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Perceptual organization and visual search processes during target detection task performance in schizophrenia, as revealed by fMRI☆

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ABSTRACT

Background: Past studies of perceptual organization in schizophrenia have demonstrated impairments binding fragmented stimulus components into unified representations. ERP and fMRI data indicate that even under conditions of adequate behavioral task performance, significant and meaningful changes in cortical and subcortical activation are present. Here, we examined, using fMRI, activation differences on a visual task wherein feature grouping was a precursor to the formation of distinct groups in the service of target location and identification.
Method: Fourteen schizophrenia patients and 16 healthy controls completed a target detection task with 2 conditions: one in which target–distractor grouping facilitates detection (the *Isolated* condition) and one in which it hinders detection (the *Embedded* condition). Stimuli were blocked by condition. Accuracy and RT data were obtained in addition to fMRI data.
Results: Patients and controls did not differ significantly in accuracy or RT in either condition. Within this context, controls demonstrated greater recruitment of brain regions involved in visual–spatial processing, and the groups differed in activity in areas known to support visual search, visual analysis, decision making and response generation.
Conclusion: These findings are consistent with past data indicating reduced processing of stimulus organization, and the subsequent use of inefficient visual search strategies, even under conditions when behavioral performance is at a high level and matches that of healthy controls.

Over the past 30 years, consistent evidence has accumulated for an impairment in perceptual organization in schizophrenia (see Uhlhaas & Silverstein, 2005 for a review). This phenomenon has been demonstrated in both medicated and unmedicated patients. It has also been revealed via paradigms in which impaired grouping leads to superior performance, compared to controls, in making a decision about a single item that is organized with distractors in such a way that normal grouping processes hinder target detection and/or identification (e.g., Place & Gilmore, 1980). Recently, the National Institute of Mental Health (NIMH)-funded Cognitive Neuroscience Treatment Research for Improving Cognition in Schizophrenia (CNTRICS) project highlighted perceptual organization impairment in schizophrenia as being a critical domain for furthering our understanding of the cognitive neuroscience of this disorder (Barch et al., 2009; Green et al., 2009). In addition to the wealth of psychophysical evidence, this decision was based on two main sets of findings. First, electrophysiological studies of perceptual organization in schizophrenia have revealed abnormalities in both specific waveforms (e.g., P1) (Doniger, Silipo, Rabinowicz, Snodgrass, & Javitt, 2001; Foxe, Doniger, & Javitt, 2001) and synchronization of gamma- and beta-band oscillations (Spencer et al., 2003; Spencer et al., 2004; Uhlhaas et al., 2006) that suggest reduced neural connectivity as its basis. Second, evidence from the brain injury literature indicates prefrontal involvement in generating top-down input during perceptual organization (Ciaramelli, Leo, Del Viva, Burr, & Ladavas, 2007), and the prefrontal cortex has been demonstrated to function abnormally in schizophrenia (Tan, Callicott, & Weinberger, 2007), although its relationship to perception in the illness has been largely unexplored.

To date, however, there has been only a single fMRI study of perceptual organization in schizophrenia (Silverstein et al., 2009). This demonstrated that schizophrenia patients were characterized

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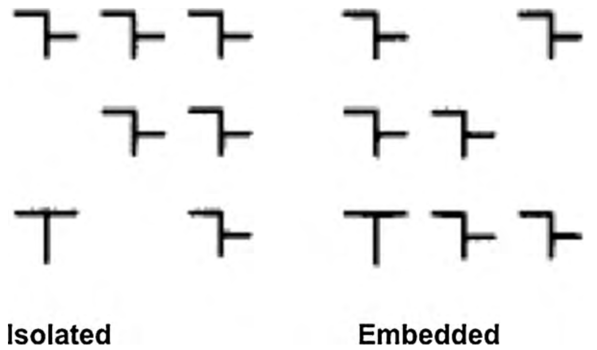

Fig. 1. Examples of stimuli used in the target detection task. Left – sample stimulus from the Isolated condition. Right – sample stimulus from the Embedded condition. In each condition, the target (T or F) could appear at any of the 4 corners, maintaining its relative position to the other elements.

by less activation in occipital regions (e.g., V2–V4) subserving integration of stimulus elements into perceptual groups, and also less activation in parietal and frontal regions involved in visual attention and amplification of the signal emerging from occipital areas. These group differences in fMRI activation were present even when the groups were matched on behavioral performance. That study investigated the relatively low-level process of integrating elements, presented within a noisy background, into a single group. In this study, we examined another, but higher-level function of grouping, that of parsing elements into multiple groups to facilitate location and identification of a target.

To do this, we adapted Banks and Prinzmetal's (1976) procedure. Examples of stimuli are shown in Fig. 1. Two conditions were utilized, one in which the nature of target–distractor grouping should enhance performance, and one in which it should hinder performance. In the former, the target (T or F) always stood apart from the group of distractors (i.e., the *Isolated* condition). In this condition, the target and distractors are (normally) automatically grouped apart and the target is attended to automatically by virtue of its being processed as "figure" relative to the larger group's "ground." After attending to the target, a single perceptual decision is required: "T" or "F." In contrast, in the latter condition, the target is always embedded within the group of distractors, and a single distractor stands out (i.e., the *Embedded* condition). In this condition, attention is also automatically directed to the single element that is outside the larger group, and so successful performance in this condition requires: (a) a redirection of attention to the larger group; (b) a time consuming serial search through this group of elements to identify the target; and (c) following each shift of attention to a different element, a decision regarding whether it is a distractor, a "T" or an "F." Normally, therefore, the Isolated condition is associated with a higher accuracy level and faster reaction time (RT) compared to the Embedded condition (Banks & Prinzmetal, 1976; Silverstein et al., 1996; Silverstein et al., 2006).

In a prior study (Silverstein et al., 1996, Study 2) both patients and controls demonstrated superior performance in the Isolated condition compared to a variant of the Embedded condition. Therefore, this context of adequate behavioral performance was ideal for examining neural correlates of performance in the absence of a generalized deficit (Silverstein, 2008). Importantly, data from electrophysiological studies (Spencer et al., 2003, 2004) indicate that even when schizophrenia patients perform normally on perceptual organization tasks, in terms of behavioral indices, abnormalities can be revealed via the physiological index. In the present study, we used fMRI to explore the extent to which patients and controls would demonstrate differences in brain activity related to visuo-spatial processing and visual search, even while demonstrating similar patterns of performance (accuracy and RT) across the two conditions described above. Specific hypotheses were as follows:

In the Isolated condition (i.e., Isolated minus Baseline):

(1) controls would demonstrate greater activation than patients in regions involved in visuo-spatial processing, but not in attentional control (since, if perceptual organization is adequate, in this condition, re-allocation of attention is not required); whereas

(2) patients would be less successful in grouping apart the target and distractors and would therefore engage in greater processing of distractor elements, requiring more activity in regions involved in attentional control and decision making.

In the Embedded condition (i.e., Embedded minus Baseline):

(3) controls would demonstrate greater activation in regions involved in attentional control and perceptual decision making (and response conflict), indicating more efficient and goal-directed serial search; whereas

(4) patients would demonstrate greater activation in non-frontal regions involving shifting attention, reflecting a more diffuse search process that is less driven by top-down control (as has been noted in prior behavioral studies, e.g., Gold, Fuller, Robinson, Braun, & Luck, 2007).

Since pre-attentive and attentive processing are required in both conditions, we had fewer hypotheses regarding group differences in BOLD signal changes in *between-condition* contrasts, for regions supporting attention. Therefore, these analyses were exploratory, although potentially important, since they are less prone to alternative explanatory accounts than contrasts involving subtraction of baseline values. Here, we hypothesized that the groups would differ in activity in regions involved in processing stimulus and response conflict, especially in the Embedded minus Isolated contrast.

1. Methods

1.1. Subjects

The sample consisted of 14 people with schizophrenia (9 men) and 16 healthy control subjects (5 men). Schizophrenia patients were enrolled either in a partial hospital or outpatient program. The groups were matched on age, education, and maternal education levels. All subjects completed a practice version of the task, and were familiarized with the scanning environment (using a mock scanner) the day before the fMRI session. Also at that session, all patient subjects were interviewed using the: (1) Structured Clinical Interview for DSM-IV Diagnosis, Patient Version (SCID-P, First et al., 1995); and (2) the Positive and Negative Syndrome Scale (PANSS, Kay, Opler, & Fiszbein, 1987), which was scored using a five factor model, including Positive, Negative, Cognitive, Excitement, and Depression symptoms (Lindenmayer, Bernstein-Hyman, & Grochowski, 1994). Medication level was assessed for patients using published conversion formulas (Woods, 2003) to generate chlorpromazine equivalent daily doses for second generation antipsychotic medications. All subjects were tested at the MRI Center at the University of Illinois at Chicago.

1.2. Stimuli

1.2.1. Task

The target was always positioned at one of the 4 corners of the array. Because there were 2 possible targets (T or F), there were eight individual stimuli in each of the two conditions. Stimuli were blocked by condition. In each block, each stimulus was shown three times, for a total of 24 stimuli in each condition. Each trial consisted of a 100 ms presentation of the stimulus, followed by a 1900 ms response period. The two active conditions followed the same order for all subjects: Isolated followed by Embedded. For each trial, subjects were asked to indicate their response (i.e., target choice) by pressing one of two buttons on a standard button box (i.e., left button for "T" or right button for "F"). Responses and latencies were automatically recorded and sent to an Access database.

1.3. Brain imaging

Each trial block lasted for 48 s with 24 brain volumes acquired, separated by a 26 s "rest" block with central fixation. This central fixation condition was included to allow the hemodynamic response function to return to baseline prior to the second block. The task began with 8 volumes (16 s) of rest to allow a period of adaptation