Cerebral Dysfunction and Childhood Psychoses

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V. Cerebral Dysfunction and Childhood Psychoses

By I. KOLVIN, C. OUNSTED, and M. ROTH

A series of recent papers (Creak, 1961, 1963; Rutter, 1966; Brown, 1963; Lotter, 1967; Schain and Yannet, 1960) have provided evidence of degrees of cerebral dysfunction in infantile autism (Kanner, 1943) and other infantile psychoses. They have demonstrated that groups of cases of infantile psychoses satisfying broadly similar diagnostic criteria have in their backgrounds a variable frequency of cerebral insult and abnormal discharge in the EEG. The diagnostic criteria in such series are of crucial importance. Imprecision and vagueness hamper comparisons between series. In childhood psychoses some investigators have excluded those cases in which there was any history or clinical evidence of organic features in an attempt to obtain a 'pure' group. This technique, while valid in delineating a syndrome, is handicapping to subsequent etiological study. For these reasons the present authors have used only age of onset and behavioural features as their ascertainment criteria it was a behavioural rather than an aetiological diagnosis.

Methods

Childhood psychoses have been divided into three groups—those beginning before the age of three; those between the age of three and five; and those beginning after the age of five. The criteria for diagnosis and the clinical phenomena of the two main groups of infantile psychosis (I.P.) and psychosis of later onset (L.O.P.) are described in the foregoing papers of this series.

Information about the perinatal history of each child was obtained from mother, paediatrician, social worker, etc., extended neurological examinations made, and EEGs recorded.

In one L.O.P. case the perinatal data were not reliably available. In 28 out of the 33 cases it was possible to undertake EEG examinations.

The children of the I.P. group being younger had more reliable early information available (46 out of 47). Forty-four had EEGs and in two of the other three there was other evidence of cerebral dysfunction.

Certain investigators (Anthony, 1958, and 1962) have pointed out that psychosis appearing after the age of three and before the age of five has a high likelihood of being organically determined. The size of this group of cases was small—three psychotics with such an onset were found. In all three there was clear-cut evidence of brain dysfunction, as described in paper II of this series.

It had been hoped to stratify the 80 cases according to varying degrees of cerebral dysfunction but the smallness of the series prevented this. Instead it was decided to divide the data into two categories, a 'pure' and a 'complicated' group, the former showing no associated anomalies.

Findings

Some relevant biographical features and the results of clinical neurological examination are listed in Tables I and II. (More detailed information is available on request from the authors.) Minor perinatal complications were ignored. Prematurity *per se* was not accepted as providing sufficient historical evidence unless relatively severe (weight below 5 lb.) or combined with other complications which could occur independently, such as respiratory distress. Where more than one perinatal risk factor was present the case was categorized in Table I according to the main complication. Where such a pattern was not clearly identifiable the case was included in the multiple difficulties category. Thus under delivery, two of the caesarean sections were breech presentations, and so were two of the L.O.P. difficult labours.

The Table provides no indication of the

TABLE I
Evidence for perinatal brain damage

	I.P. Cases ($n = 46$)		*L.O.P. Cases* ($n = 32$)	
A. During pregnancy	maternal rubella	1		
	toxemia with A.P.H.	1		
		2		0
B. During delivery	prematurity	2		
	Difficult labour	3	difficult labour	3
	caesarean section	3		
		8		3
C. Neonatal	encephalitic	2	respiratory distress	1
	massive spasms	2	Rh incompatibility	1
		4		2
D. Multiple difficulties during A, B, C		7		0
Total		21 (46%)		5 (15%)

TABLE II
Clinical signs of brain damage

	I.P. cases ($n = 46$)		*L.O.P. cases* ($n = 33$)	
A. Neurological	spasticity	1	spasticity	1
	minor motor anomaly	3	minor motor anomaly	2
	hypotonia	2		
	abnormal gait	1		
	skull asymmetry	1		
		8 (17%)		3 (9%)
B. Epileptic	massive spasms	4		
	other seizures before	3	other seizures before	4
	other seizures after	2		
		9*		4
C. EEG	low voltage record	12	low voltage record	2
	no low voltage record	32	no low voltage record	26
		44	$\chi^2 = 4{\cdot}4$	28
	abnormal record	14		9
	equivocal (includes low v.)	13		3
	normal (includes slow waves)	17		16
	epileptic, EEG and clinical	8		4
	epileptic, EEG only	6		5

* Includes one case without EEG record.

severity of the complications. There was thus a great variety of possibilities of perinatal risk factors. However when they are taken together there is a significant excess of them in the I.P. group (21 out of 46, or 46 per cent) as against the L.O.P. group (5 out of 32, or 15 per cent; $\chi^2 = 7{\cdot}7$). It can be argued that perinatal complications provide presumptive evidence of brain damage, but this carries little weight unless there is subsequent evidence of other neurological or encephalographic abnormalities. This proved to be the case for all but one out of the 5 L.O.P. cases and 7 of the 21 I.P. cases.

The 46 I.P. cases and 32 L.O.P. cases were classified in four groups as follows:

Level O—A group in whose biography, and from clinical neurological and EEG investigations, no evidence of brain damage could be found. This is called a 'Pure' group.

Level I—A group in whom a perinatal anomaly was present (prematurity, persistent breech, etc.) but no evidence of brain damage on clinical investigation.

Level II—Children with an isolated anomaly on EEG or on special investigations (X-ray of skull) and minor anomalies on neurological examination.

Level III—Those children in whom there was unequivocal evidence of brain dysfunction: a clear-cut history (e.g. of encephalitis); epilepsy; neurological signs, alone or in combination.

The numbers in each group are given in Table III. It is clear that there is a definite subgroup of cases with good evidence of brain damage.

In the following analysis the pure cases (Level O) are compared with the rest, or complicated cases.

TABLE III

Brain dysfunction in childhood psychosis

	I.P. cases ($n = 46$)			*L.O.P. cases* ($n = 32$)	
	N	%		N	%
Level O,	21	46		22	69
			$\chi^2 = 4{\cdot}1$		
Level I	7			1	
Level II	7			4	
Level III	11	24		5	15

EEG Variables and epilepsy

Normal data for young children's EEGs are not generally available and only broad judgements could be made. Table II indicates there was an excess of low voltage records (27 per cent) in the I.P. group compared to the L.O.P. group (7 per cent). There were no differences between the two psychotic groups in terms of EEG epileptic discharge patterns. If the equivocal group, which was mainly composed of low voltage or flat records, is accepted as abnormal then 57 per cent of the L.O.P. group had completely normal EEGs but only 38 per cent of the I.P. group. If equivocal records are counted as normal then 68 per cent of the L.O.P. and 69 per cent of the I.P. group had broadly normal EEGs and there was no difference between the groups. In fact the only difference between them was in the number of low voltage records (Hutt *et al.*, 1964, 1965).

There was a cluster of cases within each group with a history of epilepsy. In the I.P. group 5 cases (4 clear-cut and one dubious) had a previous history of massive spasms. Another 5 cases had typical or atypical major fits. Those with massive spasms were an interesting group—after an earlier bout of spasms they were indistinguishable in behavioural symptoms from the infantile psychotics. In 3 of the 5 cases later EEG examinations showed no abnormalities.

The interesting feature of the epilepsy in the L.O.P. group was that 3 cases had clear-cut temporal lobe epilepsy which had been present for many years before the onset of the psychosis. Another had a temporal lobe spike focus on EEG, minor neurological anomalies but no fits. Though the numbers are small this tends to confirm the findings of Slater and Beard (1963) on epilepsy and schizophrenia in adults.

Brain dysfunction and other findings

(a) *Social Class*

Elsewhere (Kolvin *et al.*, paper III) it was shown that the two groups of childhood psychoses (I.P. and L.O.P.) are linked with social class, I.P. being more common in social class I

and II and L.O.P. in social classes IV and V. Table IV shows that the cerebral dysfunction (organic) I.P. group is again class-related, the parents of many cases falling into Classes III to V whereas the parents of the pure I.P. cases were more often in Classes I and II. This underlines the well established relationship between adverse social factors (represented here by lower social class) and physical and intellectual malaise (Fairweather and Illsley, 1960 and Illsley, 1961). These results provide strong support for the view that pure infantile psychosis is linked with social class.

TABLE IV
Social Class and Brain Dysfunction

Social Class	Pure I.P.		Complicated I.P.		Total
	N	%	N	%	
I + II	12	57	5	21	17
III + IV + V	9	43	19	79	28

$p = \cdot 026$

(b) *Phenomenology*

Five comparisons were made

(i) L.O.P. complicated v. L.O.P. pure. The numbers here were too small to indicate anything other than trends.

(ii) I.P. complicated v. I.P. pure.

(iii) L.O.P. complicated v. I.P. complicated.

(iv) L.O.P. complicated v. I.P. pure.

(v) L.O.P. pure v. I.P. pure.

Most of the features examined did not appear to be related to brain dysfunction: excitement, silly giggling, perplexity, aimless wandering, perseveration, abnormal induced movements, abnormal postures and mannerisms, spontaneous movements (except impulsivity), work ability (where possible) and evidence of formal thought disorder where possible; disorder of stream of thought and alienation of thought, murmuring and whispering to voices. Some trends were found which only applied to one or other group—these are discussed elsewhere (Kolvin *et al.*, VI). Indeed few trends and fewer statistical associations were found.

Those who have witnessed the spine-chilling rage reactions of autistic or I.P. children have felt strongly that there must be an underlying organic basis. Indeed there was a trend towards more frequent rage reactions amongst the I.P. brain-dysfunction group. But this evidence by itself is not convincing enough to support an organic hypothesis. Similarly, there was a trend towards increased impulsive behaviour in the complicated I.P. and L.O.P. groups but this again was not very convincing. However, highly significantly ($p = \cdot 008$) more of the pure I.P. than the pure L.O.P. cases rejected all contact whatsoever. This could be merely a part of a general autistic retreat reaction among the I.P. group expressing itself slightly more frequently in the pure cases. The tendency towards self-scrutiny of hands and feet was more prominent among the pure than among the complicated I.P. group.

The only two behavioural features which showed associations with brain dysfunction were ritualistic behaviour and hyperkinetic behaviour. The pure I.P. group were significantly more ritualistic than the pure L.O.P. group ($p = \cdot 044$). One can only speculate about the meaning of this finding.

Finally, the complicated I.P. group were more hyperkinetic than the pure I.P. group but only at the 10 per cent level ($p = \cdot 1$). The use of the term hyperkinesis in relation to infantile psychosis needs clearer definition. When present it refers to continuous movement of a desultory non-purposeful variety rather than the seemingly purposeful switching of attention and insatiable curiosity of the brain-damaged hyperkinetic child (Ounsted, 1955). Hyperkinesis is a well-known but variable consequence of brain-damage in early childhood (Ounsted, 1955 and Ingram, 1956), and its manifestation in a group of young children with probable brain dysfunction is not unexpected. It provides at least a part explanation for some behaviour of I.P. children.

(c) *Psychological precipitants*

Psychological precipitating factors occurred to an appreciable extent (50 per cent) in the pure L.O.P. group. These included such experiences as death of a close relative, sexual assault, etc., which, though small in number, occurred significantly more frequently in this group than in the other three groups jointly ($\chi^2 = 6 \cdot 2$ with $p < \cdot 02$).

TABLE V

Phenomenology and brain dysfunction

	Pure				Complicated			
	L.O.P.		I.P.		L.O.P.		I.P.	
	N	%	N	%	N	%	N	%
No rage	15		14		7		14	
Rage	7	31	7	33	3	30	11	44
Not rejecting contact	14		4		4		7	
Rejecting contact	8	36	17	81	6	60	18	72
No self-scrutiny			6				13	
Self-scrutiny			15	70			12	48
Not-hyperkinetic			11	52			6	
Hyperkinetic			10	48			19	76
No impulsive actions	16		14		5		14	
Impulsive actions	6	27	7	33	5	50	11	44
No rituals	14		6		5		13	
Ritualistic	8	36	15	72	5		12	48

This finding leads to speculation about possible psychogenic triggers in predisposed individuals. However, with the retrospective character of some of the L.O.P. data and with the small size of the series it is unwise to theorize about unprovable causal origins.

TABLE VI

Psychological precipitants and brain dysfunction

	Pure				Complicated			
	L.O.P.		I.P.		L.O.P.		I.P.	
	N	%	N	%	N	%	N	%
None ..	11	50	17	81	7	70	20	80
Present ..	11	50	4	19	3	30	5	20

The data of this study were reorganized in order to make them comparable with Lotter's (1967) epidemiological series. The perinatal complications were given scores of 0–3 for severity in each of the three periods of pregnancy, delivery, and neonatal life and the number of cases showing such complications listed.

Rating	*Lotter*	*I.P.*	*L.O.P.*
0–2	22	30	28
3+	6 (21%)	16 (35%)	4 (12%)
Total	28	46	32

DISCUSSION

An excess of perinatal complications has previously been reported in the histories of infantile psychotic patients (Vorster, 1960, Taft and Goldfarb 1964, Knobloch and Grant, 1961). Gittelman and Birch (1967) studied a heterogenous group of 'schizophrenic children' and found a 35 per cent incidence of complications of pregnancy and delivery. In the present study, taking equivalent items, the incidence of pregnancy and birth complications (37 per cent) in the I.P. group is broadly similar to that found by Gittelman and Birch; whereas in the L.O.P. group it is very much lower (12 per cent).

The difference between Lotter's autistic and our I.P. group can quite reasonably be attributed to different selection procedures.

The significant excess of perinatal complications in the I.P. group over the L.O.P. group is unlikely to be entirely explained by the better recall by parents of younger children and the large percentage of younger children referred by paediatricians. Though the differences need to be interpreted with caution they cannot be ignored. Among the possible explanations are:

(a) organic factors acting as psychotic release mechanisms in infants with a psychotic predisposition.

TABLE VII

Comparison of epileptic fits in different series

Author	Total Cases	Fits	Percentage
Kanner (1954)	100	1 case	1
Creak (1963)	100	12 cases	12
Rutter (1967)	63	13 + 2 dubious cases	21—24
Schain and Yannett (1960)	60	21	32
Lotter (1967)	32	4	12
Present series L.O.P.	32	4 + 1 dubious	12—15
Present series I.P.	41	9 + 1 dubious	19—22

(b) physical interference, not necessarily macroscopic, with the neurophysiological pathways for integration of incoming stimuli.

The earlier studies (Kanner, 1954) of authenticated cases of infantile psychosis did not find certain and significant evidence of neurological abnormality. Creak (1963) confirmed this while others (Vorster, 1960, Goldfarb, 1961; Rutter, 1965 and 1967; Gittelman and Birch, 1967 and Lotter, 1967) have produced data suggesting a substantial degree of cerebral dysfunction.

Both Goldfarb (1961) and Gittelman and Birch (1967) studied clinically heterogeneous groups of childhood psychoses without adequate specification of diagnostic criteria. Goldfarb reported a 66 per cent incidence of neurological abnormalities in 26 cases. Gittelman and Birch rated 97 case records retrospectively for three categories of neurological dysfunction. Sixty-six per cent were negative, 13 per cent at risk (equivocal EEG, blackouts, suspected encephalitis, etc.), and 18 per cent positive (petit or grand mal; abnormal EEG, athetotic or pathological reflexes).

They considered these to be conservative estimates, for incidence rose to 75 per cent of 51 cases when results of clinical neurological examination were available. It rose further to 80 per cent when evidence either from clinical history or examination was considered. The importance of this study lies in the fact that it was of non-institutionalized children.

Rutter and Lockyer (1967) reported that 18 out of 63 (28 per cent) showed 'probable' evidence of brain-damage and 16 (25 per cent) 'possible' evidence. Lotter (1967) in his epidemiological study reported that 11 of 32 (33 per cent) showed abnormal neurological signs.

Our study shows more complicated (presumed cerebral dysfunction) cases among the I.P. than the L.O.P. (54 per cent against 31 per cent, $\chi^2 = 4 \cdot 1$). Though these percentages are lower than those found by Goldfarb (1961) and Gittelman and Birch (1967) they are substantially higher than Lotter's, possibly because they are all hospital cases. Different criteria from those of Rutter were used for rating cases as brain-damaged, and our figures are therefore not really comparable with his. Nevertheless, they all provide support for the suggestion of considerable cerebral dysfunction in infantile psychosis. The fact that 50 per cent of the cases do not show this dysfunction does not invalidate the theory, nor does the smaller percentage found in the group collected by epidemiological survey. It may be that part but not the whole of the variance is determined by cerebral dysfunction. Furthermore, as in schizophrenia where a pool of symptomatic cases (temporal lobe epileptics) collects in mental institutions, a pool of symptomatic infantile psychotics may be gravitating to hospital environments. Epidemiological research reflecting a smaller incidence of cerebral dysfunction in the general population does not invalidate its importance but rather places it in perspective in relation to the syndrome. It must also be remembered that we find more pure I.P. cases (lacking evidence of cerebral dysfunction) in the highest social class. Hence the social composition of a clinical sample may determine the precise findings.

A number of investigators have now reported on the liability to epileptic fits in infantile psychoses.

The United Kingdom hospital cases (Creak, Rutter and Lockyer and Kolvin *et al.*,) all show a higher incidence of fits than the cases ascertained by epidemiological techniques (Lotter, 1967). Rutter's work suggests that incidence of fits increases with age. The Schain and Yannett (1960) series is remarkable for the exceptionally high frequency, especially in the first two years of life (28 per cent which includes three cases of infantile spasms). This higher frequency is probably determined by biased selection, as their cases were obtained from a subnormality institution. The early onset of fits is at variance with Rutter's findings in which 10 cases had late-onset fits, but is similar to the present series where 15–17 per cent had early onset fits. Indeed in the present I.P. series the incidence of fits is a very conservative estimate as the cases have not been followed up long enough.

In spite of this disagreement over the incidence of fits in different I.P. groups one can discern a pattern. L.O.P. cases with fits had them for many years before the onset of the psychosis, whereas in I.P. cases the fits were simultaneous with or post-dated the onset of the psychosis. While in the L.O.P. cases epileptic or EEG abnormalities were localized in the temporal lobe, no unifying pattern could be discerned in the I.P. cases, although there were two sub-patterns—a group of cases with low voltage EEG's (Hutt *et al.*, 1964, 1965), and cases with infantile spasms. In the Schain and Yannett (1960) series three children had infantile spasms. In the present series there were four. Whatever the explanation for the high incidence of the syndrome of massive spasms (9 per cent) in our study it suggests one possible pathophysiological basis for infantile psychosis. We are not suggesting that infantile psychosis is generally determined by massive spasms but rather that some cases of infantile psychosis are preceded by massive spasms, just as temporal lobe epilepsy may precede adult schizophrenia. The syndrome of massive spasms is regarded as having a multifocal origin. This is interesting in view of the fact that on occasions an autistic child has been found to be suffering from a degenerative cerebral disorder (Corberi, 1926), so that the possibility of a minimal diffuse cortical condition or even a minimal multifocal cortical condition in some psychotics cannot be ignored. This hypothesis is partly supported by the subsequent development of major fits in 2 cases in this series and in 11 of the 63 cases followed up at the Maudsley (Rutter and Lockyer 1967).

The diversity of both the EEG and seizure patterns argues against a homogenous pathological process or mechanism underlying infantile psychosis. It argues for different types of structural disorganization within the central nervous system leading to a homogeneous functional aberration, for instance in the reticulocortical system as suggested by Rimland (1964). There might then be early progressive damage (and later fits) or non-progressive damage (with early fits, continuing or remitting) at different levels of this system.

The main early theory of the genesis of autism or infantile psychosis was a psychogenic one (Kanner, 1943 and 1954) which incriminated parental personalities as one of the main determining features. Subsequent research (Creak and Ini, 1960, and Kolvin *et al.*, IV) has not substantiated this theory. The present work points to important neurophysiological antecedents of infantile psychosis and complicated late onset psychosis. Indeed, the only subgroup in which there can be any speculation about possible psychogenic triggers is the pure L.O.P. group, and even in this it is doubtful.

Summary

Cerebral dysfunction has been sought in 46 children suffering from infantile psychosis and in 33 suffering from late onset psychosis in terms of anomalies in perinatal life, and by neurological and EEG examinations. 46 per cent of I.P. cases and 69 per cent of L.O.P. cases had no such evidence of dysfunction, and there was evidence that more of these pure I.P. cases came from social class I and II.

On the other hand one-quarter of the I.P. cases had very strong evidence of cerebral dysfunction, and a low voltage EEG record was much commoner in them. Roughly one-third of both I.P. and L.O.P. cases had abnormal

EEGs. It is interesting that massive infantile spasms preceded the onset of I.P. in 4 cases, while temporal lobe epilepsy was present beforehand in 3 cases of L.O.P.

Childhood psychoses are a heterogenous collection. The evidence for an organic pathology is discussed.

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