, 2013; Wolfe & Horowitz, 2017) in guiding visual attention. Location priming is an example of an effect of selection history: the location that contained a target on the previous trial tends to automatically attract attention on the following trial. In healthy individuals, evidence for this comes from studies showing faster responses when the target repeats its location from the previous trial than when it changes locations (Maljkovic & Nakayama, 1996; Tanaka & Shimojo, 1996, 2000). More recently, in a visual search paradigm similar to ours, Talcott & Gaspelin (2020) found that eye movements were automatically directed to the previous location of the target.

In the present study, we observed that initial saccades were frequently directed to the location that contained the target on the previous trial, and this location priming effect was larger in PSZ than in HCS. This is exactly what would be expected if PSZ focused their attention more intensely on the previous-trial target, creating stronger priming of that location that persisted until the next trial. These results also converge with previous RT results indicating that PSZ exhibit greater color-based priming than HCS in a priming-of-popout paradigm (Leonard et al., 2020). Note that these findings of supranormal priming effects in PSZ cannot be explained by impaired task comprehension, reduced motivation, lapses of attention, poor maintenance of task goals, and other such generalized factors. Such factors would lead to poorer encoding of the previous-trial target and therefore weaker priming.

Priming has been previously studied in schizophrenia using the *negative priming* paradigm (Tipper, 1985,2001; Fox,1995). If a stimulus feature that was present in the distractor on one trial is present in the target on the next trial, there is an increased reaction time associated with the response, due to inhibition of the feature when it was originally a distractor. It has been found that inhibition of such distracting information is reduced in PSZ (e.g., Beech et al., 1989; Park et al., 1996; Fuller et al., 2000). The location priming effects in the present study are quite different, because these effects are based on a feature of the previous-trial target rather than a previous-trial distractor. Thus, our finding of increased priming in PSZ is not inconsistent with previous studies of negative priming.

Although there may be multiple explanations for our finding of increased location priming in PSZ, this result was directly predicted by the hyperfocusing hypothesis. That is, if attention is more intensely focused on the target on one trial, then greater priming of that location would be expected on the next trial. Importantly, in PSZ our measure of location priming was associated with independent neuropsychological measures of attention, working memory and executive control, with greater priming for individual with lower scores on these neurocognitive assessments.

Conclusion

In summary, the present study found that: 1) PSZ exhibited intact top-down control and were not distracted by salient color singletons; 2) PSZ were able to suppress the singletons below the level of nonsingleton distractors just as well as HCS; and 3) Overt attention was

significantly more biased toward the location primed by the previous target in PSZ than in HCS. Thus, PSZ do not have a general deficit in inhibitory control, but they are attracted to locations primed by the previous trial.

The exaggerated priming adds to the mounting literature supporting the hyperfocusing hypothesis of cognitive impairment in PSZ (see Luck et al., 2019b). The hyperfocusing hypothesis explains a variety of attentional deficits, but it has also predicted several findings of *supranormal* effects in PSZ, such as the exaggerated location priming observed here. On the surface, the present results appear to conflict with the hypothesis of impaired inhibitory control in schizophrenia, and it will be important for future research to resolve this apparent conflict. One possible resolution is that both the singleton suppression and location priming effects examined in the present study are automatic consequences of implicit learning, whereas cases of impaired inhibitory control in PSZ may be based on paradigms that emphasize conscious goals. Given that much natural behavior involves an interplay of conscious and unconscious processes, it will be important for future research to determine if inhibitory control deficits in schizophrenia are limited to cases of conscious goals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

This study was made possible by NIH grant R01MH065034 awarded to JMG and SJL.

The University of Maryland, Baltimore (UMB) Institutional Review Board (IRB) approved the protocol HP-00054557 entitled, "*Attention, Working Memory, and Brain Electrophysiology - NIMH Grant: 2R01MH065034*"

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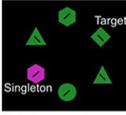
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A. EXAMPLE SEARCH ARRAYS

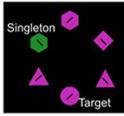


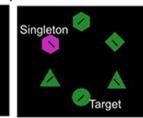




Green Target Group

Circle Target Group





Pink Target Group

Green Target Group

B. TRIAL SEQUENCE

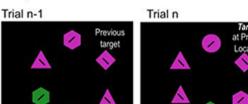
Pink Target Group



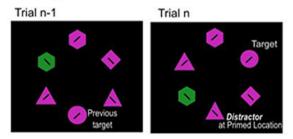
Blank 500 ms

C. LOCATION PRIMING

Repeat Location Trial



Change-Location trial



Search Array

until response

Figure 1.

A. Each participant was assigned to a target group (diamond or circle), which remained constant throughout the experiment for that participant. Participants were instructed to report the orientation of the line inside the target. Distractors were heterogeneous shapes to prevent the target from popping out. The singleton was pink among green for half the participants in each diagnostic group and green among pink for the other half. **B.** Trials began with the presentation of a blank intertrial interval screen for 500 ms, followed by a screen containing the fixation cross; this screen remained visible until the participant maintained fixation within a 1.5° radius of the central fixation point for 500 ms. The search array then appeared

Fixation

500 ms

and remained visible until the button-press response. **C.** The two types of trials with regards to location priming. The location of the target was randomly selected. On repeat-location trials, the target location from the previous trial (trial n-1) was also the target location on the current trial (trial n). On change-locations trials, the target location on the current trial was not the same as on the previous trial, so a distractor appeared at the primed location.

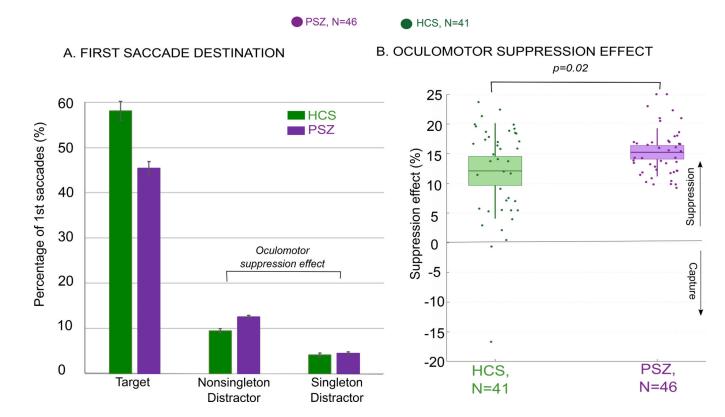


Figure 2.

A. Percentage of first saccades that landed on a given stimulus type (target, nonsingleton distractor, or singleton distractor). **B.** The individual data points indicate each's subject's mean difference score, which was used to quantify the extent to which gaze was directed toward the singleton when it was not directed toward the target. For trials on which the first fixation was not directed toward the target, we computed the percentage of trials on which the first fixation was directed to the singleton (rather than to one of the nonsingleton distractors).

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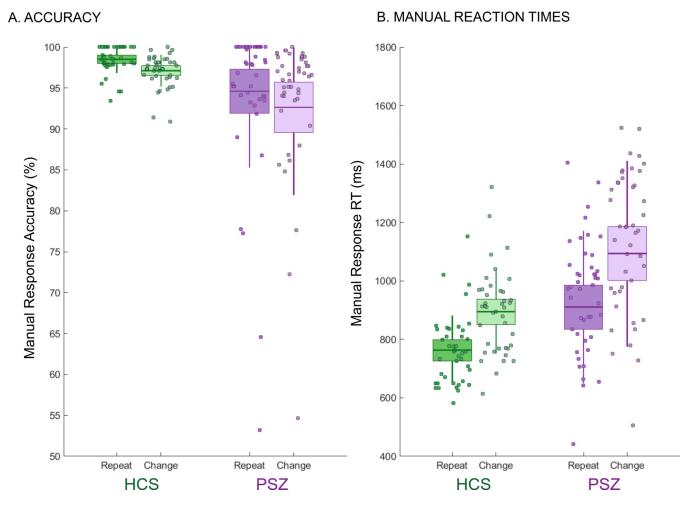
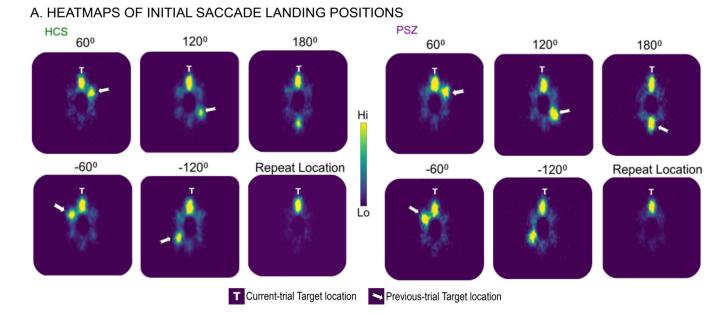


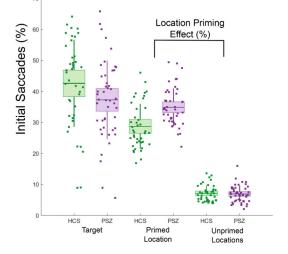
Figure 3.

A. Percent of accurate responses (in reporting the tilt of the line within the target) and **B.** manual response times when the current-trial target was at the same location as the previous-trial target (repeat-location trials, left side of each panel) versus when the current-trial target was at a different location from the previous-trial target (change-location trials, right side of each panel).



B. FIRST SACCADE DESTINATION: CHANGE LOCATION TRIALS

C. LOCATION PRIMING EFFECT



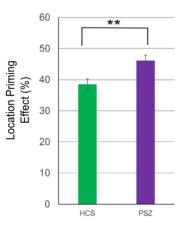


Figure 4.

A. Heat maps of first saccade destinations for each angular distance between the target and primed location (Left panel for HCS, Right for PSZ). The heat maps have been rotated so the target appears at the top (12 o'clock) position. The white arrow points to location primed by the target from the previous trial. On repeat-location trials, the target on the current trial appears at the primed location. **B.** Percentage of first saccades to each search item (Target, Primed location, unprimed location) on change-location trials. **C.** The location priming effect was calculated as the difference score between percentage of first saccades directed to the primed location versus the average unprimed location. **D.**

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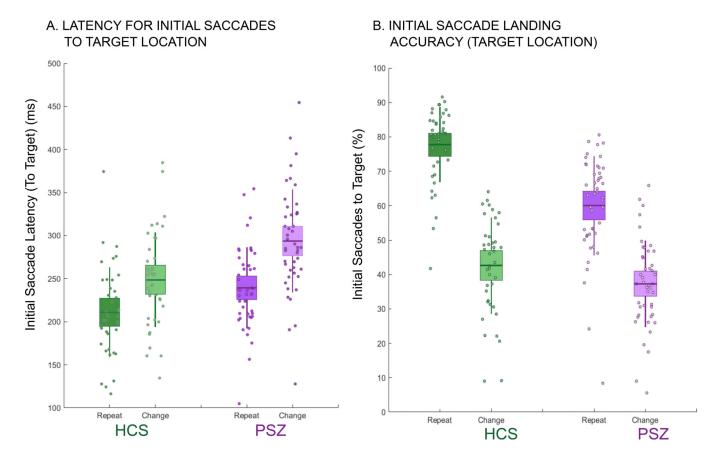


Figure 5.

A. Latency for initial saccades to the target location on repeat-location trials verses changelocation trials in each group and **B.** Percentage of saccades directed to the target location on repeat-location trials versus change-location trials in each group

Table 1:

Demographic Information (mean \pm SD)

	HCS (N=41)	PSZ (N=46)	Statistic	p value
Age	37.15 ± 10.51	37.17 ± 10.03	<i>t</i> = −0.01	0.99
Gender (F M)	17 24	14 32	$\chi^2 = 1.15$	0.28
Race (African American Caucasian Other)	17 19 5	18 23 5	$\chi^2 = 0.13$	0.94
Participant Education	15.07 ± 3.4	13.38 ± 2.88	t= 2.49	0.02
Maternal Education	14.61 ± 2.62	14.56 ± 2.77	t= 0.07	0.94
Paternal Education	14.17 ± 3.94	14.19 ± 4.18	<i>t</i> = −0.02	0.99
Neurocognitive Test Results				
WASI	112.20 ± 9.97	95.80 ± 13.03	t= 6.37	< .001
WRAT-4	109.20 ± 13.5	98.48 ± 14.15	t= 3.54	< .001
WTAR	111.41 ± 11.81	100.35 ± 17.55	t= 3.41	0.001
Overall d' from 12-AX-CPT task	3.00 ± 0.98	2.50 ± 0.96	t= 2.36	0.02
Visual WM capacity (K) from change localization task	3.08 ± 0.38	2.53 ± 0.58	t= 5.15	< .001
MCT Overall	51.62 ± 8.78	32.80 ± 13.22	t= 7.54	< .001
MD Processing Speed	53.73 ± 8.6	38.80 ± 14.43	t= 5.76	< .001
MD Attention Vigilance	49.49 ± 11.22	40.39 ± 12.47	t= 3.48	< .001
MD Working Memory	50.71 ± 12.89	38.40 ± 12	t= 4.59	< .001
MD Verbal Learning	49.78 ± 9.66	38.47 ± 8.94	t= 5.64	< .001
MD Visual Learning	47.50 ± 8.78	36.50 ± 14.14	t= 4.23	< .001
MD Reasoning	50.77 ± 12.23	42.18 ± 12.41	t= 3.19	0.002
MD Social Cognition	51.25 ± 11.77	37.89 ± 12.34	t= 5.07	< .001
Antipsychotic Medication				
CPZ dose equivalent (mg/day)		446.88 ± 431.73		
Clinical Ratings				
BPRS Positive Symptoms		2.43 ± 1.29		
BPRS Negative Symptoms		1.6 ± 0.61		
BPRS Disorganized Symptoms		1.21 ± 0.31		
BPRS Total Score		35.33 ± 10.75		

WASI = Wechsler Abbreviated Scale of Intelligence; WRAT = Wide Range Achievement Test; WTAR = Wechsler Test of Adult Reading; MD = MCCB (MATRICS Consensus Cognitive Battery) Cognitive Domain; MCT = MCCB Composite Total; WM= Working Memory; d'= D-prime; CPZ = Chlorpromazine equivalent; BPRS=Brief Psychiatric Rating Scale

See Supplemental methods for descriptive details.

Table 2:

1ST SACCADE LANDING: LATENCIES (MEAN (SD))

A. Lat	A. Latencies with respect to Singleton suppression							
	Target	Nonsingleton Distractor	Singleton Distractor					
HCS	234.73 (50.51)	196.27 (48.61)	179.36 (39.25)					
PSZ	250.61 (51.28)	223.27 (48.81)	201.92 (45.3)					
B. Latencies on Change Location Trials								
	Primed Distractor	Unprimed Distractor						
HCS	178.25(45.07)	206.14 (47.52)						
PSZ	199.85(38.75)	230.11 (58.66)						

Table 3:

Correlations

	Suppression	Priming	MD Working Memory	MD Attention Vigilance	MCT Overall	CPT d'	Change localization k	BPRS Total	Total CPZ
Suppression	_	0.069	0.425	0.247	0.333	0.237	-0.18		
	—	0.671	0.009	0.152	0.051	0.146	0.359		
Priming	-0.266	—	-0.08	-0.091	-0.098	-0.164	-0.183		
	0.077	_	0.638	0.604	0.576	0.318	0.352		
MD Working Memory	-0.045	-0.300	_	0.386	0.829	0.444	-0.032		
	0.771	0.045	—	0.022	<.001	0.006	0.877		
MD Attention Vigilance	0.128	-0.312	0.373	_	0.671	0.971	-0.057		
	0.407	0.039	0.013	_	<.001	< .001	0.786		
MCT Overall	-0.074	-0.182	0.744	0.698	_	0.683	-0.109		
	0.634	0.237	< .001	<.001	_	< .001	0.605		
CPT d'	0.195	-0.305	0.391	0.942	0.674	_	-0.013		
	0.204	0.045	0.009	<.001	<.001	_	0.948		
Change localization k	0.222	-0.263	0.583	0.305	0.536	0.339	_		
	0.153	0.089	< .001	0.05	<.001	0.028	—		
BPRS Total	0.127	0.05	0.067	-0.296	-0.327	-0.223	-0.082	_	
	0.405	0.742	0.663	0.051	0.03	0.147	0.599	—	
Total CPZ	0.184	-0.128	-0.063	-0.034	-0.243	0.02	0.07	0.374	
	0.25	0.424	0.694	0.837	0.13	0.902	0.674	0.016	

Values below the diagonal (left) are correlations for PSZ, whereas those above (right, Shaded gray) are correlations for HCS.

For each variable pair, the top row indicates Spearman's rho, and the bottom row indicates the uncorrected p value.

Values in boldface are indicate significant correlations.

MD = MCCB (MATRICS Consensus Cognitive Battery) Cognitive Domain; MCT = MCCB Composite Total; SANS=Scale for the Assessment of Negative Symptoms;

BPRS=Brief Psychiatric Rating Scale; CPZ = Chlorpromazine equivalent

k= working memory capacity; d'= d-prime