REACTION TIME AND PROGNOSIS IN ACUTE SCHIZOPHRENIA

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In the vast and often contradictory literature on schizophrenia, the reaction time (RT) differences stand out as one of the few consistently replicable findings. More recent attempts to extend these early studies, e.g., process-reactive distinctions, measures of field independence, utilizing measures of premorbid withdrawal, etc., suffer from the fact that patients receive prompt pharmacological treatment usually before they can be tested. This study was designed to study the predictive value of RT and its relationship to other predictors.

Thirty acute, male admissions with a senior staff diagnosis of schizophrenia were admitted to the study. The patients were drug-free and were not given any long acting sedatives or tranquilizers throughout the period of testing. They were hospitalized between 2 and 3 weeks when the RT’s were obtained so that the confounding effect of variations in duration of pretesting hospitalization did not pertain. The RT measure was a simple finger lift response to a quasi-random series of four stimuli: red and green lights and low and high tones. The RT data were classified according to the stimulus presented on the preceding trial. Category 1 refers to RT’s to stimuli preceded by the same stimulus. Category 2 represents RT’s to stimuli preceded by a different stimulus in the same sensory modality (ipsimodal RT). Category 3 indicates RT’s to stimuli preceded by a stimulus in the other sensory modality (cross-modal RT). Patients were classified as process or reactive on the basis of the Phillips Prognostic Rating Scale (PRS)—a measure of premorbid withdrawal. The other predictors included were marital status, social class, duration of previous hospitalization, acuteness of onset, depressive mood, abstract attitude, conceptual plasticity, and field independence. The outcome measure was the total number of nights spent in any mental institution during the 3 years of follow-up.

The results indicated that simple RT scores to light and sound were significantly correlated to length of hospitalization for both process and reactive patients. The correlations ranged from .40 to .53 and averaged .50 for the combined group. The ipsimodal and cross-modal data did not significantly improve prediction of hospitalization for process schizophrenics but did for the reactive cases. RT is not correlated with premorbid adjustment,

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thought disorder, field independence, and several other predictors of outcome. This suggests that it measures a relatively independent variable. While the clinical measure of the thought disorder was the best single predictor, the simple RT to light added 17 per cent of additional variance. This result indicates the value of using RT measures in a variety of clinical situations.

The literature on the schizophrenic reactions is a voluminous one, the size of which is in part determined by the multiplicity of the contradictions. There is a marvelous value in this since one can, on an ad hoc basis, claim that virtually anything has been demonstrated and be correct. Despite the usefulness of this contradictory literature, as a practical ego support it presents very real problems. One research strategy in coping with this state of affairs is to seek out those findings which have been consistently replicated. The reaction time (RT) studies are the closest thing to a north star in schizophrenia research.

Fifty years ago there was considerable interest in the measurement of RT in psychosis, and the early literature has been ably reviewed by Wells and Kelley (14). For the next 20 years there was continuing interest in the utilization of this measure in the study of mental illness. In 1937, Huston, Shakow, and Riggs (5) published their now classic study on RT in schizophrenia. Their tranquilizer-free schizophrenic sample showed a longer mean RT as well as significantly greater within group and within individual variation than normals. This was true for even their most cooperative patients. They concluded that their patients did not "attain as high a level of preparation as normal subjects, that the patients vary more within themselves in the height of preparation attained from reaction to reaction, and that the patients do not maintain their level of preparation as consistently as the normal subjects" (5, p. 82).

It has been demonstrated that schizophrenic subjects were unable to take advantage of a regular preparatory interval (PI) that exceeded several seconds. Rodnick and Shakow (10) carried this observation further by utilizing a PI of varying duration as an estimate of a person's ability to reach and maintain the high level of preparation or set necessary for meeting recurrent environmental stimulation. Their study revealed that even normal subjects under certain conditions were unable to take advantage of a regular PI. However, the failure to take advantage of the regular PI did not occur in the normals until some point between 20 and 25 seconds. In the schizophrenics the failure occurred after about 5 or 6 seconds. These investigators demonstrated a continuity between schizophrenic and nonschizophrenic performance, although the "major set" of the schizophrenic is more vulnerable to the intrusions of minor or task irrelevant sets. They also computed a "set index" which was devised so as to separate the schizophrenic and the normal subjects without overlap. Rosenthal et al. (11) found this index correlated at .89 with clinical evaluation of severity of schizophrenic pathology. For many reasons the war and postwar years had a different Zeitgeist in which RT experiments were deemphasized in clinical work. Despite this, Shakow remained firm in his conviction that the inability to maintain a set was a primary feature of the schizophrenic disorder and continued to publish accordingly.

Morrer (8), in the early 1940's, reported a series of experiments in which he studied RT as a function of the sequence of the modality of sensory input. He found that RT was lengthened when a stimulus was presented in a sensory modality differing
from the stimulus which preceded it. Kriegel and Sutton (6) and Sutton et al. (12, 13) independently investigated, some dozen years later, the phenomenon of a prolonged RT which was confirmed by using simple RT with three stimuli: red light, green light, high tone, and low tone. This device was used to measure the simple RT of schizophrenics and normals. Their results indicated that under certain conditions the effect of a previous sensory experience persisted longer in a schizophrenic than it did in a normal.

The role of prior events has also appeared as an important variable in the PI studies (6, 13, 18). Zahn, Rosenthal, and Shakow (16, 17, 18) have shown that the RT of schizophrenic patients is affected not only by the PI, but also by the duration of the PI relative to the PI of the immediately preceding trial. In both the Sutton and Shakow studies, immediately prior events have a disproportionate effect on the RT of the schizophrenic patient. Zubin (19) has recently considered both the modality shift and PI findings as reflecting a common effect and proposed a model involving the concept of facilitatory and inhibitory residues or traces left by prior stimulating events. In terms of this model, the findings for the schizophrenic patients are seen as evidence for a longer persistence of such traces in the schizophrenic.

Unfortunately, much of this work was done years ago when data were not collected on variables which are now recognized as important, including the more precise discrimination of subgroups of patients, such as the process-reactive distinction. The therapeutic requirements of patients today, especially with the emphasis of community psychiatry, are such that most patients are receiving pharmacological treatment before RT studies can be done. As early as 1960, Freedman, Deutsch and Deutsch (4) showed that a single dose of hydroxyzine would bring the RT of schizophrenic children closer to normal. The restriction of a population of schizophrenics to only those patients who are drug-free or who could be taken off drugs would result in the selection of a subpopulation that would be highly unrepresentative. These methodological problems have caused Shakow and some of his coworkers to go back to the original Worcester data for purposes of re-examination. A somewhat different approach to the problem was taken in the present study, since drug-free patients were available. The primary goal was to explore the relationship between RT and outcome; i.e., to ascertain the value of RT as a prognostic indicator. The rationale was that RT measured something basic to the psychopathology of schizophrenia and, therefore, should be related to outcome. The secondary goal was to study the relationships between RT and known prognostic indicators.

**METHOD**

Thirty male admissions to a psychiatric observation ward who received a senior staff diagnosis of schizophrenia were admitted to the study. At the time the sample was collected, virtually no admissions were receiving tranquilizers so that these 30 cases were representative of the population seen at the center. The patients were not given tranquilizers, barbiturates, or long acting sedatives throughout the period of testing and examination. They had been hospitalized between 2 and 3 weeks when the RT procedure was done so that the confounding effects of variation in duration of current hospitalization as well as the chronic effects of long term hospitalization did not pertain. The patients included 8 blacks, 1 Oriental, and 21 whites. Only 8 were married and living with their spouses. The age range was 19 to 42 with a mean age of 29.0 years. Twelve had prior psychiatric hospitalizations which in each case totaled less than 3 years. Of the 30 patients, 67 per cent were in Hollingshead's group V, 20 per cent...
TABLE 1
Sample Description (N = 30)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>28.97</td>
<td>8.64</td>
</tr>
<tr>
<td>Years of education</td>
<td>11.46</td>
<td>1.78</td>
</tr>
<tr>
<td>WAIS scaled vocabulary*</td>
<td>9.60</td>
<td>2.98</td>
</tr>
<tr>
<td>Hollingshead Social Index</td>
<td>59.70</td>
<td>10.83</td>
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</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whites</td>
<td>21</td>
<td>70</td>
</tr>
<tr>
<td>Single</td>
<td>22</td>
<td>73.3</td>
</tr>
<tr>
<td>First admissions</td>
<td>18</td>
<td>60</td>
</tr>
<tr>
<td>Acute onset</td>
<td>14</td>
<td>46.7</td>
</tr>
<tr>
<td>Paranoid</td>
<td>16</td>
<td>53.3</td>
</tr>
</tbody>
</table>

* Wechsler Adult Intelligence Scale.

in group IV, and 13 per cent in group III. The sample description is summarized in Table 1.

The RT scores were the latencies, in milliseconds, of simple finger lift responses to a predetermined random series of four stimuli: red and green lights and low and high tones. RT data were classified according to the stimulus presented on the preceding trial. Category 1 refers to responses to stimuli preceded by the same stimulus (simple RT). Category 2 refers to reactions to stimuli preceded by a different stimulus in the same sensory modality (ipsimodal RT). Category 3 indicates response times to stimuli which were preceded by stimuli in the other sensory modality (cross-modal RT). Scores were obtained for light and sound stimuli separately. RT's were obtained by an independent examiner who was unaware of the patients' scores on the other variables.

Every patient received the Phillips Prognostic Rating Scale (PRS), part I of which was used as the measure of premorbid object relations (9). The score on part I of the PRS was also used to separate the patients into process (N = 17) and reactive (N = 13) groups. A score of 15 was used as the dividing line. Part II was used as a measure of the precipitating events for the psychotic episode. Part III is a measure of the severity of the presenting signs of the disorder much like a quantitative mental status examination, which includes subscales for the formal signs of the thought disorder, affect, and impulsivity. The first two of these subscales were used in the study. In summary, four measures were taken from the PRS—part I, part II, and the first two subscales of part III.

The other variables that were considered were marital status, social class, duration of previous hospitalization, acuteness of onset, depressive mood, abstract attitude, conceptual plasticity, and field independence. Depressive mood was included not only because it is a known predictor of outcome but also to control for its possible effects on the RT results in the patient sample. The measure of the abstract attitude was obtained from the Benjamin Proverb Test (1) using the Meadow Scale (7). The Metalog Test (21) was used as the measure of conceptual plasticity. The Rod-and-Frame Test was used as the measure of field independence (15). These three procedures were administered and scored by separate judges independently and blindly. Two additional measures of the severity of thought disorder were included. These were a measure of the frequency of intrusion of the thought disorder into the proverb response (3) and the Index of Formal Signs (2).

The measure of the outcome was the total number of nights spent in any mental institution during the 3-year follow-up period subsequent to testing. The patients were actually followed throughout the 3-year period rather than retrospectively at the end of that time. The treating institutions were not informed of the research status of these patients so as not to introduce an additional source of variance.

RESULTS

All of the 30 patients cooperated adequately during their testing but no attempt was made to quantify their level of cooperativeness. The mean outcome indices for the
process and reactive patient groups were 506 and 269 nights, respectively. An F ratio test for the homogeneity of variance of the process and reactive groups showed at the .05 level of significance that these groups could not be assumed to be samples from the same population. The test used for comparing the mean outcomes of the process and reactive patients did not assume variance homogeneity and passed the .05 significance level. This result indicated that process patients have a significantly poorer prognosis, in terms of the length of hospitalization, than reactive patients. Having demonstrated the validity of the classification in this sample, it was necessary to show the predictive value of simple, isomodal, and cross-modal RT.

Table 2 shows that the correlation coefficients between median RT's and the outcome index varied from .26 to .60 for the various stimulus categories. Since all the correlation coefficients were positive, longer RT's were associated with a greater number of nights spent in the hospital. In general, process and reactive patients showed similar correlations for sound stimuli, but for reactions to light, process schizophrenics showed a higher correlation of outcome with RT than did reactive schizophrenics. In each of the categories, both for sound and light, the process cases showed a longer mean RT and a greater variability than did the reactive patients.

The prognostic value of the simple RT measure was further evaluated by using the standard deviation of the subjects' RT scores around the total group mean. Using a cutoff of ±1/2 sigma for simple RT to light gave a group of 9 above this point and 10 below. Of those with the longer RT, 6 had longer than average hospitalizations while 8 out of the 10 with a shorter RT had less than an average duration of hospitalization. Repeating this procedure for sound yielded accurate predictions of duration of hospitalization for 5 out of 7 cases with longer and 6 out of 8 cases with shorter RT's. Doing a simple division of the sample solely on the basis of being above or below the mean for both RT to light and duration of hospitalization yielded accurate predictions for 14 out of 20 cases with shorter hospitalization and 7 out of 10 cases with longer hospitalization. Repeating this procedure for RT to sound gave accurate predictions for 15 out of the 20 shorter hospitalizations and 7 out of the 10 longer ones.

Since the correlations in Table 2 showed a moderately strong relationship between outcome and all RT scores, it was desired to find what relationship, if any, existed between outcome and the isomodal and cross-modal retardations, independent of the simple RT correlation. For this analy-
TABLE 3
Multiple Correlation Coefficients (R) and Coefficients of Multiple Determination (R\(^2\)) for Predicting Outcome, Using One, Two, or Three Stimulus Categories

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Results for Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Process</td>
</tr>
<tr>
<td></td>
<td>R</td>
</tr>
<tr>
<td>Sound</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>.44</td>
</tr>
<tr>
<td>1 + 2</td>
<td>.44</td>
</tr>
<tr>
<td>1 + 2 + 3</td>
<td>.55</td>
</tr>
<tr>
<td>Light</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>.53</td>
</tr>
<tr>
<td>1 + 2</td>
<td>.55</td>
</tr>
<tr>
<td>1 + 2 + 3</td>
<td>.55</td>
</tr>
</tbody>
</table>

sis, multiple regression was used to determine if RT’s to category 2 and 3 stimuli added anything to the prediction of the dependent variable, the outcome index. Table 3 shows the multiple correlation coefficients (R) and the coefficients of multiple determination (R\(^2\)). For reactions to sound stimuli, the inclusion of the cross-modal RT scores (category 3) accounts for an additional 41 per cent of the variance in outcome for the reactive patients, and an additional 11 per cent for the process patients. For reaction to light stimuli, the cross-modal category did not account for any additional variance in the outcome index for either group of patients. However, there was a 39 per cent increase in the coefficient for the reactive patients when the ipsimodal category of RT’s was added to the regression equation. This effect was not evident for the process patients.

These results indicate that simple RT scores are correlated with outcome for both process and reactive patients, but the effect of ipsimodal and cross-modal shifts in a sequence of stimuli is primarily correlated with the outcome of reactive patients who have a better prognosis, and this effect differs for reactions to light and sound stimuli.

Correlations were determined between the RT scores and other common predictors of outcome: including the actual scores obtained on the four scales taken from the PRS, acuteness of onset, depressive mood, marital status, duration of prior hospitalization, abstract attitude, conceptual plasticity, the Rod-and-Frame Test, and social class. There were no significant relationships between RT—simple, ipsimodal, or cross-modal—and most of these other measures. Marital status was related to simple RT for both light (r = .36, p < .05) and sound (r = .37, p < .05), with single patients being more likely to show retardation, i.e., a prolonged RT. There was a significant relationship between conceptual plasticity and simple RT for light (r = .41, p < .05) and sound (r = .37, p < .05), with the patients showing low conceptual plasticity also showing longer RT’s. In addition, there was no relationship between the presence of depressive mood and prolongation of RT.

The relative independence of the RT measures from the other predictors suggested the value of a multiple stepwise regression utilizing the other successful predictors of outcome as well. The sample size (N = 30) makes such a multiple regression of marginal statistical validity. However, the result seemed of sufficient interest, at least for hypothesis generation, to warrant doing this procedure. These results, including the list of variables used, are presented in Table 4.

DISCUSSION

The very simplicity of the outcome index may raise questions concerning its validity as a measure of prognosis. There are many nonmedical factors that contribute to staying out of a mental hospital but do not reflect the state of the illness (e.g., availability of placement). Nevertheless, the number of nights spent in the hospital is very highly correlated with more complex measures of prognosis including the Outcome Index of Zubin and his coworkers (20) and was therefore used.
While 12 of the patients had had prior psychiatric hospitalization, the admission represented an acute exacerbation of the illness following a period of remission. The 12 patients were divided equally between the process and reactive categories and, therefore, represented a higher proportion of the cases in the reactive group (6 out of 13 vs. 6 out of 17). It is doubtful that this higher representation of readmissions biased the results since there was not a significant relationship between prior hospitalization and either classification into process-reactive schizophrenia \( r = .02 \) or duration of hospital stay \( r = -.17 \).

The absence of a relationship between depressive mood and RT indicates that the finding of delayed RT in this population of schizophrenics is not an artifact associated with the mood disturbance. The RT measures, particularly to light, are powerful prospective predictors of duration of hospital stay in acute schizophrenics. The correlations between outcome and RT, which range from .46 to .55 for the total group, are larger, for example, than that for the premorbid scale of the PRS \( r = .41 \). It is not clear from the data why simple RT to light is a better predictor of outcome than RT to sound, but the difference is a very small one. There is an interesting differential effect of modality shift on process vs. reactive schizophrenics. The modality shift accounts for very little additional predictive variance in process patients, but accounts for over 40 per cent additional variance in the reactive cases. This finding suggests the speculation that stimulus novelty or change may exert a stronger influence on or even present a greater problem for reactive patients and that the RT measure in process schizophrenics is less sensitive to environmental changes. Despite the clinical similarities which unite process and reactive schizophrenia, it is possible that the former group is more insulated from the environment. These individuals may be more insulated in the sense that it takes longer for a response to a stimulus to occur, and neural processing time is less affected by changes in the stimulus modality. This hypothesized general diminution in responsivity to the environment may be defensive in origin or part of the more fundamental pathology of the disorder. The study is not designed to test such speculations, nor to shed any light on the difference in effect of ipsi- and cross-modal shift as a function of stimulus type (light or sound). Yet, the group means for simple, ipsi-, and cross-modal RT to sound and light in process patients were higher than the corresponding group means in reactives. The means for simple RT to sound and light in process patients actually exceeded the reactive means for ipsi- and cross-modal responses. These findings are suggestive and need to be examined in an appropriately designed study.

It is interesting to note that RT is not correlated with premorbid adjustment, thought disorder, field independence, and several other established predictors of outcome. This suggests that it measures a relatively independent variable which is a new source of variance. This finding is in contrast to the premorbid scale of the PRS whose predictive value is absorbed by the measure of formal signs of thought disorder.

<table>
<thead>
<tr>
<th>Variable*</th>
<th>( R )</th>
<th>( R^2 )</th>
<th>Increase</th>
<th>df</th>
<th>( F ) ratio†</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thought Disorder Subscale (PRS)</td>
<td>.55 .30</td>
<td>.30</td>
<td>1.28</td>
<td>12.12</td>
<td>&lt; .005</td>
<td></td>
</tr>
<tr>
<td>Simple RT—light</td>
<td>.60 .47</td>
<td>.17</td>
<td>2.27</td>
<td>8.66</td>
<td>&lt; .01</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>.75 .57</td>
<td>.10</td>
<td>3.26</td>
<td>6.04</td>
<td>&lt; .025</td>
<td></td>
</tr>
<tr>
<td>Social class</td>
<td>.80 .63</td>
<td>.06</td>
<td>4.25</td>
<td>5.40</td>
<td>&lt; .05</td>
<td></td>
</tr>
</tbody>
</table>

* Other variables entered were: part I, II, and Affect Subscale of PRS; simple RT—sound; ipsi-modal RT—sound and light; cross-modal RT—sound and light; Index of Formal Signs; and frequency of intrusion of thought disorder in proverbs.
† The \( F \) ratio tests the significance of the increased multiple correlation when each successive variable is added.
The multiple regression shows that while a measure of formal signs of thought disorder is the best single predictor of outcome the simple RT to light accounts for an additional 17 per cent of the variance. This finding suggests the value of using RT measures in a variety of clinical situations where they can help to separate patients prognostically. For example, a simple division of patients on the basis of the mean simple RT correctly identified 70 per cent of the cases who were going to have either a greater or less than average duration of hospitalization. The more elaborate procedure of using the standard deviation for determining cut-off points only increased the accuracy of the prediction slightly while sharply reducing the number of patients on whom predictions could be made.

The best group of predictors consisted of the clinical rating of the formal signs of thought disorder, simple RT to light, the presence or absence of a depressive mood, and the rating of social class. While the last only accounts for an additional 6 per cent of the variance, the F ratio shows that each additional variable adds significantly to the prediction of outcome. The Index of Formal Signs, an overlapping measure of thought disorder, accounted for an additional 5 per cent in variance, thereby supporting the predictive value of measurements of the formal signs of schizophrenic thought disorder. Patients who show minimal formal signs of a schizophrenic thought disorder, a depressive mood, little retardation in RT to light, and a higher social class have the shortest hospital stay.

In summary, RT is not only an excellent predictor of duration of hospital stay in itself but, in combination with a clinical assessment of thought disorder and depressive mood, also makes possible even better predictions. It certainly seems that the former interest in RT was well founded and that additional studies are warranted today. A major defect to this study is the absence of repeated RT measures during the follow-up period. This deficiency highlights the need for longitudinal studies in schizophrenia as a function of the clinical state of the patient. We need to know what variables change and in which direction over the course of the disorder. Until this basic need is met we shall be continuing to ignore a critical source of variance.

REFERENCES


