A new paradigm emerges: visual field defects after optic nerve or brain injury are partially reversible. Using high-resolution visual field tests, areas of residual vision can be identified which are characterized by impaired vision (relative defect) with some residual capacities. By repetitively stimulating these partially damaged areas with daily computer-based visual restitution training it is now possible to enlarge the visual field. Average border shifts of 5° (range, 0 to 20°) have been found in clinical trials, and training is effective even when started years after the injury. Visual restitution training is useful for the treatment of patients with stroke, head injury, or partial optic nerve damage, as long as the patient presents some residual vision. The improved vision is maintained in most patients after training is discontinued. Brain plasticity is likely to provide the substrate for restoration of vision, opening new opportunities to treat partial blindness, which has been considered irreversible. Curr Opin Ophthalmol 2000, 11:430–436 © 2000 Lippincott Williams & Wilkins, Inc.

Patients suffering from visual deficits caused by optic nerve or postchiasmatic injury commonly experience many limitations in their activities of daily living, such as reading problems, ignoring objects or people, and bumping into things. The generally accepted paradigm that nothing can be done about this leaves little hope for the patients, because once vision is lost, restoration is considered to be impossible.

Most textbooks describe visual field impairments by subdividing the field into intact (white) and blind (black) regions, but areas of residual vision exist that are often ignored. Although it is common clinical practice that patients may have variable or uncertain performance in certain regions of the visual field, such areas of relative defect are considered to be of no therapeutic value. The irreversibility paradigm was, of course, a logical consequence of Hubel and Wiesel's [1–3] discovery that neurons in the visual cortex are highly specialized, and, consequently, much of vision research has focused on further characterizing the specialized neuronal organization (retinotopy, functional specializations of various kinds). Thus, considering the assumption that the cellular organization consists of highly specialized elements, there was no apparent hope, and therefore no need, to attempt visual rehabilitation in patients with permanent blindness.

In recent years, however, a paradigm shift has taken place. Through high-resolution diagnosis, areas of residual vision now can be identified where training visual functions help to restore some of the lost vision. These discoveries fit well with a already sizeable and continuously growing body of evidence that the visual system possesses a high degree of plasticity. The term plasticity [4] describes the ability of the brain to adapt to various experiential and structural changes (such as lesions), as seen by the following evidence:

1. After lesions of the central nervous system, animals and humans can recover visual functions considerably well, even without therapeutic intervention [5].
2. Visual receptive fields can shift their location and increase in size following deafferentation [5–7] and under different conditions of alertness [8].
3. Cells surviving an area of partial injury undergo massive molecular and cellular changes that help to overcome the loss of vision [9].
4. Practicing visual tasks in normal monkeys and humans significantly improve visual discrimination performance in normal subjects [10].
(5) Through a complex neuronal network of lateral interactions and feedback connections, visual information can reach many areas of the brain through alternative routes, thus providing a structural basis of reorganization and plasticity [11].

Therefore, the visual system, previously considered to be hard-wired, possesses a remarkable plasticity to adapt to short-term as well as long-term demands [5–22,23•].

**Diagnosis of residual vision**

Areas of residual vision are those sectors of the visual field that do not function normally but in which some visual capacities have survived the injury. These areas are not absolutely blind, and are usually referred to areas of relative defect. However, just as a glass of water may be viewed as half-full or half-empty, the term relative defect emphasizes the deficit, whereas the term residual vision stresses the residual capacities that provide an structural substrate for restoration [23•,24,25]. As Figure 1 shows, residual vision in a given patient depends both on the nature, and the relative amount, of neuronal sparing in the blind field [24], which varies considerably between patients. The most important determinant of how much residual vision remains depends on the relative number of fibers surviving the damage (Fig. 2). If only very few fibers survive, blindsight may occur, whereas a larger degree of neuronal sparing may allow conscious, although unreliable, responses (Fig. 3).

Blindsight describes the situation in which some, though nonconscious, vision exists in the otherwise blind field [20,26–30]. When visual stimuli are presented in such patients, they report that they see nothing, but when forced to guess, they respond well above chance. It has long been proposed [26] that blindsight is mediated by uninjured extra-striate pathways. However, the presence of blindsight responses in the blind regions of many optic nerve patients [30] and in isolated islands of postchiasmatic patients [20] indicates that a few spared fibers, rather than an intact, alternative pathway provide the basis for blindsight. As Figure 3 suggests, blindsight might comprise a phenomenon of residual function at a lower level of the neuronal activity spectrum.

In contrast to blindsight, we [24] use the term residual vision to indicate the presence of unreliable, though conscious, visual responses. There are just as many ways to document residual vision in the human visual system as there are ways to test normal vision. Areas of residual vision show numerous errors or omissions, including reduced reaction times, increased number of misses, or more frequent unreliable responses. Areas of residual vision are also termed transition zones [24], because they are usually located at the border between the blind and the seeing region. As Figure 1 shows, they are represented graphically in different shades of gray, depending on the degree of visual impairment. It is likely that the degree of residual vision correlates directly with the relative number of cells surviving the injury (Fig. 2). Practically speaking, areas of residual vision can be defined by the relative number of correct responses in a given location. Thus, if, for example, a small white dot is presented five times at a given location without the patient ever responding to it, this position is defined as blind. When the patient responds to the stimulus every time, vision is considered to be intact. An area of residual vision, in contrast, is apparent when between one and four responses are made. We do not place much importance on each single dot in the visual field but rather on the overall response pattern. Only when several adjacent test locations show relative impairments do we consider this to be an area of residual vision [24]. The size and location of such areas may vary considerable among patients (Fig. 1): they may be nonexistent or small (type I), of medium...
size (type II), or large and fuzzy (type III), which is most often encountered after optic nerve injury [24].

Methods to document residual vision include the following. Because of their relatively low resolution, standard perimeters used in clinical medicine are not usually sufficiently precise to demonstrate residual vision, because they generally test too few points in the visual field to delineate areas of residual vision in sufficient detail. We therefore have developed a high-resolution perimetry procedure using personal computers, and we [31,32] have written programs to perform high-resolution qualitative perimetry of the central visual field. In this manner, color and form recognition also can be examined. High-resolution perimetry procedure consists of three subprograms that present visual stimuli with random spatial distribution throughout the central visual field. PeriMa presents stationary white (ie, suprathreshold) dots on a dark background; PeriForm presents different forms, eg, lines of different orientation or letters; and PeriColor presents gray or colored squares (red, green, or blue) [32]. This set of programs permits the assessment of visual field defects with a sufficiently high spatial resolution and flexibility to obtain detailed and objective information about residual capacities of vision.

**Restoration of visual field defects**

The existence of areas of residual vision raises the question of whether patients are able to make use of such areas and to what extent dynamic changes (eg, visual improvements) are possible.

**Spontaneous recovery**

The first evidence for dynamic change in the visual system is that both animals [9•] and patients [23•,33–36] usually recover some lost visual functions spontaneously, even without any intervention. Though many clinicians have witnessed cases of recovery of vision, only few have studied them systematically. As early as 1917, Poppelreuter [37] observed spontaneous recovery from visual dysfunctions in soldiers with gunshot wounds. The soldiers showed gradual visual field enlargements, and similar observations with reports of recovery rates ranging from 7% to 85% have since been made [15,33,34,36,38–40]. In an individual patient, it is not possible to predict the extent or duration of recovery, but patients with relatively large areas of residual (>5°) vision usually recover better than patients with smaller areas [35]. Recovery in animals is usually completed within 3 weeks after injury [9•] and in humans at 3 to 6 months, though some notable examples of long-term recovery have been reported [34]. After this time point, additional improvement can be accomplished only by visual restitution training.

**Training-induced enlargements of visual field defects**

Already in the 1940s, animal studies [9•] revealed that systematic training or experience can improve visual functions. However, only in the 1980s were such studies performed. It is proposed that the nature of residual vision depends directly on the level of neuronal activation. As the continuum of neuronal activation increases, residual vision can be one of the following stages: 1) no response at all, total blindness (0% neuronal survival); 2) correct guessing without conscious awareness (blindsight); 3) uncertain responses (partial vision with some consciousness); and 4) no deficit, full vision.
were carried out with patients. Zihl et al. [40–42] found repeated testing of the visual field border (which was essentially a training-type situation) to significantly increase visual field size in patients with postchiasmatic lesions, a finding which was confirmed by others [21,23•,25,43–47], but the claims had encountered some skepticism [48]. We therefore have developed computer programs to stimulate residual vision in brain-damaged patients (visual restitution training [VRT] programs: www.nova-vision.org), initially conducting one open pilot study which was followed by two prospective, randomized, placebo-controlled clinical trials [23•,25,49].

The VRT programs run on personal computers so that visual field training can conveniently be done at home without much assistance by medical staff. Consequently, a large number of training sessions can be achieved at minimum cost. For a period of 6 months or more, each patient performs two training sessions, half an hour each, on a daily schedule. Treatment results are stored on a disk so that compliance and changes in visual field size can be recorded.

In the initial open pilot study [49], 14 patients trained with VRT for approximately 1 year. Although three untreated patients experienced a slight decrease of visual field size, most patients of the restitution (treatment) group \(n = 11\) showed a significant visual field enlargement. In a subsequent randomized, double-blind, placebo-controlled trial, 19 postchiasmatic patients were assigned randomly to either the experimental or control group [25]. After a period of 6 months (175 h total), the experimental group showed a significant increase of visual field size amounting to 29.4% above baseline (baseline =100%), corresponding to an average shift of the visual field border by 4.8° of visual angle (Figs. 4, 5). The control group had a decrease of -3.1% or -0.9°. Interestingly, the training, which was done only with white or gray stimuli, has also improved color and form recognition [43]. Four patients who did not improve in the light detection test also showed only small or no changes in form recognition and color discrimination. Thus, in patients with postchiasmatic injury, visual restitution training not only improved the function that had been trained specifically, but the effect generalized to other visual modalities, ie, color and form discrimination [43].

In a second clinical trial [25,30] with 19 patients suffering optic nerve injury, the training effect was even more pronounced. In the experimental group, visual field size increased by 73.6% over baseline, corresponding to an average shift of about 5.8°. Unlike the postchiasmatic group, patients with prechiasmatic lesions showed improvements primarily in the early stage (within 4–6 weeks) after the training had started. It is interesting to note that optic nerve patients also showed an improvement of visual acuity, but, in contrast to postchiasmatic patients, training effects did not generalize to form or color perception [43]. To determine if training simply led to an altered response sensitivity (criterion change) rather than a true visual field enlargement, we counted the number of false positive responses (ie, patient pressed a key although no stimulus was presented). Before training, all patients \(n = 38\), postchiasmatic and optic nerve patients showed an average of 8.6 false-positive reactions in response to 500 stimulus presentations. After 6 months of training, the average number of false positives was comparable, indicating that the response criterion did not change [23•].

Effects of VRT are not restricted just to the perimetric test situation, but also encompass restoration of vision transfers to other (neuropsychological) functions that are of everyday use [25]. Patients show improved performance in paper-pencil tests of visual exploration and attention; more than 70% of the patients report subjective
improvements of vision; and more than half of the patients opt to continue the laborious training protocol beyond 6 months. Thus, VRT gives the patients the opportunity to better cope with the demands of the visual environment.

Mechanisms of action
This success in training actually is not surprising when viewed in the context of recent research results. Despite its strict neuronal organization and specificity, the visual system adapts rather well to lesion-induced changes (plasticity). Although the precise neuronal mechanisms underlying visual field enlargements are still not clarified, animal experiments and clinical research have provided some insights [8,9•,12,13,18–20].

The visual system is not as hard-wired as previously assumed. Rather, there is a considerable overlap of receptive fields in the visual system, and an astonishing degree of plasticity [27] is maintained throughout life. This can be seen in both short-term and long-term changes in receptive field size and localization [7,12,13] In fact, the brain perpetually undergoes processes of rerouting information to adapt to temporary alterations, such as special demands of the environment, shifts of attention, changes in the synchronicity of neuronal activation, and more permanent changes, such as those induced by brain lesions [1–7,9•,12,13,18,19].

Receptive fields may change their location and size following injury [7,18,19], and through the process of perceptual learning, both the uninjured and the lesioned brain can improve visual performance. Furthermore, the injured visual system has a remarkable, hitherto underappreciated, capability to recover visual functions, despite a massive neuron loss of 90% or more [9•,16,50]. Because visual field enlargements in patients usually occur at the transition zones, we have proposed that partially surviving neurons and their axons within the zone of damage provide the structural basis for this plasticity [23•,25]. It is conceivable, though not yet studied, that alterations of receptive field properties take place in such areas of partial injury, the degree of which is likely dependent on experience (practice or training). Lateral interactions may be of great importance here (Fig. 6) but other postlesion cellular or molecular changes in surviving cells also contribute to plasticity [9•].

Indirect evidence that receptive field changes may be involved in restoration are provided by observations that the amount of visual field enlargement covaries with the cortical magnification factor [51]. Although there are rather fast and comparatively large shifts of the visual field border in peripheral parts of the visual field because of training, an improvement in foveal regions is more difficult to achieve [36–41]. Because receptive fields in the central region are small, and vast areas of V1 are responsible for small portions of the visual field, visual field enlargement can be induced only by very intensive stimulation. However, even very small shifts of the visual field border in or near the fovea are of much greater practical relevance for the patients, as this region is es-
sential for reading and fixating. In contrast, in the periphery, where receptive fields are large, improvements are achieved more easily. However, here, even large shifts of the visual field border are subjectively less noticeable to the patient. Beside receptive field dynamics, other mechanisms may contribute to restoration of vision, including axon sprouting, unmasking of silent synapses, and increased synaptic efficacy [9•,23•].

Whatever the cellular mechanisms may be, transition zones are the functional representation of partially damaged regions in the visual system [24], and, according to the hypothesis of minimal residual structures [16], very few neurons surviving within such areas of could be sufficient to induce notable recovery of vision (Fig. 3). We speculate that by repetitive visual stimulation of these surviving neurons in a long-term training schedule, these cells may become more efficient, perhaps by reducing their threshold of firing.

Clinical recommendations

Visual restitution training can be used routinely in neurology or neuro-ophthalmology. Based on our current experience, the following recommendations can be made:

Training should be supervised by trained health care professionals.
Training levels should regularly be adapted to the progress.
Training is useful at least for patients with pre- or postchiasmatic lesions of the central nervous system, such as patients with stroke and trauma or in patients following brain surgery.
Training should be used only by patients that have at least some residual vision.
The training program has to be tailored to the requirements of the individual patient, to be determined during an initial session of residual vision diagnosis.
To increase the probability of progress, regular training twice a day is essential. The training phase should initially last at least half a year, but, depending on the patient’s performance, may be extended.
Training should not be used by patients with photosensitive epilepsy because visual light stimulation may have adverse effects.
Training also should not be used by patients with inflammatory diseases of the eyes or central nervous system because intense stimulation may reinforce the inflammation. Training should be initiated only after the disease has subsided.

When the visual field defect is caused by a progressive illness, for example, a malignant tumor, patients should be informed that training improvements can be compromised by ongoing visual deterioration due to the illness.

Conclusions

In conclusion, neuroplasticity of the visual system provides the neurobiologic substrate for a rational and scientifically based visual rehabilitation strategy. Although complete restitution seems unlikely at present, significant visual field enlargement can be accomplished, and patients with visual field such as scotoma or hemianopia defects benefit from it. Consequently, neuropsychological rehabilitation of patients suffering from visual field defects should become standard therapy to help patients with visual field defects to regain some of their lost vision.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
• Of special interest
** Of outstanding interest
