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Perceptual plasticity in damaged adult visual systems

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ABSTRACT

Plasticity appears to be a ubiquitous property of nervous systems, regardless of developmental stage or complexity. In the visual system of higher mammals, perceptual plasticity has been intensively studied, both during development and in adulthood. However, the last few years have seen some significant controversies arise about the existence and properties of visual plasticity after permanent damage to the adult visual system. The study of perceptual plasticity in damaged, adult visual systems is of interest for several reasons. First, it is an important means of unmasking the relative contribution of individual visual areas to visual learning, adaptation and priming, among other plastic phenomena. Second, it can provide knowledge that is essential for the development of effective therapies to rehabilitate the increasing number of people who suffer the functional consequences of damage at different levels of their visual hierarchy. This review summarizes the available evidence on the subject and proposes that visual plasticity may be just as ubiquitous after damage as it is in the intact visual system. However, damage may alter visual plasticity in ways that are still being defined.

1. Definitions

Perceptual plasticity or the ability to alter perception, usually as a result of experience, takes on many forms, including perceptual learning, adaptation and priming. It is a well-described feature of mammalian visual systems throughout the lifespan (see reviews by Gilbert, Das, Ito, Kapadia, & Westheimer, 1996; Kaas, 1995). This is no surprise, given that the visual system, even in adulthood, appears to exhibit functional plasticity at every stage of processing, from photoreceptors (Smallman, MacLeod, & Doyle, 2001) to higher-level cortical areas (e.g. Zohary, Celebrini, Britten, & Newsome, 1994). As a result, the adult visual system is capable of substantial changes in sensitivity following visual stimulation (e.g. Fahle & Poggio, 2002; Gilbert, 1996; Gilbert, Sigman, & Crist, 2001; Goldstone, 1998; Ramachandran, Cobb, & Yang, 1994), deprivation (Fine, Smallman, Doyle, & MacLeod, 2002; He, Hodos, & Quinlan, 2006; Komatsu, 2006; Mendola, Conner, Sharma, Bahekar, & Lemieux, 2006) and even abnormal development, as in amblyopia (e.g. Kupfer, 1957; Levi & Polat, 1996; Levi, Polat, & Hu, 1997; Polat, Ma-Naim, Belkin, & Sagi, 2004; Simmers & Gray, 1999; Zhou et al., 2006). The present review will, following a brief description of visual plasticity in the normal, adult brain, attempt to summarize the state of the field related to perceptual plasticity after damage to the adult visual system.

2. Perceptual plasticity with an intact visual system

2.1. Task-dependent and task-independent learning

In many instances, changes in sensitivity are driven by task demands (e.g. during task dependent learning—Ahissar & Hochstein, 1993; Ball & Sekuler, 1987; Fiorentini & Berardi, 1980; Karni & Sagi, 1993a; Ramachandran & Braddick, 1973). However, evidence also suggests that the visual system can adapt to stimulus features that are subliminal, not the main focus of attention, and in some cases, not even relevant to the task (Watanabe et al., 2002; Watanabe, Nanez, & Sasaki, 2001). The major requirement for this form of perceptual plasticity is that irrelevant or subliminal stimulus features be presented synchronously with task-relevant, supraliminal features (Seitz & Watanabe, 2003, 2005), suggesting that Hebbian neural mechanisms (Hebb, 1949) may underlie this phenomenon.

2.2. A role for V1 in visual plasticity

An interesting characteristic of both task-dependent and task-irrelevant visual learning is their apparent reliance on relatively low-level, retinotopically organized areas of the visual system. The primary evidence for this comes from a large number of studies showing specificity of learning for fundamental stimulus features such as orientation (Crist, Kapadia, Westheimer, & Gilbert, 1997; Fiorentini & Berardi, 1980; Ramachandran & Braddick, 1973), spatial frequency (Fiorentini & Berardi, 1980), direction of motion (Ball & Sekuler, 1987; Vaina, Sundereswaran, & Harris, 1995), visual field location (Crist et al., 1997; Fiorentini & Berardi,

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1980; Karni & Sagi, 1991; Shiu & Pashler, 1992) and eye of presentation (Karni & Sagi, 1993a). These specificities are consistent with the smaller receptive field sizes, selectivity for stimulus attributes and ocular dominance observed in early visual cortical circuits, including primary visual cortex or V1 (Maunsell & Newsome, 1987). This notion is supported by electrophysiological recordings in monkeys (Crist, Li, & Gilbert, 2001; Schoups, Vogels, Qian, & Orban, 2001) as well as fMRI (Furmanski, Schluppeck, & Engel, 2004; Schwartz, Maquet, & Frith, 2002; Walker, Stickgold, Jolez, & Yoo, 2005) and EEG (Pourtois, Rauss, Vuilleumier, & Schwartz, 2008) studies in humans, which demonstrate functional plasticity in V1 that parallels behaviorally measured perceptual plasticity—in this case, visual learning.

2.3. A role for higher-level visual cortex in visual plasticity

A role for V1 or other low-level visual areas in perceptual plasticity does not preclude an important (albeit different) contribution of higher levels of the visual cortical hierarchy to this phenomenon (Ahissar & Hochstein, 1997; Dosher & Lu, 1998; Gilbert et al., 1996; Herzog & Fahle, 1997; Hupe et al., 1998; Karni & Sagi, 1993b; Liu, 1999; Schwartz et al., 2004). The fact that in some cases, task dependent learning is associated with a reduction in external noise and an enhancement in signal extraction, is thought to reflect plasticity in, and mediation by higher-level visual cortical areas (Dosher & Lu, 1998). Interestingly, Fine and Jacobs (2002) found that humans show more learning on tasks requiring discriminations along multiple perceptual dimensions than on tasks requiring discrimination along a single dimension. Humans also exhibited more learning when external noise was added to an otherwise unambiguous stimulus (Fine & Jacobs, 2002), suggesting perhaps, that higher level visual areas not only mediate different aspects of visual learning relative to V1, but perhaps, that they mediate larger learning effects as well.

Other evidence for the role of higher level visual areas in perceptual plasticity has come from electrophysiological recordings in primate area V4, demonstrating significant changes in both neuronal responsiveness and orientation tuning following training on a fine orientation discrimination task (Yang & Maunsell, 2004). With respect to visual motion discrimination learning, the fact that it can transfer between the two eyes and is highly specific for directions trained *if* the task is difficult (Ball & Sekuler, 1982, 1987) has implicated area MT, with its binocular, highly direction selective neurons, rather than V1, as a potential site for learning (Lu, Qian, & Liu, 2004). However, nothing in the mature visual system appears set in stone, including the visual areas mediating different aspects of visual plasticity. Indeed, when task difficulty was relaxed, training accelerated learning away from a trained motion direction (Liu, 1999; Liu & Vaina, 1998; Liu & Weinshall, 2000). Thus, a simple change in test conditions can induce a change in specificity and possibly, in the visual circuitry mediating learning.

A further level of complexity appears to exist at the highest levels of the visual cortical hierarchy. In primate inferotemporal (IT) cortex, the highest level in the ventral visual stream (Felleman & Van Essen, 1991; Ungerleider & Mishkin, 1982; Van Essen, Anderson, & Felleman, 1992; Van Essen & Maunsell, 1983), training with particular stimulus categories alters the neuronal representation of diagnostic features for the trained categories (Sigala & Logothetis, 2002). As a result, training monkeys to discriminate novel visual stimuli causes the emergence of a population of IT neurons which begin to respond selectively to the novel stimuli (DiCarlo & Maunsell, 2000; Kobatake, Wang, & Tanaka, 1998; Logothetis, Pauls, & Poggio, 1995; Sato, Kawamura, & Iwai, 1980), or which become capable of distinguishing between them (Jagadeesh, Chelazzi, Mishkin, & Desimone, 2001).

Taken together, the weight of experimental evidence supports the notion that plasticity is a ubiquitous property of the adult mammalian visual system. However, it also demonstrates significant differences in the contributions of different levels of the visual system to perceptual plasticity. While these differences are evident, the neural mechanisms that give rise to them remain poorly understood. For instance, it is often difficult to identify whether there is increased plasticity at higher levels of the visual system, or whether the amount of plasticity is constant at every level of the visual system, but its expression differs because of limitations imposed by neuronal properties specific to each processing level. It is hoped that future studies may shed some light on this issue, since understanding the potential for plasticity inherent in different processing levels of the adult visual has critical implications for the rehabilitation of visual system disorders. Indeed, the easy adaptability of the intact visual system raises interesting questions about its ability to change when critical components of the circuitry are damaged. Clearly, damage impairs vision. To what extent does it also affect perceptual plasticity?

3. Damaging different levels of the adult visual system affects perception differently

An in depth analysis of perceptual plasticity after visual system damage cannot take place without first examining the perceptual consequences of such damage. The sheer complexity of the visual system means that damage to its different components causes visual problems that differ in quality, severity and thus, functional consequence for the organism as a whole. From a simple retinotopic standpoint, there are already major differences in the effect of damage at different points along the information transfer path between the retina and primary visual cortex (Fig. 1). Retinal damage causes localized (“retinotopic”), usually complete blindness by depriving the rest of the visual system of its basic sensory input. In fact, blindness (in the form of visual field loss) results when V1 or any of its inputs (down to the retina) are damaged. However, it should be noted that the blindness that results from damage at different levels of this early visual pathway differs not only in topography (as shown in Fig. 1), but also in quality and properties. For instance, the blindness that results from V1 damage is not as “deep” or complete as that induced by retinal lesions (see discussion below).

Damage to higher-level, extrastriate visual cortex causes even more subtle, area-specific abnormalities of visual perception without frank blindness. For example, in humans, temporal cortex lesions predominantly cause abnormalities of face perception (prosopagnosia) and/or perception of complex objects and shapes (Damasio, Damasio, & Van Hoesen, 1982; Huxlin & Merigan, 1998). Motion perception abnormalities occur when the MT complex is damaged (Vaina, 1989, 1994; Zeki, 1991; Zihl, Von Cramon, Mai, & Schmid, 1991), while color vision abnormalities usually result from damage to the fusiform and lingual gyri (Bartels & Zeki, 2000; Damasio, Yamada, Damasio, Corbett, & McKee, 1980; Zeki, 1990; Zeki & Marini, 1998).

3.1. The special case of V1 damage

Among the different forms of visual cortical damage in humans, V1 damage is both the most commonly reported and the most devastating. The principal reason for this is that V1 is the main gateway through which visual information reaches the rest of [extrastriate] visual cortex (Fig. 2; reviewed by Felleman & Van Essen, 1991; Van Essen & Maunsell, 1983; Van Essen et al., 1992). As a result, unilateral damage to V1 or its primary inputs causes an inability to consciously perceive most types of visual information

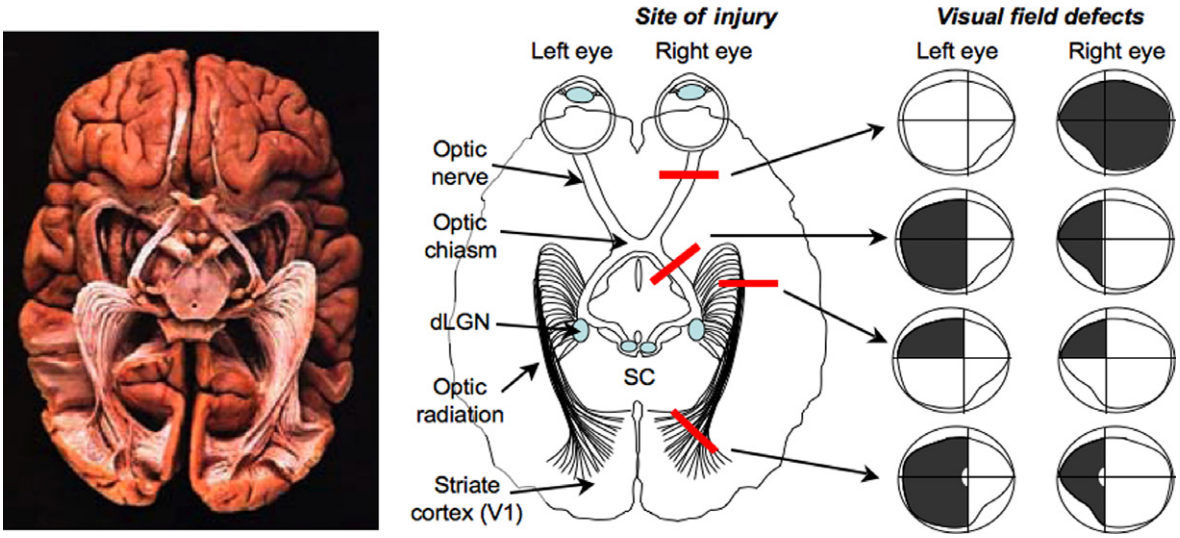

Fig. 1. Ventral view of visual pathways in the human brain illustrating the topography of visual field defects that result from damage (red bars in middle, schematic diagram) at different levels of the visual pathway. This is illustrated here only for the right hemisphere, but can clearly occur in the left hemisphere or bilaterally. Note that even for unilateral damage, there are bilateral effects on visual function once the optical chiasm is crossed. dLGN—dorsal lateral geniculate nucleus; SC—superior colliculus.

in the contra-lateral visual hemifield (see examples in Fig. 3—Cowey & Stoerig, 1991, 1995; Holmes, 1918; Teuber, Battersby, & Bender, 1960; Weiskrantz, Warrington, Sanders, & Marshall, 1974). When it affects the majority of the contra-lateral hemifield, such cortical blindness is termed a "homonymous hemianopia" or "hemianopsia". It most commonly occurs as a result of unilateral stroke, trauma, or tumor in the visual thalamus, optic radiation or primary visual cortex (Gilhotra, Mitchell, Healey, Cumming, & Currie, 2002; Zhang, Kedar, Lynn, Newman, & Biousse, 2006a).

In mammals with relatively high-acuity, color vision (including monkeys and humans), V1 damage is doubly devastating. In these animals, visual information is relayed from the retina to the primary visual cortex via a largely parallel, labeled-line system. Therefore, V1 damage destroys not only an important visual processing center (V1 itself), but also causes the retrograde degeneration of neurons in retinotopically corresponding areas of the dorsal lateral geniculate nucleus (dLGN), and subsequently, the death of a large portion of parvocellular (Pβ retinal ganglion cells in the eye (Cowey & Stoerig, 1991; Cowey, Stoerig, & Perry, 1989).

3.2. Residual vision and blindsight after V1 damage—Behavioral characteristics

In spite of retrograde degeneration at lower levels of the visual system and in contrast with the aftermath of primary retinal lesions, vision after V1 damage does not completely disappear within cortically blind portions of the visual field (e.g. Barbur, Harlow, & Weiskrantz, 1994; Morland et al., 1999; Pöppel, Held, & Frost, 1973; Riddoch, 1917; Weiskrantz, 1986, 1990, 1996). Evidence from a number of patients with V1 lesions demonstrates the existence of basic residual visual motion, form and wavelength sensitivity in the blind field (e.g. Blythe, Kennard, & Ruddock, 1987; Weiskrantz, Harlow, & Barbur, 1991; Zeki & Ffytche, 1998), findings that have been broadly replicated in monkeys with V1 damage (Cowey & Stoerig, 1995; Pasik & Pasik, 1982). Such preserved vision was originally termed "blindsight" (Weiskrantz, 1986; Weiskrantz et al., 1974) to denote the fact that it often occurred in the absence of awareness. However, more recent studies have shown that this residual vision is not simply an unconscious form of normal vision, such as might be mediated by islands of intact V1 cortex within the broader zone of damage (Gazzaniga, Fendrich, & Wessinger, 1994; Morland, Le, Carrol, Hoffmann, & Pambakian, 2004). First, it varies considerably among affected individuals, likely because the amount and precise location of damage sustained varies between individuals (Blythe et al., 1987; Morland et al., 2004). Variability in the amount of conscious vision experienced by different individuals with V1 damage has caused investigators to break up the syndrome into classes, including blindsight types I and II, with type I denoting the unconscious version of blindsight or "agnosopsia" (Zeki & Ffytche, 1998) and type II or "gnosopsia" (Zeki & Ffytche, 1998) denoting residual vision accompanied by awareness (Weiskrantz, 1986, 1997; Weiskrantz, Barbur, & Sahraie, 1995).

3.3. Residual vision after V1 damage—Underlying mechanisms

One very specific manner in which residual vision after V1 damage differs from vision with an intact visual system is that residual vision is narrowly tuned in the spatio-temporal domain (Barbur et al., 1994; Sahraie et al., 2003; Weiskrantz et al., 1991). Visual stimuli that are sensed tend to be simple (e.g. grating), with spatial frequencies around 1 cycle/deg and temporal frequencies around 10 Hz. Stimuli moving faster than about 5°/s or with a steep onset and offset are also most easily detectable (Morland et al., 1999). The most likely explanation for residual visual capacities with these specific characteristics is the existence of several pathways that can transmit information from the retina to extrastriate cortex, bypassing V1 (examples shown in red in Fig. 2). Indeed, a select number of dLGN neurons and even Pβ retinal ganglion cells are known to survive over the long term within retinotopic areas corresponding to the V1 lesion (reviewed by Cowey & Stoerig, 1991). In monkey dLGN, the survival of these cells is due to their lack of direct projection to V1. Instead, they project to extrastriate visual cortical areas, including V4 (Cowey & Stoerig, 1989), V2 (Hendry & Reid, 2000) and MT (Sincich, Park, Wohlgemuth, & Horton, 2004).

In addition, several extra-geniculocalcarine pathways bypass both the dLGN and V1, terminating directly in extrastriate visual cortex (reviewed in Cowey & Stoerig, 1991). The extra-geniculocalcarine pathway most commonly invoked in residual visual functions after V1 damage is the retinal projection to the superior colliculus (SC), hence to the pulvinar/LP complex and finally, to

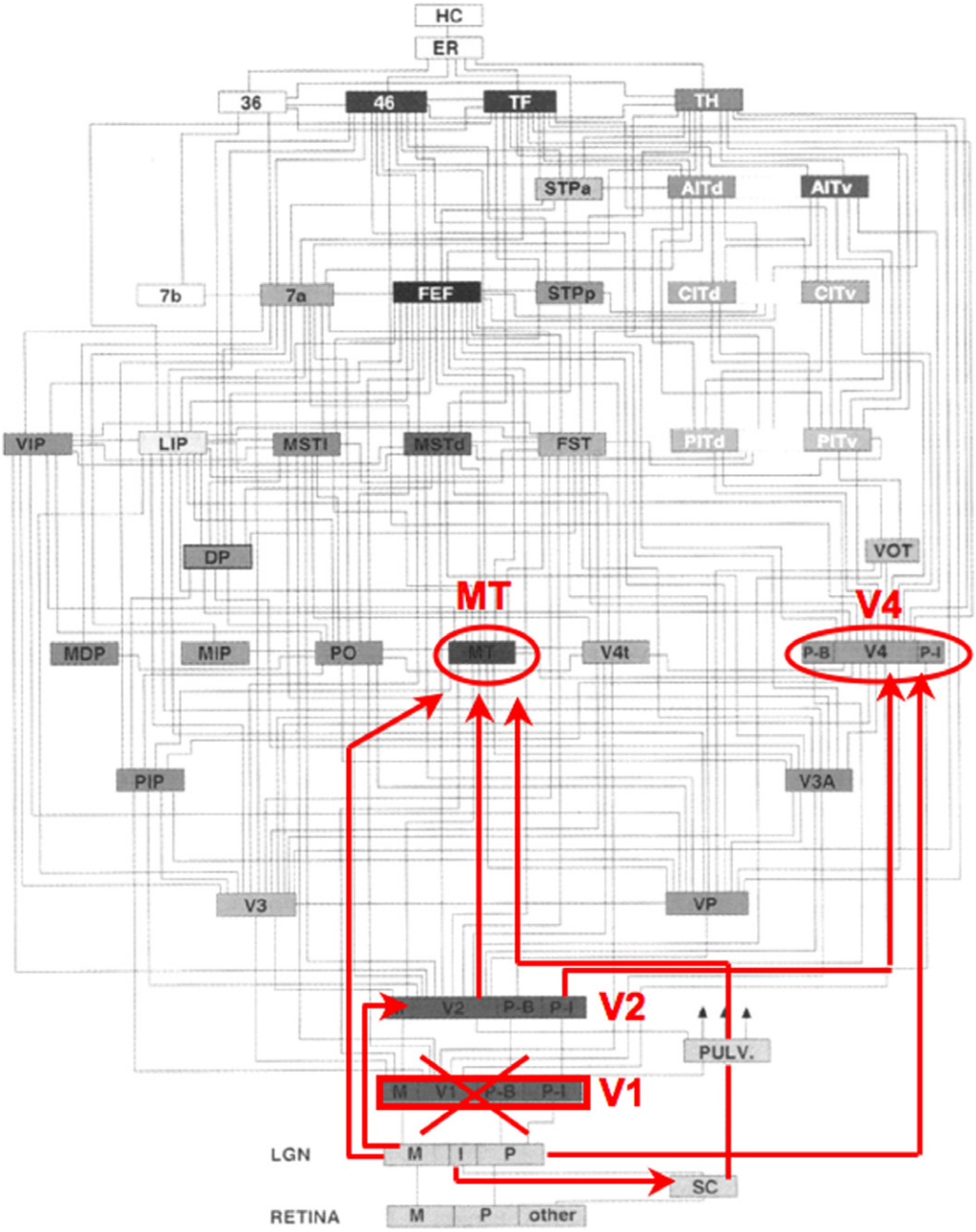

Fig. 2. Schematic representation of the connectional complexity of the primate visual system according to Van Essen and colleagues (Van Essen et al., 1992). This diagram illustrates well the serial and hierarchical organization of the system. Superimposed on this diagram in red is a connectional explanation for the preservation of residual visual functions following V1 damaged. Indeed, when V1 is damaged, visual information can still reach higher level visual areas directly, either through the lateral geniculate nucleus (LGN) or through the superior colliculus (SC)/Pulvinar. Current knowledge indicates that pathways, which bypass V1 on their way to extrastriate visual cortical areas, tend to terminate in either V4 or MT, and thus, should theoretically be capable of mediating both motion and form processing.

extrastriate visual cortex, especially to dorsal stream areas such as V5 or MT/MST (Fig. 2; Benevento & Rezak, 1976; Cragg, 1969), which are thought to be critical for many aspects of motion perception (Newsome & Paré, 1988; Pasternak & Merigan, 1994; Tootell et al., 1995; Zeki et al., 1991). Indeed, MT neurons maintain activity, including directionally selective responses after lesions or inactivation of V1 in monkeys (Girard, Salin, & Bullier, 1992; Rodman, Gross, & Albright, 1989; Zeki & Ffytche, 1998) and humans (Goebel, Muckli, Zanella, Singer, & Stoerig, 2001). However, in monkeys, additional SC removal abolishes these visual responses (Mohler & Wurtz, 1977; Rodman, Gross, & Albright, 1990; Rodman et al., 1989). In summary, damage at different levels of the adult visual system causes different types of perceptual deficits. Does it also affect visual plasticity?

4. Visual deficits are not stable—Spontaneous perceptual plasticity after damage

While we cannot categorically claim that visual perceptual plasticity is completely normal following visual system damage in adulthood, an important clue that speaks to its preservation is the fact that visual deficits that first arise after the insult are rarely stable. This pertains both to retinal damage and damage at higher (cortical) levels of the visual system.

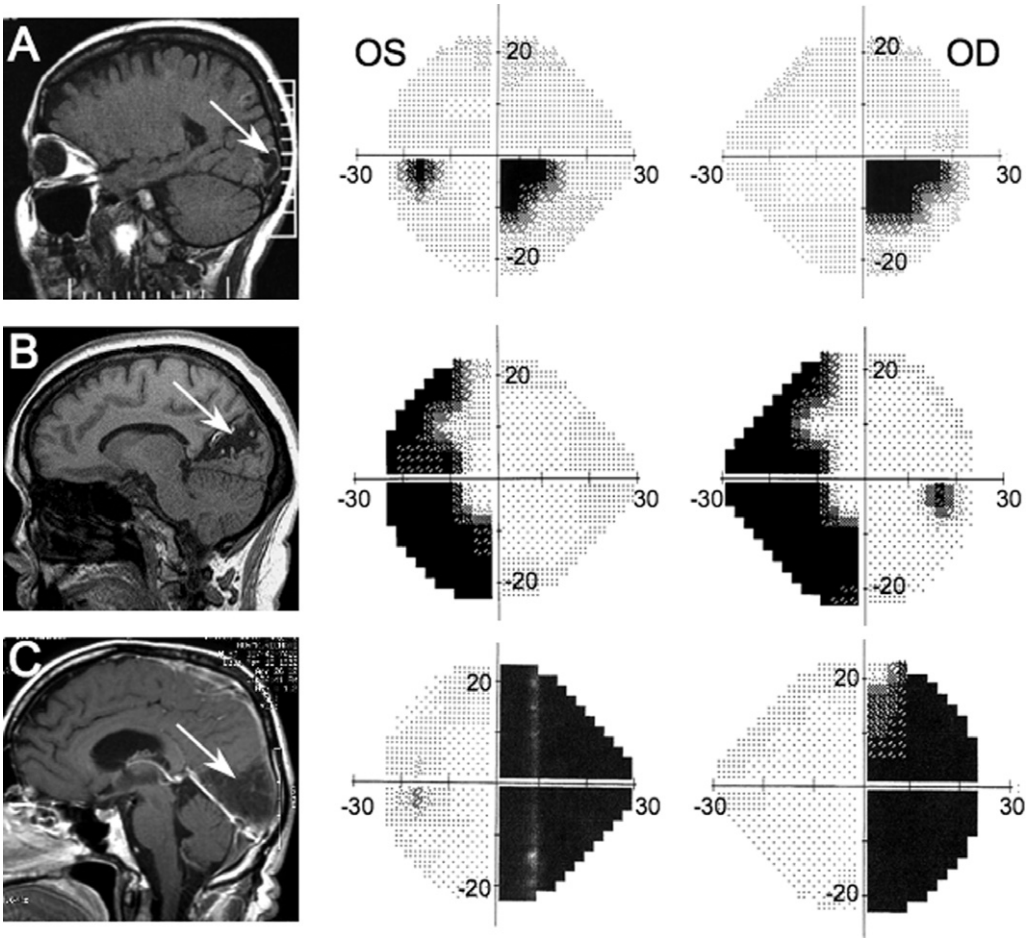

Fig. 3. Magnetic resonance images (MRI) of three different human subjects (A, B and C) who sustained unilateral, stroke-induced damage of V1 or the optic radiation during adulthood. Note the darkened, damaged areas of the brain in the occipital cortex of each subject (white arrows). Adjacent to each MRI image is that particular subject's 24-2 Humphrey visual field, measured independently through the left (OS) and right (OD) eyes. The solid black areas in each visual field indicate lack of sight. Numbers on the axes are in degrees of visual angle relative to central fixation. Note the homonymous nature of the field defects resulting from damage to V1.

4.1. Spontaneous plasticity after retinal lesions

Over time, human subjects suffering from macular degeneration, and other, relatively large retinal lesions exhibit perceptual filling-in of the resulting scotomas (blind spots), as well as distortions of visual space in and around them (Burke, 1999; Craik, 1966; Gerrits & Timmerman, 1969; Kapadia, Gilbert, & Westheimer, 1994; Zur & Ullman, 2003). Experimental evidence in several species (Calford, Wright, Metha, & Taglianetti, 2003; Darian-Smith & Gilbert, 1994, 1995) suggests that a major cellular/anatomical substrate for this phenomenon is cortical reorganization, both within and around the silenced zone of primary (and likely higher level—see De Weerd, Gattass, Desimone, & Ungerleider, 1995) visual cortex. The result is a distortion of the retinotopic map in V1 (and most likely, in other visual areas as well), with neurons in the lesion-projection zone becoming responsive to stimulation of the retina surrounding the area of damage (Calford, Schmid, & Rosa, 1999; Chino, Kaas, Smith, Langston, & Cheng, 1992; Chino, Smith, Kaas, Sasaki, & Cheng, 1995; Gilbert & Wiesel, 1992; Heinen & Skavenski, 1991; Kaas et al., 1990; Schmid, Rosa, Calford, & Ambler, 1996). Although the fundamental finding of altered neuronal responsiveness within and around the lesion projection zone in V1 and its interpretation in terms of retinotopic map alteration has been questioned (Baker, Peli, Knouf, & Kanwisher, 2005; DeAngelis, Anzai, Ohzawa, & Freeman, 1995; Smirnakis et al., 2005; Sunness, Liu, & Yantis, 2004), the observation that perceptual changes occur after retinal lesions or artificial scotomas in adult mammals remains.

The simple existence of perceptual changes after retinal damage implies that some form of perceptual plasticity exists, even if its exact mechanisms are not yet fully understood (but see evidence for possible cellular mechanisms in the more recent work of Arckens et al., 2000; Arckens, Van Der Gucht, Eysel, Orban, & Vandesande, 2000; Giannikopoulos & Eysel, 2006; Van den Bergh, Eysel, Vandenbussche, Vandesande, & Arckens, 2003). The fact that the visual system remains capable of perceptual plasticity after retinal damage is the major reason why patients who suffer from foveal or macular damage spontaneously develop one or more alternative, preferred retinal loci (PRL) of fixation (Cheung & Legge, 2005; Crossland, Culham, Kanbanarou, & Rubin, 2005; Cummings, Whittaker, Watson, & Budd, 1985; Schuchard & Fletcher, 1994). Indeed, the development of PRLs is an important aspect of occupational therapy for this patient population, allowing for the restoration, albeit to a limited extent, of reading, navigation and driving abilities (e.g. Schuchard & Fletcher, 1994; Watson, Schuchard, De l'Aune, & Watkins, 2006).

4.2. Spontaneous plasticity after V1 damage

4.2.1. Changes in visually guided behavior

There is clear indication of spontaneous perceptual plasticity after permanent damage to V1 or its immediate inputs in both hu-

mans and non-human species. Much of this evidence comes from carefully controlled clinical and laboratory studies of human subjects suffering from homonymous hemianopia (Gassel & Williams, 1966; Ishiai, Furukawa, & Tsukagoshi, 1987; Pambakian et al., 2000). Of interest is the fact that the most obvious changes noted in these subjects relate to visual behavior. Indeed, although a good number of these individuals possess residual vision in their blind field, the great majority of hemianopes significantly alter their visual behavior—and specifically, the way they distribute gaze—following their insult (Pambakian et al., 2000). For instance, when presented with point light targets at different, random sites along the horizontal meridian, visually intact controls usually fixate the targets directly (Meienberg, Zangemeister, Rosenberg, Hoyt, & Stark, 1981). Hemianopes rarely do so (Meienberg et al., 1981). Instead, when target duration and position are predictable, they perform a series of hypometric saccades that incrementally approach each target until it is found. Once target positions are learned, the saccades become hypermetric, overshooting the target by a few degrees of visual angle, and requiring a short, corrective saccade for eventual target localization (Meienberg et al., 1981). Hypometric saccades are also observed when hemianopes are asked to search static images for a small target (Zangemeister, Oechsner, & Freksa, 1995) or when searching for a visual target among distracters (Chedru, Leblanc, & Lhermitte, 1973). Indeed, hemianopes exhibit longer search times, shorter and more frequent fixations, and shorter saccades than visually normal controls (Chedru et al., 1973).

Hemianopes also spend more time looking towards their blind than their intact hemifield (Ishiai et al., 1987). This bias has been observed for numerous visual tasks, including counting dots (Zihl, 1995), viewing natural and degraded images (Pambakian et al., 2000) and detecting sudden-onset, moving targets in a three-dimensional, virtual environment (Riley, Kelly, Martin, Hayhoe, & Huxlin, 2007). It is not due to visual or attentional neglect with respect to the intact hemifield (Ishiai et al., 1987) but rather, represents a compensatory strategy that partially overcomes the loss of conscious, high-quality visual input from the affected side of space. By looking towards their blind field, hemianopes place most of the scene of interest in their intact hemifield (Zihl, 1995).

Finally, the sequential gaze patterns exhibited by hemianopes while they perform naturalistic tasks strongly suggest that they also place greater weight on visual memory representations of their visual environment, compared to age-matched, visually intact controls (Martin, Riley, Kelly, Hayhoe, & Huxlin, 2007). All these changes in visual strategy after V1 damage occur spontaneously and in the presence of normal saccade and eye movement dynamics (Martin et al., 2007; Zangemeister et al., 1995), suggesting that they are a true adaptation to the perceptual deficit rather than being due to abnormal oculo-motor control. Because patterns of gaze allocation are a good indication of the quality and quantity of visual information needed and gathered by the organism (Hayhoe & Ballard, 2005; Triesch, Ballard, Hayhoe, & Sullivan, 2003), we propose that changes in gaze strategy following visual loss should be considered a true form of perceptual plasticity.

4.2.2. Changes in the peri-lesional cortex

While there is clear evidence that organisms change their visual behavior because of cortical blindness, we known much less about specific changes in perception in the blind field over time. A change in the size of the blind field is the most commonly reported alteration. While this usually takes the form of an improvement in vision, it is usually restricted in time to the first few weeks after the insult, and in space to the border between blind and intact portions of the visual field (Zhang, Kedar, Lynn, Newman, & Biousse, 2006b). This is thought to be due to resolving inflammation around the lesion site, a return of function in neural circuits damaged but not destroyed by the insult (Poggel, Kasten, Müller-Oehring, Sabel, & Brandt, 2001; Sabel, 1997) and/or improvements in the subject's ability to perform visual field testing reliably (Zhang et al., 2006b). With very rare exceptions (e.g. Poggel et al., 2001), perimetric visual improvements are not seen after the second or third month post-lesion (Tiel & Kolmel, 1991; Zhang et al., 2006b). In addition to resolving inflammation around the lesion site, spontaneous plasticity following V1 damage may also be mediated by changes in the properties of neural circuits adjoining the lesion (reviewed in Eysel, 1997). Neurons in these perilesional circuits exhibit significant plasticity, including changes in excitability (Eysel & Schmidt-Kastner, 1991), receptive field size (Eysel & Schweigart, 1999), neurochemistry and channel properties (Barmashenko, Eysel, & Mittmann, 2003; Rumpel et al., 2000). Indeed some of the changes in LTP and ion (especially Ca^{2+}) permeability may underlie the observed changes in field size and excitability around the lesion site.

4.2.3. Changes deep within the blind field

For large V1 lesions, the question of whether residual vision deep within the blind field borders changes spontaneously over time has been more difficult to answer. This is partly due to difficulties in separating the influence of visual testing (necessary to assess "vision") from the simple passage of time. An interesting observation in one patient with stroke-induced homonymous quadrantanopia made recently by Dilks and colleagues (Dilks, Serences, Rosenau, Yantis, & McCloskey, 2007) does, however, provide some evidence for perceptual plasticity deep within the blind field after retro-chiasmatic damage. Of note is the fact that the patient in question had suffered damage not to V1 directly, but rather to the optic radiations providing input to his left upper visual quadrant representation in V1. This is important because it means that his V1 neurons, while deprived of their main visual input, were likely to have survived this lesion. Six months after his stroke, psychophysical testing revealed that the subject experienced a distorted perception of space for stimuli presented in his left lower visual quadrant—objects appeared stretched upwards into his blind, upper left quadrant. Visually guided grasping was similarly distorted: when the subject attempted to pick up objects in his lower left visual quadrant, he "overshot" the upper boundary of the target into his scotoma. fMRI confirmed little activation of the right V1 when stimuli were placed in his blind, upper left quadrant. However, stimuli placed in the near lower left visual quadrant activated the blind, upper left field representation of the right V1, suggesting that this portion of V1, after losing its normal geniculate input, had become responsive to adjacent retinotopic locations. While it is not currently possible to establish the exact anatomical and physiological substrates of such perceptual plasticity, these could include dis-inhibition of pre-existing long-range horizontal connections within V1 (Darian-Smith & Gilbert, 1995; Das & Gilbert, 1995), sprouting of new horizontal connections in V1 (Darian-Smith & Gilbert, 1994), or changes in the functional interactions between higher-level visual cortical areas and V1 (De Weerd et al., 1995; Mendola, Dale, Fischl, Liu, & Tootell, 1999; Mendola et al., 2006).

In summary, while sparse, evidence for spontaneous visual improvements after damage to low-level visual cortex does exist. Functionally, the most pronounced changes appear to involve visually guided behavior. As discussed above, this is mostly the result of subjects developing compensatory visual strategies rather than recovering lost vision *per se*. Thus, we may tentatively conclude that in spite of evidence for cellular plasticity within low-level areas, the primary form of spontaneous perceptual plasticity following damage to lower levels of the adult visual system (retina to V1), appears to be higher-level, integrative plasticity, focused

on preserving functional interactions between the organism and its environment.

4.3. Spontaneous plasticity after extrastriate cortical damage

Clear evidence of spontaneous improvements in visual perception following extrastriate cortical damage is even more difficult to find in the literature. In order to claim that changes in perception are spontaneous, experiments must first behaviorally measure the visual deficit and then monitor it over time, while differentiating whether changes observed are due to the passage of time or the repeated administration of visual testing. Very few of the many published lesion studies actually do this, making it difficult to ascertain whether spontaneous perceptual plasticity occurs after extrastriate visual cortical damage. The only claim that can be made with certainty is that most forms of extrastriate cortex damage cause long-lasting (over months to years) visual deficits. However, extrastriate visual areas were not created equal. Merigan and Pham (Merigan & Pham, 1998) noted that damage to extrastriate areas in the ventral visual pathway such as V2 (Merigan, Nealey, & Maunsell, 1993) and V4 (Merigan, 1996; Merigan & Pham, 1998; Schiller, 1993) appeared to cause more stable (and permanent) visual deficits than damage to motion processing areas in the dorsal processing stream, especially areas MT/MST in monkeys (Dursteler, Wurtz, & Newsome, 1987; Pasternak & Merigan, 1994; Yamasaki & Wurtz, 1991), or their homologues in other species—V5/MT + complex in humans (Huk, Dougherty, & Heeger, 2002; Huk et al., 2002; Huk & Heeger, 2002; Tootell et al., 1995; Watson et al., 1993; Zeki et al., 1991) and LS cortex in cats (Payne, 1993; Rudolph & Pasternak, 1996).

Furthermore, damage to several extrastriate areas, including area V4 (Merigan, 1996; Schiller, 1993), foveal prestriate cortex (Cowey & Gross, 1970; Gross, Cowey, & Manning, 1971; Iwai & Mishkin, 1968; Manning, 1971; Manning, Gross, & Cowey, 1971) and inferotemporal cortex (Britten, Newsome, & Saunders, 1992; Gross, 1971, 1973; Huxlin, Saunders, Marchionini, Pham, & Merigan, 2000; Mishkin, 1966) impairs aspects of visual learning, especially those which involve stimulus attributes or aspects of vision that rely on the damaged area for processing. Since learning is a form of perceptual plasticity, this is an important consideration. Further research is needed to assess whether this is a unique effect of extrastriate cortex damage or of damage to visual areas in the ventral processing stream.

In summary, while damage at any level of the visual system induces changes in anatomy, connectivity and function throughout the rest of the system, the functional relevance of these changes for visual perception and function seems to depend critically on the hierarchical level that has been most perturbed. With retinal damage, the loss of visual function is profound and all encompassing. However, spontaneous plasticity rapidly develops, causing changes in cortical responsiveness, perhaps even topography, but most clearly, changing higher-level usage of visual information. As a result, preferred retinal loci of fixation develop in the retinal periphery. With retro-chiasmatic damage, up to and including V1, there is residual, but largely unconscious and most definitely degraded vision. Long-term, spontaneous improvements in visual sensitivity in the blind field appear to be minimal. The most obvious spontaneous changes pertain, once again, to higher-level usage of visual information, resulting in the development of compensatory gaze strategies. It is uncertain, at this time, whether extrastriate visual cortical damage is associated with more or less spontaneous perceptual plasticity than V1 damage. But the proposed role of higher-level visual areas in perceptual learning leads us to consider to what extent training might be used to further stimulate perceptual plasticity after visual system damage.

5. Training-induced visual plasticity in damaged visual systems

5.1. Effects of training following retinal damage

Visual training, which usually involves repeated trials of a visual task, is known to alter the electrophysiological response properties of neurons in intact primary (e.g. Schoups et al., 2001) as well as higher level visual cortical areas (e.g. Salazar, Kayser, & König, 2004; Yang & Maunsell, 2004). Repetitive stimulation of visual neurons in anesthetized preparations (i.e. in the absence of a "training task") is likewise capable of altering response properties in V1 (e.g. Eyding, Schweigart, & Eysel, 2002; Eysel, Eyding, & Schweigart, 1998; Godde, Leonhardt, Cords, & Dinse, 2002). However, an important factor in being able to repetitively stimulate the visual system is the intactness of its basic sensory mechanisms, which reside in the retina. Once retinal circuitry is destroyed, it is unclear how stimulating, even repetitively, the damaged retinal locations could generate any perception, let alone perceptual plasticity of any functional benefit for the organism. Perhaps as a result of this interpretation, there have been few attempts to recover sensory function following retinal lesions. In fact, theoretically, this is unlikely to be feasible unless the retinal neurons destroyed (especially if they are photoreceptors) are replaced and their connections re-formed.

5.2. Training-induced plasticity after V1 damage—Animal studies

Most instances of training-induced perceptual plasticity after visual system damage have been reported following cortical insults. Although patients with V1 damage exhibit spontaneous and/or compensatory changes in visual behavior, they still report significant visual difficulties, especially when reading (Leff et al., 2000; McDonald, Spitsyna, Shillcock, Wise, & Leff, 2006) or navigating in the complex, dynamic visual environments of everyday life (Marigold, Weerdesteyn, Patla, & Duysens, 2007; Turano et al., 2004). This brings up the notion that spontaneous perceptual plasticity after V1 damage has significant limitations. It also delineates very real, functional consequences of these limitations for natural behavior, which we now have the opportunity to address.

Several research groups have asked whether more directed, functionally relevant perceptual plasticity might be induced after V1 damage if visual training was administered. In monkeys, visual training after V1 lesions restores the ability to detect and localize visual stimuli in their blind fields (Cowey & Weiskrantz, 1963; Mohler & Wurtz, 1977). These improvements do not occur spontaneously, but require training (Cowey & Weiskrantz, 1963), and they are largely restricted to visual field regions retrained (Mohler & Wurtz, 1977).

5.3. Training-induced plasticity after V1 damage—Human studies

In humans, our fundamental lack of knowledge about visual plasticity and the controversies that have plagued the field mean that there are currently no widely accepted treatment options available for people with visual cortical damage. Patients with V1 damage are either sent home or to "low vision" clinics where they are trained to improve their compensatory mechanisms rather than to attempt recovery of their lost vision. This is in sharp contrast with the physical therapy and motor retraining aggressively implemented to rehabilitate patients with damage to primary motor cortex (see reviews by Hallett, 2001; Taub, Uswatte, & Elbert, 2002). A major reason for this discrepancy is the dogmatic assumption that unlike motor functions, visual functions lost as a result of damage to the adult visual system cannot be recovered (Horton, 2005). This assumption has come about after multiple, but contro-

versial attempts to restore visual function in humans with V1 damage (see review by Pambakian & Kennard, 1997).

Poppelreuter (Poppelreuter, 1917) and Preobrazenskaya (cited in Luria, 1963) were perhaps the first to report on the effects of visual retraining (in this instance, reading) in such patients. A modified perimetry system was then developed to train saccadic eye movements into the blind field following V1 damage (Zihl, 1981; Zihl & von Cramon, 1985). However, the results obtained were questioned, because they reported variable, limited improvements, and did not properly control for variables such as compensatory shifts in fixation or eye movements that could affect the patients' measured visual "recovery" (Bach-Y-Rita, 1983; Balliet, Blood, & Bach-Y-Rita, 1985). A few years later, a computerized campimetry system devised by Sabel and colleagues (Kasten, Poggel, & Sabel, 2000; Kasten & Sabel, 1995; Kasten, Wüst, Behrens-Baumann, & Sabel, 1998; Sabel & Kasten, 2000), was tested and then marketed as Nova Vision's Visual Restitution Training (VRT) in a number of clinics in Europe and more recently, in the United States. This system is used on patients with either V1 or optic nerve damage and requires them to carry out in-home, daily practice of a light detection task. This task asks the subject to fixate a star-shaped spot of light while clicking a mouse button every time he or she perceives a white, bright spot of light presented at one of 500 positions on a dark computer monitor in front of them (Kasten et al., 2000). NovaVision's strategy is to intensively stimulate the border between intact and impaired portions of the visual field and thus recruit potentially intact but under-performing visual circuits (Sabel & Kasten, 2000). VRT evaluates its success by the amount of visual field enlargement attained after about 6 months of daily training. On average, the enlargement is about 5° of visual angle in size, and about 72% of patients report subjective improvements in their vision (Kasten et al., 2000). However, NovaVision's claims have recently been challenged by a report that showed visual field improvements to disappear if subjects were tested using a scanning laser ophthalmoscope, a different instrument than that used for training but one which could tightly control for the subjects' eye movements (Reinhard et al., 2005).

In order to assess whether perceptual improvements could be attained deep in the blind field of subjects with V1 damage when eye movements were tightly controlled, three groups independently carried out visual training in humans with homonymous visual field defects using three very different systems (Huxlin, 2004, 2007; Raninen, Vanni, Hyvärinen, & Näsänen, 2006; Sahraie et al., 2006). All three groups measured improvements in visual sensitivity at the trained blind field locations while monitoring eye movements using automated systems. Raninen and co-workers (Raninen et al., 2006) trained two cortically blind subjects on a luminance detection task and a letter identification task using flickering stimuli presented at 10° and 30° eccentricity on the horizontal meridian. The subjects attained up to a sevenfold improvement in sensitivity for the flickering stimuli after 1 year of training. Although improvements were not restricted to the trained locations, they were associated with changes in activity of intact visual cortical areas, as demonstrated both with neuromagnetic recordings (Raninen et al., 2006) and fMRI (Henriksson, Raninen, Näsänen, Hyvärinen, & Vanni, 2007).

Sahraie and co-workers (Sahraie et al., 2006) trained cortically blind subjects to discriminate a vertical sinewave grating from a uniform background in their blind field. Training in this study was conducted using a two-alternative forced-choice paradigm and was very specialized, in the sense that the spatial and temporal frequencies of the training stimuli were set at levels optimal for spatio-temporal channels known to survive V1 damage and mediate blindsight (Barbur et al., 1994; Sahraie et al., 2003). While they could not be monitored during in-home training, the patients' eye movements were closely monitored during laboratory verification of threshold improvements using an ASL 5000 pupillometer. This form of eye movement monitoring ensured that shifts in fixation during stimulus presentation could not explain the improvements observed.

Huxlin and colleagues (Huxlin, 2004, 2007) also precisely monitored fixation using an ISCAN RK426 pupillometer during psychophysical testing of cortically blind subjects before and after training on a global motion discrimination task (Fig. 4). Complex visual motion processing is interesting in the context of V1 damage for several reasons. First, it is significantly impaired after V1 damage and may be responsible for many of the problems experienced by this patient population in navigating and interacting with the complex, dynamic visual environments typical of everyday life. Second, the MT + complex is usually spared after V1 strokes and even appears to mediate some aspects of residual visual motion perception (see earlier discussion of blindsight). Given its well-established role in processing complex motion information (Newsome & Paré, 1988; Rudolph & Pasternak, 1999; Thompson & Liu, 2006; Vaina, Cowey, Eskew, LeMay, & Kemper, 2001), area MT and its homologues are likely to be ideally placed to mediate relearning of not just simple, but also complex motion perception in the absence of V1. Indeed, when adult humans with stroke-induced V1 damage were retrained to perform a global direction discrimination task with random dot stimuli at a single location in their blind field, their performance progressed from a complete inability to discriminate global motion direction to normal direction integration thresholds following 20–100 training sessions (i.e. 6000–30,000 trials—Huxlin, 2004, 2007). Improvements appeared to be permanent and were retinotopically restricted to retrained blind field locations. Furthermore, contrast sensitivity for direction and the ability to extract motion signals from noise both improved at the trained blind-field locations, even though they had never been specifically trained. Interestingly, the spatial and temporal frequencies at which the greatest post-training improvements in sensitivity were attained hovered around 0.5–1 cycles/deg and 10 Hz. This matches the known spatio-temporal channels thought to mediate blindsight (Barbur et al., 1994; Sahraie et al., 2003, 2006) and suggests that these channels may well play a role in mediating training-induced plasticity of complex motion perception after V1 damage. A final point of interest is that just as in the subjects trained by Sahraie and colleagues (Sahraie et al., 2006), training-induced improvements in global motion discrimination after V1 damage (Huxlin, 2004, 2007) were elicited at least 12, and in some cases 30 or more months after the subjects' strokes, a time when spontaneous visual improvements in the blind field are no longer thought possible (Zhang et al., 2006b).

5.4. Training-induced plasticity after extrastriate damage—Animal studies

The evidence for training-induced perceptual plasticity after extrastriate cortex lesions, which comes largely from animal studies, stands in contrast with the controversies that arose from attempts to retrain vision after V1 damage in humans. Training-induced perceptual improvements have been reported following lesions of area V4 in monkeys (Merigan & Pham, 1998; Schiller, 1993), areas MT/MST in primates (Bisley & Pasternak, 2000; Dursteler et al., 1987; Newsome & Paré, 1988; Newsome, Wurtz, Dursteler, & Mikami, 1985; Pasternak & Merigan, 1994; Rudolph & Pasternak, 1999; Yamasaki & Wurtz, 1991), MT/MST's homologue in the cat—the lateral suprasylvian (LS) cortex (Huxlin & Pasternak, 2004; Huxlin, Williams, & Price, 2008; Rudolph & Pasternak, 1996), foveal prestriate (Manning, 1972) and inferotemporal cortex (Britten et al., 1992; Dean, 1974; Holmes & Gross, 1984; Manning, 1972; Yaginuma, Niihara, & Iwai, 1982). In most of the studies involving V4 or MT lesions, improvements were specific to the class of visual stimuli and/or retinotopic locations trained,

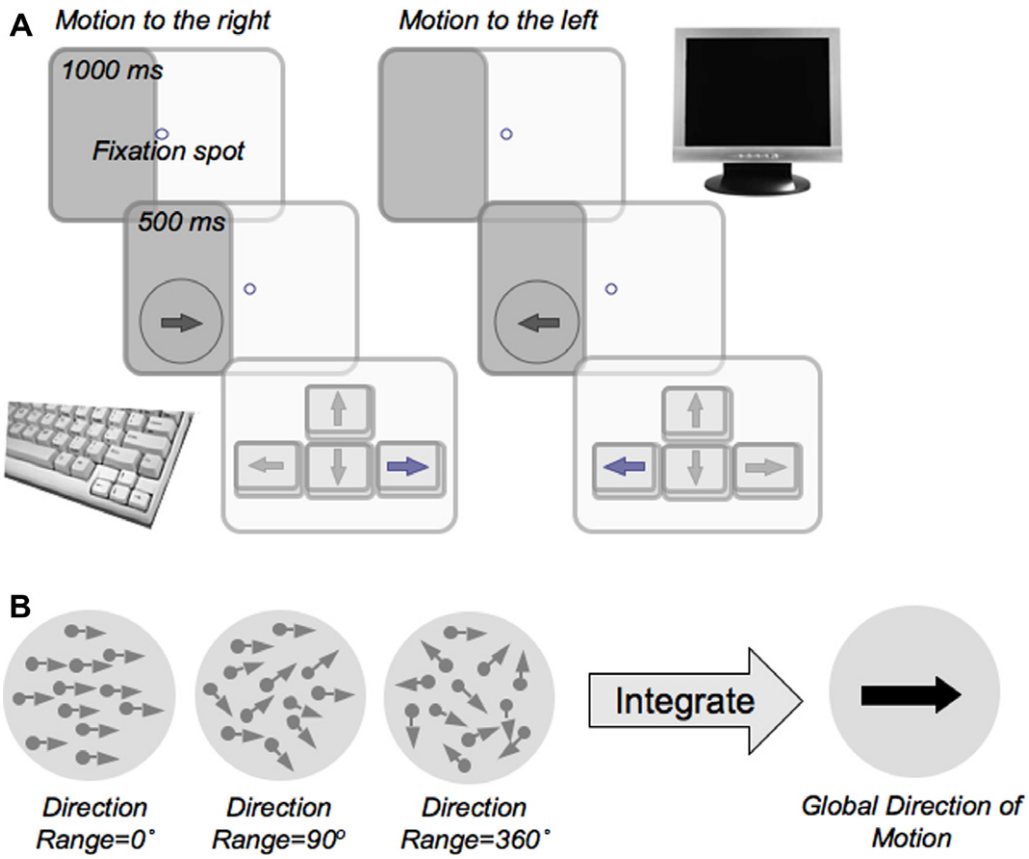

Fig. 4. Example of a psychophysical task (A) and visual stimuli (B) used by Huxlin and colleagues to train complex motion perception in the blind field of V1-damaged subjects (Huxlin, 2007), as well as of cats with extrastriate cortical damage (Huxlin & Pasternak, 2004). Each trial of this two-alternative, forced-choice, left-right direction discrimination task begins with the appearance of a spot on a computer screen that the subject is required to fixate precisely for 1000 ms. Following successful fixation, a drifting stimulus appears at a pre-selected location in the blind field (dark grey), lasting for 500 ms. The subject is required to discriminate its global direction of motion without breaking fixation from the central spot, and then indicate this perceived direction using a key press on the keyboard (or an eye movement in the case of cats). Random dot stimuli were used n which dots moved within a range of directions that was progressively increased (in a staircase) between 0 deg (completely coherent motion) and 355 deg (almost random). Accurate performance of the task required the subjects' visual system to perceive and integrate individual dot directions in the stimulus, extracting a global direction vector that was either to the left or the right.

suggesting that relatively low-level, retinotopically organized visual areas might be mediating such training-induced, post-lesion plasticity. Because retinotopically localized stimuli were generally not used to retrain primates with temporal lobe lesions, it is not know if training-induced improvements are likely to be retinotopically restricted to the retrained locations. Likewise, there appears to be little stimulus specificity in the effects of training following damage to visual areas in the primate temporal lobe. However, this may be due to the nature of the deficits being investigated, which for temporal lobe lesions, tend to involve more cognitive, mnemonic and associative deficits (see reviews by Cowey, 1994; Dean, 1974, 1976; Gross, 1971, 1973), rather than the largely perceptual deficits, which arise from damage at lower levels of the visual system hierarchy.

5.5. Training-induced plasticity after extrastriate damage—Human studies

In humans, extrastriate damage is less commonly reported than damage to V1, partly because the visual deficits are more subtle than those induced by V1 damage (specifically, extrastriate damage rarely causes visual field losses). For instance, damage to human V5 or the MT + complex, causes deficits of motion perception, often termed motion blindness (Baker, Hess, & Zihl, 1991; Hess, Baker, & Zihl, 1989; Shipp, Dejong, Zihl, Frackowiak, & Zeki, 1994; Vaina, 1998; Vaina et al., 2001; Zeki, 1991; Zihl, Von Cramon, & Mai, 1983; Zihl et al., 1991). Just as in monkeys with MT lesions, the motion deficits can be transient or permanent, more or less severe, affecting first and/or second order motion, depending on how much of MT + and surrounding motion processing circuitry has been damaged (Nawrot, Rizzo, Rockland, & Howard, 2000; Shipp et al., 1994; Vaina & Cowey, 1996). A frank attempt to retrain motion coherence thresholds in humans with unilateral cortical damage involving the MT + complex was made by Vaina and colleagues (Vaina et al., 2001). Although subjects who were thus trained exhibited improved motion coherence thresholds, in contrast with the results of carefully controlled lesion studies in animal models, the retinotopy and stimulus-specificity of improvements attained in humans did not appear tightly correlated with retraining parameters (Vaina et al., 2001). To what extent this lack of correlation is due to non-optimal training parameters, differences in the amount and type of brain damage sustained, or other uncontrolled variables remains to be determined. Significantly more work is needed before any solid conclusions can be drawn about the potential role of training in eliciting perceptual plasticity and improved visual function after permanent damage to extrastriate cortex in humans.

6. Conclusions

When considering the many, well-documented cases of plasticity and recovery following damage to motor, speech, somatosen-

sory and auditory centers of the adult mammalian brain (see reviews by Cauraugh & Summers, 2005; Engelien et al., 1995; Hallett, 2001; Musso et al., 1999; Xerri, 1998; Xerri, Benelhadj, & Harlay, 2004), one may surmise that barring major differences in structure and function between the visual system and the rest of the brain, we should be able to demonstrate some form of visual perceptual plasticity following visual system damage in adulthood. In addition, we should be able to tap such perceptual plasticity for the purpose of recovering visual functions lost as a result of visual system damage. In reality, however, solid evidence for perceptual plasticity following visual system damage is relatively sparse and its underlying mechanisms are far from understood. A direct consequence of this gap in scientific knowledge is that visual rehabilitation for those afflicted by visual system damage is still in its infancy. Most likely, it currently achieves only a fraction of the success possible if treatments were based on a better understanding of the impact of visual system damage, both on perception and plasticity. The present review does illustrate one important point however: visual perception in adult, large-brained mammals is capable of change after damage, regardless of the levels of the visual system affected. It should not be too difficult to canvas the available evidence and design the next generation of experiments whose goal should be to better characterize this phenomenon, identify its enabling mechanisms and canvas it for the improvement of vision.

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