

Study of Subarachnoid Spaces in Children With Idiopathic Mental Retardation

P. Prassopoulos, MD; D. Cavouras, PhD; M. Ioannidou, MD; S. Golfinopoulos, BSc

ABSTRACT

The aim of this study was to assess quantitatively the size of the subarachnoid space in children with "idiopathic" mental retardation. The extent of various cerebrospinal fluid compartments was measured in 106 brain computed tomographic examinations of children with idiopathic mental retardation, and the results were compared with the corresponding normative data. The third ventricle was enlarged in 77% of the cases. A mild degree of diffuse widening of the subarachnoid spaces was found in about 30% of the patients. These morphologic alterations are additional observations supporting the hypothesis that "idiopathic" mental retardation has a biologic basis. (*J Child Neurol* 1996;11:197-200).

Children with mental retardation fail to achieve expected milestones at the appropriate age, revealing psychomotor delay during early childhood or, in the mildest of cases, deficits in adaptive behavior and intellectual impairment when they are school age.^{1,2} Mild mental subnormality occurs with a prevalence of 20 to 30 per 1000, and severe subnormality has a prevalence of three to four per 1000 in the general population.¹ Children suspected of having mental retardation during pediatric screening undergo detailed developmental and medical evaluation in order to establish the existence and degree of the subnormality and associated deficits. Medical assessment attempts to investigate etiologic factors that are useful in providing information about prognosis, in planning optimal management, and in genetic counseling to the family.¹⁻³ Chromosomal abnormalities, endocrine and metabolic diseases, genetic syndromes, central nervous system malformations, and brain injury are often associated with mental deficiency.^{1,2} However, in 45% to 65% of the children with mild mental retardation and in 30% to 40% with severe mental retardation, a specific diagnosis cannot be determined, and the subnormality is characterized "idiopathic."¹

Received March 7, 1995. Received revised May 22, 1995. Accepted for publication May 23, 1995.

From the Department of Radiology (Dr Prassopoulos), University Hospital, Medical School of Crete, Iraklion, the Department of Medical Instrumentation Technology (Dr Cavouras), School of Technological Applications, Technological Educational Institution of Athens, Athens, and the Department of Radiology (Drs Ioannidou and Golfinopoulos), Aghia Sophia Children's Hospital, Goudi, Athens, Greece.

Address correspondence to Dr D. Cavouras, Department of Medical Instrumentation Technology, Technological Educational Institution of Athens, 37-39 Esperidon Street, Kallithea 17671, Athens, Greece.

In a significant number of children with idiopathic mental retardation, subtle findings on neuroimaging studies, mostly concerning cerebrospinal fluid compartments, have been reported.¹ Macro cisterna magna and cavum septi pellucidi are among those findings that in children with idiopathic mental retardation have been considered signs of mild cerebral dysgenesis rather than normal variants.^{4,5} Recent evidence has suggested that mild mental retardation might have a pathologic basis and could be associated with morphologic changes in the central nervous system as well as other somatic anomalies.^{1,6}

In this study, the extent of the cerebrospinal fluid compartments in brain computed tomographic (CT) examinations of children with idiopathic mental retardation was assessed quantitatively in order to investigate morphologic changes that may be associated with idiopathic mental retardation.

MATERIAL AND METHODS

Brain examinations of children referred for CT scan in our departments with clinical evidence of developmental disability during the last 4 years were reviewed. One hundred six children—62 boys and 44 girls, 10 months to 14 years old—finally diagnosed as having mild (97) or severe (nine) idiopathic mental retardation were selected from the optical disks of the CT units. Children with chromosomal abnormalities, metabolic diseases, congenital syndromes, microcephaly, cerebral palsy, visual or hearing deficits, or history of perinatal asphyxia, intracranial hemorrhage, severe head trauma, and central nervous system infection were not included in this study. Additionally, children with neuroimaging findings of focal brain lesion, central nervous

system malformation, or any alteration in the morphology of the subarachnoid space, such as cavum septum pellucidum or benign frontal enlargement of the cerebrospinal fluid space, were also not included in this series.

Examinations were performed on Phillips LX CT scanners with consecutive 5-mm sections in the posterior fossa and skull base and 10-mm sections in the rest of the cranium. In our departments, younger children are routinely examined after sedation with 80 to 90 mg/kg of chloral hydrate. However, in a significant number (27) of patients with idiopathic mental retardation under the age of 5 years (43 children were less than 5 years old), an additional amount of 20 to 40 mg/kg of chloral hydrate was required, and in four anesthesia was necessary. Employing the CT software, the extent of various cerebrospinal fluid compartments was estimated by the following linear measurements^{7,8}: (1) the minimum width of the bodies of the lateral ventricles; (2) the maximum distance between the anterior horns of the lateral ventricles; (3) the bicaudate nuclei distance; (4) the width of the third ventricle; (5) the width of the fourth ventricle; (6) the anteroposterior and transverse diameters of the basal cistern, which were added; (7) the anteroposterior diameter of the prepontine cistern; (8) the maximum width of the sylvian fissure; (9) the maximum width of the interhemispheric fissure; (10) the maximum width of the "true" or peripheral cerebrospinal fluid space at the frontal, temporal, parietal, or occipital regions; and (11) the maximum width of the cortical sulci. Measurements were divided by either the sum of the maximal longitudinal and transverse diameters of the skull (measurements 1 through 4 and 6) or the posterior fossa (measurements 5 and 7) in order to take into account the size and shape of the skull.⁷ The so-formed quotients (cerebrospinal fluid indices) were compared with the corresponding normative data (normal range = mean value \pm 2 SD) established in previous study.⁷ Because the normal cerebrospinal fluid indices do not differ between boys and girls,⁷ the sex of patients was not taken into account in the statistical analysis. Measurements 8 through 11 were considered abnormal if they exceeded the corresponding upper normal limits⁸ (Table 1). The cisterna magna was not evaluated because, to our knowledge, there are no normative CT data; its size has been estimated only from midsagittal magnetic resonance imaging scans.⁹ Data processing and statistical analysis were performed on a computer.

RESULTS

In children with idiopathic mental retardation, the third ventricle was found to be larger than normal (Figure 1) in 82 cases (77%), the basal cistern was enlarged in 36 (34%), and the lateral ventricles were enlarged in 29 (27%); the latter were assumed enlarged when at least two of the three lateral ventricle cerebrospinal fluid indices (measurements 1 through 3) were above the normal limits. Significant differences were found for the anterior horns ($P < .05$), bicaudate nuclei ($P < .001$), and third ventricle ($P < .001$) indices between children with idiopathic mental retardation and the group of children with normal brain CT examinations that were used for the establishment of normative data.⁷ No differences

were found for the fourth ventricle ($P > .10$) and prepontine cistern ($P > .10$) indices, and the lateral ventricles index was marginally larger than normal ($P = .05$). The fourth ventricle was widened in 13 (12%), and the prepontine cistern was widened in nine cases (9%). The sylvian fissures were found to be enlarged in 34 cases (32%), the interhemispheric cistern in 27 (25%), the peripheral cerebrospinal fluid space in 25 (24%), and the cortical sulci in 29 (27%). Significant differences ($P < .05$) for the sylvian fissures, the interhemispheric cistern, and the cortical sulci were found between children with idiopathic mental retardation and normal children. The difference for the peripheral cerebrospinal fluid space was not of statistical significance ($.05 < P < .10$). In 24 children with idiopathic mental retardation, the third ventricle was normal, as were the rest of the intraventricular and extraventricular cerebrospinal fluid compartments. Enlargement of the extraventricular supratentorial subarachnoid space and the third and the lateral ventricles was observed in all nine children with severe mental retardation; widening of the fourth ventricle and the prepontine cistern was found in seven of them. The range of values for the cerebrospinal fluid spaces and the corresponding normative data are presented in Table 1.

DISCUSSION

Brain imaging studies have a significant impact in the clinical evaluation of children with mental retardation, contributing to specific diagnosis, genetic counseling, and prognosis.^{1,3} A wide spectrum of morphologic anomalies depicted in neuroimaging studies, including intracranial calcifications, dysgenesis of corpus callosum, schizencephaly, gyral abnormalities, porencephaly, and periventricular leukomalacia, have been associated with developmental delay or mental retardation.^{1-3,10} However, in the majority of children with mental retardation, especially those with mild subnormality, an etiologic factor is not identifiable.¹¹ It has been assumed that in many cases, cultural, social, or familial factors are related to mild mental retardation.¹ On the contrary, recent evidence

Table 1. Ranges of Measurements of Cerebrospinal Fluid Spaces in Children With Idiopathic Mental Retardation and Normal Ranges*†

	Idiopathic Mental Retardation	Normal Range
Lateral ventricles	0.087-0.168	0.070-0.137
Bicaudate nuclei	0.020-0.064	0.017-0.043
Anterior horns	0.097-0.195	0.085-0.144
Third ventricle	0.008-0.022	0.003-0.012
Fourth ventricle	0.050-0.106	0.050-0.095
Basal cistern	0.142-0.206	0.102-0.161
Prepontine cistern	0.020-0.075	0.017-0.066
Sylvian fissure, mm	0-7	0-3
Interhemispheric fissure, mm	0-6	0-4
Peripheral cerebrospinal fluid, mm	0-6	0-4
Cortical sulci, mm	0-4	0-2

*From Prassopoulos and Cavouras.⁷

†Zero at the extraventricular cerebrospinal fluid compartments means that the subarachnoid space was too small to be measured.

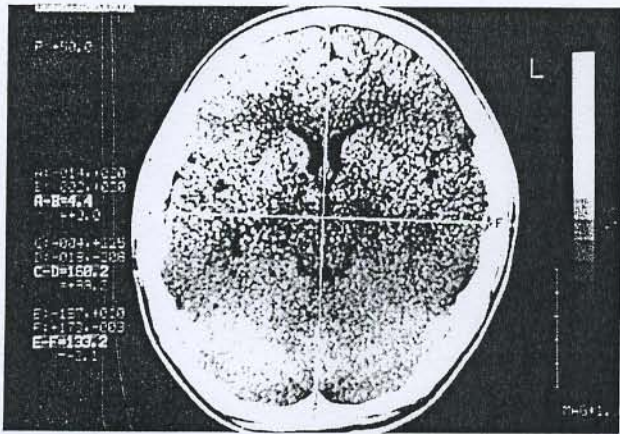


Figure 1. Third ventricular enlargement in an 8-year-old boy with idiopathic mental retardation. The third ventricular index, $AB/(CD + EF)$, was 0.015, which is above the upper normal limit.

from the fields of genetics, dysmorphology, and neuroimaging suggests that the majority of cases with mild mental retardation have a pathologic basis, and a significant incidence of somatic anomalies are associated with mild mental retardation.^{1,6} Likewise, a number of nonspecific or subtle radiologic findings have been observed in children with idiopathic mental retardation, but their contribution to the pathogenesis, clinical management, and prognosis of mental retardation has not been determined. These subtle findings, namely macro cisterna magna, persistence of a cavum septi pellucidi, and hypoplasia of corpus callosum have been considered to represent markers of cerebral dysgenesis in children with idiopathic mental retardation.^{1,4,5,12} These findings support the theory that idiopathic mental retardation has a biologic basis, and the underlying pathogenesis may be related to dysgenetic events during intrauterine brain development.¹ Furthermore, it has been anticipated that with the progress of neuroimaging methods, more such markers will be revealed.¹ According to the results of the present study, in the majority of the children with idiopathic mental retardation, the third ventricle was enlarged. In many cases, this finding did not coexist with other abnormalities and could not be interpreted on the basis of cerebrospinal fluid dynamics. Third ventricular enlargement might either constitute an additional subtle marker of cerebral dysgenesis or be the result of hypoplasia in the neighboring thalamic regions that are known to have several connections with the cerebral cortex.¹³

Quantitative methods employed for the morphometric evaluation of intracranial structures in neuroimaging studies have revealed mild morphologic variations in schizophrenia, autism, fragile X syndrome, and benign enlargement of the frontal cerebrospinal fluid spaces.^{1,8,14-16} In the present study, a quantitative assessment of the extent of the cerebrospinal fluid compartments was performed in order to examine morphologic variations associated with idiopathic mental retardation. In 27% of our patients, the lateral ventricles were

enlarged, and in 24% to 34%, the various extraventricular supratentorial cerebrospinal fluid spaces were widened, with ventricular enlargement being observed concurrently in most cases. These findings might be related to brain growth deficiency in children with idiopathic mental retardation. Reviewing the literature, we were able to find only two studies on this subject. They evaluated the subarachnoid space by visual inspection in children with nonspecific mental retardation; one¹⁷ reported a 4% and the other¹⁸ a 20% incidence of "cerebral atrophy." In the majority of our patients with prominent subarachnoid spaces, the lateral ventricles and the extraventricular cerebrospinal fluid spaces, although enlarged, had values close to the upper normal limits, suggesting a mild degree of diffuse cerebrospinal fluid space widening.

Our patients might be broadly divided on the basis of CT findings into four subgroups: those with normal size of the subarachnoid space, those with supratentorial and infratentorial widening of the cerebrospinal fluid spaces, those with enlargement of only the supratentorial subarachnoid spaces, and those with dilation only of the third ventricle. The variation in the extent of the subarachnoid space suggests either several types of underlying pathology or different degrees of central nervous system dysgenesis in children with idiopathic mental retardation. The latter is more probable, because children with severe idiopathic mental retardation had greater incidence of cerebrospinal fluid spaces widening.

In conclusion, the findings of this study—third ventricular enlargement and diffuse widening of the cerebrospinal fluid spaces—are additional observations supporting the hypothesis that there is a relationship between idiopathic mental retardation and morphologic changes in the brain. More information on this field with advancing neuroimaging technology may illuminate the pathogenesis of idiopathic mental retardation.

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