Information Processing Effect on Saccadic Reaction Time in Schizophrenia

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Summary: Information processing was tested by comparing saccadic reaction times of 13 schizophrenics and 13 normal controls under conditions where there was information provided about the duration of a warning signal to those where there was not. Saccadic reaction time measured by electro-oculogram was studied in order to minimize complicating variables associated with prior studies using manual reaction time. Supporting prior research, this study found that schizophrenics do worse when there is prior information about warning signal duration than when there is not, while in controls this was reversed. Significant enhancement of this effect with increasing age and a possible normalizing effect with greater neuroleptic dose were also found. The major limitations of this study, however, included a small N and uncontrolled medication. The authors conclude that (a) there is a schizophrenic deficit in the processing of information in order to establish a mental set necessary for preparation, (b) this deficit may be useful in confirming the diagnosis of schizophrenia in older age groups, and (c) effects of antipsychotic medication on information processing warrant further study. They hypothesize that effects of neurotransmitters on information processing and time perception, abnormalities in the frontal lobes, and information processing steps measured by evoked potential may play a role in impaired information processing in schizophrenia. Key Words: Schizophrenia—Information processing—Saccadic reaction time—Eye movements. NNBN 3:80–97, 1990

Reaction time (RT) studies, reviewed by Nuechterlein (1977), have been consistently replicated in schizophrenia (SZ) research. A significant group of studies in this regard include those that test ability to prepare for RT by providing prior

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time information about foreperiod duration, the time between onset of the warning signal and the imperative stimulus. Huston et al. (1937) reported on simple auditory–manual RT that significantly differentiated patients with chronic SZ from normals. SZ patients had a longer mean RT, and whereas in normals the RT was faster when the duration of preparatory intervals was held constant, in SZ patients this difference did not persist, indicating that they were unable to profit from this regularization. Presumably, the regular series allows the subject to learn when to expect the imperative stimulus and to prepare maximally to react to it by establishing a “mental set.”

Rodnick and Shakow (1940) replicated these results in a simple visual–manual RT study, and although Huston and Senf (1952) found the greatest impairment in set in chronic patients, lesser degrees of impairment could be found in patients with early SZ or depressive psychoses and to a smaller extent in neuroses. This last study, along with one done by Zahn and Rosenthal (1965), who found considerable overlap of acute SZ and non-SZ cases, have questioned the diagnostic utility of this measure in acute cases, although in chronic cases there is statistically significant degree of discriminability using this test. Tizard and Venables (1956) found excellent discrimination in impairment of set between chronicSZ and mentally retarded adults, suggesting that this impairment in set reflects something other than an intelligence factor.

In a visual–manual RT experiment with a variable auditory foreperiod where pitch of the sound acted as a prior time information about foreperiod duration, Mo and Kersey (1980) compared chronic SZ patients to alcoholics. When pitch was correlated with foreperiod duration, so that there was prior time information about foreperiod duration, SZ patients performed worse than when there was no correlation although it did not reach the 0.05 level of significance. Alcoholics, on the other hand, did not differ in this regard. They concluded that in SZ patients there was a suppression of preparation by expectancy, and they hypothesized that the motor preparation itself decreased the ability of their data to reach significance.

The purpose of the present study is to clarify the effect of prior time information on RT and to relate the results to current neuropathophysiological studies in SZ patients. In order to do this, we propose the study of foreperiod in the RT of saccadic eye movement. The advantages of this are many.

(a) There has been a consistent finding of a slowed simple manual RT in SZ patients (Nuechterlein, 1977). Saccadic latency, in contrast, has been shown in at least three studies to be normal in SZ patients, whether or not there was impaired smooth pursuit (Iacono and Tuason, 1981; Levin et al., 1981, 1982). If saccadic RT is affected by foreperiod conditions, then it is not likely due to a function inherent in the saccadic system itself.

(b) In the above-cited studies, visual or auditory stimuli are coupled to manual responses, thus utilizing a more complicated system of sensory motor integration.
than the visual-oculomotor saccadic response. If there is a basic SZ deficit in the handling of sensory data, then one would want to keep the processing of this data to a minimum when testing for such a deficit. The superior colliculus can directly relate visual input to oculomotor commands and the saccadic system is a discrete control system whose velocity is not under voluntary control. Eye muscles are faster than those used in a manual response, do not pull against gravity, and oculomotor neurons fire much faster than spinal motor neurons (Kandel and Schwartz, 1981).

(c) Unlike simple RT tasks, in the saccadic task the imperative stimulus is determined by a change in location (the target moves) rather than by the introduction of a stimulus.

(d) Saccades are considerably less dependent on proprioception than manual responses and proprioceptive deficits have long been suspected in SZ (Iacono and Tuason, 1981).

(e) Saccades recorded via electro-oculogram will provide highly accurate information for the measurement of RT (Iacono and Tuason, 1981; Mialet and Pichot, 1981; Lipton, 1983).

(f) Comparison of foreperiod effect on the saccadic system to that of the manual response system will provide evidence to determine whether this effect is unique to a particular system or common to both.

Antipsychotic drugs have not been found to affect simple manual RT, foreperiod effect on manual RT, saccadic latencies, or smooth pursuit eye movements (which include an initial saccade and sustained attention to a target) (Held et al., 1970; Neuchterlein, 1977; Lipton, 1983; Holzman, 1987). One study concluded that RT got better on phenothiazones although this was not tested for statistical significance (Held et al., 1970). The present study will further address this issue of drug effect on RT.

Study of the foreperiod information effect on RT may tap multiple steps in the processing of information. The prefrontal cortex governs planning, abstract thinking, the ability to change expectations in response to new data, and sequential thinking among others (Foster, 1980; Andreasen, 1988). Prior time information about foreperiod may test frontal lobe processing of this information since subjects will be required to create new expectations about foreperiod duration in response to new data and then to react.

In a review of SZ, Andreasen (1988) delineates various tests of brain structure and function that have been found to be abnormal in SZ. Computed tomography (CT) and magnetic resonance (MRI) brain imaging studies have shown increased ventricular size that does not change with age, stage of illness, or drug treatment. The most consistent correlate with CT abnormalities is cognitive impairment.

MRI reveals decreased frontal size, position emission tomography (PET) scan shows decreased prefrontal metabolism, and regional cerebral blood flow (rCBF) studies find decreased activity of the prefrontal lobes when SZ patients do the
Wisconsin Card Sorting Task or the Continuous Performance Test, both of which require the ability to change expectations to new data. SZ patients seem to have difficulty activating the prefrontal lobe when they need it. Cytoarchitectural studies of the frontal system have found changes that are compatible with an early developmental abnormality, suggesting a pathologic process that begins before the onset of clinical illness. The information processing task in the present study will likely tap the functioning of the prefrontal cortex.

Another area that tests information processing is the evoked potential studies, recently reviewed by Holzman (1987). The P300 wave, a later occurring wave on EEG during evoked potentials, reflects the cognitive work done on the stimulus, and the N100 wave, which is an early wave reflecting stimulus registration, have been found to be abnormal in SZ patients. The P300 wave is attenuated, suggesting difficulty extracting information from the stimulus. The N100 wave has shown less variation and heightened amplitude, suggesting impaired subcortical filters with abnormal amounts of information reaching the cortex. The information processing task in the present study will likely be handled by those steps measured by evoked potentials.

**METHODS**

**Subjects**

**Patients**

Thirteen patients who gave informed consent were studied from a long-term inpatient psychiatric hospital. All patients were ethnically Japanese with identical cultural backgrounds. All patients met DSM-III-R criteria for chronic schizophrenia and none had concomitant diagnosis of mental retardation. Five patients were of the paranoid subtype, three were disorganized, two were residual, two were in acute exacerbation, and one was undifferentiated. Patients were excluded from the study if they had electroconvulsive therapy (ECT) during the last 10 years or were currently on a benzodiazepine or other sedative-hypnotic or if they were unable to cooperate or understand the instructions. The patient group consisted of nine males and four females. The average age was 41.4 years with an age range of 32 to 48 years.

All patients were on a high-potency neuroleptic and 9 of 13 were concomitantly on an anticholinergic. Details of medication, symptomatology, hospital duration, and Brief Psychiatric Rating Scale (BPRS) ratings are provided below. All clinical determinations were done by the physicians currently caring for the patients without a knowledge of RT scores.

**Controls**

Thirteen controls volunteered from the staff at the medical center and were age- and sex ratio-matched to the patient group. Average ages for controls and
patients were not significantly different. Nine controls were male and four were female. The average age was 43.4 years with an age range of 35 to 50 years. Exclusion criteria were the same as in the patient group. In addition, any control with a history of a major psychiatric disorder or a first-degree relative with such a history was excluded.

Detailed questionnaires were given to all subjects in order to rule out a history of neurologic, vestibular, visual, auditory, or medical condition that might interfere with the study. Glasses were required to be worn if needed. Neurologic screening examinations were also done on all subjects with particular attention to hearing, vision, and extraocular movements to insure that these systems were intact.

**Procedures**

Subjects were seated and were instructed to watch a horizontal display panel 0.5 m away and at eye level. Heads were stabilized at the chin and forehead. The target was a 1.0 cm diameter circular red light constantly visible at center field that moved abruptly in the horizontal plane to the right or left in 20° of visual arc. Stimulus proceeded instantaneously without delay at the end of an auditory foreperiod provided by a speaker situated immediately behind the stimulus display.

The sound frequency varied in three measures (250, 500, and 1,000 Hz) as well as its duration (1, 3, and 5 s). In the correlated (COR) trials, frequency and duration covaried so that frequency could function as prior time information about foreperiod duration. The covarying combination that was used was 1 s with 250 Hz, 3 s with 500 Hz, and 5 s with 1,000 Hz. In the uncorrelated (UNC) trials, frequency and duration varied randomly so that subjects could not pre-estimate the foreperiod duration.

In both COR and UNC conditions, the same number of each of the three frequencies and durations and in the same order within each condition set were presented to all subjects. Thirty of each COR and UNC trials were given. Both COR and UNC conditions were divided into 15 trails to the right and 15 to the left. Approximately 5–10 s separated each trial, and 1–2 min rest was provided between direction changes and 5 min between the COR and UNC trial sets.

In order to study the effects of fatigue and practice on RT, sequences of the COR and UNC trial sets were reversed in one-half of both the patient and control groups. The stimulus direction reversed within these sets so that in each of the control and patient groups, there were four subgroups with differing trial set sequences.

All subjects were provided with instructions before each set of trials as to stimulus direction and the nature of the frequency–duration correlation. Three unrecorded practice trials were provided before each direction change. Subjects were
also instructed to refrain from blinking, to relax their facial muscles, to watch only the target, and to respond as quickly as possible to follow the target when it moves. Visual distraction was minimized by turning out the lights. The sound level was audible in the adjoining room, where equipment was operated, and all subjects reported that the sound was readily audible.

Eye movement was recorded via electro-oculogram (EOG) with standard EEG electrodes placed two at the inferior lateral aspects of each eye, two at the superior medical aspects, and a midforehead ground. A Nihon Kohden standard EEG machine was used with settings adjusted as necessary to maximize the EOG and to minimize EEG and EMG noise. Saccades were clearly distinguished in all cases from the EEG and EMG. Electrode position readily enabled distinction of blinks and vertical saccades from horizontal saccades. Horizontal saccades were always registered in opposing directions on the EOG, while the others were always in the same relative direction. Excessive blinking during the foreperiod or stimulus could be monitored and instructions given to the subject to refrain.

Four channels were used for recording. Channel 1 recorded foreperiod tone, channel 2 recorded the stimulus displacement, and channels 3 and 4 recorded left and right eye EOG, respectively (Fig. 1). All four channels were simultaneously recorded on a data recorder for future RT measurement.

Data Analysis

RT measurement was performed via display of recorded data on a polygraph. Vertical bars were manually adjusted to separate the interval from stimulus initi-
ation to saccadic reaction, while a computer determined the RT in milliseconds. This procedure enabled accurate RT measurement to within 2 ms. Blinks occurring near the end of the foreperiod resulted in exclusion of that trial in order to insure that a blink did not interfere with stimulus recognition.

RESULTS

Overall Comparison

Figure 2 and Table 1 display the total RT of all subjects. Controls were significantly faster in absolute RT on both the COR ($p < 0.001, t = 7.97$) and UNC ($p < 0.001, t = 3.62$) trials. In controls, COR was significantly faster than UNC ($p < 0.05, t = 2.22$) while the reverse was true for patients whose UNC was faster than COR ($p < 0.05, t = 2.14$). There was no overall difference in RT in right vs. left for either controls or patients under either condition. There were also no sex differences in RT.

<table>
<thead>
<tr>
<th>TABLE 1. Total RT control versus patient</th>
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<tr>
<td></td>
</tr>
<tr>
<td>Controls</td>
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<tr>
<td>Patients</td>
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N = Number of trials.
FIG. 3. Relative reaction times PTs versus controls. Numbers in the boxes refer to millisecond difference in RT.

**Comparison of Individual Subjects**

The disparate distributions between patients and controls were significantly different (Wilcoxon’s U test; $p < 0.05$, $U = 39.5$) (Fig. 3). Eight of 13 (62%) patients had faster UNC trials, five reaching statistical significance. Only two controls had UNC faster and none reached the 0.05 level. Nine controls (70%) had faster COR; three reached the 0.05 level and another just missed it. Four patients (30%) had faster COR; only the 22 ms faster patient reached significance. The average differences (COR minus UNC, computed from individual data) for controls of $-8.86$ ms (COR faster, SD of 15.2 ms) and patients of $+9.49$ ms (UNC faster, SD of 20.9 ms) also tested significantly different ($p < 0.02$, $t = 2.56$).

**Age Effect**

Figure 4 and Table 2 break down subjects into young and old groups. Within both groups of subjects, young and old ages differed significantly (controls: $p < 0.005$, $t = 3.77$; patients: $p < 0.005$, $t = 4.04$) while between groups the respective young and old ages did not differ.

Within both patients and controls, COR – UNC differences were significant in the old groups but not in the young (controls: $p < 0.005$, $t = 3.22$; patients: $p < 0.005$, $t = 3.02$). Between patients and controls, COR – UNC differences were significantly different in the old group but not in the young ($p < 0.05$, $t = 4.70$).
The absolute RT had a tendency to increase with age from young to old in both the control and patient groups. All comparisons reached the 0.001 level of significance except COR controls, young to old, which slowed the least, just missing the 0.05 level of significance.

Figure 5 plots the individual distribution of COR – UNC differences. After the age of 41 years, there was almost complete segregation of patients vs. controls. None of the 8 patients over 41 years of age had faster COR trials while 9 of 10 controls had faster COR ($p < 0.01, \chi^2 = 14.4$). This amounted to 94%, without overlap at 3 ms minimal difference and 88% at 6 ms. There was a significant difference in comparing the correlation coefficient of age vs. COR – UNC difference for controls ($R = -0.49$) and for patients ($R = +0.52$) ($p < 0.02, Z = 2.51$). In both patients and controls, the effect of age on laterality failed to show significant differences in either the COR or UNC conditions.

**TABLE 2. Age versus RT**

<table>
<thead>
<tr>
<th></th>
<th>COR</th>
<th></th>
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<th>UNC</th>
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<tbody>
<tr>
<td></td>
<td>N</td>
<td>M (ms.)</td>
<td>SD</td>
<td>N</td>
<td>M (ms.)</td>
<td>SD</td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Young</td>
<td>195</td>
<td>148.4</td>
<td>46.4</td>
<td>200</td>
<td>151.8</td>
<td>42.0</td>
</tr>
<tr>
<td>Old</td>
<td>172</td>
<td>158.3</td>
<td>51.2</td>
<td>168</td>
<td>178.0</td>
<td>61.3</td>
</tr>
<tr>
<td>Patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Young</td>
<td>221</td>
<td>167.3</td>
<td>39.6</td>
<td>215</td>
<td>164.5</td>
<td>38.3</td>
</tr>
<tr>
<td>Old</td>
<td>134</td>
<td>205.5</td>
<td>48.0</td>
<td>145</td>
<td>189.2</td>
<td>42.0</td>
</tr>
</tbody>
</table>

N = Number of trials.
FIG. 5. COR-UNC is the difference in milliseconds between the COR minus UNC trials.

Effect of Sequence on RT

In order to test the effects of practice and fatigue on RT, varying sequences were employed. In patients, whether the UNC condition was given in the initial or final trials, the RT was faster, and in controls it was consistently slower (Fig. 6). Although none reached the 0.05 level of significance, trends were consistent.

FIG. 6. Sequence versus reaction time.
with the significant overall results when the data for the varying sequences were combined.

In the patient group when the COR trials were first, all RTs in this sequence set were significantly slower then when the UNC trials were first (COR initial vs. final; $p < 0.05$, $t = 2.02$; UNC initial vs. UNC final; $p < 0.001$, $t = 3.46$). In controls, there were no significant differences in this regard. Thus, initial COR conditions in patients seemed to have an effect of overall slowing although UNC patients still maintained a faster position.

**Medication Data**

Medication was recorded as equivalents of haloperidol (HPD) and trihexyphenidyl (THP).

**THP**

Increasing dose was associated with slower absolute RT for both conditions (COR, $R = +0.62$, $p < 0.05$, $t = 2.59$; UNC, $R = +0.53$, $p$ almost 0.05, $t = 2.06$) (Figs. 7 and 8). For the COR – UNC difference, however, $R = +0.31$ and was
FIG. 8. COR-UNC is the difference in milliseconds between the COR minus UNC trials.

not significant. Although it did not reach the 0.05 level, the four patients on no THP tended to have faster UNC RT ($p = 0.07, t = 1.96$). The high-dose THP group did have significantly faster UNC trials ($p < 0.005, t = 2.88$).

**HPD**

In contrast to THP, increasing dose was associated with faster absolute RT (COR, $R = -0.58, p < 0.05, t = 2.38$; UNC, $R = -0.63, p < 0.05, t = 2.68$). For HPD, the COR – UNC difference ($R = -0.15$) was not significant. The low-dose HPD group, however, did show a significant COR – UNC difference ($p < 0.005, t = 3.01$).

**BPRS vs. RT**

There was a trend toward decreasing absolute RT for both the COR and UNC conditions as BPRS severity increased, the COR trials reaching significant correlation (COR, $R = -0.62, p < 0.05, t = 2.61$). For UNC ($R = -0.52, p < 0.1, t = 2.0$), this did not reach the 0.05 level. For BPRS, the severity vs. COR – UNC difference ($R = -0.33$) was not significant.

**Diagnostic/Symptom Analyses**

Because of a low $N$, results of both diagnostic and symptom breakdown were felt to have no meaning. We did note, however, that anxiety was the only symptom, with an overall trend for faster COR RT although it did not reach significance.
Hospital Duration

There was no significant correlation of either COR ($R = +0.31$) and UNC ($R = +0.31$) absolute RT or COR – UNC differences ($R = +0.10$) with hospital duration.

DISCUSSION

The major finding of this study is a significant inability of SZ subjects to utilize the COR trials in the service of faster RT, consistent with studies previously cited. Overall, the absolute RT in SZ patients was also, as in prior studies, slower than controls.

Age had a significant effect on the way SZ patients and controls responded to prior time information. Young controls seemed to be able to react quickly in either the COR or UNC conditions while older controls seemed more dependent on prior time information. In patients, however, only the young were able to benefit from prior time information. Older patients, in contrast, could not extract benefit from prior time information and in fact were slower under these conditions.

The strong association of faster UNC trials with age in the SZ group may be an indicator of basic SZ pathology. Alternatively, this may be due to an interaction of the normal aging process with a prior static neurological insult. In either case, the results point to altered information processing expressed to greater degrees in older SZ patients. Because of almost complete separation in response to experimental conditions of patients and controls over 40 years old, this test may prove to have some value in confirming the diagnosis of SZ in older age groups. More definitive results would come from future studies stratifying subjects by age before testing rather than post hoc analyses that were done in this study.

By employing varying sequences, we concluded that for both patients and controls, the effects of fatigue or practice were small relative to the effect of whether there was prior time information or not. No matter what sequence was employed, results were consistent with the significant trends seen in the groups as a whole. Intrasequence comparisons may not have reached the 0.05 level because the $N$ was one-half of that as a whole. Initial COR conditions seemed to disturb the ability of these patients to react in that both COR and UNC trials in this sequence set were significantly slower. One explanation might be that the initial COR trials impaired their ability to establish a mental set for preparation and that they perseverated on this in the later UNC trials.

Voluntary attention and motivation factors can also be assumed to be small, since if they were a major influence, one would expect even performance in both COR and UNC conditions rather than a selectively poor COR performance. All subjects willingly agreed to be subjects, participation was completely optional, and no reward was given to participate in the study. SZ patients have also been
shown to have intact voluntary attention and motivation in studies of saccadic latency as well as in studies of smooth pursuit (Iacono and Tuason, 1981; Levin et al., 1981, 1982; Holzman, 1987).

Additionally, differences between patients and controls are too large to be due to errors in the RT measurement itself.

Analysis of medication dose pointed to significant associations with absolute RT. Increasing THP dose was associated with slower absolute RT while increasing HPD dose was associated with faster absolute RT. Regarding medication effect on response to foreperiod conditions, even those patients who took no THP continued to have faster UNC trials. Along with a nonsignificant R (for THP COR – UNC difference), this supports a conclusion that THP alone was not responsible for the faster UNC trials in SZ patients. Only in the low-dose HPD group were UNC trials significantly faster. This may mean that at low neuroleptic doses, SZ patients have more trouble using the correlated cue. At higher doses, there was no significant difference between COR and UNC trials, and it seems that although some patients may have been “normalized” in their ability to use the COR prior time information in the service of faster COR trials (see Fig. 8).

Alternatively, it might be that some aspect of the patients’ symptomatology and the prescribers’ dosing in regards to the symptomatology contributed to the HPD effects. This logic also applies to THP dosing, where drug-induced parkinsonism may have been responsible for increased absolute RT and was treated with higher THP doses. There was no association, however, of THP with COR – UNC difference, and higher COR – UNC differences were seen only in the low-dose HPD group. We conclude, therefore, that while there may be other explanations for a more normal pattern of information processing with higher HPD doses, the main finding of a significant inability of SZ subjects to utilize the COR trials in the service of faster RT seems to be independent of medication dosing. The way to discern medication effects more clearly would be to test drug-free patients, or those whose drug dosages are assigned at random. This is important in light of the fact that patients were medicated and controls were not. Enhancement of information processing with antipsychotic medication warrants further study. This is important since it could provide a measurement of treatment response as well as support a role for medication in improved cognitive functioning.

In neurotransmitter terms, either a low HPD or a high THP dose reflects a relatively high D/A (dopamine/acetylcholine) ratio in the central nervous system. In this model, a high D/A ratio correlates with slow overall RT and poor ability to use foreperiod cuing in order to form a mental set. Lower D/A ratios would be associated with RT profiles more consistent with the control data. The findings of this study are thus consistent with the hypodopaminergic theories of SZ (Andreasen, 1988). Further study might employ various drug regimens and/or challenges in order to learn more about the role of neurochemistry in this area.
Another effect of antipsychotics may be to alter time perception. Maricq (1983) studied the effects of metamphetamine and HPD on time estimation in the rat and found that metamphetamine, which increases dopamine transmission, leads to an increase in the speed of the internal clock and vice versa with HPD. If dopamine is increased in SZ patients and affects temporal processing as Maricq suggests, then there may be erroneous estimation of foreperiod as cued by the COR signal. In the present study, slow COR RT at low HPD doses and improvement at higher doses would be consistent with Maricq’s finding that when he gave rats a mix of metamphetamine and HPD, the opposing effects on time estimation were neutralized. Additionally, antipsychotics have been shown to speed up rather than slow information processing (Holzman, 1987).

Unfortunately, because of a low N, neither the diagnostic nor the symptom analyses were felt to have any meaning. Because there was a trend for anxiety to cause a faster COR RT, there was no evidence that this symptom was responsible for the SZ patients’ poor ability to form a mental set.

Poor ability of SZ patients to use the COR warning cue may relate to various areas of cognitive difficulty that are suspected to be awry in SZ. Because both manual and saccadic RTs show this phenomena, the function in question must be common to both systems and lie proximal to the motor output stage in which these systems differ.

Areas in the frontal lobe concerned with sequential thinking and the ability to change expectations to new data are likely to be activated under the conditions of this study. Various lines of evidence including CT, MRI, and cytoarchitectural studies have pointed to early cerebral changes before the onset of clinical symptoms (Andreasen, 1988). In our study, we found significant, though divergent, age-related changes between SZ patients and normals so that the normal aging process coupled to an earlier defect may be a cause for these results. Although the limitations of this study could not provide brain imaging correlation, we propose a comparison of those patients who do and do not show slower RTs under COR conditions. We also propose a prospective study to follow the time course of subjects’ response to foreperiod conditions in order to clarify individual progression with age.

Evoked potential studies may provide another clue towards delineating the steps in information processing that are put to use by our study. N100 abnormalities are seen in conditions of divided attention or longer rates of stimulus presentation (Holzman, 1987). In our experiment, divided attention consists of that to the light and sound present in both COR and UNC groups. P300, however, reflecting cognitive processing of the stimuli, would more likely be included in the COR trials, where there is information about foreperiod duration. It may also be that the information reaching the cortex (reflected by N100) is more poorly filtered at the P300 stage when there is meaning to be processed. Correlation of

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our experimental conditions with evoked potential would be useful for a further understanding of this matter.

Mather (1986) studied saccadic eye movements of normals in the dark and concluded that SZ patients, although having normal oculomotor RTs, process visuospatial information less efficiently than normals. We suggest that because our study illuminates a temporal processing deficit (only temporal conditions change between COR and UNC trials), there may be a general sensory information processing deficit common to both spatial and temporal types of stimuli.

One limitation of this study is that it did not separately analyze the responses to the 1, 3, and 5 s intervals. Other studies using manual responses had reported that SZ patients were unable to improve RTs in regular compared to irregular series of preparatory intervals when these intervals were greater than 2 s in one study and greater than 4 s in another (Huston et al., 1937; Rodnick and Shakow, 1940). Having done so, perhaps we would have found less overlap with controls at the longer foreperiods.

Another limitation is the relatively small number of patients in this study. This limits the reliability of the conclusions that can be drawn from analysis of some of the data variables, such as diagnosis, symptomatology, BPRS severity, and medications. Many Japanese SZ patients are often concurrently on a benzodiazepine and could not be included in this study. This may also bias the pathology in the sample that was studied although in what way we do not know. Although DSM-III-R criteria were used, another shortcoming was the absence of research diagnoses. The limitations of uncontrolled medication dosing were discussed earlier.

Future research in this area needs to address further the effects of diagnosis, symptom cluster, severity, and medication. Studies should include nonsymptomatic relatives of SZ patients to search for genetic links and state vs. trait variables. Other psychiatric diagnoses need to be studied to discern specificity. Prospective studies to follow the progression with age and correlation with tests of brain structure and function are also needed. The present study presented the foreperiod signal via a speaker system that simultaneously stimulated both ears. Presentation of the warning signal via earphone to one ear at a time provided more conclusive evidence as to the question laterality.

A summary of the conclusions of the present study are as follows:

(a) Measurement of saccadic latency is an accurate and reliable method to study the effect of foreperiod on RT.

(b) SZ subjects had significantly slower COR trials, where there was prior time information about duration of foreperiod, while controls had significantly faster COR trial sets. This is interpreted as a general information processing deficit in SZ patients’ ability to establish a mental set necessary to prepare by expectancy. This may relate to sequencing difficulty in the frontal lobes, stages of information processing associated with the N100 and P300 evoked potential waves, abnor-
malities in time perception, and relatively high levels of dopamine in the central nervous system.

(c) Significantly slower absolute RTs were found in the SZ group, consistent with past data of slow RT in SZ patients.

(d) Increasing age was associated with increasingly significant slower COR trials in SZ patients and increasingly significant slower UNC trials in controls. These findings may be due to a normal aging process in controls while in SZ patients it may be associated with progression of the SZ pathology. Alternatively, it could be an interaction of normal aging with a prior static SZ deficit, or possibly a combination of both. This inability to establish a mental set necessary for preparation with increasing age may prove useful in confirming the diagnosis of SZ in older patients.

(e) In both groups, increasing age was associated with significantly slower absolute RTs under all conditions. While low neuroleptic dose and low BPRS were also associated with slow absolute RTs, the fact that controls on no medication and with no symptoms had increasing RT with age points strongly toward age as an important factor.

(f) Both HPD and THP had significant and opposing associations with absolute RT. Absolute RT quickened with higher doses of HPD and slowed with increasing doses of THP. While THP had little recognizable influence on experimental conditions, HPD at higher doses may enhance the ability of some SZ subjects to use prior time information in the service of establishing a mental set about the occurrence of a future event. Medication, however, was uncontrolled and confounding interactions could not be ruled out as causative for the observed medication effects. Enhancement of information processing with antipsychotics warrants further study since this could provide a measurement of treatment response and support a role for medication in improved cognitive functioning. The overall finding of slower COR RT in SZ patients, however, remained independent of medication dose in this study.

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