Chapter 36
Attention and Information Processing as Indicators of Vulnerability to Schizophrenic Episodes

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As a descriptive model, we find it useful to distinguish between vulnerability to schizophrenia which is a relatively permanent, enduring trait and episodes of schizophrenic disorder that are waxing and waning states. According to this model, episodes of schizophrenia ensue when endogenous and exogenous challengers surpass a threshold set by the individual's dispositional level of vulnerability. When such challenging events subside, the patient shows at least some degree of recovery, and sometimes even reattains his premorbid level of functioning. However, even when a schizophrenic's state has normalized, his vulnerability persists and leaves him at risk for future episodes of schizophrenia.

The various etiologic models of schizophrenia have been presented elsewhere (1). Here it will suffice to suggest that vulnerability to schizophrenia may originate in many ways. Biologic models emphasize etiologic forces arising from an individual's internal make-up: his genes, biochemistry, and neurophysiology. Field theory models stress the role of exogenous forces impinging on the maturation, learning, and immediate behavior of the individual.

The different etiologic models often agree in predicting that a particular group of individuals will be vulnerable to schizophrenia, although these predictions are based on different rationales. Most models predict that siblings of schizophrenics represent a

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group at some risk for schizophrenia, since they share numerous possible sources of vulnerability with the schizophrenic probands. These include a shared gene pool, similar intra-uterine environments, common family and community interaction experiences, exposure to the same diseases, diets, physical environments, and so forth.

Because of the evidence that disturbed sensation, perception, and attention may be central characteristics of the schizophrenic syndrome (2-4), our selection of potential vulnerability indicators has been influenced by the neurophysiologic model of schizophrenia. This model seeks the causes of schizophrenic symptoms in disorders of central nervous system functioning and the capacity to take in and process information. Disturbances of information processing have a prima-facie link with the schizophrenic psychopathologic state because patients' subjective complaints so often include altered perceptual experience, distractibility, and flooding or loss of the ability to differentiate figure from ground (2-3). Even if these disturbances do not produce or cause schizophrenia, they may serve as "culture-free" markers of that disorder or of vulnerability to it.

We are investigating a variety of information-processing indicators to distinguish between two types: those that mark the trait of vulnerability to schizophrenia and those that mark episodes of schizophrenia. The sample consists of recently hospitalized schizophrenic patients, their close-in-age siblings who have never manifested severe psychiatric disturbance, nonschizophrenic psychiatric control subjects, and healthy controls without a family history of psychiatric disturbance. Schizophrenic patients are also retested after their symptoms have subsided. We will designate as potential markers of vulnerability to schizophrenia performance anomalies that display two characteristics: (a) The characteristic is not present in nonschizophrenic psychiatric patients or healthy control individuals but does appear in both the nonaffected sibling and the schizophrenic proband, (b) The anomaly persists in "recovered" schizophrenics. Anomalies found in both groups "at risk" for schizophrenia (unaffected siblings and "recovered" patients) but bearing no relationship to the manifest psychopathologic state, would appear to be associated with the underlying vulnerability to schizophrenia. In contrast, promising candidates to mark the beginnings and ends of episodes of schizophrenia would be those characteristics that deviate only in highly symptomatic schizophrenic patients and normalize in retested "recovered" cases.

MEASUREMENT TECHNIQUES

The battery of assessment techniques consists of procedures previously found to reveal differences in the information-processing characteristics of healthy subjects, schizophrenic patients, and depressed individuals. Some techniques can be considered primarily sensory in nature; others assess physiologic, psychophysic, attentional, and language processes. All the techniques are listed below. More detailed descriptions will be given for procedures illustrating some general "methodologic maxims" that have been followed at the Biometrics Research Unit. Many of these maxims have recently been articulated by Sutton (5) as useful guidelines in designing test procedures for psychiatric research. The relevant techniques are:

1. Dichotic listening as a measure of the ability to maintain selective attention.
2. Simple reaction time to ipsimodal and crossmodal stimulus sequences, measuring the ability to shift attention.
3. Pupillary dilation to ipsimodal and crossmodal stimulus sequences.
4. Evoked potential to ipsimodal and crossmodal stimulus sequences.
5. Pupillary constriction to simple light stimuli.
8. Auditory threshold and auditory reaction time facilitation by the addition of a masking stimulus.
9. Comprehensibility of verbal utterances as measured by the cloze procedure.

**METHODOLOGIC MAXIMS**

The maxims advanced are designed to contend with a fundamental pitfall in schizophrenia research. The pitfall is that confirmation can be obtained for almost any theory of schizophrenia as long as the theory predicts that schizophrenics will perform more poorly than normal subjects on a given experimental task. Therefore, certain precautions are needed to obtain meaningful patient data and to shed light on the factors responsible for schizophrenic behavior.

1. *Test procedures should be as simple as possible.* Two forms of simplicity are desirable. (a) *The response required of the subject should be as simple as possible,* so as not to place excessive demands on the subject's willingness to cooperate or to follow complex instructions. This demand is perhaps most readily met when simple physiologic recordings are taken, as two of our procedures illustrate.

In one test, visual and auditory evoked potentials are recorded from the scalp when subjects are either told in advance (certain condition) or asked to guess (uncertain condition) whether the stimulus on the next trial will be a light or a sound. Figure 36-1 shows evoked potential waveforms recorded from 10 normal controls, 10 depressed patients, and 10 schizophrenic patients. The solid tracing represents a waveform generated in the certain condition; the dotted line shows a wave recorded under conditions of uncertainty. Both groups of psychiatric patients were tested while receiving phenothiazine medication. This sample of tracings illustrates the finding of Levit et al (6,6A) that the effect of uncertainty in enhancing a late positive component of the evoked potential (P300) is greatest in the normal group and least in the schizophrenic group. Levit also presented subjects who were naive with respect to evoked potentials with the 10 sets of three waveforms recorded in the uncertain condition. When instructed to select the "most different" waveform in each triad, subjects overwhelmingly identified the schizophrenic trace as the maverick.

In another procedure, subjects are simply asked to fixate while the extent of pupillary constriction to a single light pulse is assessed. Figure 36-2 illustrates the findings of Lidsky et al (7) comparing the pupillary reactions of recently admitted, drug-free psychiatric patients with those of normal controls. All but 7 of the 51 patients were diagnosed as schizophrenic by hospital psychiatrists. The data are presented in the form of a cumulative distribution, whereby a value on the ordinate shows the percentage of subjects whose contraction exceeds any given value on the abscissa. Results indicate that patients show reduced constriction of the pupil to light. Moreover, the reaction to light differentiates patients and normal subjects quite strikingly, such that the response distributions show only 20% overlap.
Figure 36-1. Evoked potential waveforms recorded from 10 normal subjects (N), 10 depressed patients (D), and 10 schizophrenic patients (S). Solid tracings represent waveforms generated in the certain condition. Dotted lines show waveforms recorded under conditions of uncertainty. From Levit RA (6a).

Figure 36-2. Cumulative distributions of patients and normal subjects as a function of the extent of contraction to a single light pulse. From Lidsky A, Hakerem G, Sutton S (7).
(b) Task requirements should be simple in the respect that the procedure engages few systems of psychologic function aside from the one in which the deviant process is thought to reside. For example, the crossmodal reaction time procedure was devised to test the hypothesis that schizophrenic patients experience particular difficulty in shifting attention. Rather than presenting complex cognitive stimuli that might evoke dysfunctions in high-level conceptual functioning, the procedure requires attentional switching between different modalities of simple energy stimuli. Very brief preparatory intervals of between 1.5 and 3.5 seconds are used, so as not to confound attentional switching ability with the capacity to sustain attention or to estimate the duration of long time intervals.

When simple finger-lift reaction time is tested for serially presented sequences of light and sound stimuli, schizophrenics show the predicted greater than normal lengthening of reaction time when the stimulus sequence requires them to shift their attention from one modality to another (8–9). However, it is still possible that the schizophrenic’s impairment in crossmodal sequences reflects deviant expectancies about the modality of the upcoming stimulus rather than an inability to shift attention. To control for the variable of cognitive expectations, Kriegel (9) informed subjects of whether the stimulus on each trial would be a light or a sound. Schizophrenics continue to show the greater than normal crossmodal retardation even when they are told in advance what stimulus to expect. In our current experimentation, subjects are always informed of the nature of the upcoming stimulus. Moreover, the usual procedure of verbally conveying expectancy information is being compared with another procedure in which an actual light or sound stimulus forewarns the subject. The latter, more “task-syntonic” condition, is expected to reduce the information-processing demands of the task even further by making the form of the expectancy information distinct and in the appropriate modality for each stimulus and by eliminating the cognitive translation necessary to transform verbal symbolic expectancy information into an appropriate sensory set.

2. The phenomenon of interest should be monitored in more than one response system, and, if possible, with simultaneous recording. To study the physiologic response of the brain to crossmodality shift, Levit et al (6) recorded scalp evoked potentials to stimulus sequences involving light and sound. Simultaneous physiologic and psychomotor recording were not desirable in this case because of the danger of contaminating the evoked potential with movement artifact or with cortical activity reflecting motor processes. Findings showed that, whereas depressive and normal subjects tend to have larger N1-P2 amplitudes in the crossmodal condition, schizophrenics tend to display larger amplitudes in the ipsimodal condition. In the current study, subjects tested on the crossmodal reaction time procedure are subsequently tested by simultaneous monitoring of the vertex evoked potential and pupillary dilation response to certain and uncertain crossmodal and ipsimodal stimulus sequences. By obtaining all three responses for the same subject, it will be possible to determine whether pupillary dilation and P2 amplitude preserve their previously discovered parallelism (10) and conform to the crossmodality psychomotor response pattern of any given subject.

3. If nonpsychotic psychiatric patients constitute a control group, the test battery should include at least one procedure on which this group’s performance markedly differs either qualitatively or quantitatively from that of schizophrenics and normal controls. The general rationale for including a nonpsychotic psychiatric control group in a research design is to demonstrate that a relevant performance characteristic pertains specifically to schizophrenia rather than to psychosis or to psychiatric disorder in general. If it is to be argued that different diagnostic groups suffer from discrete
disorders rather than from the same disorder with more or less severity, then test results should bear out this theory. The usual finding that normal subjects perform adequately, psychiatric controls somewhat worse, and schizophrenics very poorly conforms as well if not better to the theory of differing severity as it does to the theory of discrete functional psychiatric disorders.

A test of auditory reaction time facilitation demonstrates the desired discontinuity in performances by schizophrenics and psychotically depressed patients. Bruder et al (11) examined the extent to which reaction time to a high intensity click is reduced when the standard click is paired with a second click. Clicks were presented in a forward masking paradigm in which the more intense click preceded the less intense. Testing was done at each of three different intervals (2, 7, and 15 mseconds) separating clicks in a pair. Affectively psychotic subjects showed a significantly greater reduction in reaction time to the click pair relative to the single click than did schizophrenics and nonpatients. In fact, schizophrenic patients displayed slightly less facilitation than did healthy controls. Moreover, when the interval separating clicks in a pair was increased to 15 mseconds, affectively ill patients showed a marked decrease in reaction time not observed in either of the other groups.

4. Test procedures should be sought for which patient performance is in some sense better than normal. The auditory reaction time facilitation procedure is illustrative in that affective psychotic patients show more improvement or better facilitation than do the controls. The great advantage of such findings is that it is difficult to attribute them to extraneous factors such as the patient’s poor motivation, failure to comprehend or follow instructions, or more general problems.

The dichotic listening procedure is another technique that can yield better-than-normal patient performance. This task also will be used to illustrate three final methodologic maxims. Dichotic listening is a classic test of the ability to maintain selective attention while filtering out distracting material. The test should therefore index any tendency for schizophrenics to be excessively distractible. In this procedure, subjects wear stereo earphones and are simultaneously presented with two different verbal messages, one to each ear. The instructions are to ignore the message presented to one ear, while attending to the other message and “shadowing” or repeating it word-by-word.

When messages are presented at a fairly rapid rate, schizophrenics make more shadowing errors than controls (12–13). However, if schizophrenics are in fact excessively distractible, they should do better than controls on another aspect of the dichotic test. They should surpass healthy controls in the extent to which they process information on the irrelevant, distracting channel. Processing of the competing channel is typically assessed by asking subjects to recall or recognize words previously presented to the unattended ear. Two problems with this procedure are noteworthy. First, the subject is effectively placed in a double bind, having first been asked to ignore and then subsequently been asked to report on the competing message. Second, one must devise a way of distinguishing between two aspects of memory performance: the subject’s sensitivity, or the extent to which he has processed information on the irrelevant channel, and the subject’s criterion, or the extent to which he is willing to report having processed distracting material. Previous work on schizophrenic memory for distractors (12–13) suggests that the two variables may be difficult to disentangle, since patients and normal controls differ in their tendencies to make “false alarms,” or to claim to remember words that have not in fact been heard.
5. **Whenever appropriate, research on psychiatric patients should either control the criterion variable or obtain separate estimates of sensitivity and criterion.** One strategy to avoid the confounding of sensitivity and criterion is to have subjects show by their performance rather than tell whether distractors have been processed. This objective can be attained by presenting novel pairs of words on the unshadowed channel and by subsequently testing to see how readily subjects learn to remember these paired-associates. To the extent that a schizophrenic subject has been biased toward attending to the distracting pairs, and has begun to learn to associate them during the shadowing task, he should find it relatively easy to learn these particular word pairs in a paired-associate memory task. But should his paired-associate memory for distractors exceed that of normal subjects in an absolute sense? Almost certainly not, because the schizophrenic’s generally low level of memory ability will prevent him from being able to demonstrate an advantage in a simple group comparison. Rather than “covary out” the confounding variable of memory ability, an alternative strategy is to use an “own control” design.

6. **The own-control design can be used to control for differences between patients and normals on a confounding variable.** Two measurements can be taken in such a way that the confounding variable enters equally into both measures, and the variable of interest enters only into one. In the dichotic listening example, the group’s ability to learn to remember pairs of words presented as distractors is compared with its baseline ability to learn new pairs of words not previously presented. The relationship between the group means on the two variables is plotted for all groups, so each group serves as its own control on the variable of baseline memory ability. Regression analyses can then be used to discern the general trend or “law” relating the two variables for the majority of groups, and it can be seen whether the experimental group deviates from the general trend (16).

7. **To establish the factors responsible for a performance anomaly, it should be demonstrated that the performance pattern fluctuates as a consequence of manipulations affecting the psychologic system that is hypothesized to be responsible for the anomaly.** If schizophrenics’ deviant performance on the dichotic listening test is due to dysfunctional attention, the deviance should be normalized by manipulations that effectively engage attention. Kahneman (17) has reviewed evidence suggesting that voluntary control over attention is limited. The degree of attention invested in a task is primarily determined by intrinsic task demands rather than by volition. Spare processing capacity cannot be engaged by an easy task as readily as by a hard one.

It can be expected that the schizophrenic’s tendency toward distractibility will be most evident when the shadowing task exerts few intrinsic constraints on attention. Attention will be most free to wander when the main message is easy to predict or highly redundant. On the other hand, manipulations that engage attention by making the shadowed message difficult and unpredictable should minimize and possibly even normalize deviant attentional performance.

In a pilot experiment conducted by Spring (18), the dichotic test was administered to nonpatient controls and to hospitalized psychiatric patients diagnosed according to research criteria (19). All subjects shadowed four familiar proverbs and four matched unpredictable sentences. Proverbs and unpredictable sentences were presented in semi-randomized order and equally often to the right and left ears. Sentences were presented at such a slow rate (slightly less than one syllable per second) that very few patients or nonpatients made any shadowing errors. A set of three pairs of words (proverb pairs)
was presented as the competing message for each proverb; and a matched set of word pairs (unpredictable pairs) co-occurred with each unpredictable sentence. Sentences were matched on the syntax and Thorndike-Lorge frequency of each component word. Proverbs were rehearsed in advance to ensure familiarity. Word pairs consisted of one-syllable, high frequency words coupled to be difficult for paired-associate learning by pairing stimulus words low in imagery value with response words low in association value. When shadowing was completed, subjects were asked to memorize a list of paired words that included all proverb pairs and all unpredictable pairs in addition to nine new (neutral) pairs of words. On each memory trial, subjects studied and were tested on all 15 pairs, until the entire list was learned to a criterion of one perfect trial or until eight trials had been completed.

Distractibility was measured by a savings, or better performance, on learning to associate word pairs previously presented on the secondary tape channel, relative to baseline performance on new pairs of words. The savings on proverb pairs relative to baseline indexed distractibility when the shadowing task was predictable and the demand on attention was minimal. Savings on unpredictable pairs would indicate distractibility during a difficult, attention-engaging main channel task.

At this point it might be noted that there were many discrepancies between patients' hospital diagnoses and the diagnoses assigned according to research diagnostic criteria. The great majority of patients in the sample received hospital diagnoses of schizophrenia. Research diagnoses made with a knowledge of hospital diagnoses but blind as to test performance assigned patients almost equally across a broader range of diagnostic categories. One consequence of these discrepancies is an inadvertent drug control procedure. Among the patients receiving phenothiazine therapy were 5 of the 7 schizophrenics, 3 of the 7 depressed patients, 4 of the 7 schizoaffective depressed patients, 3 of the 5 schizoaffective manic patients, and all the 5 manic patients. There was no systematic relationship between medication and test performance across all diagnostic groups.

For all groups except schizophrenics and depressed patients, the number correct is about equal for proverb pairs and neutral pairs. The schizophrenic group deviates significantly from this trend ($t_{12} = 13.25, p < 0.01$) and shows a savings or better performance on learning pairs presented as distractors during an easy, predictable message. This finding suggests that schizophrenic patients profited from their distractibility during the shadowing task and began learning to associate the word pairs presented simultaneously with predictable sentences. Most groups appear not to have learned these associations during tape presentation—they learn the proverb pairs only as easily as the new pairs. Depressed patients also differ significantly from the main trend ($t_{12} = -21.21, p < 0.01$) but in an entirely different direction. They do not learn the proverb pairs as easily as new pairs. Instead they seem to have acquired an active inhibition that makes pairs previously presented as distractors more difficult to learn.

Figure 36-3 shows the consistency of these effects for all individuals in a group. For subjects in all groups except the schizophrenic and depressed, chance seems to govern whether there is a savings or a decrement on learning proverb pairs relative to baseline learning on new pairs. However, every single individual in the schizophrenic and depressed groups scores consistently with the trend for the mean group performance.

When the main channel message is unpredictable and, hence, should engage attention very effectively, all groups show a deficit relative to baseline in learning the associated
pairs. This "inhibition" effect is significantly more marked for the depressed ($t_2 a.r. = -10.07, p < 0.01$) and the schizoaffective depressed ($t_2 a.r. = -13.93, p < 0.01$) groups. The schizophrenics do not depart from the trend for the other groups. Thus their performance is normalized by the attention-engaging manipulation.

REFERENCES

2. Freedman RJ: The subjective experience of perceptual and cognitive disturbances in schizophrenia. *Arch Gen Psychiat* 30:333, 1974.


