Spectrum of Visual Disorders in Children With Cerebral Visual Impairment

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Cerebral visual impairment is a visual function deficit caused by damage to the retrogeniculate visual pathways in the absence of any major ocular disease. It is the main visual deficit in children in the developed world. Preperinatal hypoxic-ischemic damage is the most frequent cause of cerebral visual impairment, but the etiology is variable. The authors set out to evaluate the presence of visual disorders not attributable to any major ocular pathology in a sample of children with central nervous system disease and to describe the clinical picture of cerebral visual impairment in this cohort. One hundred twenty-one patients with central nervous system damage and visual impairment underwent a protocol developed at the authors’ center that included neurologic, neurophthalmologic, and neuroradiologic assessments (brain magnetic resonance imaging). Reduced visual acuity was found in 105 of 121 patients, reduced contrast sensitivity in 58, abnormal optokinetic nystagmus in 88, and visual field deficit in 7. Fixation was altered in 58 patients, smooth pursuit in 95, and saccadic movements in 41. Strabismus was present in 88 patients, and abnormal ocular movements were found in 43 patients. Of the 27 patients in whom they could be assessed, visual-perceptual abilities were found to be impaired in 24. Fundus oculi abnormalities and refractive errors were frequently associated findings. This study confirms that the clinical expression of cerebral visual impairment can be variable and that, in addition to already well-documented symptoms (such as reduced visual acuity, visual field deficits, reduced contrast sensitivity), the clinical picture can also be characterized by oculomotor or visual-cognitive disorders. Cerebral visual impairment is often associated with ophthalmologic abnormalities, and these should be carefully sought. Early and careful assessment, taking into account both the neuroophthalmologic and the ophthalmologic aspects, is essential for a correct diagnosis and the development of personalized rehabilitation programs.

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Cerebral visual impairment is defined as a deficit of visual function caused by damage to, or malfunctioning of, the retrogeniculate visual pathways (optic radiations, occipital cortex, associative visual areas) in the absence of any major ocular disease. This rise of cerebral visual impairment reflects not only improvements in diagnostic abilities but also advances in neonatal intensive care. Indeed, there has been an increase in the survival rate of children born preterm, individuals potentially at risk of cerebral damage (and thus of cerebral visual impairment). Hypoxic-ischemic injury is the most common cause of cerebral visual impairment in childhood. At least 60% of children with preperinatal hypoxic-ischemic damage have cerebral visual impairment. Other causes are cerebral malformations, hydrocephalus, central nervous system infections, epilepsy, head trauma, metabolic and neurodegenerative diseases, and intoxication with drugs or poisons. Cryptogenic cases are also described. The most frequent clinical manifestation of cerebral visual impairment is reduced visual acuity (of varying severity), often associated with visual field deficits. Affected
children, unlike adults with cortical blindness, have some residual visual function that shows a tendency to improve over time. Furthermore, in children, the lesion responsible for the visual disorder can involve various areas of the visual system and not only the occipital cortex. For these reasons, in children, the term cerebral visual impairment has now replaced the term cortical blindness.

Children with cerebral visual impairment can also show several peculiar behavioral signs: short visual attention span; markedly fluctuating visual performances; the need for time, environmental stability, and repetition of items to obtain the best response; and the ability, probably due to integrity of the extrageniculate pathways, to avoid obstacles when walking (“blindsight”).

In recent years, the spectrum of cerebral visual impairment has been extended to include disorders of visual information integration and processing, which are its main clinical expressions in subjects without loss of visual acuity (higher functioning cerebral visual impairment). The presence of these disorders, termed visuoperceptual disorders or cognitive visual dysfunction, is well known and has been demonstrated in preterm children with periventricular leukomalacia. Oculomotor disorders and ophthalmologic abnormalities often complete the clinical picture.

Cerebral visual impairment is prevalently a clinical diagnosis that can be supported by instrumental (neuroradiologic and electrophysiologic) findings.

Given the lack of a clear nosographic categorization of cerebral visual impairment, the aims of this study were (1) to evaluate the presence of visual disorders not attributable to any major ocular pathology in a sample of children with central nervous system abnormalities and (2) to describe the clinical picture of cerebral visual impairment in this cohort.

Materials and Methods

This study was conducted at our department’s Center of Child Neurophthalmology, which specializes in the evaluation of visual function in children and adolescents, particularly those with central nervous system disorders. All the patients referred to us are submitted to the following protocol:

1. clinical history and neurologic examination,
2. developmental (Griffiths Mental Development Scales) and/or cognitive assessment (Wechsler Scales of Intelligence), and
3. neuroophthalmologic evaluation including
   • observation of spontaneous visual behavior.
   • oculomotor assessment: fixation (absent, sporadic, unstable, stable), smooth pursuit (absent, discontinuous, normal), saccadic movements (abnormal, normal), visual axis alignment to detect strabismus (using the Hirschberg Test of corneal reflexes, the Cover Test, and the Paliaga Test), and extrinsic and intrinsic ocular motility. In addition, we look for abnormal ocular movements, such as nystagmus and paroxysmal ocular deviations.
   • visual acuity: evaluated with the maximum possible dioptric correction and using different tests depending on the subject’s age and on the severity of the clinical picture. Children up to 2 years old are evaluated using the Teller Acuity Cards, which give resolution acuity expressed in cycles per degree (cy/deg). In older children able to collaborate, several tests are used (Lea Symbols, letter optotypes), which give recognition acuity expressed in tenths. Subjects are categorized as follows: very low vision (<0.05 tenths, or <1.6 cy/deg), low vision (0.05-0.3 tenths, or between 1.6 and 9.6 cy/deg), near normal vision (0.3-0.8 tenths, or between 9.6 and 26.0 cy/deg), and normal vision (≥0.8 tenths, or >26.0 cy/deg). In subjects whose vision is not assessable, we look for signs of visual perception, both direct (object localization, movement of the head and/or limbs toward the visual target, pursuit of a moving stimulus) and indirect (postural reactions, alteration of respiratory frequency, avoiding reactions, smiling and other changes of facial expression).
   • contrast sensitivity (not assessable, reduced, normal), evaluated using the Hiding Heidi Low Contrast “Face” Test.
   • optokinetic nystagmus (absent, asymmetric, present), evaluated using a semirigid screen covered with black-and-white square patterns, bent to form an arc, or using a computer-generated random-dot pattern in front of the infant’s face.
   • visual field (normal, reduced). Because of the often young age of our children and their frequent associated motor and/or mental disabilities, traditional methods cannot always be used to define with precision the extent of their visual field. We thus assess, using kinetic perimetry and on the basis of behavioral reactions (eg, movements of the head, eyes, or a limb toward the target), the child’s ability to localize targets presented in the different areas of the visual field. The perimeter consists of 2 perpendicular black metal strips bent to form 2 arcs, each with a radius of 40 cm, with the infant in the center of the arcs.
   • stereopsis (not assessable, absent, partial, present), evaluated using the Lang Stereotest.
   • visual-perceptual assessment: in children older than 4 years with an IQ >55 and visual acuity ≥3 tenths, visual-perceptual abilities are assessed using the Developmental Test of Visual Perception, which allows the definition of a general visual-perceptual quotient, a nonmotor visual-perceptual quotient, and a visual-motor integration quotient. Patients with a general visual-perceptual quotient of less than 90 are considered to have a deficit of visual perception and are categorized as follows: 80 to 89 = below average, 70 to 79 = poor, and less than 70 = very poor visual-perceptual abilities.
   • ophthalmologic examination including assessment of refraction in cycloplegia and ophthalmoscopy.
The protocol also includes neuroradiologic examinations (brain magnetic resonance imaging [MRI], studying the optic pathways, or brain computed tomography/transfontanellar ultrasound) and neurophysiologic investigations (pattern and flash visual-evoked potentials and electroretinogram; electroencephalography; brainstem auditory-evoked potentials).

For the purposes of this study, a sample of 121 children was selected from all the patients consecutively referred to our center in the period from January 1, 2002, to June 30, 2003. This study sample included all those with central nervous system abnormalities who, at the end of the evaluation detailed above, were deemed to be affected by cerebral visual impairment, diagnosed according to the criteria set out in the introduction.2,5 We excluded all subjects whose visual deficit was clearly attributable to abnormalities of the anterior segment, inadequate correction of refractive errors, sequelae of retinopathy of prematurity, or retinal dystrophies.

The sample was made up of 50 girls and 71 boys. Almost half of these children were born at term (58/121; 47.9%), while the remaining subjects were born at ≤37 weeks gestation (63/121; 52.1%). Their mean age at clinical observation was 53.9 months (range, 3-180 months; SD, 39.7 months). Table 1 summarizes the etiologies and neurologic impairment found in the sample. As shown in the table, the most frequent etiology was hypoxic-ischemic encephalopathy, present in 81 of 121 cases (67%), and the most frequent neuromotor picture was cerebral palsy, defined according to Mutch,44 found in 88 of 121 (72.7%) patients.

Here, we describe in detail the clinical picture of cerebral visual impairment in this cohort. The instrumental data collected during the administration of the protocol will be detailed in a further report.

Results

Figure 1, in which the percentages are referred to the whole sample, shows the neuroophthalmologic findings in these patients and Figure 2 the associated ophthalmologic abnormalities. These are described in detail in the following paragraphs.

Refraction

Refractive errors were found in 96 of 121 (79.3%) patients: hypermetropia in 28 of 96 (29.2%), astigmatism in 21 of 96 (21.9%), myopia in 11 of 96 (11.4%), and associated refractive errors in 36 of 96 (37.5%; hypermetropia and astigmatism in 27, myopia and astigmatism in 9).

Fundus Oculi

Fundus oculi abnormalities were present in 53 of 121 (43.8%) patients: temporal optic disk pallor in 30 of 53 patients (56.6%; isolated in 26 patients, associated with large optic disk cupping in 4 patients), optic atrophy in 17 of 53 patients (32%; isolated in 13 patients and associated with large optic disk cupping in 4 patients), large optic disk cups in 3 of 53 patients (5.7%), and optic nerve hypoplasia in 3 of 53 patients (5.7%).

Visual Acuity

The data reported here refer to binocular visual acuity (monocular investigations being difficult to perform because of both the young age of the children and the frequent presence of associated neurologic impairment). Binocular visual acuity was reduced in 105 of 121 (86.8%) patients and was normal in the other 16 (13.2%). Of the patients with reduced visual acuity, 24 of 105 (22.8%) had very low vision (not quantifiable), 40 of 105 (38.1%) had low vision, and 41 of 105 (39.1%) had near-normal vision. All the subjects whose vision was not quantifiable showed direct and/or indirect signs of visual perception: movement of the head and/or a limb toward the visual target in 6 of 24 (25%) patients, localization in 7 of 24 (29.2%), postural reactions in 6 of 24 (25%), alteration of respiratory frequency in 6 of 24 (25%), avoiding reactions in 3 of 24 (12.5%), smiling in 5 of 24 (20.8%), and other changes of facial expression in 12 of 24 (50%).

Contrast Sensitivity

Contrast sensitivity could be evaluated in 97 of 121 (80.2%) patients but not in the remaining 24 of 121
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Figure 1. Neuroophthalmologic findings in cerebral visual impairment.

Figure 2. Ophthalmologic abnormalities associated with cerebral visual impairment.
(19.8%) because of the severity of their visual impairment. Contrast sensitivity was reduced in 58 of 97 (59.8%) patients and was normal in 39 of 97 (40.2%).

Optokinetic Nystagmus
Optokinetic nystagmus was abnormal in 88 of 121 (72.7%) patients: absent in 34 of 88 (38.6%) patients and asymmetric in 54 of 88 (61.4%). It was normal in the remaining 33 of 121 (27.3%) patients. Of the 54 patients with asymmetric optokinetic nystagmus, 39 (72%) had strabismus.

Visual Field
Assessment of visual field was possible in 78 of 121 (64.5%) patients and not possible in the remaining 43 of 121 (35.5%): in 24 patients because of the severity of their visual impairment and in 19 because of poor collaboration. The ability to locate targets presented in different areas of the visual field was impaired in 7 of 78 (9%) patients; no impairment was observed in the remaining 71 of 78 cases (91%).

Stereopsis
Stereopsis was evaluated in 82 of 121 (67.8%) patients. It could not be evaluated in the remaining 39 of 121 (32.2%) patients because of poor collaboration (15 cases) or severity of the visual impairment (24 cases). Stereopsis was absent in 71 of 82 (86.6%) patients, partial in 3 of 82 (3.7%) patients, and present in 8 of 82 (9.7%) patients. Of the 71 in whom it was absent, 67 (94.4%) had strabismus.

Oculomotor Abilities
Fixation was absent in 24 of 121 (19.8%) patients, sporadic in 2 of 121 (1.7%), unstable in 32 of 121 (26.4%), and stable in 63 of 121 (52.1%). Smooth pursuit was absent in 26 of 121 (21.5%) patients, discontinuous in 69 of 121 (57%), and normal in 26 of 121 (21.5%). Saccadic movements were absent in 24 of 121 (19.8%) patients, abnormal (ie, dysmetric in both the horizontal and vertical planes) in 17 of 121 (14.1%), and normal in 80 of 121 (66.1%). To shift their fixation, the patients with abnormal saccadic movements adopted compensatory strategies, such as brusque head movements, blinking, or both; they also presented hyperfixation and conjugate gaze spasms (upward and lateral). Visual exploration, or scanning, involving a succession of saccadic eye movements was consequently impaired, as were serialization activities (eg, counting a series of objects).

Alignment of the Visual Axes
Strabismus was present in 88 of 121 (72.7%) patients: 51 of 88 (57.9%) had esotropia, and 37 of 88 (42.1%) had exotropia. Of the 97 of 121 subjects able to fixate, 25 (25.7%) showed variability of the strabismus angle (ranging between 10° and 35°). Three (3.4%) of the 88 patients with strabismus exhibited a shifting pattern (esotropia to exotropia).

Extrinsic and Intrinsic Ocular Motility
Extrinsic ocular motility was evaluated in 95 of 121 (78.5%) patients; this evaluation was not possible in the remaining 26 of 121 (21.5%) patients because of the absence of fixation and smooth pursuit. Extrinsic ocular motility disorders were found in 43 of 95 (45.3%) patients: an abduction deficit in 25 of 43 (58.1%), upshoot in adduction in 9 of 43 (20.9%) with a “V” pattern (inferior oblique overaction) in 6, dissociated vertical deviation in 5 of 43 (11.6%), an isolated elevation deficit in 2 of 43 (4.7%), and a monocular adduction, elevation, and depression deficit associated with partial ptosis in 2 of 43 (4.7%). Evaluation of intrinsic motility revealed sluggish pupillary reactions in 34 of 121 (28.1%) patients and normal responses in the remaining 87 (71.9%).

Abnormal Ocular Movements
Abnormal ocular movements were found in 43 of 121 (35.5%) children. Nystagmus was found in 23 of 43 (53.5%): manifest in 20 of 23 (86.9%) and latent in 3 of 23 (13.1%). The manifest nystagmus was horizontal-jerky in 14 children, horizontal-pendular in 3, and cyclorotatory in 3. We found other abnormal eye movements in 20 of 43 (46.5%) patients: 7 of 20 (35%) children had erratic eye movements (all 7 were unable to fixate and had nonquantifiable visual acuity, only indirect signs of visual perception, and sporadic light perception), 9 of 20 (45%) had paroxysmal ocular deviations (these 9 children all had very low or low vision but with quantifiable visual acuity), and 4 of 20 (20%) showed a preferential looking strategy, probably exploiting their peripheral vision, and erratic eye movements in the other gaze positions.

Visual-Perceptual Abilities
Children older than 4 years with an IQ >55 and visual acuity >3 tenths (27 of 121) underwent assessment of their visual-perceptual abilities. The presence of a visual-perceptual disorder was found in 24 of 27 (88.9%) patients: a global reduction (general visual-perceptual quotient, nonmotor visual-perceptual quotient, visual-motor integration quotient) in 8 of 24 (33.3%) patients, a reduction of both the general visual-perceptual quotient and the visual-motor integration quotient in 7 of 24 (29.2%), of both the general visual-perceptual quotient and the nonmotor visual-perceptual quotient in 3 of 24 (12.5%), and of the visual-motor integration quotient alone in 6 of 24 (25%).
Discussion

Children with central nervous system abnormalities often present visual deficits, frequently classifiable as cerebral visual impairment. The results of our study showed that the clinical manifestations of cerebral visual impairment are extremely heterogeneous and frequently associated with ophthalmologic abnormalities, even though the picture of cerebral visual impairment, by definition, does not include major ocular pathologies.

In accordance with literature findings, fundus oculi abnormalities and refractive errors were extremely common in our sample. The former typically involved the optic nerve, whereas the macula and the peripheral retina were generally spared. Indeed, the presence of optic atrophy or temporal optic disk pallor, in isolation or associated with large optic disk cupping, was the most frequent fundus oculi abnormality in our sample. This finding might be attributable to axonal loss due to damage caused, through the phenomenon of regressive transsynaptic degeneration, to the geniculostriate pathways. The effects of the above phenomenon have also been demonstrated in vivo in other parts of the visual system, such as the lateral geniculate body.

Refractive errors were found in more than three quarters of our sample, and hypermetropia, isolated or associated with astigmatism, was the most frequent of these.

This is in line with the findings of other ophthalmologic studies of children with cerebral visual impairment. Myopia, on the other hand, was less frequent in our sample, possibly because we excluded subjects with severe retinopathy of prematurity, a condition frequently associated with myopia.

Loss of visual acuity, which is prevalent in the diagnosis of cerebral visual impairment, emerged as the main clinical manifestation in our sample. Often associated with reduced contrast sensitivity, it must always be evaluated — and was evaluated — with the maximum possible dioptic correction. The extent of this deficit, which is the expression of impairment of central vision due to involvement of the geniculostriate visual pathways, ranges from forms so severe that residual vision is not even quantifiable to milder forms. Like Dutton and Good et al., we maintain that it is possible to find normal visual acuity in a small percentage of children with cerebral visual impairment. In our sample, who had normal visual acuity, the visual deficit manifested itself through oculomotor abnormalities or visual-spatial problems, impaired eye-hand coordination, or impaired recognition of faces or objects. In this study, we performed only a screening of these visual-cognitive disorders based on the Developmental Test of Visual Perception. We are currently in the process of developing a more in-depth protocol for investigation of these dysfunctions, which will be presented in a future study. Despite this limitation, it is important to note that 88.9% (24 of 27) of the subjects in whom they could be investigated presented these disorders.

Our study, confirming findings in the literature, emphasizes that cerebral visual impairment can manifest itself through disturbances of visual perception and integration, which, according to Good et al. and to Dutton and others, are more typical of subjects without loss of visual acuity (higher functioning cerebral visual impairment). These visual-cognitive disorders — expressions of dorsal or ventral stream malfunctioning — may escape notice during follow-up in the first years of life, becoming evident only at school age through graphomotor or visual-spatial problems, impaired eye-hand coordination, or impaired recognition of faces or objects. In this study, a number of our children had difficulty performing voluntary saccades in both the horizontal and the vertical planes and used compensatory strategies such as head movements and blinking to shift fixation from one object to another; the same subjects showed hyperfixation and gaze spasms. This picture, which is termed oculomotor dyspraxia and is associated with impaired visual scanning, emerged more clearly when the patient’s head was kept still.

Strabismus was a common finding. Esotropia was the most frequent form, but as reported elsewhere, exotropia is also possible in subjects with cerebral visual impairment. Our results indicate that strabismus in cerebral visual impairment may be characterized by specific
trains, namely, angle variability (this was actually found in the entire sample of Salati et al\textsuperscript{31}) and a shifting pattern (esotropia to exotropia), even though only a small percentage of our cases exhibited this pattern. There are several possible explanations for the strabismus in cerebral visual impairment,\textsuperscript{30,31} but further studies are needed to clarify beyond doubt its underlying causes.

A high percentage of our patients (78.5\%) also presented extrinsic ocular motility disorders, whose significance is still unclear. In some cases, these disorders may be attributable to cranial nerve palsies: for example, the abduction deficit could be associated with a sixth cranial nerve palsy, the upshoot in addiction with a fourth cranial nerve palsy, and the adduction, elevation, and depression deficit and partial ptosis with a third cranial nerve palsy. Follow-up studies are needed to confirm this hypothesis.

Quite a large percentage of our patients with cerebral visual impairment, usually those with optic atrophy, had sluggish pupillary reactions. This finding contrasts with the original definition of cortical blindness in adults.

Furthermore, contrary to the old belief\textsuperscript{37} that children with cerebral visual impairment cannot present nystagmus, except in the presence of a coexistent bilateral anterior visual pathway disorder\textsuperscript{23} (a belief based on the fact that an intact geniculostriate pathway is a prerequisite for the genesis of nystagmus), we, like others,\textsuperscript{3,9,28,30,31} found nystagmus in nearly a quarter of our patients. Two possible interpretations of the nystagmus in cerebral visual impairment have been advanced: (1) secondary extension of the damage to the anterior visual pathways, due to the phenomenon of retrograde transsynaptic degeneration, and 2) alteration of the visual integration circuits involving the premotor commands for ocular movements\textsuperscript{29,30}.

Erratic eye movements or paroxysmal ocular deviations, which have already been described elsewhere,\textsuperscript{31} were also present in our sample. Both of these abnormalities, erratic eye movements in particular, were typical of the children with severe visual impairment. The paroxysmal ocular deviations were mainly oriented upward and sideways and rarely downward, and they lasted a few seconds, which supports the finding of Salati et al,\textsuperscript{31} according to whom these disorders constitute a supranuclear gaze disturbance related to the neurologic damage responsible for the cerebral visual impairment.\textsuperscript{31} Electroencephalography with video recording excluded epilepsy as a possible cause of these abnormalities in our patients.

In conclusion, our study allows us to affirm that cerebral visual impairment, as reported by Good et al,\textsuperscript{2} can manifest itself through a variety of clinical signs and symptoms, apparently reflecting the possible involvement of various parts of the retrogenticulate pathways. Our study confirmed that the most striking symptom is reduced visual acuity, even though a characteristic of cerebral visual impairment, unlike cortical blindness in adults, seems to be the conservation of a degree—even minimal—of residual vision.

Other well-documented symptoms include visual field deficits, reduced contrast sensitivity, optokinetic nystagmus, and stereopsis abnormalities. Oculomotor disturbances are also frequent, and these, together with visual-cognitive dysfunctions, seem to characterize the clinical picture of higher functioning cerebral visual impairment. Cerebral visual impairment is often associated with ophthalmologic abnormalities.

Early and careful assessment of these subjects, taking into account both the neuroophthalmologic and the ophthalmologic aspects of their visual deficit, is thus essential for a correct diagnosis and necessary for the development of personalized rehabilitation programs. Furthermore, given that some abnormalities in cerebral visual impairment (refractive errors, strabismus) are treatable, they should be carefully sought out to exploit any residual vision and to reduce the risk of amblyopia, which would worsen the visual prognosis of these children.

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