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Minor malformations in mental retardation of various aetiology

by

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The frequency of minor malformations was determined in 246 mentally retarded children with an I. Q. ranging from 37 to 67. According to the probable aetiology, the patients were divided into 4 groups: Down syndrome (n = 29), other genetic causes (n = 22), perinatal and postnatal environmental damages (n = 68), and unknown aetiology (n = 127). One thousand consecutive newborn infants served as controls.

The mean number of minor malformations per subject was the highest in patients with Down syndrome (3.38) and other genetic disorders (2.00). It was significantly lower in the mentally handicapped of unknown (0.88) and of environmental origin (0.37). The number of multiple minor anomalies was high in the genetically determined conditions and the smallest and nearing the control value in the exogenic group.

The results support the idea that the presence of minor malformations, and especially of multiple ones, refers to the prenatal onset of mental deficiency.

Minor malformations are in themselves harmless structural variations. They may occur in completely healthy individuals, but their frequency is much higher in subjects with congenital disorders. A positive correlation between minor malformations and childhood behaviour anomalies and mental retardation has been demonstrated in several investigations [3, 4, 6, 17, 18, 19, 21, 22, 23, 24]. Most of these studies, however, dealt with mental retardation or "brain damage" in general, irrespective of aetiology. The present paper reports on mentally handicapped children in whom efforts were made to clarify the cause of subnormality.

MATERIAL AND METHODS

A total of 246 institutionalized mentally retarded children, 153 boys and 93 girls, was involved in the study. Their age varied from 4 to 17 years (mean, 11.4 years). The mean I.Q. (Binet—Simon) was 55, with a range of 37 to 67.

The following examinations were carried out in each child: pedigree analysis, paediatric and neurologic status, electroencephalography, audiology, buccal X-chromatin, lymphocyte Y-chromatin, serum cholesterol, uric acid, thyroxine, TSH, amino acid chromatography, urine screening tests for sugar, protein and mucopolysaccharide excretion.

In suspicious cases the above methods were complemented with more detailed biochemical, cardiologic, radiologic, ophthalmologic, cytogenetic and dermatogly-

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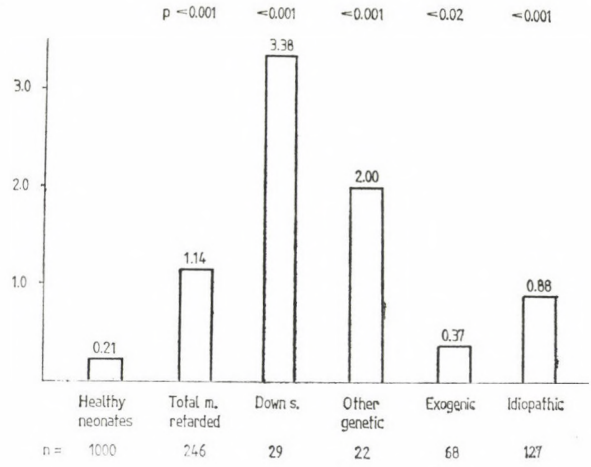

FIG. 1. Mean number of minor malformations per child in the different aetiological groups of mental retardation. The p-values represent significance againts the control neonates

phic investigations. Special care was taken to get information about perinatal events.

By means of these methods the children could be grouped according to aetiology as follows.

(1) Genetic disorders (51 patients = 20.7%).

(a) 29 children with Down syndrome

(b) 22 subjects with other genetically determined abnormalities, including 4 chromosome aberrations, 10 inborn errors of metabolism, and 8 specific syndromes.

(2) Perinatal and postnatal environmental injuries (68 children = 27.6%). Clearly detectable perinatal and postnatal meningitis and encephalitis, asphyxia, trauma, kernicterus, and very low birth weight (< 1250g) were included in this group.

(3) Idiopathic mental retardation (127 patients = 51.6%). In some of these cases the family history referred to a possible familial form with multifactorial inheritance. The data on the relatives, obtained partly from physicians, partly from parents, and partly from teachers, were so heterogeneous and sometimes unreliable that we gave up to form an independent group from these patients and combined them with the children in whom absolutely nothing related to a possible aetiology. No teratogenic damage could be verified retrospectively.

Since our patients were institutionalized at different ages with the most various anamnestic data, no control children corresponding in age, social class, parental education, previous and accompanying diseases could be examined. Thus, the results were compared with those of a new series of 1000 consecutive apparently healthy newborn infants. Minor malformations were scored in both of these babies and in the mentally retarded patients in exactly the same way as in our previous survey of neonates [10].

RESULTS

As compared to healthy neonates, the frequency of minor malformations was significantly higher in the mentally retarded children. When the prevalence values were expressed as minor malformation per child, and analysed according to aetiology, the highest figures were found in the patients with Down syndrome (3.38)

TABLE I

Proportion of children with 0, 1, 2, 3 or more minor anomalies in relation to whether or not they had major malformation

	Children with 1 or more major malformations				No major malformation			
	0	1	2	≥3	0	1	2	≥3
Controls (n = 1000)					834 (83.4%)	129 (12.9%)	32 (3.2%)	5 (0.5%)
Down syndrome (n = 29)	—	—	—	7 (24.1%)	—	—	2 (6.9%)	20 (69.0%)
Other genetic (n = 22)	1 (4.6%)	2 (9.1%)	3 (13.6%)	3 (13.6%)	2 (9.1%)	4 (18.2%)	4 (18.2%)	3 (13.6%)
Exogenic (n = 68)	1 (1.5%)	1 (1.5%)	—	—	49 (71.9%)	11 (16.2%)	5 (7.4%)	1 (1.5%)
Idiopathic (n = 127)	1 (0.8%)	1 (0.8%)	1 (0.8%)	—	53 (41.7%)	45 (35.4%)	19 (15.0%)	7 (5.5%)

and with retardation of other genetic origin (2.00) (Fig. 1).

The lowest frequency was obtained in subjects in whom the retardation was attributed to environmental factors (0.37), while the mean of the idiopathic group was significantly higher (0.88).

The proportion of children with multiple minor anomalies with or without associated major malformations was very similar in the normal neonates and in the mentally handicapped of environmental origin (Table I).

A higher number of multiple birth defects was seen in the idiopathic group, but major malformations were very rare. In the genetically determined cases both major defects and multiple minor anomalies were relatively common.

A total of 279 minor malformations was identified in the 246 mentally subnormal children. This number was too small to evaluate the significance of the individual anomalies in the different groups of patients. The distribution of minor birth defects differed, however, from that found in the normal neonates; the higher frequency of antimongoloid palpebral slant in the mentally subnormals was conspicuous. Further common features were: upward palpebral slant, hypertelorism, ear deformities, preauricular tags and pits, simian crease, mamillary and hallucal abnormalities.

DISCUSSION

Excellent aetiological surveys of mentally subnormal children have been reported [1, 2, 5, 7, 8, 14, 15, 16]

but because of differences in severity and origin of the material and in the methods of investigation, the results are hardly comparable. Our findings are, however, in accordance with the tendencies in other surveys; about 13% of the patients had chromosome aberrations and it was possible to establish a causal diagnosis in some 50% of the cases.

Minor malformations have not or only superficially been dealt with in previous studies. Thus, for instance, Mounoud et al [14] demonstrated a 2- to 4-fold increase in the frequency of epicanthus, fistula auris congenita and simian crease in idiopathic mental retardation. Similar results were published in the basic work of Smith and Bostian [19]. When examining children with ventricular septal defect, with cleft lip and palate, and with idiopathic mental retardation excluding cases of known genetic and environmental origin, they found the highest frequency of associated minor anomalies in the group with idiopathic mental retardation. According to these authors the discovery of multiple associated anomalies suggests that the defect of brain function is also a congenital abnormality. In harmony with an earlier Hungarian survey [6], our results, too, confirm this conclusion. The prevalence of minor malformations was significantly higher in the mentally retarded children, but when distinction according to probable aetiology was made, remarkable differences were obtained. Irrespective of Down-patients, a very high frequency and many multiple anomalies were seen in the group of genetically determined cases, where minor malformations indirectly verified the prenatal onset and sometimes even the timing of the problem in morphogenesis [20]. At the same time, only a slight increase in the frequency of minor anomalies was found in the group of environmental cases. Multiple malformations were very rare among these children; this seemed to be an evidence of the perinatal or postnatal origin of the mental defect.

The children with idiopathic mental reatardation showed intermediate values. This was probably due to the fact that this group was a mixture of undetectable familial cases, of defects of hitherto unknown genetic and teratogenic origin, and of birth injuries and postnatal causes. It is likely that the composition of "idiopathic" groups was similar in the previous surveys too. The adjective "idiopathic" refers to the lack of knowledge and information but the retarded individual must have had either a prenatal or a perinatal/postnatal defect. Therefore we emphasize the importance of individualization also in the evaluation of minor malformations.

The presence of minor anomalies, and especially of multiple ones, may support the diagnosis of genetic or teratogenic mental retardation, whereas the absence of minor birth defects may refer to a perinatal or postnatal brain damage. For that reason we recommend thoroughly to examine the mentally retarded children for minor malformations. Further,

we propose to screen newborn infants for minor anomalies and for other factors often associated with congenital disorders, i.e. intrauterine growth retardation and positive family history [9, 13]. Based on this principle, a simple score was elaborated in our department which proved to be useful in the early recognition and eventual prevention of mental retardation [12].

The diagnostic value of the different minor malformations is certainly different. This study could not essentially contribute to this question; still, in agreement with our earlier observations [11, 12], the significance of antimongoloid palpebral fissures, hypertelorism, preauricular pits, simian crease, mamillary and hallucal abnormalities was confirmed in this material, too.

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