Review Article

Visual Perception in Preterm Children: What Are We Currently Measuring?

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ABSTRACT

Over the past two decades, cerebral visual impairment has been recognized as a principal deficit in preterm children, and in particular those with cerebral palsy. We review the current knowledge of visual processing deficits in these children, and provide an overview of the tools for assessing cerebral visual impairment. Commercially available instruments are usually directed at evaluating visuospatial skills rather than detecting object recognition difficulties. Particularly in children aged 3 years or younger and in children with multiple handicaps, cerebral visual impairment is difficult to diagnose. This difficulty may be attributable to limitations specific to the instrument, such as a test that is inappropriate for age, or to child-specific limitations such as motor impairment or speech delay. We therefore include an overview of relevant neuroimaging findings reported in these children, focusing on the most recent imaging modalities. Novel techniques such as diffusion tensor imaging may provide sensitive markers of cerebral visual impairment in situations where clinical diagnosis is difficult, and such approaches may allow for early intervention.

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Introduction

Since the 1970s, the survival of preterm born children born has steadily improved [1]. In particular, an increase in survival of 25-73% was reported for infants born before 26 weeks of postmenstrual age [2]. Although this positive evolution raised concerns that the burden of disability in this population would demonstrate a similar increase, a decrease in significant disabilities such as cerebral palsy and severe visual and hearing problems was reported during the last decade [3]. However, a spectrum of more subtle cognitive deficits has become apparent with age [4]. Deficits in the domains of executive functioning, attention, language, behavior, and learning skills were reported, particularly in extremely preterm children, and these difficulties tend to persist into school age and adolescence [4,5]. This finding is reflected in the current definition of cerebral palsy, which includes accompanying disturbances on the sensory and perceptual levels, leading to limited activity and participation [6].

Within this spectrum of “new” cognitive deficits, cerebral visual impairment has emerged as a major problem, and its occurrence is not restricted to extremely preterm children or children with brain abnormalities [7]. Although the problem is becoming better understood, the exact definition of cerebral visual impairment is still under debate, and diagnostic approaches vary widely [8,9]. Cerebral visual impairment not only occurs in association with other deficits, but by itself exerts a major impact on other developmental domains, and this renders the clinical picture of the individual child with cerebral visual impairment very complex. Probably as a consequence of these factors, solid research efforts to address the development of rehabilitative strategies for cerebral visual impairment are lacking.

This review aims to provide an overview of the visual processing deficits occurring in preterm children, of the diagnostic tools in current use to assess cerebral visual impairment, and of neuroimaging findings reported in association with cerebral visual impairment.

Development of visual function in healthy, term children

A great deal of research has been directed at understanding the maturation of sensory function in preterm babies, and these efforts initially relied on behavioral measures. Daum et al. [10] reported in 1980 that fixation and ocular pursuit are present from postmenstrual age 34 weeks. In their research, they used the “œil de boeuf,” a cardboard disc with concentric black and white circles presented to the baby at a distance of 20-30 cm. In 1982, Morante-Boeuf, a cardboard disc with concentric black and white circles presented to the baby at a distance of 20-30 cm. In 1982, Morante et al. [11] described the development of a preference for patterns and gratings after postmenstrual age 30 weeks. Subsequently, Tsuneishi et al. succeeded in eliciting visual evoked responses in preterm infants as of postmenstrual age 24 weeks [12]. With increasing age, the waveform of visual evoked responses changed,
and a positive deflection (N1) was discovered at around age 34 weeks [13].

Enhanced extraterine visual experience was revealed to accelerate the maturation of these visual evoked responses significantly, but not that of the electroretinogram [14]. Ricci et al. [15] also showed that extraterine visual experience positively influenced the maturational aspects of visual function relating to ocular stability and tracking, but not those relating to attention at distance and the perception of color contrast. Therefore, subcortically mediated functions were assumed to mature more rapidly with extraterine visual exposure than aspects of visual function that required cortical input, because the maturation of those aspects depended more on postmenstrual age. However, in children with brain lesions such as periventricular white matter injury, periventricular hemorrhage, and occipital lesions, the maturation of visual evoked responses demonstrated a manifest delay, the extent of which was related to the degree of neurologic abnormality [16].

Behavioral and electrophysiologic methods enabled researchers to demonstrate that visual acuity in preterm children changed from a 160-minute to a 40-minute arc between postmenstrual ages 30 and 40 weeks. Van hof-van Duin [17] indicated that visual acuity dramatically increases before age 1 year (from fourfold to tenfold), reaching an adult level of acuity (1-minute arc) at age 3-5 years. Visual acuity may be defined as the visual capacity to discriminate fine detail, and according to the stimulus, three categories are discerned: detection acuity (the detection of a small object against a plain background), resolution acuity (the discrimination of individual elements in repetitive patterns), and recognition acuity (the discrimination of fine detail of an optotype). In 1989, recognition acuity had already been demonstrated to involve not only the eye and the occipital brain areas, but also the temporal and parietal cortex, along with the eye and the occipital brain areas.

Along with the maturation of lower-order visual functions, various cortical visual functions reach maturity, each at specific ages. For example, orientation selectivity is considered mature at age 8 weeks. From birth, human infants preferentially attend to face-like patterns. A newborn first recognizes its mother’s face on the basis of information from both the outer contour of the head and hairline, and the internal configuration of eyes, nose, and mouth [18]. After age 6 weeks, recognition is based solely on the internal configuration of the face. Very early on, infants also detect biologic motion, can discriminate that motion from other forms of motion, and show preferential attention for upright human movement, a preference crucial in the ability to recognize people and make social contacts [19]. Visual attention is a process that matures more slowly, and that continues until school age [20]. After a phase of alertness between birth and age 8-10 weeks, the orienting system becomes fully functional during the first 6 months. In this period, the duration of looking decreases, reflecting an improved ability to disengage attention. Afterward, infants develop an ability to manifest sustained attention, enabling them to explore objects in the environment. Finally, at around age 18-24 months, the frontal cortex undergoes further development, enabling toddlers to begin looking at complex visual displays such as television [21].

Before age 16 months, form-processing and motion-processing abilities have also begun to develop, but these are not complete until age 4 years [22].

**Lower-order visual function in preterm children**

Overall, preterm children are at risk for developing visual disorders, irrespective of a history of retinopathy of prematurity. Visual acuity is significantly reduced in preterm children with neurologic problems, such as those that develop after asphyxia and intraventricular hemorrhage [23]. Studies reported not only a reduction in resolution, but also in recognition acuity. Acuity was demonstrated to be normal in infants with prolonged flares or periventricular leukomalacia grades 1 and 2, but it was clearly affected in infants with periventricular leukomalacia grades 3 and 4 [7,24]. However, in preterm children attending mainstream school, decreased visual acuity was reported to occur two to three times more frequently than in term-born peers [25,26]. These problems with visual acuity can be ascribed principally to refractive errors. High myopia, in particular, confers a risk for developing anisometropia and secondary visual disorders such as amblyopia and strabismus [27]. However, such early reductions of visual acuity are reportedly subject to “catch-up” by age 5 years [28].

The prevalence of strabismus in preterm children varies from 3% in infants without retinopathy of prematurity, to 57% in 5-year-old children born at a postmenstrual age of less than 28 weeks. The presence of brain lesions partly accounts for this wide range in prevalence [25,27]. Considerable variation exists in the type of strabismus, but the proportion of children with divergence-type strabismus is known to be higher in preterm than in term children. This knowledge is important for purposes of detection, because the presence of strabismus affects the development of binocular vision, including stereo acuity [28].

In addition to deficits in acuity and eye alignment, preterm children also run a higher risk for reduced contrast sensitivity and visual field loss [26].

**Visual perception/higher-level visual processing in preterm infants**

A structural framework for visual perception

Cerebral visual perception is an important and early developing aspect of brain function. Visual processing is complex, and in its first phase involves a relay of sensory signals from the retina to the visual cortex (striate cortex or area V1). This relay is responsible for the initial processing of visual information. Lesions in the striate cortex primarily lead to reduced visual acuity, contrast sensitivity, and color detection, and a loss of visual field. From the striate cortex onward, information is processed by the extrastriate areas. In a simplified view, these extrastriate regions are organized as two streams, i.e., ventral and dorsal. The ventral stream runs from the striate cortex to the middle and inferotemporal regions, and plays a role in the recognition of colors, objects, shapes, faces, and route finding [20,29]. These representations are stored for future reference, and help build visual memory. The dorsal stream also starts in area V1 but orients its fibers to the posterior parietal cortex, and plays a role in processing complex visual information. It is also responsible for online unconscious visual processing, which allows for the visual guidance of movement. Goodale and Milner [29] introduced the terms “What” (vision for perception) for the ventral stream, and “How” (vision for action) for the dorsal stream.

From the posterior part of the brain, visual information is led to V5, a specific projection area where motion is detected. This area is responsible for the recognition of radial flow and translational motion, which enables us to detect the approach to an object or to distinguish figures from their background, among other abilities. Biologic motion is processed in both the temporal lobe and parietal areas, where posterior portions of the superior temporal sulcus represent the intersection within this distributed network [19]. Finally, visual attention is regulated by both the posterior parietal and frontal areas [20,30]. Figure 1 illustrates the different brain areas involved in visual processing.
The clinical spectrum of visual perceptual deficits in children

The term “cerebral visual impairment” was introduced in the 1990s to describe deficits of visual perception in children. It was pragmatically defined as “a neurological disorder caused by dysfunction of the retrochiasmatic visual pathways and projection areas in the absence of major ocular disease” [9]. Although this deficit was formerly designated “cortical visual impairment,” it was revealed to derive more frequently from the subcortical white matter than from the cortical mantle, and hence the term “cerebral” was introduced [7,8]. However, different views on the definition of cerebral visual impairment have persisted in the United States and Europe. In the United States, the term “cortical visual impairment” continues to denote deficits in acuity and visual fields as a result of brain damage, and less emphasis tends to be placed on perceptual visual dysfunction. In contrast, in the European literature, the term “cerebral” is used. Low visual acuity is not a prerequisite for diagnosis, as Fazzi states in her definition [9].

Both definitions imply that cerebral dysfunction is present. However, in addition to this primary pathophysiologic mechanism, the clinical spectrum of cerebral visual impairment also relates to secondary limitations caused by the underlying disorder. For example, in children with cerebral palsy and poor head stability, the establishment of visual referents may be compromised [31].

Because of the enormous plasticity of the developing brain, lesions occurring during development induce a reorganization of maturing functions. In adults, deficits in visual perception attributable to an anatomically defined lesion can be readily diagnosed on the basis of the selective loss of visual-cognitive abilities, whereas the complex of signs in children is variable and not as straightforward [32]. Signs depend not only on the causative lesion itself (if a lesion is even present), but on when the injury occurred. Table 1 contains an overview of potential visual deficits encountered in children, using the current neurocognitive working model (with ventral and dorsal streams) as a basis. However, not all signs occur simultaneously, and neither are they persistently present. They can change over time according to a child’s developmental stage, and according to whether or not a child has acquired strategies to compensate his deficits.

From a clinical point of view, one could therefore argue that the best model to approach dysfunctional development is that of Frith [33]. Frith described a three-level framework, i.e., biologic, cognitive, and behavioral, all three of which may be influenced by the environment. With respect to cerebral visual impairment, this framework may be useful in linking the behavioral picture of an individual child via the affected visual modalities to the underlying cause. For example, a child with a right-sided occipital lesion (biologic) and hence a left-sided visual field loss (visual) will run into obstacles on his left side (behavioral). The International Classification of Functioning, Disability, and Health also integrates personal factors into its framework [34]. This model emphasizes the interactions between a disorder and contextual factors, and particularly focuses on implications of the impairment of body structure and function on the activity and participation level of an individual. This approach is very valuable when rehabilitation is considered (Fig 2).

The clinical spectrum of cerebral visual impairment in preterm children

Cerebral visual impairment is typically diagnosed in association with periventricular leukomalacia, a characteristic lesion in children born between 28 and 32 weeks of gestational age [35,36].
association explains why cerebral visual impairment represents a major comorbidity in preterm children with cerebral palsy, and more specifically in those with spastic diplegia. In the 1960s, Abercrombie et al. [37] reported on visual, perceptual, and visuomotor impairments in diplegic children, and those findings were reproduced by many others [38-40]. However, visual perceptual problems were also reported in late preterm children without brain damage [41].

In school-age children, a diagnosis of cerebral visual impairment is principally rendered on the basis of a failure to recognize abstract drawings and to reproduce figures of increasing complexity. However, in children under age 5 years or in children with associated brain damage and central motor problems, many tests are not reliable, either because the test is inappropriate for age, or because the child presents with specific limitations such as motor impairment or speech delay. Although this lack of reliability has led to the use of questionnaires to aid in diagnosis, one of which has been published [42], the diagnostic value of these questionnaires is unknown. Referring to the framework of Frith [33], we note that clinicians often rely on behavioral signs to make a diagnosis, rather than on formal testing. However, because these behavioral signs reflect a child’s restrictions in activity and participation, they currently form the basis of treatment.

Next we describe the visual perceptual deficits observed in preterm children, and the tools in use to document them.

Visual attention

Although preterm children run a strongly increased risk of developing visual attention problems, they are not often formally tested for these problems. Based on studies using habituation and dishabituation paradigms, evidence exists that the development of early visual attention in preterm infants is not optimal [15,43]. These deficits increase with age, resulting in shortened periods of sustained attention in the toddler age group [23]. Studies in school-age children are sparse. In a study of 45 7-9-year-old children born very preterm, Shum et al. [44] observed that relative to 49 full-term control subjects, a significant difference occurred in performance on the visual attention subtest of NEPSY, a neuropsychologic assessment battery for children between ages 3 and 12 years that assesses six domains: Social Perception, Executive Functioning/Attention, Language, Memory and Learning, Sensorimotor Functioning, and Visuospatial Processing [45].

Visuospatial abilities

The Beery-Buktenica Developmental Test of Visual-Motor Integration is widely used to assess visual perceptual abilities [46]. The Visual-Motor Integration test consists of three subtests. First, in the copy task, the individual is asked to copy geometric forms, arranged in order of increasing difficulty. Second, the visual perception task uses the same geometric forms, but asks the subject to search for a specific form in a series of similar forms. Third, in the motor coordination task, the subject is asked to copy these same drawings in a frame. The copy task is used most frequently in research. This task relies predominantly on visuomotor abilities, and can be used in children in a broad age range from 2.5 years to adulthood. With this test, 10-45% of preterm children were observed to perform below their age level, with their performance level depending on the age at which they were tested and the presence or absence of associated brain lesions [47-49].

Motor free tests, such as the Test of Visual Perceptual Skills—Revised, the Developmental Test of Visual Perception, or the Motor Free Visual Perception Test, assess different categories of visual perceptual skills: visual discrimination, visual memory, visual-spatial relations, visual form-constancy, visual sequential memory, visual figure ground, and visual closure [50-52]. These tests can be performed within an age range of 4–18 years. Overall, significant disability, defined as a total score less than percentile 5 for all subtests, was present in 11–20% of children with a history of preterm birth. This prevalence increased when gestational age or birth weight decreased (17% of children with a birth weight of <750 g were affected), but was unaffected by global intelligence quotient [53,54].

Visuospatial abilities can also be tested by three subtests of the NEPSY: route finding, which evaluates the understanding of visuospatial relationships and directionality; arrows, in which children are asked to judge line orientation and direction; and design copying, which assesses visuomotor integration when two-dimensional figures are copied on paper [45]. Normal values are available for an age range of 5–16 years. Marlow et al. [55] demonstrated in a large cohort of extremely preterm children that scores for visuospatial performance differed from those of term-born peers by 1.6 standard deviations. This deficit remained significant after controlling for global intelligence quotient.

Only one study has investigated spatial neglect by using the Bells Test cancellation task [56] in preterm children versus a group of age-matched and sex-matched term control subjects [49]. The authors reported no difference in speed, but documented a difference in accuracy.

Table 1. Clinical features of cerebral visual impairment

<table>
<thead>
<tr>
<th>Ventral Stream Impairment</th>
<th>Dorsal Stream Impairment</th>
<th>Additional Ophthalmologic Cues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired recognition of faces, objects, shapes, letters, or gestalt</td>
<td>Impaired ability to handle complex scenes in two-dimensional and three-dimensional space</td>
<td>Unilateral or bilateral lower visual field loss</td>
</tr>
<tr>
<td>Impaired visual memory</td>
<td>Impaired visual search</td>
<td>Loss of acuity</td>
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<tr>
<td>Impaired orientation</td>
<td>Impaired visually guided movement of upper and lower limbs</td>
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<tr>
<td>Impaired visual attention</td>
<td>Impaired perception of motion</td>
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<tr>
<td>Impaired motion perception</td>
<td>Additional Ophthalmologic Cues</td>
<td></td>
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</tbody>
</table>

* Children typically present with a complex combination of these features.
Object recognition

In the Hooper Visual Organisation Test, the patient is asked to identify 30 objects, represented as puzzle pieces [57]. The test relies mainly on concept formation, visual analysis and synthesis, and on labeling familiar objects, and can be used from age 6 years onward. In a group of 216 extremely low birth weight children older than age 6 years, Jakobson et al. [58] observed no differences in performance on this test, independently of whether brain lesions were documented by ultrasound in the neonatal period.

The L94 Visual Perceptual Battery is another object recognition test, comprising eight visual perceptual tasks for which normative data are available for children aged between 2.75 and 6.5 years. In five computer tasks, the child is asked to identify everyday objects, and thus is tested for semantic and perceptual categorization (for an overview and examples of individual subtasks, see Stiers et al. [35] and Fig. 3). In a study by van den Hout et al. [59], impairment indicated by the L94 was particularly evident in preterm children with periventricular leukomalacia, but also in children with transient periventricular echo densities. Later on, impaired L94 results were observed to be increased in children born between 30 and 37 weeks of postmenstrual age with cerebral palsy, and the severity of impairment increased when periventricular leukomalacia was present [36].

Finally, Fazzi et al. [9] studied 22 preterm born children with brain damage, using a neuropsychologic battery that evaluates not only form, object, and spatial recognition, but also visual memory. They identified object recognition difficulties in 70% of subjects. Visual memory was also significantly deficient, a finding confirmed by others [60]. The authors also investigated face perception, with four out of 20 preterm children performing poorly.

Perception of motion

In addition to form recognition and visuospatial problems, preterm children exhibit impaired sensitivity to motion coherence, which is thought to depend on the functional integrity of V5 [61]. Jakobson et al. [62] demonstrated significant associations between motion-defined form-processing deficits and problems with visual search, stereopsis, visuococonstructive and graphomotor skills, motor development, and performance intelligence quotient. Moreover, the presence of retinopathy of prematurity and mild periventricular leukomalacia exerted a negative influence on motion sensitivity. These results suggest that the assessment of sensitivity to motion-defined forms may allow for the early identification of preterm children at greatest risk for visual problems associated with dorsal stream impairment.

Their findings were reinforced by Birtles et al. [63] and Guzzetta et al. [64]. These groups found that the performance of preterm children on global motion perception was diminished, irrespective of whether brain damage was present. In the experimental conditions in which the perceptual task could be accomplished by relying on form information, the sensitivities of preterm children without brain lesions were similar to those of age-matched healthy children, whereas preterm children with brain lesions performed less well.

In addition to deficits in the recognition of global motion and form coherence, the recognition of biologic motion is also impaired in preterm children [65,66]. Biologic motion is crucial for a variety of daily-life activities such as adaptive social behavior and safe self-locomotion. Klin et al. [67] found that in children with autism spectrum disorder, the perception of biologic motion was impaired as of age 2 years. In a comparative study of 23 5-9-year-old children who were born at less than 32 weeks of gestation and who exhibited no major disabilities, Taylor et al. [66] demonstrated a clear reduction in sensitivity to biologic motion relative to normal control subjects. At older ages, these children exhibited better sensitivity, but the results remained significantly worse than in their term peers. When deficits in biologic motion perception were evident, they occurred either as an isolated problem or in combination with deficits in global form perception, global motion perception, or both.

Correlation of visual perception with cranial imaging findings

Structural magnetic resonance imaging

Because cerebral visual impairment was first recognized in children with cerebral palsy or acquired brain damage, imaging studies initially focused on this group of children. Cerebral visual impairment was first thought to derive only from lesions in the cortical mantle, i.e., the occipital lobe [68]. However, subcortical and white matter lesions were also observed to underlie cerebral visual impairment [7,59]. A few years later, the excellent overview of Dutton and Jacobson [69] described the wide spectrum of conditions in which cerebral visual impairment has been diagnosed. This spectrum included brain malformations, periventricular leukomalacia, and occipital damage attributable to infections or hypoxic-ischemic encephalopathy, but also closed head injuries and hydrocephalus. As a consequence, structural magnetic resonance imaging was thought to correlate in a nonspecific way with signs of cerebral visual impairment.

However, in preterm children, bilateral periventricular leukomalacia and unilateral lesions are associated with visual perceptual impairment. Van den Hout et al. [59,70] demonstrated a strong correlation between visual perceptual impairment (measured with the L94 visual perceptual battery) and the presence of cortical damage or peritrigonal white matter damage (even if unilateral) and the size of the lateral ventricles. A better visual prognosis was evident when the splenium of the corpus callosum was preserved. Laterality clearly played a role, because right temporal lobe damage in the patients of Van den Hout et al. [59,70] was associated with problems of recognition, whereas this finding was less clear for left temporal damage, an area responsible for orientation and navigation. Further, Ortibus et al. [36] demonstrated that the presence of periventricular damage correlated with the extent of visual perceptual signs.

Other authors studied the impact of central gray matter damage and reported thalamic and cerebellar atrophy in nearly half of their studied children with visual perceptual problems [71,72]. Moreover, the white matter volume of the cerebellum could predict test scores on the copy and visual perception subtasks of the Beery-Buktenica Developmental Test of Visual-Motor Integration, whereas the volume of the thalamus predicted only the scores of the copy subtask. When these structures were found to be intact, this finding was associated with normal visual function.

The absence of structural lesions, however, does not guarantee intact circuitry. This finding became clear when cerebral visual impairment was described in children without structural brain damage, e.g., in children with velocardiofacial or Williams syndrome [73,74].

Diffusion tensor imaging and tracking

The understanding that structural magnetic resonance imaging cannot provide sufficiently detailed information on the prognosis of cerebral visual impairment underscores the need for improved imaging techniques. Diffusion tensor imaging is a new, noninvasive magnetic resonance modality that can demonstrate the orientation and integrity of white matter fibers in vivo by measuring fractional
anisotropy [75]. Verhoeven et al. [76] elegantly illustrated the maturation of white matter from infancy to adolescence using this method. In preterm children, however, the integrity of the global white matter seems generally deficient [77,78]. Behrman et al. [79] reported more specifically on a correlation of optic tract integrity and visual maturity in preterm neonates by testing visual fixation. In a cohort of 36 premature neonates at gestational ages from 29–41 weeks, optic radiation fractional anisotropy correlated significantly with scores from the visual fixation tracking assessment, independent of gestational age. Using a more comprehensive visual assessment battery, Bassi et al. [80] demonstrated that fractional anisotropy of the optic tract correlated with visual assessment scores in preterm neonates, and this relationship remained significant when gestational age at birth, postmenstrual age at time of scanning, and the presence of lesions on conventional magnetic resonance imaging were taken into account. Moreover, this correlation was specific to the optic radiations, and thus did not reflect a general problem of the white matter.

Figure 3. Subtests from the L94 Visual Perceptual Battery. (Reprinted with permission from Ortibus et al. [36].)
In a group of low birth weight children assessed at age 15 years with low scores on the Beery-Buktenica Developmental Test of Visual-Motor Integration, Skranes et al. [81] documented low fractional anisotropy values in the external capsule, the posterior part of the internal capsule, and the inferior longitudinal fasciculus.

Voxel-based morphometry

Voxel-based morphometry is a recently developed method to examine the regional and subregional microstructural brain changes associated with prematurity. Using this method in preterm adolescents, Nosarti et al. [82] and Kessler et al. [83] documented significantly lower white matter volumes in the cingulum and corticospinal tract, but also in the superior and inferior longitudinal fascicules. The cingulum is (among other areas) involved in spatial attention. The superior and inferior longitudinal fascicules are thought to be associated with dorsal and ventral stream function, respectively.

Functional magnetic resonance imaging

Functional magnetic resonance imaging allows for a noninvasive investigation of neural activity by interpreting dynamic changes in blood oxygen level-dependent signals [84]. Studies of young, healthy children reported considerable variability, because both positive and negative blood oxygen level-dependent signal responses could be identified within the same study population. Whether this heterogeneity is attributable to technical issues with the stimulus paradigms, to analytical procedures, or to genuine physiologic differences in the developing brain remains unclear.

In adults, functional magnetic resonance imaging can be used to map multiple visual areas. Stiers et al. [85], for example, asked adults to passively view simple stimulus sequences, consisting of static object photographs alternating with videos of movement through natural indoor and outdoor scenes, and with a control fixation task. They demonstrated that even the processing of short sequence stimuli involved multiple visual areas, in both the ventral and dorsal areas of the brain.

Narberhaus et al. [86] performed an assessment of visual perceptual learning processing (by means of encoding, recognition, and same/different discrimination) in a cohort of very preterm-born adults compared with control subjects. Despite good task performance, Narberhaus et al. [86] found that different neural networks were activated. During encoding, the test subjects exhibited increased blood oxygen level-dependent signal responses relative to control subjects in the left caudate nucleus, the right cuneus, and the left superior parietal lobule, and decreased signal responses in the right inferior frontal gyrus. During recognition, they exhibited increased signal responses relative to control subjects in the right cerebellum and bilaterally in the anterior cingulate gyrus.

Active functional magnetic resonance imaging experiments in preschool children are difficult to perform because of limited cooperation in this age group. Passive functional magnetic resonance imaging, on the other hand, is a feasible examination for assessing visually and motor system plasticity in the developing brain. We expect this form of passive functional magnetic resonance imaging to be a useful tool for assessment in other age groups.

Plasticity of the visual system: clinical variety explained?

Evidence exists that the motor system exhibits significant plasticity. Hopefully, this would also be the case for the visual system [89]. Experiments with functional magnetic resonance imaging demonstrated that Braille reading leads to activation of the visual cortex in adults who have been blind from an early age. In contrast, in healthy control subjects, only the sensorimotor cortex was activated during this task [90]. Therefore, during adulthood, remarkable residual plasticity remains when vision is lost either temporarily or permanently. The important questions regarding children, however, involve whether alternative brain areas are capable of substituting the function of the visual cortex or the visual association areas, whether these areas are slower to mature when they are damaged, and whether interpretation is more time-consuming because of the use of alternative pathways. Answering these questions will be important when envisaging early diagnoses of cerebral visual problems and early intervention.

According to evidence from studies in healthy animals, the enrichment of an environment that produces increased visual experience also gives rise to an increase in visual acuity [91]. Studies of children with congenital cataracts and blindness also indicate that early visual experience builds the infrastructure for later learning, and this finding involves both the dorsal and ventral streams [92]. In a cohort of children with congenital cataracts, the global motion coherence threshold was significantly higher in children with bilateral rather than unilateral disease, whereas in the unilaterally affected group, the thresholds were only slightly higher than in normal control subjects [93].

Bova et al. [94] reported on the spontaneous recovery of higher visual function in the case report of a child who underwent gastroenterologic surgery at age 2 years 6 months, and who acquired bilateral occipital damage resulting in complete and bilateral visual loss. The authors described how the child was able to localize light in the lower visual field, imitate hand movements, and recognize moving cars. Over a time frame of 4 years, nearly every visual function had recovered. At age 6 years and 8 months, however, the child still failed tests evaluating memory for location, complex visuospatial design, and recognition of overlapping figures, gestalt, and unusual perspectives. The authors concluded that in comparison to adults, visual recovery in children seems more extensive, but that it is incomplete and occurs randomly over long periods of time [95].

The proposed mechanisms for the recovery observed in children are based on the assumption that functional tissue remains within a lesion, or that a reservoir of neuronal cells and synapses is available [92]. This assumption, however, is extremely difficult to document clinically in individuals with early brain damage, because such evaluations rely on behavioral responses, and active cooperation in such situations is not possible [96]. However, these mechanisms were studied in part using diffusion tensor imaging tractography. Seghier et al. [97] followed an infant who had manifested a perinatal stroke and unilateral visual field loss. They assessed visual system recovery by combining diffusion tensor imaging and event-related functional magnetic resonance imaging at ages 12 and 20 months. At age 20 months, event-related functional magnetic resonance imaging indicated significant activation in the visual cortex of the injured left hemisphere that had not been evident at age 12 months. These observations were reinforced by the finding of structural modifications on diffusion tensor imaging.

Finally, an interesting concept to explain the enormous clinical variability is based on the developmental origins theory, in which gene-environment interaction is considered central. Cell differentiation and migration are influenced by both genetic programs and the environment. Alterations in these processes, e.g., by a mutation...
or an insult, may lead to disconnected circuits and disturbed development. Particularly among children in whom a lesion cannot be documented, this hypothesis is intriguing [98].

Conclusions

With age, during both intrauterine and postnatal life and throughout the acquisition of skills, the developing brain undergoes significant changes in functional organization. Not surprisingly, therefore, preterm birth exerts long-lasting effects on brain development, including the domain of visual function. Importantly, cerebral visual impairment can occur in the absence of any identifiable brain lesion. On the other hand, secondary limitations, e.g., in children with cerebral palsy, may contribute to the emergence of visual perceptual problems.

The term “cerebral visual impairment” is used to denote visual perceptual deficits that can appear over time. Diagnoses of cerebral visual impairment have relied mostly on the formal testing of visuospatial abilities, e.g., because the available object recognition batteries are not appropriate for children under age 6 years. Assessments of motion and form coherence have thus far been performed only in the research setting. Furthermore, in children with multiple handicaps, standardized assessments are not appropriate, and in these cases, clinicians are forced to rely on observational information. Therefore, the development of a comprehensive test battery for young children and for those with multiple handicaps should be regarded as a priority.

As the model of Frith [33] states, behavioral signs are ultimately the result of a disturbance at the biologic level. Therefore, an alternative approach to study whether visual perception is intact would involve correlating clinical signs with measures of impairment at the neuroanatomic level. Given the evidence that the ventral and dorsal streams may be impaired in the absence of structural lesions to the brain, recent imaging techniques (e.g., diffusion tensor imaging) are emerging as promising tools to study the functional integrity of white matter in children. A problem in need of further clarification involves the contributions of cerebellar and central grey matter maldevelopment to the visual perceptual and visuomotor deficits in preterm children. A combination of intact circuits is probably required for visual perceptual function to develop normally [99]. Functional magnetic resonance imaging may be the appropriate technique to bring insights to this complex problem.

We hope that studying the link between early damage and clinical signs will enable clinicians to predict visual problems at an early stage in preterm children, and to begin interventions soon after discharge from the neonatal unit, exactly when brain plasticity is at its highest potential.

Until then, rehabilitation programs will rely on trial and error. Indeed, some stimulation programs to encourage visual recovery were reported in the literature, but the results are difficult to interpret, in particular because every patient with cerebral visual impairment is different [100]. In any case, stimulation programs should benefit from the growing understanding of mechanisms involved in the plasticity of the brain and of the effects of enriched environments. Ultimately, however, any individual rehabilitation program should be designed as a patient-tailored treatment.

References


