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Schizophrenia patients show augmented spatial frame illusion for visual and visuomotor tasks

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Abstract

Previous research has identified several key processes of visual perception and visually guided action that are implicated in schizophrenia. Yet, it is not well understood whether similar or different brain mechanisms mediate the abnormalities in these two processes. To explore this issue, we examined visual and visuomotor processing in schizophrenia, utilizing an illusion known as the Roelofs effect. This illusion refers to the spatial mislocalization of an object within an off-centered frame, with the object appearing to be shifted towards the opposite direction of the frame offset. In this study, localization of the object was measured either by a direct visual response or by an immediate or delayed visuomotor (reaching-to-touch) response. Patients demonstrated significantly greater magnitudes of the Roelofs effect in all response modes, indicating the existence of excessive spatial contextual effects of the frame during the processing of visual and visuomotor information, and when the two types of information are integrated over a delayed visuomotor response condition. These results provide evidence for a hypothesis of improper inhibitory control as a common mechanism underpinning abnormal visual and visuomotor processes in this mental disorder.

Introduction

Schizophrenia patients often exhibit abnormal behaviors that are difficult to understand from the perspective of any single brain mechanism. To better understand the complex nature of impaired behavioral performance in this mental disorder, one should consider comparisons of the information processing among different brain mechanisms. Recent studies have identified several key perceptual and motor processes that are implicated in schizophrenia (O'Donnell et al., 1996, Carnahan et al., 1997, Chen et al., 1999, Javitt et al., 2000, Butler et al., 2008, King et al., 2008). Yet, it remains unclear whether commonalities exist among the brain mechanisms mediating abnormalities in visual perception and visually guided action.

Information for visual perception and visually-guided action is processed in separate cortical systems (Ungerleider and Mishkin, 1982, Livingstone and Hubel, 1988, Goodale and Milner, 1992, Bridgeman et al., 1997). The dorsal system mediates the processing of visual information for action (i.e., the 'action' system), whereas the ventral system mediates the processing of visual information for perception (i.e., the 'perception' system). It is important to note that, despite the anatomical and functional differences, these two parallel visual processing systems must interact in support of perception and action. One prominent

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example of this interaction is that the inputs from the perceptual system significantly influence information processing in the action system when a temporal delay is imposed between the presentation of visual stimuli and the initiation of visuomotor response (Bridgeman et al., 1997, Bridgeman et al., 2000). Different theories attempt to explain this delayed visuomotor response. One theory conjectures that, when delayed, visuomotor responses rely primarily on information from the perception system (Goodale and Milner, 1992). Another theory proposes that the perceptual modulation impacts planning, but not execution, of delayed visuomotor responses (Glover and Dixon, 2002). Despite the differences, both theories assert that information processing in the perception system plays a significant role in the delayed visuomotor responses. These dynamic interrelationships provide an opportunity for studying individual as well as interactive mechanisms pertinent to abnormal visual perception and visually-guided action in schizophrenia.

In this study, we adapted a spatial localization illusion paradigm - the Roelofs effect - for investigating visual and visuomotor processes. The Roelofs effect refers to the appearance of an object within an off-centered frame as being shifted towards the opposite direction of the frame offset (Roelofs, 1935) (Figure 1). The simplicity of this paradigm allows the use of identical stimuli to evoke both visual perception and visually-guided action. The visual and visuomotor forms of this illusion have been used to assess the two information processes, one for perception and the other for action (Goodale and Milner, 1992, Bridgeman et al., 1997). The delayed visuomotor form has been used to assess the modulation of visually-guided action by visual perception (Milner et al., 1999).

To evaluate the influence of inputs from early visual processing which are implicated in schizophrenia (Butler and Javitt, 2005), contrast detection was also assessed, using static and dynamic visual stimuli. The two types of stimuli are processed in the parvocellular and the magnocellular pathways, respectively (Merigan and Maunsell, 1993, Chen et al., 1996). These two pathways provide basic sensory signals for visual perception and visually-guided action.

Methods

Subject

Thirty-three schizophrenia patients and 34 normal controls participated in this study. The subjects were included based on the following general criteria: 1) right-handedness, 2) no history of any neurological disorders (such as seizure or stroke) or head injuries, 3) IQ > 70, 4) age between 18 and 66 years old, and 5) no substance abuse in the six months prior to participation.

Patients were recruited from McLean Hospital and the greater Boston area. Diagnoses were based on a structured clinical interview, the SCID-IV (First et al., 1994), which was conducted by experienced clinicians who were blind to the purposes of this study, and on a review of all available medical records. Seventeen patients had a diagnosis of schizophrenia and 16 patients had a diagnosis of schizoaffective disorder. All patients were medicated on antipsychotic drugs (mean CPZ = 502 mg, SD = 415 mg). The Positive and Negative Syndrome Scale (Kay et al., 1987) was administered to the patients (positive subscale = 15.4, SD=6.9; negative subscale=14.4, SD=5.8; general subscale=28.4, SD=8.8). Healthy controls were recruited from the local community. They were screened for the absence of Axis I psychiatric disorders using a standardized interview based on the SCID-I/NP (First et al., 2002). The two groups were matched on average age and sex.

The Wechsler Adult Intelligence Scale - Revised (verbal components) (Wechsler, 1981) was administered to all participants. The participants had normal or corrected to normal vision,

as assessed by the Rosenbaum Pocket Vision Screener. Table 1 provides demographic information of the participants.

Stimulus and apparatus

The target for spatial localization was a white spot (0.2 degrees in radius) on a black background (Figure 1). It was displayed in one of five locations (-2.75 , -1.375 , 0 , 1.375 , 2.75 degrees) along the horizontal axis of a computer monitor. A rectangular frame (20 degrees in width and 15 degrees in height) was presented and accompanied the target. The frame was centered at one of three locations (0 , -3.3 or 3.3 degrees) (Figure 1). In each trial, the target and the frame were presented for 1000 msec. In between trials, a small cross appeared at the center of the visual field to aid fixation. The stimuli were programmed via VisionShell software on a Mac G4 computer (Apple Computer, Inc.). The computer monitor (Accusync LCD, NEC, Inc.) was mounted with a 17" touch frame using acoustic wave technology (Intellitouch, ELO), and thus was touch-sensitive.

For visual contrast detection, the target was a sinusoidal grating. The grating was either temporally modulated (5 Hz) and had a low spatial frequency (0.5 cycles/deg - a dynamic stimulus), or was not temporally modulated (0 Hz) and had a middle spatial frequency (4 cycles/deg - a static stimulus). Each trial included two temporal intervals during which the target and a blank screen were presented. The order of the two presentations was randomized across trials. The stimuli were programmed via VisionShell software on a PowerPC computer (Apple Computer, Inc.) adapted with a luminance attenuator, which allowed fine gradations in contrast (Pelli and Zhang, 1991). The grating orientated vertically and was displayed through a circular window (19 degrees of visual angle) for 300 msec.

The testing was conducted in a room where no other lighting sources were available except for that provided by the computer monitor.

Procedure

Subjects performed three spatial localization tasks and a visual contrast detection task in separate sessions.

Visuomotor task

In each trial, subjects were asked to poke the center of the target location on the touch-sensitive monitor with their right index finger, immediately after the offset of the target and the frame presentation. Spatial coordinates (x, y) for all finger touches made during the performance of the task were recorded.

Delayed visuomotor task

Subjects were asked to poke the target location on the monitor with the right index finger, two seconds after the offset of the target and the frame presentation. An auditory tone indicated the end of the two-second delay when subjects needed to provide a finger-touch response. Spatial coordinates (x, y) for all finger-touches made during the performance of the task were recorded.

Visual task

Subjects were asked to verbally report the perceived location of the target immediately after the offset of the target and the frame presentation. Each perceptual response was among five alternative forced choices - far left, left, central, right or far right - corresponding to the five possible target locations. Subject's perceptual response in each trial was recorded by an experimenter using a keyboard.

Contrast detection task

Subjects were asked to indicate which of the two temporal intervals in each trial, the first or the second, contained the target (grating) by pressing one of two designated keys. The contrast level of the target changed from trial to trial according to a two-alternative forced choice staircase procedure (3-down and 1-up, that is, decreasing stimulus strength (contrast level) after 3 consecutive correct responses and increasing contrast level after each incorrect response). The staircase stopped after 12 reversals. This procedure identified 79% correct threshold point on a psychometric function (Levitt, 1972, Chen et al., 2004).

The order of the tasks was counterbalanced among subjects. For the visual, visuomotor and delayed visuomotor tasks, each combination of target and frame positions was presented eight times throughout a testing session. With five target positions and three frame positions, a total of 120 trials were administered for each of the three tasks. During testing, the subject's head was stabilized on a chin-rest. For the contrast detection task, the trial number depended upon the subject's online responses, typically ranging from 35 to 45 trials for each of the two stimulus conditions. Cumulatively, the duration of testing across sessions was about 40 minutes.

Results

A three-way ANOVA (frame position $\times$ group $\times$ task) showed that the frame position significantly affected subjects' response to target position ($F=163.2$, $p<0.001$): the target appeared shifted away from the frame position (Figure 2). There was also a significant interaction between frame position and group ($F=8.1$, $p<0.001$), indicating that frame position had a greater effect on patients than controls. Additionally, there was an interaction between frame position and task ($F=4.3$, $p=0.002$), indicating that the effects of frame position varied among tasks. The main effect of group was not significant, due to the significant interaction between group and frame position. The interaction between group and task was, however, not significant, indicating the group differences were similar across tasks.

To further evaluate the effect of frame position (i.e., the Roelofs effect) for different tasks, we measured the differences in subjects' responses between the left and the central frames, and between the central and the right frames (right field vs. left field). This difference allowed for quantification of the magnitude of the Roelofs effect created by frame offsets.

For the visuomotor task, a two-way ANOVA (field $\times$ group) showed a significantly greater Roelofs effect in patients than in controls ($F=7.0$, $p=0.009$, effect size (ES)=0.48). The field effect and the interaction between group and field were non-significant, indicating that the left and right fields were similarly affected by the frame shift in both groups. For the delayed visuomotor task, a two-way ANOVA (field $\times$ group) showed a significantly greater Roelofs effect in patients than in controls ($F=6.7$, $p=0.011$, ES=0.45). The field effect and the interaction between group and field were non-significant. For the visual task, a two-way ANOVA (field $\times$ group) showed a significantly greater Roelofs effect in patients than in controls ($F=14.3$, $p<0.001$, ES=0.66). The field effect and the interaction between group and field were non-significant.

Patients' performance on the delayed visuomotor task was predicted by their performance on the visual and immediate visuomotor tasks. Using backward stepwise regression, we found that the performances on the visual and visuomotor tasks, two independent factors, accounted for a large proportion of variance in performance on the delayed visuomotor task ($R^2 = 0.61$), and both factors remained in the model as significant predictors (immediate visuomotor task, $t=2.60$, $p = 0.014$, ES=0.17; visual task, $t=2.90$, $p = 0.007$, ES=0.21). For

the control group, the total amount of variance accounted for was larger ($R^2 = 0.86$), but performance on the immediate visuomotor task was the only significant predictor ($t=10.89$, $p < 0.001$, $ES=0.78$ versus $t=1.77$, $p = 0.09$, $ES=0.08$ on the visual task).

For the contrast detection task, the group difference in perceptual thresholds, defined as minimum contrast level at which subjects achieve 79% accuracy level, was significant for the dynamic stimulus ($t=2.7$, $p=0.008$), but not for the static stimulus ($t=0.14$, $p=0.89$) (Figure 3).

The Roelofs effect, averaged across the left-shifted and right-shifted frames for each subject, was not correlated with the contrast detection thresholds in the patient group. In the control group, moderate correlations were found between contrast detection thresholds for the dynamic stimulus and the Roelofs effect for the two visuomotor tasks (intermediate: $r=0.34$, $p=0.04$; delayed: $r=0.46$, $p=0.02$). None of the correlations between magnitude of the Roelofs effect and PANSS scores or CPZ levels was significant.

Discussion

The Roelofs effects were significantly greater in schizophrenia patients than in healthy controls. This group difference applied to the visual, visuomotor and delayed visuomotor tasks.

Commonality in visual perception, visually-guided action and their interaction

The commonality of these greater spatial contextual effects in patients supports the notion that a similar impairment mechanism underlies visual perception and visually-guided action in the mental disorder. The excessive nature of the spatial contextual effects among patients also points to improper inhibitory control over spatial context as a candidate mechanism responsible for the abnormal behaviors.

The spatial-contextual effect here represents a surround effect modulating a central response. Previous studies have found *reduced* perceptual grouping of spatial context in schizophrenia (Silverstein et al., 2000, Dakin et al., 2005, Yoon et al., 2009), suggesting weakened connection of collateral neural units involved in processing central and surrounding signals. This study however found *greater* spatial contextual effects in patients, suggesting that altered surround suppression exists in their visual systems. The stimuli constitute one significant difference between this and previous studies. In the previous studies listed above, the stimuli used for the central target and context were similar (gratings of various forms). As such, the processing of similar central and surrounding signals may involve specialized or localized mechanisms. On the other hand, the present study used different stimuli for central target (dot) and context (frame). Using global motion stimuli (random dot pattern), one of our previous studies also found an increased surround effect in patients (Chen et al., 2008b). The processing of central and surrounding signals that differ categorically or are global in nature may involve very different or more broadly tuned mechanisms. Thus, the different contextual effects in patients' results may be due to the involvement of the separate mechanisms that are differentially impaired in opposing ways in schizophrenia.

The apparent incongruity in patients' performance and the underlying mechanisms may not be accidental, given theoretical and empirical findings on brain organization in this mental disorder. For example, schizophrenia has been conceptualized as hyperdopaminergia at the subcortical level and hypodopaminergia at the cortical level (Davis et al., 1991). Brain imaging studies have found both abnormally reduced and amplified cortical activity in patients during performance of visual tasks (Renshaw et al., 1994, Chen et al., 2008a). From

this perspective, patients' abnormal behaviors should not be simply interpreted as either decreased or increased capacities of information processing. Rather, their performance change from one spatial organization task (e.g. decreased perceptual grouping) to another (e.g. increased spatial contextual effects) may be a perceptual consequence of the drastic change of brain activity levels when different types of information processing mechanisms are involved. Our result of excessive contextual effects in patients indicates that the influence of the surrounding frame is not properly suppressed when making perceptual decision, pointing to an abnormal inhibitory control in processing the relevant visual information.

The excessive spatial frame effect in patients agrees with some general concepts of information processing in schizophrenia. Hyper-responsiveness to the environment in patients was observed as early as Bleuler's time (Bleuler, 1950). Modern electrophysiological studies have found sensory gating deficits in schizophrenia patients (Braff et al., 1977), the consequence of which is an overflow of sensory inputs during information processing. At the basic visual processing level, excessive surround suppression on motion perception of a central target has been found in patients (Chen et al., 2008b), and in un-medicated patients sensitivity to a simple visual stimulus is heightened (Chen et al., 2003). Patients' greater spatial context modulation may be associated with poor filtering of sensory information, which would allow amplified influence of irrelevant information (frame) on the relevant task (localizing central target). The results of this study highlight excessiveness or 'hyper-responsiveness' as a behavioral manifestation of abnormal inhibitory control in this mental disorder.

Two recent studies indicate that perceptual judgment during the Roelofs illusion involves the parietal cortex. An fMRI study found that superior parietal cortex and precuneus were specifically activated for the Roelofs illusion task (Walter and Dassonville, 2008). Another study found that a patient suffering bilateral lesion of dorsal visual stream demonstrated a similar Roelofs illusion to controls, suggesting that the perceptual judgment of the visuomotor behavior may depend upon other non-dorsal visual streams (Coello et al., 2007). Based on these results, schizophrenia patients' augmented visual response during the Roelofs illusion (as found in this study) may not be associated with the conventional ventral system (or the temporal cortex), as alluded earlier, nor with the conventional dorsal system (or the dorsal parietal cortex). Instead, the augmented visual response may involve the superior part of the parietal cortex. The neural substrates of visually-guided action during the Roelofs illusion are unknown at this point. A single brain system has been suggested to account for visual perception and visually-guided action during the illusion, due to the result of similar shifts in reference-frame bias obtained from the saccade and anti-saccade paradigms (Dassonville et al., 2004). As such, our data from the visual and visuomotor paradigms would point to the same brain system, namely the superior parietal cortex, as one possible neural substrate for the augmented Roelofs illusion in schizophrenia.

Functionally, the converging results from the paradigms used in this study suggest that abnormal inhibition plays an important role in visual perception and visually guided action in schizophrenia. The revelation of such a mechanism helps to design further studies on the neural substrates of both visual and visuomotor deficits.

Interaction between visual perception and visually-guided action

It has long been hypothesized that schizophrenia is a disorder of brain disorganization (Bleuler, 1950, Friston, 1998). Anatomical studies have increasingly found evidence for altered connectivity among different parts of schizophrenic brains (Kanaan et al., 2005, Kubicki et al., 2007). Abnormal electrophysiological responses in schizophrenia patients have also been found when multiple brain systems are involved (Butler and Javitt, 2005,

Stephan et al., 2006). How these abnormalities in brain structures and in brain functioning are associated with patients' behavior is not completely understood. One critical question is whether individual abnormalities in specialized brain systems give rise to abnormal behavioral responses, or if interactions among specialized brain systems also contribute. Patients' increased Roelofs effect in the delayed visuomotor response condition suggests one form of such interaction: namely, that the modulation of the visually-guided action by the visual perception is altered in this mental disorder.

How visual perception and visually guided action are implicated in schizophrenia is a more complex question than previously thought. Using a visual illusion during size estimation, a recent study found that the behavioral performance mediated by the dorsal system was selectively impaired, whereas behavioral performance mediated by the ventral system was relatively spared in patients (King et al., 2008). Other studies, however, have found abnormal spatial contextual effects in schizophrenia during perceptual tasks mediated primarily by the ventral system (Silverstein et al., 2000, Must et al., 2004, Uhlhaas et al., 2006). The present study found abnormally increased Roelofs effects in both visual and visuomotor tasks, a result implicating both visual and visuomotor processes. One major disparity among these studies was the content and configuration of the spatial context. When one stimulus was surrounded by other stimuli, spatial contextual effects differed between groups (e.g., (Uhlhaas et al., 2006) and this study). However, when spatial context involved only two stimuli displayed side-by-side, no group difference was found (King et al., 2008). Thus, the way and the extent to which contextual processing is implicated appears to be an important factor determining the impairment of the two parallel visual systems in schizophrenia.

Imposing a delay between target offset and initiation of visually-guided action provides a condition under which the visual and visuomotor processes interact. This temporal delay allows the visuomotor process to be fed with inputs from the visual process (Bridgeman et al., 2000). These visual inputs are crucial, since representation of target location in the visuomotor process begins to degrade approximately one second after target offset (Wong and Mack, 1981, Abrams and Landgraf, 1990). The delayed visuomotor response therefore must rely upon an interaction between the perceptual inputs and the remaining target representation in the visuomotor process (Milner et al., 1999, Himmelbach and Karnath, 2005, Rossit et al., 2009). This interaction is evidenced by the increased Roelofs effect exhibited in both groups during the delayed visuomotor response condition, as compared to the immediate visuomotor response condition. Patients' greater magnitude of the Roelofs effect in the delayed condition (Figure 3) suggests that abnormal spatial contextual processing occurred while the information processing for visually-guided action was modulated by visual inputs.

The regression analysis shows that controls' performance in the delayed visuomotor task was predicted by that in the visuomotor task, but not by that in the visual task. In patients, this relationship is extended to the visual task, i.e. the performances in both visual and visuomotor tasks are significant predictors of the performance in the delayed visuomotor task. This relationship pattern indicates that abnormality in visual perception constrains also the performance in visually-guided action in schizophrenia.

Implications for the understanding of and behavioral interventions for schizophrenia

For spatial localization of a target, the visual process tends to take contextual information into account, but the visuomotor process does not (Loomis et al., 1992, Pagano and Bingham, 1998). Consistent with this notion, this study found that the magnitude of the Roelofs effect is largest in visual perception (Figure 3) and smallest but not negligible in visually-guided action (Figure 3). These findings indicate that spatial context differentially

influences spatial localization during the visual as well as visually-guided action modes. During the delayed visually-guided action mode, it is not completely clear whether patients' increased effects are due to either altered visual inputs being fed into processing for visually-guided action or due to altered coordination between the perceptual inputs and the remaining representation of target location (after the delay) in the visuomotor process. To differentiate these two kinds of abnormal interactions, future studies should include a series of temporal delays (both shorter and longer than the 2 sec delay used in this study), for which the representation of target location in the visuomotor process may either remain robust or be further decayed.

The visual and visuomotor processes receive inputs from early processing - namely, that within the parvocellular and the magnocellular pathways, respectively (Ungerleider and Mishkin, 1982, Van Essen, 2005). Given that the early visual system is deficient in schizophrenia (Butler and Javitt, 2005), its influence on the functioning of the visual and visuomotor processes in patients needs to be considered. In this study, patients' performance on contrast detection was deficient for the dynamic stimulus, yet its correlations with performance on the visuomotor tasks, as well as on the visual task, were non-significant. These correlations were significant in the control group, though. These results are consistent with the notion that hierarchical information processing from low to high levels, available in controls, may be interrupted in patients, and that independent abnormalities exist at the level of visual and visuomotor processes. This notion is consistent with the result that patients' performance on the visual and visuomotor tasks was not correlated with the levels of their clinical symptoms. A recent study, however, found that in schizophrenia several abnormal visual illusions are associated with early visual processing deficits (Kantrowitz et al., 2009). Thus, how basic visual sensitivity contributes to the perception of visual objects in schizophrenia merits further investigation.

Contextual information is a vital aspect of all spatial landscapes in which humans operate. Patients' excessive responses to this information may abnormally affect their visually-guided behaviors. It is therefore useful for patients to learn to appropriately reference the spatial context of central targets before acting on them. Compared to training for cognitive functioning, training for visuomotor functioning has, as of yet, been insufficiently explored in schizophrenia. Understanding the similarities and differences of the mechanisms underlying abnormal visual perception and visually-guided action, and incorporating both kinds of behavioral training into intervention should yield new insights for the improvement of the quality of patients' lives.

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Figure 1.

Illustration of stimuli used to induce Roelofs effect. The top, middle and bottom panels are for three frame positions (left-shifted, center and right-shifted). In each panel, the target can appear in one of the five positions (far left, left, center, right or far right). The outer boundary represents the computer screen on which the frame and the target were displayed. Identical stimuli were used for visual, immediate and delayed visually-guided actions.

Figure 2.

Averaged perceived or touched positions for the visual, immediate and delayed visuomotor task conditions. In each panel, the x-axis represents target position whereas the y-axis represents subjects' responses. The dotted line indicates veridical responses to the target positions (i.e. no Roelofs effect). The filled and open symbols are for controls and patients, respectively. Error bars represent ± 1 standard errors. For the visual task (bottom row), subjects' responses are determined by converting the data derived from the five-alternative choices to corresponding target positions. For the visuomotor (top row) and delayed visuomotor (middle row) tasks, subjects' responses are finger-touched positions on the touch-sensitive screen.

Figure 3.

Summary of group responses for all task conditions. The left panel is for the visual, immediate and delayed visuomotor tasks, whereas the right panel is for the contrast detection task. In each panel, the x-axis represents groups and tasks, whereas the y-axis represents the Roelofs effects, defined as the differences between subjects' responses under the central frame condition and under the left- or right-shifted frame condition. The filled and open bars are for patients and controls, respectively. Error bars represent ± 1 standard errors.

Table 1

Demographic Characteristics of the Sample

	Sex	Age (year)	Education (year)	Verbal IQ [*]
HC (n=34)	F=17 M=17	41.5 (15.1)	15.8 (2.1)	111.8 (11.2)
SZ (n=33)	F=15 M=18	42.5 (20.5)	14.1 (1.6)	101.4 (12.0)

Group Mean (Standard Deviation)

HC- Healthy control; SZ – schizophrenia;

F- female; M- male

* based on the WAIS-R (Wechsler, 1981)