NEUROPSYCHOLOGICAL REHABILITATION
2006, 16 (4), 377–396

Psychology Press
Taylor & Francis Group

Visual restoration in cortical blindness: Insights from natural and TMS-induced blindsight

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Unilateral damage to visual cortex of the parietal or occipital lobe can cause the patient to be unaware of contralesional visual information due to either hemispatial neglect or hemianopia. It is now known that both neglect and hemianopia result from the disruption of a dynamic interaction between cortical visual pathways and more phylogenetically primitive visual pathways to the midbrain. We consider the therapeutic implications of these cortical–subcortical interactions in the rehabilitation of hemianopia. We start with the pheonmenon of "blindsight", in which patients with hemianopia can be shown, by implicit measures of visual detection or discrimination, to process visual information without conscious awareness. Some variants of blindsight have been postulated to recruit subcortical processes, while others may reflect compensatory optimisation of processing of spared visual cortex. Both mechanisms may offer opportunities for innovative strategies for rehabilitation of visual field defects. We relate the neural mechanisms that have been proposed to underlie blindsight to those that have been suggested to underlie the recovery of visual function after rehabilitation. It is suggested that the similarity and overlap of the neural processes supporting blindsight and recovery of visual function might provide insights for effective rehabilitation strategies for restoring visual functions.

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http://www.psypress.com/neurorehab DOI:10.1080/09602010500435989

INTRODUCTION

In this article, we use the term unawareness to refer to the lack of a subjective perceptual experience of a visual event, regardless of whether or not that event has been processed by the visual system. Metaphorically, and along the lines of various models of consciousness that have been advanced, visual information that we are unaware of is therefore information that is not on a global workspace, is not on the stage of a Cartesian theatre, or does not have fame in the brain (Dehaene & Naccache, 2001; Dennett, 2001). Unilateral damage to the primary visual cortex, or to the visual association cortex, often causes the patient to become unaware of contralesional visual information because that information is no longer processed by neural structures essential for the generation of visual awareness.

Lesions of posterior association cortex frequently cause the syndrome of hemispatial neglect. Unawareness, in this case is due to inattention. The loss of awareness is not sharply demarcated in retinotopic co-ordinates but, rather, is contralesional to the focus of attention—regardless of where the unattended object is in the visual field (Behrmann & Moscovitch, 1994; Behrmann & Tipper, 1994; Driver, Baylis, & Rafal, 1993; Driver & Halligan, 1991; Posner, Walker, Friedrich, & Rafal, 1987). By contrast, complete destruction of the primary visual cortex (or geniculostriate afferents in the optic radiations) results in hemianopia. Since the primary visual cortex in the occipital lobe, which receives the majority of retinal efferents via the lateral geniculate nucleus of the thalamus, is retinotopically organised (Holmes, 1918; Hubel & Wiesel, 1977; Tootell, Silverman, Switkes, & De Valois, 1982), focal lesions to any given part of it lead to a corresponding retinotopically determined scotoma (Holmes, 1918).

Under certain circumstances, distinguishing between neglect and hemianopia can prove challenging. Assessments and diagnoses of patients may also be complicated by the fact that many patients may present with both neglect and hemianopia or may have a complex form of a visual disorder that may be a hybrid between the two (e.g., see case report by Nadeau & Heilman, 1991). Nonetheless, some differences are typically apparent between patients with a pure hemianopia and a pure form of neglect. With confrontation testing, for example, both neglect as well as hemianopic patients will systematically miss visual events presented to their contralesional fields. However, patients with neglect will more frequently miss a contralesional visual stimulus when presented simultaneously with an ipsilesional one. Furthermore, detailed neuropsychological testing can be utilised to reveal several other visual performance differences between these types of patients. Whereas neglect patients will fail to explore and detect lines or objects on the contralesional side of space, hemianopic patients can compensate for their deficit by moving their eyes contralesionally to bring previously undetected stimuli

into their seeing field. Performance of neglect and heminopic patients on line bisection tasks also clearly differs, usually with only neglect patients showing ipsilesional biases on bisection performance (Halligan & Marshall, 1988; but see Ferber & Karnath, 2001).

Hemianopia and neglect also differ in terms of their prognosis for recovery and compensation. While most patients with hemispatial neglect improve, and many recover, hemianopia is usually permanent. Nevertheless, patients with hemianopia often compensate spontaneously (Zihl, 2000)—and a persistent hemianopia is less disabling than persisting neglect. This is, perhaps, surprising when one considers that, unlike hemianopia in which damage to primary visual cortex completely eliminates the processing (even unconscious processing) of all but the most simple visual features, this is not the case in patients with hemispatial neglect. Indeed, it has been shown that in spite of the dramatic exclusion from consciousness of neglected stimuli, perceptual processing of them can proceed to the level of semantic classification (Berti & Rizzolatti, 1992; McGlinchey-Berroth et al., 1993) and that preattentive vision parses the scene to extract figure from ground (Driver et al., 1993), group objects and define their primary axes (Driver, Baylis, Goodrich, & Rafal, 1994), and prioritize the location of objects that are not perceived consciously for subsequent orienting (Danziger, Kingstone, & Rafal, 1998). Indeed, not only is semantic information encoded outside of awareness, but it has been shown that selection for awareness occurs at the latest stage of information processing just prior to response (Baylis, Driver, & Rafal, 1993; Rafal et al., 2002).

By contrast, hemianopic deficits traditionally had been considered to be complete and irreversible in humans. Even in selected patients in whom processing without awareness has been demonstrated (we consider this phenomenon of blindsight later), it has for the most part been limited to processing only of simple visual features. Nevertheless, studies in non-human primates have shown evidence of some recovery of function with experience and training (Cowey, 1967; Mohler & Wurtz, 1977). Here we describe some of the mechanisms that may be responsible for the demonstrated recovery of visual function in humans and focus on the mechanisms responsible for blindsight and the potential for exploiting them therapeutically in rehabilitating visual function after damage to the occipital cortex.

Restoration of vision after cortical blindness: The Sprague effect

A cardinal principle guiding rehabilitation is that lesion-induced deficits may not be understood simply in terms of the absence of a putative function that is normally mediated by the lesioned tissue. Rather, the pathological behaviour reflects the re-organisation of dynamic interactions of the region with other interconnected structures. In the case of blindness due to lesions of visual

cortex, we need to consider the remote effects of the lesion on midbrain visual circuits. The geniculostriate pathway is a recent development in evolution, emerging only in mammals. In sub-mammalian vertebrates, all visual input to the brain is via the optic tectum of the midbrain. This pathway mediates reflexive orienting—the visual grasp reflex—to visual signals and the basic processing of visual stimuli.

In mammals the optic tectum is referred to as the superior colliculus (SC); and the fact that visual cortex lesions cause complete loss of visual awareness indicates that the retinotectal pathway, in humans, does not normally mediate conscious visual experience. Nevertheless, the primary visual cortex is directly connected to the SC, and the parietal lobes are connected to it via the pulvinar nucleus of the thalamus. Loss of visual awareness after lesions of either primary visual cortex or visual association cortex reflects dysfunction throughout this cortico–subcortical network.

Sprague first demonstrated that visual orienting is mediated by a dynamic interaction between the cerebral cortex and the midbrain pathways for reflexive orienting (Sprague, 1966). In a classic experiment, cats were rendered blind in one visual field by unilateral extirpation of occipital and parietal cortex. It was then shown that orienting towards the contralesional field was restored if the opposite superior colliculus was removed. This finding indicates that loss of vision after lesions of visual cortex reflects dysfunction not only of the damaged cortex, but also the remote disruption of subcortical visual pathways that might otherwise afford some recovery of visual function. This pioneering work gave us the first clues to how recovery from blindness might be facilitated.

Two approaches to rehabilitation of blindness due to lesions of visual cortex

This review focuses on the recovery of vision in heminaopia, and considers two potential strategies. The first is to optimise function of the unlesioned subcortical pathways through procedures that facilitate or release the subcortically mediated visual grasp reflex—thereby bringing the stimulus to the sighted region of the fovea. This might be termed the "bottom-up" approach. The second strategy is to train patients to strategically search into the region of the scotoma—the "top-down" approach.

We begin by considering the phenomenon of "blindsight"—the demonstration of visual processing in the absence of awareness—and then consider how this phenomenon might inform rational approaches to rehabilitation.

BLINDSIGHT IN HEMIANOPIC PATIENTS

Blindsight refers to the above chance performance of cortically blind patients on forced-choice visual discrimination tasks despite being unaware of the

visual stimulation (for review, see Stoerig & Cowey, 1997; Weiskrantz, Warrington, Sanders, & Marshall, 1974). Patients with blindsight can, for example, accurately localise visual stimuli with hand or eye movements and/or discriminate different types of visual events (e.g., shape, wavelength) well above chance, but without any awareness.

Three major explanations have been postulated for this residual vision. These are not mutually exclusive; each may apply in some patients but not in others (Morland et al., 2004):

1. Extrageniculate mediation through subcortical pathways. Visual information transmitted through the retinotectal pathway, or some other subcortical pathway (e.g., retino-pulvinar (Williams, Azzopardi, & Cowey, 1995), is projected to extrastriate visual cortex, and is sufficient to drive visually guided behaviour without awareness. Based on the demonstration of accurate localisation with saccadic eye movements, a function that involves oculomotor processes of the superior colliculus, it has been suggested that the retinotectal or secondary visual pathway may mediate some residual visual functions in patients exhibiting blindsight (Perenin & Jeannerod, 1975; Poppel, Held, & Frost, 1973; Weiskrantz et al., 1974). Furthermore, the retinotectal pathway projects through the pulvinar into the dorsal stream of the extrastriate cortex (Kaas & Huerta, 1988), which has been suggested to be involved with vision for action in the absence of awareness (Goodale & Milner, 1992; Milner & Goodale, 1995). Consistent with this anatomy, in addition to generating accurate visually guided saccades to unseen targets, patients with visual field deficits and blindsight have also been shown to accurately point towards visual stimuli presented within their scotoma (Blythe, Kennard, & Ruddock, 1987; Perenin & Jeannerod, 1975, 1978; Weiskrantz et al., 1974).

2. Geniculoextrastriate mediation. Direct projections from the lateral geniculate to extrastriate cortex may be sufficient for some visual discrimination—and even for some "sensation" that patients do not experience as actually "seeing". This mechanism has been postulated, for example, to mediate some discrimination of wavelength, since collicular neurons do not have colour opponency (Stoerig & Cowey, 1989, 1991). This mechanism also may account for the Riddoch effect (Sincich, Park, Wohlgemuth, & Horton, 2004)—a sensation of motion that some hemianopics report (Zeki & Ffytche, 1998).

3. Partial sparing of primary visual cortex, with sufficient preservation of cortical processing for stimuli to reach objective but not subjective threshold. (Fendrich, Wessinger, & Gazzaniga, 1992; Wessinger, Fendrich, & Gazzaniga, 1997). This explanation, positing "islands" of spared cortex, has

been ruled out in some blindsight patients based on behavioural/perimetric (Kentridge, Heywood, & Weiskrantz, 1997) and neuroimaging (Barbur, Watson, Frackowiak, & Zeki, 1993; Stoerig, Kleinschmidt, & Frahm, 1998; Zeki & Ffytche, 1998) findings, but may nonetheless be responsible for blindsight in some patients.

Whether blindsight may be due to superior colliculus function or remnants of spared cortex, or some combination thereof, there is one clear difference between these two accounts of blindsight: while only a small minority of patients with occipital cortex damage may have some sparing of cortical tissue, the majority of patients with occipital cortex damage, including those with spared cortex, have intact superior colliculi. Therefore, according to the retinotectal account, most patients should exhibit blindsight, but the reported prevelance of it has traditionally been relatively rare (Blythe et al., 1987; Marzi, Tassinari, Aglioti, & Lutzemberger, 1986). However, a more recent study in progress with a larger group of patients and with more extensive probes for unconscious processing suggests that the majority of patients may have blindsight (Sahraie, personal communication), providing some support for a retinotectal account of blindsight.

Despite claims of cortical involvement in blindsight, and even though not all patients with visual cortical damage may exhibit it, there has been a large body of evidence implicating superior colliculus involvement in different forms of blindsight. For example, Rafal et al. (1990) tested three patients, each with a dense homonymous hemianopia, to examine whether extrageniculate vision may be responsible for unconscious processing (i.e., blindsight). In that study, the patients made saccadic eye movements or manual button-press responses under monocular conditions to seen targets on the ipsilesional side of space. On half of the trials, a distractor was presented in the contralesional, blind hemifield. Although the patients never reported seeing these distractors in their blind hemifield, their saccadic latencies to the seen target were significantly delayed in comparison to the no distractor trials (see Figure 1). Furthermore, this effect was more robust for distractors in the temporal hemifield, which has more projections into the superior colliculus than the nasal hemifield (but see Williams et al., 1995). Based on this asymmetry, as well as the known contributions of the superior colliculus in generating saccadic eye movements (Kaas & Huerta, 1988; Munoz & Wurtz, 1995; Posner & Cohen, 1980; Robinson & McClurkin, 1989), it was concluded that the retinotectal pathway leading to the superior colliculus was involved with the unconscious processing of distractors. A more recent study, however, failed to replicate this unconscious distractor effect in a larger group of hemianopic patients (Walker et al., 2000), suggesting that this indirect measure of blindsight may not be as robust and detectable in all patients with visual cortex damage and sparing of the superior colliculus.

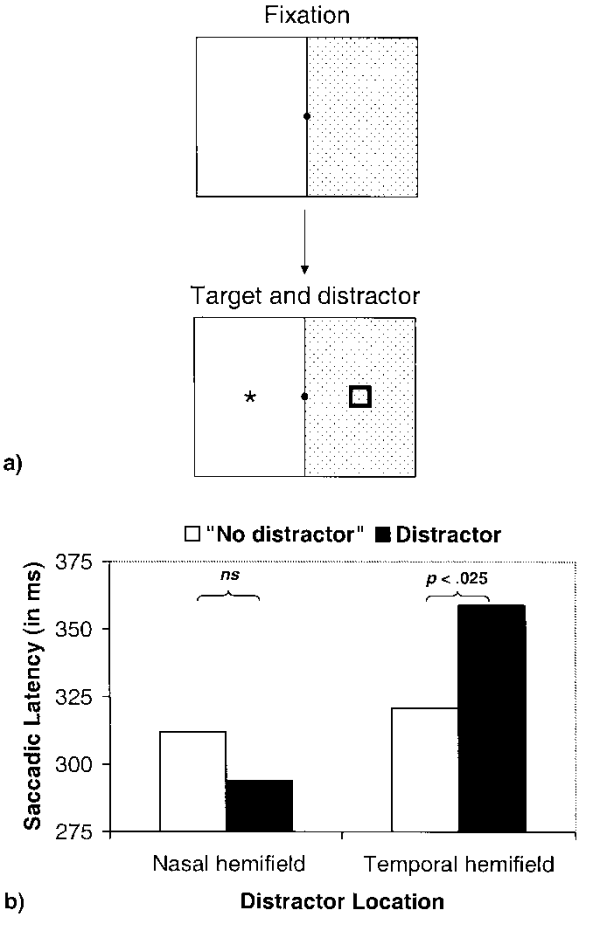


Figure 1. (a) The stimuli used in the study by Rafal et al. (1990) examining the effects of unseen remote distractors on target responses in hemianopic patients. Following fixation, the patients were asked to move their eyes to a target presented in the normal hemifield while distractors were presented in the blind hemifield depicted here by the stippled region. (b) The saccadic latencies for conditions with distractors in the nasal (left) and temporal (right) hemifields averaged across three patients. Note that the "no distractor" trials contained a distractor that was presented after the saccade was made.

Furthermore, using a similar type of task, but only requiring a button press response rather than a localisation task, Marzi and colleagues demonstrated a redundancy gain (i.e., faster simple detection responses to targets in the good hemifield when a simultaneous stimulus was placed in the hemianopic hemifield), but only in a small proportion of patients (Marzi et al., 1986; Tomaiuolo et al., 1997). This facilitation from unseen redundant stimuli

also has been proposed to be a function of subcortical mechanisms. However, if such were the case, it is again unclear why not all patients with visual cortex damage show this redundancy gain effect. One possibility may be that with stimuli presented into a scotoma of a patient, there are both inhibitory (i.e., distractor effects) in addition to facilitatory (i.e., redundancy gain) effects and the net results of slower or faster reaction times may be dependent on the task, with some tasks showing the former, whereas others showing the latter or a null effect.

Additional evidence for retinotectal involvement in blindsight, and validating the naso-temporal asymmetry as a marker for collicular mediation, was demonstrated in a different type of target localisation task by Dodds and colleagues (Dodds, Machado, Rafal, & Ro, 2002). This study examined a patient with a homonymous hemianopia as a result of visual cortex damage from a stroke. In a forced-choice location discrimination task, the patient demonstrated a higher proportion of correct verbal guesses of the location of visual targets (i.e., more blindsight) when the target stimuli to be discriminated were projected to the temporal hemifield under monocular viewing conditions as compared to nasal hemifield conditions. This result is important in that it suggests that retinotectal function may be assessed in non-oculomotor tasks (i.e., without saccadic eye or reaching hand movements) and may have the ability to influence verbal reports and awareness.

EXPLORATION OF BLINDSIGHT USING TRANSCRANIAL MAGNETIC STIMULATION

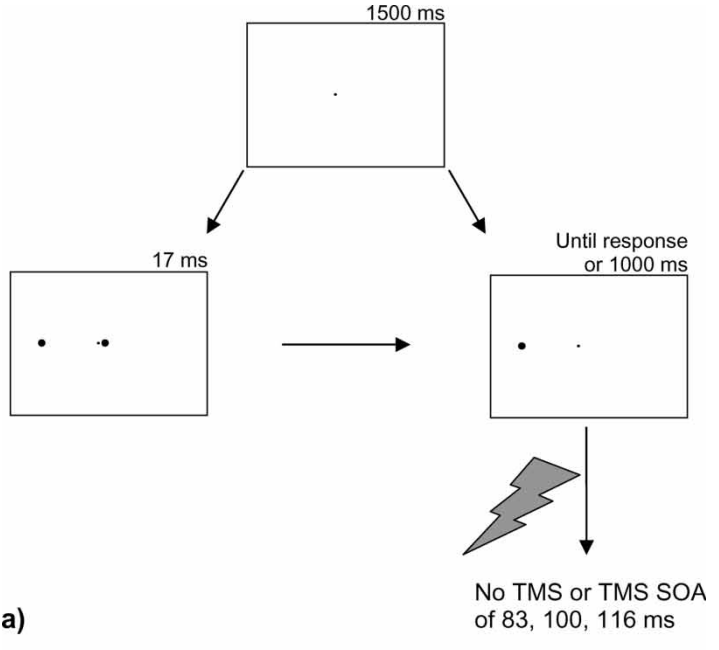
Inconsistencies of blindsight in studies of hemianopic patients may have to do with methodological differences, patient selection, or many other potential factors. We have been examining whether transcranial magnetic stimulation (TMS) (for reviews on TMS, see Hallett, 2000; Jahanshahi & Rothwell, 2000; Robertson, Theoret, & Pascual-Leone, 2003; Walsh & Cowey, 2000) might be used to consistently induce blindsight-like behaviour in normal observers. If possible, these TMS-induced visual dysfunctions might provide an additional and converging means for studying blindsight. Further, because the extent and chronicity of the "virtual" lesion created by TMS is under experimental control, extraneous factors such as diaschesis and/or reorganisation of brain function would play minimal roles in any measured blindsight effects.

In the first study, the unconscious distractor effect paradigm used by Rafal et al. was modified and adapted so that TMS could be used to induce a transient blindness of the distractor in otherwise normal seeing observers (Ro, Shelton, Lee, & Chang, 2004). Since the TMS pulse primarily affects cortical surface structures rather than deeper tissue, the extent of the

scotoma induced by TMS is limited to approximately 1 degree of visual angle in the fovea. In these studies, saccadic eye movements or manual button presses were made to targets appearing in one of four peripheral locations (see Figure 2). On the critical trials, a TMS pulse was given that induced visual suppression of a near foveal distractor. When the participants were unaware of these distractors, as assessed after each trial, we found that saccadic eye movement latencies were nonetheless delayed by these unconscious distractors. Importantly, this unconscious distractor effect was not present when the participants were making indirect button press responses on a keypad placed in front of them. Thus, a form of blindsight was induced with TMS and was similar to that observed in patients with naturally occurring lesions.

In another TMS study, we have also demonstrated spared discrimination processes independent of saccadic eye movements (Boyer, Harrison, & Ro, 2005). In both experiments of this study, the visual cortex was first localised with TMS by finding a coil position on the posterior brain that, when stimulated, induced a transient scotoma. After visual cortex localisation, participants were asked to judge the orientation of a bar in one experiment or the colour of a disk in the other experiment, each of which was presented within the scotoma. The participants were asked to only report that the orientation of the bar or the colour was perceived when he or she was aware of the orientation or colour of the stimuli. Otherwise, the participants were asked to guess the orientation of the bar or the colour of the disk and to provide a confidence rating. Our results showed that even though the participants were unaware of the orientation or colour of the stimulus, they nonetheless guessed significantly above chance on the orientation of the bar and the colour of the disk. Interestingly, some of our participants reported "having a sense" of the orientation of the bar much like patients with Type II blindsight who often "felt" that something was presented, but were unable consciously to perceive it (cf., Poppel et al., 1973; Weiskrantz et al., 1974; Zeki & Ffytche, 1998). Perhaps as a consequence of this sense or feeling, confidence ratings in our experiments were highly correlated with their accuracy performance on these judgement tasks, suggesting that their subjective experiences may have been influenced by unconscious processes.

These TMS results demonstrating spared orientation and colour processing without primary visual cortex demonstrate that TMS can be used to induce more traditional forms of blindsight (i.e., above-chance discrimination) and provide further support for the existence of a geniculoextrastriate pathway that bypasses V1 and awareness (Sincich et al., 2004; Stoerig & Cowey, 1989, 1991). Since both orientation and colour cannot be effectively discriminated by the superior colliculus, the most plausible pathway supporting these visual discriminatory behaviours without V1 and awareness may be a direct



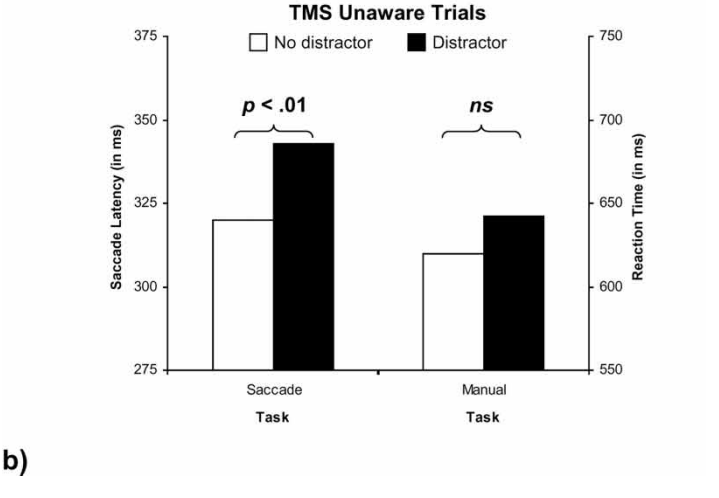


Figure 2. (a) The stimuli used in the TMS study by Ro et al. (2004) examining the effects of unseen distractors on target responses. On half of the trials, a distractor was presented along with the peripheral target (downward left arrow), whereas on the other half of the trials no distractor was presented (downward right arrow). (b) The saccadic latencies for trials with unconscious distractors were significantly slower than trials without a distractor, but no difference was measured in the manual button press task.

geniculate pathway into area V4 of extrastriate cortex, which contains a high proportion of feature-selective and colour-opponent cells (Desimone, Schein, Moran, & Ungerleider, 1985; Gallant, Braun, & Van Essen, 1993; Zeki, 1980). Along with previous anatomical tracer studies that have provided evidence for the existence of this lateral geniculate nucleus to V4 pathway (Fries, 1981; Yukie & Iwai, 1981), our results suggest that this pathway may also play a functional role in direct visual stimulus attribute processing without any awareness.

Taken together, these studies using TMS and patients with visual cortical damage strongly suggest that intact retinotectal and/or geniculoextrastriate functioning may be crucial and responsible for some forms of blindsight. These findings further suggest that recruitment or training of these retinotectal and/or geniculoextrastriate pathways may be advantageous in the restoration of visual function after primary visual cortex damage. As most patients with visual cortex damage and resulting cortical blindness will have an intact superior colliculus, it might be possible to train or encourage patients to advantageously utilise their retinotectal functions, and perhaps even remnant extrastriate processes when still intact, to enhance visual awareness.

RETINOTECTAL FUNCTIONS VS. REORGANISATION/ RECOVERY OF VISUAL CORTEX

Based on this selective review of blindsight, we now consider its therapeutic implications; specifically, that the mechanisms supporting blindsight may also be promoted to rehabilitate and restore some vision after visual cortex damage. Studies in non-human primates suggest that the mechanism for the recovery of visual function after damage to the primary visual cortex may be a function of the superior colliculus in the midbrain (Mohler & Wurtz, 1977; Zihl & von Cramon, 1979). Mohler and Wurtz, for example, demonstrated recovery of visual orienting to stimuli presented within a practised region of a surgically induced scotoma in monkeys. Subsequent to this recovery, a lesion placed in the homologous visual representation of the ipsilateral superior colliculus eliminated this recovery effect. This demonstration of reorganisation and restoration of visual function in monkeys, as well as findings suggesting superior colliculus contributions to blindsight (see above), suggest that similar reorganisation might be seen in humans after occipital cortex damage, despite the notions that recovery of visual function is unlikely due to the hard-wired nature of the visual system.

Interestingly, a subset of patients with blindsight report being subjectively aware of the presence of some visual information, but do not experience any visual phenomena. This form of blindsight, referred to as Type II blindsight (e.g., see Cowey, 2004), may indicate that some patients may be able to

access and interpret some of the unconscious processing of visual information and consequent behaviours through other visual processing mechanisms, such as the coding within the superior colliculus for reflexive eye movements towards "unseen" events. Thus, training patients to compensate for their visual deficits by relying on known properties of the extrageniculostriate pathways may prove to be a fruitful endeavour for restoring visual loss. Although there have been many attempts at rehabilitating cortical blindness, including what we refer to as peripheral techniques, such as the use of prisms to redirect light from blind regions of space (Peli, 2000; Rossi, Kheyfets, & Reding, 1990), our focus here is on the rehabilitation of visual function through central means and their relations to blindsight. Specifically, we focus on the methods that have examined the rehabilitation of visual function by attempts to induce the reorganisation and/or utilisation of different brain structures and functions with training or instruction.

The earliest approaches to restitution were based on bottom-up stimulation, in which detection or eye movement responses were made to visual signals presented in the blind field. One form of visual field loss rehabilitation examined by Zihl involves repeated stimulation within and specifically near the borders of blind regions of a patient's scotoma (Zihl & von Cramon, 1979). Another form of rehabilitation employs saccadic eye movement training (Kerkhoff, Munssinger, & Meier, 1994; Zihl, 1980, 1981; Zihl & von Cramon, 1985). Patients are repeatedly presented with visual targets within their scotoma and are instructed to generate saccadic eye movements to these "unseen" targets. As mentioned above, the ability of patients with visual field deficits as a consequence of post-geniculate damage to make accurate saccadic eye movements has been repeatedly demonstrated (e.g., see Poppel et al., 1973, and the above section on blindsight; Weiskrantz et al., 1974). This may involve the recruitment of the superior colliculus in the visual processing of stimuli presented within the scotoma. Interestingly, this repeated saccadic eye movement or localisation training leads to increases in perimetric maps of visual field size. Thus, by perhaps promoting the use of retinotectal vision, visual field sizes may be increased. As with the rehabilitation techniques involving repeated stimulation and detection of peripheral targets placed in the scotoma (see below for more details), however, eccentric fixation may also be responsible for the reported perimetrically measured visual field increases following this form of training.

Kasten, Sabel, and their colleagues have reported a new method of potentially rehabilitating visual loss using what they refer to as visual restitution training (Kasten, Poggel, & Sabel, 2000; Kasten, Wust, Behrens-Baumann, & Sabel, 1998). Conveniently for patients as well as therapists, these training procedures are implemented on standard computers and can be done in the comfort of the patient's own home. The technique presents a stimulus, dynamically changing in size, near the fovea in the sighted visual field. The

stimulus is slowly moved across the midline until it disappears in the scotoma. The disappearance is signalled by the patient, at which point the stimulus is moved back into the sighted field; and the process successively repeated. By systematically working at the boundaries of the scotoma, it was shown that the boundary of the scotoma could be moved and the field of vision expanded. In a subsequent study, the effects were shown to generalise to chromatic stimuli (Kasten et al., 2000).

It has been suggested that these types of rehabilitation procedures involving stimulation of blind regions in a patient's visual field, especially the borders, leads to increased sensitivity in detecting the presence of lights within the trained region by restoring the function of cortical tissue, such as islands of spared cortex (Fendrich et al., 1992; Wessinger et al., 1997), or in this particular case the shores of dysfunctional tissue surrounding the lesion. Unfortunately, however, this restoration of vision has been questioned, inconsistent, and simply may be a consequence of eccentric fixations or other methodological shortcomings (e.g., see Balliet, Blood, & Bach-y-Rita, 1985) or may only be possible in certain types of patients (Pambakian & Kennard, 1997). Furthermore, it is unclear whether these presumed expansions of visual fields for simple detection of stimuli might provide lasting functional benefits and improvements in more complex, real-life visual tasks.

Although more recent studies have attempted to control fixation by implementing tasks at fixation (Kasten et al., 1998, 2000), many of these tasks involve the detection of a change in colour of the fixation point, which is sufficiently simple and could likely have been accurately performed with modest degrees of eccentric fixation. Furthermore, since the restorative effects were much more pronounced when the patients knew where the targets would appear, and the recovery expanded the borders by an average of only a few degrees, fixating a position a few degrees towards the scotoma might well be responsible for the seemingly expanded visual field while also still allowing for accurate performance on the central "fixation" task. These highly promising techniques therefore require further verification with systematic means of measuring and controlling fixation (e.g., by using a Purkinje eye tracker and image stabilisation methods as in the studies by Fendrich and colleagues, 1992).

Schendel and Robertson (2004) demonstrated increases in visual field size and detection when a hemianopic patient placed his arm near the visual stimuli. Their patient with a homonymous hemianopia was better able to detect visual targets when his contralesional hand was placed near the source of visual stimulation. Studies in non-human primates demonstrate visual fields of cells in premotor cortex that are anchored to the hand (Graziano, Yap, & Gross, 1994). This finding suggests that projections to the premotor cortex, perhaps through the superior colliculus and dorsal processing stream, may be involved with the increased detection with an

outstretched hand. Although a central target detection task was required in an attempt to ensure fixation, eye movements were not directly monitored and image stabilisation methods were not used, as with the studies by Kasten and colleagues. Thus, it is also unclear whether Schendel and Robertson's results might have been due to eccentric fixations that were larger when the contralesional hand was outstretched in space. The less than perfect accuracy rates on the central fixation task suggest that deviated gaze may have played some role in their effects.

The studies reviewed thus far may all be considered "bottom-up" strategies in which visual (and proprioceptive in the case of Schendel & Robertson, 2004), stimulation is used to "pull" the patient's attention and eye movements into the scotoma. Most rely on a collicularly mediated visual grasp reflex. However, subcortical pathways may not be spared in some patients; another approach is then needed. Pambakian et al. (Pambakian & Kennard, 1997; Pambakian, Mannan, Hodgson, & Kennard, 2004) used a visual search task that encourages patients to strategically explore their blind field to find a specific visual feature in a cluttered display. Not only did search performance improve after training in many patients, there was also a demonstration of sustained improvement in tasks of daily living.

One of us (Rafal) has had the opportunity to observe the effectiveness of this approach in a patient treated by Sophie Hayward and Carolyn Young in conjunction with Alidz Pambakian. This 29-year-old woman had sustained a severe traumatic brain injury 12 years earlier. She posed an unusual clinical challenge that highlights the importance of tailoring therapy based on the particular circumstances of each individual patient. Hemiparesis and diplopia had recovered, but she was left with persistent hemianopia—for which she had not compensated at all, and which left her with severe visual disability. A magnetic resonance imaging scan revealed that there was not only occipital lobe damage, but also lesions in the pulvinar nucleus of the thalamus and the dorsal midbrain. This case is instructive in demonstrating that subcortical pathways are involved in spontaneous compensation for hemianopia. Given subcortical damage in this patient, it seemed unlikely that a "bottom-up" strategy (e.g., saccadic training) would be effective. She was treated using the protocol developed by Pambakian and Kennard (1997) and showed gratifying improvement in her visual capabilities in everyday activities.

SUBCORTICAL CONTRIBUTIONS TO BLINDSIGHT: IMPLICATIONS FOR VISUAL REHABILITATION

The projections into the superior colliculus continue on through the pulvinar into the dorsal visual processing stream of the brain (Goodale & Milner,

1992; Kaas & Huerta, 1988; Milner & Goodale, 1995). Thus, by training patients to generate saccadic eye or reaching hand movements into the scotoma, the patients might frequently detect targets with a considerable degree of accuracy and may even allow the patients to become aware of stimuli within their impaired visual field. Consistent with this notion, the accuracy in localising targets with saccadic eye movements only becomes possible in some patients when the patients are explicitly made aware of this possibility (Zihl, 1981). Thus, restoration of vision may be more prominent if patients are not only made aware of this possibility, but may also prevent the formation of learned nonuse (Ro et al., in press; Taub, Harger, Grier, & Hodos, 1980; Taub, Heitmann, & Barro, 1977), which occurs when patients attempt to compensate for deficits by relying only upon intact function, such as with frequent head movements or eye movements into the blind region for conscious visual processing. In the case of visual cortex damage, patients with visual field loss may experience learned nonuse of their extrageniculate vision due, perhaps, to the initial lack of conscious awareness of the processing occurring in spared visual areas of the brain. However, instructions to the patients to attempt to process and guess about information within their blind hemifields may be highly beneficial for inducing some recovery of vision.

In addition to being involved with oculomotor function and likely responsible for various blindsight phenomena, the superior colliculus has also been demonstrated to be directly involved with the reflexive orienting of attention (Kustov & Robinson, 1996; Rafal et al., 1988; Robinson & Kertzman, 1995). A study of one hemianopic patient has demonstrated an intact inhibition of return (IOR)—a delay in detecting visual targets at previously cued locations that has been suggested to influence attentional and oculomotor processes (see Klein, 2000 for a review). In that study, IOR was generated by a cue within the hemianopic field of a patient and assessed by taking advantage of the environmentally-based aspect of the IOR phenomenon (Danziger, Fendrich, & Rafal, 1997). The patient then moved his eyes so that a cue and a target presented at the same location in space were presented successively onto blind and seeing portions of the retina (see Figure 3). The same magnitude of IOR was measured in the blind and seeing portions in this one patient, suggesting that attentional and visuomotor processes remained intact within the blind region. An elegant study by Kentridge, Heywood, and Weiskrantz (1999) has further implicated a role of the superior colliculus in unconscious visual processing and attentional orienting by demonstrating that unseen visual events nonetheless induced an attentional orienting response to specific locations in an impaired field of a hemianopic patient.

Based on such evidence, and the strong relationship between attention and consciousness, it is conceivable that patients with visual field deficits

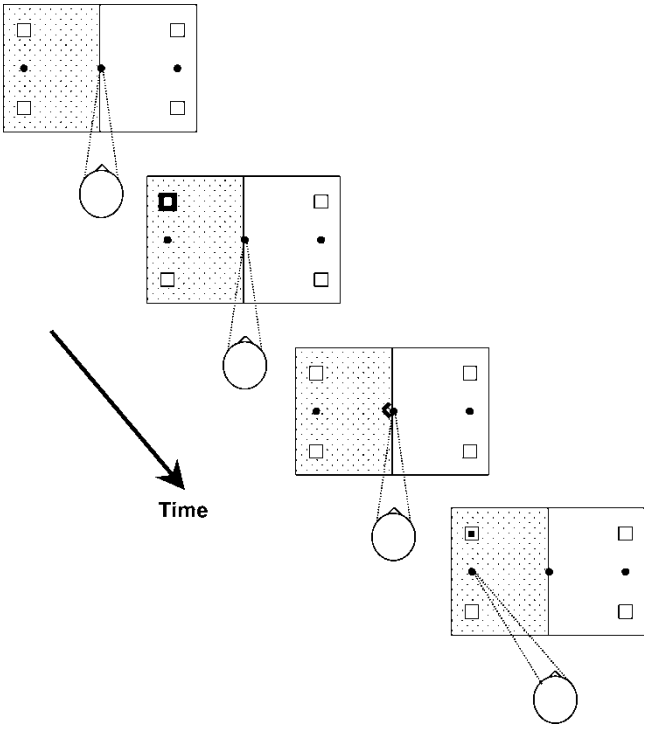


Figure 3. The stimuli used by Danziger et al. (1997) examining IOR in the left hemianopic field of a patient with right visual cortex damage. Following central fixation by the patient, a cue was presented in one of the four boxes. Following the cue, the patients were instructed to move their eyes to the fixation point within the hemifield indicated by a central arrow. A target then appeared at the previously cued spatial location, as shown in this illustration, or in the uncued location within the same hemifield.

consequent to primary visual cortex damage might be able to use such reflexive attentional orienting mechanisms of the superior colliculus and blindsight to eventually influence visual awareness. Anecdotal reports from patients suggest that although there is unawareness of visual events, they sometimes have the sense or impression that something was presented, which may be a function of reflexive orienting and may influence their ability to localise and discriminate at above chance levels (i.e., show blindsight). Thus, systematic explorations for enhancing visual awareness through retinotectal functions warrant further exploration. With insights from what we have learned from blindsight and by further examining residual vision in patients with visual field deficits, further clues for effective means of rehabilitating vision might then be provided.

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