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CHAPTER 12

Blindsight, conscious vision, and the role of primary visual cortex

Petra Stoerig*

Institute of Experimental Psychology II, Heinrich-Heine-University Düsseldorf, 40225 Düsseldorf, Germany

Abstract: What is the role the primary visual cortex (V1) in vision? Is it necessary for conscious sight, as indicated by the cortical blindness that results from V1 destruction? Is it even necessary for blindsight, the nonreflexive visual functions that can be evoked with stimuli presented to cortically blind fields? In the context of this controversial issue, I present evidence indicating that not only is blindsight possible, but that conscious vision may, to a varying degree, return to formerly blind fields with time and practice even in cases where functional neuroimaging reveals no V1 activation.

Keywords: primary visual cortex (V1); visual neuropsychology; blindness; blindsight; training; visual field recovery

Stunning controversies

The role that the occipital lobes, and specifically the primary visual cortex, play for vision has been debated for over a century. As early as 1878, Munk (1881) reported that a unilateral ablation of the monkey's occipital convexity resulted in a hemianopic, and bilateral extirpation in a complete cortical blindness. In contrast, Ferrier (1886) was convinced that bilateral removal of the greater portion of the occipital lobes caused no appreciable impairment of vision. Although methodological progress both in the precision of ablation in animals and in assessing the extent of destruction in man have led to a general acceptance of Munk's view — complete unilateral destruction or denervation of the primary visual cortex (V1) causes cortical blindness in the contralateral hemifield — the debate still continues. One of its aspects regards the permanence of the blindness. According to the classical doctrine held by the vast majority of clinicians, neurologists as well as ophthalmologists, the blindness will stay for good unless spontaneous recovery occurs within months; if it does, the damage is reversible. The contrary view traces its origins to Riddoch's (1917) early report on appreciation of movement in fields of cortical blindness, and holds that even conscious vision is possible without V1 (Zeki and ffytche, 1998). Remarkably, this divide extends to the implicit visual functions that remain in fields of cortical blindness, and has come to be known as blindsight (Sanders et al., 1974; Weiskrantz et al., 1974). According to the view advocated by Campion et al. (1983) and Fendrich et al. (1992), these nonreflexive but implicit visual functions depend on islands of surviving tissue in the primary visual cortex. This assumption is opposed by those who hold that these functions must depend on the extrageniculo-striate cortical projections rather than residual V1 (see Stoerig and Cowey, 1997, for review). Thus, V1 is at the same time presumed to be: (1) required for blindsight as well as for conscious vision and (2) required for neither conscious vision nor blindsight.

*Corresponding author. Tel.: +49-211-811-2265; Fax: +49-211-811-4522; E-mail: petra.stoerig@uni-duesseldorf.de

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"Vision is a more complex function than most people realize" (Livingstone and Hubel, 1988)

In the retina, the distribution of light falling into the eye is first translated into patterns of neuronal discharges by the retinal ganglion cells. These differ morphologically as well as functionally, with major distinctions regarding spatial and temporal resolution, sensitivity to light, and specificity to wavelengths. They project the retino-recipient nuclei that lie in the hypothalamus, the thalamus, and the midbrain. The lion's share of direct retinofugal projections goes to the dorsal lateral geniculate nucleus (dLGN) of the thalamus where the axons of different ganglion cell classes contact neurons in different layers. The vast majority of dLGN projection neurons send their output to the primary visual cortex situated in the occipital lobe, about as far from the eyes as possible. In this "cortical retina," topographical relationships are preserved. In addition, inputs that originate in different types of retinal ganglion cells remain segregated not only by targeting different subdivisions of the main input layer 4, but also by virtue of their target neurons projecting onwards to functionally distinct subregions both within V1 itself and in the second visual cortical area V2. Like further stations in the feed-forward stream of information, V2 receives input not only through V1 but also from subcortical visual nuclei including the dLGN (Yukie and Iwai, 1981). The next tier of visual cortical areas includes V3, V4, and V5/MT, which preferentially process different types of visual information, indicating that they receive dominant feed-forward input originally generated by different retinal ganglion cell classes. Although functional specialization of visual cortical areas is widely accepted nowadays, its extent is still somewhat controversial on the basis of physiological evidence (Zeki, 1978; van Essen, 1985; Livingstone and Hubel, 1988; Gross, 1992; Cowey, 1994); even the processing of visual motion, for which the area V5/MT appears unequivocally specialized, has just been reported to invoke area V4 if motion adaptation takes place (Tolias et al., 2005).

As a rule of thumb, neurons have increasingly large and complex receptive field properties further upstream their visual area. Neurons in visual cortical areas extending into the temporal lobes respond preferentially to images of houses or places, to faces and gestures, and even to individuals (Perrett et al., 1982; Kanwisher et al., 1997; Kanwisher, 2001; Jellema and Perrett, 2003); they generalize over viewpoints and other stimulus particulars. In contrast, neurons in visual areas of the parietal lobes increasingly take account of where some stimulus is, or moves toward, in relation to not only to the retinal locus of stimulation but also to the subject's ever-changing bodily coordinates. These observations have given rise to the concept of two visual streams (Ungerleider and Mishkin, 1982): a dorsal, occipitoparietal one involved in visuomotor preparation; and a ventral, occipitotemporal one involved in stimulus identification. Areas in both streams receive input (1) from earlier visual areas, (2) via several routes from subcortical nuclei, and (3) from yet higher cortical areas to which they also project. In addition, they have extensive lateral connections that allow crosstalk between dorsal and ventral pathways (Fig. 1).

Lessons from lesions

Although the anatomical and physiological studies of the visual system have profoundly advanced our

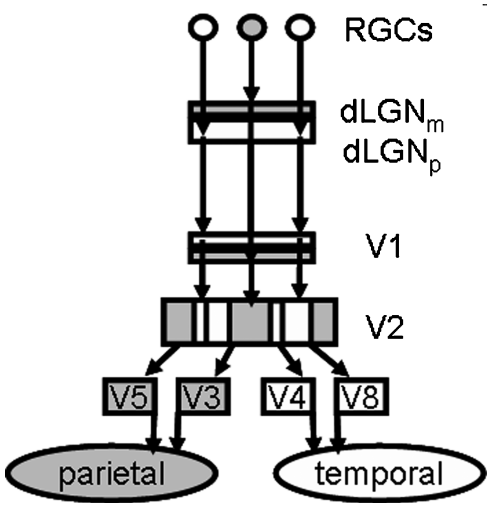

Fig. 1. The very simplified schema illustrates the functional segregation that originates in the retina and permeates the entire visual system all the way into parietal, temporal, and frontal cortices.

understanding of the visual system's functional architecture, they cannot by themselves reveal which pathways and cells contribute to conscious and which contribute to unconscious or implicit visual functions. Rather, it is through the study of the functional consequences of lesions to different parts of the system that we have learned that the primary visual system plays a much more prominent part in conscious vision than the retino-extra-geniculo-striate cortical projections. Careful neuropsychological observations of human patients with circumscribed lesion, alongside behavioral studies on animals with experimentally induced lesions, show that different levels of unconscious or blind and conscious vision remain following destruction of different parts of the system.

The neuroendocrine responses represent the lowest level of vision. They have even been demonstrated in patients who were totally blind as a result of pathologies which affect the retinas or the optic nerves. Although these patients retained no appreciation of light, their plasma melatonin levels varied in a light-dependent circadian manner. Czeisler et al. (1995) also showed that wearing a blindfold abolished this modulation, demonstrating that it is indeed through the eyes that the effect is enabled.

The next level of visual functions is that of reflexive responses. While Czeisler et al.'s (1995) patients retained no pupillary light reflexes, these and other visual reflexes may remain in patients with more centrally located lesions of the visual pathways. Such reflexive responses can also be elicited in totally blind patients; indeed, a blink reflex has even been reported in brain death (Keane, 1979).

The third level of blind visual function has been observed in patients whose lesions destroy or denervate the primary visual cortex. Most commonly, such lesions are caused by vascular incidents, but traumatic and neoplastic insults are also common causes of the ensuing cortical blindness. In the much more common cases where the lesion is confined to one hemisphere, such destruction causes a field of homonymous cortical blindness in the contralateral hemifield. Unilateral V1 destruction can spare the optokinetic nystagmus (Pasik et al., 1959; ter Braak and van Vliet, 1963) as well as a variety of pupillary reflexes that in addition to the pupillary light reflex indicate responses to chromatic and spatial information (Barbur, 2004). In addition, psychosensory effects such as the stimulus probability reflex, which elicits larger pupil dilation to rare targets (Beatty, 1986), have recently been demonstrated in response to stimuli presented in the cortically blind field (C. Loose and P. Stoerig, in preparation; Fig. 2). Moreover, patients can voluntarily initiate nonreflexive visual responses to blind field targets. They include saccadic and manual localization of stimuli presented

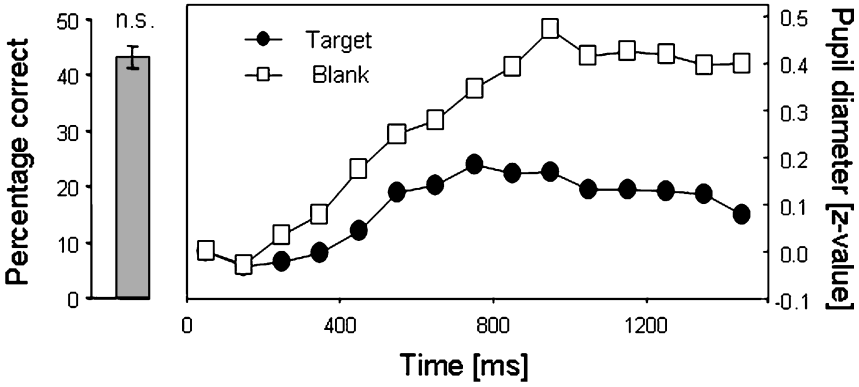

Fig. 2. Although patient KE showed no evidence of detecting the 5° gray disk at a negative log contrast of 0.61 to the white background (left), his pupil responded with a late dilation to the presentation of rare (20%) blank trials (right). As no stimulus was presented, the dilation reflects the low probability of blank stimuli, and is of psychosensory origin rather than stimulus driven. Note that pupil traces are based on "Target" responses only, so as not to confound stimulus and response probabilities.

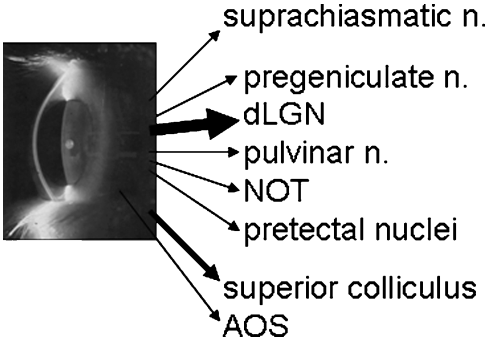

Fig. 3. The retinofugal pathways target more than 10 nuclei in different brain regions. These nuclei transmit the visual information to others, some of which also receive a direct retinal input, either via these or directly to visual cortical areas.

in the blind field (Pöppel et al., 1973; Weiskrantz et al., 1974), as well as discrimination of absence vs. presence of a stimulus (Stoerig et al., 1985), of absence or presence of stimulus motion (Perenin, 1991), and of stimuli of different orientations, flux, motion direction, and wavelength (Fig. 3; see Weiskrantz, 1986, 1990; Stoerig and Cowey, 1997, for reviews). As the patients report no perception of the stimuli, demonstration of these functions requires methods that do not rely on a considered report, but circumvent the experienced blindness. The most commonly used forced choice approach requires the patients to guess whether a stimulus was presented, where it was presented, or which one of a two possible stimuli was briefly presented in the blind field. Alternatively, processing of a stimulus in the blind field is inferred if it influences responses to targets presented in the normal hemifield. If, for example, a patient responds faster to a seen target in the normal field when simultaneously and unbeknown to him an additional stimulus is presented in the blind field, the reaction time difference indicates that the blind field stimulus has been effectively processed (Marzi et al., 1986). Capturing the dissociation between perception and performance, this phenomenon has been termed "blindsight" (Weiskrantz et al., 1974). Covering nonreflexive visual functions, it represents the highest level of visual function in the absence of a conscious stimulus representation (Stoerig, 1999).

Nonreflexive responses to unseen information have also been demonstrated in patients who, due to circumscribed lesions of extrastriate cortical areas, have lost conscious color (Meadows, 1974), form (Benson and Greenberg, 1969; Farah, 1990), or motion perception (Zihl et al., 1983). Patients with such selective visual deficits can implicitly respond to the visual feature(s) that are no longer consciously represented (e.g., Heywood et al., 1991; Milner and Goodale, 1996); indeed, the implicit processing can allow the conscious detection of stimulus properties, as when an achromatopsic patient detects the border between two abutting fields of different colors although he cannot see the colors themselves. In blindsight, where the conscious representation of all stimulus attributes are lost, such perceptual effects have been invoked by presenting the stimuli so that they straddle the border between the blind and the remaining normal visual field (see Pöppel, 1986; Marcel, 1998, for examples).

Neuronal pathways to blind vision

Anatomy and physiology

The light-dependent plasma melatonin modulation very likely depends on a sparse retinal projection to the nucleus suprachiasmaticus of the hypothalamus. It is involved in entraining the circadian rhythms to the day-and-night cycle. Of the retinorecipient nuclei, this one lies closest to the eyes, above the optic chiasm, and receives its retinal input from a small population of retinal ganglion cells that has been described in the rat (Moore et al., 1995). Whether the melanopsin-containing light-sensitive ganglion cells that have recently been described in rats and monkeys (see Foster, 2005, for summary) also project to this nucleus is presently unknown. Although functional segregation of optic fibers is more obvious in the tract than in the optic nerve (Reese and Cowey, 1988), the axons of the cells that project to the suprachiasmatic nucleus could travel more dorsally in the tract en route to their target nucleus, and thereby escape destruction in some of the pathologies that cause a peripheral blindness.

The visual reflexes are mediated by retinal projections to a variety of subcortical nuclei. The pupil light reflex involves the pretectal nuclei, which forward their output to the Edinger–Westphal nucleus receives the output of the pretectal nuclei (Magoun and Ranson, 1935; Beatty, 1986). The optokinetic nystagmus involves the retinal projections to the nucleus of the optic tract (Hoffmann, 1989), and processing of optic flow involves the three nuclei that form the accessory optic system (Simpson, 1984). Cells in the superior colliculus respond well to moving borders (Marrocco and Li, 1977), and play an important part in programming saccadic eye-movements (Mohler and Wurtz, 1976; Waitzman et al., 1991). Furthermore, collicular microstimulation improves performance in a spatially selective manner even during fixation (Müller et al., 2005), and collicular deactivation causes visual hemineglect (Sprague and Meikle, 1965; FitzMaurice et al., 2003). The nucleus is involved in cross-modal integration (Meredith and Stein, 1985), and even participates in perceptual decision-making (Horwitz et al., 2004), indicating that it contributes not only to reflexive orienting responses, but to nonreflexive functions as well.

If fibers traveling to the extra-geniculate nuclei leave the optic tract before the lesion, or escape its destructive effects in some other fashion, their target nuclei may still mediate visual responses, albeit often impaired, in patients who retain no conscious vision.

The nonreflexive visually guided responses that can be elicited in fields of cortical blindness probably make use of all pathways that survive the effects of a striate cortical lesion. This is indicated by a long series of experiments on monkeys who, in addition to occipital resection, were subjected not only to increasingly larger cortical lesions, but also to selective destruction of subcortical nuclei (see Pasik and Pasik, 1982, for review). The results show that manual and saccadic localization depend on the midbrain, and are severely disturbed when the superior colliculus is damaged in addition to V1 (Mohler and Wurtz, 1977; Feinberg et al., 1978). In contrast, rough luminance discrimination remained possible even with large cortical lesions combined with subcortical ones unless the lateral pretectum was destroyed (Pasik and Pasik, 1973). In addition to the extra-geniculate retinal pathways, the projection neurons that survive the retrograde degeneration of the dLGN that follows ablation of V1 (Van Buren, 1963; Mihailovic et al., 1971) may contribute to blindsight. Although the degeneration transneuronally affects the retinal ganglion cell of which roughly 50% die in this much slower process (Van Buren, 1963; Cowey, 1974; Cowey et al., 1989; Weller and Kaas, 1989), the survivors continue to project both to the extra-geniculate nuclei, including the pulvinar and the pregeniculate nucleus which is exempt from retrograde degeneration (Dineen et al., 1982), and to the degenerated dLGN (Kisvárday et al., 1991).

The retino-recipient nuclei that have been physiologically investigated after striate cortical ablation showed responsivity to stimuli presented in the cortically blind field (see Payne et al., 1996, for review). Furthermore, all of them project directly (like the dLGN and the pulvinar) or indirectly (like the superior colliculus) to extrastriate visual cortical areas. Different extrastriate visual cortical areas differ in the extent to which they continue to respond to information from the blind hemifield. Dorsal stream areas appear to retain more responsivity (see Bullier et al., 1994, for review). Nevertheless, despite evidence showing that area V5/MT displays the most robust responses after both cooling (Girard et al., 1992) and ablation of V1 (Rodman et al., 1989), even area MT's relative independence from V1 input is not reported consistently (Collins et al., 2005). What direction selectivity remains seems to depend on input from the superior colliculus and was abolished when it was also lesioned (Rodman et al., 1990). Whereas neither V2 nor V4 retained more than a very small number of neurons responding to the contralateral hemifield when V1 was ablated or cooled (see Bullier et al., 1994, for review), visual responses were still evoked from neurons in the polymodal cortex of the superior temporal cortex (Bruce et al., 1986).

Functional neuroimaging

Functional neuroimaging studies of human patients confirm that extrastriate visual cortex in the lesioned hemisphere continues to respond to stimulation of the blind hemifield. Although the

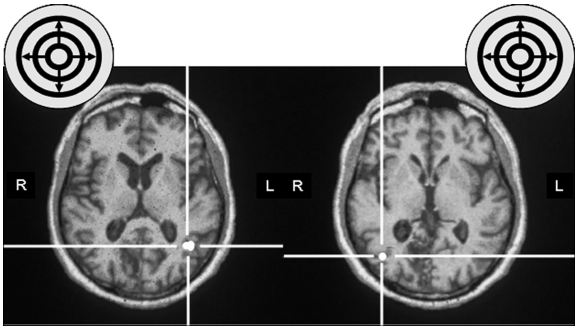

Fig. 4. Functional magnetic resonance images of patient HK obtained 3 months after a vascular lesion destroyed his right striate cortex. A circular stimulus of expanding bright and dark rings activated the human motion complex hMT+ along with early visual cortex in the normal hemisphere when presented to the normal right hemifield. When presented to the cortically blind left hemifield, the same stimulus evoked no detectable response in early visual cortex V1/V2; nevertheless, the ipsilesional motion complex was activated.

majority of published studies were performed on patients whose lesions had occurred years before the imaging took place (e.g., Goebel et al., 2001), our unpublished results also show activation of the ipsilesional human motion complex hMT+ relatively early postlesion. An example taken 3 months after the insult is shown in Fig. 4; no concomitant activation in areas V1/V2 was found. However, we have not detected hMT+ activation in all the patients we have studied early after the insult, so that the patients' neuroimaging results are in good agreement with the physiological data from monkeys. These too demonstrate the most robust responses in areas MT/V5 and its satellites, i.e., corresponding to the motion complex, but do not report it in all instances.

Blindsight has also been attributed to small islands of primary visual cortex that are supposed to survive the lesion. This explanation is based on the data of a patient who demonstrated significant evidence of detection and discrimination only if the stimuli were presented at a particular position in his blind field, but not when they were presented at a number of alternative positions (Fendrich et al., 1992). However, other patients do not show such a pattern of blindsight confined to spatially isolated islands (e.g., Stoerig and Pöppel, 1986; Stoerig, 1993; Kentridge et al., 1997). In addition, neuroimaging failed to reveal evidence for activation within the lesioned primary visual cortex in several instances (Barbur et al., 1993; Stoerig et al., 1998; Goebel et al., 2001), visually induced activation in occipitopolar cortex was not shown to correspond topographically to the "blindsight position" in Fendrich et al.'s (1993) patient, and finally, residual V1 cortex cannot explain the evidence in monkeys or patients in whom this cortical area was completely resected. Like any tissue that escapes the lesion and its degenerative consequences, small islands of V1 tissue, if they survived within the damaged region, could be recruited to serve the residual visual functions; however, the bulk of evidence on both species indicates that such a contribution is not prerequisite to blindsight.

Together, the body of anatomical, physiological, and neuroimaging data indicates that blindsight is not just mediated subcortically, but that several extrastriate visual cortical areas retain or regain visual responsivity. As this applies to both monkeys and humans, it disproves the contention that blindsight is blind because it does not invoke any cortical processing. This idea had been put forward in the context of evolutionary corticalization to explain why patients became blind following destruction of primary visual cortex, while other mammals including monkeys still displayed visually guided behavior (Klüver, 1942; Weiskrantz, 1963; Weiskrantz and Cowey, 1963, 1967). It was only by using forced choice procedures as applied in animal research that human patients were shown to also possess such capacities (Pöppel et al., 1973). To complete the cycle, by offering our hemianopic monkeys the option to respond "no target" to blind field stimuli they localized almost perfectly when not having this option, we could show that they consistently responded "no target" on target trials (Cowey and Stoerig, 1995). Like human patients, the monkeys thus behaved as if targets they could localize were not targets at all, suggesting they too had blindsight.

Functional significance of unconscious vision

The light-dependent modulation of melatonin secretion that has been demonstrated, even in

patients in whom no other visual functions were found, entrains our circadian rhythms to the day-and-night cycle. Disturbances of sleep patterns result from their failure (Sack et al., 1991; Siebler et al., 1998), indicating that they influence function in an indirect but important way.

The visual reflexes protect the eyes from overexposure to light, as the pupil light and the blink reflex, that is also elicited by fast approaching objects mediate orienting responses, and alert the organism to the sudden appearance of potentially relevant stimuli. Whereas the relatively immediate loop linking the sensory input to the reflexive motor responses is indicative of their basic relevance, the functional significance of the nonreflexive responses that are characteristic of blindsight may appear less obvious. If blindsight was exclusively a laboratory phenomenon, demonstrable in experiments which force the patients to guess the stimulus or its location, it would contribute to our understanding of the functional neuroanatomy of the visuomotor systems, but not help the patients in their daily life. Although this issue has not been extensively studied, marked improvements in the visually guided behavior have been documented in a monkey who underwent bilateral ablation of primary visual cortex. This monkey, Helen, was extensively studied (Humphrey, 1970, 1974) and showed no evidence of spatial vision for the first 19 postoperative months. Training her, first with moving, then with stationary objects, continuously improved her ability to look and reach for them, but still there was no evidence for depth vision for as long as she remained largely confined to her cage. Five years after the onset of blindness, Helen was moved to a new lab where at first no testing room was available. Humphrey then took her on a leash into the open field and woods. He describes her development as follows:

> To begin with, […] these walks were fairly hazardous. She continually bumped into obstacles, she collided with my legs, and she several times fell into a pond. But then, day by day, there was an extraordinary change in her behaviour. On the one hand she began to systematically anticipate and skirt round obstacles in her path, while on the other she began actually to approach the trees in the field, turning towards them as we passed by, walking up and reaching out to grasp their trunks (Humphrey, 1974, p. 244).

In fact, according to video documentation, Helen eventually appeared quite like a normal monkey. Although pathology revealed a small sparing of V1 that corresponded to a peripheral part of the upper right quadrant of the visual field, she did not appear to use this remnant to locate objects, but rather looked at them directly before reaching out.

Blindsight and plasticity

Blindsight without feedback

It is obvious from the wealth of data published on blindsight that what is tested, and how it is tested, makes a big difference as to whether or not positive results are revealed. For example, the incidence of statistically significant movement detection and discrimination varies between 0 and 100% of patients tested. Perenin (1991), who tested patients with hemianopia as well as complete cortical blindness, used large fields of black dots. These would either move or remain stationary, or move from left to right or right to left, respectively. The patients solved the motion detection as well as the direction discrimination task with ~90% correct performance. At the other end of the spectrum, Barton and Sharpe (1997) tested 10 patients with cortically blind fields, using a random dot kinematogram (RDK), and found that not one was able to discriminate the direction of the moving dots even at 100% coherence. A more recent study in which three patients were tested with different types of moving patterns that included both a single bar and an RDK confirmed that all were able to detect motion in all instances, but could distinguish its direction only for the single bar (Azzopardi and Cowey, 2001). GY, a patient with long-term experience with tests of his residual visual functions, participated in this experiment, and showed this same pattern of results despite his repeatedly reported excellent ability to

distinguish the direction of a single moving target (Barbur et al., 1980; Weiskrantz et al., 1995).

To specifically address the issue of blindsight learning, we used a different type of moving stimulus. A red-and-blue spiral, 5° across and with a mean luminance of 8 cd/m^2, was presented for 500 ms per trial on a white 10 cd/m^2 background. It would, or would not, rotate around its own axis in a motion detection task, and would rotate clockwise or counterclockwise in a motion discrimination task. The rotation depended on local elements and avoided global stimulus translation. As we were interested in whether patients would improve with practice, we presented both tasks for 8–12 consecutive series of 100 trials each, and analyzed performance per series as well as overall. 11 patients with fields of cortical blindness participated; one was the already mentioned GY. Upon each presentation, patients pressed one of the two response keys to indicate whether or not the spiral had been rotating, or whether it had rotated clockwise or counterclockwise. Both on- and offset of the stimuli was signalled with a brief sound to inform the patients when to attend and when to respond. The two stimuli had equal probability. Their position was adjusted to each individual field defect, and eye movements were monitored throughout to ensure that any evidence of discrimination would not reflect unstable fixation.

The results showed that of the 11 patients, 6 performed above chance ($P<0.05$ or better, χ^2 test) in the motion detection task when performance was collapsed over the series. In addition, in nine subjects the level of performance improved over the course of the series. To learn whether the improvement was significant for the group, rates of false responses to stationary stimuli ("moving"/stationary) were subtracted from those of correct responses to moving stimuli ("moving"/moving) to provide an index of discrimination that is independent of subjects' response bias. The resultant difference values for the first and the last series were used in a paired comparison test that yielded a significant advantage in favor of performance in the last ($Z = -2.045$; $P_{1\text{—tailed}} = 0.021$, Wilcoxon). Fig. 2A shows percentage correct values for three of the patients in the first and last series. Note that patient GY performed best of all subjects.

As can be seen in Fig. 5B, the corresponding values were lower for the motion direction task. This finding agrees with the published results of Perenin (1991) and Azzopardi and Cowey (2001), and confirms that in the blind field direction discrimination is more difficult than detection of motion. Nevertheless, six patients performed significantly in this task. Rotation direction discrimination, albeit clearly difficult under the present conditions, is thus possible in cortically blind fields. Whether the discrimination reflects the use of rotation rather than RDKs, whether the spiral's color contrast made a difference, or whether the size of the individual elements that move together

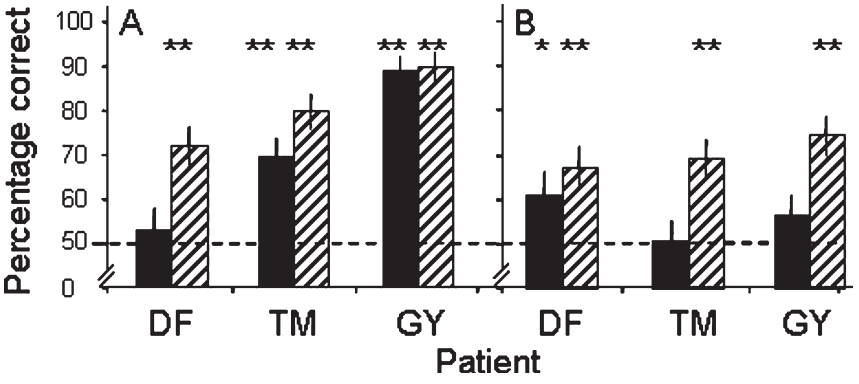

Fig. 5. Results of rotation detection (A) and rotation direction discrimination (B) in three of the patients. For each, performance in the first (black bars) and last (striped bars) of the 100 trial series is shown. Note that all patients performed better in the rotation detection than in the rotation direction discrimination, and the improvement was significant for the group only in the former task. Asterisks indicate whether performance was significant (*$p<0.05$; **$p<0.005$).

plays a role cannot be decided at present. Group analysis of the rotation direction discrimination revealed no statistically meaningful difference between first and last series; nevertheless, two of the three patients shown in Fig. 5B, TM and GY, showed evidence for perceptual learning in the form of a significant positive correlation between the discrimination index (''clockwise''/clockwise – ''clockwise''/counterclockwise) and the series (TM: $\rho = 0.738$, $P_{1\text{–tailed}} = 0.018$; GY: $\rho = 0.745$, $P_{1\text{–tailed}} = 0.011$).

To learn which of the many factors that are likely to underlie the differences in blindsight performance contributed most to the interindividual variability in the two rotation tasks, we performed a hierarchical regression analysis. Factors entered to explain the performance included the patients' age, their age at lesion, the size of the lesion as estimated on the basis of the T1-weighted MR images, the rough size of the field defect, the length of time during which each had regularly or irregularly participated in blindsight testing, and the age at which they had begun to do so. The results showed that of these factors, the overall length of blindsight experience, which varied from 0.2 to 20 years, correlated highest with performance in the motion detection task ($p = 0.002$); this factor alone explained 57% of the variance ($R^2 = .568$; $p = 0.005$). For the motion direction discrimination, none of the same factors explained a significant part of the variance.

In addition to confirming that some tasks are more difficult to solve than others, the results of the spiral experiment support the notion that blindsight is subject to learning. This is in agreement with results of Bridgeman and Staggs (1982) as well as Zihl and colleagues (Zihl, 1980; Zihl and von Cramon, 1980; Zihl and Werth, 1984). Both groups tested localization in the cortically blind fields of their patients, and found that performance improved with practice when pointing (Bridgeman and Staggs, 1982) or saccadic responses were required (Zihl, 1980; Zihl and von Cramon, 1980; Zihl and Werth, 1984). It is interesting in the context of perceptual learning that the practice effect transferred to stimuli of lower contrast in the patient tested by Bridgeman and Staggs (1982), and even to a different function in the three patients of Zihl and von Cramon (1980). The latter patients were first required to blink whenever a 116 in., 100 ms stimulus was presented to the blind field; blank stimuli were used for control comparison. 480–600 trials were given, and all patients' blink responses to targets, but not to blank control stimuli, increased. Then the same stimulus was presented at seven different positions from 10° to 40° off fixation on the horizontal meridian, and the patients were asked to initiate a saccade to where they guessed the stimulus had appeared. Localization accuracy was compared to results of a similar series conducted before the blink response experiment, and was found considerably improved in two of the patients. In addition to task- and stimulus-specific perceptual learning, transfer of practice effects has thus been demonstrated.

Blindsight with feedback

It is noteworthy that these effects have been reported although the patients did not receive feedback in any of these studies. This is a general feature of testing blindsight in humans, but not in monkeys with primary visual cortex ablation. Monkeys, unlike humans, are usually rewarded for responding correctly, as part of the procedure required to ''explain'' their task. As feedback is likely to facilitate learning, we have used it in the following localization task.

The patient is seated in front of a hemi-cylindrical training perimeter. It is studded with red light emitting diode (LED) buttons which are spaced ~7° apart laterally. Fixating the central one that is lit throughout the series, the subject presses a start key. This causes a second LED to light up; simultaneously, a sound is emitted from a central loudspeaker integrated into the setup; this sound informs the patient that a LED is on but does not provide a cue to its position. The patient is told beforehand which meridian(s) is active, and has to find the lit LED as quickly as he can with either hand, but without moving his eyes. As targets appear on either side of fixation, half of them will be visible to a patient with a complete hemianopia. The sound continues until the proper LED has been pressed, which extinguishes both the light

and the sound, thereby informing the patient that he has hit the correct LED. The computer registers all LEDs pressed per trial as well as the search time from stimulus onset to the hit.

In November, 2004, patient BT presented with a complete hemianopia to the left that resulted from a large lesion (an arteriovenous malformation had been embolized and extirpated in 1999) that destroyed the largest part of his right occipital lobe. He was tested with the LEDs on the horizontal meridian, which are schematically presented in Fig. 6. Median search times for an early test conducted in February 2005 are compared to the corresponding data from a similar series collected 4 months later; BT had in the meantime been trained in both target detection and localization. The results shown in Fig. 7 are based on 15 responses per LED, and reveal a reduction in search times for the data from the blind field ($Z = -2.173$, $P_{1\text{—tailed}} = 0.0014$; Wilcoxon).

The improvements observed over time in the few studies devoted to blindsight learning may explain why positive results are somewhat more common in cortically blind monkeys. Whereas patients are often tested on a very limited number of presentations, monkeys may receive hundreds or thousands of trials to learn whether they will reach the criterion or not. Clearly, all the factors that influence the results in studies of human patients also affect the monkeys'. The task is important, and so is the extent of the lesion that is often not confined to primary visual cortex. Lesion size affects the extent of transneuronal retrograde retinal ganglion cell degeneration (Cowey et al., 1999), as well as visually guided behaviors, as has been systematically studied in monkeys (see the section on "Neuronal pathways to blind vision"). In addition, the age at lesion, usually lower for the monkeys, contributes. Considerably more extensive rewiring has been demonstrated in monkeys following early striate cortical damage "which results in neuronal compensations, and in the sparing of certain classes of visually guided behaviors that do not occur following equivalent damage sustained in adulthood" (Payne et al., 1996, p. 742). Indeed, the age at lesion, and not the age at the beginning of blindsight testing which is closely correlated with age at lesion in monkeys but not human patients, was the second most predictive factor of individual performance in the rotation detection task. The amount of experience with blindsight testing was the first.

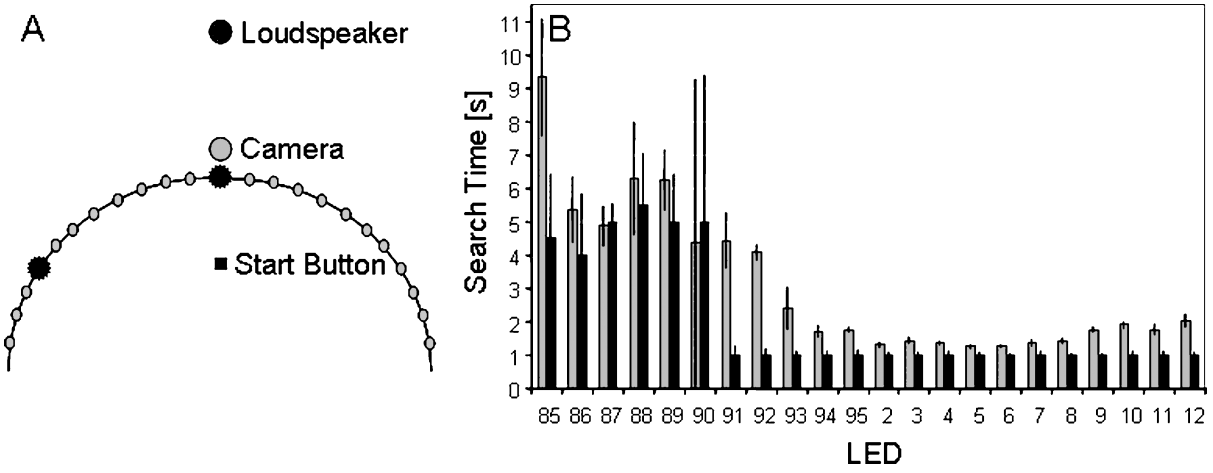

Fig. 6. Manual localization was tested in a training perimeter. The horizontal meridian that was used for patient BT is drawn on the left. The central LED served as fixation. When the patient pressed the start button, the target LED lit up, and a sound buzzed for as long as it took the patient to find and press it; this extinguished both the light and the sound. Median search times ($n = 15$ per LED, $\pm$the Semi Interquartile Range) represent data collected ~4 months apart. BT reported detecting the first LED to the left of fixation when it lit up, because of light emanating from it, but insisted that he had no information as to the location of the other targets, and found himself to be only guessing.

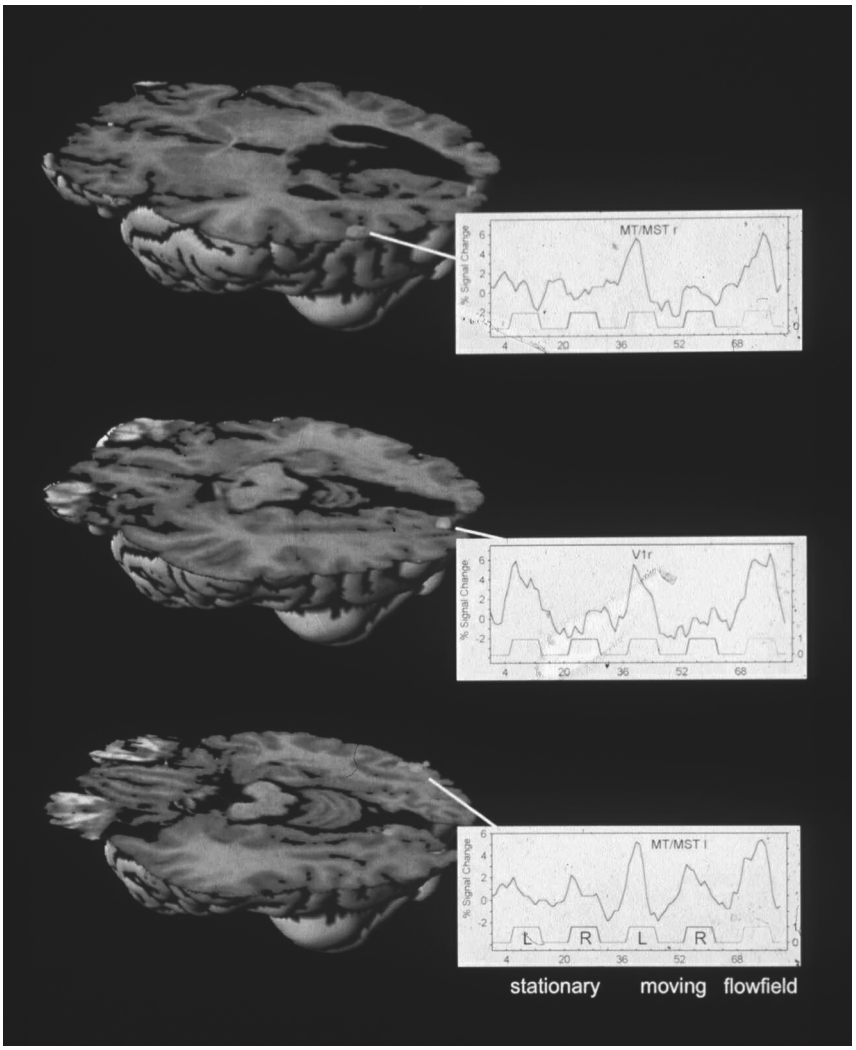

Fig. 7. Functional neuroimaging data of patient GY show strong ipsilesional activation in response to a rotating spiral presented in the hemianopic field. Unlike presentation of the same stimulus in the normal field which caused activation both in the motion complex and in V1, no V1 activation is detected anywhere within the lesioned calcarine cortex.

The blind in blindsight

The hypotheses that have been put forward regarding the blind in blindsight address the role of the primary visual cortex in conscious vision. The major ones suggest that (1) conscious vision is lost because the extrastriate visual cortex depends on the massive geniculo-striate cortical input, (2) conscious vision depends on the back-propagation of signals from the higher visual cortical areas, and (3) both output of and input to primary visual cortex are required.

According to the first hypothesis, V1 is important because the quantitatively lesser extra-geniculo-striate cortical routes to the higher visual cortex are insufficient to render vision conscious. A critical amount, or organization, of visual cortical activation would be required for that purpose, but is not reached without the massive geniculo-striate-extrastriate input. Whether the

processing that V1 performs before it transfers its output to the next stages of processing is also important is not known. Neuroimaging data from human subjects performing a challenging detection task at contrast threshold showed that a large, stimulus-independent response in the early visual cortical areas V1–V3 predicted behavioral performance, which was best when this response was large (Ress et al., 2000). Due to its being stimulus independent, the authors interpret this finding as manifestation of attentional processes. Whether it is attention or some other endogenous fluctuation, its co-varying with performance indicates that the state of the early cortices determines whether weak stimuli are processed in a manner that allows them to become consciously represented. Whether it is the output signal of these cortices, or whether it is the signals that the higher extrastriate regions send back to the early areas including V1, which is in some way insufficient when V1 is destroyed, is still open; destruction of V1 compromises both the feed-forward and the feedback signals. A role for the latter is suggested by elegant physiological studies in awake behaving monkeys, where activity patterns in V1 differentiated figure and ground in difficult segmentation tasks only when the animals succeeded in the task (Supér et al., 2001). The figure–ground differentiation, when observed, only started at ~90 ms after figure onset, suggesting that back-propagated signals with their longer latencies play an important role in performance. Lamme et al. (1998) proposed that feedback connections are essentially involved in rendering vision conscious, while the feed-forward flow is required for fast behavioral responses that are not always linked to stimulus awareness. However, since we presently have no procedures that selectively disrupt either the back-projections or the feed-forward ones, it is not known whether loss of back-propagated information by itself produces blindness. Consequently, we do not know whether one type of transfer is more important than the other, or whether, as assumed in hypothesis (3), both are required for conscious vision.

More precisely, this should read veridical conscious vision because nonveridical vision, such as hallucinations (Kölmel, 1984; Lepore, 1990) and phosphenes (Cowey and Walsh, 2000), can occur in fields of cortical blindness. This demonstrates that the brain retains the capacity to produce some kinds of vivid conscious vision even when V1 is destroyed (Stoerig, 2001). Therefore it may not be the primary visual cortex that is inexpendable for conscious vision as such, but rather a sufficient amount of appropriate activity. According to this view, such activity would arise spontaneously in release excitation, or be induced by magnetic or electrical stimulation, but it would not be evoked by the retinal input that still reaches the visual cortex via extra-geniculo-striate cortical routes. This suggestion not only agrees with the evidence but also allows for the possibility of some conscious vision to return to the cortically blind field. If the plastic changes that depend on training and age at lesion strengthen the extrastriate cortical activation, shrinkage or thinning out of the blind field might ensue.

The sight in blindsight

Patient GY was already mentioned in the section "Blindsight and plasticity". He suffered his lesion when he was 8 years of age. This relatively early lesion should, together with his long-lasting and intensive experience with testing his hemianopic field, predestine him for a recovery of at least some conscious vision, if that is possible when just a small macular sparing remains of the affected hemifield. In fact, and despite his often, and somewhat unfortunately, being referred to as a blindsight subject, GY has been known to acknowledge awareness of stimuli for a long time. Indeed, Barbur et al. (1980) already mentioned that he sees "dark shadows" in response to flashed targets, and entitled a later positron emission tomography (PET) study of GY "Conscious visual perception without V1" (Barbur et al., 1993). However, GY has not only used visual terms such as "dark shadows" to describe his sensations, but also denied "seeing" the stimuli he detected, discriminated, and acknowledged to be aware of. It is on the basis of studying this subject that Weiskrantz (1998) suggested a distinction of blindsight type I and II; type I is the original form of blindsight which is observed in the absence of acknowledged

awareness, whereas type II allows for "nonvisual" awareness of visual stimuli. Nonvisual, abstract rather than phenomenal awareness is not experienced in normal veridical vision; therefore, if GY's hemianopic visual functions were indeed "nonvisual" in this sense, visual stimuli presented to his normal field should not evoke a similar type of awareness. Arguing that a perceptual match, if it existed, would show that his hemianopic vision was visual, Stoerig and Barth (2001) attempted to find a stimulus condition which when presented to GY's normal hemifield would evoke the same kind of sensation that more prominent stimuli evoke in his hemianopic field. Having presented a series of degraded stimuli to the good field which GY always discarded upon first sight as being "visual", we eventually hit upon a match when we presented a moving bar not defined by luminance contrast but by coherent shifts in a grainy texture (see <www.ebarth.de/demos/gy>). Comparing this stimulus in the good field to a moving luminance-defined bar in the hemianopic field produced not only a perceptual match, but also closely similar discrimination performance (Stoerig and Barth, 2001). We concluded that GY has some type of low-level phenomenal vision rather than abstract conscious access (Block, 1995) in his affected hemifield.

As none of the functional neuroimaging studies in which he participated (Barbur et al., 1993; Sahraie et al., 1997; Zeki and ffytche, 1998; Baseler et al., 1999; Goebel et al., 2001) produced any evidence for activation within his lesioned V1, GY's vision in the hemianopic field must — at least as far as this conclusion is warranted when no pathological data are available — be mediated by the extra-geniculo-striate cortical pathways. If, as argued above, the strength of the extrastriate activation was important for the conscious rendering of stimuli, GY ought to show relatively strong patterns of activation in response to targets presented to his hemianopic field. This expectation gained support when a stronger response was observed in GY's motion complex when he discriminated the direction of a single moving dot in his hemianopic field in his "aware" rather than "unaware" mode (Zeki and ffytche, 1998). In addition, the ipsilesional activation that occurred in roughly the same region when the red-and-blue spiral was presented to GY's hemianopic field was remarkably strong not only when compared to that evoked by presenting the same stimulus to the good field, but also to data from other patients (Goebel et al., 2001; see also Fig. 4). Both findings agree with the hypothesis that the strength of extrastriate cortical activation is at least one of the critical factors determining whether or not a stimulus is consciously represented.

More evidence for a route to extrastriate cortex that bypasses V1 comes from a study of a different patient who suffered a stroke at an age of 19 (Schoenfeld et al., 2002). Like GY, this patient performed above chance in motion and color change experiments, and reported perceiving moving objects in his affected hemifield. Presentation of motion and color change stimuli in the hemianopic field during functional neuroimaging yielded pronounced activation in ipsilesional extrastriate cortical regions, although even at low threshold ($p < 0.1$) no activity was detected within the lesioned V1, and magnetoencephalography revealed earlier stimulus-locked responses in hMT+ than in V2.

Our own data on a patient, who suffered a stroke in the territory of the posterior cerebral artery when he was 58 years, both confirm and extend these results. HK's ipsilesional motion complex responded to moving blind field stimuli already within 3 months of his lesion when no color-evoked responses could be detected (see Fig. 4). A year and regular weekly tests later, his ipsilesional ventral cortex also responded to color. It is probably safe to assume that the blindsight training contributed to this change despite his higher age at lesion. Moreover, HK also increasingly reports receiving "signals" from his hemianopic field, and performs at >90% correct in some tasks (but not others).

Blindsight and recovery

While these three patients — GY, HK, and Schoenfeld et al.'s patient — appear to have recovered some more or less low-level vision in large regions of their hemianopic fields, shrinkage of the

blind field has been observed in others. Zihl and von Cramon (1985) reviewed 55 cases of patients who had undergone systematic localization training, and reported that this led "in the majority of patients, to an enlargement of the visual field" (p. 335). Like Sabel and colleagues who trained their patients specifically along the borders between the normal and the blind field (Kasten et al., 1998a), the authors attribute the enlargement to recovery of reversibly damaged striate cortical tissue (Kasten et al., 1998b). While both groups have reported specific effects in the trained regions, our own blindsight training rather seems to produce shrinkage of the absolute portion of the defect from the periphery inwards (see Stoerig, 1998). A remarkable case is that of patient FS whose trauma-induced damage destroyed the temporal lobe and deprived the visual cortex of its afferents. This caused a hemianopia that had already become incomplete, albeit with macular splitting, when I first saw him several years after his accident. He continued to participate in experiments (see Pöppel, 1985, 1986; Stoerig, 1987; Goebel et al., 2001, for examples), and now presents with a strip of homonymous blindness extending along the horizontal meridian. This strip is still broadest in the central hemifield, but remarkably, the vision that slowly returned over the years has become normal in the recovered regions above and below (Fig. 8).

Together, these results demonstrate not only that the visual system is capable of remarkable plasticity, but also that different mechanisms are likely to mediate the different types of recovery.

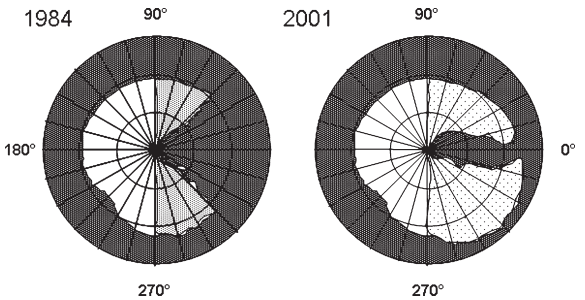

Fig. 8. Visual field plots of patient FS are based on a combination of dynamic and static perimetry using a 116 in., 320 cd/m^2 white target on a 10 cd/m^2 white background.

These range from the recovery of low-level vision within largely unchanged defective field borders to shrinkage of the blind field in stimulated regions or in extensive, predominantly peripheral portions of the defect. Striate cortex is very likely involved when it is still available, and may enable recovery of visual awareness that more closely resembles that of normal vision. However, the low-level conscious visual functions seen in Scheonfeld et al.'s patient, in GY, and in HK appear to be possible without a contribution from ipsi- or contralesional V1. Thus, V1 does not seem necessary for the recovery of some low-level vision. Probably the most remarkable case to date is that of FS, where visual stimulation of the recovered visual field produced only extrastriate cortical activation (Kleiser et al., 2001). How the brain's plasticity is engaged to invoke these changes, and how they can best be strengthened and harnessed to serve recovery of vision, requires further investigation.

Conclusion

Although the controversies regarding the role of V1 in conscious vision are bound to continue, a large body of data from monkeys and human patients demonstrates that blindsight does not depend on surviving islands of striate cortex. Furthermore, varying degrees of conscious vision can return to previously absolute fields of blindness. This not only is true within weeks or months postlesion, but can evolve in a long-term process that, like blindsight, seems to depend on challenging the system's plasticity by forcing the subject to respond to blind field targets. While striate cortex will be involved whenever the lesion allows it, the brain's plastic capacities allow functional improvements even when V1 is destroyed or denervated and the lesion occurs late in life.

Abbreviations

dLGN	dorsal lateral geniculate nucleus
V1	primary visual cortex or striate cortex
V2	second visual cortical area
V3, V4, V5	extrastriate visual cortical areas
MT (= V5)	middle temporal area

hMT+	human motion complex that includes adjacent motion-sensitive areas like MST and FST
RDK	random dot kinematogram

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