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General introduction

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INTRODUCTION

To understand and interact with the world around us, we humans are highly dependent on the quality of our senses (vision, hearing, touch, smell, and taste), cognition and motor abilities. An extensive network is involved in the processing of sensory information, and includes the sensors, such as eyes, ears and skin, and our brain. People are inclined to use their own sensorial input and interpretation of the world around them as reference. This makes it difficult or even impossible for people with effectively working senses to imagine, understand and acknowledge what it is like to be sensorially impaired, as in people with a visual impairment. To understand and recognise sensorial impairments, we need knowledge of sensorial systems and functions, and the effect that function loss or impairment has on interaction with our environment. Vision in particular, is regarded as the primary sense for developing many skills. Therefore, in this thesis, I focus on visual impairments in children.

Children that need special support because of a visual impairment

It is generally recognised that congenital low vision or blindness[1] negatively influences a child's development of cognitive, motor, communication and social skills.[1-6] To stimulate development in children with low vision and blindness, early intervention and habilitation is preferred. In the Netherlands, early intervention and habilitation are offered by special services for people with visual impairments. Because such services are funded by health insurances - originally the Exceptional Medical Expenses Act (AWBZ) and since January 2015 the mandatory health insurances -, eligibility requirements have to be met. These eligibility requirements, originally designed for adults, are based on the definitions of low vision and blindness as described in the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)[7] and involve two visual functions: visual acuity and visual field (Table 1).

Visual acuity is the ability to see or resolve details of a retinal image when tested at maximum contrast (black/white), whereas visual field is defined as the area that can be seen when looking straight forward.

1 Although this term suggests that there is a total lack of vision, there may be some vision left.

Table 1. Definition of low vision and blindness as described in ICD-10 H54, 1993.

In the better eye with best possible correction	Definition	
	Low vision	Blindness
Visual acuity	less than 6/18 and equal to or better than 3/60	less than 3/60
	or	or
Visual field	less than 30 degrees and equal to or better than 10 degrees	less than 10 degrees

Although visual acuity and visual field are important properties, there is more to this than meets the eye when it comes to visual perception, the ability to recognise and interpret visual aspects of the surrounding environment. Visual perception highly depends on the development of an extensive brain network and several visual functions, which are assigned to different brain areas. It starts with processing light that falls on the retina. The retinal information is conveyed via the optic nerve and lateral geniculate nucleus (LGN) to the primary visual cortical areas, such as the occipital lobe (V1), and extrastriate areas (V2). Next, the visual brain can be described in a simplified hierarchical model with two anatomically and functionally distinguishable main streams: the ventral stream and the dorsal stream.[8, 9] The ventral stream ends in the inferior temporal cortex and is involved in object[10, 11] and face recognition.[11] The dorsal stream leads into the posterior parietal cortex and extends towards the anterior parietal and posterior frontal cortex, and is involved in motion perception,[12, 13] visuomotor integration,[10] visual attention,[14, 15] and object recognition in suboptimal representations.[16, 17]

Habilitation specialists generally acknowledge that a lack or loss of cerebral visual functions can impede a child's development and participation as well. Thus cerebral visual disfunctions, for example, may hinder the ability to visually recognise persons or objects or to perceive motion.[18-20] Difficulties in the perception of a person's identity hinder discrimination of familiar and unfamiliar persons, and proper social communication. Object recognition problems not only complicate learning by means of objects, but make exercises in schoolbooks, which often contain illustrations, difficult or even impossible to do. Visual spatial attention and motion perception are essential for understanding and predicting the constantly changing world around us. For blind people or people with impaired visual motion perception, crossing a street without aids such as traffic lights with a signal system is very risky, especially now that car engines become more silent. The combination of spatial awareness and motion perception also helps us to direct our object handling, such as catching

a ball or pouring a cup of tea. From a social interaction perspective, it also enables us to predict what other people intend to do.

Visual impairments, either mild, moderate or severe, can have a major impact on daily life functioning. When children with mild visual impairments grow older, they may experience more difficulties when it comes to educational methods towards more self-regulation, and demands on communicative and social skills. This may lead to an increase of referrals to specialised services and special schools, similar as has been suggested for children with autism.[21] A thorough but tailored diagnostic process and the ability to diagnose mild cerebral visual impairments become of a greater importance.

Diagnosing cerebral visual dysfunctions in children

In 2005, when we started this project, the ophthalmological guideline for referral to special services for people with visual impairments exclusively mentioned low and subnormal vision (visual acuity ≤ 0.5), visual field defects, reading problems as result of high hyperopia (farsightedness) and glare (interference of light) as referral criteria.[22] In the updated guideline of 2011[23] specific attention is asked for cerebral visual impairment, but no specific referral criteria are given and only risk groups with 'mental retardation', low birth weight, and cerebral paresis were mentioned. Once children are referred, they enter a diagnostic process, which routinely includes history taking and an assessment of oculomotor functions, visual acuity, visual fields and contrast sensitivity. Only if cerebral visual dysfunctions (e.g. problems with visual attention, object or face recognition, motion perception or visuomotor abilities) are suspected to cause problems in daily life, further assessment is done.

For the decision to start further assessment, the cause and type of visual impairment in combination with the experienced problems in daily practice, as reported by parents or teachers, are considered relevant. Visual impairments are grossly divided into cerebral (or central) visual impairments (CVI) and ocular (or peripheral) visual impairments (OVI). CVI is mainly caused by brain damage or brain dysfunction. Low vision and visual field loss may also be caused by brain damage (CVI) as well as by ocular disorders (OVI). It is important to realise that children with CVI can have normal visual acuity and normal visual fields.[24] Currently, the following groups of children are considered at risk for cerebral visual dysfunctions: children with cerebral palsy, children with intellectual disability and prematurely born children.[24] The prevalence of CVI in developed and developing countries is still unknown. Brain damage or brain dysfunction is considered the most common cause of low vision and blindness in developed countries.[25, 26]

A few reasons why epidemiological knowledge on cerebral visual dysfunctions in children is limited are:

1. the effect of brain plasticity: the course of development in children with early brain damage is unpredictable, a certain brain area can take over the function of affected brain areas. As a result, the presentation of problems, including visual problems, may be heterogeneous in a group with comparable brain damage.
2. a-specific testing of visual functions: several brain functions interact and thereby making it difficult to disentangle the specific function that caused the abnormal or weak performance, e.g. a child might be unable to name a picture due to a language problem, a visual perceptual problem or did not pay attention to the picture;
3. the difficulty in recognition of problems: cerebral visual dysfunctions may be difficult to recognise in children with other prominent problems, such as motor or intellectual disabilities;
4. the availability and applicability of diagnostic tests: not all cerebral visual functions can be assessed with diagnostic tests with quantitative outcomes; moreover, many tests are not applicable in very young children;
5. the limited accessibility of certain groups of children to expert services: many children with unrecognised cerebral visual dysfunctions, especially among those visiting special schools, rehabilitation centres, and day care centres for children with intellectual disabilities are not referred yet.

Aim of this scientific project and contents of this thesis

Without a valid basis of scientific knowledge on the epidemiology of cerebral visual dysfunctions and evidence on their impact on daily life, adaptation of the eligibility requirements is very unlikely. As a result, children with cerebral visual dysfunctions, especially those without a diagnosis of low vision or blindness, are at risk for denial of the support they are in need of. Prior to investigating the prevalence of cerebral visual dysfunctions, it is required to get a clear overview of the wide spectrum of functional impairments. During a meeting of a Dutch expert working party in 2006, professionals involved in the signalling, referral and early assessments, such as youth healthcare physicians, paediatricians, intellectual disability physicians and paediatric ophthalmologists, indicated that they needed clear guidelines how to recognise children at risk for cerebral visual dysfunction, apart from the above-mentioned risk groups. They requested a test or screening questionnaire, because most paediatricians and youth healthcare physicians were unfamiliar with even the existence of cerebral visual impairment. Many professionals had difficulties with the

recognition of typical behaviours and problems associated with it.[27] Professionals involved in the expert diagnostic process indicated multiple problems, such as the lack of neuropsychological tests for children under the age of four years. As a result, they are forced to rely on structural observations with no or limited quantitative outcome measures. In addition, they stressed the lack of quantitative tests for specific cerebral visual functions applicable to children older than four years, with a special emphasis on motion perception tests. Still, most tests have been developed for normally sighted children, excluding children with low vision. Therefore, the effect of low vision on test outcomes is unknown. The presence of a cognitive impairment can also affect the performance of perception tests. That raises a very practical question: what entry should be used when using norm tables: the developmental or the chronological age of a child?

Study approach

Neuropsychology aims to understand how behaviour and cognition are influenced by brain functioning. During several tests, the processing of visual information plays an important role, because many tasks consist of visual representations. Here, the ability to visualize a complete whole even when presented incomplete information or a partial picture, also known as Gestalt, is crucial for optimum performance. The general aim of my thesis was to provide new information to advance evidence-based diagnostic procedures in children at risk for cerebral visual dysfunction (children with brain damage), which ultimately should be efficient (burden and costs, use of valid tests).

I decided to focus on school-aged children with a developmental age between 4 and 7 years. The selected tests are relatively easily to integrate in the assessment and provide a quantitative outcome of cerebral visual functions associated with dorsal stream vulnerability of the visual system. Here, I consider object recognition under suboptimal conditions, motion perception, visuomotor abilities and visual attention as dorsal stream functions.

Data collection

We assessed oculomotor functions, visual acuity, visual fields and contrast sensitivity, performance age, object recognition under suboptimal conditions, motion perception, visuomotor abilities and visual attention in children at risk for cerebral visual dysfunction (children with brain damage) as well as in children not at risk (normally developing children and children with ocular disorders).

In **Chapter 2**, we focus on early recognition by e.g. youth healthcare physicians, paediatricians, intellectual disability physicians, ophthalmologists. We studied whether the crowding ratio (ratio between single optotype and multiple optotype acuity), or ratios between grating and optotype acuity, could help to discriminate between children considered at risk for cerebral visual dysfunctions (children with brain damage) and children not at risk for cerebral visual dysfunction (normally developing children and children with ocular disorders), given the different detection goals in the care supply chain.

In Chapter 3-6 we focus on the expert assessment of cerebral visual dysfunctions. **Chapter 3** is a short introduction into motion perception, including current insight into its representation in the brain, different aspects of motion perception, and available diagnostic approaches. In **chapter 4**, a systematic review is presented of the scientific literature on motion perception tasks, to evaluate whether there is substantial evidence that motion perception tasks are valid and reliable to be used in clinical practice as well as epidemiological research, i.e. tasks are applicable, norm values are available and reliable, and motion perception problems have been demonstrated in at risk groups.

Consequently, motion perception becomes a central part of my studies. Based on neuropsychological assessment, I address the following topics: 1. the relation between chronological age, performance age and motion perception task outcomes and whether we should use chronological age or performance age as an entry of norm tables in the diagnostic process in at risk groups (**Chapter 5**), and 2. whether specific (isolated) motion perception problems are present in children with brain damage (**Chapter 6**).

Chapter 7 addresses object recognition, and specifically the question whether children with brain damage and problems with object recognition under suboptimal conditions either have a general dorsal stream dysfunction or have selectively impaired dorsal stream functions.

Chapter 8 and 9 result from a collaboration with the Vestibular and oculomotor research group at the department of Neuroscience, Erasmus MC. The rationale for this collaboration was the availability of a method to test visual processing functions in children aged younger than 4 years and in children as well as adults with severe intellectual disabilities. The method depends on automated tracking of reflexive and goal-directed eye movements towards specific visual stimuli using a remote eye tracker system. In **Chapter 8**, the viewing behaviour to three different coherent motion stimuli is assessed in terms of reaction time and fixation quality.[28] The data are obtained in typically developing children aged 0-12 years and may serve as normative data. In **Chapter 9**, I investigated the ability of children with OVI and CVI to

visually integrate parts of the representation into a whole. In clinical practise, the subtest Gestalt Closure of the Kaufman Assessment Battery for Children second edition (KABC-II) is frequently used for this purpose. Here, this test was combined with eye tracking to be able to combine the performance with the obtained viewing behaviour.

Finally, in the general discussion, **Chapter 10**, the outcomes and limitations of this study are discussed, as well as implications for clinical practice and research.

Remarks on terminology

Terms like cortical visual impairment or cerebral visual impairment (CVI) can cause confusion about the visual functions of interest. The term visual impairment is often used to indicate low vision and blindness. In the above text and in the following chapters the term visual impairment is used for both low vision and blindness and cerebral visual dysfunctions.

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