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Increased developmental deviance and premorbid dysfunction in early onset schizophrenia

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Abstract

Abnormal neurodevelopment and poor premorbid function have been described in schizophrenia. It is unclear whether abnormalities in these domains are increased in patients with early onset schizophrenia (EOS; onset before the 18th birthday) and whether they act to precipitate the earlier onset of the disorder. To address these questions, we collected information based on maternal interviews about the premorbid function of 40 adolescents with recent onset schizophrenia and an equal number of healthy controls using the Developmental Scale Score, the Premorbid Schizoid and Schizotypal Trait Scale (PSST) and Premorbid Adjustment Scale (PAS). Data on the PSST and PAS were also available in 54 patients with adult onset schizophrenia (AOS; onset after the 20th birthday). Compared to healthy controls, EOS patients had (a) delayed speech milestones, difficulties in reading and spelling and greater overall developmental deviance; (b) poor premorbid adjustment in childhood, which became even more deviant in adolescence particularly in boys and (c) more schizophrenia spectrum traits. Both premorbid adjustment and personality traits were more abnormal in patients with increased developmental deviance suggesting the possibility that they represent different manifestations of ongoing abnormalities in developmental processes. EOS patients had more impaired premorbid adjustment in adolescence and schizophrenia spectrum traits compared to AOS cases. Age of onset was related to developmental deviance, premorbid schizophrenia spectrum traits and childhood adjustment in EOS patients only.
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1. Introduction

The neurodevelopmental hypothesis of schizophrenia is based, at least in part, on the presence of premorbid impairments seen in childhood and adolescence in individuals who later develop schizophrenia. Studies of adult onset schizophrenia have found evidence of developmental delay mostly in speech and language (Ambelas, 1992; Jones et al., 1994), motor deficits (Walker and Lewine, 1990; Walker, 1993), poor premorbid social functioning (Watt, 1972; Watt and Lybensky, 1976; Jones et al., 1994; Done et al., 1994; Olin and Mednick, 1996; Cannon et al., 2001) and increased schizophrenia spectrum traits (Foerster et al., 1991; Cannon et al., 2001).

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Aberrant neurodevelopment may be even more relevant for schizophrenia with onset in childhood or adolescence (early onset schizophrenia (EOS)). Kolvin et al. (1971), in his seminal work in 1971 on 33 children with Late Onset Psychosis (equivalent of the current concept of EOS), found that 87% of them were premorbidly odd and had developmental delays nearly exclusively in speech. More recent studies of EOS have consistently reported abnormalities in speech, language and motor development (Watkins et al., 1988; Alaghband-Rad et al., 1995; Hollis, 1995; Nicolson et al., 2000), premorbid social deviance ranging from disruptive behaviour to withdrawal (Watkins et al., 1988; Russel et al., 1989; Alaghband-Rad et al., 1995; Hollis, 1995; Nicolson et al., 2000) and difficulties with academic performance (Alaghband-Rad et al., 1995; Nicolson et al., 2000). However, the issue of increased prevalence of social and personality difficulties in EOS as compared to adult onset schizophrenia has not been directly tested.

The evidence summarised above confirms the presence of premorbid impairment in several domains in a substantial number of patients with EOS. However, there are several key issues that are still unresolved. The aim of the present study was to address three questions: (a) whether impairments in development, social adaptation and aberrant personality traits are more prevalent in EOS compared to adult onset schizophrenia; (b) whether they occur independent of each other and (c) whether abnormalities in these domains precipitate an earlier onset of schizophrenia. To address these questions, we studied adolescents with EOS as neurodevelopment may have a more salient role in triggering schizophrenia at an unusually early age.

2. Methods

2.1. Subjects

2.1.1. Patients

Forty adolescents fulfilling criteria for schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders: Fourth edition (DSM-IV; American Psychiatric Association, 1994) were recruited over a 3-year period from adolescent inpatient units in south London. All admissions with psychosis were assessed as described below, and 73% of the patients were included in the final study sample.

2.1.2. Healthy comparison subjects

Forty subjects, without a personal history of psychiatric disorder or family history of psychosis, were recruited from the community via advertisement. They were matched to the EOS patients on age (within 6 months), gender and parental socio-economic status.

EOS and control subjects were excluded if they had (a) current neurological disorders or family history of hereditary neurological disorders, (b) a history of head injury resulting in loss of consciousness and (c) alcohol or substance abuse in the preceding 6 months. Patients were also excluded if they had a comorbid DSM-IV Axis 1 disorder.

EOS patients and comparison subjects were recruited as part of the Maudsley Early Onset Schizophrenia Study, which examines the clinical and neurobiological underpinnings of schizophrenia with onset before the age of 18. After complete description of the study to the subjects, and the parents of subjects below the age of 16, written informed consent was obtained.

2.1.3. Adult onset schizophrenia (AOS) comparison subjects

Fifty-four patients fulfilling DSM-VI criteria for schizophrenia were also selected from a database of 79 schizophrenic patients who had been recruited from local services and voluntary organizations for other studies conducted in our section. They were selected based on their age of onset of psychosis (after the 20th birthday) and on the availability of information regarding premorbid function and personality obtained by the same scales as those used in the EOS sample.

2.2. Assessment

2.2.1. EOS patients

Diagnoses were made on the basis of interviews by qualified psychiatrists, medical records, and information from family members and treating physicians. Age of onset of schizophrenia was based on the age when patients first clearly manifested either delusions or hallucinations. Psychopathology was assessed using

the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1989).

2.2.2. Healthy comparison subjects

These were selected following parental interview either in person or over the phone and personal interview of the subjects.

Confirmation of diagnosis or its absence was based on the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First et al., 1997). For those subjects under the age of 16 (21 controls and 18 patients), the interview was supplemented by the KID-SCID (Matzner et al., 1997).

2.2.3. AOS patients

For these patients, diagnoses were also based on personal interviews, medical records, and information from family members and treating physicians. Confirmation of diagnostic status in these patients was based on either the SCID or the Schedule for Affective Disorders and Schizophrenia- Lifetime Version (SADS-L) (Spitzer and Endicott, 1978).

Parental socio-economic status was determined for all subjects according to the Standard Occupational Classification (Office of Population Censuses and Surveys, 1991).

For all subjects (EOS and AOS patients and controls), information regarding premorbid development was based on maternal interviews. Premorbid function was assessed using the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982). This scale assesses premorbid function in childhood (up to the age of 11) and in adolescence in the areas of social interaction, peer relationships, scholastic performance, and adaptation and interests using an 8-point scale (0–7) of increasing deviance with explicit anchor points. The original scale contains the additional item of psychosexual adaptation in adolescence for subjects over the age of 16, which was not included, as it did not apply to the majority of the EOS sample.

Premorbid Schizoid and Schizotypal Traits (PSST) were assessed on a seven-item scale, where each item is rated on a 4-point (0–3) scale of increasing deviance using explicit anchor points (Foerster et al., 1991). The items cover sociability, demonstrative affect, suspiciousness/sensitivity, ideas of reference/perceptual distortions, speech and antisocial behaviour as a solitary or peer-related activity.

In addition, mothers of EOS cases and controls were asked about the age when their children spoke their first words, walked unaided, and achieved bladder and bowel control. They were also asked to complete the Developmental Scale that assesses speech, motor function, enuresis, encopresis and reading difficulties. For each domain, a rating of 0 suggested no problems reported by the mother, a rating of 1 denoted the presence of problems as shown in Table 2, and a rating of 2 was reserved for those children who had been referred to professionals for their developmental problems. In order to reduce the number of comparisons, children with ratings of 1 or 2 were grouped together.

2.3. Statistical analysis

Pearson's χ^2 and Student's *t*-tests were used to compare the distribution of categorical and continuous data, respectively, between the different groups.

2.3.1. Comparisons between EOS subjects and controls

Univariate analysis of variance was used to compare differences in developmental milestones with diagnosis and gender as factors. Multivariate analysis of variance was used to compare the subjects' scores on PAS and PSST items with diagnosis, gender and total developmental score as independent factors. General Linear Model Repeated Measures analyses were used to examine within subject changes in PAS items' scores from childhood to adolescence with gender, diagnosis and developmental score as between subject effects.

2.3.2. Comparisons between EOS and AOS subjects

Multivariate analysis of variance was used to compare EOS to AOS patients' scores on PAS and PSST items with group and gender as independent factors.

2.3.3. Predictors of age of onset

The relationship of the total developmental score, the total scores on the PAS for childhood and adolescence and PSST with age of onset was examined using multiple regression analyses separately in EOS and AOS patients.

3. Results

3.1. Demographic characteristics

There were no differences in age ($t = -0.4$, $df = 78$, $p = 0.6$), gender (Pearson's $\chi^2 = 0.2$, $df = 1$, $p = 0.5$), handedness (Pearson's $\chi^2 = 2.2$, $df = 2$, $p = 0.3$) or parental social class (Pearson's $\chi^2 = 4.9$, $df = 4$, $p = 0.2$) between EOS subjects and controls. AOS patients were significantly older than EOS patients ($t = 14.0$, $df = 92$, $p = 0.0001$), but did not differ in gender distribution (Pearson's $\chi^2 = 0.2$, $df = 1$, $p = 0.6$), handedness (Pearson's $\chi^2 = 1.1$, $df = 2$, $p = 0.1$) or parental social class (Pearson's $\chi^2 = 5.0$, $df = 4$, $p = 0.2$) (Table 1).

3.2. Clinical characteristics

EOS patients had a significantly earlier age of onset of psychosis ($t = 12.1$, $df = 92$, $p = 0.0001$). Thirty-two EOS patients were on regular antipsychotic medication, while eight were medication-free at the time of assessment. AOS patients were all on antipsychotic medication.

3.3. Comparison of EOS subjects to controls

3.3.1. Early development

Univariate analysis of variance with diagnosis and gender as factors and the mean age subjects reached developmental milestones for speech, walking, bladder and bowel control as independent variables showed a significant effect of diagnosis only for speech ($F = 4.70$, $df = 1$, $p = 0.03$). There was also a significant effect of gender ($F = 4.19$, $df = 1$, $p = 0.04$) and gender by diagnosis interaction ($F = 4.40$, $df = 1$, $p = 0.04$) for the same variable, both in favour of females.

The subjects' scores on the developmental scale are shown in Table 2. The two groups differed significantly in their reading ability (Pearson's $\chi^2 = 4.21$,

Table 1
Demographic characteristics of the sample

	EOS schizophrenics, $N = 40$	AOS schizophrenics, $N = 54$	Controls, $N = 40$
Age (years) Mean (S.D.)	15.58 (2.24)	37.00 (9.73)	15.79 (2.06)
Age of onset (years) Mean (S.D.)	14.10 (2.10)	22.90 (3.96)	–
Sex (% male)	50	57.40	50
IQ Mean (S.D.)	80.98 (19.27)	100.48 (20.88)	104.97 (15.19)
Handedness (% right)	80.0	71.4	79.5
Social class (% 1–3)	75.0	67.5	70.5

Table 2
Developmental scale scores

	EOS schizophrenics	Controls	p value
Speech: No. of patients (%)			
No problems	32 (80.0)	36 (90.0)	ns
No first words by age 3 or grammar or pronunciation difficulties at school entry	3 (7.5)	3 (7.5)	
Professional help sought	5 (12.5)	1 (2.5)	
Motor: No. of patients (%)			
No problems	39 (97.5)	40 (100.0)	ns
Could not walk unsupported by age 2	1 (2.5)	0 (0)	
Professional help sought	0 (0)	0 (0)	
Encopresis: No. of patients (%)			
No problems	39 (97.5)	38 (95.0)	ns
Soiling after the age of 4 for at least once a week	1 (2.5)	2 (5.0)	
Professional help sought	0 (0)	0 (0)	
Enuresis: No. of patients (%)			
No problems	35 (87.5)	39 (97.5)	ns
Bed or daytime wetting after the age of 5 for at least once a week	5 (12.5)	1 (2.5)	
Professional help sought	0 (0)	0 (0)	
Reading: No. of patients (%)			
No problems	29 (72.5)	37 (92.5)	0.04
Reading or spelling difficulties	5 (12.5)	(3) 7.5	
Professional help sought	6 (15.0)	0 (0)	
Developmental score: No. of patients (%)			
No problems in any area	24 (60.0)	33 (82.5)	0.02
Problems in or more areas	8 (20.0)	6 (15.0)	
Professional help sought for one or more areas	8 (20.0)	1 (2.5)	

Table 3
Premorbid adjustment scale

Mean (S.D.)	Early onset schizophrenics	Adult onset schizophrenics	Controls
Childhood			
Isolation	2.70 (1.46)	2.67 (1.15)	1.92 (0.91)
Peer relationships	2.85 (1.54)	2.21 (1.19)	1.52 (0.67)
Scholastic performance	3.09 (1.33)	3.15 (1.2)	2.20 (1.04)
School adaptation	2.18 (1.40)	2.13 (1.2)	1.35 (0.86)
Interests	2.75 (2.09)	2.55 (1.6)	1.52 (1.17)
Total score[a]	2.86 (1.49)	2.54 (0.98)	1.70 (0.67)
Adolescence			
Isolation	3.19 (1.62)	3.11 (1.40)	1.92 (1.09)
Peer relationships	3.48 (1.96)	2.40 (1.37)	1.4 (0.81)
Scholastic performance	4.09 (1.37)	3.61 (1.45)	2.51 (1.07)
School adaptation	3.22 (2.23)	2.75 (1.35)	1.69 (1.07)
Interests	3.16 (2.23)	3.25 (1.94)	1.43 (0.88)
Total score[a]	3.85 (1.76)	3.02 (1.14)	2.17 (0.88)

[a] Total score = sum of all preceding items divided by their number.

$df = 1$, $p = 0.04$) and overall developmental score (Pearson's $\chi^2 = 5.0$, $df = 1$, $p = 0.02$).

3.3.2. Premorbid adjustment

The subjects' mean scores and standard deviations are shown in Table 3. Comparison between patients and controls for premorbid adjustment during childhood was based on multivariate analysis of variance with the PAS childhood items' scores as dependent variables and diagnosis, gender and developmental score as independent factors. There was a significant effect of diagnosis ($F = 4.95$, $df = 6.52$, $p = 0.0005$) and developmental score ($F = 3.12$, $df = 12{,}106$, $p = 0.001$), but no effect of gender ($F = 1.29$, $df = 6.52$, $p = 0.27$). Similarly, comparison between patients and controls for premorbid adjustment during adolescence was based on multivariate analysis of variance with the PAS adolescent items' scores as dependent variables and diagnosis, gender and developmental score as independent factors. In this analysis, there was a significant effect of diagnosis ($F = 3.91$, $df = 5.51$, $p = 0.004$) and developmental score ($F = 2.65$, $df = 10{,}104$, $p = 0.006$). Although the effect of gender just failed to reach statistical significance ($F = 2.21$, $df = 5.51$, $p = 0.06$), the interactions between gender and diagnosis ($F = 3.92$, $df = 5.51$, $p = 0.004$), as well as that between diagnosis, gender and developmental score were significant ($F = 2.36$, $df = 5.51$, $p = 0.05$), both showing more impairment in males.

Repeated measures analysis was used to examine the change in each of the PAS items from childhood to adolescence between patients and controls using gender and diagnosis as between subject factors. There was a significant change over time for social isolation ($F = 6.06$, $df = 1$, $p = 0.01$), which was more pronounced in patients ($F = 4.37$, $df = 1$, $p = 0.04$), particularly males ($F = 4.37$, $df = 1$, $p = 0.04$). For peer relationships, change over time was only significant for male cases ($F = 13.42$, $df = 1$, $p = 0.001$). Scholastic performance showed a significant change over time ($F = 27.69$, $df = 1$, $p = 0.0005$), which was more pronounced in patients ($F = 6.51$, $df = 1$, $p = 0.01$) without any evidence of a gender effect ($F = 0.05$, $df = 1$, $p = 0.81$). Scholastic adaptation also changed over time ($F = 16.73$, $df = 1$, $p = 0.0005$) without any effect of gender ($F = 0.49$, $df = 1$, $p = 0.48$) and only a marginal effect of diagnosis ($F = 2.93$, $df = 1$, $p = 0.09$). There was no overall change in interests over time ($F = 0.74$, $df = 1$, $p = 0.79$) and no effect of diagnosis ($F = 1.47$, $df = 1$, $p = 0.22$).

3.3.3. Premorbid schizoid and schizotypal traits

The subjects' mean scores and standard deviations on items of this scale are shown in Table 4. Multivariate analysis of variance revealed a significant main effect of diagnosis ($F = 4.25$, $df = 8.56$, $p = 0.0005$), gender ($F = 3.42$, $df = 8.56$, $p = 0.003$) and developmental score ($F = 4.17$, $df = 8.56$, $p = 0.001$).

Table 4
Premorbid schizoid and schizotypal traits

Mean (S.D.)	EOS schizophrenics	AOS schizophrenics	Controls
Social isolation	2.00 (1.05)	1.71 (0.74)	1.25 (0.54)
Demonstrative affect	1.71 (0.92)	1.32 (0.670)	1.47 (0.78)
Suspiciousness/ sensitivity	1.74 (0.81)	1.53 (0.72)	1.42 (0.54)
Thought content/ beliefs	2.20 (2.49)	1.21 (0.53)	1.20 (0.60)
Speech	1.55 (0.99)	1.15 (0.45)	1.10 (0.37)
Antisocial behaviour with peer group	1.35 (0.77)	1.30 (0.78)	1.45 (0.55)
Antisocial behaviour alone	1.58 (0.95)	1.34 (0.76)	1.25 (0.49)
Total score	11.65 (5.13)	9.52 (2.28)	9.15 (2.53)

The interaction between diagnosis and gender was not significant ($F=1.65$, $df=8.56$, $p=0.13$), but that between diagnosis and developmental score was significant ($F=3.01$, $df=8.56$, $p=0.007$). Post hoc univariate analyses showed that the effect of diagnosis was significant for social isolation ($F=14.58$, $df=1$, $p=0.0005$), abnormal thoughts and beliefs ($F=13.81$, $df=1$, $p=0.0004$), speech ($F=6.63$, $df=1$, $p=0.01$) and general assessment ($F=11.51$, $df=1$, $p=0.001$). The interaction between diagnosis and developmental score was significant for social isolation ($F=4.06$, $df=1$, $p=0.04$), and abnormal thoughts and beliefs ($F=8.70$, $df=1$, $p=0.004$).

3.4. Comparison of EOS and AOS subjects

3.4.1. Premorbid adjustment

There was no significant difference between EOS and AOS patients in premorbid social adjustment in childhood ($F=1.78$, $df=5.76$, $p=0.12$) and no effect of gender ($F=1.04$, $df=5.76$, $p=0.39$). However, EOS patients showed significantly more deviant social adjustment in adolescence ($F=11.42$, $df=5.76$, $p=0.0001$). There was a significant effect of gender ($F=2.34$, $df=5.76$, $p=0.03$) and a gender by group interaction ($F=2.29$, $df=5.76$, $p=0.04$) with male EOS patients being significantly more deviant in adolescence than male AOS patients.

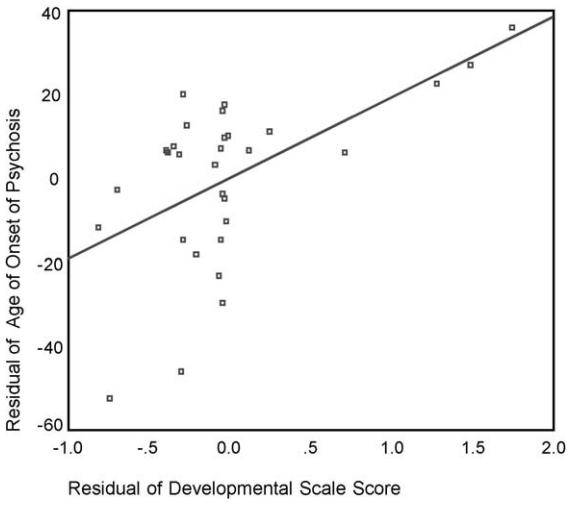

Fig. 1. Partial regression plot of the relationship between age of onset of psychosis and development scale score in EOS.

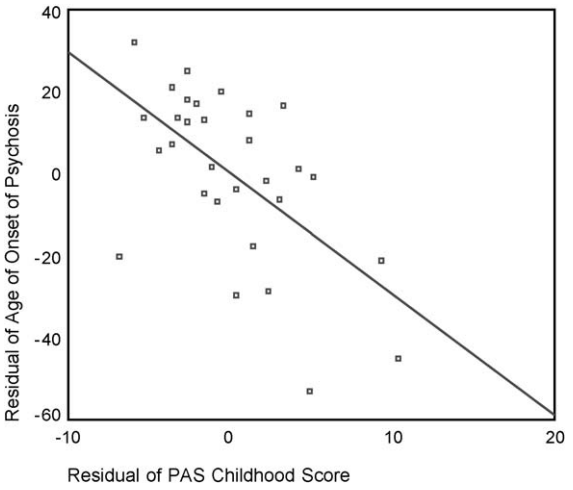

Fig. 2. Partial regression plot of the relationship between age of onset of psychosis and PAS childhood score in EOS.

3.4.2. Premorbid schizoid and schizotypal traits

There were significant difference between EOS and AOS patients in total PSST scores ($F=5.98$, $df=7.77$, $p=0.01$) and a significant gender interaction ($F=4.69$, $df=5.76$, $p=0.03$) with male EOS patients being more deviant. Post hoc comparison showed that EOS patients had significantly higher scores on items rating abnormal affect ($F=4.0e$, $df=7.77$, $p=0.04$), odd beliefs and experiences ($F=9.54$, $df=7.77$, $p=0.003$) and odd speech ($F=5.50$, $df=7.77$, $p=0.02$).

3.5. Relationship with age of onset

In the regression analysis, age of onset of psychosis for the EOS sample was predicted by the developmental score ($B=0.54$, $t=3.51$, $p=0.001$), the total PAS score in childhood ($B=-1.00$, $t=-3.78$, $p=0.001$) and by the PSST total score ($B=0.59$, $t=2.22$, $p=0.03$). The partial regression plots showing the relationship between age of onset of psychosis and the above three variables are shown in Figs. 1–3.

The regression analysis was repeated for the AOS patients using the same variables with the exception of the developmental score that was not available in these patients. Neither premorbid functioning (PAS total childhood score $B=0.35$, $t=1.59$, $p=0.11$; PAS total adolescence score $B=-0.19$, $t=-0.09$, $p=0.92$) nor

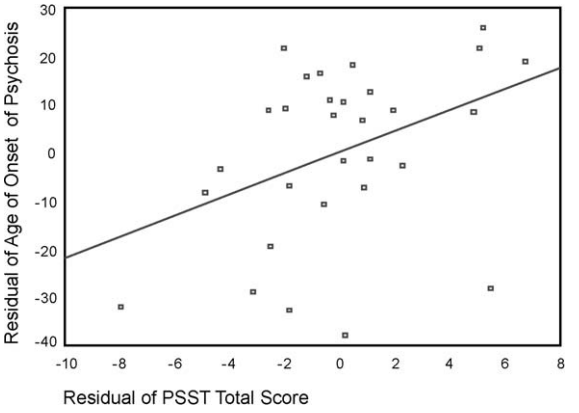

Fig. 3. Partial regression plot of the relationship between age of onset of psychosis and PSST total score in EOS.

schizophrenia spectrum traits ($B = -0.27$, $t = -1.82$, $p = 0.07$) predicted the age of onset in the adult onset sample.

4. Discussion

4.1. Early development

We found that the main developmental delays in patients with EOS were in speech and language. EOS cases had delayed speech milestone, as well as more reading and spelling difficulties compared to normal controls. Males were more vulnerable than females with regards to speech development. Speech and language delays or impairment have been consistently reported in 43–55% of patients with childhood onset schizophrenia (Kolvin et al., 1971; Watkins et al., 1988; Nicolson et al., 2000). Language impairment was present in 19.4% of our sample, which is lower than that reported in studies of childhood onset schizophrenia. This difference is probably due to the adolescent as opposed to childhood onset of schizophrenia in our patients. This view is also supported by Hollis (1995) who studied a sample of 61 psychotic children and adolescents, and found that onset of schizophrenia before the age of 13 was associated with higher impairment in speech or language than adolescent onset.

With respect to motor function, this was measured using the Developmental Scale that was designed to detect unequivocal deviations from normality to avoid recall biases. Even so, 3% of the patients in our sample could not walk unaided by the age of 2. Direct comparison with other studies is hampered by marked differences in the aspects of motor function examined and the clinical characteristics of the patients studied. Kolvin et al. (1971) also noted that only 3% of developmental delays were due to a cause other than speech or language. Watkins et al. (1988) found motor impairment in 64% of his patients, but he included both delayed milestones and poor coordination; in addition, his group consisted only of eight patients whose age of onset of schizophrenia was below 10 years. Hollis (1995) reported motor disturbance in 31% of his subjects, but he included symptoms of restlessness, stereotyped movements and poor coordination, which were not assessed in this study. Nicolson et al. (2000) found motor impairment in 57.1% of their sample of schizophrenic subjects, but again the criteria were wide including not only delayed motor milestones but also poor coordination and abnormal repetitive movements. In an analysis of a subgroup of the above sample (Alaghband-Rad et al., 1995), the rate of motor impairment was 17% when restricted to delayed walking only (as in our study), which is, however, still five times higher than what we found. However, in their sample, developmental motor delays were more likely in those schizophrenic children that met either at least one (36%) or all the criteria for infantile autism (13%). It would seem from the above that although subtle motor abnormalities are common amongst preschizophrenic EOS children, clearly identifiable impairment is noticeable only in a small minority.

Impairment in at least one area of development sufficiently severe to elicit help seeking behavior was present in almost 20% of our cases compared to 2.5% of controls. Although this is a very indirect measure of severity, it has the advantage of being least affected by recall biases and it does suggest that in EOS patients pronounced neurodevelopmental abnormalities are almost 10 times higher than in a carefully matched group from the general population.

4.2. Premorbid adjustment

We found that preschizophrenic children had poorer adjustment than normal controls even since childhood and that this deteriorated further as they

progressed into adolescence. Premorbid adjustment in childhood and adolescence was closely associated with developmental impairment in both genders. As patients progressed to adolescence, the most significant impairments identified were social isolation and poor scholastic performance. Boys were more pronouncedly affected, in terms of peer relationships and social isolation.

Similar results of impairment in premorbid functioning have been reported in a number of studies. Hollis (1995) found that a premorbid history of social withdrawal was significantly more common in cases of EOS compared to nonpsychotic patients. Two studies on treatment resistant EOS cases ascertained at the National Institute of Mental Health (NIMH) (Alaghband-Rad et al., 1995; Nicolson and Rapoport, 1999) have found that there had been concerns from parents and teachers about the social development and academic performance of more than half of their subjects who had significantly higher total PAS score than the normal for that age group.

There is also evidence to suggest that these premorbid abnormalities may show some degree of specificity to schizophrenia. Asarnow and Ben-Meir (1988) compared children with schizophrenia, schizophrenia spectrum, depression and dysthymic disorders and found that the first two groups were significantly more impaired on all PAS ratings and were more likely to show patterns of chronic dysfunction.

Cannon et al. (2001) reported that social withdrawal and disturbed relationship with peers or adults other than family members were more common in those children who developed schizophrenia rather than affective disorders later in life.

Impairment in premorbid functioning particularly in social adaptation (Offord and Gross, 1969; Hans et al., 1992; Olin and Mednick, 1996) and scholastic performance (Offord and Gross, 1969; Jones et al., 1994; Olin and Mednick, 1995) has been repeatedly found in studies of adult onset schizophrenia. In this study, we directly compared premorbid adjustment as measured by the PAS between EOS subjects and those with adult onset schizophrenia. We found that early onset cases were more deviant than adult onset patients during adolescence and not childhood, and this effect was more pronounced for male EOS subjects. This finding ties in with the significant increase in deviant social behaviour that we have observed in EOS patients compared to their age matched controls which was also more pronounced in male patients.

Our study suggests that abnormalities in premorbid adjustment both in childhood and adolescence are closely associated with abnormal neurodevelopment. Existing neurodevelopmental theories of schizophrenia have been criticized for the lack of a proposed mechanism, whereby early, possibly prenatal, neurodevelopmental deviance, could account for the fact that overt psychopathology is not apparent until later in life. The present study provides some evidence to support the notion that early development deviance and premorbid function may both be manifestations of abnormalities in developmental processes exerting their influence beyond the prenatal phase into childhood and adolescence.

4.3. Premorbid schizoid and schizotypal traits

Our study confirms the presence of a number of schizophrenia spectrum traits during the premorbid phase of EOS. These features were more pronounced in EOS than AOS subjects. In addition, EOS patients were more deviant in terms of bizarre ideas/perceptions, restricted affect and odd speech. Our results are in line with a recent prospective birth cohort study (Poulton et al., 2000) that found that children reporting delusional beliefs and hallucinatory experiences at age 11 were 16 times more likely than the rest of their cohort to be diagnosed with a schizophrenia spectrum disorder 15 years later. These findings suggest that the PSST items most commonly endorsed by parents of EOS patients are indeed predictive of later schizophrenia.

Within the EOS sample, we found a significant interaction between a history of developmental deviance and the presence of social isolation and abnormal thoughts and beliefs in those subjects who later developed schizophrenia. This offers further, albeit indirect, support that developmental deviance, abnormal premorbid function and premorbid schizophrenia spectrum traits may be different, but associated manifestations of on-going abnormalities in developmental processes.

4.4. Association with age of onset

With regards to the clinical picture, the present study suggests that developmental impairment, schizophrenia spectrum traits and poor childhood

adjustment act to precipitate an earlier onset of schizophrenia. However, in our sample, this effect seems to be more relevant for patients with adolescent onset schizophrenia rather than for those with adult onset disorder. Most previous studies have reported an association between poor premorbid functioning and schizophrenia spectrum traits and an earlier age of onset of schizophrenia (McCreadie et al., 1994; Gupta et al., 1995; Jablensky and Cole, 1997). However, our findings suggest that this effect may not be present throughout the entire range of age of onset, but may be more relevant to those with an adolescent onset.

4.5. Methodological issues

The main limitation of this study is its retrospective design. Our data were based on maternal recall and thus recall bias cannot be excluded. As far as we know, there are no published data regarding the possible influence of parental recall bias for the scales used in this study. There are considerable practical difficulties in validating these scales against objective and contemporaneously obtained measures because information on premorbid adjustment and schizoid or schizotypal traits are not routinely collected by any health or educational agency. The accuracy of recall of parents of schizophrenic as opposed to those of healthy offspring has been assessed for perinatal and birth complications. Such studies suggest that the type of errors does not seem to differ between diagnostic groups (O'Callaghan et al., 1990; Cantor-Graae et al., 1998; Buka et al., 2000). With regards to the scales used in this study, the threshold for deviation from the normal trajectory is quite high in the Developmental Scale and incorporates objective measures such as the involvement of professionals for developmental problems. In the case of the PAS, Alaghband-Rad et al. (1995) completed PAS ratings for childhood items only in a sample of 23 patients with childhood onset schizophrenia. The authors had access to most patients' school and medical records to supplement the information from parental interviews. The mean total PAS childhood score in that was 2.33, which is very similar to the score obtained from the childhood items of PAS in this study (2.89). In addition, abnormalities in premorbid adjustment and schizoid/schizotypal traits have been repeatedly shown in studies of early (Alaghband-Rad et al., 1995; Hollis, 1995; Cannon et al., 2001) and adult-onset schizophrenia (Offord and Gross, 1969; Jones et al., 1994; Olin and Mednick, 1996). The consistency of the results across studies mitigates against their being an artifact of parental recall bias.

In conclusion, our data suggest that developmental deviance and abnormalities in premorbid social interaction and language-related functions act to precipitate an earlier age of onset in schizophrenia. The effect of these factors on age of onset is more pronounced for adolescent than adult onset patients. Early developmental deviance continues to play a significant part in influencing social function and personality traits beyond childhood, and this effect may be more pronounced in males.

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