Perceptual and attentional asymmetries in schizophrenia: further evidence for a left hemisphere deficit

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Abstract

Increasing evidence suggests the presence of a lateralizing attentional deficit in schizophrenia. In the present study, 23 unmedicated patients with schizophrenia (mean age = 32.1 years) and 14 age- and sex-matched normal subjects were studied with the Global/Local Task to provide converging evidence for the presence of a left-hemisphere-associated attentional deficit in schizophrenia. This task is sensitive to the integrity of mechanisms involved in discriminating local and global elements of stimuli. Previous research has linked the discrimination of local targets to left hemispheric processes and the discrimination of global targets to right hemispheric processes. As predicted, patients were impaired in the detection of local level targets, consistent with a left hemispheric deficit. The degree of impairment correlated with the patient's level of auditory hallucinations. These results are consistent with previous studies showing an asymmetrical attentional deficit in schizophrenia and left hemispheric dysfunction. The correlation between this deficit and auditory hallucinations is consistent with a hypothesized relationship between this symptom in schizophrenia and left temporal pathology.

Keywords: Laterality; Attention; Left hemisphere; Hallucinations auditory; Schizophrenia

1. Introduction

Attentional pathology is one of the most clinically apparent and widely studied aspects of the psychopathology of schizophrenia (Braff, 1993). Results obtained with a diverse range of procedures, from pen-and-paper measures (Tomer and Flor-Henry, 1989), to dichotic listening tasks (Wexler and Heninger, 1979; Green et al., 1994), to spatial cuing tasks (Posner et al., 1988; Strauss et al., 1991, 1992; Carter et al., 1992, 1994; Nestor et al., 1992), suggest the presence of lateralizing abnormalities of attention in schizophrenia. These results have often been interpreted as indicating deficits in left-hemisphere-related attentional processes. This interpretation has, in turn, generated a number of hypotheses about the neurobiological
substrates of attentional dysfunction in schizophrenia (Early et al., 1989; Carter et al., 1994).

Tomer and Flor-Henry (1989) reported that unmedicated patients with schizophrenia who performed a dot-cancellation task tended to neglect the right side of space. Using a spatial cuing task, Posner et al. (1988) reported a ‘neglect-like’ pattern of performance in a group of acutely ill, mostly medicated patients. This pattern resembled that seen in individuals with left parietal lesions. In studies of chronic schizophrenia, Carter et al. (1994) and Nestor et al. (1992) reported that this group failed to show the normal reaction time disadvantage associated with detecting a target appearing in the right visual field after the appearance of a cue instructing them to attend to the left visual field. These studies suggest a spatial attention deficit in schizophrenia characterized by abnormalities in processes located in the left hemisphere.

In the experiment described below, we sought to provide further evidence for the presence of dysfunction in left hemispheric attentional mechanisms using a procedure from cognitive neuropsychology known as the Global/Local Task. Studies in normal and brain-injured subjects suggest that performance of specific aspects of this task depends on processing mechanisms localized in the left hemisphere, particularly left superior temporal and temporo-parietal regions. During this task, subjects are presented with hierarchically constructed stimuli (large letters or forms made up of small letters or forms; see Fig. 1) and are required to identify the occurrence of targets that can appear at either the global or the local level of the stimulus (global = the large letter, local = the small letter).

On the basis of initial results using this procedure, Navon (1977) proposed that global attributes of a stimulus be analyzed first, with subsequent analysis of local elements. This theory of global precedence has been superseded with the recognition that many factors determine the relative speed of processing of the local and global elements of stimuli, including sensory factors (such as visual angle or the retinal location of the stimulus), pattern-recognition factors (discrimination vs. detection), and attentional factors (stimulus response compatibility, spatial uncertainty, and instructional set) (Lamb and Robertson, 1988). It is generally accepted that there are at least two cortical processing pathways for the perceptual analysis of hierarchical stimuli, one biased toward processing at the local level, and one toward the global level (Navon, 1981; Robertson et al., 1988; Robertson and Lamb, 1991). Research in normal subjects, who were presented with Navon type stimuli (e.g., see Fig. 1) in the right or left visual field, demonstrated that local stimuli presented in the right visual field were processed faster than global stimuli (Martin, 1979; Sergent, 1982) and that global targets presented in the left field were processed faster than local targets (Sergent, 1982). This finding was replicated and extended by Robertson et al. (1993) in commissurotomized patients who showed a left > right field advantage for global targets and a right > left field advantage for local targets. We have also replicated this finding in normal subjects (Carter et al., unpublished data). These findings have led to the elaboration of a computational model for global and local processing, in which the left hemisphere weights local information more heavily than global information, and vice versa for the right hemisphere. This difference in weighting appears to be driven by the relative amounts of low and high spatial frequency information present in the stimuli (Hazeltine and Ivry, 1994; Ivry and Robertson, 1996). Global targets contain lower spatial frequencies than local targets, independent of the overall size of the stimulus.

In a series of recent studies, Robertson and colleagues have confirmed that the left hemisphere has a processing advantage for local targets while the right hemisphere has an advantage for processing global stimuli (Robertson et al., 1988; Lamb et al., 1989). These studies of patients with focal brain lesions have also suggested that the temporal-parietal junction may have unique importance for the lateralizing aspects of performance on the Global/Local Task. For example, lesions involving the inferior parietal lobule impair the subject’s ability to allocate attention strategically to one or the other level to improve target discrimination at that level. More important for the study of schizophrenia, lesions of the left superior temporal gyrus and left temporo-parietal junction impair the subject’s ability to detect tar-
gets at the local level, while lesions of the right superior temporal gyrus impair target detection at the global level.

A number of studies have suggested that lateralizing cortical pathology, particularly of the left temporal lobe, is associated with auditory hallucinations in schizophrenia. For example, Barta et al. (1990) reported that volume reduction of the left superior temporal gyrus was correlated with the intensity of patients' auditory hallucinations. Using positron emission tomography with $^{18}$F-deoxyglucose, DeLisi et al. (1989) found that hallucinating patients showed increased metabolism of the left superior temporal gyrus. Finally, Green et al. (1994) reported that hallucinating patients showed a loss of the normal right ear advantage during a dichotic listening task while nonhallucinating patients did not, a finding that was interpreted as indicating a deficit in left temporal cortical functioning.

On the basis of evidence that schizophrenia is associated with a left lateralizing attentional deficit and findings suggesting that pathology in the left superior temporal gyrus is associated with the development of auditory hallucinations, we made the following predictions about Global/Local Task performance in schizophrenia: (1) Patients with schizophrenia will show a pattern of impairment on the Global/Local Task consistent with the presence of a left lateralizing lesion, specifically a deficit in identifying local targets. (2) The severity of patients' local deficits will be positively correlated with the intensity of their auditory hallucinations. (3) Results using Posner's covert orienting of attention task (Posner et al., 1988; Strauss et al., 1991, 1992; Carter et al., 1992; Nestor et al., 1992) suggest that the ability to use a location cue to control visual attention in order to benefit detection performance is normal in schizophrenia. Therefore, we predicted that the ability to use a cue to attend to either the global or the local level of the stimulus (associated by Robertson et al. with the integrity of the inferior parietal lobule) would be intact in schizophrenia.

2. Methods

2.1. Subjects

Participants were 23 outpatients who met DSM-III-R criteria for schizophrenia as determined by the Structured Clinical Interview for DSM-III-R (Spitzer and Williams, 1986) and 14 normal control subjects. Patients were entered in a clinical trial and had been withdrawn from antipsychotic medication at least 2 weeks before testing. Two patients had been treated previously with haloperidol decanoate and had received their last shot 9 and 10 weeks before testing. Some patients had continued to use anticholinergic medications up to 4 days before testing, and six had used short-acting benzodiazepines, chloral hydrate, or diphenhydramine intermittently during their neuroleptic-free washout period. These subjects took no medications for 24 h before testing. Patients had been ill for a mean of 11.3 (SD = 7.8) years. They scored in the mild to moderate range on core symptoms of the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962). The mean total BPRS score was 39.6 (SD = 11.8). Normal subjects were recruited by advertisement and had no lifetime history of mental disorder and no first degree family history of psychotic disorder. Fourteen normal subjects were matched with patients for age (patients: mean = 32.1 years, SD = 5.3; normal subjects: mean = 31.3 years, SD = 5.5 years; t = 0.47, df = 35, P = 0.65), sex (patients: 18 males, 4 females; normal subjects: 10 males, 4 females; $x^2 = 0.64$, df = 1, P = 0.43), and years of parent's education (patients: mean = 13.3, SD = 2.53; normal subjects: mean = 13.0, SD = 3.64; $t = 0.23$, df = 34, P = 0.82). There was one left-handed subject in each of the two groups. All subjects had normal or near-normal visual acuity measured by Snellon testing. All subjects gave written informed consent on the day of testing. Both patients and normal subjects were paid for their participation.

2.2. Procedures

Stimulus presentation was controlled by an Everex tempo 386 PC and presented in the center of a Princeton color monitor. Subjects' heads rested on a chin rest 295 mm from the screen. Stimuli subtended visual angles of $6.6 \times 4.2^\circ$ at the global level and $1.2 \times 0.7^\circ$ at the local level, which in previous studies produced a reliable local advantage in normal subjects. Response timing was to 1-ms resolution and was controlled by the
Fig. 1. Stimuli for the Global/Local Task were large letters made up of small letters. Stimuli were presented at the center of the computer screen and subjects responded with a right key press to an S or a left key press to an H (one of the two stimuli was always present). Within a given block of trials, the two targets, as well as two distractor letters (an E or an A), occurred with equal probability. In the unbiased condition, the targets occurred randomly at either the global level (the large letter) or the local level (the small letter). In the global bias condition, 75% of targets appeared at the global level and 25% at the local level. In the local bias condition, 75% of targets appeared at the local level and 25% at the global level.

8253 chip. Stimulus timing was tied to the vertical sync pulse. The target letters were S and H (Fig. 1), and the distractors were E and A. Each stimulus contained one target and one distractor crossed with the global and local levels. Each of the two targets occurred with equal frequency at a given level throughout the experiment. Stimuli were presented one at a time in the center of the visual field for 100 ms, to control for eye movements. Subjects responded by pressing the left button of a response box if an H was present in the stimulus and the right button if an S was present. They were not required to report the level at which the target appeared. One of the two targets was always present at either the global or the local level. Reaction times were recorded to the nearest ms. The subject's response initiated the 1000-ms intertrial interval. The next trial began with a 500-ms warning tone followed by the stimulus. Three blocks of 64 trials were presented. One block was unbiased (a 0.5 probability of targets appearing at the global or local level). In the other two blocks, the probability of a global or local target was systematically varied to evaluate the patient's ability to control visual attention. One of these blocks was biased locally (75% probability of targets appearing at the local level); the other was globally biased (75% probability of targets appearing at the global level). Subjects were informed of the probability schedules and encouraged to use them to improve their performance when appropriate. The order of the blocks was either global bias/no bias/local bias or local bias/no bias/global bias. Half of the subjects were presented one order, and the remainder the other order.

2.3. Analysis
Analyses of reaction time data were conducted on block medians as the measure of central tendency with an analysis of variance of mixed design. One-tailed comparisons were used when directional hypotheses were being tested. All other comparisons were two-tailed.

3. Results
3.1. Level effect
Seven patients were unable to perform at a level where reaction times were reliable (≤ 20% errors) with the brief presentation times used in the present study and their reaction time data were excluded from the analysis. All normal subjects had ≤ 20% errors. There were no differences between patients who performed to criterion and those who could not on any of the demographic variable (all P < 0.35). The nonperformers did tend to be more severely ill, however, as reflected by higher total scores on the BPRS (performers: total BPRS score = 36.3, SD = 9.5; nonperformers: mean = 45.9, SD = 13.7, t = 1.97, P < 0.07). The two groups did not differ on the severity of auditory hallucinations (t = 0.57, df = 21, P < 0.58).

To test our hypothesis that patients with schizophrenia would have a deficit in processing stimuli at the local level (independent of strategic effects), median reaction times for correct responses in the unbiased block of trials were cast into an ANOVA with group as the between-subjects factor and target level as the within-subjects factor. Patients were slower overall than normal subjects (F = 4.0, df = 1.27, P < 0.06). As
predicted by our hypothesis, the group \times level interaction was significant \((F = 3.0, df = 1.27, P < 0.05, \text{one-tailed})\). Normal subjects showed the expected local advantage (31 ms), while patients showed the opposite pattern of performance. Patients were 48 ms slower in detecting local targets than global targets. Fig. 2 shows median reaction times for each group, target level, and bias condition.

3.2. Correlation with auditory hallucinations

To test the hypothesized relationship between impaired local processing and auditory hallucinations, we calculated a difference score between local and global reaction times and computed the correlation coefficient between this score and the score on the BPRS hallucinations item (patients who had only visual or olfactory hallucinations were given a score of 1). Fig. 3 shows the regression line for the significant correlation \((r = -0.58, P < 0.01, \text{one-tailed})\). Patients who had the highest levels of auditory hallucinations showed the greatest deficit in detecting local level targets. In contrast, there was no significant correlation between the local bias score and either the total BPRS score or the BPRS negative factor score (Kane et al., 1988) (both \(P < 0.46\)).

3.3. Bias effect

We evaluated the effect of biasing attention
strategically on performance by contrasting performance under the two bias conditions (local and global) in an ANOVA with group, target level, and bias level as factors. Patients tended to be slower than normal subjects \( (F = 3.9, df = 1.27, P < 0.06) \). The expected normal interaction between bias and level was present \( (F = 49.8, df = 1.27, P < 0.001) \), and did not interact with group \( (F = 0.07, df = 1.27, P > 0.78) \). This finding suggests that both patients and normal subjects could use attention strategically to improve their performance.

### 3.4. Errors

While the analysis of reaction time performance has been the more sensitive index of lateralized cortical damage in studies of brain-injured subjects, the pattern of errors made during task performance usually parallels that of reaction times. The same parallel was found in the current experiment. All subjects were included in the error analysis, since there was no a priori reason to exclude subjects with high error rates. In the no-bias condition, normal subjects made an average of 4.4% errors at the local level and 8.7% errors at the global level. Patients made an average of 13.6% errors at the local level and 15.7% at the global level. For the patients, error performance was in the same direction as reaction time performance (loss of local advantage), and reaction times did not correlate with error rates in either the patients or the normal subjects (all \( P < 0.38 \)). Thus, it does not appear that a speed-accuracy tradeoff was reflected in the reaction time results. However, the interaction of group and target level was not significant \( (F = 0.54, df = 1.34, P < 0.47) \). Paired \( t \) tests indicated that normal subjects tended to show a significant local bias in error rates \( (t = 2.1, df = 13, P < 0.06) \), while patients did not \( (t = 0.09, df = 21, P < 0.28) \). When this analysis was limited to patients whose data were included in the reaction time analysis, the pattern of results was identical. Although the group \( \times \) target level interaction was not significant, normal subjects showed a strong trend toward a local advantage (4.4% local errors, 8.7% global errors, \( P < 0.06 \)), while patients showed a much smaller and statistically nonsignificant local advantage (6.7% local errors, 8.5% global errors, \( P < 0.32 \)).

The effect of biasing error performance was evaluated through the introduction of a probability manipulation. Under local bias conditions, normal subjects made 3.3% errors to local targets and 6.6% errors to global targets; under global bias conditions, they made 6.7% errors to local targets and 9.5% errors to global targets. Under local bias conditions, patients made 17.5% errors to local targets and 21.9% errors to global targets; under global bias conditions, they made 18.2% errors to local targets and 12.5% errors to global targets. The group \( \times \) bias interaction was significant \( (F = 7.3, df = 1.34, P < 0.01) \), reflecting the preponderance of global level errors in normal subjects (which paralleled the local advantage for reaction times). The group \( \times \) bias \( \times \) level effect was marginally significant \( (F = 3.1, df = 1.34, P < 0.09) \), again reflecting the preponderance of global errors in normal subjects, regardless of bias. In contrast, patients actually allocated attention
more effectively across level according to bias. These results parallel the reaction time data, which suggest a loss of local processing advantage and an intact ability to use the expectancy bias to improve target discrimination in patients with schizophrenia.

4. Discussion

Consistent with our hypothesis of a left hemispheric deficit, when attention was not biased through probability manipulation to one level or another, unmedicated patients with schizophrenia showed a loss of the normal reaction time advantage in the detection of targets occurring at the local level of stimuli in the Global/Local Task. In addition, there was a significant correlation between the patient's level of auditory hallucinations and the degree of local level deficit. According to the model proposed by Robertson et al. (1988), this finding is consistent with other studies that suggest a relationship between the presence of auditory hallucinations and left superior temporal gyrus pathology. Since this is the first report to use this procedure to study neuropsychological functioning in schizophrenia, these findings should be considered preliminary, until replicated.

A frequent concern in the analysis of results of reaction time experiments in patient groups is the issue of differential versus specific deficits (Chapman and Chapman, 1978). Our results suggest that impaired discrimination of local level targets reflects a specific information-processing deficit for two reasons: (1) In the case of a generalized deficit, patients' performance will be worst on that component of the task which is most difficult. Normal subjects in this study had most difficulty (as reflected by longer reaction times and higher error rates) with global level targets. A generalized performance deficit would predict greater difficulty with global targets in the patients and an accompanying increase in the magnitude of the local processing advantage seen in normal subjects. However, patients showed faster response times for the more difficult global level, and slower response times for the easier local level — a reversal of the normal pattern. (2) Patients showed no impairment in controlling attention between levels, as evidenced by their performance with the bias manipulation. Thus, although they were generally slow to respond, patients showed a selective impairment on that aspect of global/local performance reflecting the ability to discriminate local level targets.

The localization of neuropathology in schizophrenia remains a critical unanswered prerequisite for understanding the pathophysiology of this common and devastating illness. The prefrontal and temporal cortex remain prime candidate regions for further study. Recent proposals, however, have sought to widen the scope to the investigation of other brain regions. Pearlson et al. (1996) recently proposed that schizophrenia is a disorder of heteromodal association cortex (HASC), a hypothesis based upon a review of neuropathological and neuroimaging findings and the increased vulnerability to insult that the relatively late maturation of these regions conveys. A disorder of HASC implies that in addition to the prefrontal and superior temporal cortex, the parietal cortex is also affected by the neuropathological processes underlying schizophrenia. The impaired performance in the discrimination of local level targets showed by unmedicated patients with schizophrenia is similar to that seen in neurological subjects with lesions of the left superior temporal gyrus and adjacent left temporo-parietal junction. The intact ability to focus attention strategically between levels seen in this group suggests that inferior parietal lobule substrates of selective attention may be intact in these patients. It also suggests that the notion that patients with schizophrenia have impaired attentional control requires qualification. As noted above, several studies using the covert orienting paradigm in schizophrenia suggest that patients may benefit from valid spatial cues to improve detection times to the same degree as normal subjects. For a task to reveal deficits in attentional control in schizophrenia, the additional constraint required may be for the task to be more capacity demanding (Nuechterlein and Dawson, 1984; Braff, 1993).

Neuropsychological accounts of auditory hallucinations have recently focused on the notion of a failure of self-monitoring (Feinberg, 1988; Frith and Done, 1988), as a result of which self-
generated speech is misidentified by patients as originating from an external source. It has been proposed that the neural substrate for this failure is hippocampal dysfunction, although direct evidence is lacking. Although self-monitoring deficits have been identified in schizophrenia, these findings have not been associated specifically with auditory hallucinations (Frith and Done, 1988; Leudar et al., 1994). An alternative to a self-monitoring failure underlying this process is suggested by the recent work of Ramachandran et al. (1992). This investigator has observed that limb amputees often develop new somatosensory maps (1992). This redistribution, in turn, results in distinctly abnormal perception. These observations suggest the hypothesis that altered connectivity in the superior temporal gyrus, where primary sensory cortex and areas involved in language representation and speech production are juxtaposed, may result in altered representational processes in which intended speech is remapped as perceptual information. Impairment in other functions of superior temporal cortex, such as the discrimination of spatial frequencies indexed by the Global/Local Task used in this study, may serve as a marker of the altered connectivity underlying this effect.

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