Thought Disorder in Schizophrenia: Cognitive and Neuroscience Approaches

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Abstract

Research with schizophrenics is reviewed in the areas of the startle reflex, subject-initiated evoked potentials, and two-stimulus evoked potentials. A hypothesis of an early (pre-100 ms) information-processing deficit is posited and further refined by results presented from brain evoked potentials during a backward-masking experiment. The implications of these findings for the speech component of schizophrenic thought disorder are speculated upon, with specific reference to failures of temporal sequencing control that may underlie schizophrenic speech dysfunction and may be attributable to defective thalamic control. Recent neuroanatomical findings of abnormalities in the hippocampus and thalamus of schizophrenics are presented, and considered as likely contributors to the early information-processing deficits posited.

A defect may exist in the early (less than 100 ms) information-processing ability of schizophrenics. This hypothesis, we believe, is supported by preliminary findings (reported below) from our work with topographical mapping of the brain electrical activity observed during a backward-masking experiment with schizophrenics and controls. Further support for this hypothesis may be found in paradigms that have explored the startle reflex, subject-initiated evoked potentials, and two-stimulus evoked potentials in schizophrenics. This hypothesized defect may constitute a fundamental element in schizophrenic thought disorder when viewed from the perspective of current models of information processing. It may explain certain aspects of dysfunctional speech in schizophrenics.

Johnson (1985) has advanced a hypothesis of an early information-processing defect in schizophrenia. While our hypothesis is similar, it is elaborated somewhat by inclusion of brain potentials in backward masking and by consideration of recent neuroanatomical and electrophysiological findings which allow hypotheses to be formulated concerning the brain mechanisms that may underlie the early information-processing defect.

A formal theoretical framework for information processing (from the psychological or cognitive science perspective) dates back to Broadbent (1958). In simplistic terms, this theoretical framework views information processing in the brain as taking place in a series of somewhat discrete stages. An initial sensory store (sometimes called the “icon” store or “iconic” image) is posited to last at most a second and, more likely, a few hundred milliseconds. This stage is believed to have a vast storage capacity but very limited duration. A subset of this information is thought to be extracted from the sensory store, transformed into a short-term memory store, and relayed through a central processing stage at which point decisions are made about the degree of further processing needed for the new information. The central processing stage is believed to be the point at which resource allocation is made toward further information processing. One of the resources available through the hypothetical central processor is the lexicon or language faculty. Up to this point we are describing mostly the “input” stage of information processing. The “output” stage in information-processing theory is...
usually referred to as “response organization” and is conceptualized to follow decisions as to the category membership of the information and the response requirements pertinent to it. It is implicitly assumed that the response requirement (which may reflect the current “state” of the organism) feeds forward in time to determine which features will be extracted from the next sensory store. Thus, a dynamic and on-going information processing system is in perpetual operation, sensitive to and interactive with the needs of the organism and changes in the environment.

This account of information-processing theory is highly oversimplified, and the concept of an “iconic” stage has been strongly criticized as unnecessary by Haber (1983), although this view is clearly not shared by some other investigators in their commentary on Haber (1983). It is both impractical and unnecessary for our purposes, in this article, to delve further into this controversy, but it is worthwhile to note that Broadbent’s (1984) reformulation of his earlier outlook still includes the construct of a sensory store which possesses many of the attributes ascribed to the “icon” above. Perhaps the most important conceptualization which we would like to adduce is that information may be processed in brains (in the cognitive sense) by a process of changing one form of representational code into another form of representational code. In all likelihood, the processes whereby the code is represented are different from the processes whereby the code is changed from one form to another (see Broadbent 1984, for further discussion of this point).

For many years the language and concepts of information-processing theory have been used to “dissect” the cognitive abilities of schizophrenics, and the process continues with some controversy. Thus, deficits have been posited at the level of the sensory store or the speed/efficiency of feature extraction from it (Saccuzzo, Hirt, and Spencer 1974; Braff, Callaway, and Naylor 1977; Saccuzzo and Schubert 1981; Braff and Saccuzzo 1985). Other theorists have attributed schizophrenic information-processing deficits to slowed central processing (Yates 1966; Yates and Korboot 1970) or to failures in response organization (Hemsley and Richardson 1980). It is, of course, perfectly possible that defects in schizophrenic information processing may be manifest at each of these stages, but from our point of view, the intactness or otherwise of the earliest stages must be fully ascertained, because defects at this point may well also account for later (e.g., response organization) deficits. This proposal is justified in that information-processing theory posits to some considerable extent a “serial” process. It is therefore a logical corollary of this theoretical framework that an inadequately constituted sensory code or feature extraction from it will result in a short-term memory (or working memory—Broadbent 1984) that is an inadequate representational code of the stimulus events and their potential significance or response organization demands.

Adler et al. (1982) and Freedman et al. (1983) have reported data which indicate that when two auditory (click) stimuli are presented with an interstimulus interval (ISI) varying from 500 ms to 2 seconds, the response of normal subjects is to attenuate the P酢 component of the evoked potential (EP) to the second stimulus. The amount of attenuation varies from 90 percent at 500 ms (ISI) to 30-50 percent at 2 seconds (ISI). Schizophrenics, on the other hand, do not attenuate the P酢 component by more than 15 percent at 500 ms (ISI) and may even show an increased amplitude to the second stimulus at 2 seconds (ISI). The authors of these reports have argued strongly for an interpretation that involves defective input or “gating” control of structures which should selectively attenuate input to the cortex. However, these data may also speak to the concept of defective control of temporal sequencing and integration in the brains of schizophrenics. If we posit (as do Adler et al. 1982, and Freedman et al. 1983) that the attenuation of aspects of brain response to secondary input following a primary event is a “normal” function in the processing of information, then one possible implication of such a formulation is that the brain structures which control such events are acting like the absolute and relative refractory periods which follow the discharge of single neuronal cells. The further implication is that in schizophrenics, failures in inhibitory processes which allow for such refractoriness are implicated in early information processing. If we restate the argument in terms of its consequences for schizophrenia, we can hypothesize a situation in which the processing of a primary event is “overwritten” by a secondary input because of a failure to attenuate the strength of the afferent volley generated by the second event.

Such a formulation has important implications for hypotheses concerning the malfunction of early “preattentive” store in schizophrenia. It suggests that the actual formation of the sensory store could be defective apart from additional malfunctions in feature extraction from it. In short, the data of Adler...
et al. and Freedman et al. mentioned above could indicate some malfunction in the "time constant" with which information is handled by the schizophrenic brain. This conceptualization is also consistent with previous work by Shagass (1976) and Shagass et al. (1979), who observed enlarged early components of EPs in schizophrenics to be followed by diminished later components. A plausible explanation offered by these investigators is that inadequate attenuative processing is occurring in the early handling of information in the schizophrenic brain and that this stage is followed by an active inhibitory process on the part of the patient to reduce the consequences of this early failure. However, as the later components of the EP are indicative of higher order categorical decision process and response organization stages, then it is highly likely that the schizophrenic is sacrificing the richness of later stage information processing in an attempt to compensate for early registrative malfunction.

The startle reflex, which has been studied in both human and nonhuman species, is also of relevance to our discussion for two reasons. First, it is organized at a level below the cortex and involves the lateral tegmental area of the midbrain reticular formation (Leitner et al. 1981) and, more particularly, the nucleus reticularis pontis caudalis (Leitner, Powers, and Hoffman 1980). Second, it displays modification by a weak "leading" stimulus which precedes the startle-evoking stimulus (Graham 1975; Hoffman and Ison 1980). The leading stimulus is most effective in reducing the startle response in human subjects if it precedes the startle-producing stimulus by about 100 ms.

This reduction, however, is not so great in schizophrenics as in controls (Braff et al. 1978) and, as such, may reflect temporal sequencing failure in schizophrenics, as hypothesized above, but involving in this instance primarily lower brain structures. The implications for schizophrenia are that available information cannot be temporally organized to protect the schizophrenic from the startling effects of subsequent stimulus events.

There is a short time constant information processing system acting up to 240 ms intervals which is associated with blink amplitude inhibition and latency facilitation. This system is thought to serve a preattentive filtering function by allowing rapid information processing. Since blink (and startle) reactions are inhibited by antecedent stimulation, they are less distracting and more quickly elicited (latency facilitation), allowing for rapid processing of stimuli. The deficit we see in schizophrenics is consistent with a dysfunction in this early protective mechanism which would correlate with information overload and subsequent cognitive disruption in schizophrenia. Braff et al. (1977) have described "over-reactivity" with cortical evoked potentials in similarly brief interstimulus intervals. The two findings are syntonie: when perceptual filters are impaired, as indexed by either blink reflexes or evoked potentials, there is a tendency to be flooded by environmental cues. [Braff et al. 1978, p. 343]

The EP findings of Braff, Callaway, and Naylor (1977) are also of importance to our discussion. Schafer and Marcus (1973) demonstrated that normal subjects showed a reduction of EP amplitude when they were allowed to initiate the onset of the EP stimulus themselves. This reduction in amplitude still held with delays of up to 4 seconds between subject initiation of the stimulus and its occurrence. Braff, Callaway, and Naylor (1977) showed that the amplitude reduction effect was less adequately displayed by schizophrenics with short delays of 250 ms. Again, these data indicate that short time constant information handling is defective in schizophrenics, who appear to need a longer interval to organize accommodations to the strength of incoming information.

Data from the startle reflex and self-stimulation EP paradigm cited above have been combined with the work of Adler et al. (1982) and Freedman et al. (1983) in a most thought-provoking paper by Johnson (1985). It is Johnson's conclusion that there is an overactivation of sensory input in schizophrenia which is directly due to the failure of an inhibitory mechanism, some of the attributes of which he described as follows:

it is proposed that a mechanism exists which will respond with inhibition to any small change in stimulus intensity, the amount of inhibition corresponding to the amount of change. The inhibition begins within 100 ms of the change and continues for more than two seconds. It attenuates arousal created by external stimulation during this time, at an early or low level in the brain, before the activity has been relayed to higher neural systems. [Johnson 1985, p. 432]

Much of the data mentioned above might be accounted for in some fashion a primary stimulus fails to "engage the attention" of the schizophrenic. Thus, the leading stimulus in the startle paradigm carries rapidly processable data (to the normal brain) that a startling event will take place. We suggest that in the schizophrenic brain the significance of the primary stimulus is either lost or the information it conveys cannot be used in time to
mobilize adequate defenses. In Schneider and Shiffrin's (1977) formulation, this may indicate that an "automatic" (i.e., fast and involving minimal cognitive effort) information-processing system is available to the normal subjects but not available to the schizophrenics, who must rely on a slower and more cognitively effortful "controlled" information processing. In short, the primary stimulus event engages some form of attentional process in normals but fails to do so in schizophrenics.

Such a conceptualization might also be applied to the Adler et al. (1982) and Freedman et al. (1983) paradigms with the following results: If the first stimulus engages (in an "automatic" manner) the attention of the normals, then the attenuation of the P50 EP component to the second stimulus event may indicate a protective inhibition that will ensure adequate processing of the primary event. In the schizophrenics, however, if the attentional engagement did not take place, then there would be no need for an attenuation of the EP events associated with the second stimulus, leading to the observed results.

A subtle but perhaps important question raised by these studies is the distinction between the early engagement of attentional processes (and therefore the speed and accuracy with which the early sensory store is formed and information extracted from it) versus the vulnerability of the early sensory store to disruption and distortion by subsequent stimulus events. To examine this question, we have measured the EPs associated with performance on a backward-masking task. The backward-masking paradigm by which a brief stimulus event is presented to a subject (and its afterimage obliterated) has consistently shown a schizophrenic deficit (Saccuzzo, Hirt, and Spencer 1974; Braff, Callaway, and Naylor 1977; Saccuzzo and Schubert 1981; Braff and Saccuzzo 1985).

In our adaptation of this paradigm, a fixed stimulus exposure duration (of nine letters in a rectangular 3 x 3 array) is followed by a noise mask, and a partial report (of the middle line) is required from the subject. As the EP is measured throughout, we can observe the brain electrical events temporally concurrent with both the target stimulus and the masking stimulus. The brain electrical response to the target stimulus should therefore index some aspects of the early engagement of attentional processes when the subject is placed under an information-processing load. The EP events following the onset of the masking stimulus should indicate something of the brain events associated with the vulnerability of the early sensory store to disruption. To elaborate more fully on this reasoning: If the brain electrical activity were identical (in schizophrenics and controls) during the appearance of the target stimulus, then we would conclude that the early attentional engagement did not differ between the groups. We would then hypothesize that the masking stimulus produced a differential effect and would expect to see this reflected in differential brain electrical activity following the masking stimulus. If, on the other hand, a difference in brain electrical activity were observed between schizophrenics and controls during the target stimulus (and before the mask appeared), then we would conclude that the engagement of attentional processes was different between the groups even at this early stage. If this latter result were found along with a similar brain response to the mask in both schizophrenics and controls, then we would conclude that the deficits behaviorally observed in schizophrenics (in this task) might have been due to a failure of the target stimulus to engage the attentional processes of schizophrenics fully and that their performance deficit was not due to excessive vulnerability of their early sensory store to destruction by a secondary event (a mask in this case).

Methods

Subjects. All experimental subjects have been recruited and diagnosed (by Research Diagnostic Criteria) using identical instruments and personnel as reported in this issue by Spohn et al. (in fact, a number of the subjects are common to both studies). The reader is referred to that article for a more exhaustive description. Briefly, 19 schizophrenics (5 unmedicated and 14 medicated), 15 patient controls (4 unmedicated and 11 medicated) with the Research Diagnostic Criteria diagnosis of bipolar illness or schizophrenia, or schizoaffective disorder were compared with 31 normal controls. All groups were equated as far as possible for age (in the 18- to 55-year range) and all were male. All subjects consented to participation after full disclosure of the protocol. The patient control group allows for exploration of the specificity of findings to schizophrenia.

Backward Masking. Full technical details of our computer-controlled methodology will be reported elsewhere. Briefly, as shown diagrammatically in figure 1: A target 3 x 3 array of letters was presented (within 4 degrees visual angle) to both eyes. This stimulus followed a dim fixation point, which disappeared 1 second
Figure 1. Schematic representation of stimuli and timing for a backward-masking paradigm, incorporating measurement of both high and low frequency evoked potentials

before presentation. The letters of the array were easily readable and composed of dots, computer generated, and displayed on a fast-decay-phosphor oscilloscope screen. The entire 3 x 3 array can be created on the screen in less than 1 ms. Stimulus duration was a fixed 150 ms. The screen was blank for a further 100 ms, allowing a total stimulus availability of 250 ms including afterimage. A masking stimulus composed of exactly the same number of dots then appeared for 10 ms. The dots occupied the same block space as the letters on the screen and appeared as a 3 x 3 array of small masks. Thus, the perceived brightness of the mask was identical to that of the 3 x 3 array of letters, being composed of the same number of elements (dots) with the same brightness (Z axis gain) but rearranged into a meaningless “noise” array within the same area occupied previously by a letter. The 10 ms mask produced a 95–99 percent correct detection rate in normal subjects.

Increasing the mask duration to 15 ms produced a decrement in normals to about 70 percent correct detection, as revealed by pilot experimentation. The 10 ms mask duration was selected to allow normal subjects to perform close to ceiling scores. Subjects gave a partial report and were trained (before EP recording) to report only the middle line and never any other letters were arranged for each presentation according to a computer-controlled random sequence generator. The experiment required 50 artifact-free trials under each of two conditions (on separate days). In the first condition, the subject performed as described above, in the second, a small set of horizontally oriented chevrons “>” appeared at the outer edges of the center line. These chevrons constituted a form of postmask probe and appeared (dim but clearly visible) 300 ms following the offset of the mask.

When the probe was used, it remained visible until the experimenter reoriented the subject that a new trial would begin in about 10 seconds at which time it would disappear to be followed by the fixation spot at the beginning of a new trial. Intertrial interval was variable from 45–65 seconds as the experimenter waited until the subject was correctly head inclined (monitored by closed-circuit video) and the on-line electroencephalogram (EEG) monitor showed no artifacts and no eye movement. Each individual trial was repeated (but the letters changed) if it produced a computer-detected brain wave artifact. The subjects sat in a reclined (but not recumbent) position in a dimly lit room, which was quiet but not acoustically isolated.

Brain Wave Recording. The EEG was recorded from the full 10/20 system referenced to linked ears and with eye movement detection set at a very high gain. The latter is necessary to detect blinks and more subtle eye movements, and to reject any trial in which they occur. As this paradigm involves detection and report of letter strings, there is a danger that eye movements may cause distortion of later components of the EP. Stringent precautions were taken to avoid this. The 20 channels (19 of the 10/20 system plus eye movements) were recorded with a bandwidth of 0–10 kHz, and the 20 channels were then filtered into two separate outputs from each channel. Data reported here are from the low frequency bandwidth (.5–40 Hz-3 dB points). Data recording began 100 ms prestimulus and continued 900 ms poststimulus (for a total of 1000 ms). In addition, a high frequency bandwidth was recorded (300–3 kHz-3 dB points), beginning 10 ms prestimulus and continuing for 35 ms.
into the 3 X 3 array. Recording then terminated in this bandwidth and began again (for 35 ms) at the onset of the mask and again (for 35 ms) at the onset of the postmask probe or at exactly the same time point if the probe was not used. The low frequency channels were digitized at 400 Hz/channel, and the high frequency channels were digitized at 20,000 Hz/channel. All channels were recorded in pure parallel with a separate analog-to-digital converter on each. The low frequency and high frequency data streams were interleaved after digitation and relayed by direct memory access to the core memory of a PDP 11/34 computer (Digital Equipment Corporation). When low frequency and high frequency were recorded together, the total data input speed was 400,000 samples/second. These methods are highly technically demanding. High frequency data from this experiment will be reported elsewhere.

Data Reduction. Each trial was stringently checked by on-line computer for artifact. The artifact rejection was exceptionally conservative, and overvoltage detection on any one channel rejected the entire trial. The summed EPs for all channels and the sums of squares for each channel (trial by trial) were computed on line and the data stored on disk. The sums of squares data will not be reported here. The summed EPs (for each subject) were graphically displayed and checked visually for any possible artifacts. Data from normal subjects, schizophrenics, and patient controls were separately summed to produce grand mean profiles and also subjected to t-test statistical probability mapping (SPM) as recommended by Duffy, Barrels, and Burchfield (1981). The SPM maps are the only analyses presented here. In the future, we shall be reporting results acquired by multivariate approaches.

Results

The postmask probe stimulus did not produce any within-subject changes in the EP waveforms (or in correct responses). This finding is of interest and will be discussed below. The backward-masking paradigm produced a difference in performance range in the groups. Normals performed in the range of 95–99 percent correct responses, schizophrenics performed in the range of 50–70 percent correct responses, and, on the basis of preliminary analyses, patient control subjects performed at 55–90 percent correct responses. We may therefore tentatively conclude that the backward-masking paradigm differentiates schizophrenics from normals but not necessarily from patient controls, and that the postmask probe does not affect the EP waveform on a within-subject basis.

The most interesting finding is that the schizophrenics are differentiated from normal by an EP epoch which extends from approximately 80 ms to about 103 ms poststimulus. Figure 2 shows the grand mean EP waveforms for schizophrenics and normals, and figure 3 shows the SPM of comparison of brain topography of both groups at the 95 ms poststimulus point, where the differences are maximal between the schizophrenics and normals. (Figures 2 and 3 are redrawn by hand from color graphic computer topographical maps.) No other epoch of the EP waveform shows reliable differences between schizophrenics and normals. In addition, the schizophrenics depart from the patient control sample at 80–100 ms in the same way that they depart from normals. The patient control sample did not differ from normals at this epoch or at other times in the EP waveform.

The foregoing results presentation is both partial and brief as befits reports from work in progress. The conclusions drawn must therefore be highly tentative, and may change with the addition of more subjects and more rigorous (multivariate) analysis. If this reservation is held firmly in mind, the following comments may be in order.

The addition of the postmask probe was incorporated to test, in a simple manner, the possibility that a small low-information-carrying event might differentially alter the backward-masking performance (or the EPs) of the schizophrenics and normals. The tentative conclusion is that it does not alter the performance of any group; thus, simple formulations of schizophrenics' vulnerability to disruption by any stimulus events occurring while information is being processed are not upheld. One of the hypotheses under test here is that the brain potentials evoked by the mask may be of greater amplitude, regional distribution, or duration in the schizophrenics and, as such, may be "overwriting" the ongoing processing of the 3 x 3 array, hence demonstrating neurologically a possible mechanism for schizophrenic deficit in this task. This hypothesis is not borne out, and we find no evidence so far to this effect. From figure 2, however, we can see that a small amplitude but clearly discernible waveform in the 80–105 ms epoch in normals is not apparent in schizophrenics. This waveform is temporally coincident with the target stimulus presentation, which continues until 150 ms. A tentative conclusion might be that these EP waveform differences speak to early...
Evoked potentials were obtained from the paradigm shown in Figure 1.

Information registration differences between schizophrenics and normals, or, more particularly, to the time period during which the sensory store is actually being formed. Alternatively, we might say that the target stimulus has engaged some attentional process in the normals but failed to do so in the schizophrenics.

Discussion

At this juncture we again call attention to the tentative nature of our data (due to the small number of subjects involved) and consequently the tentative nature of our conclusions and interpretations.

Nonetheless, some interesting points can be made about the potential significance of the findings. The lack of a well-defined negative-going wave in the 80-105 ms epoch in the schizophrenics appears to be a reasonably strong finding and favors an interpretation of the nonengagement of some early attentional component in these subjects. Perhaps the data also speak to the fact that this early attentional dysfunction may take the form of an inadequacy in forming the early sensory store in the sense of Broadbent (1984). The failure to observe any significant EP differences (between schizophrenics and normals) at later time epochs than approximately 100 ms is perhaps a much weaker finding for the following reason: The early (pre-100 ms) EP events have a much smaller peak amplitude/latency variability (on a between-subjects, within-groups basis) than events in the later epochs (200 ms and beyond). In other words, those subjects who display an N100 wave will perhaps have a within-group variability of 10 ms, and thus a peak amplitude of the component somewhere between 95 and 105 ms. This is not the case with later components, where the “time window” within which the P300 EP component has its peak amplitude, for example, may range from 280 ms to 400 ms depending to some extent on the experimental paradigm but also on a substantial between-subjects, within-groups variability.

For these reasons, although our 80-100 ms negative wave is quite small in amplitude, due to its lesser peak amplitude/latency variability, it may be “easier” (i.e., require fewer subjects) to demonstrate a significant between-groups effect predicated upon a small within-groups variability.

By the same logic, it will be more difficult (i.e., require more subjects) to demonstrate a later EP epoch (between-groups) difference (if it exists) due to the greater variability of these components as described above. For these reasons, we feel much more confident that an early (pre-100 ms) group difference exists than we do that a later EP epoch
Figure 3. Statistical probability map

Normal (31)
Schizophrenic (19)

95 ms poststimulus

Statistical probability mapping follows the procedure of Duffy, Bartels, and Burchfield (1981). The significance of t-test comparison between schizophrenics and normals is shown. See figure 2 for evoked potential waveforms.

difference does not exist. Larger subject numbers in each group should increase this confidence in the future.

Before we proceed to more speculative discussion in the language and neurophysiological areas of schizophrenia, this may be an appropriate place to make two additional observations: the first concerning the \(N_{100}\) EP wave form, and the second concerning a neurophysiological finding that may have some importance for early information processing.

A negative-going wave peaking at approximately 100 ms (latency largely determined by experimental conditions) has been recorded in human subjects in a wide variety of experimental paradigms. Recent data from Baribeau and Laurent (1985) suggest that this wave is indexing some aspect of “input channel selectivity” or stimulus filtering set (largely based on the work of Parasuraman 1978). The wave that we have observed to differentiate schizophrenics from normal may be the same wave or closely related. Accordingly, the attribution of this wave as indicating “predecision processing of signals in conjunction with target identification and categorization” (Desmedt, Huy, and Bourguet 1983, p. 272) agrees closely with our interpretation. Findings which indicate that the \(N_{100}\) is sensitive to manipulation of directed attention (Parasuraman 1980) and to processing demand (Callaway and Halliday 1982) may further substantiate this claim. Schizophrenic children have been examined by Strandburg et al. (1984) and were found to deviate from normal children in failing to increase the \(N_{100}\) component as a function of information-processing demand. The authors interpret this finding (along with other EP findings) as indicative of a failure “to regulate processes involved in the mobilization and direction of attention and the discrimination of target stimuli” (p. 251).

With such considerations in mind, we have begun to contemplate a situation wherein target stimuli (in the experimental laboratory setting) have some “inherent” or “automatic” attribution of potential significance assigned to them in the brains of normal subjects but not in the brains of schizophrenics. One possible implication of such an outlook is that the “automatic” or “inherent” significance is attributable to the functioning of a very fast (but crudely analyzing) information-processing system which gets some representation of the target stimulus all the way from the input sensors, through the brainstem, and into the cortex in a very preliminary representational form. This “fast” input could then be used to mobilize attentional resources faster than a finer grained input-analyzing system. The credibility of such an outlook is largely predicated on its neuro-anatomical feasibility. Recent data (Van der Kooy and Kolb 1985) indicate that an important brainstem structure, the globus pallidus, has axonal projections directly to the cortex as well as projections to the
subthalamic nucleus and the paraventricular thalamic nucleus. Our suggestion is therefore that two routes of information relay to cortex are available: a faster (but minimally analyzing) system from brainstem structures and a slower (but more "neural-integrative") route through the thalamus and, hence, by thalamic relay to the cortex. The implication is that the "fast" route of information "preprocessing" is either not used or cannot be used by the schizophrenics. Although these ideas are highly speculative, they represent a preliminary attempt to account for fairly widespread findings by other investigators as well as ourselves in schizophrenic adults and children. In any event, the globus pallidus and thalamus have demonstrably important functions in language information processing, and we will return to this aspect of our discussion below.

The thematic orientation of this issue of the Schizophrenia Bulletin is thought disorder, and it is therefore appropriate to make more explicit the links between thought disorder as seen clinically and information processing as viewed in experimental psychopathology.

The crucial element here is schizophrenic speech, itself the subject of considerable recent controversy (Schwartz 1982; Chaika and Lambe 1985; Lanin-Kettering and Harrow 1985). We do not intend to join this controversy but rather to bring to it some concepts from the work presented above and suggest at least one method to test these concepts.

Thought disorder as diagnosed clinically is almost totally dependent upon examination of the speech of schizophrenics. It is our assumption that deviant schizophrenic speech is not predicated upon defects in the language faculty of schizophrenics, but instead reflects defects in their information-processing abilities as indicated by the material presented above. This assumption shares some ground with recent work from Grove and Andreasen (1985) where certain aspects of language were found to be intact in schizophrenia but a short-term memory deficit was strongly indicated. We therefore propose a trichotomy division between speech (which can be observed and recorded), language (the "knowledge" component that cannot be observed but is inferred from behavior), and thinking (which is loosely equated with information processing in our exposition).

From Schwartz (1982), it may be concluded that schizophrenics do not have difficulties at the level of the meaning of words but may have severe difficulties at the level of sentence use and sentence comprehension. The important addition in the transition between use of words and use of sentences is that a "time buffer" has been added in the case of the sentence. In other words, the early material in the sentence only acquires "meaning" in the context of the later material in the sentence (and vice versa), and the early material must be held in some temporary store or "buffer" until the later material arrives.

Recent EP evidence shows very clearly (Kutas and Hillyard 1984; McCallum, Farmer, and Pocock 1984) that a semantically incongruous ending to a sentence will produce a characteristic EP waveform (the N_{400}). The data of McCallum, Farmer, and Pocock (1984) further show that this N_{400} ("incongruous" response) starts to develop very early in time relative to the onset of the incongruous word. This strongly suggests that a contextually driven expectancy is set up by the subjects, as a function of the early material in the sentence. This expectation may form a (forward-projected) semantic "template" for an expected ending to the sentence; if it does not occur, a very rapid detection of the incongruity results, faster than would be possible if the later material in the sentence required more complete processing. In all likelihood, this is a normal and essential function for conversational ability in humans and is a likely candidate for defect in schizophrenics in the light of the information-processing defects posited above. We would argue that early components in the sentence may not engage sufficient attentional resources (in the schizophrenic) so that a contextually driven expectancy is inadequately generated with which to ascertain the meaning of later sentential elements. Such a process would also be held to occur in "reverse," whereby an inadequately represented early sentence component may not be amenable to semantic modification in the light of a later sentence component. In this formulation, we contend that we are directly addressing the phenomenon of thought disorder (as diagnosed clinically) and that schizophrenics' difficulties at the level of sentence use and comprehension may be predicated upon early information-processing dysfunction.

To test this possibility, replications of the Kutas and Hillyard (1984) and McCallum, Farmer, and Pocock (1984) experiments are needed with schizophrenics. In such paradigms, we would strongly hypothesize that the N_{400} EP will not appear (as in normals) to semantic incongruity or, alternatively, that the N_{400} will be of reduced amplitude and the point at which the "incongruous" EP waveform begins to depart from the semantically congruous waveform will be later in time. In the latter case, we would interpret such results to indicate that a contextually driven
expectancy is not being used to enable rapid detection of incongruity in schizophrenics and, consequently, that a more complete (and slower) processing is required for the incongruous material. If such results are observed, they may well underlie failure of "discourse editing" in schizophrenia discussed by Schwartz (1982) and Grice (in commentary to Schwartz, 1982, in the same article). We shall return to this material below in relation to recent studies of the thalamus in language and thalamic post-mortem findings in schizophrenia.

In light of recent findings, it is possible to speculate on the neurological underpinnings to the early information-processing defect posited above. Findings with various forms of ERPs, as well as recent post-mortem findings in schizophrenics, are pertinent here.

The brainstem EP shows a series of small waves within about 10 ms that index the earliest stages of stimulus input to the brain, mostly below the level of the thalamus.

A small number of studies have examined the brainstem EP in schizophrenics (see Brecher and Begleiter, 1985. for a brief review as well as new data from nine schizophrenic patients). The general consensus is that schizophrenics do not differ from normal in this earliest stage of stimulus input. However, the brainstem EP is notoriously variable, even in normal subjects, and most studies have not tested an adequately large patient or control population to make a definitive statement possible. Patterson et al. (1985) have topographically mapped the auditory brainstem EP and preliminary data show subtle topographical differences between schizophrenics and normals which may lead, with greater subject numbers, to the identification of a subpopulation of schizophrenics outside the normal range on this measure.

Interestingly, the patient control population of Patterson et al. (1985) (schizoaffectives and bipolars) showed much of the same subtle aberrations as the schizophrenic population. It is therefore possible that subtle deviations of the brainstem EP are not specific to schizophrenics, but may be sensitive to a more generalized psychotic or affective component.

If we accept for the moment that the electrophysiological indicators of stimulus input at the brainstem level do not indicate pathology, then we must ask why abnormal ERPs are observed in schizophrenics at 50 ms (Adler et al. 1982: Freedman et al. 1983) and beginning at 70 ms, peaking at approximately 95 ms in the data that we have reported above. This time frame is coincident with complex interactions of the thalamus, limbic brain, and cortex. Recent research has shown direct thalamic involvement in EPs in the 18-24 ms time frame (Kudo and Yamadori 1985), as well as a specific thalamic negativity temporally coincident with the surface-recorded P300 waveform (Katayama, Tsukiyama, and Tsubokawa 1985).

In addition, the hippocampal gyrus has been shown to be a specific dipole generating source for the 200-300 ms epoch of the EP when recorded by electromagnetic radiation (Okada, Kaufman, and Williamson 1983). It is therefore reasonable to look at possible thalamic and hippocampal sources for the underpinnings to some EP abnormalities in schizophrenia.

Kovelman and Scheibel (1984) have reported data which demonstrate profound disarray in the hippocampal CA1/CA2 layers of post-mortem schizophrenic brains. A tentative interpretation of their data suggests a pathological continuum from normal subjects through borderline schizophrenic conditions to intractable chronic schizophrenia. For our purposes, if these data are considered along with the EP studies of Halgren et al. (1980), who directly examined hippocampal and amygdala unit discharge activity (coincident with surface-recorded activity), then they strongly suggest that abnormal hippocampal influences may be seen in the surface-recorded EP and that abnormal limbic brain components may underlie some EP findings in schizophrenia.

The complete thalamus of post-mortem schizophrenic brains has been examined by Adams and Oke (in preparation, personal communication) with specific reference to its regional neurochemical constituents. Their data show a particularly marked alteration of the noradrenalin-to-dopamine ratio in many regions of the thalamus, with a considerably greater concentration of dopamine than is seen in the normal post-mortem brain. The importance of these data is heightened by the fact that unusually accurate and detailed clinical records are available for these subjects.

These data are again tentative indications that the thalamus may be contributing to neuroanatomical underpinnings of abnormal surface-recorded EPs in schizophrenia.

Both the (various) thalamic nuclei and the hippocampus and amygdala in the limbic brain are crucially important neurointegrative centers controlling the interactions of brainstem and cerebral cortex (for a more complete discussion, see Pay 1980, 1981, 1982). Certain aspects of thalamic function may be directly observable with the 40 Hz EP technique (Spydell, Pattee, and Goldie 1985), and replication of such experiments may demonstrate the
intactness or otherwise of these functions of the thalamus in schizophrenia.

Perhaps a more important consideration is that certain aspects of schizophrenic dysfunction are currently attributed to the frontal cortex. For example, Levin (1984a, 1984b) has elegantly argued the case for a dysfunction in frontal eye-field control of smooth pursuit eye tracking in schizophrenia. While such attribution may be partially correct, it must be borne in mind that the exceptionally complex internal structure of the frontal cortex is partly defined by the pathways that project to it from the anterior and mediodorsal thalami and from the limbic brain. A fine-grained analysis of these interactions has recently been reviewed and integrated by Reep (1984). It may therefore be concluded that defects in the anatomical structure of hippocampus and neurochemical abnormalities in the thalamus, as previously discussed, may be playing some part in what appears to be an abnormality in various frontal cortex functions in schizophrenia.

On a more behavioral level and following our previous discussion of abnormalities of speech in schizophrenia, a most elegant and provocative theoretical model of "spoken language formulation" is given by Crosson (1985). In this model, the thalamus plays a central role in relaying arousal information (received from the basal ganglia and, most particularly, the globus pallidus) to the cortex and also in timing the release of formulated language (Wernicke's area) for motor programming (Broca's area). Crosson's model allows for intactness in the classical language and speech areas while still permitting speech defects to occur through the type of abnormal temporal sequencing (thalamically mediated) that we have posited in schizophrenia on the basis of EP and startle reflex data.

In conclusion, we have presented preliminary findings from a backward-masking experiment in which the EP data are consistent with an interpretation of an early information-processing dysfunction in schizophrenic patients which may account for their reported deficit behaviorally in this task. When such findings are considered along with data from startle reflex experiments, self-initiated EP paradigms, and findings in paired stimulus EPs, then a plausible hypothesis of abnormalities (of a generalized nature) in temporal sequencing control of information processing in schizophrenia is generated. Such a hypothesis, when considered in the light of recent reports of anatomical abnormalities in the hippocampus and thalamus of schizophrenics, produces in our opinion a compelling theoretical framework within which abnormalities in schizophrenic verbalization may be understood both behaviorally and neurologically. Such a formulation is not inconsequential as it strikes at the heart of the verbal behavior of schizophrenics, upon which the clinical diagnosis of thought disorder is fundamentally based.

References


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