A Neurophysiological or Brain-function Model for Schizophrenia

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I Introduction

In the attempt to determine the possible etiological sources of schizophrenic behavior we have postulated the following set of models:

(1) ecological (2) developmental (3) learning (4) genetic (hereditary) (5) internal environment and (6) neurophysiological or brain function model. It is the last named model that we are concerned with here.

Let us first indicate that not one of these six models by itself can provide both the necessary and sufficient basis for the development of schizophrenia. It is rather the interaction of these causal forces working in conjunction that can probably be regarded as both necessary and sufficient. Nevertheless, because of the abysmal ignorance that surrounds the causes of schizophrenia we must first try to determine how far each of these models can take us by itself, before we invoke its interactions with the others. This we will proceed to do with the neurophysiological model.

If any of these models are to be tested for their tenability we must first develop hypotheses emanating from these models for experimental investigation. Thus, if we adopt the genetic model, we can hypothesize that identical twins must show a high concordance for schizophrenia,
higher at least than dizygotics; show, and then proceed to test this hypothesis in pairs of twins, one of whom is the proband for schizophrenia. We need to develop or apply techniques for determining zygocity, measures of environmental similarity, etc. in order to test the hypothesis. Similarly, in testing the tenability of any of the other models we must develop suitable hypotheses, develop tools, and proceed to test.

The gross behaviors which are noted clinically in schizophrenics and which constitute the basis for the diagnosis of this disorder are so molar in character that it is futile to try to resolve them into their underpinnings relative to the six causal factors we have stipulated. While persecutory ideas, for example, can be related to the ecological niche that the patient emanates from (that is why the Russian patient is chased by OGPU while the American must be pursued by the FBI) or to the other models as well, it would be very difficult to relate such observations to the origin of the persecutory idea without making a more intensive examination of the single individual, his prior history, etc. To try to determine the neurophysiological basis for persecutory ideas is, at the present time, beyond our capacities. We do not even know how to start such an investigation. For this reason, investigations of the neurophysiological basis of schizophrenia must begin at a much simpler level.

The particular ways the schizophrenic differs from other mental patients and normals might have been of some use in this connection. Clinical psychological tests have for a long time been used for such differentiation, but the validity as well as the reliability of these tests have never been well established. In a survey of clinical psychological tests for diagnosis
and prognoses carried out in the early 50's we were forced to give up any hope that the available projective and personality tests would be of value. Instead we turned to the classic categories of human responses to stimulation categorized as physiological sensory perceptual psychomotor and conceptual and have tried to determine whether the pattern of response across these categories differentiates patients from normals. We developed a Mendelejeff-like table relating response to type of stimulus (discuss Mendelejeff table).

It is quite clear that as we move from energy stimuli to signal and symbol stimuli, the role of prior experience, cultural influence, and schedules of reinforcement begin to enter. Since schizophrenics are bound to differ from normals in these respects, we will concentrate as far as possible on energy stimuli that are relatively free of prior experience.

The term neurophysiological may require a bit of explanation. We are trying to group together under this rubric the psychophysical, physiological and general psychophysiological approaches all of which have some bearing on the functioning of the central nervous system especially the brain. In terms of our Mendelejeff table we shall deal with physiological, sensory, perceptual and psychomotor responses, omitting the conceptual because of their high-cultural and experiential loading.

Experimentally there have been three types of approaches: (1) experiments relating cognitive behavior to schizophrenia, e.g. perceptual constancy, (2) experiments related to physiologically based responses, e.g. arousal level, energy integration and (3) experiments related to sensory information
processing, e.g. thresholds. While these three types of experiments have their own distinctive features, we shall regard them as subsumed by the last named type -- information processing -- since we believe the techniques used in such experiments usually involve the assessment of the information processing that is carried on by the central nervous system.

Before we begin our presentation we need to point out that the literature on information processing in schizophrenia has an old tradition dating back to Kraepelin and earlier. Despite its wealth, it suffers from several handicaps. First, is the problem of diagnosis which is one of the fundamental stumbling blocks in communicating findings of both clinical and research import. Second is the dependence of many of the tasks on prior experience, acculturation and cooperation of the patient. Third is the development of new techniques such as signal-detection theory and its implication for separating the sensitivity of the central nervous system to stimulation from certain attitudinal factors which are independent of such sensitivity. As a result, much of the earlier literature is only of historical value and is no longer dependable as a guide for current and future work. For this reason, we shall limit our approach to only a few of the more reliably based approaches in our own laboratories and in those of our colleagues who are equally aware of the shortcomings of the earlier data and have taken steps to correct their procedures accordingly.
II Neurophysiological Model

We would like to present our psychophysical and physiological findings in the context of the rationales for undertaking this work and even more so in the context of the methodological problems which the specific experiments are designed to overcome.

The rationales for applying a neurophysiological approach to mental disorders is the hope of either objectifying or measuring the observations of the clinician on the characteristics and behavior of the patients belonging to a given category or to find some kind of indicator of central nervous system functioning on these same patients. Both of these aims are linked to the overall goals of obtaining measures which may assist with diagnostic problems, hopefully cross-culturally, as well as clues which may be relevant to the question of etiology for that illness. Kety has noted some time ago that the subtlety and complexity of undertaking biochemical research in mental illness as well as the kinds of artifacts which may arise in the application of biochemical analyses of blood, urine and other body tissues make it highly desirable that some clues to what might be being looked for could be supplied to the biochemist from other fields, not the least of all psychology.
The nature of the clinical impressions that the psychophysicist may undertake to objectify need not concern us here. They are many and varied and rarely have any compelling arguments for picking one above another as being a key or root symptom. Thus various investigators have attempted to objectify the general observation of perceptual disorder. Others have been concerned with the common observation of psychomotor retardation, and so on. We have argued in the past (Zubin & Kietzman) for the importance of studying the temporal processing of stimuli as being an important dimension to study. We have further argued that phenomena which occur relatively rapidly in time, in the first 1000 msec or less, might be somewhat less susceptible to contamination by cultural and conceptual variables. Of course even this criterion must be applied with great deal of care since no matter how short the span of time one might be dealing with the cultural or conceptual contamination may arise in determining the attitude or point of view that the subject brings to the presentation of the stimuli and nature of the task he must perform in relation to them.

It might seem paradoxical that one would undertake to measure psychophysical performance if one is concerned with obtaining some reflection of central nervous system functioning.
in a particular illness. Why not measure physiological performance directly? However, as will emerge later it turns out that it is often more illuminating to measure a psychophysical reflection of central nervous system function than to obtain a measure of central nervous system function directly. We will develop this theme as I go along but at this point let me just give you one example of the difficulties in interpreting physiological data. In our evoked potential research we found that the average evoked potential waveforms obtained from clearly schizophrenic patients to stimuli which told the subject whether his guess was right or wrong are very dramatically different from those obtained for clearly depressive patients and for normal subjects. These waveforms are so unusual in their conformation, and frankly so "messy," that we had no difficulty getting completely naive subjects to distinguish the schizophrenics' waveform by asking them to indicate which were most different from the rest. Subjects who had never seen evoked potential waveforms before would almost invariably pick out the schizophrenic waveform as the one that was most different. It would seem then that here we have very dramatic evidence of the operation of the "crooked" molecules that may be involved in determining schizophrenic thought. But this is not so! In fact we know from our research that the evoked potential is enor-
mously sensitive to the general psychological state of the
subject as well as to his interpretation of his task and of
the role of the stimulus in relation to the task. Therefore what we may have is no more than a demonstration that
physiology faithfully represents the different psychological
state with which the patient approaches the task and if we
could induce a similar state of uncertainty or indecision in
the normal, he would show similar distortions in his evoked
potential. I should note in passing that the clearcut depressive patients who had no conceptual
disorganization of the kind that one finds in schizophrenia
had waveforms which were in fact very similar to those
of the normal subjects—only slightly smaller in amplitude
and very slightly later in latency of the various components
of the averaged evoked potential waveform.

How then can one use psychophysical measures to obtain
more valid indicators that it is the physiology or anatomy or biochemistry
of the nervous system that is at fault in obtaining par-
ticular differences between some group of patients and
other groups of patients and normals. It is certainly true
that all the problems of obtaining reliable and meaningful
measurement that the patient brings with him into the physio-
logical laboratory are also present in the psychological laboratory. In fact we have just argued that it is quite possible and even likely that the physiological differences were obtained as a result of differences in psychological state. The complexities of the task may be too much for the patient. He may be less cooperative or less attentive. He may be concerned with his troubles, may be listening to his hallucinations, and may care very little about this apparently meaningless task we put before him. Paradoxically we may often obtain meaningless results because the patient is too motivated, too anxious, and too concerned with the results of his performance and as we all know a very high degree of anxiety and motivation often lead to poor performance as well. We had found that for these and perhaps other reasons the nature of the tasks that we present to the patient must be extremely simple. While there are a few occasional patients who can learn to give reliable data in highly complex and difficult discriminations, the majority of hospitalized patients perform at chance levels in this type of task.

We have, however, been successful in developing or utilizing five strategies for coping with the problem presented by the difficulty of testing patients and obtaining what we feel are valid indicators of the central nervous system differences between certain groups of patients and normals despite the hazards described above.
STRATEGY 1.

Simplicity of the task

We have almost always used reaction time, and simple reaction time at that, to measure differences in performance of patients to different kinds of stimuli. In other words we may present in a particular experimental design five different stimuli in random order successively, but the subject need make no conscious discrimination among the stimuli. Whichever stimulus occurs, all the subject has to do is lift his finger as rapidly as possible. The rationale which is well established in the psychophysical literature and confirmed in our laboratory is that different stimuli (although between them no conscious discrimination is required) will give different reaction times. For example, we might present in different trials either a stimulus package which consists of a 25 dB click by itself or a stimulus package which consists of a 25 dB click followed 15 msecs later by a 10 dB click. If the reaction time to these two stimulus packages is different, e.g., if the reaction time to the double click is faster than the reaction time to the single click above, then we have direct evidence that the central nervous system was capable of appreciating the difference between these two stimulus packages.

Of course the reaction time of schizophrenic patients and to some extent of most hospitalized psychotic patients is much slower than
normals to all stimuli. But this brings into play our second strategy.

**STRATEGY 2.**

*Own control design*

While statisticians have often been quite irritated at our reluctance to use classical analysis of variance designs in which different individuals are used in each cell of the analysis of variance matrix, we have always argued that this is not a feasible or desirable strategy in comparing mental patients with normal performance. It is well known that the variability among psychotic patients is quite high. This arises presumably both from the nature of specific illnesses, the nature of the hospital setting, and perhaps the fact that the different patients are suffering from different illnesses although we may with our current limited knowledge be classifying them as being in the same group. I will return to this problem from another point of view later in my talk.

It, therefore, becomes an exercise in futility to have different groups of subjects for each experimental condition. Rather for both patients and normals we test each subject on all conditions which we want to compare. Of course, we use care to randomize our experimental conditions so that subjects cannot with any ease assume different attitudes to given experimental conditions, e.g., the attitude "this is a challenging condition I will try harder" or "this is a very difficult condition, I give up on this one" or "this is an easy condition, I don't have to try so hard" and so on. We, therefore, use the difference
among experimental conditions as the measure or measures representing each subject. Sometimes we have used, rather than raw differences, covariance analyses or still other strategies proposed by Dr. Fleiss, our statistician. We are aware, of course, that such strategies do not unequivocally cope with the fact of level differences between groups of subjects such as differences in speed of reaction time between patients and normals, or in another form of the same problem it does not really cope with the problem of initial value where we know that one performance is close to an optimum there is less room for it to change than when a performance is in the middle of a given range. We have nevertheless used with some success the own control design. We continue to be aware that a number of converging operations are necessary to unequivocally prove any case. For example, difficult as this may be, it is desirable to find some patients who perform in the reaction time range of the normals to see whether our findings hold for them as well.

Our major finding within the context of applying primarily the own control design has been the fact that schizophrenic patients have longer reaction times than normals when the immediately preceding trial is in a different sensory modality than when the immediately preceding trial is in the same sensory modality. The patients appear to be disproportionately retarded by a shift of sensory modality in sequential trials. Even though the stimulus of the previous trials occurs several seconds before. In a critical
control experiment, we have been able to eliminate the possibility that this difference arises from a difference in bias or expectancy on the part of the patients. We were able to show that a greater crossmodal retardation is found in patients than in normals even when the subject is told prior to each trial what the sensory modality of the stimulus would be.

STRATEGY 3.

Controlling the criterion variable

I will touch on this strategy only lightly because we have not made any direct use of it in our laboratories. It is based on the fact that signal detection theorists have been able to demonstrate that they can obtain two independent measures in threshold situations, one is called $d'$ which is the measure of sensitivity and the other, which is called beta, which is a measure of criterion. The basic advance consists of the fact that it can be demonstrated both logically and experimentally than these two measures can be obtained independently of each other. This is an important step forward since one of the important sources of attitudinal differences between patients and normals is the relative degree of cautiousness that these different groups may exhibit with respect to saying "yes, they see a difference" at a particular difficult threshold level of stimulus presentation. Patients even when performing well do tend to be more cautious than normals. They want to see a clear change before they are willing to say "yes, it is indeed different."
It turns out that it is indeed this cautiousness which accounts for the earlier reports that schizophrenic patients had a lower critical flicker fusion frequency. What Clark, Brown and Rutschmann have in fact shown is that rather than being deficient in sensitivity, they require a slower rate of alternation between light and darkness before they are willing to say that the stimulus is flickering—they are simply more cautious. They want to see a clear flicker before they are willing to say that the light is flickering. By classical psychophysical methods such a bias yields an apparently lower sensitivity. In fact, when measures of sensitivity are obtained which are for one reason or another independent of the criterion variable, it turns out there is no difference in sensitivity to the rate at which light and darkness must alternate before flicker is detected. It has all been a reflection of the degree of cautiousness on the part of the patients! This classical paper by Clark, Brown and Rutschmann has cut the underpinnings from a great deal of research comparing the sensitivity of patients and normals which were done by classical psychophysical techniques. It is not that we know at this time that there are no differences in sensitivity on these many variables that have been measured, but rather that we don't know whether those differences which have been reported are due in fact to differences in sensitivity, or whether they are differences in the degree of cautiousness. If the performance depends on cautiousness, it does not add anything new to our knowledge.
STRATEGY 4.

Accuracy indicators

In the detection theory method a stimulus let us say at close to absolute threshold is either presented or not presented in any given trial and the subject in each trial must say either "yes, there was a stimulus," or "no, there was not a stimulus." Thus, his overall rate of saying "yes," whether or not a stimulus was present, gives us a measure of his willingness to say "yes," in other words a measure of his criterion; whereas the proportion of saying "yes" when a stimulus was actually presented so that the response was correct or a 'hit' when related to his proportion of saying "yes" when a stimulus was not presented, so that the response was in error or a 'false alarm', gives us a measure of sensitivity (ratio of proportion of hits to false alarms) which is independent of criterion. This method clearly has accuracy indicators since we know how to weigh the subject saying was presented because we know of his readiness to say "yes," when a stimulus "yes" when a stimulus is not presented. If he says yes equally frequently regardless of whether the stimulus is present or absent, we conclude that he is merely guessing, as the proportion of yes to the presence of the stimulus increases and the proportion of yes to the absence of the stimulus declines correspondingly, we can conclude that his detection of the presence of the stimulus is increasing. Of course, the complementary case is also true, we know the meaningfulness of his saying "no" when a stimulus is not presented by knowing the rate at which he says "no" when a stimulus is presented.
Another technique which has the advantage of eliminating from consideration the criterion is the three interval forced-choice method.

Instead presenting the subject with the choice of saying yes or no for the presence or absence of the stimulus, the forced choice method presents three successive intervals which two of the stimuli are alike and the third is different.

The three interval forced-choice method has the additional advantage of having an accuracy indicator. In the
typical forced-choice method there are three observation intervals and the target stimulus, or the stimulus which is different, is presented in only one of the three intervals. The subject must always pick the odd stimulus in one of the three intervals. We know the meaning of his correct choices by being able to weigh them against his willingness to pick intervals in which the stimulus is not presented. Thus if he picks the target stimulus only as frequently as the non-targeted, we can conclude that his choice is a chance guess. In this situation, furthermore, the criterion is eliminated by the fact that the subject must in effect always say "yes." since he must always pick one of the three intervals, and there is no way in which the subject can exercise a desire to be more or less cautious.

By using a three interval temporal forced-choice method as just described we were able to demonstrate that hospitalized mental patients in general have lower absolute thresholds than normal subjects for auditory clicks. While this difference between patients and normals was only of the order of 4 decibels, when we subsequently separated the patients by diagnostic classification it turns out that particularly one group of patients, those who are called moody-disorganized — that is they show both symptoms of depression and symptoms of conceptual disorganization, have an average of 9 db lower threshold than normals.
STRATEGY 5.

Better patient performance

While the use of forced-choice methodology controls the criterion problem very well and also gives us a safeguard against falsely attributing to patients a better performance than they can actually accomplish, it does not solve our fundamental problem. One can argue very persuasively that the patients who had poorer thresholds than normals were simply less attentive or less motivated than normals and, therefore, they made more errors in their forced-choice. Presumably according to this argument, had the patients been in a state which had permitted them to be fully attentive and cooperative they might have obtained just as good thresholds as the normals. There is only one satisfactory antidote to this argument and this would arise if we could demonstrate a particular task in which patients were able to perform better than normals. If this performance is better than that of normals, it is not possible to attribute this better performance to poorer attention and cooperation on the part of patients. We have so far obtained two instances of better performance on the part of patients.

In the auditory version we presented randomly either a click which was 25 decibels above each subject's absolute threshold followed
15 milliseconds later by a click which was 10 decibels above the subject's absolute threshold, of the more intense click, the 25 decibel click, by itself. Subjects were to lift their finger from a key as rapidly as possible to the presentation of either stimulus package. We found that for normals the average reaction time to the paired clicks, the 25 followed by the 10, was only very slightly better and faster than the average reaction time to the 25 db click by itself. However, for the patient group as a whole, and particularly for the moody-disorganized patients described above, there was a much larger improvement in reaction time for the paired clicks than for the single intense click presented by itself. Here then we have evidence that the patients are benefitting more from the presence of the 10 db click than were the normals. The moody disorganized patients are in this sense more "sensitive" to the presence of that 10 db click and in that sense performing better.

Perhaps the visual version of this experiment is an even more convincing case of better performance. There were two 2-millisecond flashes of light, which in one stimulus package were separated by 2 milliseconds and in another stimulus package were separated by 0 milliseconds -- in effect in the second case it was a 4 msec flash of light. Note that here the two stimulus packages have the same
total amount of light energy, however, in the one case the light energy is distributed over 4 msec and the other case the same amount of light energy is distributed over 6 msec. As is known from the Bunsen-Boscope law, if the stimulus duration lies within the critical duration period, then the response will be identical to these two packages of light because when stimuli are within the critical duration period, the total energy determines the level of response since none of the energy gets lost. If, however, one of the stimulus packages exceeds critical duration, some of the energy gets lost, and the response to the two light equal energy packages would be different.

These two stimulus packages were presented at random and subjects were instructed to lift their finger as rapidly as possible whenever stimulus package appeared. For all our normals — we do not yet have comparable studies for patients — these two packages are perceptually identical. Normal subjects cannot by any means distinguish between a given package of light which is distributed over either 4 msec or 6 msecs. Similarly in their reaction time response, normals show absolutely no difference in reaction time between these two packages of light. However, schizophrenic patients do have significantly longer reaction time —-----------------------------
than to the 6 msec package of light to the 4 msec package of light.

From this we infer that for schizophrenics, critical duration is shorter than 6 milliseconds, therefore, they are not able to utilize the total energy when it is distributed over 6 msec to generate their reaction time response, and, since some of the energy gets lost, their reaction time is longer for the 6 msec package than for the 4 millisecond package.

What do we mean when we say that the schizophrenics are performing better than normals? What we mean in the visual version is that they can make a discrimination albeit by the speed of their motor response, that normals cannot make by any kind of response whatsoever. If you like, the schizophrenics are more sensitive to the way light is distributed over time than normals are. This is true even though the overall level of reaction of the schizophrenic patients for both light packages is longer than the reaction time of the normals. In further experiments with normals we found that even with procedures that produce a lengthening of their reaction time, we were unable to get them to produce differences in speed of reaction time to the 6 millisecond package of light as opposed to the 4 millisecond package of light. It should be noted, however, that what we have done here is taken advantage of a kind of fluke. It is fairly likely that the visual
system particularly at close to threshold intensities is built to integrate energy over time. One can easily imagine that this in an evolutionary way would be an advantage to an organism that must detect the presence of enemies in relative darkness. A given amount of light reflected from an object which is at a greater distance and, therefore, dimmer than the same amount of light from a near object, may nevertheless be detected equally. Since energy is integrated temporally, this increases the possibility that a longer look at the distant dimmer stimulus would permit its detection to the same degree as a nearer stimulus which may appear brighter. By looking longer at the distant dimmer object, compensation for its dimness occurs as long as the temporal factor is below critical duration. Furthermore, its distance permits the longer look necessary for detection before the predator approaches. Organisms whose critical duration was too short must have fallen prey to their predators and thus did not survive. Schizophrenic patients presumably because of some defect in their nervous system are not as able to integrate energy over time for as long a period as normals. We have taken advantage of this by creating a design where that very inability results in their demonstrating a discrimination that normals cannot make.

**Strategy 6.**

*Iterative procedures*

All the above five strategies are addressed to the design of the psychophysical tasks that the subjects are performing. However, we are faced with at least as serious a problem in defining the nature of the independent variable, namely the group to which the subject belongs. We can, of course, be arbitrary about this and call normal any one who is recruited applicants to the United States Employment Service or from a university, and a patient any one who is in a mental hospital, but some years ago when we applied scaled mental interview results
a more objective description of all subjects we found that as many as half of our "normals" did not clear as normal on our rating scales and similarly about half of our patients who had been diagnosed as schizophrenic by two different psychiatrists at two different hospitals did not clear as schizophrenic on our rating scales. When we limited our samples to the schizophrenics and to the normals who were assessed as such by the rating scale we found that the experimentally determined retardation or reaction time was both larger and less variable. It is clear that, for proper evaluation of differences on objective measures, we require better classification of our subjects.

We do not in fact know in advance which group of patients will have lower or higher absolute thresholds. We do not know in advance which group of patients will have shorter or longer critical durations. Nor do we know in advance which group of patients will show greater retardation due to shift of sensory modality. We admit that we very often develop rather ingenious hypotheses to cover up our ignorance, but we think it is better to make a clean breast of it and to say in advance that we are ignorant. Given that confession, and given the fact that we apply the same set of structured interview rating scales to all subjects, what we can do after the results are in
is to see in fact which group of patients it is that differs in what way from normals. Now, I know that here we are violating the rules of statistical inference in which the hypothesis must be made in advance and that, therefore, our conclusions become much more tentative, but the gain justifies this loss in power. What we must do when taking this approach is to treat our rather formal experiments as pilot experiments and say "yes" we did obtain a statistically significant difference between group X and group Y, but because we defined our group post hoc this cannot be taken as valid statistical inference. The experiment must be replicated, this time with the finding of the previous experiment now used as a hypothesis which is made in advance before the result can be taken seriously. Furthermore, we gain even greater power in our inferences from subsequent replications, if for some of these replications, we define our groups not on the basis of their rating scale performance, but on the basis of a particular kind of performance on our psychophysical measure. Here we are interchanging our independent and dependent variables and saying that our hypothesis is that the individuals who perform a particular way on our psychophysical measure will turn out to be a particular kind of patient. In still further construct validating operations we can make efforts to find out what other properties this particular
group of patients has, for example, if they have lower auditory absolute thresholds, do they also have lower visual absolute thresholds. Are they, or are they not the same patients who have shorter critical durations? Furthermore, we can make similar inroads into our rating scale categories. We have an arbitrary definition of the moody-disorganized group. We already have some evidence that the definition of moody should not include because this scale does not help in differentiating the moody-the anxiety scale. We don't know the relative merits of the various scales which are grouped under the concept of disorganization. In the case of the critical duration findings they were strongest in schizophrenic patients who showed evidence of thought disorder. This impels us to attempt to further refine our definition of thought disorder, perhaps even to develop a more objective measure of thought disorder which is not dependent on subjective scaling.

After clustering the patients into subgroups in accordance with their performance on laboratory tests and interview status, we could proceed to see whether the members of each of the subgroups have in common such characteristics as response to specific treatments, duration of hospitalization and type of outcome on follow-up. These
could validate the groupings or break them up into further subgroups.

What I have described, therefore, to you is the history of our continuing effort. Our ultimate objective is to be able with some precision to define various subgroups of patients cross-culturally and define them in such a way that we can have some indication which ones are suffering and which are not suffering from some kind of central nervous system insult and perhaps what kind of central nervous system insult it is. At this point we could go the biochemist and ask him what else can he tell us about the specific subgroups of patients which we have found. We should also note that it is at this point that our physiological measures such as our evoked potentials can become even more powerful. We can now look not only at evoked potentials to standard stimuli for different groups of patients which have been rigorously defined by psychophysical methods, but we can even go ahead and look at the potentials evoked by the very stimuli which utilized for determining the subgroups into which our patients fall. Thus we can examine the evoked potentials which characterizes our patients while they exhibit short critical duration to see if the evoked potential also differentiate them from their fellows with longer critical durations. In other words, we can examine the evoked potential concomitants of the other psychophysiological behaviors which differentiate the subgroups.
III Significance of neurophysiological findings.

The differences in information processing between schizophrenics and other mental patients and normals present us with an interesting paradox. The behaviors which bring the schizophrenic to attention are gross behavioral deviations whose connection with the subtle laboratory findings such as critical duration for energy integration, higher auditory thresholds, cross-modality retardation in reaction time, generally slower reaction time, and smaller amplitudes in the evoked potential, are at best difficult to trace. What possible connection might exist between our findings and the schizophrenic disorders?

The total disorder is so encrusted with so much varying life experience that it defies analysis; all one can do is describe it. We have had 22 centuries of such descriptions, dating back to the Hindu Ayure-Veda, The Caraka Samhita (1949), but understanding still eludes us. By dealing with behavior that is relatively free of prior experience and cultural influence, as we do when we limit ourselves to these brief laboratory tasks, we are attempting to obtain differentials between schizophrenics and normals that reflect a basic substrate of brain functioning in the processing of information.

If the difference between schizophrenia and normality can be demonstrated to begin at the information-processing level, for example,
we may be able eventually to understand why the world looks so
different to the schizophrenic, and yet demonstrate that his behavior
is consistent and predictable though systematically deviant from
normal expectancy in some basic substrate. Such differences may
yield the culture-free indicators we so desperately need when
studying subcultural groups or when making cross-cultural comparisons.
By depending on interviewing methods or clinical tests alone, or
on techniques highly dependent on prior reinforcement history, such
as perceptual constancy or higher mental functions, we cannot
escape the cultural bias inherent in such techniques. It is hoped
that culture-free indicators may help us detect deviations that
would be either falsely occluded or spuriously introduced when culture
dependent techniques are used.

Perhaps these simple differences which differentiate the
schizophrenic -- his inability to shift as readily, his shorter
critical duration, his lower amplitudes in evoked potentials and
the different patterns produced psychomotorically as contrasted
with perception under the influence of uncertainty, reward, punish-
ment, etc. -- constitute the real building blocks of schizophrenia.
He begins to feel different and appears to his friends to be
different because of the small discrepancies in his behavior. Once
these differences become recognized by him and by his peers, the
rest of schizophrenia begins to develop. In other words, schizophrenia is "caused" by these small losses of pain in the game of life — the rest of schizophrenia is merely an epiphenomenon. We realize that this is a highly controversial point of view, but this is what we have come to believe is a possible, though not yet probable, explanation of some types of schizophrenia. In short — schizophrenia occurs in a vulnerable individual when subjected to sufficient stressors — and his vulnerability may be detectable in the differential patterns of his central nervous system.