NEW ADVANCES IN CHILD NEUROPHTHALMOLOGY

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ABSTRACTS

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E. Fazzi
ORAL COMMUNICATIONS

CORTICAL/SUBCORTICAL INTERACTION: VISUAL MOTION SYSTEMS IN THE NORMALLY AND ABNORMALLY DEVELOPING BRAIN

O. Braddick

Department of Experimental Psychology, University of Oxford, UK

Two distinct brain systems respond to the direction of visual motion. The first, subcortical, is functional at birth and controls optokinetic responses (OKN) but not the visual perception of moving targets. The second, cortical, develops in the postnatal months. Interactions between these systems reveal the course of normal development and provide indicators of atypical development.

A signature of the immature, purely subcortical system is an asymmetry between the nasal and temporal directions of OKN in monocular viewing. This asymmetry normally disappears as the developing cortical system comes to provide a descending input to the subcortical system, but it may persist if there is a persisting deficit in cortical binocular interaction, e.g., in strabismus.

Early asymmetries in the VEP to a horizontally oscillating pattern suggest that, as well as a descending influence of cortical on subcortical motion systems, ascending asymmetrical signals from midbrain nuclei also have an effect on cortical motion processing.

Cortical-subcortical interactions are also revealed by asymmetrical OKN in cases of unilateral cerebral damage. Hemispherectomised infants initially show a pattern indicating bilateral subcortical function. However, in the absence of normal input from the cortex on one side, the subcortical response ipsilateral to the lesions becomes non-functional. Beyond a few months of age, the signature of unilateral cerebral damage is a deficit of OKN towards the damaged side, rather than the nasal/temporal asymmetry of the normal immature system.

VISUAL ASSESSMENT BASED ON NEW NEUROBIOLOGICAL MODELS OF VISUAL DEVELOPMENT

J. Atkinson

Visual Development Unit, University College London, UK

From research in our Visual Development Unit, we have devised new visual assessment methods, appropriate for infants and young children, based on our neurobiological models of visual development. These models suggest an initial separation in the onset of function for visual subcortical and cortical systems, with the neonate using a largely subcortical system and the cortex starting to function during the first 6 months of life. There is also differential onset of function in the two cortical streams, with the so-called ‘dorsal’ stream (for action control and spatial relations) starting to function later than the ‘ventral’ stream (for discrimination and recognition of objects and faces). Different dorsal ‘action’ systems control selective saccadic eye/head movements and selective reaching and grasping, with the eye movement system functional before the manual system. The development of systems underpinning visual selective attention is integrally connected to development within both ventral and dorsal streams.

Our new methods have been used, together with more conventional clinical procedures, to assess abnormalities in infants and young children with ophthalmological problems (significant refractive errors of long and short sightedness including astigmatism, poor focussing/accommodation, strabismus, cataract and visual problems associated with dyslexia) and in clinical populations, including infants and children with developmental delay, cerebral palsy, infants who have undergone hemispherectomy, Williams syndrome, autism, term/preterm infants with focal and diffuse perinatal brain abnormalities (imaged on US and MRI) and children with hemiplegia.

The methods to be described include a) Orientation Reversal Visual Evoked Potentials (OR-VEP) for assessing the onset of visual cortical function and as a prognostic indicator of neurological development; b) the Fixation Shifts paradigm for assessing early disorders of visual selective attention; c) ABCDEFV - Atkinson Battery of Child Development for Examining Functional Vision - for assessing sensory visual, visuomotor, visuo-perceptual, visuo-cognitive and spatial disorders in infants and young children from birth to 5 years; d) tests comparing dorsal and ventral stream function: orientation matching and posting in the ‘post box’ task, form and motion coherence threshold measures.

Using these methods we find that:

a) from our screening programmes, normally developing children who have had significant hyperopia (including hyperopic astigmatism) have a significantly greater risk of strabismus and amblyopia, but that partial refractive correction (by wearing spectacles) in infancy can reduce this risk. There is also a significant difference in visuo-cognitive, visuomotor and spatial development in the pre-school years for children who were hyperopic in infancy and those who were emmetropic;

b) infants with early hemispherectomy initially show evidence for subcortical control of optokinetic responses in both directions of eye movements horizontally, which changes after about 5 months of age to a loss of control from the damaged hemisphere, despite the intact subcortical system on both sides;

c) infants with perinatal brain damage show remarkable recovery of visual function even with extensive damage to classical visual occipital areas. However, damage involving basal ganglia (seen on structural neonatal MRI) is associated with poor recovery of visual function. This can be found even when the occipital cortex appears structurally intact;

d) many infants and young children with a range of developmental disorders, including hemiplegia, Williams syndrome and autism, show greater impairment of performance on motion coherence compared to form coherence. Williams syndrome children also show deficits in the post box task in posting but not matching the orientation of the letter to the post box aperture.

We propose the hypothesis of ‘dorsal stream vulnerability’, with differential plasticity in the two cortical streams, which may be common to a number of paediatric anomalies of development.

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ADVANCES IN THE DIAGNOSIS AND TREATMENT OF CORTICAL VISUAL IMPAIRMENT

W.V. Good
Smith-Kettlewell Eye Research Institute
San Francisco, California, USA

Cortical visual impairment, also termed cerebral visual impairment (CVI), is the leading cause of vision impairment in children in developed regions of the world. CVI usually occurs in preverbal or non-verbal children, thereby making quantitative assessment of vision in these children difficult. In order to study new interventions for CVI, better diagnostic tools are required. The objective of this presentation is to discuss new methods for vision assessment and ways in which these methods may lead to improved rehabilitation and treatment.

We used 3 types of visual acuity assessment in children with CVI: clinical assessment; behavioral assessment (grating acuity measured using Teller Acuity Cards), and sweep visual evoked potential threshold assessment (grating, vernier acuity, luminance variation). Children with CVI ranged in age from 5 months old to 10 years old. The various methods were compared. In the luminance study, age-matched control subjects who did not have CVI were measured for comparison. All investigations were performed with permission from our local research board, and with the express and written permission of parents.

All 3 measures agree and are useful in identifying children with CVI. Acuity thresholds are better using the VEP assessment, compared to behavioral or clinical. Results suggest that children with CVI have better grating acuity thresholds under low luminance conditions. Normal children see better under high luminance conditions, as expected.

The results of these studies suggest that the VEP is a useful tool for the quantitative measure of vision in children with CVI. The sweep VEP offers the advantage of measuring a variety of vision functions (grating, vernier, contrast sensitivity, thresholds under different luminance conditions). Results can be used to help interpret the effect of new medical interventions that are designed to reverse or prevent damage to the cerebral cortex in children. Results from these studies also suggest that a battery of tests on children with CVI can be used to formulate a plausible and evidence-based approach to rehabilitation.

OCULOMOTOR DYSFUNCTION IN CEREBRAL VISUALLY IMPAIRED CHILDREN

G. Giammari Aldè, A. Cavallini, R. Salati, R. Borgatti
Regional Centre of Visual Impairment in Childhood, IRCCS “E. Medea” Institute, Bosisio Parini, Lecco, Italy

We set out to describe ocular motility in a sample of patients affected by cerebral visual impairment (CVI) of hypoxic-ischaemic origin and to describe the clinical evolution of some of them.

The sample consisted of subjects ranging in age from 2 to 16 years. In all cases CVI was associated with MRI-verified damage of the cerebral visual system. A complete ophthalmological and neurological assessment was performed. Behaviour of gaze was studied in four conditions: during scanning of the surrounding environment, fixation, execution of saccades and pursuit. In addition, strabismus, nystagmus and paroxysmal ocular deviations were evaluated. Ocular motility was studied by video recording the patients’ eye motility.

Each pattern of ocular motility studied revealed profound alterations in all the subjects examined. Typical features of ocular motility in CVI were: impaired fixation (84%) and smooth pursuit (96%), defective coordination of saccades (93%), impaired visual scanning (88%), paroxysmal ocular deviations (78%), the presence of variable angle strabismus (86%), and nystagmus (46%). In our sample, most improvements take place before two years of age, but improvements are possible up to 6-7 years of age. A worse evolution could be expected in seriously impaired children who fail to improve by the age of two. Fixation is the most important feature for a better prognosis.

Oculomotor disabilities characterize the lack of gaze coordination found in children with brain damage; an early and detailed evaluation of ocular motility in subjects with CVI is important, especially when rehabilitation is planned.

VISUAL OUTCOME AT SCHOOL AGE IN CHILDREN WITH NEONATAL ENCEPHALOPATHY: CORRELATION WITH BRAIN MRI

E. Mercuri
Department of Paediatrics, Hammersmith Hospital London, UK, Institute of Child Neuropsychiatry, “Sacro Cuore” Catholic University of Rome, Italy

The aim of this study was to assess various aspects of visual function at school age in children with neonatal encephalopathy.

Thirty children born at term, who had neonatal encephalopathy and had early and serial neonatal MRI, were assessed using a battery of visual tests. This included measures of crowding acuity (Cambridge crowding cards), stereopsis (TNO test) and visual fields. The results of the visual assessment were compared to the type and the extent of the lesion observed on neonatal MRI.

All the children with severe basal ganglia lesions were untestable in the first year of life and were still untestable at school age. The degree of visual impairment at school age was similar to that found in the first year in children with diffuse lesions but not in children with focal infarcts. Only 28% of the 16 children with focal infarct presented some abnormalities of visual function. Visual abnormalities were more frequent in children with lesions involving the main branch of the middle cerebral artery and were less frequently associated with lesions in the ter-
ritory of one of the cortical branches of the middle cerebral artery. The presence of visual abnormalities was not always associated with the involvement of optic radiations or the occipital primary visual cortex. Abnormal visual fields were found only in children who also developed hemiplegia.

LEBER’S CONGENITAL AMAUROSIS: AN OVERVIEW


Dept of Child Neurology and Psychiatry,
IRCCS C. Mondino Foundation, University of Pavia
* Early Intervention Center for Visually Impaired Children, Robert Hollman Foundation, Cannero Riviera, VB
** Dept of Ophthalmology, IRCCS S. Matteo Hospital, University of Pavia, Italy

Leber’s congenital amaurosis (LCA) is the earliest-onset and most severe form of inherited retinal dystrophy. It is characterised by blindness or severe hypovision at birth or in the first 6 months of life. A genetic pathology with an autosomal recessive pattern of inheritance, it accounts for 10-18% of all cases of congenital blindness. Its incidence is 2-3 cases per 100,000 live births. The electroretinogram is markedly reduced or extinguished (in both photopic and scotopic responses); VEPs can be altered or extinguished; the appearance of the fundus is variable. Oculo-digital signs are pathognomic.

Mental retardation (although the application of scales standardised for sighted children has led to its incidence being overestimated), cerebral malformations and/or systemic abnormalities, particularly renal ones, are described as frequent associated defects. The psychomotor development of subjects affected by LCA is peculiar and specific instruments are required for its evaluation.

The main question on which researchers (in both the clinical and genetic fields) are currently concentrating their efforts is that of the clinical and genetic heterogeneity of LCA. From this perspective, we have begun a research study whose objectives are:

– to study the clinical aspects and the natural history of the disease;
– to define a new classification on the basis of ophthalmological, neurological and clinical data and on the evolution of the clinical picture;
– to perform genetic diagnosis concentrating on known genes;
– to investigate the pedigrees of relatives of LCA patients (especially consanguineous relatives) and to conduct linkage analyses;
– to define with precision the criteria for the differential diagnosis of LCA versus, in particular, Joubert and Senior-Loken syndromes;
– to identify subjects at risk of renal insufficiency;
– to develop a plan for early intervention.

Our working strategies, implemented in the pursuit of the above aims, are the following:

– collection of details of new cases brought to our attention;
– the carrying out, in all LCA subjects, of the following investigations: neurological, ophthalmological, cognitive and behavioural evaluations; VEPs and ERG, brain MRI, complete abdominal US, BAEPs, hand X-ray, EEG, metabolic investigations (lactic and pyruvic acid, very long-chain fatty acids, aminoacids in the plasma and urine, muscle enzymes);
– search for mutations on known genes;
– collection of lymphoblastoid lines of affected subjects and their families, thereby establishing an inexhaustible source of DNA;
– search for the genes responsible for Joubert and Senior-Loken syndromes.

This research is using all the clinical and diagnostic facilities of the Centre of Child Neuroophthalmology at the IRCCS C. Mondino Foundation in Pavia and the laboratories of other centres that have agreed to take part in the project.

We are collecting data regarding 40 subjects with LCA and this project is expected to result in:

– precise description of clinical subforms (simple, complex, syndromic) and genotype-phenotype correlation;
– characterisation of cases according to the trend (stable, worsening, improving) of their ophthalmological picture;
– establishment of the natural history of the disease;
– clarification of the incidence of mental retardation and of the characteristics of cognitive development of affected children;
– description (also by age group) of the neuropsychological and behavioural profile of affected subjects;
– identification of subjects at risk of developing renal insufficiency;
– precise description of the neuroradiological features of LCA.

Our preliminary data confirm that LCA is a heterogeneous entity, which can present as an isolated ocular pattern, or associated with neurological and systemic abnormalities, and support the need for a multidisciplinary approach.
CEREBRAL VISUAL IMPAIRMENT IN CHILDREN: VISUAL FUNCTION ASSESSMENT


Dept of Ophthalmology, IRCCS S. Matteo Hospital, University of Pavia, *Regional Centre of Visual Impairment in Childhood, IRCCS E. Medea Institute, Bosissio Parini, Lecco, ** Dept of Child Neurology and Psychiatry, IRCCS C. Mondino Foundation, University of Pavia, Italy

Cerebral visual impairment (CVI) indicates the presence of a visual deficit due to a congenital or an early-acquired cerebral lesion, usually of the retro-geniculate visual pathway. CVI is frequently associated with ophthalmological abnormalities (nystagmus, strabismus, refractive errors, optic nerve atrophy) and other neurological disorders, i.e., cerebral palsy, epilepsy, mental retardation; CVI can be considered one of the major causes of visual handicap in children in developed countries.

The assessment of vision in early infancy is of great importance due to the role it plays in a child’s development: vision is involved particularly in a child’s perceptive, motor and mental development. The possibility to recognize as early as possible the warning signs of sight deficit is fundamental to get a correct diagnosis and to begin a specific rehabilitation. We report a detailed protocol for the diagnostic and functional assessment of suspected visually impaired young children. The protocol considers: neurological assessment, ophthalmological examination (ocular motility, refraction, pupillary reflexes, fundus oculi assessment), electrophysiological examinations (VEP, ERG), visual function assessment (sensory-perceptual and oculomotor abilities, behavioural signs in response to bright light), neuroimaging (MRI).

The aim of this protocol is not just diagnostic but also rehabilitative: it is a prerequisite for an early specific rehabilitation programme.

DTVP FINDINGS IN CHILDREN WITH PERIVENTRICULAR LEUKOMALACIA


Dept of Child Neurology and Psychiatry
* Child Neuroradiology Unit, IRCCS C. Mondino Foundation, University of Pavia
** Dept of Ophthalmology, IRCCS S. Matteo Hospital, University of Pavia, Italy

We set out to define higher visual disabilities related to periventricular leukomalacia (PVL) using the Developmental Test of Visual Perception (DTVP). Correlations were sought between DTVP results and neuroradiological and neuroophthalmological findings.

The DTVP was administered to 20 children (m/f:10/10), aged between 4 years 1 month and 10 years 8 months (mean: 5 years 9 months), presenting with: spastic diplegia; PVL documented by brain MRI; normal or near normal visual acuity; mild-moderate upper limb functional impairment. The mean General Visual-Perceptual Quotient was below normal, showing a great variability among the patients. Despite this, an uneven DTVP profile characterised by significant difference between the visual motor integration quotient and the non motor visual perceptual quotient (p<0.001), and a poor result on the Closure subtest (identification of whole figures from incomplete visual information) was observed in all the subjects. This profile reflects a deficit in eye-hand coordination and in praxic-constructional abilities, and the presence of a disorder in the sphere of simultagnosia, and could be the expression of malfunctioning of the occipital-parietal pathway of visual integration, the so-called “dorsal stream,” a hypothesis reinforced by neuroradiological findings of deep parietal white matter signal alterations in addition to peritrigonal white matter alterations typical of PVL.

TRANSYNAPTIC DEGENERATION OF LATERAL GENICULATE BODIES IN CHILDREN AFFECTED BY CEREBRAL VISUAL IMPAIRMENT


Dept of Child Neurology and Psychiatry
* Child Neuroradiology Unit, IRCCS C. Mondino Foundation, University of Pavia
** Dept of Ophthalmology, IRCCS S. Matteo Hospital, University of Pavia, Italy

Cerebral visual impairment (CVI) is the leading cause of bilateral visual impairment in Western countries. It is characterised by bilateral impairment of visual functions caused by damage to the CNS. A common cause is periventricular leukomalacia (PVL) following perinatal hypoxic-ischemic brain injury. Diagnosis of CVI is based mainly on clinical signs but damage to the posterior visual pathways is frequently documented on brain magnetic resonance (MR) in children with PVL. The lateral geniculate body (LGB) is the thalamic relay nucleus of the geniculate visual pathway. Lesions at this level have frequently been demonstrated by pathological examinations – following transynaptic degeneration of these nuclei secondary to pregeniculate or postgeniculate interruption of visual pathways – but seldom documented on brain MR. In this study we investigate MR alterations of visual pathways and in particular of LGBs in 20 children affected by CVI and cerebral palsy. The presence of a small, symmetrical area of T2 prolongation in the exact site in which the LGBs are located – consistent with gliosis – was considered indicative of LGB damage. Neuroophthalmological findings are compared with a control group of 20 children with a similar clinical and neuroradiological picture, except for LGB damage. Comparison between the two groups shows higher incidence of optic nerve atrophy, lower visual acuity, and higher incidence of disorders of ocular motility (saccades and smooth pursuit) in children with LGB damage. These findings suggest that MR signal alterations in LGBs, probably attributable to transynaptic degeneration, can also extend to the optic nerve and lead to poorer visual outcome.
This unusual case of Miller Fisher syndrome (MFS) started with a bilateral areflexical mydriasis and a slight failure of accommodative-convergence. Ocular-movement abnormalities developed progressively with a palsy of the upward gaze and a bilateral internuclear ophthalmoplegia to a complete ophthalmoplegia. In the serum of this patient, high titers of an IgG anti-GQ1b ganglioside and anti-cerebellum anti-Purkinje cells in particular, were found. The role of these findings and clinical implications in MFS are discussed.

**SIGNIFICANCE OF AN INTEGRATED REHABILITATIVE APPROACH: CASE REPORT OF A CHILD WITH CORTICAL VISUAL IMPAIRMENT IN CEREBRAL PALSY**

P. Caldironi, T. Battistin, M. Vinciati, L. Pinello*

Robert Hollman Foundation, Diagnosis and Rehabilitation Center for Visually Impaired Children, Padua
* Paediatric Ophthalmology Service, Department of Paediatrics, University of Padua, Italy

Our aim was to underline the significance of an integrated rehabilitative approach in work with disabled children.

We describe the case of a 4-year-old child, diagnosed at birth with cerebral palsy. He developed a spastic tetraparesis and a severe cortical visual impairment.

He came to our centre 2 years ago, having received intense visual stimulations for a period of one year.

Upon arrival the child was very withdrawn, not communicating and not perceiving light contrast clearly. Moreover he was very irritated by any kind of visual stimulation and visual tests. So we decided to start a rehabilitative project, in which the visual component was less intense and more complicated process. Many factors must be taken into account, and these differ from case to case.

Correct identification and access to devices should be structured around several stages – analysis, intervention, support and monitoring/follow-up – based on a series of fundamental principles:

- the characteristics of the individual;
- the intended use of the proposed equipment;
- the individual’s expectations and attitudes;
- the influence exerted by the context and the features of the same;
- personalization of equipment and training.

This implies the presence of a group of trained professionals, supported by a duly organized and equipped center.

**FUNCTIONAL EVALUATION AND REHABILITATION OF SEVERELY VISUALLY IMPAIRED CHILDREN (0-4 YEARS)**

J. Lanners, E. Goergen

Early Intervention Center for Visually Impaired Children, Robert Hollman Foundation, Cannero Riviera (VB), Italy

Description of the early intervention rehabilitation programme used at the Robert Hollman Foundation, Lake Maggiore, Northern Italy, with particular emphasis on the concept of Functional Low Vision Evaluation and rehabilitation of severely visually impaired and/or multi-handicapped children (0-4 years).

The authors describe the basic principles of functional evaluation of residual vision in severely visually impaired children, applying the fundamental criteria of “early low vision training” as devised by Dr. Barraga (USA), with addi-
tional input from other American and European methods. In particular, it highlights the main aspects of the visual and oculomotor reactions of such children in early childhood, and offers suggestions for possible visual rehabilitation.

**OPHTHALMOLOGICAL FINDINGS IN SPINA BIFIDA**

L. Pinello, C. Bortolin*, F. Rodeghiero**, A. Menegotti, P. Drigo*

Paediatric Ophthalmology Service
* Paediatric Neurology Clinic, Department of Paediatrics, University of Padua
**Orthoptic Service, Eye Clinic, University of Padua, Italy

Of the numerous problems that spina bifida (SB) patients face, visual apparatus impairments are often considered late and are not covered extensively in the literature. As far as the alteration of the ocular motility is concerned, 44% (26/59) of our patients revealed a manifest squint and only 3% (two patients) suffered from a latent squint. The most frequent type was a convergent squint (80%). Nystagmus, observed in 32% of the subjects, was mainly horizontal. These disorders are strongly connected with the presence of hydrocephalus, with or without shunt, and with the cerebral anomalies typical of these patients (Chiari 2 and midline anomalies). Visual acuity outcomes were good (8-10/10) in 82% of the cases (contrary to what is commonly reported in the literature) and mild (4-7/10) in 18%. None of the patients manifested low vision. Refraction defects were present in 59% (34/59) of the patients. The authors underline the importance of serial neuro-ophthalmic examinations, from birth or from diagnosis, to allow ophthalmological treatments to be tailored to children suffering from SB and also enable these subjects to attain and maintain a good visual standard.

They also allow the subtle symptoms of endocranial hypertension to be observed sooner. An early discovery and correct treatment of visual problems improves cognitive and motor performance as well as the autonomy of SB patients.

**OPTIC PATHWAY (AND HYPOTHALAMIC CHIASMATIC) GLIOMAS: VISUAL OUTCOME IN 25 CHILDREN**


Paediatric Ophthalmology Service
* Paediatric Neurology Clinic
** Paediatric Onco-haematology Clinic, Department of Paediatrics, University of Padua, Italy

Hypothalamus and optic pathway gliomas (H/OPG) usually occur in children under the age of 5. The treatment of H/OPG is a controversial issue. For a variety of reasons, the numerous reviews reporting treatment outcome of children affected by H/OPG are difficult to interpret.

This study focuses mainly on the visual outcome of a cohort of 25 children (12 males and 13 females) affected by an H/OPG followed by the Paediatric Neuro-oncology Programme of the Paediatric Department of the University Hospital of Padua, in accordance with homogenous treatment guidelines. The median age at diagnosis was 4 years (range: 3 months - 14 years); 7 of the 25 had neurofibromatosis 1 (NF1). The median follow-up was 54 months. Due to the young age of many of these children, a complete ophthalmological examination was not always possible. Evaluation was based on the preferential looking technique, LH chart (Lea Hyvarinen chart for determining visual acuity), contrast sensitivity test, colour vision test, visual field, orthoptic and ophthalmoscopic examinations. Initial therapy was surgical resection in 3 patients, radiation in 13 (52%), chemotherapy in 5 (20%) and no treatment (“wait and see”) in 7 (28%). One patient died of tumour progression.

Of the 25 children, 11 maintained good vision (V.A. 8/10 - 10/10), 10 fair vision (5/10 - 7/10), 3 children had low vision (V.A. 4/10 or less) and only 1 child became legally blind (V.A. 1/20).

Of 17 children with visual field follow up, 7 improved, 7 remained stable and only 3 became worse.

This study confirmed the good prognosis of these children and thus the importance of a “treatment approach” aiming to guarantee quality of life as much as reasonably possible, which in this context means function. The authors underline the importance of serial neuro-ophthalmic examinations together with MRI in the management of visual pathway gliomas in infancy and childhood.

**CORRELATION BETWEEN CUP DISK ESCAVATION ANALYSED VIA HRT AND VISUAL EVOKED POTENTIALS IN CHILDREN AFFECTED BY CVI**


Dept of Ophthalmology, IRCCS S. Matteo Hospital, University of Pavia
* Biometrics Service, IRCCS S. Matteo Hospital, Pavia
** Dept of Child Neurology and Psychiatry, IRCCS C. Mondino Foundation, University of Pavia
*** Regional Centre of Visual Impairment in Childhood, IRCCS E. Medea Institute, Bossio Parini, Lecco
**** Anaesthesia Service, IRCCS S. Matteo Hospital, Pavia, Italy

Previous studies report various degrees of optic nerve damage associated with cerebral visual impairment (CVI): pale nerve, optic hypoplasia or optic nerve cupping. A tran-synaptic degeneration is generally invoked to explain the involvement of optic nerves in CVI. The aim of our study was to investigate optic nerve fibre loss using the Heidelberg Retina Tomograph (HRT) and Flash Visual Evoked Potentials (FVEP).
Using the above methods, we examined, under general anesthesia, five children (aged 3-10 yrs) affected by CVI and showing neuroradiological signs of cerebral damage. We considered all the parameters tested with HRT (disc area, rim area, cup volume, rim volume, mean retinal nerve fiber layer (RNFL) thickness, mean cup depth, max cup depth, cup shape measure) as well as the FVEP delays and the amplitude of the pIV wave. We correlated the results using Pearson’s correlation coefficient (r).

A good correlation, for the right eye, was found in the following parameters: delay of pIV and disc area (r: -0.75), rim area (r: -0.52), rim volume (r: -0.46), mean RNFL thickness (r: -0.53); pIV amplitude and disc area (r: 0.41), rim area (r: 0.50), mean RNFL thickness (r: 0.80); for the left eye there was a good correlation between: delay of pIV and cup volume (r: -0.56), mean cup depth (r: -0.51), max cup depth (r: -0.67); pIV amplitude and rim volume (r: 0.57), max cup depth (r: 0.61), cup shape measure (r: -0.63).

The data of outstanding interest were the following:

- Delay of pIV and disc area (r: -0.75), rim area (r: -0.52), rim volume (r: -0.46), mean RNFL thickness (r: -0.53); pIV amplitude and disc area (r: 0.41), rim area (r: 0.50), mean RNFL thickness (r: 0.80); for the left eye there was a good correlation between: delay of pIV and cup volume (r: -0.56), mean cup depth (r: -0.51), max cup depth (r: -0.67); pIV amplitude and rim volume (r: 0.57), max cup depth (r: 0.61), cup shape measure (r: -0.63). In our sample the morphological parameters (tested using HRT) correlated well with the functional ones (tested with FVEP); in particular the most affected eye gave the worst results in both examinations.

**OPTIC HEAD NERVE TOPOGRAPHY ALLOWS DETECTION OF STRUCTURAL DAMAGE TO THE OPTIC DISK IN CEREBRAL VISUAL IMPAIRMENT**

R. Salati, C. Bertone*, R. Borghetti, E. Fazzi**, A. Cavallini, G. Giannini Aldè, P.E. Bianchi*

Regional Centre of Visual Impairment in Childhood, IRCCS E. Medea Institute, Bassioo Parini, Lecce
* Dept of Ophthalmology, IRCCS S. Matteo Hospital, University of Pavia
** Dept of Child Neurology and Psychiatry, IRCCS C. Mondino Foundation, University of Pavia, Italy

The study aimed to describe objectively the features of optic nerve damage in cerebral visual impairment (CVI). Twenty-two patients, aged 3-13 years (mean 7 years), affected by CVI of hypoxic-ischemic origin underwent examination using the Heidelberg Retina Tomograph (HRT) (5 under general anesthesia). HRT provides a three-dimensional map of optic disk topography and reveals structural damage to the optic nerve. The results were compared to those of 88 age-matched normal control subjects.

The data of outstanding interest were the following:

- Disk area was 2.028 mm² in the sample versus 2.468 mm² in the control group; cup/disk ratio was 0.286 in the sample versus 0.166 in the control group; thickness of the ganglion cell fiber layer was 0.1497 mm in the sample versus 0.2142 in the control group.

The study demonstrated that the optic nerve in CVI patients is smaller (disk area), presents an enhanced excavation (cup/disk ratio), and a thinning of the nerve fiber layer, due to fiber loss. These data confirm the presence of optic damage, even in patients with normal or nearly normal optic disk appearance. This damage may affect vision in addition to the lesions on the retrochiasmatic visual pathway, typical of CVI subjects.

**OSCILLATIONS AND VISUALLY DEPENDENT POSTURAL STABILIZATION IN CONGENITAL NYSTAGMUS**

G. Savino, A. Salerme, S. Russo, D. Colucci, S. Di Girolamo, A. Dickmann

Dept of Ophthalmology and
* Dept of Otorhinolaryngology,
Sacred Heart Catholic University of Rome, Italy

The visual, somatosensory and vestibular systems together contribute to the maintenance of postural equilibrium. Afferent inputs interact and the information is analyzed centrally by the cerebellum, cerebral cortex and basal ganglia. The final result of this analysis is the generation of motor outputs aimed at maintaining postural control. The aim of the study was to verify whether the changes in postural control in our group of patients are due to ocular oscillations or to reduced visual acuity, since both conditions may be responsible for a reduced vision-dependent postural stabilization.

Nine patients (mean age: 23.3 years) affected by congenital nystagmus (CN) with anomalous head position and 10 healthy subjects as controls (mean age: 25.6 years) were enrolled in the present study. The nystagmographic curve was recorded for each patient using a magnetic search coil (EPM S3000 Scalar). Both groups underwent a complete postural evaluation. Dynamic posturography (Equitest, Neurocom int.Inc.Clackamas, Oregon, USA) was performed. The sensory organization test (SOT) consists of six different conditions, each lasting 20 s. These were repeated three times so as to obtain more stable values. All patients were evaluated as follows: 1. Head in primary position; 2. Head in primary position and gaze rotated to the position of blocked nystagmus; 3. Head in primary position with prisms that block or reduce ocular oscillations. The control group was submitted to the following conditions: 1. Head in primary position and without filters; 2. Head in primary position and gaze rotated in lateroversion; 3. Head in primary position during application of Bangert’s filters. Data were analyzed using the SPSS statistical package and employing non-parametric tests for unpaired samples (Mann-Whitney U test).

Our results were as follows: In normal subjects, the sensory analysis showed a reduced visual score with Bangert’s filters compared with the primary position. In congenital nystagmus patients, a statistically significant improvement of the overall postural control (composite) was present in the blocking position vs the primary position.

Normal subjects vs CN patients: significant differences were noted between the primary position in CN patients and the primary position in normal controls. A significant difference was also found between normal controls wearing Bangert’s filters and CN patients in primary position.

Our data strongly support the role of ocular oscillation in visual-dependent postural control, since postural impairment recovered under any condition when ocular oscillations were abolished, despite differences in visual acuity.

The impaired postural control in patients affected by congenital nystagmus is mainly due to ocular oscillations, with reduced visual acuity creating a secondary effect.
NEUROBEHAVIOURAL ADAPTATIONS IN CEREBRAL VISUAL IMPAIRMENT


Dept of Child Neurology and Psychiatry,
IRCCS C. Mondino Foundation, University of Pavia
* Dept of Ophthalmology, IRCCS S. Matteo Hospital,
University of Pavia, Italy

We set out to evaluate the frequency and mode of expression of neurobehavioural adaptations, described by some authors as typical symptoms of cerebral visual impairment (CVI), in order to characterise the clinical picture and visual function of subjects affected by this pathology.

Thirty subjects with CVI associated with other motor and/or cognitive handicaps, divided into two groups according to visual acuity (severely visually impaired or blind), underwent evaluations of visual function and extended observations. These were used to ascertain the presence of direct and indirect neurobehavioural signs of visual perception as well as possible stereotyped behaviours.

All the subjects showed these adaptations, with direct signs being found to be more frequent in sight-impaired than in blind subjects; a similar pattern, but characterised by a less marked discrepancy between the values of the two groups, emerged for the indirect signs. Stereotyped behaviours were observed only in the blind subjects. This study underlines the importance of detecting neurobehavioural signs in children with CVI as this allows a better semiological definition of the visual disorder and thus a correct neuroophthalmological diagnosis, essential in order to establish a targeted rehabilitative programme and to help families interact with children.

BRAIN MR STUDY OF THIRTY-FIVE CHILDREN AFFECTED BY LEBER’S CONGENITAL AMAUROSIS

Child Neuroradiology Unit
* Department of Child Neurology and Psychiatry
** Department of Neuroradiology,
IRCCS C. Mondino Foundation, University of Pavia, Italy

Leber’s congenital amaurosis (LCA) is the earliest and the most severe form of inherited retinal dystrophy, which shows an autosomal recessive pattern of inheritance. Its incidence is 2-3 per 100,000 live births and it is responsible for 10-18% of cases of congenital blindness. The diagnostic criteria currently used, although yet to be agreed upon, for the diagnosis of LCA were proposed by De Laey in 1991:

- blindness or severe lack of vision at birth or in the first six years of life;
- poorly reacting pupils;
- pendular nystagmus;
- oculo-digital signs (pressure and rubbing of the eyes etc);
- electroretinogram showing extinguished or markedly reduced responses in both the photopic and scotopic states;
- absence of or altered visual evoked potentials;
- variable appearance of the fundus (normal or ‘salt and pepper’).

In addition to these ocular signs, a series of symptoms, such as mental retardation and multisystemic anomalies like renal, cardiac or skeletal alterations are revealed relatively frequently and are thus considered part of the LCA picture. In the literature there are few reports dealing with the MR findings presented by children with LCA. From these, it emerges that neither morphological nor signal alterations along the course of the primary visual pathway have ever been detected, either in traditional studies or in diffusion studies. In some isolated cases brain alterations have been detected, both lesional, having the appearance of probable demyelinating alterations, and malformative. In particular, there has been more than one report of paediatric LCA presenting in association with rhombencephaloschisis, usually considered a casual link. In this study we evaluate the neuroradiological examinations of thirty-five young patients who came to our notice with congenital blindness, and in whom LCA was diagnosed only if the above diagnostic criteria were fully satisfied. Our MR findings confirmed the normal resonance signal of the structures of the primary visual pathway in all the patients. We were also able to observe the MR examinations of children aged 2-3 months, in whom the myelination process was within the correct range for this age group. The normal morphology of the structure of the retrochiasmatic visual pathway was preserved; in two cases the chiasma and in one case the optic nerves were thin. In the majority of subjects a certain degree of enophthalmos was present, with the eyeballs often smaller than usual, flattened but without alterations at the level of the retina. In the cases we observed, we did not come across any focal or diffuse signal alterations of the white matter of specific significance or relevance. In three patients (two of whom were siblings) an anomaly of the posterior fossa was evident, which was found to be Molar Tooth malformation. They presented mild clinical signs (hypotonic trunk and gait ataxia) attributable to a cerebellar pathology; the clinical symptoms as described by Joubert were not evident. In two of these subjects a renal pathology was revealed, found to be nephronophthisis, prompting the diagnosis of Senior-Loken disease. The three patients also had a residual visual acuity that was higher than that seen in the rest of the sample. In our view these findings suggest that the association of LCA with rhombencephaloschisis and nephronophthisis cannot be considered casual. It remains to be established whether all patients affected by LCA present an increased risk of cerebellar and renal anomalies or whether this may be the case only in a subgroup characterized by a more complex form of LCA. From this perspective, a brain MR examination in young patients with congenital amaurosis could help to identify those affected by cerebellar anomalies. Our findings, if confirmed in a larger sample and by genetic analysis, could have an important positive prognostic value for residual visual acuity. They could also contribute to predicting the likelihood of future renal failure and thus make it possible to plan a screening programme of the renal functions of such children.

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