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Child and Adolescent (Early Onset) Schizophrenia: A Review in Light of DSM-III-R[1]

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Early onset schizophrenia (EOS) is defined as that beginning in childhood or adolescence (under 16 or 17). Studies of EOS are infrequent, and comparative adult figures not always available, but tentative conclusions may be drawn. EOS is more common in males; symptomatology is often undifferentiated; frequencies of homotypic family disorder, premorbid schizotypal personality, and neurodevelopmental abnormalities high; outcome poor but only slightly worse than in adults; response to psychotropic drug treatment probably similar though not properly tested; and confusion with psychotic bipolar disorder particularly common. Onset before language is developed presents special diagnostic difficulties. There are a few reports of autistic children developing schizophrenia but this requires replication. Differences from adult schizophrenia are more marked when onset is in childhood than in adolescence but all are quantitative rather than qualitative suggesting that the disorders are the same and that there should be no separate category for children or adolescents.

INTRODUCTION

Schizophrenia is one, if not the major, contributor to the cost of psychiatric services in most countries (see Sharfstein & Clark, 1978). But, as Andreasen (1987) pointed out, there is considerable conflict as to how schizophrenia should be defined and each definition varies with the population encompassed, the clinical picture, and the outcome (see also

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Westermeyer & Harrow, 1988). With the immense popularity of DSM-III and its successor, DSM-III-R, the fact that this represents only one definition and one that, by the criterion of 6-month duration, necessarily worsens the prognosis, has probably been overlooked. Nevertheless, the ineluctable fact is that for clinical purposes, DSM is now the standard and forms the main focus here.

This review is concerned with early onset schizophrenia (EOS), that is, where the disorder develops in childhood or adolescence (say, under 16 or 17). Within this age group, there is a subgroup, beginning before age 13 usually referred to as "prepubertal." Since this term speaks to a biodevelopmental state which cannot be defined precisely by age, the term "Very Early Onset Schizophrenia" (VEOS) is used when the onset is less than 13 years of age. Thus, unlike prepubertal, VEOS does have a precise meaning.

Reviewing EOS is complicated by the fact that from about 1960 to the appearance of ICD-9 and DSM-III in 1979/1980, all psychotic disorders of childhood were officially aggregated into a single category "childhood schizophrenia." This, combined with often inexact criteria, makes disentangling EOS from autism and other psychoses in many studies from this period very difficult. There have been a few useful reviews specifically addressing aspects of early onset schizophrenia more or less as defined in DSM-III (Beitchman, 1985; Kolvin & Berney, 1990; Prior & Werry, 1986) but, unfortunately, the vast general literature on schizophrenia seems to pay little credence to EOS—yet there is reason to believe that young age may reflect a number of critical issues as follows.

Diagnostic

1. Are adult and early onset schizophrenia diagnostically the same disorder as ICD and DSM now state? (It should be noted that only certain symptoms, change in adaptive function, duration, and some exclusion criteria are used for diagnosis.)

2. If diagnostically the same as the adult disorder, is EOS still sufficiently distinctive to merit a separate, *developmental* subcategory within schizophrenia similar to the current *symptomatological* ones of catatonic, disorganized, residual, paranoid, or undifferentiated?

3. Does a diagnosis of EOS, using the same criteria as in adults, exclude some psychotic children who probably have schizophrenia (false negatives)?

Other Features

Here the issue is whether or not EOS resembles the adult disorder in terms of nondiagnostic characteristics or correlates. The DSM-III-R (American Psychiatric Association [APA], 1987) manual lists these areas as: (a) associated features, (b) age at onset, (c) course, (d) impairment, (e) complications, (f) premorbid personality, (g) predisposing factors, (h) prevalence, (i) sex ratio, (j) familial pattern, and (k) differential diagnosis.

There is much merit in following this schema here because DSM does not reference its conclusions in any way, nor does it focus on EOS particularly. There is thus a danger that what is there could be taken as necessarily true of EOS and become part of an unsubstantiated folklore. Treatment is not addressed in DSM but will be in this paper, briefly, for completeness.

THE REVIEW

This follows the usual lines of a critical review. Studies were confined to those in English. All were reviewed directly and previous reviews cited above were used only to confirm conclusions. Studies were subject to usual methodological scrutiny. However, because of the paucity, standards have had to be relaxed somewhat, and this should be borne in mind in evaluating the findings.

The most critical methodological problem was that of diagnosis. To be admissible, the diagnosis of schizophrenia had to be based on DSM-III criteria or an approximate equivalent of a psychotic state characterized by hallucinations, delusions, or other first-ranked symptoms used in DSM. The lumping of all childhood psychoses together in the 1960s and much of the 1970s and/or rather vague or overly encompassing criteria noted above, meant that with two exceptions (Kolvin, 1971; Makita, 1966), only studies since 1975 have been acceptable. There is an old literature prior to 1960 which is less muddled and at least of historical interest (see Eisenberg, 1957; Prior & Werry, 1986).

There were only a handful of studies that qualified. Because the studies by J. Asarnow, R. Asarnow, Caplan, Russell, and Watkins all use more or less the same subject pool in varying numbers and for varying purposes, they are treated as a single set named "the UCLA group" and arbitrarily cited as Russell, Bott, and Sammons (1989) except where specific findings from individual studies apply.

The study by Makita (1966) is quoted here because, despite its informality and paucity of detail, it is clear that modern schizophrenic diagnostic

Table I. Characteristics of Studies of EOS

	Makita	Kolvin et al.	Eggers 1978 (Eggers 1989)[a]	Green et al. (Green 1986)[a]	Volkmar et al.	UCLA Group	Werry et al.
I. Diagnosis							
1. Criteria	Adult type	First rank symp Other schizp.	Bleulerian First rank,	DSM-III	DSM-III	DSM-III	DSM-III-R
2. Method	?Psych exam	?Chart review ?Psych exam Consensus	Chart review Follow up Informants	Chart review Consensus	Chart review Blind Consensus	Chart review K-SADS/DICA etc. kappa 0.88	Chart review Followup SCID Consensus checks
3. Comparison	Autism, COPDD[b]	Autism	Discards at FU (Schizoaffect)	Autism, Conduct	Autism, COPDD Schizotypal	STPD Depression & comorbidity	Discards at FU Bipolar
II. Sample							
1. Source	Ch. psych. clinic	Ch. psych. clinic	Ch. psych. clinic	Ch. psych clinic	Ch. psych clinic	Ch. psych clinic	Ch. psych clinic
2. Number of Ss	32	33	57(41)[a]	40(24)[a]	14	18-35	18
3. Sex ratio M/F	?	2.66:1	1:1.28	2.33:1	?	2.6-2.2:1	1.5:1
4. Age of onset							
Range	10-15	?7-13+[c]	7-13	5-12	7-14	3-11	9-15
5-10	2	4[c]	11	36	7	24[c](2<5)	1
11-12	1	6[c]	46	4	3	9[c]	5
13-15	29	23[c]		0	2	2[c]	12(1 @ 15)
16+	0		0	0	0	0	0
5. Social class	?	All	?	No I,II	?	I,II 64%	All
6. Country	Japan	UK	Germany	USA	USA	USA	New Zealand

[a]Parentheses refer to second study by same author(s).
[b]COPDD = Childhood Onset Pervasive Developmental Disorder.
[c]Age seen - onset not stated.

criteria were applied and it deserves recognition because it anticipated, by several years, the classic study by Kolvin (1971) which proved the most influential one in re-separating schizophrenia, autism, and other psychotic disorders in children and adolescents.

EARLY ONSET SCHIZOPHRENIA

Acceptable studies together with their main methodological features, are set out in Table I. It can be seen that most of the studies rely on informal methods, chart reviews, and consensus diagnosis by two psychiatrists. Though some kept data extractors/diagnosticians blind (e.g., Volkmar, Cohen, Hoshino, Rende, & Paul, 1988), only the UCLA group (Russell et al., 1989) observed, in addition, high-quality reliability methods, structured interview, and data capture techniques, and then not necessarily all the time or in all cases. Two of the studies (Eggers, 1978, 1989; Werry, McClellan, & Chard, 1991) were able to validate the diagnosis by long-term outcome and found substantial error rate in initial diagnosis. However, both these studies relied on diagnoses made in the past — sometimes more than 10 years previously — so that this error should not be interpreted as necessarily applying to the most recent studies which in general are more exact, especially in their diagnostic criteria.

The widely quoted study by Kydd and Werry (1981) is not included and is now repudiated as applying to EOS because the recent follow-up study (Werry et al., 1991) showed that a significant number of cases had bipolar disorder not schizophrenia. This finding of misdiagnosis of early mood disorder as EOS is not new (Bashir, Russell, & Johnson, 1987; Carlson, 1990; Joyce, 1984; Steinberg, 1985). There is reason to believe from the symptomatology, course, and family history, that the study by Eggers (1978) may still be subject to this error to some degree despite his argument to the contrary because his diagnostic methods are not described in detail. In fact, he subsequently (1989) changed about 25% of the outcome diagnoses to schizoaffective disorder. While an earlier study suggested that closer attention to mood symptoms might help prevent this error (see Carlson, 1990), the concurrence of mood disorder and EOS in some patients in the UCLA studies (J. Asarnow & Ben-Meir, 1988; Russell et al., 1989) suggests that strict adherence to DSM-III criteria may not have solved this diagnostic problem entirely.

Two other studies (Cantor, Evans, Pearce, & Pezott-Pearce, 1982; Jordan & Prugh, 1971) which appeared in the review by Beitchman (1985) were not considered suitable because the diagnostic criteria were unclear and there was insufficient detail for validation of the diagnosis. Although some of their cases were schizophrenic, there is a strong suspicion that a

significant number were not. It will be recalled that Bender came in for considerable criticism for an overliberal definition of schizophrenia in the 1960s (see Kydd & Werry, 1981) and while Cantor et al. (1982) defined a problem — that of the preverbal child — there was a retreat from the strict DSM criteria which cannot be considered legitimate in the absence of careful study including follow-up.

Sometimes studies not in the general review are cited because they make particular points such as that of Cantor et al. (1982). One of these is a study of all psychotic children and adolescents to age 19 (N = 1,084) seen for the first time in state facilities in Erie County and New York City 1968–1976 (Bettes & Walker, 1987). Though selection criteria were positive and negative schizophrenic symptoms, not diagnosis, the minimum age when first seen was 5, which makes inclusion of autistic patients unlikely. It offers valuable information on the developmental and gender aspects of schizophrenic symptoms seen in EOS and in a large sample though whether or not the subjects all had schizophrenia is unprovable.

DIAGNOSTIC ISSUES

Nosological Similarity between Adult and Early Onset Schizophrenia

The diagnosis of schizophrenia in DSM-III-R is based solely upon three criteria: symptomatology, severity of disturbance of function, and duration, so that proof of similarity must rest entirely upon demonstrating that such criteria are found in children and adolescents too.

All studies in Table II show that DSM-III-R adult-type symptomatology of delusions, hallucinations, incoherence, catatonic behavior, flat/inappropriate affect — all accompanied by marked deterioration in function and a prodrome/active/residual phase lasting 6 months or more — can be found in children and adolescents.

Thus there is general agreement among investigators that a clinical syndrome that resembles that of adult schizophrenia can be found in children and adolescents and supports a position that early onset schizophrenia should not be differentiated from the adult form — unless there is a serious problem with false negatives (see below).

Early Onset Schizophrenia as a Subcategory

Not surprisingly, concern has been expressed (e.g., Cantor et al., 1982; Caplan, Guthrie, Fish, Tanguay, & David-Lando, 1989; Volkmar et al.,

1988; Watkins, Asarnow, & Tanguay, 1988) that though the basic symptomatology may be similar, since the symptoms of schizophrenia are mostly cognitive (e.g., hallucinations, thought disorder), developmental (and intellectual) level will create differences in symptomatology. This might be thought reason for a separated subcategory of childhood schizophrenia. Subcategorization in DSM-III-R is based in all except one subcategory (residual) entirely upon which of three types of primary clinical symptomatology: paranoid, catatonic, disorganized, or all three (i.e., undifferentiated), predominate. Thus a systematic and qualitative age-dependent variation in predominant clinical symptomatology could be an argument for a separate subcategory.

What evidence then is there for age-dependent variation in predominant symptomatology? There seems to be some agreement across studies which have addressed this issue (Bettes & Walker, 1987; Eggers, 1978; Russell et al., 1989; Watkins et al., 1988; Werry et al., 1991) that well-formulated and stable delusions are less frequent in EOS especially in VEOS, though this is not unanimous (Green et al., 1984; Volkmar et al., 1988). All seem to agree that hallucinations, disorganized thinking, and flattened/inappropriate affect are characteristic of EOS, though there may be developmental differences in the type of thought disorder (Caplan et al., 1989; Caplan, Perdue, Tanguay, & Fish, 1990). Catatonic symptoms may be less frequent though the precise frequency in adults is not well described.

Only two studies (Eggers, 1978; Werry et al., 1991) actually assigned subcategories and they are in conflict, though the almost 50% of undifferentiated subtypes in the New Zealand study is more consistent with the general symptomatological picture of other studies.

In summary, EOS may show some age-dependent symptomatological patterns in which undifferentiation and disorganized thought are more characteristic than delusions especially at younger age levels, and the pattern of disturbed thinking may be somewhat different. However, such features can easily be encompassed within the existing subcategories and while probably more common in EOS, are by no means confined to it. This seems to argue against a separate subcategory. It should be noted that in general, only the UCLA group have used methods of studying symptoms that pass beyond the mere clinical and some of these (e.g., Caplan et al., 1990) hint there may be some symptomatological differences in children which are worthy of proper testing using a comparative adult sample, not merely relying on studies by others.

While the type and distribution of basic symptoms may be the same as in the various adult subcategories, so far there has not been much attention to whether or not there are *additional* symptoms peculiar to children

Table II. DSM-III-R Diagnostic Features of Studies

	Makita	Kolvin et al.	Eggers 1978 (Eggers 1989)	Green et al. Green 1986	Volkmar et al.	UCLA Group	Werry et al.
1. Delusions	?	57%	?68% (rare <10)	50%	{ All	63%	41%
2. Hallucinat.	?	81%	Frequent			83%	35%
2.1 Auditory	?	81%	Commonest	85%	?	80%	29%
2.2 Visual	?	30%	?50%	48%	?	37%	06%
2.3 Other	?	36%	Sometimes	8%	?	23%	12%
3. Thought Dis.	Yes	60%	?	80%	?	40%	24%
4. Catatonic	Yes	?60-80%	?Unusual	30%	?	?	25%
5. Flat/Inapp Aff.	Yes	>60%	?	80%	?	74%	82%
6. Changed Function	Yes	?	Yes	Yes	Yes	Yes	Yes
7. Psychotic Mood Dis. Excluded	?	?	Yes At followup	?Yes	?Yes	Yes	Yes At followup
8. Signs 6/12	?	?No	?No	?Yes	?Yes	Yes	Yes
9. Prodrome	?	?Unusual	?	?	?	50% (>8)	90%
10. Residual Phase	?	?	Most	?	?	?	Some
11. Subtypes							
11.1 Catatonic	A few	?	?4%	?	?	?	25%
11.2 Disorgan.	Most	?	?14%	?	?	?	6%
11.3 Paranoid	?	?	?68%	?	?	?	13%
11.4 Undiff.	?	?	?14%	?	?	?	47%

which might warrant a special subcategory such as is the situation, for example, with the subcategory of residual schizophrenia.

False Negatives

Several authors (Cantor et al., 1982; Caplan et al., 1989, 1990; Kolvin, 1971; Reid, 1989; Volkmar et al., 1988; Watkins et al., 1988) have defined two areas of concern that are largely peculiar to children or the domain of child psychiatry like mental retardation.

Absence or Immaturity of Language. The first is that positive symptoms of schizophrenia are dependent on language and so in those children too young or too handicapped to have language, the diagnosis could be impossible to make. Immaturity of language and cognition may also be a problem, since some of the observed phenomena in adults require functions like logic and listener-sensitive skills which develop only in later childhood (Caplan et al., 1989, 1990). In fact, there are preliminary indications that there is some relationship between chronological (and mental) age and positive symptoms (Bettes & Walker, 1987; Caplan et al., 1989, 1990). So far, the earliest age at which most investigators agree that schizophrenia has been diagnosed is 6–7 (Eggers, 1978; Green et al., 1984; Kolvin, 1971; Volkmar et al., 1988, Werry et al., 1991), though there has been one case reported at 5 years 7 months (Green & Padron-Gayol, 1986) and one at age 3 (Russell et al., 1989). The studies by Caplan et al. (1989) show that most of the cognitive positive symptoms are demonstrable as early as 5 years of age but below that remains an open question. There is also the problem of those older than 5 who lack sufficient language to report schizophrenic symptoms. This must thus remain as a possible cause of false negatives in the severely mentally retarded or severely autistic (Reid, 1989). Only careful studies (including long-term follow-up) of children without or with very restricted language who show a marked change in function at some point after age 5, can answer this question.

Insidious Onset. As all studies show, EOS schizophrenia, especially VEOS, is often of insidious onset and the criterion of marked deterioration in function may prevent or make difficult the diagnosis even when the symptoms are present. Cantor et al. (1982), Kolvin (1971), Volkmar et al. (1988), and Watkins et al. (1988) felt this was a problem but Green et al. (1984) did not.

However, this problem is not confined to children but bedevils adult psychiatry as well and has led to the notion of simple schizophrenia and of schizophrenia spectrum disorder (see Caplan et al., 1990, and differential diagnosis below).

OTHER FEATURES OR CORRELATES

The question here is to what extent children and adolescents diagnosed as having schizophrenia using adult criteria have the characteristic correlates of the disorder as found in adults (see Table III).

Associated Features

This area is not well reported but what there is suggests that as in adult schizophrenia as reported in DSM-III-R, a wide variety of associated symptoms, including antisocial and affective, can be expected.

Age at Onset

The youngest age reported so far and that very recently, is 3 (Russell et al., 1989) and before that 5 years 7 months (Green & Padron-Gayol, 1986). Since the study of schizophrenia in children is recent and sparse, and there are special diagnostic problems very early (discussed above), it seems premature to apply any age limitation to the diagnosis. It is noticeable that the age limit seems to be creeping down with the evolution of diagnostic sophistication in child psychiatry, though onset before 6 should be considered to be requiring more replication. Cases before age 13 (VEOS) are infrequent though large urban area centers in the United States with a special interest in psychotic children (Green & Padron-Gayol, 1986; Russell et al., 1989; Volkmar et al., 1988) show that it occurs frequently enough to be a routine consideration in the differential diagnosis of children showing a marked deterioration in behavior. There is a significant increase in frequency after 11–12 (Eggers, 1978; Kolvin, 1971; Makita, 1966; Werry et al., 1991) though there is a paucity of studies in the 13–15 age group. As noted, there has been a tendency to define puberty by age rather than by physical state and so it is quite unclear at the moment whether this increase is related to *age* or to *puberty*.

Onset and Course

There is agreement that onset is more likely to be insidious in VEOS (J. Asarnow & Ben-Meir, 1988; Green & Padron-Gayol, 1986; Kolvin, 1971) but there is conflict about adolescence, with Eggers (1978) and Werry et al. (1991) showing high rates of acute onset (defined as less than 1 year) and Kolvin (1971) a preponderance of insidious onset.

It is often stated that the earlier the onset the more likely the course to be chronic; but there are very few outcome studies and even these show that VEOS is not always associated with a poor outcome (Eggers, 1978; Werry et al., 1991). Since VEOS is highly associated with insidious onset, which is a known ominous predictor (Westermeyer & Harrow, 1988), it is possible that there has been in the past confounding of insidiousness and age of onset (Kydd & Werry, 1981).

There has been little study of adolescent-onset schizophrenia but what there is suggests it runs a rather similar variety of courses (recovery, relapsing, chronic) as do adult forms (Eggers, 1978, 1989; Werry et al., 1991). There are insufficient studies to say if there is any greater tendency to chronicity, the two studies of outcome (Eggers, 1978, 1989; Werry et al., 1991) not being in agreement (49% vs. 83%). The New Zealand study supports a high level of chronic disability, though at 83%, this was only slightly more than adult figures of around 75% (Westermeyer & Harrow, 1988).

Impairment

There appear to be no features in EOS beyond those listed in DSM-III-R, as reported in all studies so far, except possibly issues related to education. Given that schizophrenia is known to produce profound cognitive impairment in adults (Aylward, Walker, & Bettes, 1984) this seems only a social-development variation, not a distinctive feature. As already noted, because of the increased association with poor premorbid function in VEOS and possibly EOS in general, plus the necessarily longer impact on life-span, it is likely that end impairment will be worse; but unless duration is partialled out and *change* in function the dependent measure used, it will be unclear as to whether this is due to the disorder itself, to premorbid features, or longer duration.

Complications

In adults, the lifetime risk of suicide is about 15% with most occurring within the first 10 years of the illness (Cohen, Test, & Brown, 1990). In EOS, the risk of suicide or accidental death directly due to the psychosis appears to be between 5–15% (Eggers, 1978; Werry et al., 1991). Numbers are too small and follow-up periods too short in some subjects to make precise comparisons with adult figures beyond noting that suicide is a definite risk.

Premorbid Personality

The possible implications of premorbid personality are twofold: predisposing/etiological (see below) or in influencing treatment and outcome (see above). There is clear agreement that in EOS there is a high frequency of premorbid abnormality (54–90%) and the earlier the onset, the more likely the abnormality (J. Asarnow & Ben-Meir, 1988; Eggers, 1978; Green & Padron-Gayol 1986; Kolvin, 1971; Watkins et al., 1988). There is also agreement that a type of abnormality often seen is that of an odd, anxious, isolative child often called "schizoid" or schizotypal which is consistent with studies in adults (see R. Asarnow, Asarnow, & Strandburg, 1989) and the idea of schizophrenia spectrum (J. Asarnow & Ben-Meir, 1988). It is difficult to tell whether these abnormalities are more common in EOS since direct comparison with properly matched adults have not been done and DSM-III-R is rather vague saying only that abnormality is often described.

Predisposing Factors

The etiology of schizophrenia is unknown though views range from totally biogenic to the result of a complex and variable biopsychosocial interaction (see Carpenter, 1987; Goldstein, 1987). As Carpenter (1987) pointed out, in the absence of good knowledge, medical science proceeds by looking for correlates. DSM may therefore be considered a little presumptuous by arbitrarily listing the following correlates as "predisposing" though the adult literature especially high-risk research (on offspring of schizophrenic parents) suggests that some of the cognitive and brain damage/dysfunctional indicators below may be true vulnerability factors (Carpenter, 1987; Goldstein, 1987). Even so, they are found most often in persons without schizophrenia. There is also the problem that if the factor is a feature of the disease (e.g., cognitive dysfunction), its role in predisposition may be difficult to establish except in expensive and time-consuming longitudinal risk studies or family pedigree studies which restrict findings to familial types of schizophrenia, probably less than 15% of the total (Goldstein, 1987).

Social Class. All studies of EOS are of clinic patients with a preponderance of inpatients carrying presumed selective referral bias; so that it is not possible to say whether there is any increase in lower socioeconomic groups as noted in DSM-III-R, though there is support for this in some studies (Green & Padron-Gayol, 1986; Kolvin, 1971) but quite the reverse in others (Russell et al., 1989; Werry et al., 1991).

Cognitive and Intellectual Dysfunction. The hypothesis of schizophrenic spectrum disorder posits a predisposing (familial) cognitive dysfunction (R. Asarnow et al., 1989) as one of the fundamental vulnerabilities. This has been the subject of only one study in EOS that lent support (J. Asarnow, Goldstein, & Ben-Meir, 1988). In some studies, subjects in the mentally retarded range have been excluded (Bettes & Walker, 1987; Russell et al., 1989). Where it is not, lowered IQ (in the retarded or borderline range) has been found in 10–20% of patients in several studies, which seems increased above what would be expected by chance (Eggers, 1978; Green & Padron-Gayol, 1986; Kolvin, 1971; Reid, 1989; Werry et al., 1991). Without comparative studies of other diagnostic groups from the same clinics, caution in interpreting this is needed though it is entirely consistent with other research in schizophrenia which shows lowered IQ in preschizophrenic children and adolescents (Aylward et al., 1984). The suggestion that mental retardation established after the onset of the disorder may be secondary to the schizophrenic process (Aylward et al., 1984; Bettes & Walker, 1987) is not supported by the observations of poor academic progress premorbidly in the majority of such cases in one study of EOS (Werry et al., 1991).

Brain Damage/Dysfunction. There is good evidence to show that schizophrenia is sometimes associated with evidence of brain damage such as ventricular enlargement (Meltzer, 1987) which in some cases can reasonably be inferred to have preceded the onset of the disorder. High-risk research has also shown that schizophrenia has a probable association with preexisting brain damage/dysfunction of a "softer" neurodevelopmental type (R. Asarnow et al., 1989; Goldstein, 1987). In EOS, any association with brain damage is not supported when criteria are properly "neurological" (Kolvin, 1971; Werry et al., 1991), but it is if neurodevelopmental indicators such as lowered IQ, language, and other developmental delays/abnormalities are combined and all admitted in evidence (Kolvin, 1971; Watkins et al., 1988; Werry et al., 1991). Further, there is reason to believe that the frequency of neurodevelopmental anomalies is likely to be underreported as it depends on the punctiliousness of obtaining accurate information in the preschool years and on the age at which subjects are seen. No study seem to match that by Watkins et al. (1988) in this respect and it reports the highest frequency.

Psychological Factors. As Goldstein (1987) pointed out, most research in this area has concentrated on stressors presumed to come from family relationships and, despite years of research (much of it of poor quality), any predisposing relationship to schizophrenia is still unclear though not disproven. In EOS, there is too little research though there are some studies that would be supportive of further investigation (J. Asarnow et al., 1988; Kolvin, 1971; Eggers, 1978; Werry et al., 1991).

Table III. Nondiagnostic Descriptive Features

	Makita	Kolvin et al.	Eggers 1978 (Eggers 1989)	Green et al. Green 1986	Volkmar et al.	UCLA Group	Werry et al.
1. Associated features	?	Perplex., rages Stereotyp. Behav.	12% Crimes	Wide variety	?	30% Conduct 37% Mood	?
2. Age of onset	10-15	?7-13+	7-13	5-12	7-14	3-11	9-15
3. Onset	?	Acute 33% (<11 = 28%)	Acute 90% (10 = 36%)	Acute 25% (<11 = 10%)	? ?	Acute 10%	Acute 90%
4. Course	?	?	50% Good/fair 11 Most chronic	?	?	?	50% GAF↓20 points
5. Impairment	?	Severe	66% (15 yr on)	Severe	?	Mn GAF 29	93% GAF<51
6. Complications	?	?	5% Suicide 15 Year FU	?	?	?	5% Suicide
7. Premorbid personality		87% Odd 58% Schizoid.	54% Introverts (59%)	80% abnormal (after age 2)	?	86% Abnormal ADD/CD 40% 26% "Odd"	70% Abnormal Odd, solitary
8. Predisposing							

8.1 Develop disord.	?	49%	?	?	?	Most till 3-4	?
8.2 IQ 70-80	?	13%	?10%	18%	?	Excluded	22%
8.3 Stressors	?	42%	22%	?	?	?	?
8.4 Disturbed fam.	?	62%	58%	?	?	79%	33%
9. Sex ratio M/F	?	2.66:1	1:1.28	2.33:1	?	2.6-2.2:1	1.5:1
10. Fam Hx schiz.	?	11% parent	42% all	?	?	?	?18% 1st deg.
11. Fam. Hx Mood D	?	?	18% all (7%)	?	?	?	?25%
12. Differential							
12.1 Autism	Age 3	Kanner triad valid	—	DSM-III valid None autistic	DSM-III valid None autistic	26% "Autistic features"	None autistic
12.2 Schizotypal person dis.	—	—	—	—	Less severe & no change	Less severe & no change	Less severe & no change
12.3 Mood with psychosis	—	Episodic mood in a few	46% cyclothymic episodes (28% schizoaffect at re-review)	—	—	37% Depressed comorbidly	20% Bipolar at FU (discarded)

Prevalence

No good epidemiological data on EOS are available though clinic figures reviewed here suggest that VEOS is rare and significant numbers are found only in megalopoles like New York or Los Angeles. EOS is infrequent though rising in prevalence with each year from 13 on (Bettes & Walker 1987, Eggers, 1978; Werry et al., 1991).

Sex Ratio

In adults, sex ratios are equal, though the mean age of first admission, and presumptively of onset, in females is about 7 years older (34) than in men (27) (Zigler & Levine, 1981). In contrast, males outnumber females in all studies except one (Eggers, 1978); but there is a distinct age effect, in that those reporting the highest ratios of around 2.5:1, except in one case (Kolvin, 1971), are of VEOS (Bettes & Walker, 1987; Green & Padron-Gayol, 1986; Russell et al., 1989). Studies of the 13- to 15-year age group suggest that parity is getting closer (Bettes & Walker, 1987; Eggers, 1978; Werry et al., 1991). It is of interest that in EOS in general, gender may not affect symptomatology (Bettes & Walker, 1987).

Familial Pattern

Pedigree and twin studies of schizophrenia have consistently confirmed that in some cases there must be a genetic basis though the frequency in first-degree relatives is under 10–15% (Goldstein, 1987). Studies of EOS reporting this (Eggers, 1978, 1989; Kolvin, 1971; Werry, et al., 1991) find an increased family history of schizophrenia but the small samples, varying inclusions of first- and second-degree relatives and the unstated or informal methodology used, make exact estimates and hence comparisons with adult schizophrenia uncertain. However, Hanson and Gottesman (1976) did feel two studies were adequate for proper genetic analysis and found some evidence in favor of a raised frequency (possibly double) in EOS. It is also noteworthy that both Eggers (1978) and Werry et al. (1991) reported increases in mood disorders in EOS families too. The reported frequency of depressive symptoms (J. Asarnow & Ben-Meir, 1988) or even frank mood disorder (Russell et al., 1989), the cycloid nature of some of Eggers cases, and the misclassification of some EOS bipolars as schizophrenic (Werry et al., 1991), all suggest that this increase in mood disorders in families may reflect some persistent diagnostic problems with early onset psychoses rather than a true bill.

TREATMENT

DSM does not discuss this and since the emphasis here is on taxonomy of schizophrenia, treatment is covered only briefly. Reviews by Kane (1987) of adult schizophrenia and McClellan and Werry (1991) of EOS should be consulted for more detail. As McClellan and Werry pointed out, there is very little research on treatment in EOS and therefore it is necessary to extrapolate from the assumption that EOS and adult schizophrenia are the same disorder or, more likely, group of disorders.

Kane (1987) emphasized that to treat schizophrenia one must have a good grasp of the time frame of schizophrenia (weeks or months), its phases (prodromal, active, recuperative/recovery, and residual), and its relapsing tendency.

Pharmacotherapy with antipsychotic (neuroleptic) drugs is the cornerstone of treatment. In spite of what is believed, there is no evidence to support the view that pharmacotherapy is ineffective in EOS and the very few studies made suggest the contrary (see McClellan & Werry, in press). No active neuroleptic has been shown to be any more effective than any other against the disorder, particular subtypes or symptoms, or individuals (Kane, 1987). The persistent failure historically of any newly introduced antipsychotic drug to prove its superiority, suggests that skepticism about putative advantages of clozapine in refractory cases is prudent. However, side effects do differ in number and type (primarily preponderance of atropinic or of extrapyramidal) and individual drugs may be preferred on this account rather than on efficacy. Dosage is a difficult issue which has been surprisingly poorly researched. There is a threshold level but high-dose regimens (above about 600 mg/70 kg in chlorpromazine equivalents) are now shown to be no more effective than lower ones. Higher doses may be needed during the active phase than during recovery or for maintenance and for short-term control of very disturbed behavior. While neuroleptics do not cure the disorder they can mitigate acute psychotic symptoms and prevent relapses in a majority. There are some patients who respond poorly and some do just as well without medication, but they are a minority. Failure to understand the time frame of the disorder results in unnecessary changes in type of medication, high dosage, polypharmacy, resort to ECT, and premature cessation of medication. The most serious problem with medication is compliance. Serious side effects like neuroleptic malignant syndrome are rare with the exception of tardive dyskinesia which is usually mild and apparently nonprogressive in the majority of cases (Kane, 1987). Older age is the variable most clearly associated with severity of tardive dyskinesia.

In contrast to the clear-cut role of medication, the role of psychosocial treatments is vexatious because research in this area has been of poorer quality than in pharmacotherapy (Goldstein, 1987; Kane, 1987). There has also been a marked shift away from trying to cure schizophrenia toward mitigating the disability and preventing relapse, mostly along behavioral lines. There is enough evidence to this point to sustain the commonsense belief that rehabilitation-oriented psychosocial management is worth prosecuting. The effect of family interventions in preventing relapse may have promise, as may the hypothesis of some synergistic interaction between medication and psychosocial interventions in some patients (see Goldstein, 1987).

DIFFERENTIAL DIAGNOSIS

Only concerns particularly relevant to EOS are discussed here. It should be pointed out that DSM-III brought a new era to clinical diagnosis in which criteria were made explicit. It is impossible to remember exactly what the criteria for even common disorders are and accurate diagnosis is dependent on a willingness by clinicians to accept this fact as given and *use the manual. not their memories* in diagnosis. It also calls for punctilious history-taking and examination. The advent of the personal computer has opened the door to both a more systematic history-taking and examination derived from structured interviews developed for research and epidemiological studies, and to diagnostic decisions trees which help to keep the diagnoser "honest." Good software for both these is becoming increasingly available. Although no substitute for clinical judgment, they are important aids to accurate diagnosis.

Autism

This is distinguished by the absence or transitoriness, insignificance, or insufficiency of the key positive schizophrenic symptoms as opposed to the prevasiveness and predominance of the characteristic language patterns, unrelatedness, and other key symptoms of autism (Green et al., 1986; Green & Padron-Gayol, 1984; Kolvin, 1971; Volkmar et al., 1988). Onset before age 2–3 and the absence of a normal period of development are also indicative of autism, though some schizophrenic children have been abnormal since infancy (Watkins et al., 1988). The premorbid abnormality is less pervasive and developmentally catastrophic in schizophrenia. There is probably less difficulty distinguishing autism from schizophrenia than

from schizotypal disorder where "oddness" is more characteristic than schizophrenic symptoms (see below).

Bender believed that autism and schizophrenia were simply developmental variations of the same disorder (see Kydd & Werry, 1981) but this view was subsequently soundly rebutted by Rutter (1972) and made official in ICD-9 and DSM-III. As noted above, Cantor et al. (1982) seemed to argue for a partial return to Bender's position or that of DSM-II on the developmental grounds that schizophrenic symptoms cannot exist in preverbal children and thus that psychosis may be schizophrenic. This issue has been discussed in more detail above.

However, whether or not children with autism can subsequently become schizophrenic, either independently or by having a greater vulnerability, is another issue. DSM seems to admit that this can occur by the addition of a special diagnostic criterion (#F) which emphasizes that if autism has been diagnosed previously, hallucinations or delusions must now be prominent.

There is no reason à priori that the two should not coexist (Watkins et al., 1988) coincidentally (though given the low frequency of schizophrenia and lower frequency of autism, this would be rare), or indeed, if early brain damage facilitates the onset of both disorders, the risk could well be raised. In fact, there are now reports that both disorders may coexist (Petty, Ornitz, Michelman, & Zimmerman, 1984; Watkins et al., 1988) but that the onset of schizophrenia will be much later than that of autism (ordinarily after age 5). Such reports are rare and the Yale group (F. R. Volkmar & L. J. Cohen, personal communication, 1990) have not found any schizophrenia in 163 cases of autism. The UCLA group are unique in reporting a significant premorbid rate of autism or childhood onset PDD (COPDD) (Watkins et al., 1988) but recently this seems to have been muted as less than sufficient for the full diagnosis of autism (Russell et al., 1989). Coexistence of autism and schizophrenia should be regarded as theoretically possible but requiring replication.

Schizotypal/Schizoid Disorder

This should not be a problem if DSM-III-R criteria are followed, since schizotypal disorder lacks the requisite active phase with positive symptoms. Occasionally, it may present some difficulty especially where there is a lifelong history of abnormality and/or continuing deterioration with no clear point of onset and/or presence but insufficiency of positive symptoms (J. Asarnow & Ben-Meir, 1988; Cantor et al., 1982; Caplan et al., 1990; Volkmar et al., 1988). The problem in EOS is no different from

that of schizotypal disorder in general, except for the possibility of onset in preverbal children or those without language precluding the appearance of some of the positive symptoms necessary for the diagnosis of schizophrenia (Cantor et al., 1982; Volkmar et al., 1988). In doubtful cases there could be merit in a diagnostic trial of antipsychotic medication and in the development and employment of more precise methods of studying positive symptoms (see Andreasen, 1987; Caplan et al., 1989, 1990).

Mood Disorders

There is now good evidence that when the presentation of major depression or mania in adolescence or childhood is accompanied by psychosis, the differential diagnosis from schizophrenia may be very difficult especially in bipolar disorder (Bashir et al., 1987; Carlson, 1990; Joyce, 1984; Steinberg, 1985; Strober, Hanna, & McCracken, 1989; Werry et al., 1991) since there is a large overlap in schizophrenic and affective symptomatology (Apter, Bleich, & Tyano, 1987; Bashir et al., 1987; Carlson, 1990; Russell et al., 1989). The error operates largely to misclassify mood disorder as schizophrenia (Bashir et al., 1987; Carlson, 1990; Joyce, 1984; Werry et al., 1991). Rules for the differentiation of mood disorder and schizophrenia are given in DSM-III-R. Strober et al. (1989) emphasize premorbid social withdrawal/anxiety, insidiousness of onset, mood incongruent delusions/hallucinations, and protractedness as characteristic of schizophrenia. Homotypic family history may be helpful in bipolar disorder (Werry et al., 1991). Nevertheless, the picture in children and adolescents may become clear only with time and calls for punctilious follow-up of all cases of EOS (Werry et al., 1991).

Organic Disorders

These are best diagnosed by finding a clear-cut physical cause, but this is not always easy. Dementias in childhood are rare and usually characterized by marked intellectual decline and neurological signs, rather than positive symptoms (see Gudex & Werry, 1990). Delirium is more likely to be confused with schizophrenia since hallucinations and ill-formed delusions may be present, and not all children with delirium are clearly seriously physically ill. However, with careful examination, including neuropsychological testing where necessary, it will be found that disorientation is not present in schizophrenia and intellectual function is better preserved though not unaffected (see Aylward et al., 1984). Drug-induced states are evanescent, whereas untreated schizophrenia is not. On the whole though,

psychiatric aspects of delirium and dementia have been little studied in children (Gudex & Werry, 1990) so their phenomenology is unclear.

Other Psychoses (Psychoses Not Elsewhere Classified)

This is a heterogeneous group of disorders described below.

Schizophreniform Disorder. This disorder resembles schizophrenia but lacks only the 6-month duration criterion (for any combination of prodromal, active, and residual phases). Of course, many schizophreniform disorders subsequently prove to be schizophrenia after 6 months of observations has elapsed or upon recurrence.

Brief Reactive Psychosis. This psychosis requires only one of the positive symptoms of incoherence, nonspecific delusions or hallucinations, or catatonic behavior, substitutes emotional turmoil for social dysfunction, adds two new requirements (for a clear, obvious, and major stressor and adds three exclusionary criteria: a duration of greater than 1 month before full recovery, a premorbid schizoptypal personality, and a prodromal phase). Great care is needed in making this questionable diagnosis since there is a close similarity with the criteria for schizophrenia not helped by the substitution of an internal state common in acute schizophrenia (emotional turmoil) for its external consequences (social dysfunction), allowing the admission of stressors that may result from the onset of schizophrenia, and a duration that is possible in the first episode of what turns out subsequently to be schizophrenia.

Schizo-Affective Disorder. This term has a variety of meanings but the one used in DSM requires that the patient must have had at one time, *both* a diagnosable mood and schizophrenic disorder concurrently *and* at another time, psychotic symptoms without mood disorder. As already noted, distinguishing between mood disorder and schizophrenia is sometimes very difficult, and in a sense, schizo-affective disorder represents the point at which this differentiation becomes impossible (see Eggers, 1989; Werry et al., 1991).

Psychosis Not Otherwise Specified (Atypical Psychosis). This is a situation when there is psychosis but not sufficient criteria to meet one of the other categories. Whether this is a "real" category in its own right, rather than one in which some key features of another disorder are lacking but will become clear in time, remains to be established. Some of these cases will prove to be malingering or dissociative states. Inconsistent and outlandish symptomatology and/or rapid fluctuations between psychotic and normal states should raise suspicion.

CONCLUSIONS

This review argues for abandoning the vague terms of adolescent, childhood, and prepubertal schizophrenia by the substitution of an age-related category of Early Onset (under 16 or 17 or some similarly agreed limit) and a subcategory of EOS, Very Early (before 13), though there would be no objection to the use of prepubertal if it were based on proper physical criteria rather than on age. Studies of EOS are infrequent and most are incomplete in details. However, they suggest that EOS seems similar to later forms of schizophrenia apart from greater male predominance (about 2.5:1), some developmental variations in symptomatology (less differentiated), and possibly, an increased frequency of family history of schizophrenia, premorbid personality, and neurodevelopmental abnormalities — especially in VEOS. Autism and schizophrenia may possibly occur together, though rarely, and of different times of onset. The lower limit of onset of schizophrenia has been increasingly challenged and there seems little reason at this stage to posit a lower limit. There may be some false negative errors in the diagnosis of EOS especially before age 6 because of the requirement of a significant change in function and in preverbal, retarded, or young patients because of the language-based nature of some of the critical diagnostic criteria; but such criteria probably do less harm to research and clinical practice than more liberal ones that run the risk of including false positives where the real diagnosis was schizotypal or schizoid personality disorders, since this seems to be a much more common state than true schizophrenia (e.g., Volkmar et al., 1988). Early onset bipolar disorder clearly presents the major problem in differential diagnosis with the error heavily in favor of misdiagnosing bipolar disorder as schizophrenia (over 50% error rate in the Werry et al., 1991, study). It is crucial that clinicians and researchers be aware of this problem. There are insufficient data to make firm judgments on a number of nondiagnostic issues such as epidemiology, family history, outcome, and response to antipsychotic drugs. In the meantime, especially in management, it is prudent to assume the similarity of, and extrapolate from, adult to early onset schizophrenia. It is plausible that EOS will prove more homogeneous in etiology and with less time for adventitious distortions and hence obfuscations of brain function and structure. On these grounds, it is an heuristic subgroup for research. Because of the infrequency of EOS, there is a need for well-designed, comprehensive, multicenter studies and to establish outcome, for prospective studies which will make predictors of outcome more discernible.

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