

Predictors of later schizophrenia and affective psychosis among attendees at a child psychiatry department[†]

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Background Schizophrenia has been linked with psychological problems in childhood but there is little information on precursors of affective psychosis.

Aims To compare childhood psychological antecedents of adult schizophrenia and affective psychosis.

Method Childhood item sheets, which give standardised information on signs and symptoms of mental illness in the year preceding assessment are completed for all attendees at the children's department of the Maudsley and Bethlem Royal Hospital. We examined item sheet data on individuals with an adult diagnosis of schizophrenia ($n=59$) or affective psychosis ($n=27$) and a comparison group with no adult mental illness ($n=86$) (all had attended the department).

Results Abnormal suspiciousness or sensitivity and relationship difficulties with peers are associated with later schizophrenia. In contrast, affective psychosis is associated with childhood hysterical symptoms and disturbances in eating.

Conclusions Childhood psychological precursors for schizophrenia and affective psychosis differ and do not simply reflect non-specific psychiatric disturbance in adolescence.

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Longitudinal research shows that many mental disorders do not arise *de novo* in adult life but have roots further back in childhood (Rutter, 1984; Caspi *et al*, 1996). Schizophrenia is associated with significant impairments in childhood, but little work has yet been carried out on affective psychosis. Longitudinal prospective studies are an ideal way to study childhood precursors of adult psychotic illness, but the length of the follow-up period and the large sample sizes required make this a prohibitively costly exercise. One approach is to use existing general population birth cohorts (Done *et al*, 1994; Jones *et al*, 1994), but although such samples have the advantage of an epidemiological design, they usually have few data on psychological symptoms in childhood, and have low statistical power to study relatively rare disorders such as schizophrenia. Data collected from attendees at child psychiatric clinics can overcome both of these difficulties. We have utilised a valuable resource of standardised psychological data collected over many years from a large child psychiatric service to examine predictors of later psychosis.

METHOD

Childhood information

Since 1968 the Children's and Adolescents' Department of the Maudsley and Bethlem Royal Hospital has used a computer-based system of clinical data gathering, storage and retrieval (Thorley, 1982). This system uses a structured data recording sheet called an item sheet that employs Likert-type scales and is completed in addition to the usual medical file. The first part of the item sheet covers clinical symptoms and signs that have occurred within the previous 12 months, and is completed by the assessing psychiatrist within 2 weeks of the child's initial assessment (which comprises a mental state examination and a parental interview).

Each symptom on the item sheet is rated by the clinician as absent ('0'), minimal or dubious ('1') or definitely present ('2'). The list of symptoms and socio-demographic variables recorded on the item sheets comprises the following.

- (a) *Emotional symptoms*: abnormal suspiciousness or 'sensitivity'; morbid anxiety; morbid depression; specific phobias; obsessions/compulsions/ruminations; suicidal ideas or attempts; hypochondriasis; morbid irritability; school refusal; abnormally elevated mood/hypomania; depersonalisation; derealisation; conversion hysterical symptoms.
- (b) *Somatic symptoms*: disturbance of eating (pica, faddiness, refusal); disturbance of sleeping; pains of mental origin; encopresis; enuresis; non-epileptic disturbance of consciousness.
- (c) *Disturbance of relationships*: overt disturbance of: child–mother relationship; child–father relationship; relationship with other adults (e.g. teacher); patient–sibling relationship; relationships with other children (isolation, failure to make friends); autism/social withdrawal; social disinhibition.
- (d) *Speech and language*: disorder of rhythm; disorder of articulation; disorder of comprehension, disorder of production; elective mutism.
- (e) *Motor disturbance*: tics; other abnormal repetitive movements; clumsiness or poor coordination; restlessness or fidgetiness; gross overactivity; hypoactivity; habitual manipulations (thumb-sucking, rocking, etc.).
- (f) *Antisocial behaviour*: defiance or lying; stealing; destructiveness; truancy; running away; sexual misbehaviour, fighting/bullying, etc; violent assault; taking drugs; other substance misuse; cruelty to animals; other antisocial behaviour.
- (g) *Socio-demographic and administrative variables*: main referral agency; duration of child's psychiatric disorder; patient status at time of admission; school attended; special school/day unit attended; special educational needs; employment; legal status; current parental situation; number of children under 17 years in the household; ordinal position; twin; seen by psychiatrist previously; seen by paediatrician for psychological disorder; brought before juvenile court previously; place of residence; country of

[†]See editorial, pp. 395–396, this issue.

birth of mother; country of birth of father; country of birth of child; occupation of father or main breadwinner.

Cases

All discharge summaries from the Maudsley Hospital Adult Psychiatric Service up to 1993 were searched for a unique identifying code signifying that patients had previously attended the Children's and Adolescents' Department of the Maudsley and Bethlem Royal Hospital between 1968 and 1989. Discharge summaries with a diagnosis of psychosis were entered into the OPCRIT system (version 3.2) (McGuffin *et al*, 1991) to give ICD-10 diagnoses (World Health Organization, 1992). In total, 56 cases fulfilling ICD-10 criteria for schizophrenia and 24 fulfilling ICD-10 criteria for affective psychosis (defined as bipolar affective disorder or severe depression with psychotic symptoms) were identified.

Comparison group

The next four children, of the same age and gender, who were registered at the clinic after the index psychosis case were taken as the initial 'raw' comparison group. We then undertook a follow-up study in order to identify a final comparison group who had no mental illness in adulthood, and to identify those individuals who later developed psychosis and had been treated elsewhere. Tracing was carried out in three stages:

- (a) names and dates of birth of the 'raw' comparison group were matched against the National Health Service Central Register at the Office of Population Censuses and Surveys (now the Office for National Statistics), which gave the name of the relevant Family

Health Service Authority (FHSA) for each subject;

- (b) each FHSA was contacted to request the names of the general practitioner for each subject;

- (c) we then wrote to each general practitioner requesting information on the adult psychiatric history of the subject who was registered with them, enclosing a questionnaire.

Using these methods, we located general practitioners for 256 subjects. The general practitioners for 203 subjects agreed to participate in the study. From this group we identified 86 individuals who had never suffered any mental illness in adulthood, and these were taken as the 'final' comparison group. Nine individuals were found to have an adult diagnosis of schizophrenia and four had a diagnosis of affective psychosis. In order to increase statistical power, we decided to add these individuals to our original case group. The remainder of the traced comparison group had suffered non-psychotic psychiatric disorders in adulthood.

Final sample

We identified 65 childhood attendees with an adult diagnosis of schizophrenia and 28 childhood attendees with an adult diagnosis of affective psychosis, comprising 20 cases with bipolar disorder and 8 cases with psychotic depression. Our comparison group comprised 86 childhood attendees who had not suffered mental illness in adulthood. We could not locate childhood item sheets for six subjects with schizophrenia and one subject with affective psychosis. The final sample available for analysis thus comprised: 59 subjects with

schizophrenia; 27 subjects with affective psychosis; 86 controls.

Statistical analysis

We included only variables rated as 'definite' (score=2) on the item sheets in our analysis. Odds ratios and confidence intervals were calculated to measure the association between each variable from the item sheet separately with later schizophrenia or affective psychosis. Items that were associated significantly with schizophrenia or affective psychosis at the 5% level on the univariate analysis then were entered into a multivariate analysis. Stepwise logistic regression was used to identify those variables that were independently associated with later schizophrenia or affective psychosis. Analyses were performed using STATA v.5 (Stata Corporation, 1995).

RESULTS

Sample characteristics

Table 1 presents the socio-demographic characteristics for the three groups of subjects: schizophrenia, affective psychosis and comparison. There were no significant overall differences between the groups on gender, socio-economic group (defined by parental occupation) (Goldthorpe & Hope, 1974) or referral status (tertiary or local). Subjects were assessed at the children's department when they were aged between 13 and 14 years on average, so were, strictly speaking, in early adolescence rather than childhood at that time. Their assessments usually occurred some 3-5 years before a diagnosis of schizophrenia or affective psychosis. However, 12 of the schizophrenia group (20%) and 12 of the affective psychosis group (44%) were

Table 1 Socio-demographic characteristics of subjects with childhood item sheet data¹

Variable	Schizophrenia (n=59)		Affective psychosis (n=27)		Comparison group (n=86)		Test statistic ² (d.f.)	P value
	No.	%	No.	%	No.	%		
Male	37	(62.7)	11	(40.7)	50	(58.1)	4.6 (2)	0.1
SEG I, II	9	(20.0)	8	(44.4)	18	(26.6)	5.4 (2)	0.2
SEG III, IV, V	36	(80)	10	(55)	50	(73.4)		
Tertiary referrals	8	(13.5)	2	(7.3)	14	(16.3)	1.4 (2)	0.5
Mean age at assessment (s.d.)	14.1	(2.7)	13.8	(2.5)	13.4	(3.05)	1.13 (2, 170)	0.3
Mean age at diagnosis (s.d.)	19.4	(4.3)	17.0	(3.6)	N/A			

SEG, socio-economic group.

1. Values are missing for 32 subjects (5 schizophrenia, 9 affective psychosis, 18 comparison).

2. For categorical variables, the χ^2 -test was used; for continuous variables, F-test was used.

already diagnosed with psychosis while attending the children's department. These are called the 'early-onset' cases (onset before age 17 years) and analyses are carried out both with and without these cases.

Univariate analysis

Variables from the item sheets that were associated significantly with later schizophrenia are presented in Table 2. Fifteen variables (nine symptom variables and six socio-demographic variables) were associated significantly with later schizophrenia on univariate analysis. Odds ratios could not be calculated for four variables ('elective mutism', 'hypoactivity', 'in-patient status on referral' and 'twin') because they did not occur in the comparison group. The strongest univariate association was between the symptom of 'abnormal suspiciousness or sensitivity' and later schizophrenia, with an odds ratio of about 10. Three symptom variables ('disturbance of relationship with other adults', 'disturbance of relationship with peers' and 'autism/social withdrawal') that were concerned with aspects of interpersonal relationships (outside the family) were associated significantly with later schizophrenia. Because the three variables were felt to be describing the same underlying phenomenon, they were combined into one variable called 'relationship difficulties

(extrafamilial)' for the multivariate analysis. Other symptom variables associated with later schizophrenia were: 'morbid depression', 'morbid irritability/temper tantrums' and 'disturbance of sleeping'. There was no association with speech and language disturbance (apart from 'elective mutism'), motor disturbance or antisocial behaviour. Among the sociodemographic variables, 'family psychiatric history', 'previous psychiatric assessment', 'residing in a children's home or other type of institution' or 'parent born in the Caribbean or Africa' were associated significantly with later schizophrenia.

Symptoms associated with affective psychosis on the univariate analysis are presented in Table 3. The strongest associations were with hysterical symptoms (which, because of low base rates of endorsement, was a combination variable comprising 'depersonalisation', 'conversion hysterical symptoms' and 'non-epileptic disturbance of consciousness') and 'gross overactivity', with odds ratios of about 20. 'Morbid depression', 'hypochondriasis' and 'disturbance of eating' also were associated significantly with affective psychosis. Among the antisocial behaviours there was a positive association with 'violent assault', but 'stealing' was significantly less likely to occur than among the comparison group. There were no associations with speech and

language disturbance. Among the socio-demographic variables, 'family psychiatric history' and 'referral by another psychiatrist' were associated positively with affective psychosis. Odds ratios could not be calculated for the symptoms of 'hypomania' and 'hypoactivity' or for the socio-demographic variable 'in-patient on referral' because they did not occur in the comparison group.

Multivariate analysis

All variables that were associated significantly with schizophrenia or affective psychosis on univariate analysis were entered into multivariate analyses. Table 4 shows the variables that were associated independently with schizophrenia and affective psychosis after logistic regression. The final model for schizophrenia comprised two symptom variables ('abnormal suspiciousness or sensitivity' and 'relationship difficulties') and two socio-demographic variables ('family psychiatric history' and 'past psychiatric contact'). The positive predictive power of the model for this sample of child psychiatric clinic attenders was 81.2% (26/32 cases correctly classified) and the model sensitivity was 65%. Adjusting for gender made no difference to the model. When we examined the 'Maudsley' cases only, the associations did not change. When the early-onset cases were excluded, the

Table 2 Association between item sheet variables and schizophrenia

Item sheet variable	Odds ratio (95% CI)	Schizophrenia		Comparison group	
		% Reporting variable	No. ¹	% Reporting variable	No. ¹
Symptoms or signs in the past year					
Abnormal suspiciousness or sensitivity	9.86 (3.4–28.6)	43	51	7.1	70
Autism/social withdrawal	5.21 (1.6–17.3)	24	50	5.7	70
Morbid irritability/temper tantrums	3.32 (1.4–7.7)	32.7	58	12.8	86
Disturbance of relationship with peers	2.97 (1.5–5.9)	53.4	58	27.9	86
Disturbance of sleeping	2.63 (1.2–6.0)	30.5	59	14.3	84
Morbid depression	2.48 (1.2–5.2)	39.6	58	20.9	86
Disturbance of relationships with other adults	2.12 (1.1–4.4)	41.1	56	24.7	85
Elective mutism	–	7.8	51	0.0	70
Hypoactivity	–	3.9	51	0.0	70
Socio-demographic variables					
Family psychiatric history (parent or sibling)	3.99 (1.7–9.2)	46.8	47	18.1	72
Past psychiatric history (child)	3.73 (1.1–13.2)	65	55	37.4	83
Currently in institution or children's home	2.69 (1.0–7.5)	19.3	57	8.1	86
Parent born in Caribbean or Africa	2.63 (1.1–6.1)	39	49	19.4	67
Twin	–	5.2	58	0.0	86
In-patient status on referral	–	17.5	57	0.0	86

1. Number with available data on item sheet.

Table 3 Association between item sheet variables and affective psychosis

Item sheet variable	Odds ratio (95% CI)	Schizophrenia		Comparison group	
		% Reporting variable	No. ¹	% Reporting variable	No. ¹
Symptoms or signs in the past year					
Hysterical symptoms ²	24.2 (2.6–224)	26.3	19	1.5	69
Gross overactivity	19.3 (2.1–173)	18.5	27	1.2	86
Hypochondriasis	10.6 (1.1–107)	11.1	27	1.2	86
Disturbance of eating	4.7 (1.4–15.4)	25.9	27	6.9	86
Violent assault	4.9 (1.2–19.8)	19.2	26	4.6	86
Morbid depression	2.5 (1.02–6.1)	48.0	27	27.1	85
Stealing	0.2 (0.04–0.9)	7.7	26	29.1	86
Hypomania	–	21.1	19	0.0	70
Hypoactivity	–	5.3	19	0.0	70
Socio-demographic variables					
Family psychiatric history (parent or sibling)	6.12 (2.2–17.2)	54.2	24	18.1	72
Referral by another psychiatrist	3.61 (1.3–10.1)	34.6	26	12.8	86
In-patient status on referral	–	15.4	26	0.0	86

1. Number with available data on item sheet.
 2. Includes depersonalisation, conversion hysterical symptoms and non-epileptic disturbance of consciousness.

Table 4 Independent association between schizophrenia, affective psychosis and item sheet variables: final models

Item sheet variable	Odds ratio (95% CI) for all cases	Odds ratio (95% CI) for adult-onset cases only (> 17 years)
Schizophrenia		
	<i>n</i> =59	<i>n</i> =47
Abnormal suspiciousness or sensitivity	21.5 (4.9–94.8)	12.4 (2.6–59.8)
Family psychiatric history (parent or sibling)	4.68 (1.4–15.6)	3.46 (0.9–12.1)
Past contact with psychiatrist or psychologist	3.54 (1.1–11.4)	2.67 (0.8–8.9)
Relationship difficulties (extrafamilial)	3.34 (1.04–10.7)	4.22 (1.2–14.7)
Affective psychosis		
	<i>n</i> =27	<i>n</i> =15
Hysterical symptoms	26.24 (2.03–339) ¹	22.4 (0.96–520) ¹
Disturbance of eating	15.67 (1.9–124) ¹	19.5 (0.85–447) ¹
Family psychiatric history (parent or sibling)	5.54 (1.3–24.13) ¹	25.7 (2.4–274.0) ¹

1. Adjusted for confounding by gender.

association with ‘relationship difficulties’ became stronger. The associations with ‘past psychiatric history’ and ‘family psychiatric history’ were no longer statistically significant, although the odds ratios remained above 2. The final model for affective psychosis comprised three variables: ‘hysterical symptoms’, ‘disturbance of eating’ and ‘family psychiatric history’. The positive predictive power of the model for this sample was 63.6% (7/11 cases correctly classified) and the model sensitivity was 43.8%. The likelihood ratio test showed that gender made a significant difference to the model, so the odds ratios are presented after adjustment for gender. The wide confidence intervals for ‘hysterical

symptoms’ reflect the loss of precision due to the 25 missing values in the comparison group. After excluding the early-onset cases, the association with ‘family psychiatric history’ became stronger but the associations with ‘hysterical symptoms’ and ‘disturbance of eating’ were no longer significant.

DISCUSSION

Strengths of the study design

The main strength of this study was the availability of standardised ratings, made on first assessment at a child psychiatric clinic, which cover most aspects of childhood psychopathology. The content validity

and reliability of the item sheet data has been shown to be very high (Thorley, 1987; Goodman & Simonoff, 1991). Although the data were collected for other reasons and cannot encompass all the questions that one would possibly wish to address, it is rare to find such a detailed source of psychological data covering a large sample of children on whom information is available for adult outcome. Our study is unique in including a relatively large group of children who develop affective psychosis in adulthood, because previous studies have either not studied such children or had very small numbers (Pritchard & Graham, 1966; Zeitlin, 1986). Another strength of the study design is the

follow-up strategy to determine the adult psychiatric status of the comparison group, which increases the sensitivity of the associations reported in this paper.

Limitations

A limitation of this study design is the possible lack of representativeness of our findings. Our sample represents adults who were sufficiently disturbed as children to be seen in a child psychiatric clinic that accepted both local and tertiary referrals. Strictly speaking, therefore, our results apply only to prediction of later psychosis among children who attend child psychiatric clinics. However, we will discuss the similarity of our results to findings from epidemiological general population samples, and show that there may be a wider application for our findings. In addition, by choosing as the comparison group children who had not suffered from mental illness in adulthood we hoped to find a comparison group as close as possible to a general population control group. Another limitation of this study is that some of the children were diagnosed with psychosis while still in the children's department. However, such diagnoses would have been made, in most cases, after a period of inpatient evaluation and not on the initial assessment, and the assessing psychiatrist would not have distinguished between schizophrenia and affective psychosis at that time. In addition, when we conducted our analysis without these early-onset cases, it made little difference to the findings. We feel, therefore, that we have identified precursors for psychosis rather than prodromes.

Comparison with previous work on schizophrenia

The two childhood symptoms independently associated with later schizophrenia in this study were 'abnormal suspiciousness or sensitivity' and 'relationship difficulties (extrafamilial)'. Relationship difficulties and social withdrawal in childhood and adolescence have long been known to be risk factors for schizophrenia and have been found in previous work on precursors of schizophrenia among child psychiatric clinic attendees (Offord & Cross, 1969; Hartman *et al*, 1984; Ambelas, 1992). Indeed, a review of this literature revealed so much evidence of pervasive social isolation that Garmezy (1974) deemed it

"the fundamental dimension that is most integral in the developmental histories of schizophrenics". Our study had the power to distinguish between different types of relationship and found that familial relationships in childhood were not disturbed to the same extent as relationships with peers and other adults (usually teachers). Findings of relationship difficulties preceding schizophrenia are not confined to child psychiatric clinic samples. Two large cohort studies of male conscripts have found that poor social functioning at ages 16–18 years was the strongest predictor of later schizophrenia (Malmberg *et al*, 1998; Davidson *et al*, 1999). General population birth cohort studies have found problems with socialisation at even earlier ages: in the 1946 British birth cohort (National Survey of Health and Development), a preference for solitary play was apparent by 4 years of age among children who later developed schizophrenia (Jones *et al*, 1994). However, the inability to relate effectively with peers during childhood is probably a non-specific predictor of psychiatric and social morbidity, and we cannot determine the degree to which peer rejection contributes to this morbidity or is merely a marker of risk (Brown & Dodge, 1997; Hollis & Taylor, 1997).

The strongest risk factor for schizophrenia in this study was 'abnormal suspiciousness or sensitivity' in childhood and adolescence, and this was independent of relationship difficulties. Few studies have examined this symptom separately, and it may have been incorporated into many of the earlier reports of relationship difficulties. One exception is the Swedish conscript study (Malmberg *et al*, 1998) mentioned above, which found that reporting oneself as 'more sensitive than others' at age 18 years was a risk factor for schizophrenia, and conscripts who endorsed this symptom, in combination with 'having fewer than two close friends', 'preferring to socialise in small groups' and 'not having a steady girlfriend', were 30 times more likely to develop schizophrenia than their peers. Accumulation of exposure to these four variables was associated with a linear increase in the risk of developing schizophrenia: a dose–response relationship (Malmberg *et al*, 1998). Reports of childhood experiences by patients with schizophrenia also describe 'hypersensitivity' as a prominent feature (Wagner, 1996). Investigation of the neuropsychological basis of this symptom in childhood may give insight into the development of psychotic phenomena.

Comparison with previous work on affective psychosis

The literature regarding childhood precursors of affective psychosis is less clear than for schizophrenia. There is evidence for pre-morbid social impairment although to a lesser degree than in schizophrenia (Cannon *et al*, 1997). In the 1958 British birth cohort study (National Child Development Study), boys who later developed affective psychosis were rated as more hostile to other children and more restless at age 7 years but these differences had disappeared by age 11 years and otherwise they were very similar to the control group (Done *et al*, 1994; Crow *et al*, 1995). This is the first study to demonstrate that childhood hysterical symptoms and eating problems can precede adult affective psychosis, but these associations have wide confidence intervals, are based on small numbers of cases and need replication in other samples.

Genetic risk factors

It is well known that both schizophrenia and affective psychosis have substantial genetic components; having a first-degree relative who suffers from bipolar disorder or schizophrenia increases the risk for the illness in probands by 6–10-fold (Sham, 1995). We found that children who developed either schizophrenia or affective psychosis were more likely to have a family history of psychiatric illness in a first-degree relative, but we had no information about the exact nature of the psychiatric illness in the relatives. A previous study of Maudsley Child Psychiatric Clinic attendees found that the presence of any psychiatric illness in relatives was a significant predictor of early-onset affective disorder (Guth *et al*, 1993).

Disagreement with previous studies

The schizophrenia group were more likely to have been seen by a psychologist or psychiatrist previously, emphasising that psychological difficulties began at a very early age. We were initially surprised to find no evidence for motor or language developmental impairments in our pre-psychosis sample (apart from elective mutism, which was noted in about 8% of the schizophrenia group but did not occur in the comparison group). Our explanation is that the item sheets only rated symptoms or signs occurring over the past 12 months, and would therefore not detect very early

developmental impairments. Previous studies of child psychiatric clinic populations that have found such impairments have examined early-onset patients only or have used maternal interview information recorded in case notes (Guth *et al*, 1993; Hollis, 1995; Sigurdsson *et al*, 1999).

Implications of our findings

Our findings suggest that the premorbid precursors for schizophrenia and affective psychosis differ and do not simply reflect non-specific psychiatric disturbance in adolescence. There appear to be separate 'tracks' leading from suspiciousness, sensitivity and social difficulties to schizophrenia, and from eating disorders/hysterical symptoms to affective psychosis. An interesting question (which we cannot answer from our data) is whether these childhood problems are markers of the neurocognitive substrate of schizophrenia or affective psychosis, or are independent risk factors for the disorder. At a general population level, the predictive power of individual childhood symptoms is low (social difficulties are common and schizophrenia is rare) (Malmberg *et al*, 1998). However, within the context of a child psychiatric clinic the predictive power of our model was relatively high. Our study demonstrates the benefits of moving from a risk factor approach to a 'risk model' approach to the prediction of adult psychosis, including not just symptoms but also measures of genetic risk, psychiatric history and demographic variables.

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CLINICAL IMPLICATIONS

- Symptoms detected on routine childhood psychological assessment can predict adult psychotic illness.
- There appear to be separate childhood precursors for schizophrenia and affective psychosis.
- Information on family psychiatric history, in combination with childhood psychological symptoms, can increase the power of predictive models for later psychosis.

LIMITATIONS

- Our results, strictly speaking, apply only to children who attend a child psychiatry service.
- Predictive power of childhood symptoms is generally low in the general population, owing to the high prevalence of childhood difficulties and the rarity of adult psychotic outcomes.
- Symptom precursors of affective psychosis found in this study will need replication in other, larger samples.

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