Eur Arch Psychiatry Clin Neurosci (1991) 241:126–130

European Archives of Psychiatry and Clinical Neuroscience

Laterality in Schizophrenia

A Reaction Time Study*

Joanne Fishman[1], Fred Schwartz[2], Elizabeth Bertuch[2], Barbara Lesser[2], Deborah Rescigno[2], and Barbara Viegener[2]

[1] Psychiatry Service St. Lukes/Rooseveld Hospital and [2] Department of Psychiatry, Cornell University Medical College, Westchester Division, The New York Hospital

Summary. A laterality study in schizophrenia was carried out by measuring reaction time (RT) in a baseline condition and while subjects were engaged in a concurrent task. In the baseline condition, a clinical measure of psychoticism was associated with differential slowing with the right hand in schizophrenic dextrals but not in a control group of affective dextrals. The concurrent task suppressed the effect of psychoticism on RT performance. The results suggest that left-hemisphere deficits in schizophrenia are state dependent, and so not necessarily due to cortical dysfunction.

Key words: Schizophrenia – Reaction time – Laterality – Psychoticism

Introduction

This study investigated hemispheric laterality in schizophrenics and a control group of affective disorders with a reaction time (RT) paradigm. Performance with each hand was studied in a baseline condition and while subjects were engaged in a concurrent task (dual-task or time-sharing condition). A measure of clinical psychoticism was also obtained. It was anticipated that the concurrent task and the level of psychoticism would increase processing demands on the hemisphere dominant for language, thus yielding a laterality effect.

RT deficits are well documented in schizophrenia (Nuechterlein 1977), but also occur in affective illness (Schwartz et al. 1989). Work from our laboratory suggests that RT slowing is due to psychoticism, in that deficits were obtained in a schizophrenic sample, but also in affectively ill patients with a history of psychotic symptoms (Schwartz et al. 1989). Patients with such a history, however, may or may not be floridly psychotic at the time of testing. Conflicting findings have been reported on the correlation of clinical psychoticism and RT performance (Hamilton and Salmon 1962; Rosenthal et al. 1960; Zahn 1980). It is thus not clear whether clinical state influences RT performance.

There is growing evidence of left hemisphere dysfunction in schizophrenia (Crow et al. 1989). Walker and McGuire (1982) reviewed the experimental literature on laterality effects up to that time and concluded that the findings were inconsistent, but added that schizophrenics were consistently slower when processing information in the left hemisphere, thus identifying RT as a measure of choice in studies of laterality. In addition, left hemisphere dysfunction in schizophrenia appears to be associated with the severity of psychotic symptomatology (Bruder 1983; Galderisi et al. 1988; Gur et al. 1988). These diverse findings provide a rationale for studying hemispheric laterality with a RT paradigm while evaluating the patients' clinical state.

Time-sharing or dual-task paradigms have been used to study normal differences in cerebral laterality (see Kee and Cherry 1990). The concurrent tasks employed include paragraph reading and anagram solution. Kinsbourne (reviewed by Boles 1979) obtained a left hemisphere decrement in visual attention with a concurrent memory task in three separate studies; Boles (1979), however, failed to replicate this finding. No data exist using a concurrent memory task with schizophrenic subjects. The present study employed a memory load as the concurrent task, in part because it is easily administered during the interstimulus interval, and because both a memory load and psychotic symptoms are processed covertly.

Subjects and Methods

Experiment 1: a laterality study with schizophrenic and affectively ill subjects

Twenty schizophrenic and 26 affectively ill inpatients at the New York Hospital-Cornell Medical Center agreed to participate after granting informed consent. Diagnosis was based on Research Diagnostic Criteria (Spitzer et al. 1981), using the Schedule for Affective Disorders and Schizophrenia (Endicott and Spitzer 1978), the patient's history, and course in the hospital.

* From a doctoral thesis completed at the New School for Social Research

Four nurse collaborators rated the patients' symptoms for the week prior to testing, using the 18-item Brief Psychitric Rating Scale (BPRS; Overall and Gorham 1962). Two clinical measures were abstracted from the BPRS: a psychoticism index (the sum of the thought disturbance and hostile-suspicious factors), and a withdrawal-retardation index (the sum of the anergia and anxiety-depression factors). The BPRS factors are described by Guy (1976). The withdrawal-retardation index was included to provide a contrast to the clinical index of psychoticism. The anergia and anxiety-depression factors were combined to form this index, based on the correlation of the anergia scale with independent measures of depression (Whiteford et al. 1987).

All subjects were right-handed, as assessed by a 12-item hand-preference questionnaire (Annett 1970). A right-hand choice on eight or more items was considered dextral (Flor-Henry 1976). Handedness, in turn, was used to establish that the left hemisphere was dominant for language (Hicks 1975; Kraft et al. 1987).

The total sample consisted of young adults (mean age, 26.5 years) with numerous prior hospitalizations (mean = 4.0); the two diagnostic groups did not differ in these variables. Twelve of the schizophrenics were male and 8 female, while 6 of the affective disorders were male and 20 female. The schizophrenics had significantly higher overall severity of symptoms ratings (*M* BPRS score = 46.10, SD = 11.25) than the affective group (*M* BPRS score = 35.69, SD = 8.08). Additionally, 85% of the schizophrenics were on neuroleptics, compared with 58% of the affectives, and 73% of the affectives were on antidepressants or lithium, compared with 35% of the schizophrenics.

A traditional visual RT procedure was used, with the light stimulus in the center of the visual field. Subjects responded to the light stimulus after a warning tone by lifting their forefinger from a telegraph key (simple baseline RT condition). The interstimulus intervals were 2.5, 3.0 and 3.5 s, in a counterbalanced order. In the time-sharing condition, RT was measured under the same conditions as above while subjects simultanteously engaged in a short-term memory task. Specifically, subjects were given a different auditory call-sign on each trial following the warning tone (e.g., 6H2). They were instructed to repeat the call-sign after they had responded to the light stimulus. Recall accuracy for the cell-sign was 100%. The experimental apparatus was fully automated by the use of a Lafayette Instrument's tone and light, a programmable timer, a digital clock and a printer (Lafayette Instrument, Layayette Indiana, USA). Response times less than 90 ms were discarded as anticipatory errors. In both diagnostic groups, an equal number of subjects started this procedure with either their right or left hands. One block of simple RT trials and two blocks of time-sharing trials were administered using each hand. Each bloc consisted of 18 trials, for a total of 3×8 or 54 trials per hand. There was a rest period between hands during which the handedness questionnaire was administered.

Results

A logarithmic mean was obtained for each block of trials and averaged across subjects. The log means had homogeneous variances across diagnostic groups. The geometric means (the antilog of the log mean) by diagnosis and condition are listed in Table 1. Data analysis was by way of a Groups (2) × Hand (2) × Task (2) analysis of variance with repeated measures on the last two factors. The results demonstrate that subjects responded slower in the time-sharing condition than in the baseline condition ($F = 40.95$, $df = 1.44$, $P < 0.001$). A laterality effect was tested by the Hand × Task and the Groups × Hand × Task interactions; neither interaction was significant ($F < 1.00$). Performance with the right and left hands was nearly identical, replicating the findings in normals (Moscovitch 1986) and schizophrenics (Niwa et al. 1983).

Table 1. Geometric means for RT performance by schizophrenics and affective disorders by hand and condition

Hand	Schizophrenics		Affectives	
	SRT	*TS*	*SRT*	*TS*
Right	271	360	227	295
Left	272	362	229	295

The table lists the geometric means (antilog of the logarithmic mean) in ms by hand, diagnosis and condition: SRT = simple RT; TS = RT during time-sharing

We next considered laterality effects due to clinical state. A laterality effect is defined as a relative slowing with the right hand, partialling (controlling for) RT with the left hand. This process can be visualized if one imagines a regression line with positive slope between right-hand RT (Y-axis) and left-hand RT (X-axis). Subjects above the regression line are slower than expected with their right hand, based on performance with their left hand; subjects below the regression line are faster than expected. The difference of the raw score from the regression line – a residual score – is the measure of laterality. The effect of clinical state is determined by correlating the BPRS indices with these residuals.

In actual practice, the above analysis was accomplished by multiple regression, partialling performance with the contralateral hand, and then sequentially adding Groups, Psychoticism, and the Groups × Psychoticism interaction to the regression equation. The same statistical steps were followed to evaluate the effect of withdrawal-retardation on the measure of laterality. It should also be understood that partialling performance with the contralateral hand suppresses error variance, and so greatly increases the power of the statistical tests. In particular, individual differences in RT latency are mostly eliminated, as the residuals are completely independent of performance with the partialled hand.

The partial correlation coefficients from the multiple regression analyses are listed in Table 2. The coefficients for the combined sample are equivalent to main effects in an analysis of variance. A significant Groups × Psychoticism interaction was obtained in the simple (baseline) RT condition. Partial correlation coefficients were therefore obtained for each diagnostic group seperately and are also listed in Table 2.

A plot of the residuals against psychoticism indicates that schizophrenics rated high in psychoticism were slower with their right hand than expected, based on performance with their left hand; conversely, those low in psychoticism were faster than expected with their right hand, based on performance with their left hand (partial $r = 0.61$). The same pattern emerged when left-hand performance was the dependent variable and right-hand performance was partialled (partial $r = -0.52$). Table 2 indicates that: (1) a laterality effect due to psychoticism was obtained in the baseline RT condition and restricted to the schizophrenic group; (2) the introduction of a con-

Table 2. Partial correlation coefficients between RT variables and clinical variables

Variable/ hand	Combined group	Schizophrenics	Affectives
Psychoticism			
SRT/right	0.43[b]	0.61[b]	0.00
SRT/left	−0.36[a]	−0.52[a]	0.00
TS/right	0.10		
TS/left	−0.05		
Withdrawal-retardation			
SRT/right	0.08		
SRT/left	0.17		
TS/right	0.39[b]		
TS/left	−0.31[a]		

[a] $P<0.05$; [b] $P<0.01$

Table 3. A cross-tabulation of subjects high or low in psychoticism by whether they were slower in baseline RT with the right hand (R > L) or slower in baseline RT with the left hand (L > R)

Psychoticism	Schizophrenics		Affectives	
	Low	High	Low	High
R > L	1	7	5	6
L > R	6	0	4	3

The subjects were subdivided into the top and bottom third of the distribution of the psychoticism scale for each diagnostic group separately

current task suppressed the effect of psychoticism on RT performance in the schizophrenic group; and (3) right-hand (lateralized) slowing due to withdrawal-retardation was obtained in the time-sharing condition in both diagnostic groups.

Table 3 presents a simpler demonstration of the laterality effect due to psychoticism. The subjects in the top and bottom third of the distribution for psychoticism in each diagnostic group were identified. For these subjects, a tabulation was made as to whether baseline RT was slower with the right or the left hand. The results indicate that schizophrenics high in psychoticism were slower with the right hand, whereas schizophrenics low in psychoticism were slower with their left hand. No such pattern was found in the affectively ill subjects.

Experiment 2: a laterality study with normal controls

A normal group (mean age = 28.9 years) was studied with the same procedure as in Experiment 1, using a portable Gebrands RT unit (Gebrands, Arlington Massachusetts, USA). As with the patient sample, a laterality effect due to a memory load was not obtained ($F<1.00$). RT was slowed during the concurrent task by 41 ms ($F=34.62$, $df=1.20$, $P<0.001$), compared with 78 ms in the combined patient group.

Discussion

We replicated Boles (1979), in not obtaining a laterality effect due to a memory load in either a patient or a normal sample. Unexpectedly, the memory load mediated the effect of clinical symptoms on RT performance. In the baseline condition (simple RT), a laterality effect was obtained in the schizophrenic group but not in the affective controls. The effect was that schizophrenic patients rated high in psychoticism were relatively slower with their right than their left hand, whereas those rated low in psychoticism were relatively slower with their left than their right hand. Two points need to be made about this finding. The first is that relative slowing is independent of whether patients had slow, average, or fast RTs overall, as the correlation of the residuals and performance with the partialled hand is by definition zero. Relative slowing therefore does not mean that patients high in psychoticism had slow RTs; it only means that they were slower than expected, based on performance with the contralateral hand. The second point is that we obtained two laterality effects, both of which require explanation. A right-hand decrement in subjects rated high in psychoticism is consistent with the laterality literature, which suggests that schizophrenia is associated with left-hemisphere deficits. Why, then, was there a left-hand decrement in schizophrenics rated low in psychoticism? This may have been a medication effect, as will be discussed below.

Interpretation of a left-hemisphere decrement in the schizophrenic group is based on the assumption that psychotic symptoms are especially likely to involve activity in the hemisphere dominant for language. There would then be relatively greater interference or slowing with motor activity organized in the same cerebral hemisphere. This is a time-sharing model and has been used by Kee and Cherry (1990) to explain why a verbal task interferes with motor performance in normals using their right hand. The absence of a comparable left-hemisphere effect in the affective controls is consistent with the laterality literature (Bruder 1983), although this statement begs the question. Speculatively, psychotic symptoms may involve a different mechanism in schizophrenic and affective disorders. Specifically, psychotic phenomena in schizophrenia may be related to a failure to control focal awareness and hence to screen out task-irrelevant mental activity. Indirect support for this hypothesis comes from our finding that the introduction of a memory load in the time-sharing condition suppressed differences in laterality associated with psychoticism. By analogy, this is comparable to the finding that overt vocalization tends to suppress auditory hallucinations in schizophrenic patients (e.g., Green and Kinsbourne 1989).

The introduction of a memory load in the time-sharing condition resulted in a relative decrement in right-hand performance in patients rated high in withdrawal-retardation. This was true for both diagnostic groups. The introduction of a concurrent task to the RT paradigm slows performance (Table 1) and presumably requires greater effort and concentration, as reported spontaneously by subjects. It seems plausible that such effort is mediated verbally through self-instructions and that the withdrawal-retardation scale is, in part, a measure of motivation or willingness to exert effort as task difficulty increases.

As noted above, the central finding in this study was of a laterality effect in the schizophrenic sample due to psychoticism. No such effect was found in the affective controls. The two groups, while fairly comparable, differed as expected in medication regimen, with the majority of the schizophrenic patients on a neuroleptic, and with many receiving anticholinergic drugs. A reasonable question, then, is whether medication could account for the laterality effect in the schizophrenic group. The literature indicates that anticholinergic agents mostly effect memory; in addition, one study with normals found no effect of scopolamine on RT (reviewed by Spohn and Strauss 1989). All major reviews have concluded that neuroleptics do not appear to affect simple RT (Medalia et al. 1988; Nuechterlein 1977; Spohn and Strauss 1989). Most of the studies reviewed by these authors nevertheless were potentially confounded, as the unmedicated controls usually had a prior and recent history of neuroleptic treatment. In a study using mostly never-medicated controls, Cleghorn et al. (1990) found that neuroleptics actually improved RT in the medicated group. This is understandable if we assume that neuroleptics reduce psychoticism and that psychoticism slows RT. A more central issue is whether or not neuroleptics have lateralized effects. This question only applies to the schizophrenic sample, as no laterality effect was found in the affective controls. The study of laterality effects due to neuroleptics is a relatively new area of investigation. Buchsbaum et al. (1987) reported that neuroleptics tend to normalize hemispheric asymmetries in schizophrenia. Two recent studies reported that neuroleptics improved left-hemisphere performance in schizophrenic patients, whereas right hemisphere performance deteriorated (Tomer 1989; Tomer and Flor-Henry 1989). Our results are readily integrated with these findings. We assume that the schizophrenic patients who were high in psychoticism had not yet stabilized on neuroleptics and so continued to demonstrate a relative decrement in right-hand (left-hemisphere) performance. The patients low in psychoticism had stabilized on neuroleptics, and so had improved performance with their right hand but now demonstrated a decrement with their left hand. In this formulation, we merely assume that neuroleptics normalized left-hemisphere performance by reducing psychoticism. The deleterious effect of neuroleptics on right-hemisphere performance has no ready explanation in the literature.

The results of this study warrant replication and further clarification. As noted previously, a number of disparate studies have reported that left-hemisphere dysfunction in schizophrenia is associated with the severity of psychotic symptoms (Bruder 1983; Galderisi et al. 1988; Gur et al. 1988). The implication is that left-hemisphere dysfunction is state-dependent in at least some schizophrenic patients. This would explain the diversity of findings in the experimental literature on laterality effects in schizophrenia, as patients most likely were tested at different points in their treatment regimen. A state-dependent decrement that is normalized with neuroleptic treatment is also consistent with neurochemical theories of schizophrenia. The RT paradigm may provide a convenient method for investigating hemispheric laterality in schizophrenia, as the method is easily administered and is readily varied experimentally.

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