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Article

Delayed onset of inhibition of return in schizophrenia

Abigail Larrison-Faucher[a,b,*], Kevin A. Briand[a], Anne B. Sereno[a]

[a]*W.M. Keck Center for the Neurobiology of Learning and Memory, Department of Neurobiology and Anatomy, University of Texas-Houston Medical School, MSB 7.160A, 6431 Fannin, Houston, TX 77030, USA*
[b]*Center for Molecular and Behavioral Neuroscience, Rutgers, the State University of New Jersey, Newark, NJ, USA*

Abstract

Peripheral visual cues occurring before a subsequent target result in an almost immediate facilitatory and then a later inhibitory effect on target detection. In a detailed parametric investigation, the authors compared schizophrenic subjects (SCZ) and control subjects (CONT) to examine whether they showed any differences in the time course of these nonpredictive peripheral cuing effects. Subjects fixated a central position and made saccadic responses to visual targets. Targets were presented 10° to the left or right of fixation and were preceded at various time intervals by visual cues. Targets occurred with equal probability in either the same position as the cue or in the opposite, uncued location, and 10 delay periods were used corresponding to stimulus onset asynchronies (SOAs) of 66, 79, 106, 133, 159, 226, 305, 505, 705, and 1000 ms. All subjects showed facilitation for short cue–target delays and inhibition of return (IOR) for longer delays. SCZ, however, showed an apparent shift in the time course of cuing effects in the form of a delayed onset of IOR. Using a task of reflexive orienting, these results support findings of a delayed rather than an absent inhibitory process in medicated SCZ. © 2001 Elsevier Science Inc. All rights reserved.

Keywords: Attention; Eye movements; Schizophrenia; IOR

1. Introduction

Schizophrenic subjects (SCZ) show deficits on a broad range of tasks that are proposed to involve inhibitory attentional processes, such as sensorimotor gating, latent inhibition, priming, antisaccades, and covert orienting (Freedman et al., 1997; Lubow et al. 2000; Beech et al., 1989; Sereno and Holzman, 1995; Posner et al., 1988). With somewhat lesser frequency, investigators have also examined the performance of SCZ on the inhibition of return (IOR) paradigm. Findings of impaired performance in SCZ on the well-established inhibitory attentional paradigm of IOR have been variable.

In the standard IOR task, a subject fixates a central point during the presentation of a nonpredictive peripheral cue. Even though the cue does not indicate the subsequent target location, these cues do affect response times (RTs). Specifically, at short delays between the cue and target presentation, i.e., short stimulus onset asynchronies (SOAs), subjects show faster RTs to targets appearing in cued locations. This enhanced performance is referred to as facilitation. However, if the time interval between the cue and target presentation is increased, i.e., long SOAs (typically, more than 200 ms), subjects now show delayed or inhibited responses to stimuli appearing in the cued locations. This increase in RT is known as IOR.

Previous studies examining performance by SCZ on IOR tasks have demonstrated conflicting results (Carter et al., 1994; Huey and Wexler, 1994; Fuentes and Santiago, 1999; Sapir et al., 2001). The primary points of contention are whether SCZ show normal IOR with respect to time course and amplitude. Huey and Wexler (1994) first demonstrated enhanced and prolonged facilitation and diminished IOR in medicated SCZ. In the same year, Carter et al. (1994) reported an absence of IOR in a subgroup of paranoid patients only, while normal IOR was reported for a group of undifferentiated SCZ. None of these subjects were on medication at the time of testing. Fuentes and Santiago (1999), however, reported normal

Abbreviations: CONT, Control subjects; EM, Eye movements; IOR, Inhibition of return; LVF, Left visual field; RT, Response time; RVF, Right visual field; SCZ, Schizophrenic subjects; SOA, Stimulus onset asynchrony

* Corresponding author. c/o Anne B. Sereno, Department of Neurobiology and Anatomy, University of Texas-Houston Medical School, MSB 7.160A, 6431 Fannin, Houston, TX 77030, USA. Tel.: +1-514-274-9768.

E-mail address: abigailfaucher@hotmail.com (A. Larrison-Faucher).

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performance in medicated SCZ when measuring the amplitude of the IOR effect. Finally, Sapir et al. (2001) demonstrated no IOR using a task presenting a single cue, and a reinstatement of IOR using a double cuing, or cue-back paradigm. In summary, approximately half the studies examining IOR report performance deficits, while half show no performance differences between control subjects (CONT) and SCZ.

Many factors may affect the time course of spatial cuing effects, such as task difficulty, nature of the response, and practice effects (Klein, 2000; Maylor, 1985; Lambert and Hockey, 1991; Khatoon et al., submitted for publication). And although not yet studied systematically, factors such as cue–target luminance, eccentricity of cues and target, cue duration, the presence or absence of a central fixation point, the number and relation of the chosen SOAs, and so forth, might each affect the time course of IOR. Rarely are these factors consistent between studies investigating IOR in SCZ, and possibly any of these factors, which vary substantially between investigative groups, might account for inconsistent findings.

Sapir et al. (2001) proposed that the incongruencies reported between research groups might be explained by differences in the methods used to control or shift spatial attention. In order to obtain IOR, attention must be first shifted to the cued position in response to the peripheral cue, and then shifted away. IOR reflects the difficulty to return attention to the initially cued position. In some studies, the addition of a second cue presented at fixation is used in the IOR task in order to quickly draw attention away from peripheral cue and speed the onset of IOR. This manipulation has been referred to as the cue-back procedure and has been shown to have significant effects on the time course of IOR. Specifically, cuing attention back to fixation results in an earlier onset of IOR, apparently shifting the time course of the cuing effect relative to the single cue condition where this second cue is omitted (Briand et al., 2000).

Interestingly, previous experiments that reported either delayed or absent IOR in SCZ administered tasks with peripheral cues followed by targets with no intervening stimuli, i.e., no cue-back (Huey and Wexler, 1994; Carter et al., 1994; Sapir et al., 2001). Sapir et al. (2001) proposed that the reported differences between investigative groups could be related to the presence or absence of a cue-back in the experimental design. They addressed this issue by performing two parallel experiments in which they systematically changed the stimulus presentation and compared performance in SCZ and CONT. In the first experiment, using the standard IOR paradigm with no cue-back, Sapir et al. reported a significant increase in the amount of early facilitation, and diminished or absent IOR in SCZ.

In the second experiment (Sapir et al., 2001), a cue-back was included in the task design to determine if indeed the cue-back was responsible for the normalization of IOR as seen by Fuentes and Santiago (1999). Although the importance of keeping all variables constant between the tasks was emphasized, in order to accommodate the presentation of the cue-back, the cue–target intervals were changed from 100, 300, or 1200 ms in Experiment 1, to SOAs of 350, 700, and 1200 ms in Experiment 2. Sapir et al. (2001) reported normal IOR amplitude in their schizophrenic group in the experiment involving the cue-back.

Sapir et al. (2001) concluded that the cue-back to fixation acted to reinstate IOR, and normalized differences between SCZ and CONT. This conclusion, however, may be incomplete due to a minimal sampling of the attentional time course. Note that the SOAs chosen for the cue-back experiment did not examine facilitation at any time point (minimum SOA of 350 ms). Therefore, the point at which facilitation shifted to inhibition (the crossover point) was not measured. This is also true for the only other study using a cue-back procedure (Fuentes and Santiago, 1999) in which only the magnitude of IOR was measured (SOAs equaled 900 and 1200 ms) and therefore the issue of whether the crossover point differed in SCZ could not be addressed. Using a more prolonged time course, Huey and Wexler (1994) initially indicated a delay in the onset of IOR using no cue-back. No studies, to date, can confirm if using a cue-back procedure normalizes this delayed IOR onset. The cue-back task design administered with a full range of SOAs would be able to address the issue of whether the IOR deficit is persistent or transient.

The present study examined performance in medicated SCZ and normal CONT in a cue-back IOR task. Ten different SOAs were chosen, including several early SOAs as well as the more often examined later points, in order to measure facilitation, IOR, and an estimated time course and crossover point from facilitation to inhibition in SCZ and normal subjects. This study was designed to more precisely determine the presence or absence of a normal time course of facilitation and IOR in medicated SCZ using a cue-back procedure. We expect that given a thorough testing of performance across a full range of SOAs, SCZ may fail to show normal IOR onset even when a cue-back to fixation is included in the task design.

2. Methods

2.1. Subjects

Fourteen SCZ (3 females, 11 males) and 14 CONT (5 females, 9 males) completed the IOR task. SCZ were recruited from outpatient clinics. All subjects were stable and taking neuroleptic medications at the time of testing. Diagnoses were schizophrenia ($n=12$) or schizoaffective disorder ($n=2$). Informed consent was obtained from all subjects before participating and subjects were debriefed following completion of the experiment.

2.2. Task

The orienting task employed was a modified version of the IOR paradigm described by Posner and Cohen (1984). Fig. 1 illustrates our task.

Subjects were required to fixate a central point and to maintain fixation during the brief presentation of a peripheral cue, a brightening of the central fixation point and a variable interval. Ten intervals were chosen to create effective SOAs between the initial peripheral cue and target onset of: 66, 79, 106, 133, 159, 226, 305, 505, 705, and 1000. The target was presented with equal probability in the cued or uncued location. Subjects were required to respond to the target by making an eye movement (EM) to the target location. EMs prior to the target onset resulted in a cancellation and a random representation of the trial. Subjects were run through a practice session of 16 trials before being tested in the full IOR task. The IOR task consisted of 160 trials with 16 trials for each of the 10 SOAs.

Details of the EM analyses are presented elsewhere (Larrison et al., 2000). Briefly, EMs were analyzed online with respect to latency to respond and errors. Latency was defined as the time elapsed between the onset of the target and the beginning of the EM to the target location and is referred to as RT. If fixation was not maintained prior to the target onset, the trial was cancelled online, and rerun later in the session. Errors consisted of anticipations and incorrect responses. Anticipations constituted responses made in non-physiological time intervals with respect to the target onset (less than 90 ms) and incorrect responses were made up of responses made to the nontarget location with RTs over 90 ms. All errors were eliminated from calculations of cell means and were analyzed separately.

2.3. Data analyses

2.3.1. Response time

RT data were submitted to a three within-factors, one between-factor repeated-measure ANOVA. The within factors included Cuing (cued, uncued), SOA (10 chosen SOAs), and Laterality (left target, right target). The between factor was Group (SCZ, CONT). Analyses of RT data were performed twice, once using cell means and once using cell medians. There were no differences for any main effects or interactions noted using these separate measures, and therefore, from this point forward, only means are reported.

2.3.2. Planned comparisons

Planned comparisons were performed to determine whether the cuing effect differed between our groups. Schizophrenic and control RT data of cuing effects were compared at each separate SOA.

2.3.3. Errors

Error data were broken down into anticipations (responses made before 90 ms) and errors (responses made to the nontarget location after 90 ms). These two types of errors were each analyzed using the same repeated-measure ANOVA as was used for RTs (Cuing, SOA, and Laterality — within factors, Group — between factor).

3. Results

3.1. Sample

Comparisons between our control and patient group revealed no difference for age, gender, or smoking status. The average age of patients was 38.0 (S.D. 8.0) and the average age of controls was 36.2 (S.D. 6.8). Twelve of the 14 patients, and 10 of the 14 controls smoked cigarettes regularly. There was a small but significant difference between our two groups for education, with SCZ averaging 12.7 years (S.D. 1.4), and the CONT averaging 13.8 years (S.D. 1.5), $F(1,24) = 11.4$, $P < .05$. We are aware of no data indicating differences in performance on orienting tasks due to education level. Other patient information regarding diagnosis, medication, and age of onset (when available) is

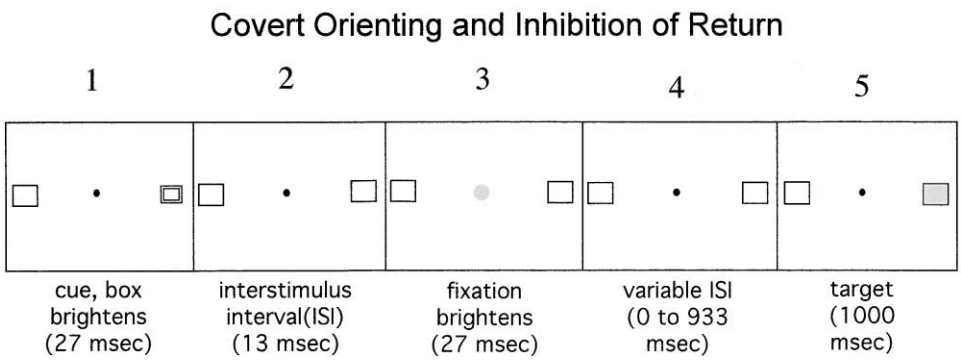

Fig. 1. The task of covert orienting and IOR. Subjects were required to fixate a central point and to maintain fixation throughout the first four frames of the trial. Frame 1: A peripheral cue was presented randomly to the left or right of fixation. Frame 2: The cue offset for a brief interval stimulus interval (ISI). Frame 3: The central fixation brightened (the cue-back procedure). Frame 4: For each trial, 1 of 10 variable intervals were used to measure cue effects at SOAs of: 66, 79, 106, 133, 159, 226, 305, 505, 705, and 1000 ms. Frame 5: The target appeared with equal probability in the cued or uncued location. Subjects responded by making an eye movement to the target location. A cued trial is shown.

Table 1
Subject information for schizophrenic patients participating in the IOR task

Subject	Age	Gender	Education	Diagnosis	Medication	Onset
PT01	45	M	14	Paranoid	Resperidol 3, Mellaril 50	23
PT02	33	M	11	Paranoid	Resperidol 4 mg	18
PT03	39	M	15	Paranoid	Haldol 5 mg, ACh	25
PT04	45	M	12	Paranoid	Resperidol 3 mg	21
PT05	31	M	13	Paranoid	Zyprexa 20 mg	23
PT06	44	M	13	Paranoid	Prolixin 5 mg	20
PT07	41	F	14	Paranoid	Resperidol 3 mg	35
PT08	50	M	16	Undifferentiated	Resperidol 2 mg, Bz	20
PT09	48	F	11	Schizoaffective	Stelazine 8mg, Bz, E	25
PT10	34	M	13	Paranoid	Chlorprmzn 200mg, H, TC	UNK
PT11	47	M	15	Undifferentiated	Prolixin, ACh	UNK
PT12	36	M	9	Paranoid	Clozaril, Dep	18
PT13	43	F	11	Schizoaffective	Prolixin, Dep, E, ACh	UNK
PT14	20	M	12	Paranoid	Zyprexa 10 mg, Dep	15

Bz = benzodiazepines, E = antiepileptics, TC = tricyclic antidepressants, H = antihistamine, Dep = Depakote, ACh = anticholinergic.

presented in Table 1. All subjects were taking antipsychotic medication at the time of testing. Antipsychotic dose information is presented when available. Only one subject (PT01) was on more than one antipsychotic, and a relatively few number of subjects took additional psychotropic medications.

3.2. Response time

As expected, there was a significant main effect for both Cuing and SOA, and moreover, these two factors interacted significantly, $F(9,234) = 9.12$, $P = .0001$. This was due to the well-described effect of Cuing in the IOR task. Subjects were faster to respond to the cued position at short SOAs, and this reversed at longer SOAs when subjects were slower to respond to the cued position (Fig. 2). However, there were no further interactions between Cuing and SOA for Group or any other factor.

There were no significant Group differences for RT. However, there was a small trend for the main effect of Group, resulting from an overall increase in RT in the patient group, $F(1,26) = 3.26$, $P = .08$. This did not significantly interact with Cuing $F(1,26) = 2.07$, $P = .16$; nor with SOA, $F(9,234) = 1.26$, $P = .25$ (Fig. 2).

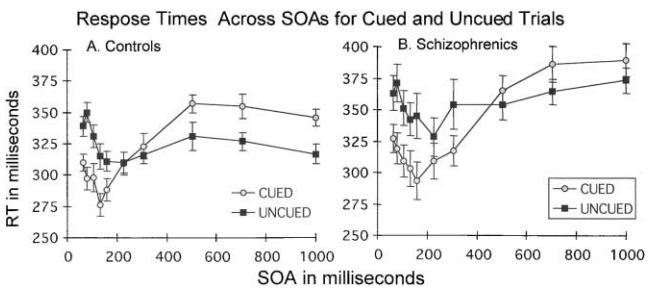

Fig. 2. The effect of Cuing on RT. Notice the minimum RT is followed by a gradual and sustained increase in RTs to the cued side. There were no significant differences between our schizophrenic and control groups for RTs.

There were no main effects or interactions for Laterality for RT data. Subjects were slightly faster overall to right targets for both cued and uncued trials, although this was not significant, $F(1,26) = 2.5$, $P = .18$, and this was true for both SCZ and CONT. There were no interactions between Laterality and Cuing for any interaction, including the highest level interaction Laterality × Cuing × Group × SOA, $F(9,234) = 0.91$, $P = .51$. Table 2 shows laterality data for facilitation and inhibition in SCZ and CONT across the 10 SOAs. Crossover points from facilitation to inhibition did not significantly differ in left and right hemifields but were seen at later SOAs for SCZ compared to CONT.

3.3. Planned comparison

The comparison of cuing effects at each SOA indicated a significant difference between our groups at only the 305-ms SOA, $F(1,234) = 5.40$, $P < .02$. No other points were significant (P values for all other SOAs were as follows: 66 ms, $P = .74$; 79 ms, $P = .93$; 106 ms, $P = .64$; 133 ms, $P = .93$; 159 ms, $P = .12$; 226 ms, $P = .32$; 505 ms, $P = .43$; 705 ms, $P = .73$; 997 ms, $P = .50$). Fig. 3 demonstrates cuing effects (uncued minus cued RT) for SCZ and CONT. In addition, data collected by the authors using the identical paradigm in 40 normal task-naïve subjects (Faucher, 2001) are presented as a historical reference.

Table 2
Laterality of the cuing effect in SCZ and CONT

SOAs	66	79	106	133	159	226	305	505	705	1000
Left										
CONT	36.2	41.7	40.9	25.9	18.6	7.7	**−12.6**	**−4.5**	**−24.6**	**−34.7**
SCZ	34.7	57.4	38.1	59.1	73.5	21.8	49.5	**−7.0**	**−31.7**	**1.7**
Right										
CONT	22.5	65.3	24.8	50.3	27.0	**−5.1**	**−1.9**	**−47.5**	**−31.5**	**−23.1**
SCZ	36.6	46.5	45.2	20.1	30.4	18.2	24.4	**−15**	**−11.3**	**−34.2**

Cuing effects as measured by cued–uncued RTs at each of the 10 SOAs. Inhibitory cuing effects are in bold.

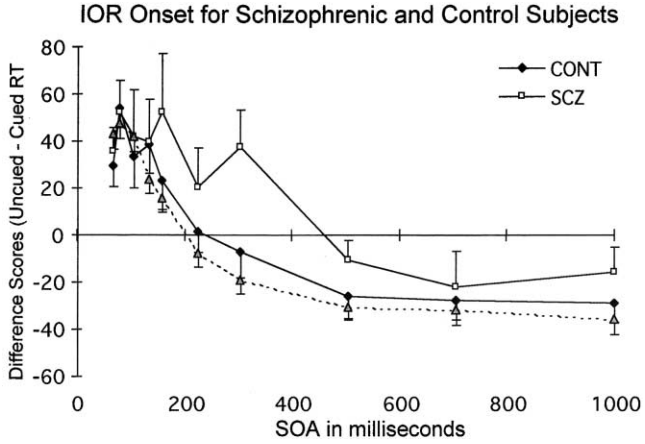

Fig. 3. Difference scores demonstrate the delayed onset of IOR in SCZ compared to CONT. Cuing effects at SOA 305 differed significantly between SCZ and CONT. Additional reference data from our laboratory (gray dashed line) collected from 40 task-naïve subjects participating in the identical task design is presented for comparison (Faucher, 2001).

The reference data closely follow the curve seen for the CONT from the present study further emphasizing the difference in task performance by the SCZ.

3.4. Error rates

The overall error rate was low. On average, subjects made a total of 4.2 ± 2.1% errors (± S.D.) during the 160-trial session, this included both anticipations and incorrect responses. Of these errors, SCZ made more incorrect responses than CONT (SCZ 4.3 ± 2.5%) (CONT 2.4 ± 1.8%), but made fewer anticipations than CONT (SCZ 0.8 ± 0.6%) (CONT 1.1 ± 0.9%).

3.4.1. Anticipations

There was a main effect of SOA on anticipations, $F(9,234) = 3.99$, $P < .01$ (Fig. 4A). This factor also interacted with Cuing, $F(9,234) = 4.26$, $P < .01$, this was due to a significant increase in anticipations at SOAs of 226 and 305 at the cued location. There were no significant differences between our groups for anticipations, both SCZ and CONT showed this pattern.

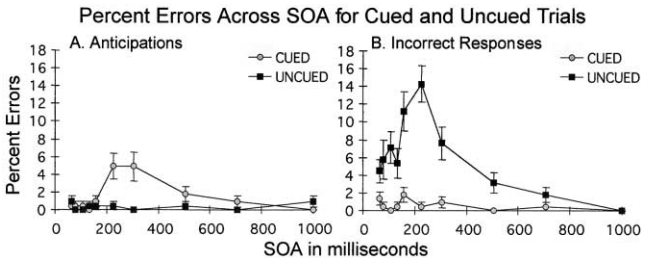

Fig. 4. Percentage of errors for all subjects across the 10 SOAs. There was an increase in errors at the SOAs 226 and 305 for anticipations and a peak in incorrect responses at SOA 226 that fell off to zero by SOA 1000. This error pattern across SOAs was striking and held for both SCZ and CONT.

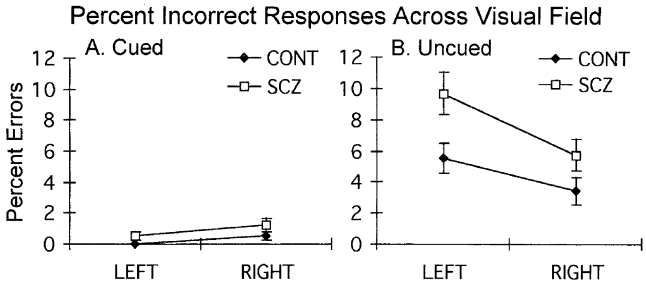

Fig. 5. SCZ showed an increased percentage of incorrect responses. There were no group differences with respect to Laterality (LEFT target, RIGHT target). There was a significant Laterality × Cuing effect due to increased errors to RVF targets for cued trials, and an increased rate of errors to LVF targets for uncued trials.

3.4.2. Incorrect responses

There was a main effect of SOA on incorrect responses, $F(9,234) = 8.12$, $P < .001$. This again interacted with Cuing, $F(9,234) = 5.95$, $P < .001$. As for anticipations, this was due to a significant increase in errors at SOAs of 159, 226 and 305. Unlike the case with anticipations, these errors were made almost entirely to the uncued location (Fig. 4B). There was a main effect of Group on incorrect responses, $F(1,26) = 5.29$, $P < .05$. This was due to the increased rate of errors by the schizophrenic group as mentioned above. However, there were no interactions between Group and any other factor. SCZ showed the same overall pattern of errors across SOAs as did CONT.

There was a significant interaction between Laterality and Cuing for incorrect responses, $F(1,26) = 7.13$, $P < .01$. This effect was due to an increased number of EMs made in error to the right visual field (RVF) (Fig. 5). For cued trials, subjects made more errors to RVF targets (rightward EM). For uncued trials, subjects made more errors when presented with LVF targets (rightward EM, after RVF cue). This did not further interact with GROUP, $F(1,26) = 0.51$, $P = .47$ (Fig. 5). There were no significant group differences in any laterality measures for our error analyses.

4. Discussion

This study used a nonpredictive peripheral cuing paradigm and examined facilitation and IOR at 10 different SOAs in medicated SCZ and CONT. All subjects showed facilitation at SOAs of 159 ms and less and IOR at SOAs of 505 ms and greater. However, SCZ significantly differed from CONT at SOA 305, where CONT showed IOR and SCZ continued to show facilitation.

While even the 10 SOAs used in the present experiment do not allow a precise measure of the crossover point from facilitation to IOR to be determined, this point can be estimated. One rough method of estimating this crossover point is to linearly interpolate between the last SOA showing facilitation and the first showing IOR (Klein, 2000).

Using such a procedure, CONT crossed from facilitation to inhibition at about 226 ms, whereas SCZ did not cross to inhibition until over 450 ms (see Fig. 3). This is consistent with a previous report by Huey and Wexler (1984) and Sapir et al. (2001) indicating a prolonged facilitation or a delay in the onset of IOR in SCZ compared to CONT.

4.1. Enhanced facilitation or delayed inhibition in schizophrenia

It has been proposed that facilitation and inhibition as measured by the IOR task represent two dynamically interacting functions (Tipper and Weaver, 1998). This study cannot directly differentiate between these two effects. Therefore, it is possible that our results reflect an enhanced or prolonged facilitatory processing component in our SCZ, rather than an aberrant inhibitory process (Sapir et al., 2001; Huey and Wexler, 1994). Certain details of the data presented here may be relevant in understanding IOR versus facilitation differences between our groups. It should be recognized that the SCZ show a normal magnitude of facilitation at early SOAs. More interesting, perhaps, is the pattern of RTs to the cued location for the schizophrenic and control groups. Both groups show decreasing RTs, that reach a minimum at 133 for CONT and 159 for SCZ (see Fig. 2). After this minimum in cued RTs, normal subjects show an RT slowing represented by a steadily increasing curve. This abrupt transition is not as striking for SCZ. SCZ show a somewhat slower rising curve just following the RT minimum, and a more rapidly rising RT curve only after the 305 SOA. The explanation for this pattern might be better discerned with the inclusion of a neutral cuing procedure in future studies. The use of a neutral cue would allow a determination of whether there is an enhancement of facilitatory processes that then gives the appearance of a delay in the normal IOR onset.

4.2. Inability to disengage attention

One proposed component of orienting is the need to disengage attention from the previously attended stimulus. The failure to disengage from the cue stimulus could produce a pattern of prolonged facilitation at cued locations. Thus, the apparently delayed appearance of IOR in our SCZ might reflect a failure to disengage attention from the cued location, rather than a delayed buildup of IOR per se. We do not think this account is a likely explanation for our findings, since we specifically used a cue-back procedure to ensure that attention would be drawn away from the initially cued location. In addition, previous research using a neutral cuing procedure suggests that SCZ do not show a failure to disengage attention on a similar orienting task (Sapir et al., 2001).

4.3. Object- versus location-based IOR

Further speculation on the differences we report between groups relates to the recent description of multiple forms of IOR. Tipper and Weaver (1998) and Tipper et al. (1991, 1994) have described the presence of two apparent forms of IOR: one based on location, and the other on object representation. Object-based IOR decays fairly quickly, whereas location-based IOR is constant and prolonged. Therefore, the changes noted in IOR at the period of IOR onset only, as reported here, might represent a selective dysfunction in object-based IOR. Whereas, the presence of normal IOR at longer SOAs might indicate a normally functioning location-based IOR. Also worth noting is a proposed anatomical model of these inhibitory processes. Tipper et al. suggested that location-based IOR utilizes subcortical structures, whereas object-based IOR requires cortical circuitry. This would be consistent with numerous studies indicating a cortical dysfunction as central to schizophrenia (for review, see Levin, 1984). A study specifically designed to assess object- versus location-based IOR in schizophrenia would perhaps be able to provide insight on these issues.

4.4. Laterality effects

There were no differences with respect to laterality between our patient and the control group. Since all of our subjects were medicated at the time of testing, this finding is consistent with previous reports indicating that medication normalizes laterality differences between patient and control groups (Maruff et al., 1995). However, we do report an overall effect of laterality. This was due to both our patient and control groups making faster responses to RVF targets. This enhanced RVF effect is consistent with other data from our lab showing slightly faster RTs to RVF targets (Sereno and Holzman, 1996; Larrison et al., 2000). This bias may represent an increased sensitivity of the RVF, or may simply reflect a speed accuracy trade off, as subjects also tended to make more rightward EMs in errors and anticipations.

4.5. Errors and response inhibition in IOR

Although the overall error rate was low, the overall pattern of errors across SOA was striking. By far, the majority of errors made by both patients and CONT occurred at the SOAs of 159, 226, and 305. These SOAs correspond roughly to the time points at which the transition from facilitation to IOR occurred (see Figs. 2 and 3). There was a slight increase in incorrect responses in our SCZ compared to CONT, but the pattern of errors across SOA did not differ between the groups. The normal pattern of errors in this paradigm is not at this time well understood. One possibility is that the instability of responses at the time of IOR onset represents a partial function of IOR. The dramatic fall off in errors with increasing IOR might suggest that IOR is a stabilizing force with respect to response. This is consistent with some models of action-based visual attentional systems (Tipper et al., 1998). This model proposes

that visual information flows automatically into action-based representations and that inhibitory mechanisms shape the responses to avoid chaotic or overresponding.

4.6. Manual versus saccadic responses

The experiment reported here measured saccades to targets as the response mode. This is in contrast with previous studies of IOR in SCZ, which have required a key press response. There are three important points to be made concerning this aspect of our procedure. First, our study extends the results of earlier studies which have reported abnormalities of IOR in SCZ by demonstrating that this pattern can be obtained even if response mode differs substantially, i.e., using EMs rather than manual responses. Secondly, saccadic responses are commonly used to investigate IOR in normal populations. Thus, our use of target-directed saccades rather than manual key press responses is not unusual from the standpoint of the wider IOR literature. Finally, there is no evidence that would suggest that response mode, per se, could have been responsible for the group differences reported here. Studies of IOR in normal populations generally have used both manual and saccadic responses interchangeably, ignoring the possible role of response factors in IOR. However, Briand et al. (2000) have reported time course differences between two different versions of an IOR task in normals. Specifically, saccadic responses to targets (as used here) showed a shift to IOR sooner than did manual key press responses to targets (Briand et al., 2000). Although there may be more than one reason for the differential time courses, one important factor appears to be related to the directness of the response (Khatoon et al., submitted for publication). In this study, simple, target-directed responses such as saccades or pointing to the target switch to IOR fairly quickly (within 200 ms), whereas the transition to IOR appears to become delayed or even absent (at an SOA of 1000) as the stimulus–response mapping becomes more indirect or complex (e.g., such as pressing a key or using a mouse to indicate target location). Hence, we believe that a target-directed saccade task, being a more direct response, may in fact be less likely to generate spurious differences in IOR time course between SCZ and normal subjects than would a manual version of an IOR task. Thus, while it is by no means proven that IOR is the same when measured using saccadic or manual responses, we believe that saccadic responses offer a simpler and perhaps cleaner paradigm for studying this phenomenon.

4.7. Medication effects

The present studies were performed in schizophrenic patients taking neuroleptic medications, and therefore, it is not possible to determine to what extent an attentional dysfunction compared to a medication effect contributed to the results. In the only study examining nonmedicated subjects using a single cuing procedure, IOR was reduced even at SOAs as late as 1000 ms for a subgroup of paranoid SCZ (Carter et al., 1994). This would suggest that the medication may have acted to normalize attentional performance of SCZ, to the point where they differed from CONT at only a single SOA. Again, it will be important to examine the whole time course and try to separately distinguish enhanced facilitation from reduced or delayed IOR. Future research using a more detailed time course and testing medicated and nonmedicated subjects will be needed to clarify the role of medication in the findings reported here.

5. Conclusions

The authors present data using a covert orienting task that measures facilitation and IOR in SCZ and CONT. Previous studies have shown contradictory results utilizing similar tasks. This study was intended to clarify these findings by examining intermediate time intervals that have been previously excluded. Examining these intermediate intervals demonstrated that there was a shift in the time course of IOR in SCZ that appeared as a delay in the onset of IOR. These findings lend support to previous studies of impaired inhibitory attentional mechanisms in schizophrenia.

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