

Homonymous hemianopia and related visual defects: Restoration of vision after a stroke

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The term homonymous hemianopia refers to visual impairment due to a post-chiasmatic brain lesion. Mammalian neurons of the central nervous system do not have the ability to regenerate. However, the cerebral cortex shows plasticity in certain cases. Motor or speech disorders due to frontal lobe brain damage can be improved with well-directed rehabilitation techniques. If such plasticity is possible, it raises the question whether specialized training could improve a cortical visual disorder. There is need for simple visual training which could be used in rehabilitation. A few different approaches have been developed to treat patients with hemianopia: (1) substitution including special devices, such as optical prisms; (2) compensation using intact residual abilities – especially training of eye movements; (3) restitution which is based on stimulating the blind hemifield. The third method of rehabilitation is the most controversial; however, it has the largest potential. To support concepts of the targeted rehabilitation outlined here, first: further development of the theory of plasticity in visual pathways is required and second: the efficacy of the rehabilitation procedures has to be demonstrated by clinical evidence. We review methods and approaches of hemianopia rehabilitation and treatment. We also review results of contemporary clinical studies and meta-studies.

Key words: homonymous hemianopia, cerebral stroke rehabilitation, scotoma, visual field deficit

ABBREVIATIONS

HHA – homonymous hemianopia,
LGN – lateral geniculate nucleus,
(f)MRI – (functional) magnetic resonance imaging,
(M)ANOVA – (multivariate) analysis of variance,
V1, V2, V3, V4, V5/ MT – (primary and secondary)
visual cortical areas,
VEP – visual evoked potentials,
VFE – visual field expansion,
VRT – visual restitution training/ therapy

INTRODUCTION

Vision is a major sensory input to the human brain. Half of the afferent neuronal fibers projecting to the brain originate from the eyes. Intact visual

abilities are an important condition enabling us to orient ourselves in our world. There are obvious limitations of orientation due to visual and oculomotor disorders. Patients with some form of hemianopia are diagnosed in significant numbers. Pambakian and Kennard (1997) reported that 50% of all neurological admissions into hospitals in the United Kingdom are due to a stroke and 30% percent of them are reported to have hemianopia. Numbers of hemianopic patients reported in the Czech Republic are similar and somewhat lower due to differences in diagnostics and classification of nosological units (Mikulik et al. 2010).

Visual impairments are present in 20 to 40% of patients in neurological rehabilitation centers (Leys et al. 2007). According to a life table analysis by Reding and Potes (1988) a deficit in vision and spatial perception can cause slowdown of the rehabilitation progress in physiotherapy. Hemianopia or scotoma caused by stroke is also a signal that a primary disease (for example atherosclerosis or hypertension) is a

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Received 25 November 2012, accepted 12 June 2013

cause of the cerebral stroke. Such a patient is in a danger of repeated cerebro-vascular accidents and the primary disease must be treated. At the same time, coordinated rehabilitation should prevent recurrence of such accidents. Therefore, the rehabilitation of hemianopia has its logic. However, visual rehabilitation program on a larger scale is still missing in most rehabilitation centers and clinics. The reason for this omission is the frequent argument that lesions of the lateral geniculate nucleus (LGN) and striate cortex lead to a permanent loss of vision. According to recent findings, this does not always have to be true. Experimental work on monkeys and humans proved that despite the destruction of the striate cortex, some visual functions could be retained (Humphrey and Weiskrantz 1967, Ptito et al. 1991). Various methods of treatment have been developed to date, some with clearly positive results.

This mini-review is divided into three parts. Descriptions of homonymous hemianopia and other different visual impairments due to brain damage are presented in the first part. In the second part, different methods of hemianopia treatment are described. Future possibilities of treatment are discussed in the third part of this paper.

VISUAL IMPAIRMENTS DUE TO CENTRAL LESIONS

Homonymous hemianopia (HHA) can be congenital, but mostly it is an acquired condition caused by stroke, traumatic brain injury, tumors, infections or surgery. The term denotes verbatim “half-blindness of the same side in both eyes”. More precisely it is a deficit in half of the perimeter in both eyes due to contralateral post-chiasmatic brain lesion. The loss of one quarter of visual field on one side in both eyes is referred to as homonymous quadrant hemianopia. Pathogenesis of HHA includes mainly ischemic strokes in 70% of cases. The rest is caused by tumors, hemorrhages and other lesions (Fujino et al. 1986).

Approximately 20 to 30% of all patients in neurological rehabilitation centers are reported to have a homonymous visual field disorder. Hemianopia is connected with lesion in: (1) the occipital lobe in 40%, (2) the parietal lobe in 30%, (3) the temporal lobe in 25% and (4) the remaining 5% in the optic tract and the LGN (Fujino et al. 1986). In 7% of all cerebral infarctions both hemi-fields are affected, which results in

cerebral blindness. According to Kerkhoff (1999) patients face three main visual behavioral problems: (1) impaired eye movements (including saccades) leading to defective visual and spatial exploration, (2) hemianopic reading deficit (hemianopic alexia) because of the parafoveal field loss and (3) deviated subjective mid line. More than 60% of patients with hemianopia have limited or no awareness of their impairment (Kerkhoff 2000, Koch 2004).

Impaired eye movements due to visual field deficit also cause wrong exploration patterns and deteriorated visual search. This defect is characterized by shorter saccades within the scotoma. These impaired saccades result in the prolonged exploration time of a scene and can lead to significant problems in daily life such as inability to navigate around various obstacles (cars, people and other objects). It also causes a cognitive deficit while extracting information from a visual scene (Kerkhoff 1999). Patients with visual field disorders spontaneously develop limited compensating oculomotor strategies. Patients with homonymous hemianopia tend to halve a line too close to the border of their scotoma. This is to the right in right-sided hemianopia in a horizontal line and vice versa.

Reading impairment (hemianopic alexia) is caused by a loss of parafoveal field (parafoveal scotoma). This reduces the size of the perceptual window for reading. Rayner and McConkie (1976) defined the perceptual window as the central area in the visual field, where letters can be recognized by one-time fixation of the eyes. This corresponds approximately to 13 characters to the right and 6 characters to the left, assuming a left-to-right (western) reading direction. The left parts of single words contain more information needed by (western) readers to identify a word. The right part of a perceptual window is used to lead the eyes. Therefore, patients with left-sided visual defects tend to make more reading errors due to false identification of the initial letters of words. Patients with right-sided defects are reported to have a significant decrease in reading speed (Kerkhoff 1999). Hemianopic alexia is standing apart of heterogeneous group of more common developmental dyslexia, where defective multi-sensory processing including visual and attention disorders is also involved (Hari and Renvall 2001).

Visual acuity is normal in patients with hemianopia except in cases where the optic tract is involved (Zihl 2011). Visual acuity impairment can occur due to the eye fixation to the healthy part of visual field out of a

defect. Therefore, clinical findings show that it may be reduced after brain lesions. This is caused by a combination of factors such as reduced contrast sensitivity, impaired visual search and inaccurate fixation.

Photopic and scotopic foveal adaption is a cortical ability to adapt continuously to an increasing or decreasing level of illumination in both color (day) and color blind (night) illumination ranges. This is another mechanism of adaptation apart from the retinal photochemical adaptation of rods and cones. Foveal adaptation deficits are reported in occipital lobe lesions mainly due to posterior cerebral artery infarction. It could also be caused by cerebral hypoxia or brain trauma. Patients with reduced photopic adaptation often complain about being blinded while leaving a room for outside. Reduced scotopic adaptation leads to night blindness in the dark and there is need of a higher illumination level during nighttime to illuminate near objects. Patients with a combined disorder can bear only a smaller range of illumination (Kerkhoff 2000).

Stereo vision defects can occur due to lesions in different brain areas. Posterior cerebral lesion, especially area V2 lesion, leads to a deficit in local stereopsis. (The deficit is local within a visual scene.) That means a deficit in extracting stereo disparity cues from a few visual elements (Julesz 2006). It is more frequent in right-sided lesions. Normal stereo vision or stereopsis denotes a depth sensation created by processing a stereo pair of two different images of an object as seen by both eyes. Global stereopsis (in contrast to local stereopsis) is the ability to extract a global form from many disparity signals. It is frequently affected due to temporal lesions. Stereo disparities are encoded in all association visual cortical areas. At the object, "Gestalt" level, neural coding of three-dimensional objects depth takes part in the parietal cortex. Normal visual space perception is a subjective three-dimensional perception of width, height and depth of objects and a scene.

All these particular visual disorders, together with their locations and clinical findings are listed in an order from low level visual information processing to higher level visual disorders in Table I. Visual information is processed in two main streams ("What" and "Where" pathways). Visual information leaves the striate cortex and travels to the temporal lobe (to the ventral stream, "What" pathway). This pathway is involved in object identification. The dorsal stream, "Where" pathway, terminates in the parietal lobe and processes

spatial information. Locations of all the defects reflect this general division of the secondary visual areas (Koch 2004). Impairments in face and object recognition together with the spatial defects are rare, because the corresponding capacities reside in the two separated streams. Similar tables for comparison can be found in Kerkhoff (2000) and in Zihl (2011, p. 27).

More often visual defects are associated with partial or full unawareness of the defect. The terminology of these phenomena is virtually simple, as all four combinations of visual discrimination and awareness are possible: gnosis as a normal condition, gnosis denoting the condition of awareness without discrimination, agnosia as discrimination without awareness and finally pure anosia (Zeki and Ffytche 1998). This introduces visual processing defects caused by defect in areas out of the visual pathway.

OTHER CONDITIONS ASSOCIATED WITH VISUAL IMPAIRMENTS

Visual space perception defects occur mostly due to lesions of parietal cortex typically in the right (non-dominant) hemisphere (Sakata et al. 1997). Similar defects can be also a part of the hemineglect syndrome. This syndrome, also called hemiagnosia, unilateral neglect, hemispatial neglect, spatial neglect, or simply neglect is a condition in which a deficit in attention to and awareness of one side of perceptual space is observed (Heilman et al. 1998). Space perception defects are also caused by bilateral lesions in the temporal and occipital lobe, by bilateral occlusion of the posterior cerebral artery, or by some other cause, for example by hypoxia, or encephalitis.

Blindsight is a well-documented ability of cortically blind to respond by motor visual tracking of a moving object without any subjective awareness of this ability (Humphrey and Weiskrantz 1967, Schmid et al. 2010). Some patients can be objectively diagnosed as being cortically blind and are not at least aware of their residual sight abilities of this kind (Wilimzig et al. 2008). As mentioned above, (in definitions of gnosis, gnosis, agnosia and anosia) there exist all possible combinations of visual perception and visually guided action, with and without awareness/consciousness, together with more subtle variants of patients' performance in tests tailored to their conditions (Zeki and Ffytche 1998). In normal conditions, many variants of attended and unattended perfor-

mance can be under voluntary control in psychophysical testing of control subjects. The example of the blindsight syndrome shows the possible division of higher visual processing into conscious and unconscious components (Koch 2004).

Visual agnosias are described in Zihl (2011, p. 185): “Visual agnosia is the inability to recognize, interpret, or comprehend the meaning of visual stimuli. This disorder is modality-specific, (because) objects can be recognized in the auditory or tactile modality.” Visual agnosias include various types of agnosia: object agnosia with a more general defect than face agnosia, known also as prosopagnosia, topographagnosia with a defect of visual orientation in an environment and pure alexia, inability to read. Prosopagnosia is associated with a lesion in the fusiform gyrus (Hegde and Van Essen 2000).

Balint’s syndrome is inability to perceive the visual field as a whole (simultan-agnosia), difficulty in fixating the eyes (ocular apraxia), and inability to move the hand to a specific object by using vision (optic ataxia).

Other functions of the sensory integration across modalities can be also affected due to stroke. One example is the binding of sound objects to visual objects presumably producing that sound (Kopco et al. 2009). Even though the exact mechanism of the binding is not known to date, particular forms of the neglect syndrome can be localized to specific cortical areas and connection fibers (see Corbetta et al. 2005). One working hypothesis of the binding problem states that the binding of perceptually connected objects and parts of one object is realized through rhythmic cortical activity within the gamma frequency band. The experimental physiology in monkeys studying mechanisms of binding and other neural mechanisms of visual associative processing have been a subject of review in this journal in past by Eckhorn and coauthors (2004) and therefore we refer to this article and move directly to the clinical aspects of the visual rehabilitation.

DEVELOPMENT OF THE VISUAL DEFECTS AND TREATMENT APPROACHES

Before we discuss any treatment approaches, it should be noted that in some cases vision can recover spontaneously. Recovery of partial visual impairment due to a stroke is fully developed usually within 48

hours. Approximately 10% of patients fully recover. Approximately 50% experience partial recovery. It depends on the localization of lesion and collateral vascular system. Any other prospect of spontaneous improvement in vision after 3 months of onset is futile. Recovery of vision after a traumatic lesion is more frequent. Large areas of visual field frequently recover, though with unstable function (Pambakian and Kennard 1997).

Three main approaches have been developed to treat hemianopia: (1) Optical aids, (2) substitution (visual strategies training) and (3) visual field restoration (rehabilitation addressing neural plasticity). The field of view can be expanded with optical aids using an intact visual field to see objects in an otherwise blind hemifield. Compensating techniques is an attempt to help with adaptation to the damage by using intact visual abilities. It may be the only method with proved positive results at the present time. Restorative training is aimed at retaining lost visual abilities. This last method is based on the hypothesis of neuronal plasticity. It is the most ambitious method, considering the prolonged training of a blind visual field. However, recent studies have not confirmed its initially claimed impact definitively.

Optical aids

Various optical aids have been developed to treat hemianopia to increase the view of the blind hemifield. These include special enhancements with prisms, mirrors, telescopes and closed circuit television monitors. Their main purpose is to (1) relocate the hemifield in the sight of patient or (2) to expand the visual field. The relocation in just one eye raises a lot of technical questions of how one visual field replaces the other, to what extent the oculomotor system will react with compensatory strabism, how this address the visual plasticity. These questions are discussed in the literature related to comensatory optical aids (Peli 2000, Ross et al. 2012). In any case, expanding the field using prism is an option worth the effort (Pambakian and Kennard 1997, Pambakian et al. 2005).

Binocular sector prisms involve their application in the hemianopic sides of both lenses. The application creates a relocation of view for a patient looking sideways through the prisms; however, it also generates scotoma in a straight gaze. Research on

one trial group with these prisms concluded with significant improvement in visual spatial tests under laboratory conditions; however, it failed in activities in daily life. Dolezal (1982) reported on a cortical adaptation to the condition with a chronic use of binocular glasses from a viewpoint of experimental psychology, yet the impracticalities of such glasses described therein outweigh their possible benefit. Expanding the field of view can be reached with a monocular sector prism. This prism, however, leads to central diplopia. This last optical aid mentioned here has been introduced into clinical practice in recent years by Peli (2000) and collaborators and tested successfully by Bowers and coworkers (2008). The other types of aids mentioned above have never been widely used because of their impractical qualities.

Requirements for optical aids are therefore: (1) expansion of view rather than relocation, (2) function within all gaze directions, (3) avoiding central (and creating peripheral) diplopia and (4) substitution for central and peripheral vision interplay. The optical aid designed by Peli (2000) is closest to these conditions.

Peli (2000, Fig. 1) has designed a monocular sector prism placed across the whole length of spectacle lens both above and under the pupil on the side of the hemianopia which expands the peripheral view in all lateral gazes. It creates peripheral diplopia, which is a natural condition in subjects with normal vision. It leads to isotropy in peripheral vision that is often seen as an adaptation strategy in patients with congenital homonymous hemianopia (Peli 2000). Patients with Peli's prisms reported improvement in their activities of daily life, avoiding obstacles and locating objects. From the time of the introduction of these prisms, several clinical studies have been conducted. For example, Bowers and colleagues (2008) have shown in a single group study of 43 patients with hemianopia that majority of the patients continue wearing the prisms even after one year. Ross and coauthors (2012) tested 8 patients for different visual phenomena caused by the prisms.

Optical aids and magnification software can serve patients with chronic low visual acuity. Patients with low photopic and scotopic adaptation might benefit from using darkened glasses to reduce glare. The various aids discussed here can also increase reading speed.

Substitution

Substitution refers to specialized training to improve natural adaptation strategies in patients with hemianopia. At the present time we must admit that rehabilitation techniques aimed at restoring the visual field are

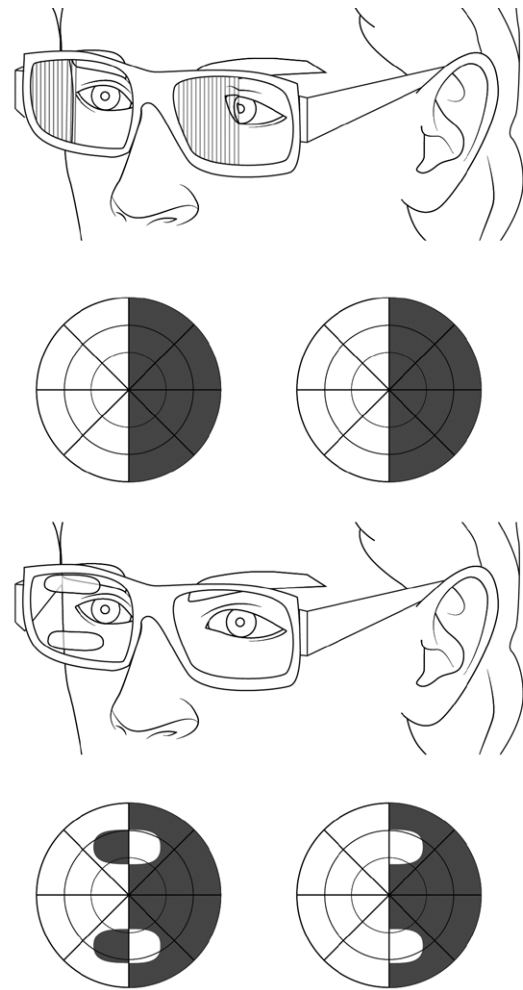


Fig. 1. Glasses with prisms used for homonymous hemianopia rehabilitation. Top: Glasses prescribed in past consist of binocular sector prisms (Fresnel prisms), same on both eyes, placed with base to the affected side. Visual field plots show schematic of (right side) scotoma in the homonymous hemianopia, Left: in left eye, Right: in binocular viewing. Bottom: Prisms designed by Peli (2000) are worn only on one (affected side) eye. They are restricted to the upper and lower peripheral fields only and extend across the majority of the width of the lens (for details see Peli 2000, Ross et al. 2012). Visual field plots show visual field changes with prism, Left: in prism-eye-only viewing and Right: in binocular viewing. This type of one-eye-only prism extends the binocular visual field in HHA.

limited. Compensatory eye movements explain the positive results of the early original visual field training studies (Zihl 1995). As described above, approximately 70% of patients with hemianopia tend to have disorganized visual exploration strategies. These are characterized by small amplitude saccades towards scotoma, frequent repetition of scan paths, increased search time, beginning with a visual search in the blind hemifield and a lack of larger saccades to overview an entire scene (Kerkhoff 1999). Visual exploration training can be useful for hemianopia patients to develop more effective visual exploration strategies. Implemented studies have confirmed that 10 to 25 training sessions in a 6-week period can be effective for hemianopia patients to adopt these strategies (Zihl 1995).

A study by Kerkhoff and others (1994) of 92 patients with hemianopia reported an expansion of visual search view from 10 to 30 deg (angular degrees) within 8 visual training sessions. Another study of 22 patients by the same authors describes the shortening of visual search times and improvement in activities of daily life after the training (Zihl 1995).

Computerized methods are used during the training. Patients are encouraged to enlarge their saccadic amplitudes towards the blind side by locating light stimuli in their scotoma. Later systematization of visual search is introduced. Patients carry out tasks requiring serial and parallel visual search (Koch 2004). Indication criteria for the training are pure occipital brain lesions without parietal or thalamic damage and with relative awareness of the scotoma. Negative factors are diffuse lesions, peripheral visual defect or oculomotor impairment (nystagmus, sight pareses, see Kerkhoff 1999). Some studies report better results with flickering stimuli, such as Raninen and coauthors (2007), yet in other studies the use of flicker remains controversial.

Reading impairment (hemianopic alexia) is frequently present in patients with para-central scotoma. In this condition, the length of the perceptual window for reading is reduced. As field restoration techniques are very limited, training is based on improvement of oculomotor reading mechanisms (Kerkhoff 1999). Treatment starts after a test of reading problems. It begins with reading text with short high frequency words that fit in the undamaged part of the perceptual window. Next follows reading of more complex words, searching for words in a text and a scanning reading

technique. Studies by Kerkhoff and colleagues (1994) and Zihl (1995) focusing on hemianopia training showed improvement in reading speed and accuracy. Patients with right hemianopia needed more training sessions to achieve a significant level of improvement.

Visual field restoration

Clinical trials attempting to restore deficient visual fields are based on the hypotheses of plasticity persisting in central nervous system through adulthood. Recent studies in humans, monkeys and other mammals showed that processes of axonal and dendritic sprouting, processes of unmasking alternative neocortical pathways, neurogenesis and other remodeling processes take place in adulthood and are dependent on experience and training (Balliet et al. 1985, Marsalek and Santamaria 1998, Macias 2008). These processes could therefore be supported and enhanced in specific rehabilitation. One particular theory assumes that neuronal plasticity should be higher in hierarchically higher cortical regions and lower in early visual areas. Restitution of the primary visual cortex should therefore be more limited than the restitution of the higher visual association areas of the parietal and temporal lobe (Brodthmann et al. 2009). Based on these hypotheses, restorative visual training aims at restoring the visual field inside the scotoma together with central filling in mechanisms (Koch 2004).

A research group led by Zihl and von Cramon (1979, see also Zihl 2011) tried to stimulate the border of scotoma with repetitive visual stimuli. Their results were optimistic in reporting an average visual field extension of 5 deg (angular degrees) and an even larger dramatic improvement in individual cases. However, any other research group failed to find any visual field increase in hemianopia patients (Balliet et al. 1985, Pollock et al. 2011).

Later research group of Kasten and Sabel (1995) revived visual field restitution training. They designed computer software called Visual Restitution Therapy (VRT). The software can be customized to meet the patient's individual hemianopia. Patients fixate a central point. At the same time visual stimuli are presented in the border between their blind and seeing fields. This supposedly activates residual neurons that are in the ischemic transition zone. This training can be conducted on a personal PC and requires 1 hour every day for 6 months. Visual field enlargement of 5

deg was reported in 95% of patients. That enlargement represents sufficient improvement to restore the perceptual window for reading.

However, these studies were criticized for their inaccurate measurement of the visual field increase (Pollock et al. 2011). The perimeter has been measured by the means of a VRT program which could not allow

firm eye fixation. Laser ophthalmoscopes and micro-perimeters were used to assure exact eye fixation in later study of Kasten and others (2008). Using this more accurate technique, no significant improvement in the visual field has been found in patients after VRT. The hypothesized visual field increase was probably created by eye movements.

Table I

Types of visual disorders		
Type of visual impairment	Clinical picture	Typical lesion location, lobe and/ or area
Homonymous hemianopia	The name arises from the observation that visual field defects are on the same side in both eyes.	Occipital lobe – primary visual area, also virtually all other parts of the central visual pathways, occipital, temporal, parietal lobes, lateral geniculate nucleus, and optical tract.
Visual acuity impairment	Frequently arises as a secondary impairment, due to the use of visual field remote from fovea.	Postchiasmatic lesions.
Eye movements and convergence defects	Altered convergence fusion. Reduced visual sustained attention in near work conditions. Feeling of eye strains. Reading difficulties. Reduced reading duration.	Occipital lobe, area V2, midbrain lesions, oculomotor pathways and nuclei.
Foveal adaption defect	Impairment of adaptation to both day and night, illumination alterations.	Occipital lobe, posterior thalamic lesions.
Hemianopic alexia	Reading impairment.	Occipital lobe, parafoveal regions.
Cortical blindness	Complete visual field loss, certain visual abilities can be retained, within a blindsight syndrome.	Bilateral damage to occipital lobe.
Stereo vision defects	Losses of either local object, or global space perception.	Occipital lobe, area V2, temporal lobe, parietal lobe.
Balint's syndrome	This syndrome is inability to perceive the visual field as a whole (simultanagnosia), difficulty in fixating the eyes (ocular apraxia), and inability to move the hand to a specific object by using vision (optic ataxia)	Disseminative, parieto-occipital lesions.
Apperceptive agnosia, associative agnosia and prosopagnosia	Visual apperceptive agnosia is inability to recognize objects, with retained ability to describe them. Associative agnosia is impairment in assigning meaning to a perceived stimulus. Prosopagnosia is a specific variant of object agnosia notable by inability to recognise faces.	Bilateral temporal and occipital areas. Prosopagnosia – fusiform gyrus of temporal lobe.
Blindsight	Ability to respond by motor visual tracking despite the overall visual loss in full cortical blindness.	Loci are same as in cortical blindness.

Visual disorders arising from stroke or other acquired brain damage or injury, arranged from low level visual disorders to higher order visual disorders.

A study by Roth and colleagues (2009) compared flicker stimulation training of the blind hemifield to exploratory saccade training. It reported a significant improvement in accuracy and speed of visual tasks performed by the group after saccade training. No improvement after flicker stimulation was reported. The visual field remained stable in both groups.

Repetitive training of binocular vision leads to a significant improvement in the contra-lateral to homonymous hemianopia training. Training of fusional amplitude using dichoptic methods lead to stereopsis and reading improvement. This may be considered as pure restorative training (Kerkhoff 2000).

Deficits in visual spatial perception due to parietal lobe lesions recover nearly completely after the training according to Kerkhoff's (2000) study. It is based on patients performing actions towards a specific object in space (assembling pieces together, pointing at location of objects).

Rehabilitation after a stroke has been a topic of numerous clinical studies. Also meta-studies have been conducted. They are based on extensive search in clinical literature and their aim is to compare the studies after their statistical parameters have been unified and made comparable. They identify relevant studies, according to whether they use randomized controlled trials and standardized statistical approaches and methodology. Based on the extent to which they conform to standards, the studies are typically classified into several classes and some of them are excluded. Afterwards, normalization is performed to make the studies comparable. Among these studies, 12 randomized clinical trials have been selected by Bowen and Lincoln (2007), 87 studies have been reviewed by Cicerone and coworkers (2005) and 13 studies have been processed by Pollock and others (2011). Table II summarizes reports on clinical studies collected here with participant numbers (or alternatively with a note identifying a meta-study). Pilot studies with $n=1$ or 2 patients and also physiological studies on healthy volunteers have not been included. The three meta-studies are included for comparison. Type of the study and methods used are summarized in the Table II. The target of visual function and the results of the studies are mentioned only in highly abbreviated description.

DISCUSSION OF EXPERIMENTAL STUDIES AND PROSPECTIVE REHABILITATION STRATEGIES

Even if it is admitted that VRT has no significant influence on visual fields, many patients claim subjective improvement in their activities of daily life after the training. This can be explained by an increase of attention in their blind hemifield stimulated by VRT light stimuli (Poggel et al. 2006). However, the improvement can be also caused by the behavioral improvement *per se* and by more frequent eye movement towards the blind field. Any ability to adopt new eye movement strategies assumes changes in brain regions connected to vision. The plasticity in connections can also explain changes in cortical activities of the blind hemifield observed during electro-physiological studies by visual evoked potentials, VEP. To date, the electro-physiological methods such as the VEP do not represent high spatial sensitivity diagnostic procedure in hemianopic patients due to its limited resolution in the localization of the brain disorder. In most cases VEPs show characteristic findings, where the side and extension of the lesion can be inferred to some extent from the VEP. Studying latencies, amplitudes and other objective electro-physiological aspects of visual stimulation is of a prospective diagnostic use, commonly discussed under the term of the event related potentials (ERP, see Hruby and Marsalek 2003).

Changes of both VEP and functional magnetic resonance imaging (fMRI) have been observed after the VRT procedures. A study based on 5 patients with chronic lesions after a stroke reported an improvement of VEP in 3 patients after the training (Julkunen et al. 2003).

Patients with a lesion in the V1 area with homonymous hemianopia are not consciously aware of stimuli presented in their blind field. Humprey and Weiskrantz (1967) were the first to notice that these subjects are capable of motor tracking and locating visual stimuli while at the same time not being aware of this capacity themselves. This phenomenon called blindsight has been briefly mentioned above. Numerous careful reproductions of these observations confirmed that the performance of these subjects is consistent and its success rate is much higher than merely a statistical difference. The subjects themselves believe that they are only guessing. Conscious vision is probably not needed in all aspects of visual motor behavior. It suggests the

Table II

Listing of clinical studies with methods and brief outcome summaries

Reference	Number of patients, types of defects	Study type	Methods	Conclusions related to rehabilitation
Balliet et al. 1985	12 patients with homonymous hemianopia	Single group study	Restitution training, following Zihl and von Cramon (1979)	“Visual field increases are not trainable.”
Bowen and Lincoln 2007	Total 306 subjects/ 12 studies of neglect patients	Meta-analysis	Meta-analysis	“Patients with neglect should continue to receive general stroke rehabilitation.”
Cicerone et al. 2005	Total 1801 subjects/ 47 studies	Systematic review	Systematic review of literature from 1998 through 2002	“Overall analysis reveals differential benefit of cognitive rehabilitation in 37 of 47 studies.”
Fujino et al. 1986	140 patients with homonymous hemianopia	Retrospective study	Diagnostic review	No recommendations regarding the rehabilitation.
Julkunen et al. 2003	5 stroke patients	Single group study	Visual field expansion computer training	“Visual field defects resulting from stroke can be partially restored even in the chronic phase.”
Kasten and Sabel 1995	11 patients	Non-randomized controlled study	Visual field expansion computer training	“The treatment group displayed a reliable enlargement of visual field size.”
Kerkhoff 1999	313 patients with visual field defect	Systematic review of own clinical data	Compensatory treatments, trainings and rehabilitation	„The amount of visual field recovered is limited to 5–12 degrees in 90% of these patients.”
Kerkhoff et al. 1994	22 patients with homonymous hemianopia	Chi square tests	Visual field expansion and saccadic training, as described in Kerkhoff et al. (1992)	„Training (...), improves performance in functional visual activities.“
Peli 2000	12 patients with homonymous hemianopia	Single group study	Visual field training with the use of glasses with prisms	“Most patients reported substantial improvement in function.”
Poggel et al. 2006	23 patients with post-geniculate brain lesions	Using several statistical tests and showing confidence level	Visual field expansion, with use of statistical tests, see Marques de Sa (2007)	„This effect (of attentional cueing) may be relevant for designing new strategies to permanently improve vision during neuropsychological rehabilitation.“

Table II (cont.)

Listing of clinical studies with methods and brief outcome summaries				
Reference	Number of patients, types of defects	Study type	Methods	Conclusions related to rehabilitation
Ptito et al. 1991	4 hemispher-ectomized patients	Single group study	Visual field diagnostics	No recommendations regarding the rehabilitation.
Reding and Potes 1988	95 patients with unilateral hemispheric stroke	Study of three groups using life table analysis	Sample cumulative analysis	No recommendations regarding the rehabilitation
Roth et al. 2009	28 hemianopic patients	Variance analysis, ANOVA	Saccadic training and flicker training	„Visual field size remained constant after both treatments.“
Zihl 1995	60 patients with homonymous hemianopia	Multivariate variance analysis, MANOVA	Perimeter training and flicker training	„After training, all patients showed a significant improvement in visual searching.“
Zihl and von Cramon 1979	12 patients with post-chiasmatic visual field defect	Single group study	Perimeter training and flicker training	„The improvement was restricted to the training period-no spontaneous recovery was observed between or after the periods of training.“

Table lists number (*n*) and type of patients, types of studies, methods used and results of studies

existence of extra-striate visual-motor pathways, whereby information might travel through LGN directly to higher extra-striate cortical areas (Weiskrantz et al. 1995). Such visual capacities might be also utilized in the future processes of neuro-visual rehabilitation.

Another phenomenon is based on the gaze dependent modulation of neuronal activity. It has been demonstrated that activities of certain cortical areas including V1, V2, V3 and V5/MT are modulated by the orbital position of an eye in an alert monkey (Bradley et al. 1998). Nadeau and coauthors (1997) described a study of one patient's transitional improvement of scotoma by turning her head towards the side opposite to the lesion while fixating her gaze straight ahead. The patient with a lesion in the right occipital lobe and left hemianopia reported the vanishing of his scotoma while turning his head to the left. The exact mechanism of the cortical filling in and analogous processes is not known to date; however, existence of such phenom-

ena assumes neuronal activity modulation dependent on gaze direction.

According to a neuro-imaging study by Henriksson and others (2007), visual training of a blind hemifield leads to changes in the intact hemifield. In the study, a patient with a two-year history of hemianopia was trained with visual stimulation aimed to his blind hemifield. The functional MRI results showed representation of the blind hemifield in ipsi-lateral intact visual cortical areas, specifically in V5/MT. This raises the question whether cortical ipsi-lateral change in the visual cortex can be found in patients with hemianopia independent of the visual stimulation history.

Spontaneous reorganization in the visual system after its injury is still not sufficiently understood to date. A study of plasticity in the visual cortex by Brodtmann and colleagues (2009) indicates that the dorsal stream may play the key role in cortical reorganization after striate cortex injury. Brodtmann and coworkers (2009) support their view by observation that "dorsal extra-striate neurons (specifically in area

V5/MT) retain visual responsiveness in the presence of deactivated V1 (striate cortex), whereas the ventral extra-striate regions seem more reliant on intact striate function.”

Our primary aim was to review biological, unique aspects of visual restoration and rehabilitation. The clinical studies reviewed use variable degree of statistical approaches to assess how the quality of patients’ lives changes and how could be possibly improved.

In their systematic review, Cicerone and coauthors (2005) summarize recommendations of how to properly conduct a clinical study and what conclusions for the cognitive rehabilitation can be drawn from properly documented studies. The simplest variant of such a hypothetical study should compare two groups, for example with and without visual defects, or with and without rehabilitation. Also erudite statistical methods should be used, as is discussed in the last paragraph of this review. In the meta-studies discussed here, some of the papers cited are scrutinized regarding whether their methodology and statistics are not biased. Subsequently, a meta-statistics is produced reporting virtually no positive outcome and prospect for the patients (Bowen and Lincoln 2007, Pollock et al. 2011).

Not all the primary studies included in Table II used the clinical randomized trial approach, in which the obvious two groups to compare would be with and without specific rehabilitation. Some of the studies obtained significant results using standardized statistical tests. An alternative method would be to use Bayesian (that means conditioned) statistics to sort out among the causes which are difficult to homogenize. Several studies used variants of analyses of variance (ANOVA), which are amongst the simplest statistical methods of comparison, assumed the methods of diagnostic and therapeutic procedures are standardized. A review of statistical methods suitable for clinical trials can be found in a book by Friedman and colleagues (1998). Without the statistical software used by professional statisticians, who should also spend some time understanding the factual, fundamental, and not only technical aspects of the studies, application of the statistical methods would be hardly possible. The review of the statistical software can be found in a book by Marques de Sa (2007). In the neighboring research fields of psychology, psychophysics and other cognitive sciences, one can find ready to use recipes and also critical advice of how to design clinical studies even

with low numbers of patient subject to adhere to reproducibility and standardization. As mentioned above, Bayesian methods should be applied more frequently due to the higher variability of medical data. One example of all is a collection of examples of Bayesian method applications in Wagenmakers (2007).

CONCLUSIONS

Vision is based on a complex system involving cooperation of different cortical visual areas. Due to lesions of particular areas, different impairments can occur. Visual hemifield defect is a common impairment resulting in a well-defined disability. Various treatment approaches have been tested to rehabilitate lost visual abilities. It has been found that training of eye movements including saccades can bring positive results although we are not aware to date of a control study indicating this with a rigorous statistical background. Restorative rehabilitation programs addressing neuronal plasticity have not so far shown effects in larger than small perimeter improvement due the use of present methods. Recent studies showing neuronal cortical plasticity in adulthood may promise future development in vision rehabilitation. At the present time the effect of visual restorative training is limited. Yet most studies discussed in this review underscore the effects of cognitive rehabilitation and further needs for our deeper understanding of the underlying physiological processes.

ACKNOWLEDGMENTS

Supported by the Czech Ministry of Health program NT 11532 „Medical Technology Assessment“ at the Czech Technical University and by the Czech Ministry of Industry and Trade project MPO FR-T13/ 869 at the Charles University in Prague. We thank the two anonymous reviewers for helpful comments, Eli Peli and Jiri Vrana for discussions, Tomas Mika and Helen Nathan for copy-editing. Special thanks are due to Jiri Kofranek and Veronika Sykorova for technical assistance.

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