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Children with a schizophrenic disorder: neurobehavioral studies

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Abstract This paper summarizes retrospective and cross-sectional neurobehavioral studies of schizophrenic children. Retrospective studies of schizophrenic children reveal that during early childhood, prior to the first onset of schizophrenic symptoms, most schizophrenic children showed delays in language acquisition and/or impairments and delays in visual-motor coordination. These impairments appear to be developmental delays rather than fixed neurobehavioral impairments, because cross-sectional studies conducted when the children are at least 10 years of age, after the first onset of psychosis, fail to detect the same deficits. The results of behavioral, cognitive/neuropsychological studies as well as the study of event-related potentials measured during performance of cognitive tasks suggests that schizophrenic children suffer from limitations in processing resources. It is argued that the developmental delays observed in schizophrenic children represent the greater time it takes them to automate certain skills. The delay in automation may reflect their limited information-processing capacity.

Introduction

There often appears to be a significant delay (more than 2 decades) between the hypothesized first onset of brain lesions and the initial appearance of positive symptoms of schizophrenia. Postmortem studies suggest that brain lesions emerge very early (in many instances during fetal development) and involve congenital, static pathology of the limbic system and prefrontal cortex (Weinberger 1987). To explain the delay of symptom onset Weinberger and colleagues (1987) have proposed that schizophrenia is a "neurodevelopmental disorder in which a fixed brain lesion from early in life interacts with certain normal maturational events that occur much later" (Weinberger 1987), p. 660). What is "pathophysiologically" distinct about schizophrenia is neither the location nor the cause of the "lesion," but is, instead, the interaction between this "lesion" and the normal course of maturation of the neural system affected by it (Weinberger 1987, p. 660). The lesion remains relatively silent until early adulthood when the normal maturation of certain brain structures, notably dorsolateral prefrontal cortex, occurs.

This neurodevelopmental model provides a useful framework to begin to understand the complex pathways from central nervous system (CNS) dysfunction to the symptoms of schizophrenia. In this paper we present neurobehavioral data that can inform neurodevelopment models of schizophrenia. These data are products of our ongoing family genetic study of schizophrenic children. Our research project's working assumption is that schizophrenia is a disorder involving impaired CNS functioning. For many patients there may be a genetic basis for the CNS disturbance. We are studying schizophrenic children because prior research (for reviews see Fish 1977; Asarnow 1995) suggests that they might represent a more homogeneous and more severe form of schizophrenia in which the CNS dysfunction is more readily discernable than in adult-onset schizophrenia.

This paper summarizes and integrates two complimentary sets of data that help elucidate the nature of the neurobehavioral impairment in schizophrenia. The first set of data are the results of studies that retrospectively characterize neurobehavioral development in schizophrenic children. These studies reveal that prior to the onset of psychotic symptoms there are certain neurobehavioral impairments. The second set of data are the results of cross-sectional studies that examine cognitive/neuropsychological functioning, thought and language disorder, and event-related potentials to delimit the cognitive processes impaired in schizophrenic children.

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Subjects and methods

The children included in the studies summarized herein were ascertained and diagnosed by the UCLA Childhood Schizophrenia Research Program. A case registry maintained by the Los Angeles County Department of Mental Health, containing demographic information and diagnostic data, was used to identify the agencies in Los Angeles County that were most likely to treat schizophrenic children. We then selected agencies from which to recruit subjects.

To be included in the study the children had to have an onset of schizophrenic psychosis prior to 13 years of age. The best-informed parent was first interviewed about the child's history of psychiatric symptoms; then the child was interviewed. Interviews were conducted by an experienced clinician using a semistructured interview, the Kiddie-SADS-E (Orvaschel and Puig-Antich 1987) supplemented by the psychosis and mood disorders sections of the K-SADS-P to provide more detailed coverage of the severity of psychotic and mood symptoms. In addition, hospital and school records were reviewed. The clinician interviewing the parent and child reviewed the diagnostic interviews as well as ancillary information with a second clinician to arrive at a consensus diagnosis. Only children who obtained consensus diagnoses of DSM-III-R (1987) schizophrenia were included in the UCLA Childhood Schizophrenia Research Program. Children were excluded if they were retarded (Full Scale IQ < 70), had a history of CNS diseases that could produce psychotic-like symptoms (e.g., temporal lobe epilepsy), or had taken drugs that could produce psychotic symptoms. Normal children were drawn from local school districts that have children who are demographically comparable to the schizophrenic children.

Different subsets of our cohort of schizophrenic subjects are included in the various studies summarized herein. To indicate the demographic characteristics of this group of children, we have summarized the demographic characteristics of the entire cohort in Table 1.

Precursors of psychotic symptoms in schizophrenic children

To identify the precursors of psychotic symptoms in schizophrenic children we (see Watkins et al. 1988 for details of this study) employed a follow-back design similar to that used in studies of adult schizophrenia (Watt and Lubensky 1976) in which school, hospital, and other early records of a group of children who subsequently developed schizophrenia were examined and objectively rated.

Two rating scales were used to characterize the children: a DSM-III Symptom Rating Scale and the Achenbach Child Behavior Checklist (CBCL; Achenbach and Edelbrock 1983). The DSM-III Symptom Rating Scale was used to rate each symptom of schizophrenia, schizotypal personality disorder, childhood onset pervasive developmental disorder and infantile autism included in DSM-III. The CBCL provided broad coverage of behavioral problems associated with a wide variety of child psychiatric disturbances that were not covered by the Symptom Rating Scale.

Table 1 Characteristics of schizophrenic children

	Mean	SD
Age in years (*n* = 47)	10.5	1.9
Peabody Picture Vocabulary Test-Revised (*n* = 47; Full-scale IQ)	93.9	14.7
Gender (*n* = 47)		
Males:	34	
Females:	13	
Handedness (*n* = 45)		
Right:	40	
Left:	5	

Symptoms were rated at each of four age ranges: 0–30 months, 31 months to 5 years 11 months, 6 years to 8 years 11 months, and 9 years to 11 years 11 months.

A symptom-rating database was developed by obtaining copies of records from all hospitals, clinics, schools, physicians and other relevant professionals seen by the children prior to entry in our study. This symptom-rating database provided multiple contemporaneous accounts of each child's behavior, medical status, and school performance in each of the four age ranges.

The majority of schizophrenic children had significant developmental delays beginning in infancy. Gross deficits in language development or no language prior to 30 months were reported in 72% of the schizophrenic children. Motor development problems were also seen in schizophrenic children including delayed milestones and poor coordination in 72% and hypotonia in 28%. Comparison across the four age ranges showed clearly that the frequency of language deficits in the schizophrenic children gradually decreased.

There appeared to be two somewhat different patterns of symptom development prior to the onset of psychotic symptoms in these children. The children with the most severe language problems had a number of other autistic-like symptoms including peculiar speech, pervasive lack of responsiveness, and self-mutilation. The balance of the children tended to have less severe language problems and no autistic-like symptoms.

The children with the more severe language problems and other autistic-like symptoms generally manifested schizophrenic psychotic symptoms one age range earlier (during the 6 year to 8 years 11 months) than the balance of the children. During this age range the schizophrenic symptoms consisted primarily of incoherence, loosening of associations, other symptoms of formal thought disorder, and flat or inappropriate affect in 71% of the children, with only two showing diagnostically significant delusions or hallucinations. By the 9 years to 11 years 11 months age range, however, 71% of these children developed diagnostically significant delusions and hallucinations in addition to formal thought disorder and flat or inappropriate affect. Differences in symptoms between children with and without autistic-like symptoms faded with age as rates of hallucinations and delusions increased for both groups in the 9 years to 11 years 11 months age range.

The other group, schizophrenic children without autistic-like symptoms, showed a gradual worsening of symptoms. Although less disturbed during infancy than children with autistic-like symptoms, most of these children also had significant developmental delays beginning in infancy. Most of the children *without* early histories of autistic-like symptoms first manifested schizophrenic psychotic symptoms during the 9 years to 11 years 11 months age range. During the age range immediately preceding the onset of psychotic symptoms, 82% of these children were rated as *both* socially impaired and presenting with at least one of the following prodromata of schizophrenia identified in prior research: excessive anxiety and panic, constricted or inappropriate affect, magical thinking, suspiciousness, and undue social anxiety and hypersensitivity to criticism.

Interestingly, given other data suggesting that depressive symptoms are associated with more positive outcomes, children *without* autistic-like symptoms showed more depressive symptoms on the CBCL at the time of the onset of the schizophrenic episode when compared with children *with* autistic-like symptoms. Prior to the first onset of psychotic symptoms, symptoms associated with the hyperactive factor of the CBCL were observed in over 50% of both groups of children including: speech problems, clumsy, acts too young for age, poor school work, daydreams, cannot concentrate, impulsive, hyperactive, and confused.

Follow-back analyses conducted by J. Asarnow and colleagues (Asarnow and Ben-Meir 1988; Asarnow et al. 1995) using a sample composed of schizophrenic children who had been psychiatric inpatients (a small subset of whom were also in the Watkins et al. 1988 sample) revealed that schizophrenic children were likely to have an insidious onset of disorder with only 1 of 21 schizophrenic children presenting with an acute onset. When compared with a group of child psychiatric inpatients with major depression, schizophrenic children showed significantly poorer levels of overall premorbid adjustment, as well as significantly poorer premorbid functioning in the area of peer relationships, scholastic performance, school adaptation, and interests. Schizophrenic children did show variability in the level of premorbid adjustment, with the subgroup of schizophrenic children with depressive symptoms tending to show higher levels of premorbid adjustment.

Overall, there were far more severe symptoms and far more social impairment prior to the onset of schizophrenia in these children than is seen in the childhood histories of schizophrenic adults. The gender differences found in our cohort of schizophrenic children paralleled those reported in the early histories of adult schizophrenics, where males are more likely to show early signs of deviant development than females (Goldstein 1980; Mednick et al. 1978).

Early developmental delays and/or neurobehavioral impairments similar to those described during the premorbid periods of childhood-onset schizophrenics have also been observed among children considered at risk for schizophrenia based on schizophrenia in their biological parents. These include transient delays in gross motor and/or visual-motor development (see Fish et al. 1992 and Asarnow 1988 for reviews).

Table 3 Neuropsychological performance in schizophrenic and normal children

Test	Schizophrenic children (n = 15) Mean ± SD	Normal children (n = 15) Mean ± SD
Benton Judgement of Line Orientation (number correct)	19.18 ± 7.17	21.29 ± 4.40
Peabody Picture Vocabulary Test (standard score)	93.6 ± 12.73	98.07 ± 18.55
Purdue Peg Board (standard score)		
Dominant hand	78.00 ± 9.27	95.13 ± 12.71*
Nondominant hand	78.90 ± 12.49	97.33 ± 13.50*
Both hands	72.90 ± 8.65	89.85 ± 15.03*
Rey's Tangled Lines (scaled score)	45.30 ± 16.79	56.64 ± 16.62
Seashore Rhythm (standard score)	90.93 ± 14.74	110.92 ± 15.09**
Token Test (standard score)	82.13 ± 13.60	99.07 ± 14.84**

* $P < 0.05$
** $P < 0.005$

Neuropsychological functioning in schizophrenic children

Survey of neuropsychological functions

This section summarizes some key findings from a series of studies conducted in R. Asarnow's laboratory that surveyed a range of neuropsychological functions using performance tasks shown to be sensitive to focal brain damage in patients with neurological disease (see Asarnow et al. 1995 for details). The tasks included in that survey are described in Table 2. Table 3 summarizes the results of the survey.

The goal of this survey was to identify the task demands and/or experimental conditions that elicit the least and most impairment in the performance of schizophrenic children. This is a critical first step in delimiting the cognitive processes that are impaired in schizophrenic children. The studies used either well-validated clinical neuropsychological tasks or experimental versions of those tasks.

The following sections focus on measures of language and motor functioning, because early delays and impairment were observed in these functions in our retrospective studies. Do these impairments persist when the children are between 10 and 13 years old and have already experienced their first schizophrenic episode?

Language functioning

The schizophrenic children in these studies scored within the normal range on the verbal comprehension factor of

Table 2 Functional domain and putative brain substrates for neuropsychological tests

Test	Functional domain	Putative brain substrate
Benton Visual Form Discrimination Test (match)	Visuoperceptual	Right hemisphere
Benton Visual Form Discrimination Test (memory)	Visuoperceptual + memory	Right hemisphere + left hemisphere?
Benton Judgement of Line Orientation	Visuoperceptual	Right hemisphere (posterior parietal)
Benton Visual Retention Test (copy)	Visuoperceptual + graphomotor	Right hemisphere
Benton Visual Retention Test (memory)	Visuoperceptual + graphomotor + memory	Right hemisphere + left hemisphere?
Block Design (modified)	Visuoperceptual + graphomotor	Right hemisphere
Peabody Picture Vocabulary test, revised	Receptive vocabulary	Left hemisphere
Purdue Pegboard	Fine motor speed	Right and left hemisphere
Rey's Tangled Lines Test	Visual tracking	Frontal
Seashore Rhythm Test	Auditory perception	Right temporal
Token Test	Receptive language +memory	Left hemisphere
Wisconsin Card Sorting Test	Shift of set + concept formation	Frontal?

the WISC-R (Asarnow et al. 1987), which includes the Information, Similarities, Vocabulary, and Comprehension subtests. In addition, the schizophrenic children score within the normal range on the Peabody Picture Vocabulary Test – Revised (Dunn and Dunn 1981), a measure of receptive vocabulary (Schneider and Asarnow 1987).

The schizophrenic children do show impairments, however, on two other tasks that require the processing of auditory stimuli and are sensitive to damage to the temporal lobe of the language-dominant hemisphere. Schizophrenic and normal children were administered the Token Test from the Multilingual Aphasia Examination (Benton and Hamsher 1989). The Token Test screens for receptive aphasia by requiring subjects to follow oral instructions of increasing complexity. Inspection of Table 3 reveals that schizophrenic children made significantly more errors than normal controls on this test. Schizophrenic children had particular difficulty understanding complex grammatical transpositions or instructions that involved carrying out sequences of behavior involving multiple steps (Watkins et al. submitted).

Schizophrenic children also performed significantly worse than normals (Watkins et al. submitted) on the Seashore Rhythm Test (Seashore et al. 1960; see Table 3). This test measures the processing of nonlinguistic, auditory stimuli by requiring subjects to reproduce a rhythym by tapping on a table rhythms that are presented aurally.

The schizophrenic children's pattern of performance on the Seashore Rhythm and Token tests does not indicate central impairments in the primary processing of auditory stimuli. Rather, it appears that the errors made by schizophrenic children on these two tasks (one using linguistic and the other nonlinguistic stimuli) may reflect impairments in attention and/or memory, because both tasks require subjects to sustain attention and to remember sequences of verbal instructions (on the Token Test), and to attend, remember, and reproduce sequences of nonverbal auditory stimuli (on the Seashore Rhythm Test).

Fine motor functioning

Visual motor coordination and fine motor speed were examined (Watkins et al. submitted) in schizophrenic children using the Purdue Pegboard (Tiffin 1968). The Purdue Pegboard requires subjects to place small metal pegs into a line of small holes as rapidly as possible. Schizophrenic children performed significantly worse than normal control children and the standardization sample on the Purdue Pegboard using the dominant hand, nondominant hand, or both hands. Impairments in visual motor coordination have also been observed in the children of schizophrenic parents (Fish 1977; Fish et al. 1992; Marcus et al. 1985; Walker and Emory 1983) as well as schizophrenic adults (Manschreck 1983). That schizophrenic children are impaired bilaterally on the task is *not* consistent with models that schizophrenic patients suffer from dysfunctions confined to only one hemisphere.

Perceptual functioning

Schizophrenic children obtained normal scores on the perceptual organization factor of the WISC-R (Asarnow et al. 1987). The subtests included in the perceptual organization factor are Picture Arrangement, Picture Completion, Object Assembly, and Block Design. In addition, schizophrenic children perform within normal limits (Schneider and Asarnow 1987) on the Benton Judgement of Line Orientation Task (Benton et al. 1975), a task that requires subjects to discriminate among lines that differ only in angular orientation.

Watkins et al. (submitted) recently examined in some detail a more circumscribed aspect of visual perception, form discrimination abilities, using two tests. One task, the Visual Retention Test (Benton 1974) assesses form discrimination abilities by requiring subjects to draw designs. A second task, the Visual Form Discrimination Test (Benton et al. 1977), assesses form discrimination abilities by requiring subjects to pick one of four comparison designs that match a sample design placed above the comparison stimuli. This makes much fewer demands on graphomotor functions than the Visual Retention Test. Figure 1 presents the results of this study. Schizophrenic and mental-age-matched normal children did not differ in their ability to discriminate between simultaneously presented designs (Visual Form Discrimination Test) or to reproduce a design by copying (Visual Retention Test).

When memory demands were added to both tasks, however, schizophrenic children showed impairments relative to normal control children (Fig. 1). A 15-s delay was interposed between the presentation of the design and when the subject was allowed to begin drawing the design on the Visual Retention Test. On the Visual Form Discrimination Test, after a 10-s presentation, the sample was removed so that the subject matched the comparison stimuli to their memory of the standard stimulus. The schizophrenic children performed significantly worse than the matched normal controls on both tests in which subjects were required to hold the sample stimulus in short-term memory before responding.

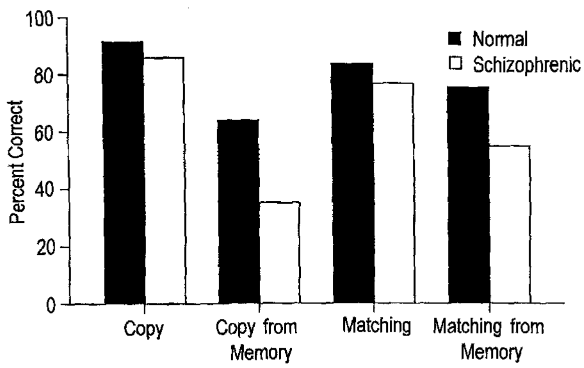

Fig. 1 Visual Retention Test and Visual Form Discrimination Test: Mean scores for schizophrenic and normal control children when subjects copy or discriminate between designs in conditions with and without memory demands. (Reprinted with permission of Schizophr Bull)

The two Benton tests are sensitive measures of the kinds of visual-spatial impairments found in patients with focal lesions involving the right posterior cortex (Lezak 1983). The normal performance of schizophrenic children on the Visual Retention and Visual Form Discrimination tests indicates that they do not suffer from the types of visual-spatial impairments typically found in patients with focal lesions confined to the right posterior lobe. In contrast, adding a memory demand to these tests elicited impaired performance in schizophrenic children regardless of whether they responded by simple pointing or by copying a design.

Conclusions

It appears that rote language skills and simple perceptual functions are not impaired in schizophrenic children. In contrast, schizophrenic children perform poorly on a number of tasks that tap fine motor speed and/or place extensive demands on attention and/or short-term memory.

Cognitive/neuropsychological tasks tap multiple cognitive processes. Which of those processes is responsible for the impaired performance shown by schizophrenic children? In the next section we briefly review a series of studies examining visual attention, which attempt to isolate the cognitive processes that are impaired in schizophrenic children.

Studies of visual information processing

This section summarizes a series of studies (see Asarnow and Sherman 1984 and Asarnow et al. in press for details) designed to further delimit the cognitive processes that are impaired in schizophrenic patients. We attempted to accomplish this by determining which of the multiple cognitive processes tapped by a forced choice, span of apprehension task, is impaired in schizophrenic children. The span of apprehension task was originally developed by Estes and Taylor (1964) to provide an index of the rate of visual information processing. This task detects dysfunction not only in actively psychotic schizophrenic patients, but also in individuals vulnerable to schizophrenia, including schizophrenic adults in clinical remission and the unaffected first-degree relatives of schizophrenic probands (see Asarnow et al. 1991 for a review).

Our attempts to isolate the cognitive processes impaired by schizophrenia are guided by information-processing models. Information-processing models describe "the structures and processes by which individuals register, encode, select, maintain, transform, store and retrieve information" (Nuechterlein and Asarnow 1989). Early information-processing models emphasized the role of structural limitations on cognitive functions. Modern information-processing models, in contrast, acknowledge the role of processing resources (capacity) in setting limits on the information processing that can be carried out in a fixed unit of time. Processing resources are broadly conceptualized as the limited fuels, processes, and skills that are available at a given moment to enable performance of cognitive tasks (Hirst and Kalmar 1987).

In Experiment I (Asarnow et al., submitted), schizophrenic, mental-age-matched normal children, and a group of younger normal children were administered the same span of apprehension task used in studies af adult schizophrenics and their relatives. Subjects were told that either a "T" or "F" would be flashed briefly (for 50 ms) on a backward projection screen along with other letters. They were instructed to report after each trial which of the two target letters had been presented. The target stimulus was embedded in arrays containing either 0, 2, 4, or 9 *nontarget* letters. Subjects received four scores, which were the number of correct detections of the target stimuli for each array size. Schizophrenic children showed impaired performance relative to mental-age-matched normals on the five- and ten-letter arrays of the span task, but not on the one- and three-letter arrays.

The results from Experiment I suggest that all groups of subjects were engaged in serial search when performing on the partial-report span task. Serial processing demands focal attention. It is characterized by directing attention "serially to different locations, to integrate the features within the same spatio-temporal 'spotlight' into a unitary percept" (Treisman and Gelade 1980). One of the defining characteristics of a serial mode of processing is that there is an incremental cost (increased reaction time or errors) when subjects are required to detect targets in displays with increasing numbers of distractors. This is exactly what happened on the Estes and Taylor span task in Experiment I. As the number of distractors increased from 0 to 2 to 4 to 9, the target detection rates for all groups decreased. The fact that the schizophrenic children and the younger normals showed a greater "cost" with increased number of distractors than mental-age-matched normal suggests that their serial search is either initiated more slowly or employed less efficiently than that of the older normal group.

A convergent result emerged from Experiment II of Asarnow and Sherman (1984). Visual scan paths were studied by modifying the stimulus matrix so that each target stimulus appeared eight times in each quadrant. When the target is in the upper quadrants, as opposed to the lower quadrants, both the schizophrenics and the mental-age-matched normals showed a significantly greater probability of correctly detecting the target. This suggests that both the schizophrenic and older normal children consistently began their serial search in the upper quadrants, and that their iconic image of the stimulus display faded before they could adequately process the lower quadrants.

The results of Experiments I and II suggest that both schizophrenic and normal children use serial search to detect the target on partial-report span tasks. Schizophrenic children appeared to be delayed in the initiation of serial search and/or carry out serial search more slowly than normal children (see Sherman and Asarnow 1985). Serial search requires effort, and, therefore, makes extensive demands on processing resources.

In contrast, on another version of the span task (a full-report task) that makes considerably less demands on processing resources, schizophrenic children reported as many letters as mental-age-matched normals (Asarnow and Sherman 1984, Experiment III). The full-report span task makes greater demands on iconic memory (a large capacity visual memory store that stores information for 200–400 ms) and immediate memory and less demands on serial search than partial-report span tasks.

Cognitive processes impaired in schizophrenic children

Our survey of neuropsychological functions and detailed studies of visual attention generally yielded converging results. The tasks that elicit impaired performance in schizophrenic children tap a wide diversity of computational functions across sensory modalities. A key characteristic that differentiates the tasks that elicit impaired performance in schizophrenic children from those that do not is that they make more extensive demands on processing resources. This is consistent with the hypothesis developed in earlier reviews of cognitive/neuropsychological studies of schizophrenic children (Sherman and Asarnow 1985; Asarnow et al. 1986; Asarnow et al. in press) and adults (Nuechterlein and Dawson 1984) that schizophrenic individuals have subtle limitations in processing capacity.

Psychophysiological studies of the processes involved in the mobilization and allocation of processing resources are important complements to our behavioral studies.

ERP indices of processing deficits in schizophrenia

We have recently completed a series of studies of ERPs recorded while schizophrenic children performed information-processing tasks such as the span of apprehension task (Span; Strandburg et al. 1984, 1991, 1994a) and the continuous performance task (CPT; Strandburg et al. 1990, 1994b). Several decades of studies of mental chronometry using ERPs has yielded a lexicon of ERP components with fairly well-established neurocognitive correlates (Donchin et al. 1978; Hillyard and Kutas 1983). These components can be used to parse the sequence of neurocognitive events in such a way as to determine more precisely the nature of information-processing deficits in schizophrenic children and adults.

ERP components studied

In our ERP studies we have focused primarily on four components: contingent negative variation (CNV), hemispheric asymmetry in the amplitude of the P1/N1 component complex, processing negativity (Np), and a late positive component (P300). The CNV provides a measure of orienting, preparation and readiness to respond to an expected stimulus. Most authors acknowledge that there are at least two separate generators of the CNV: an early frontal component believed to be an orienting response to warning stimuli, and a later central component associated with preparedness for stimulus-processing and response (Rohrbaugh et al. 1986). In the Span task the CNV is apparent as a slowly developing frontal negative wave between the warning and Span stimuli. In the CPT task a CNV-like process develops frontally just prior to each of the continuously repeating stimuli.

Normal individuals typically have larger visual P1/N1 components over the right cerebral hemisphere. We have compared hemispheric laterality between normal and schizophrenic individuals in many of our studies. Differences in this lateralization during visual information-processing tasks could reflect either differences in the strategic utilization of processing capacity of the hemispheres or a lateralized neural deficit.

The Np is a family of negative components that occur within the first 400 ms after the onset of a stimulus, indicating the degree to which attentional and perceptual resources have been allocated to stimulus processing. Because the Np waves occur contemporaneously with other components (P1, N1, and P2), they can best be seen in difference potentials resulting from the subtraction of nonattend ERPs from attend ERPs (Hillyard and Hansen 1986; Naatanan 1982).

Finally, the P300 is a frequently studied index of the recognition of stimulus significance in relation to task demands. The P300 is a positive wave occurring as early as 300 ms after a task-relevant stimulus. In the case of tasks as complex as the Span or CPT, the P300 is seen between 400 and 500 ms poststimulus.

Consistent ERP results in schizophrenia

Table 4 summarizes by component the ERP results from six studies of schizophrenic children or adults undertaken in our laboratory. We review the components in the order that they appear. All of the studies summarized in this table resulted in rather large and robust performance differences between groups in both the accuracy and reaction times of signal detection responses. Thus, the behavioral paradigms were successful in eliciting information-processing deficits in these patients. Of interest were the ERP differences that are associated with the behavioral deficits.

The CNV differences between normals and schizophrenics were not consistently found across our various studies. In the Span task (which includes a warning interval) all possible results have been obtained (normals > schizophrenics; normals = schizophrenics; and normals < schizophrenics). For the CNV-like negative wave occurring in the CPT task, no group differences were found in either experiment. Because our warning interval was short and the wave was largest frontally, the CNVs in both tasks were most likely the early wave related to orienting. Thus, differences in prestimulus orienting do not seem to reli-

Table 4 Information-processing tasks in schizophrenic children and adults: summary of evoked-potential studies. CPT continuous performance task; CNV contingent negative variation; *N*p processing negativity; P300 late positive component

Paper[a]	Task	Group tested	CNV	P1/N1 asymmetry	*N*p	P300
1984	Span	Schizophrenic children	Norm > schiz	Norm > schiz	Norm > schiz[b]	Norm > schiz
1990	CPT	Schizophrenic children	Norm = schiz	Norm > schiz	–	Norm > schiz
1991	Span	Schizophrenic children	Norm = schiz	Norm > schiz	Norm > schiz	–
1994 a	Span	Schizophrenic adults	Schiz > norm	Norm > schiz	Norm > schiz	Norm > schiz
1994 b	CPT	Schizophrenic children	Norm = schiz	Norm > schiz	Norm > schiz	Norm > schiz[c]
In preparation	Idiom	Schizophrenic adults	Norm > schiz	–	–	Norm > schiz

[a] Authors of all papers are Strandburg et al.
[b] Larger task-difficulty increase in N1 amplitude in normals than schizophrenics
[c] Normals had larger P300 than schizophrenics for targets in the single-target CPT task

ably account for the poor performance of schizophrenics on these tasks.

The literature from CNV experiments on schizophrenia from other labs has also been somewhat checkered, although the preponderance of studies seem to favor a smaller CNV in schizophrenics (see review by Pritchard 1986). It may be that a longer warning interval than used in our experiments (500 ms in the Span and 1250 ms ISI in the CNV) and the consequent elicitation of a later CNV process is necessary for observation of preparatory abnormalities in schizophrenics.

In every study summarized in Table 4 where processing negativities have been measured, Nps have been found to be smaller in schizophrenics. This deficit has been seen in both children (Strandburg et al. 1984, 1991, 1994 b) and adults (Strandburg et al. 1994 a), and in both the Span (Strandburg et al. 1984, 1991, 1994 a) and CPT (Strandburg et al. 1994 b) tasks. By way of contrast, we recently studied a group of attention-deficit hyperactivity-disorder (ADHD) children on the CPT task and found no evidence of smaller Np in ADHD children. Thus, a diminished Np amplitude is the earliest consistent ERP index of schizophrenic information-processing deficit in our research. These results suggest impaired allocation of attentional and perceptual resources.

There is general consensus from studies of processing negativities in channel selective attention tasks (Nd) that adult schizophrenics produce less attention-related endogenous negative activity than do normals (see reviews by Cohen 1990 and Pritchard 1986). Our results complement this finding in adults using a discriminative processing task and extend these findings to childhood-onset schizophrenia. Both Michie et al. (1990) and Baribeau-Braun et al. (1983) have argued that reductions in the amplitude of processing negativity in schizophrenics results from impairments in executive functions responsible for the maintenance of an attentional trace. For example, Baribeau-Braun (1983) observed normal Nd activity with rapid stimulus presentation rates, but reduced amplitudes with slower rates, suggesting that the neural substrates of Nd are intact, but improperly regulated. Knight et al. (1981) have demonstrated that individuals with frontal lobe lesions resemble schizophrenics in this regard, in that both groups do not show increased processing negativity to attended stimuli in auditory selective attention tasks.

Reduced amplitude P300 in schizophrenic adults has been found in a large number of studies in a wide variety of experimental paradigms (reviewed by Pritchard 1986). As can be seen in Table 4, we have also consistently observed smaller P300 amplitude in studies of both schizophrenic children and adults, in the Span, CPT and idiom recognition tasks. P300 latency was also measured in two of these studies. Although prolonged P300 latency was found in one study (Strandburg et al. 1994 b), no differences were found in another (Strandburg et al. 1994 a). The majority of ERP studies have reported normal P300 latency in schizophrenics (Pritchard 1986).

Absence of right-lateralized P1/N1 amplitude in visual ERPs has been a consistent finding in all five of our studies using the CPT and Span tasks. Thus, our data demonstrate that abnormally lateralized electrophysiological responses, related either to lateralized dysfunction in schizophrenics or a pathology-related difference in information-processing strategy, is a consistent aspect of both adult- and childhood-onset schizophrenia. These results are perhaps consistent with the results of others suggesting abnormal patterns of hemispheric laterality in schizophrenics (e.g., Tucker and Williamson 1984).

Summary

Our ERP studies of schizophrenic adults and children performing discriminative processing tasks suggest that the earliest reliable electrophysiological correlate of impaired discriminative processing in schizophrenics is observable in the Np component. Thus, it appears that schizophrenics are deficient in the allocation of the attentional resources necessary for efficient and accurate discriminative processing. Although diminished amplitude processing negativities have been observed in ADHD in auditory paradigms (Satterfield et al. 1990; Loiselle et al, 1980), Np was found to be normal in ADHD children during our visual CPT task (Strandburg et al. submitted). Thus, the diminished Np in visual processing may be specific to schizophrenic pathology. Later ERP abnormalities in schizophrenics (e.g., diminished amplitude P300) may be a "downstream" product of the uncertainty in stimulus recognition created by previous discriminative difficulties, or may be additional neurocognitive deficits. Abnormalities in later ERP components are not specific to schizophrenia, having been reported in studies of ADHD children (reviewed by Klorman 1991).

Finally, although the absence of P1/N1 asymmetry in the visual ERPs of schizophrenics is contemporaneous with the diminished Np, the fact the Np amplitude varies with the processing demands of the task, whereas P1/N1 asymmetry does not, suggests that it is the Np deficit that plays a greater role in the information-processing deficits manifested by schizophrenic children.

Implications for neurodevelopmental model

Our retrospective studies of the neurobehavioral antecedents of psychotic symptoms in schizophrenic children, cross-sectional studies of neurobehavioral functioning, and ERPs provide findings that can inform neurodevelopmental models of schizophrenia. Our retrospective studies of neurobehavioral development in schizophrenic children indicate that well in advance of the first onset of psychotic symptoms, schizophrenic children manifest certain neurobehavioral impairments. During infancy and early childhood their language acquisition is slow (particularly for expressive language), and gross motor functioning is impaired. Somewhat later there are impairments in fine motor coordination. These neurobehavioral impairments may be early manifestations of the brain lesions posited by neurodevelopmental models. As noted above, in the neurodevelopmental model, these brain lesions are thought to be silent. The results of our studies, as well as studies of children at risk for schizophrenia, suggest that the lesions are silent only in the sense that they do not immediately produce active psychotic symptoms. It is worth noting that the expressive language and motor skills are subserved by structures in the frontal lobes. It is these areas where many of the early brain lesions are also found (Weinberger 1987).

There is an interesting disparity between the results of our detailed cross-sectional neurobehavioral assessments and the results of the retrospective studies of neurobehavioral development prior to the onset of psychotic symptoms. As noted herein a great majority of schizophrenic children were slow to acquire expressive language. For example, the children were delayed in speaking in two- and three-word phrases. Curiously, the results of the neuropsychological evaluations conducted when the children were 9 years of age revealed that simple expressive and receptive language skills were among the *least* impaired functions in these children. It appears that the early impairments in language function were delays, not static neuropsychological deficits. On the other hand, when schizophrenic children had to process complex verbal and nonverbal information (e.g., by holding it in short-term memory while they executed a sequence of actions), their performance was impaired. A parallel situation obtains in regard to motor functioning. There were delays in motor functioning involving gross motor coordination. At age 9 years schizophrenic children did not show impairments in gross motor functioning. They did, however, show impairments on the Purdue Pegboard, a measure of speeded motor performance that places extensive demands on fine motor speed and motor coordination. Placing cognitive systems under time pressure (e.g., increasing the amount of information that must be processed in a fixed unit of time) makes greater demands on processing resources (Kahneman 1973). This constellation of findings indicating a delay in the acquisition of certain skills yet residual problems when the skills have to be performed under conditions involving more effortful processing, may offer some important insights into the neurobehavioral impairments in schizophrenia.

What mechanisms could produce this constellation of delayed acquisition of skills, which even once acquired are not necessarily deployed as efficiently? Impairments can still be revealed by putting the system under time pressure, for example. The developmental delays might be an analog of a delay of automatization of skills. Research examining the ontogeny of skilled motor performance and perceptual discrimination learning may provide a useful framework for elucidating the mechanisms underlying the developmental delays observed in schizophrenic children.

It appears to be the case that schizophrenic children are most likely to be delayed in acquiring those skills (e.g., speaking in two- and three-word utterances) that are at the cusp of development (i.e., emerging skills that are just coming on-line developmentally). It is not the case that schizophrenic children are unable to speak in two- and three-word utterances; rather, they are delayed in the acquisition of the skill because some months later they can speak in two- und three-word utterances.

Developmental delays may be analogous to a delay in learning a skill. Why should schizophrenic children show delays in learning skills? An intriguing answer to this problem emerges from our previous hypothesis that schizophrenic children have a reduced processing capacity. Controlled processes are used when an individual is first attempting to learn a skill. For example, on tasks such as the span of apprehension controlled processes modify long-term memory and are used to search the arrays and decide responses. As practice proceeds these responses become automated, i.e., they make less demands on processing resources. In this way the limited controlled processing system lays down the "stepping stones" of automatic processing (Schneider et al. 1984). Reduced processing resources can lead to deficient development of automatic operations. It can particularly lead to a delay in the time taken to make a task automated (i.e., make it resource-free). Perhaps the developmental delays we have observed in schizophrenic children represent in a broader time scale the greater time it takes schizophrenic individuals to automate certain information-processing tasks in the laboratory. There is a reciprocal relationship between automatic and controlled processes. Reduced availability of processing resources leads to greater limitations on controlled processes, which in turn leads to slow development of automatic processes. Subsequently, reduced utilization of automatic operations requires that resources demanding controlled processes be used for more components of the task, which further reduces the amounts of available resources. The reduced amplitude of the NP ERP component which is consistently observed in both child and adult onset schizophrenic patients is consistent with the hypothesis that processing resources are reduced in schizophrenia. "It is this cascading system of interactions between automatic and controlled processes, which allows a limited capacity central processor to carry out very complex cognitive tasks in normal persons, that appears to be somehow disrupted in patients with schizophrenia" (Granholm et al. 1991).

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References

Achenbach TM, Edelbrock CS (1983) Manual for the child behavior checklist and the revised behavior profile. Department of Psychiatry, University of Vermont

American Psychiatric Association (1987) Diagnostic and statistical manual of mental disorders (DSM-III-R), 3rd edn. American Psychiatry Association revised, Washington, DC

Asarnow JR (1988) Children at risk for schizophrenia. Schizophr Bull 14:613–632

Asarnow JR (1995) Childhood-onset schizophrenia: an annotation. J Child Psychol Psychiatry (in press)

Asarnow JR, Ben-Meir S (1988) Children with schizophrenia spectrum and depressive disorders: a comparative study of premorbid adjustment, onset pattern and severity of impairment. J Child Psychol Psychiatry 29:477–488

Asarnow JR, Tompson MC, Goldstein MJ (1995) Childhood-onset schizophrenia: a follow-up study. Schizophr Bull 20:599–618

Asarnow RF, Sherman T (1984) Studies of visual information processing in schizophrenic children. Child Dev 55:249–261

Asarnow RF, Sherman T, Strandburg RJ (1986) The search for the psychobiological substrate of childhood onset schizophrenia. J Am Acad Child Psychiatry 26:601–614

Asarnow RF, Tanguay PE, Bott L, Freeman BJ (1987) Patterns of intellectual functioning in non-retarded autistic and schizophrenic children. J Child Psychol Psychiatry 28:273–280

Asarnow RF, Granholm E, Sherman T (1991) Span of apprehension in schizophrenia. In: Steinhauer SR, Gruzelier JH, Zubin J (eds) Neuropsychology, psychophysiology, and information processing, vol 5 of Handbook of schizophrenia. Elsevier, Amsterdam, pp 335–370

Asarnow RF, Asamen J, Granholm E, Sherman T, Watkins JM, Williams M (1995) Cognitive/neuropsychological studies of children with a schizophrenic disorder. Schizophr Bull 20: 647–670

Asarnow RF, Asamen J, Sherman T (1995) Visual information processing in schizophrenic children: a replication and extension (submitted)

Baribeau-Braun J, Picton TW, Gosselin J (1983) Schizophrenia: a neurophysiological evaluation of abnormal information processing. Science 219:874–876

Benton AL (1974) Revised visual retention test (4th edn). The Psychological Corporation, New York

Benton AL, Hamsher K deS (1989) Multilingual aphasia examination (2nd edn), Iowa City, IA: Benton Laboratory of Neuropsychology, Division of Behavioral Neurology, Department of Neurology, University Hospitals

Benton AL, Hannay HJ, Varney NR (1975) Visual perception of line direction in patients with unilateral brain disease. Neurology 25:907–910

Benton AL, Hamsher K deS, Stone B (1977) Visual retention test: visual form discrimination, Iowa City, IA: Division of Behavioral Neurology, Department of Neurology, University Hospitals

Cannon TD, Mednick SA, Parnas J, Schulsinger F, Praestholm J, Vestergaard A (1993) Developmental brain abnormalities in the offspring of schizophrenic mothers: I. Contributions of genetic and perinatal factors. Arch Gen Psychiatry 50:551–564

Cohen R (1990) Event-related potentials and cognitive dysfunction in schizophrenia. In: Hafner H, Gattaz WF (eds) Search for the causes of schizophrenia, vol II. Springer, Berlin Heidelberg New York, pp 342–360

Donchin E, Ritter W, McCallum W (1978) Cognitive psychophyiology: the endogenous components of the ERP. In: Callaway E, Tueting P, Koslow S (eds) Event-related brain potentials in man. Academic Press, New York, pp 349–442

Dunn LM, Dunn LM (1981) Peabody picture vocabulary test revised. American Guidance Service, Circle Pines, Minnesota

Estes WK, Taylor HA (1964) A detection method and probabilistic models for assessing information processing from brief visual displays. Proc Natl Acad Sci USA 52:446–454

Fish B (1977) Neurobiologic antecedents of schizophrenia in children. Arch Gen Psychiatry 34:1297–1313

Fish B, Marcus J, Hans SL, Auerbach JG, Perdue S (1992) Infants at risk for schizophrenia: sequelae of a genetic neurointegrative defect: a review and replication analysis of pnadysmaturation in the Jerusalem Infant Development Study. Arch Gen Psychiatry 49:221–235

Goldstein MJ (1980) The course of schizophrenic psychosis. In: Brim OG, Kagan J (eds) Constancy and change in human development. Harvard University Press, Cambridge, Mass, pp 325–358

Granholm E, Asarnow RF, Marder SR (1991) Controlled information processing resources and the development of automatic detection responses in schizophrenia. J Abnorm Psychol 100:22–30

Hillyard SA, Hansen JC (1986) Attention: electrophysiological approaches. In: Coles MGH, Donchin E, Porges SW (eds) Psychophysiology: systems, processes, and applications. Guilford, New York, pp 227–243

Hillyard SA, Kutas M (1983) Electrophysiology of cognitive processing. Ann Rev Psychol 34:33–61

Hirst W, Kalmar D (1987) Characterizing attentional resources. J Exp Psychol 116:68–81

Kahneman D (1973) Attention and effort. Prentice-Hall, Englewood Cliffs, NJ

Klorman R (1991) Cognitive event-related potentials in attention deficit disorder. J Learning Dis 24:130–140

Knight RT, Hillyard SA, Woods DL, Neville HJ (1981) The effect of frontal cortex lesions on event-related potentials during auditory selective attention. Electroencephalogr Clin Neurophysiol 52:571–582

Lezack M (1983) Neuropsychological assessment. Oxford University Press, New York

Loiselle DL, Stamm JS, Maitinsky S, Whipple SC (1980) Evoked potential and behavioral signs of attention dysfunction in hyperactive boys. Psychophysiology 17:193–201

Manschreck TC (1983) Psychopathology of motor behavior in schizophrenia. In: Maher BA (ed) Progress in experimental personality research, vol 12. Academic Press, New York, pp 53–99

Marcus J, Hans SL, Mednick S, Schulsinger P, Michelsen N (1985) Neurological dysfunctioning in offspring of schizophrenics in Israel and Denmark: a replication analysis. Arch Gen Psychiatry 42: 753–761

Marcus J, Hans SL, Auerbach JG, Auerbach AG (1993) Children at risk for schizophrenia: The Jerusalem Infant Development Study: II. Neurobehavioral deficits at school age. Arch Gen Psychiatry 50: 797–809

Mednick SA, Schulsinger F, Teasdale TW, Schulsinger H, Venables PH, Roch DR (1978) Schizophrenia in high risk children: sex differences in predisposing factors. In: Serban G (ed) Cognitive defects and the development of mental illness. Brunner/Mazel, New York, pp 169–197

Michie PT, Fox AM, Ward PB, Catts SV, McConaghy N (1990) Event-related potential indicies of selective attention and cortical lateralization in schizophrenia. Psychophysiology 27: 207–227

Naatanen R (1982) Processing negativity: an evoked potential reflection of selective attention. Psychol Bull 92: 605–640

Nuechterlein KH, Dawson ME (1984) Information processing and attentional functioning in the developmental course of schizophrenic disorders. Schizophr Bull 10: 160–203

Nuechterlein KH, Asarnow RF (1989) Perception and cognition. In: Kaplan HI, Sadock BJ (eds) Comprehensive textbook of psychiatry V. Williams and Wilkins, Baltimore

Nuechterlein KH, Edell WS, Norris M, Dawson ME (1986) Attentional vulnerability indicators, thought disorder, and negative symptoms. Schizophr Bull 12: 408–426

Orvaschel H, Puig-Antich J (1987) Schedule for affective disorder and schizophrenia for school age children: epidemiologic version. Medical College of Pennsylvania, Eastern Pennsylvania Psychiatry Institute

Pritchard WS (1986) Cognitive event-related potential correlates of schizophrenia. Psychol Bull 100: 43–66

Rohrbaugh JW, McCallum WC, Gaillard AWK, Simons RF, Birbaumer N, Papakostopoulos D (1986) ERPs associated with preparatory and movement-related processes: a review. In: McCallum MC, Zappoli R, Denoth F (eds) Cerebral psychophysiology: studies in event-related potentials. (EEG Suppl 38, pp 189–229) Elsevier, Amsterdam

Satterfield JH, Schell AM, Nicholar TW, Satterfield BT, Freese TE (1990) Ontogeny of selective attention effects on event-related potentials in attention-deficit hyperactivity disorder and normal boys. Biol Psychiatry 28: 879–903

Schneider SG, Asarnow RF (1987) A comparison between the cognitive/neuropsychological impairments of non-retarded autistic and schizophrenic children. J Abnorm Child Psychol 15: 29–46

Schneider W, Dumais ST, Shiffrin RA (1984) Automatic and controlled processing and attention. In: Parasuraman R, Beatty J, Davies J (eds) Varieties of attention. Academic Press, San Diego, Calif, pp 1–27

Seashore CE, Lewis D, Sactveit JG (1960) Seashore measures of musical talents. The Psychological Corporation, New York

Sherman T, Asarnow RF (1985) The cognitive disabilities of the schizophrenic child. In: Sigman M (ed) Children with emotional disorders and developmental disabilities: assessment and treatment. Grune and Stratton, New York

Strandburg RJ, Marsh JT, Brown WS, Asarnow RF, Guthrie D (1984) Event-related potential concomitants of information processing dysfunction in schizophrenic children. Electroencephalogr Clin Neurophysiol 57: 236–253

Strandburg RJ, Marsh JT, Brown WS, Asarnow RF, Guthrie D, Higa J (1990) Event-related potential correlates of impaired attention in schizophrenic children. Biol Psychiatry 27: 1103–1115

Strandburg RJ, Marsh JT, Brown WS, Asarnow RF, Guthrie D, Higa J (1991) Reduced attention-related negative potentials in schizophrenic children. Electroencephalogr Clin Neurophysiol 79: 291–307

Strandburg RJ, Marsh JT, Brown WS, Asarnow RF, Guthrie D, Higa J (1994 a) Reduced attention-related negative potentials in schizophrenic adults. Psychophysiology 31: 272–281

Strandburg RJ, Marsh JT, Brown WS, Asarnow RF, Higa J, Guthrie D (1994 b) Continuous processing-related ERPs in schizophrenic and normal children. Biol Psychiatry 35: 525–538

Strandburg RJ, Marsh JT, Brown WS, Asarnow RF, Guthrie D (1994 c) Attentional processing in ADHD and schizophrenic children: late negative ERP activity. Psychophysiology 31: S96

Strandburg RJ, Marsh JT, Brown WS, Asarnow RF, Guthrie D (1995) Event-related potential correlates of linguistic information processing in schizophrenics. (in preparation)

Tiffin J (1968) Purdue pegboard. Science Research Associates, Chicago

Treisman AM, Gelade G (1980) A feature-integration theory of attention. Cogn Psychol 12: 97–136

Tucker DM, Williamson PA (1984) Asymmetric neural control systems in human self-regulation. Psychol Rev 91: 185–215

Walker E, Emory E (1983) Infants at risk for schizophrenia: offspring of schizophrenic parents. Child Dev 54: 1269–1285

Weinberger DR (1987) Implications of normal brain development for the pathogenesis of schizophrenia. Arch Gen Psychiatry 44: 660–669

Watkins JM, Asarnow RF, Tanguay PE (1988) Symptom development in childhood onset schizophrenia. J Child Psychol 29: 865–878

Watt NF, Lubensky AW (1976) Childhood roots of schizophrenia. J Consult Clin Psychol 44: 363–375

Watkins J, Asarnow RF, Williams M (1995) Qualitative variation in neuropsychological test performance in schizophrenic children