International meeting of the French society of neurology 2012

Rehabilitation of damage to the visual brain

Rédéducation après lésion du cerveau visuel

S. Ajina\textsuperscript{a,b,*}, C. Kennard\textsuperscript{b}

\textsuperscript{a} FMRIB Centre, University of Oxford, John Radcliffe Hospital, Headley Way, Oxford OX3 9DU, UK
\textsuperscript{b} Nuffield Department of Clinical Neurosciences, 6th floor West Wing, John Radcliffe Hospital, Headley Way, Oxford OX3 9DU, UK

INFO ARTICLE

Article history:
Received 12 July 2012
Accepted 23 July 2012
Published online 13 September 2012

Keywords:
Homonymous hemianopia
Rehabilitation
Eye movements
Neuroplasticity
Stroke

ABSTRACT

Homonymous visual field loss is a common consequence of stroke and traumatic brain injury. It is associated with an adverse functional prognosis and has implications on day-to-day activities such as driving, reading, and safe navigation. Early recovery is expected in around half of cases, and may be associated with a return in V1 activity. In stable disease, recovery is unlikely beyond 3 and certainly 6 months. Rehabilitative approaches generally target three main areas, encompassing a range of techniques with variable success: visual aids aim to expand or relocate the affected visual field; eye movement training builds upon compensatory strategies to improve explorative saccades; visual field restitution aims to improve visual processing within the damaged field itself. All these approaches seem to offer modest improvements with repeated practice, with none clearly superior to the rest. However, a number of areas are demonstrating particular promise currently, including simple web-based training initiatives, and work on neuroimaging and learning. The research interest in this area is encouraging, and it is to be hoped that future trials can better untangle and control for the number of complicated confounds, so that we will be in a much better position to evaluate and select the most appropriate therapy for patients.

© 2012 Elsevier Masson SAS. All rights reserved.

RÉSUMÉ

Une perte du champ visuel homonyme est fréquente après un trauma crânien. Elle est associée à un pronostic visuel défavorable avec des implications pour la vie de tous les jours comme la conduite, la lecture et la navigation en sécurité. Pour la moitié des cas, on peut espérer une récupération avec retour d’un niveau d’activité V1. Pour une maladie stabilisée, la récupération est peu probable après trois mois et à six mois la perte est irréversible. L’approche rééducative a trois objectifs, avec des techniques et des tâches de succès variables: aides visuelles afin d’élargir ou relocaliser le champ visuel affecté; entraînement des mouvements oculaires à partir des stratégies compensatoires afin d’améliorer les saccades exploratrices; restitution du champ visuel pour améliorer le traitement visuel au sein même du champ endommagé. Lorsqu’elles sont répétées, ces différentes approches semblent permettre des améliorations modestes, sans avoir un effet clairement supérieur au repos. Cependant un certain nombre d’interventions, dont

* Corresponding author. FMRIB Centre, University of Oxford, John Radcliffe Hospital, Headley Way, Oxford OX3 9DU, UK.
E-mail address: sara.ajina@ndcn.ox.ac.uk (S. Ajina).

0035-3787/$ – see front matter © 2012 Elsevier Masson SAS. All rights reserved.
1. Introduction

It is widely recognised that stroke is the most frequent cause of homonymous visual field defects (HVFD), with an estimation that between 40-86% of isolated HVFD are caused by posterior circulation ischaemia (Smith, 1962; Fujino et al., 1986; Trobe et al., 1973; Zhang et al., 2006a). Other common aetiologies include traumatic brain injury, tumour (each < 15%), and less frequently brain surgery and demyelination (Zhang et al., 2006a), with causative lesions most commonly in the occipital lobes (45%) and optic radiations (32.2%).

In the UK alone, there are approximately 150,000 new cases of stroke a year, with between 8-26% left with persistent hemianopia (Gilhotra et al., 2002; Gray et al., 1989), which may be closer to 30% acutely (Haerer, 1973). Figures vary quite extensively, however, with variable population demographics, measurement techniques, and reporting biases.

Stroke is also considered to be the most common cause of disability in adults (Hankey, 1999), and is likely to increase in the future with an aging population. Importantly, HVFDs in such patients are associated with an adverse functional prognosis, including likelihood of discharge home (Schlegel et al., 2003), mobility, and survival (Haerer, 1973; Gray et al., 1989). Functionally, HVFD may impair day-to-day activities including driving, reading and obstacle avoidance, which can cause reduced participation in social activities and quality of life (Trauzettel-Klosinski, 2011). At the other end of the spectrum, it is also worth noting that HVFDs often go unreported, perhaps overlooked or under-prioritised by clinicians, or because patients learn to compensate for their deficit (Zhang et al., 2006a; Gilhotra et al., 2002).

2. Natural history

2.1 Early recovery

There has been some debate about how quickly recovery of HVFD takes place after brain injury, with reports varying from two weeks (Gray et al., 1989) to one year (Trauzettel-Klosinski, 2005). Zhang et al. (2006b) reviewed the medical records of 254 consecutive patients with HH over a 15-year period, and performed a regression analysis to determine probability of improvement (reduction in VFD more than 10° horizontally or 15° vertically) as a function of time after injury. Although this was not a prospective study and follow-up varied between patients, they suggested that at 1 month there was a 50-60% chance of recovery, which fell to around 20% at 6 months. They continued to see a similar improvement beyond 6 months, although changes were attributed to improvement in the underlying disease or cognitive ability to undergo testing.

No cases with stable underlying brain disease such as stroke continued to improve beyond 6 months, with most occurring within 3 months.

These results are consistent with prospective stroke studies (Tiel and Kolmel, 1991; Gray et al., 1989) including Celebisoy et al. (2011) who used automated perimetry to document recovery in 32 patients with occipital lobe infarct at 6 months. They found improvement in the peripheral zones of the lower quadrants, with worst prognosis associated with striate cortex involvement and greater lesion size.

More recently, two studies have utilised brain imaging to monitor the neural changes over this “recovery period”. Raposo et al. (2011) observed eight patients with posterior cerebral artery stroke using fMRI at three time points: within 30 days of stroke, then at 1 and 3 months later. Visual stimuli targeted motion and colour separately to each hemisphere. When compared to control stimuli, colour in the blind field only activated V4 by the third time-point (contralaterally), at which time there was also activation of ipsilesional V1 compared to rest. In contrast, both moving and static checkerboards seemed to activate contralateral V5 at the first two time-points, then ipsilesional V5 at 3 months. Behaviorally, half of subjects at the start could already identify direction of motion from a choice of four, whilst only two correctly identified colour over chance. Over time, this improved for all patients such that average success was around 70% for colour, and 85% for motion. The reason for a lack of true motion effect (moving vs. static stimulation) on fMRI is unclear, and does not correspond with the behavioural findings. The authors suggest it may be due to the small stimulus size, however the overall findings are interesting and encourage further work to be undertaken. Polonara et al. (2011) only investigated recovery in one individual, but also employed DTI. They also found that recovery in the acute phase (although slightly earlier, at 1 month post-stroke) is associated with a return in V1 activation, together with a restoration of tract integrity in the ipsilesional optic radiations.

2.2 Residual function and spontaneous functional adaptation

In the chronic phase after injury, it appears that HVFDs become more static, and it is this stage, which is most difficult to treat. Numerous studies have suggested that during this chronic phase, patients may adopt compensatory eye movement strategies to assist with their deficit (Pambakian et al., 2000; Zihl, 1995). Whilst healthy controls fixate mostly at the centre of a patterned image, hemianopes paradoxically concentrate on the blind hemifield, thus shifting it into view (Ishiai et al., 1987). This has been shown in a number of different tasks such as viewing images of real scenes (Pambakian et al., 2000), and whilst assembling wooden
models (Martin et al., 2007) – although in the latter this was not seen in every participant.

Hemianopes may also adopt strategies for refixating between targets (Meienberg et al., 1981), for example performing a number of increasing hypometric saccades (stairstep) before finding the target or overshooting by a few degrees together with a short, corrective saccade to foveate the target. These mechanisms, however, are not ideal as an increased number of refixations, together with somewhat disorganised scanning leads to longer search times and possible omission of relevant objects (Zihl, 1995). More recent research suggests that which gaze strategies are employed vary according to lesion site, and as a function of task demand (Hardiess et al., 2010).

3. Blindsight

As well as compensation to simply shift the field of view to the unaffected side, some work has suggested that saccadic eye movements (Barbur et al., 1988) and obstacle avoidance (Striemer et al., 2009) can be influenced by unseen stimulation within the blind hemifield.

“Blindsight” refers to the observation that certain stimuli within the blind hemifield can undergo processing and influence behaviour despite the individual often being completely unaware of their presence (Weiskrantz et al., 1974; Weiskrantz, 1987). It suggests that even within the chronic phase when standard perimetry demonstrates a HVFD, certain aspects of visual abilities including motion, colour, and contrast detection are retained, with the degree of subjective awareness varying considerably across different manipulations (Weiskrantz, 2004). This was initially attributed to surviving “islands” of V1 (Fendrich et al., 1992), however there is now substantial evidence to the contrary (Stoerig et al., 1998). Indeed, stimuli with specific spatio-temporal properties are particularly effective at eliciting blindsight, with this ability perhaps even present in the majority of patients with V1 damage (Sahraie et al., 2008).

Two main pathways are reputed to subserve blindsight, with evidence existing for both. One involves subcortical projections from the retina to superior colliculus and pulvinar, which then project to other visual cortical areas bypassing the damaged V1. The other projects directly from surviving LGN neurons to extrastriate cortex.

Several studies demonstrate activation of the superior colliculus during VHFD stimulation (Barbur et al., 1993, 1998; Sahraie et al., 1997). Similarly, primate studies involving selective destruction of V1 and superior colliculus show manual and saccadic localisation become severely disturbed (Feinberg et al., 1978). In contrast, more recent work shows a clear causal role for LGN pathways. Non-human primates can detect targets presented within a scotoma caused by V1 damage, associated with contralateral extrastriate fMRI response (Schmid et al., 2010). Chemical inactivation of the LGN then abolishes virtually all activity, which returns once inactivation is reversed.

Although these results lend support for alternate pathways mediating blindsight, they do not explain whether activation comes from intact residual pathways, or some innate ability of the human cortex to reorganise following injury. This remains a controversial discussion, with important implications on treatment.

4. Plasticity in the visual system?

Despite certain limitations, diffusion-weighted MRI offers a unique method to explore non-invasively the organization of white matter in the living human brain. Two important studies have employed this technique with probabilistic tractography following V1 damage. Leh et al. (2006) looked at four patients with previous hemispherectomy for intractable epilepsy. They subdivided patients into those with and without indirect blindsight, and suggested that those with blindsight showed unique contralateral connections from superior colliculus to visual, parietal, and prefrontal areas as well as to the posterior part of the internal capsule, which were not present in the alternate group or healthy controls.

Bridge et al. (2008) used similar techniques in a well-described blindsight patient, GY. They showed that normal pathways bypassing V1 from LGN to extrastriate cortex remain intact. They also demonstrated two new connections absent in healthy controls, from contralesional LGN to ipsilesional extrastriate cortex, and extrastriate cortico-cortical connections bilaterally. Both studies should be interpreted with the caveat that the original brain damage occurred early in life, when it is suggested that plasticity is more viable. However, recovery of motor function after stroke is often attributed to cerebral reorganisation (Ward et al., 2003), and other examples of plasticity following visual pathway damage in adulthood have been reported (Dilks et al., 2007; Henriksson et al., 2007; Raninen et al., 2007).

5. Rehabilitative approaches

Irrespective of the presence or absence of unconscious processing, hemianopic patients remain significantly impaired in day-to-day life. Here we detail the rehabilitative approaches designed to offer both practical improvements to the sighted field, as well as techniques designed to improve vision with training. There are currently three main approaches, incorporating a number of techniques of varying popularity and evidence. These include the use of visual aids, a number of eye movement training techniques, and attempts to restore the deficit itself, so-called visual field restitution (VRT).

5.1. Optical aids

A number of optical devices can be used to improve perception of the visual scene by expanding or relocating the visual field. This is most commonly achieved through use of prisms, which are fitted onto spectacles on the side of the field loss, and reflect images onto the functional side of the retina. Other devices used in the past include mirrors that can be partially reflecting, or dichroic, causing a disparity in colour between the reflected and transmitted images (Cohen, 1993).

Prisms can be fitted binocularly or monocularly, with the former providing only visual field relocation and not expansion, and the latter providing field expansion only when gaze
is directed into the prism. This can be a problem if the prism is restricted to the hemianopic field, but can be resolved by stretching the prism out across the whole lens. Another problem can be central diplopia, which is often disorientating to the patient.

To preserve vision and prevent central diplopia, monocular prisms can be fitted separately to the upper and lower parts of the lens. Peli (2000) tested this technique using a 40 dioptre prism in 12 patients with HVFD. In all but one patient they found a field expansion of 20°, with subjective improvement in nine. A further multi-centre evaluation of peripheral prism glasses was carried out by Bowers et al. (2008). They found that 47% patients still wore the prism glasses more than 8 hours a day after 12 months, finding subjective benefit in obstacle avoidance.

5.2 Eye movement training

5.2.1 Visual search

The idea that explorative eye movements can be enhanced to provide an improvement in visual perception and obstacle avoidance has been around for decades, although it has received somewhat of a resurgence in the last few years. The general principle is based upon the earlier description that visual search in these patients is often unsystematic and time-consuming, thus reducing the ability to appreciate the visual scene as a whole (Zihl, 1995). Explorative training tries to manipulate the compensatory strategies seen in patients, to an advantageous outcome.

In earlier work, subjects were trained to make large saccadic eye movements to targets in the blind field using sizeable Tubingen perimeters. Findings were encouraging and suggested that a period of training such as 8–23 half hour sessions were enough to generate altered search strategies (Zihl, 1995). Even “blindsight”-guided training, using 100ms targets, appeared to show an improvement in the ability to detect and localize stimuli (Zihl and Von Cramon, 1980). It was, however, difficult to see how this would translate into real-world effects.

Pambakian et al. (2004) adapted the technique by offering a portable, low cost method for training visual search. They recorded more functional outcomes including completion of activities of daily living (ADL), and a visual disorder questionnaire. Seventy-six percent of patients had a significant improvement in visual search response times, which persisted for 1 month post-training and was not attributable to practice. Three patients became slower for both blind and sighted fields, although this appeared to be a trade-off for a dramatic improvement in error rate. Functionally, there was a small overall improvement in ADL times and self-reported performance in crossing the road and finding objects. Another more recent technique that can be carried out at home via a computer-based ramp-step search paradigm also appears promising, with a significant improvement in search reaction times after only one training period (Jacquin-Courtois et al., 2012).

Nelles et al. (2001) provided patients with 4 weeks of two daily 30-minutes sessions practicing visual search, and showed similar improvements lasting 8 months after training. They went on to use functional imaging to investigate whether there was any change in brain activation (Nelles et al., 2009, 2010), in the same way that motor training in the healthy adult is associated with a change in BOLD signal (Karni et al., 1995).

Unfortunately, training was started only 8 weeks post-stroke, thus introducing the significant confound of natural progression, as well as the fact that patients were undergoing general post-stroke rehabilitation at the time! Nevertheless, they found an increase in contralesional extrastriate activity during hemifield stimulation in the scans taken 4 weeks after training was complete, which was not present in controls. They also showed increased ipsilesional extrastriate activation during visually-guided saccades. It is interesting that the most notable changes occurred some time after training was complete. This could certainly represent a gradual evolution of the learning effect (Karni et al., 1995). It would, however, be important to rule out other factors to clarify these results.

There are very few randomised controlled trials within this area, with one comparing digit-search to flicker training on explorative saccadic behaviour (Roth et al., 2009). They concluded that search training was superior on various measures including reaction times and number of fixations in the blind versus sighted hemifield. This was a positive step as patients were recruited in the chronic phase and were randomly allocated to treatment groups. However, it did not address the role of attention on training effect, which is an important point to consider.

Lane et al. (2010) compared a standard exploratory training paradigm to attentional training, although in the former they did not provide instructions for how participants should move their eyes (generally this is specified in other studies). In an attempt to make both tasks as similar as possible, attentional training also involved “search” for targets within 1° of fixation. Results were mixed and dependent upon which search test was used to measure outcome. In a “find the number” test within the trained field-of-view, there was significant improvement in reaction times after exploratory training, but none after attentional training. In the visuomotor test, both showed improvement, even if attentional training had already been given. For the most difficult “projected search” test (outside the trained field), both tasks caused improvement, but there was no additional gain when exploratory training followed attentional training. These results highlight the importance of attention in training, although further work needs to be done to fully understand its contribution to rehabilitation trials to date.

5.2.2 Alexia & reading

Both Lane et al. (2010) and Roth et al. (2009) amongst others have also shown that visual search training does not translate to improve reading speed. Indeed, search strategies do not address the small, step-wise eye scanning or specific part of the visual field that is required to read left-to-right text (Zihl, 1995; Schuett et al., 2008). Hemianopic alexia is an important consequence of hemianopia and can be particularly debilitating. It is also receiving particular attention at the moment.

In research substantiating the above views, Schuett et al. (2012) performed the first cross-over rehabilitation study to look for transfer of training-related improvements between reading and visual exploration training. Reading training required patients to read a presented word out loud, before
rapide et de chaînes de mots successives, selon le type de tâche à réaliser.

Lors de la lecture, la supragnathie est un problème majeur, car elle peut entraîner des lacunes de perception visuelle. L’utilisation de méthodes de rééducation pour supprimer ou réduire la supragnathie est donc une approche importante.

Rééducation de la vision de champ restituée (VRT)

La VRT est un terme générique utilisé pour décrire une variété de méthodes de rééducation ciblant différents types de défauts visuels. Les méthodes de VRT visent à restaurer ou à améliorer la perception visuelle dans des zones du champ visuel qui ont été endommagées ou perdues.

La VRT a été proposée pour la première fois dans les années 1980 par Zihl et von Cramon pour traiter les patients avec des lacunes visuelles. Ces méthodes ont été progressivement adaptées et perfectionnées pour répondre aux besoins des patients souffrant de défauts visuels complexes.

La VRT est généralement utilisée après un traumatisme cérébral ou un accident vasculaire cérébral, mais elle peut également être utilisée pour d'autres types de défauts visuels. Les méthodes de VRT sont souvent combinées avec d'autres formes de rééducation ciblant d'autres aspects de la fonction visuelle.

5.3. Visual field restitution (VRT)

5.3.1. Border-field VRT

La VRT est souvent utilisée pour traiter les patients souffrant de lacunes visuelles unilatérales, tels que ceux dont les yeux sont endommagés d’un côté. La VRT vise à restaurer ou à améliorer la perception visuelle dans la zone du champ visuel en regard de l’endommagement.

Une méthode de VRT populaire est l’utilisation de stimulations visuelles répétées dans le champ visuel restant (Plant, 2005). Cette méthode vise à entraîner le cerveau à réaliser des saccades visuelles dans les zones du champ visuel restant, ce qui peut améliorer la perception visuelle dans ces zones.

5.3.2. Blindsight VRT and perceptual learning

Alors que la VRT est souvent utilisée pour traitement des patients souffrant de lacunes visuelles unilatérales, elle peut également être utilisée pour traiter des patients souffrant de lacunes visuelles bilatérales. Les méthodes de VRT sont souvent combinées avec d’autres formes de rééducation ciblant d’autres aspects de la fonction visuelle.

La VRT est une méthode de rééducation qui a montré des résultats prometteurs pour la restauration ou l’amélioration de la perception visuelle chez les patients souffrant de défauts visuels complexes. Elle peut être utilisée indépendamment ou conjointement avec d’autres formes de rééducation ciblant d’autres aspects de la fonction visuelle.
Whether one can expect a functionally useful improvement in conscious vision will need to be determined.

Huxlin et al. (2009) used perceptual learning to train patients to discriminate global direction of moving dots in a random dot kinetogram (RDK) via a staircase learning procedure. After training for several thousand trials, patients became able to correctly discriminate direction for coherent dots, and also attain normal direction integration thresholds. Interestingly, whilst not specifically trained for, there is also an improvement in contrast thresholds for direction, measured using drifting sine-wave gratings. This is important because it shows that perceptual relearning of motion direction is possible and can be translated to stimuli distinct to those used in training (Das and Huxlin, 2010). All these studies, however, demand very long training periods with retinotopic-specific learning taking considerably longer than might be expected for perceptual learning in healthy subjects. It is therefore important to understand the mechanisms behind these findings, and a number of recent neuroimaging studies have offered some early insight into these.

6. Functional imaging of rehabilitation

Henriksson et al. (2007) investigated the effects of training on changes in fMRI and MEG activation. Training involved a difficult detection task of flickering discs and recognition of flickering letters twice a week over 2 years. They found that after training, stimulation of the blind hemisphere with a large reversing checkerboard activated contralesional V5, as well as V3a, and to a lesser extent V3, dorsal V2, and a border region between V1 and V2d. Although only MEG and not fMRI were measured before training, no initial MEG response was found. Behaviourally, two patients improved on flicker detection and subjective reports of real-world navigation, but made no gains on static perimetry (Raninen et al., 2007), highlighting again the specific nature of improvements.

As discussed earlier, Nelles et al. used fMRI to study the effects of eye movement training. In the study looking at hemifield stimulation (Nelles et al., 2010), they also used a reversing checkerboard to invoke visual activation, this time recording changes pre- and post-training. They found that even at baseline, there was significant activation bilaterally in extrastriate areas, strongest in the contralesional hemisphere, which increased further 4 weeks after training was complete. This is interesting but highlights the discrepancies still present, as other studies have suggested stimulation of the blind hemifield (without training) activates ipsilesional extrastriate cortex (Goebel et al., 2001).

In a retinotopy fMRI study pre- and post-VRT, Raemaekers et al. (2011) find early visual cortex receptive field changes, but suggest that they can only account for small, local visual field increases, and are insufficient to account for the larger visual field improvements seen in some of their patients. Even in the healthy state, to what extent perceptual learning relies on local changes in receptive fields of neurons in early visual cortex remains strongly disputed (Bao et al., 2010).

Overall the evidence is mixed, but proponents suggest there is growing support for some sort of plasticity-driven process employing either ipsi- or bilateral intact visual cortex.

We have already discussed the possibility of altered cortico-cortical, thalamocortical, or subcortical pathways in certain patients with blindsight (Leh et al., 2006, Bridge et al., 2008). It may be possible therefore for similar pathways to become recruited during training. Whilst far from clear, this avenue is certainly generating enthusiasm for future research (Stoerig, 2008).

7. Conclusion

There are a number of rehabilitative techniques currently available, most of which offer specific and non-transferrable improvements in vision. No treatments to date claim to be able to fully restore vision to the damaged hemifield, although this remains the goal for restitution and plasticity-based research groups. The approach in other laboratories remains more pragmatic, focusing on the most effective ways to compensate for the deficit rather than looking for recovery. At this stage, it appears that separate, specific therapies would need to be employed to maximise improvements in vision. As most therapies require repetitive training over a prolonged period, this would be extremely time-consuming for patients and would be very difficult for them to adhere to. Ideally we would see a more integrated, single therapy that could provide the best outcome in terms of visual search, field size and patient experience. It is also important, as well as improving the quality of future studies through larger sample size and better control for attention, placebo-effect, and disparate outcome measures, to look closer at the mechanisms involved in recovery and plasticity after visual cortex damage. This may allow better focus for future research, and creation of more effective options for rehabilitation.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Acknowledgements

SA is supported by the Wellcome Trust (WT096001/Z/11/Z) and CK by the NIHR Oxford Biomedical Research Centre.

References


Kasten E, Strasburger H, Sabel BA. Programs for diagnosis and therapy of visual field deficits in vision rehabilitation. Spat Vis 1997;10:499–503.


