Published in final edited form as:

Annu Rev Neurosci. 2012 ; 35: 91–109. doi:10.1146/annurev-neuro-062111-150356.

Primary visual cortex, awareness and blindsight

David A. Leopold^{1,2}

¹Unit on Cognitive Neurophysiology and Imaging, Laboratory of Neuropsychology, National Institute of Mental Health (NIMH)

²Neurophysiology Imaging Facility, NIMH, National Institute of Neurological Disorder and Stroke (NINDS), National Eye Institute (NEI)

Abstract

The primary visual cortex, or V1, is the principal telencephalic recipient of visual input in humans and monkeys. It is unique among cortical areas in that its destruction results in chronic blindness, leading to speculation that it may have a special or direct role in generating visual awareness. To explore this issue we review experiments that have used two powerful paradigms, psychophysical visual suppression and chronic V1 ablation, each of which disrupts the ability to perceive salient visual stimuli. We focus on recent studies from the nonhuman primate using anatomical, neurophysiological and behavioral paradigms to understand V1's role in perception. We also review findings pertaining to the basis of unconscious vision, or blindsight, that can occur after V1 damage. We conclude that the critical role of V1 in primate vision follows naturally from its position as a bottleneck of visual signals, but that there is little evidence to support its direct contribution to visual awareness.

Keywords

V1; visual perception; blindsight; cortical lesion; awareness; consciousness; neuropsychology; cerebral cortex; thalamus

Understanding the relationship between neural activity and subjective perception is one of the most fascinating and challenging goals of modern neuroscience. In the domain of vision, damage to the primary visual cortex, or V1, but not any other cortical region, abolishes visual awareness and leads to chronic blindness. This observation, combined with data from electrophysiological and functional magnetic resonance imaging (fMRI) studies in human and nonhuman primates, has raised speculation that neural activity in V1 might have a direct and critical role in the generation of a percept.

The present article reviews experiments that shed light on this fascinating topic. We survey experiments pertaining to the visual phenomena of perceptual suppression and blindsight in an attempt to understand the role of V1 in conscious and unconscious vision. In doing so, we refer to diverse features of V1, whose anatomical connections, complex laminar organization, and electrophysiological response profile have been studied extensively in the monkey. Throughout the review, emphasis is placed on discoveries in the last decade. By necessity, several relevant topics are not discussed or are mentioned only in brief. Such topics include neural correlates of perception in V1 pertaining to paradigms other than visual suppression (reviewed in (Tong, 2003)), perceptual correlates outside of V1, and perceptual

impairments following cortical lesions in areas other than V1. We do not attempt to provide a comprehensive review of blindsight, and refer the reader to recent overviews by pioneers of the field (Cowey, 2010; Stoerig, 2006; Weiskrantz, 2009). A considerable portion of this review is devoted to describing pathways that carry retinal image information to the cortex, the details of which are important for understanding both the determinants of V1 activity during perceptual suppression and the basis for unconscious visual performance during blindsight.

EXPERIMENTAL INROADS TO THE UNCONSCIOUS

We begin in this first section by briefly describing the two featured paradigms (see **Figure 1**). The next section reviews the modulation of sensory responses in V1 during perceptual suppression, including some strikingly different findings obtained by single-unit and fMRI studies. This is followed in the third section by a survey of experiments that give insight into V1-independent vision during blindsight. The fourth and final section draws upon these and other findings to evaluate the particular role of V1 in visual awareness.

Perceptual suppression can render a normally salient visual stimulus completely invisible. Stimulus paradigms that induce perceptual suppression are an important component of the psychophysicist's toolbox, as they shed light on unconscious sensory processing. Such paradigms include binocular rivalry (Blake and Logothetis, 2002), motion-induced blindness (Bonneh et al., 2001), visual masking (Breitmeyer and Ö men, 2006), and various dichoptic stimulus sequences collectively termed “flash suppression” (Wolfe, 1984; Tsuchiya and Koch, 2005; Wilke et al., 2003). Psychophysical experiments have demonstrated that during perceptual suppression certain stimuli, though completely invisible, can penetrate the first stages of cortical processing. In doing so, they can generate adaptational aftereffects (Blake et al., 2006), guide manual grasping behavior (Roseboom and Arnold, 2011), and recruit spatial attention (Lin and He, 2009).

An example of a flash suppression stimulus sequence is shown in **Figure 1a**. In this particular paradigm (Wilke et al., 2003), a salient target stimulus is first presented alone on the screen, often monocularly, for several hundred milliseconds. After this period, a binocular field of randomly moving dots appears in the periphery. This sequence induces the target stimulus to vanish abruptly from perception and remain entirely invisible for several seconds, provided the moving dots remain on the screen. The probability of target suppression is a function of several stimulus parameters, such as the speed at which the dots are moving. In a typical monkey neurophysiological experiment, these parameters are adjusted to induce the target to disappear on approximately 50% of the trials. Then, based on the monkey's perceptual report, neural responses to an identical physical stimulus are compared when the target is subjectively visible or invisible (Wilke et al., 2006; 2009; Leopold et al., 2003). This approach allows one to assess the relationship of a given neural response to the perceptual awareness of a stimulus, and the results from the visual cortex are discussed in the next section.

Blindsight refers to the ability of cortically blind patients and experimental animals to use visual information to guide behavior in the absence of visual awareness (Weiskrantz, 2009). Human blindsight subjects are able to orient to and even answer questions about stimuli presented to the blind part of the visual field. However, when questioned, they report being entirely unaware of the stimuli to which they are responding (Sanders et al., 1974). This situation can be somewhat perplexing for the subject. In their seminal paper, Pöppel and colleagues (Pöppel et al., 1973) asked their subject to direct his eyes to the target, to which he replied, “How can I look at something that I haven't seen?” Nonetheless, the subject was still able to carry out the task. This paradoxical phenomenon of *blindsight* is not simply due

to low-functioning vision, but is instead due to a unique uncoupling between subjective visual perception and visually guided performance (Azzopardi and Cowey, 1997). Moreover, it only occurs when damage is restricted to V1, and is generally not present when the damage extends into the extrastriate cortex (Weiskrantz, 2009).

The blindness that follows damage to the V1 in humans appears to be common among primates, but not true for other mammals, probably they have more visual relay projections from the thalamus to other cortical areas, thus bypassing the primary visual cortex (Preuss, 2007; Funk and Rosa, 1998). Despite nominal blindness, the existence of some residual vision following V1 lesions in the macaque has been recognized for more than half a century (Klüver, 1941). In the weeks following the surgical removal of V1, macaques gradually recover the ability to use visual information to guide hand and eye movements to stimuli in the “blind” (lesion-affected) part of the visual field (Isa and Yoshida, 2009; Mohler and Wurtz, 1977; Humphrey, 1974; Feinberg et al., 1978). In formal testing they can discriminate simple patterns on the basis of spatial frequency, shape, texture, and color (Miller et al., 1980; Schilder et al., 1972; Dineen and Keating, 1981), but important aspects of their vision are gone forever, such as the capacity to visually recognize food, objects, or faces of familiar individuals (Humphrey, 1974). Importantly the residual vision in macaques indicates a dissociation between awareness and visually guided behavior. When visual perception was tested using both forced choice and detection tasks, macaques were able to respond correctly to a stimulus in the blind field during the forced choice task, but then, under the same visual conditions, indicate in the detection task that no stimulus was presented (Cowey and Stoerig, 1995; Moore et al., 1995). While it is impossible to precisely determine the subjective experience of a cortically blind monkey, or human for that matter, these experiments indicate that macaques exhibit the hallmarks of blindsight and are therefore a good model for studying V1-independent vision in the human.

PERCEPTUAL SUPPRESSION OF VISUAL RESPONSES IN V1

We now focus on perceptual suppression, asking how the visibility of a stimulus affects neural responses in V1. This approach of correlating neural activity with subjective perception has been used to investigate whether V1 might contribute directly to visual awareness. However, before reviewing the effect of perceptual suppression on cortical neurons, we begin with a survey of the basic anatomy and physiology of the ascending pathways carrying sensory information to V1. In human and monkeys, nearly all visual information reaches the cortex through a primary visual pipeline that passes from the retina to the lateral geniculate nucleus (LGN) to V1. Reviewing this basic circuitry is necessary in order to understand how perceptual signals might influence V1's basic sensory responses. The components of this pathway will also be relevant to the discussion of blindsight in a later section.

Converging visual signals in V1

The input from the LGN to V1 consists of multiple parallel sensory pathways whose characteristic response properties originate in the retina (for a recent review, see (Schiller, 2010)). In the macaque, LGN-projecting retinal ganglion cells have a wide range of morphologies and physiological response profiles, which are often classified into three main groups: $P\alpha$, $P\beta$, and $P\gamma$. The $P\beta$ cells, projecting almost exclusively to the parvocellular LGN layers, comprise over 80% of ganglion cells in the macaque. They have a “midget” dendritic morphology, which gives them small receptive fields for detailed form vision. Electrophysiologically, they exhibit sustained responses and typically show red/green color opponency in trichromats. The $P\alpha$ neurons comprise roughly 10% of the ganglion cells. Their primary target is the magnocellular layers of the LGN, though they also project to several other target structures as well, described later. Their “parasol” morphology translates

to large, integrative receptive fields. Electrophysiologically, they tend to respond transiently and without γ color selectivity. The remaining ganglion cells are often grouped together as $P\gamma$, although their morphology and physiological properties are quite diverse (Schiller and Malpeli, 1977). The $P\gamma$ axons terminate in the interlaminar zones of the LGN, ventral to each magno- and parvocellular layer. The interlaminar zones are strongly associated with the koniocellular pathway, whose neurons are immunoreactive to calcium binding proteins CAMKII or calbindin D28K (Hendry and Yoshioka, 1994; Casagrande, 1994), and carry blue/yellow color opponent signals (for reviews, see (Nassi and Callaway, 2009; Hendry and Reid, 2000)). In the marmoset, injection of retrograde tracers into the koniocellular layers labels the bistratified $P\gamma$ cells in the retina (Szmajda et al., 2008).

Each ganglion cell type then relays its signals through unusually strong synapses in the LGN to V1, where the pattern of afferent projections is known in detail (for reviews, see (Nassi and Callaway, 2009; Lund, 1988; Peters et al., 1994)). Briefly, neurons from the magno- and parvocellular LGN compartments (carrying $P\alpha$ and $P\beta$ signals, respectively) project to separate sub-compartments of layers 4C and 6. Koniocellular projections (carrying $P\gamma$ signals) terminate within and above layer 4A (**Figure 2A**). The LGN projections to layer 4C are much stronger than those to layer 6. However, the intracortical projection from layer 6 to layer 4C is also prominent, and may be an important factor in determining the overall strength of visual responses (Callaway, 1998; Douglas and Martin, 2004). Layer 6 neurons also transmit channel-specific visual signals back to the LGN in an organized fashion, with upper tier neurons projecting to the parvocellular layers and lower tier neurons projecting to the magnocellular layers and possibly also to koniocellular layers (Briggs and Usrey, 2009).

In addition to its LGN input, area V1 also receives afferent input from a large number of extrastriate visual cortical areas, including V2, V3, V4, MT, TEO and TE (reviewed in (Salin and Bullier, 1995; Barone et al., 2000)), the inferior pulvinar (Benevento and Rezak, 1976), the amygdala (Freese and Amaral, 2005) and the claustrum (Baizer et al., 1997). Aside from the claustrum, which sends its densest projections to layer 4, each of these structures projects primarily to the supragranular layers. In fact, ventral stream extrastriate cortical areas V4, TEO and TE project exclusively to layer 1. This fact is important for understanding perceptual modulation in V1, as it suggests extrastriate modulation of V1 activity might be expected to affect synaptic activity in the supragranular layers.

Before we turn to how perceptual suppression affects V1 responses, we briefly review some basic features of V1 electrophysiology, including its laminar response profile and the contribution of different inputs. The responses of a given V1 neuron will be shaped to different extents by the LGN afferents, feedback from other cortical areas, input from subcortical areas, and a very large number of synaptic inputs from within V1 itself (Douglas and Martin, 2004). It is possible to directly isolate and measure spikes arriving into V1 at the LGN terminals, provided V1 neurons are first inactivated (for example, using the GABA agonist muscimol). This approach was used in a recent study to demonstrate the laminar segregation of LGN inputs based on their chromatic selectivity (Chatterjee and Callaway, 2003). The primary influence of these spiking afferents can be seen using a technique called current source density analysis, which computes the flow of extracellular ionic currents thought to derive from synchronized postsynaptic potentials (Schroeder et al., 1991). Following an abruptly flashed stimulus, a current sink is induced with a short latency in layer 4C, followed tens of milliseconds later by current sinks in the supragranular and infragranular layers (see **Figure 2b**). This characteristic spatiotemporal evolution of excitatory synaptic activity from the middle layers toward the laminae above and below is thought to reflect feedforward processing of visual information through the cortical microcircuitry (Mitzdorf, 1985), and is consistent with the laminar distribution of spiking response latencies (Nowak et al., 1995). In addition to evoked responses, spontaneous

activity also appears influenced by LGN afferents, even in darkness. Ongoing spiking activity is markedly higher in the LGN-recipient layers compared to other layers (Snodderly and Gur, 1995) (**Figure 2c**), as is high frequency (“gamma”) local field potential (LFP) power (Maier et al., 2010). Recent work has revealed other basic measures of V1 activity that are not as obviously derived from the pattern of LGN inputs. One study using a variant of current source density analysis found that the sustained response to a stimulus was localized roughly 500 μ m below the initial transient sink in layer 4C (Maier et al., 2011) (**Figure 2d**). Another study revealed two distinct laminar zones of LFP signal coherence, with a boundary between them near the bottom of layer 4C (Maier et al., 2010) (**Figure 2e**). The extent to which these latter findings can be explained by the LGN input, reverberation within the V1 microcircuit, or corticocortical feedback remains to be determined.

Given the multiple anatomical inputs impinging on V1 and its physiological response profile that appears largely, but not entirely, determined by its LGN afferents, we next pose the following question: Does perceptual suppression affect responses to visual stimuli in V1? A simple answer to this seemingly straightforward question has proved to be much more difficult than anticipated.

Modulation of visual responses during perceptual suppression

The neural basis of perceptual suppression has been investigated in both macaques and humans using several of the psychophysical tools discussed in the previous section. Single-unit and fMRI studies largely agree that perceptual suppression modulates neural responses to stimuli throughout the visual cortex, particularly at the highest stages of the cortical hierarchy (Sheinberg and Logothetis, 1997; Kreiman et al., 2002; Fisch et al., 2009; Tong et al., 1998). At intermediate stages, such as areas MT and V4, the correlates of perception are mixed throughout the population of neurons (Logothetis and Schall, 1989; Wilke et al., 2006), and individual cells change their sensitivity to perceptual suppression based on the structural details of the inducing stimulus (Maier et al., 2007).

Within V1, monkey electrophysiology and human fMRI studies have found nearly opposite results during perceptual suppression. Single-unit experiments in the macaque have consistently found that the visibility or invisibility of a stimulus has minimal if any effect on the firing of V1 neurons (Leopold and Logothetis, 1996; Gail et al., 2004; Leopold et al., 2005; Keliris et al., 2010; Wilke et al., 2006; Libedinsky et al., 2009), in agreement with theoretical work suggesting that activity in V1 does not contribute directly to visual awareness (Crick and Koch, 1995) (but see (Tong, 2003) for a different perspective). Compared to single-cell responses, there is somewhat more modulation of the local LFP signal (Gail et al., 2004; Wilke et al., 2006; Maier et al., 2008b). However, this change is small relative to control trials in which the same stimulus is physically removed (**Figure 3b**). However, the fMRI modulation in V1 during perceptual suppression is much stronger, resembling the physical control condition (Polonsky et al., 2000; Lee et al., 2005; Tong and Engel, 2001; Haynes and Rees, 2005; Wunderlich et al., 2005). As a result, the same paradigms used to argue against the role of V1 in awareness based on monkey electrophysiology have been used to argue for its role in awareness based on human fMRI.

To investigate the basis of the discrepancy, a recent study in monkeys combined fMRI and electrophysiological methods in V1 during perceptual suppression (Maier et al., 2008a). During conventional visual stimulation, fMRI blood oxygenation level-dependent (BOLD) and electrophysiological responses, including spiking and LFP, were in good agreement. However, during perceptual suppression the signals diverged markedly, even though they were measured from the same patch of tissue. During invisible periods, fMRI responses dropped to levels similar to that of a control condition, in which the stimulus was physically removed. By contrast, spiking responses were just as high during invisible periods as during

visible periods, again indicating that neural spiking rates in V1 are unaffected by perceptual suppression (**Figure 3c**). Responses of the LFP showed some significant perceptual modulation, but proportionally much less than the BOLD signal. Thus the BOLD and spiking signals were fundamentally different in their responses (Logothetis, 2002), and the level of the discrepancy was strongly dependent on a cognitive variable, in this case perceptual visibility. This latter finding may be related to other examples of signal discrepancies in V1, such as hemodynamic response modulation observed in the absence of single unit modulation during spatial attention (Posner and Gilbert, 1999) and during the expectation of an impending visual stimulus during a periodic behavioral task (Sirotnin and Das, 2009).

Why might BOLD signals show decreased responses in V1 to perceptually suppressed stimuli while spiking responses do not? One possibility is that signals reaching V1 elicit synaptic activity that causes a hemodynamic response but is never translated into changes in the rate of action potentials. Initial results from one study indicate that synaptic activity in the supragranular layers, but not in the deeper layers, drops significantly during perceptual suppression (Leopold et al., 2008). Since cortical areas V4 and TE send their projections exclusively to the supragranular layers of V1, the reported activity changes could reflect feedback from extrastriate areas, where neural activity is known to modulate with perceptual suppression. It is tempting to speculate that such synaptic modulation might affect V1 BOLD responses, but it remains a puzzle why such modulation would have virtually no effect on neuronal spiking. This issue clearly warrants further investigation.

Thus single-unit modulation during perceptual suppression provides no evidence in support of V1 playing a direct role in visual awareness. In the next section we explore the same point from a rather different perspective, reviewing the neural basis of unconscious vision following damage to V1.

BLINDSIGHT: RESIDUAL VISION FOLLOWING V1 DAMAGE

The phenomenology of blindsight has two principal features. The first is blindness, or the loss of visual awareness associated with V1 damage. The second is the capacity of blind individuals to use unconscious visual signals to guide behavioral responses. In this section, we address the second of these features, leaving the loss of visual awareness as a topic for the final section. Understanding the basis of residual vision during blindsight, including its unconscious nature, again requires knowledge of anatomical connections. We begin this section by describing neural projections to the extrastriate cortex that are thought to underlie blindsight behavior (Weiskrantz, 2009).

Anatomical pathways to the extrastriate cortex

All retinal image information reaching the cerebral cortex ascends through synapses in the dorsal thalamus, either in the LGN or the pulvinar. Retinal projections to the LGN were reviewed earlier. In addition, a very small number of ganglion cells, primarily P γ and P α , target the inferior pulvinar (O'Brien et al., 2001; Cowey et al., 1994) along with several other projection targets in the forebrain, situated at distinct positions along the neuraxis (see **Figure 4a**). Approximately one-tenth of ganglion cells send descending projections to the SC in the midbrain. Like the pulvinar, the SC receives primarily P γ and P α inputs (Perry et al., 1984; Perry and Cowey, 1984). Sparser projections terminate in the pregeniculate nucleus and in several nuclei in the hypothalamus and pretectum (Stoerig and Cowey, 1997). Some ganglion cells are thought to send collateral projections to multiple targets, such as to both the LGN and the SC (Crook et al., 2008). In addition to their direct retinal input, both the LGN and the pulvinar also receive projections from the SC, suggesting a potential midbrain relay to each of the two structures (May, 2006; Harting et al., 1991). Thus there are

at least four potential pathways by which retinal information can reach the dorsal thalamus (1-4 in **Figure 4b**).

In addition, both the LGN and pulvinar project to both V1 and extrastriate visual cortex. Of particular interest for blindsight are the direct pathways from the thalamus to the extrastriate cortex (C and D in **Figure 4b**). These projections have been extensively investigated using retrograde tracers injected into the extrastriate cortex, which leads to dense labeling in the pulvinar and much sparser labeling in the LGN. The LGN labeling, though sparse, has been observed in many experiments (reviewed in (Rodman et al., 2001) and (Sincich et al., 2004)). Much of the dense labeling in the pulvinar can be attributed to its role as a corticocortical relay (Shipp, 2003; Sherman, 2005). However, a portion of the retrogradely labeled pulvinar neurons, and all the labeled LGN neurons, are candidates for relaying visual information from either the SC or the retina to the extrastriate cortex.

A closer examination of these pathways reveals that the extrastriate-projecting neurons in the LGN are most commonly found in the interlaminar zones. Retrograde injections into dorsal (MT) or ventral (V4) stream extrastriate cortex reveal that more than half of extrastriate-projecting neurons label positively for CAMKII and calbindin, suggesting that these neurons are part of the koniocellular pathway (Sincich et al., 2004; Rodman et al., 2001). However, unlike the koniocellular neurons that project to the superficial layers of V1, neurons sending projections to the extrastriate cortex have large cell bodies with a multipolar morphology, suggesting that the term koniocellular may be inappropriate. Strangely, the LGN projections to extrastriate cortex terminate neither in layer 4, which is characteristic of feedforward thalamic projections, nor in the supragranular layers, which is characteristic of modulatory thalamic connections (Jones, 1998). Instead, the inputs are primarily directed to layer 5, where neurons project to the thalamus, striatum and midbrain (Benevento and Yoshida, 1981). It is interesting to speculate that this laminar pattern of LGN input to extrastriate cortical areas might be related to the unconscious nature of the visual signals used during blindsight.

Establishing that a pathway relays visual information to the cortex is more challenging. Based on the sheer number of retinal projections to the LGN, it seems likely that extrastriate-projecting LGN neurons would receive direct retinal input and would be able to send it to the extrastriate cortex. This possibility is supported by the finding that, in marmosets, presynaptic afferents to MT-projecting neurons in the koniocellular layers contain synaptophysin, which is thought to be a signature of retinal terminals (Warner et al., 2010). Putative retinal afferents were also found on MT-projecting neurons in the histochemically-defined P_{Im} subregion of the inferior pulvinar (Warner et al., 2010).

Establishing visual pathways through the SC is even more difficult, since there are two synapses that must act as relays. As reviewed above, P_α and P_γ ganglion cells project to the superficial layers of the SC. Within the superficial layers, a subset of neurons sends projections to the LGN and a different subset to the inferior pulvinar (May, 2006). In the case of the pulvinar, initial anatomical findings in the owl monkey did not find sufficient spatial overlap between SC terminals and MT-projecting neuron cell bodies to support such a relay (Stepniewska et al., 1999). However, recent experiments in the macaque using disynaptic tracing with a rabies virus (Lyon et al., 2010) and electrophysiological identification of neural connections with antidromic and orthodromic stimulation (Berman and Wurtz, 2010) argue strongly that such a relay does exist. In fact, both studies identified two distinct SC relays through the pulvinar to area MT, one being P_{Im}, the same subdivision that receives direct retinal afferents, and the other localized in the region of the inferior pulvinar immediately adjacent to the LGN. There is also evidence supporting a relay from the SC to extrastriate cortex through the LGN. The SC terminals are found primarily in the

interlaminar zones, which, as discussed, is similar to the distribution of most of the extrastriate-projecting neurons (Benevento and Yoshida, 1981; Stepniewska et al., 1999). This pattern is consistent with the projection pattern observed in a wide range of mammals (Harting et al., 1991). However, one study found that the laminar pattern of disynaptic labeling in the SC following extrastriate injections in areas MT and V3 was more consistent with the pulvinar route than the LGN route, suggesting that the colliculopulvinar pathway dominates, at least to certain extrastriate areas (Lyon et al., 2010).

Based on these neuroanatomical and neurophysiological studies, each of the four potential pathways carrying visual information from the retina to the extrastriate cortex (retina-LGN-extrastriate, retina-pulvinar-extrastriate, retina-SC-LGN-extrastriate, and retina-SC-pulvinar-extrastriate) is a viable candidate to bypass V1. It is important to point out, however, that these results were established in intact animals. It is well known that following V1 lesions a number of very significant changes take place to the visual system at many levels, which we describe in the next section.

Changes to the visual system following a V1 lesion

In the weeks following a restricted ablation of V1, massive retrograde degeneration decimates the portion of the LGN corresponding to the extent of the lesion. The outcome is a near complete loss of magnocellular and parvocellular neurons in the LGN (Mihailovi et al., 1971). Then, over a period of months and years, the degeneration cascades to the retina, and kills half of the P β ganglion cells (Cowey et al., 1989; Weller and Kaas, 1989). The interlaminar regions of the LGN, where some neurons project directly to multiple regions of the extrastriate cortex, do not degenerate nearly as much (Cowey, 2004), nor do the retinal projections to the SC (Dineen et al., 1982). Moreover, the extrastriate-projecting neurons that survive within the LGN are much larger than normal (Hendrickson and Dineen, 1982) and stain positively for calbindin D28K (Rodman et al., 2001), suggesting that the koniocellular system may be strengthened following the lesion. One study found that some of the retinal input to the remaining geniculocortical neurons projecting to V4 was mediated by GABA-ergic interneurons, and that a portion of the ganglion cells themselves stained positively for GABA (Kisvárdy et al., 1991). It was subsequently shown that a small proportion of retinogeniculate neurons are GABA-positive in the normal monkey optic nerve and optic tract (Wilson et al., 1996). These findings suggest that transmission of visual signals through the LGN to extrastriate cortex is fundamentally altered following V1 damage, with significant changes to the types of viable relay neurons, the distribution of retinal and collicular inputs, and quite possibly the balance of excitation and inhibition, as the system recovers.

Extrastriate visual responses without V1

Electrophysiological experiments in anesthetized macaques first demonstrated that neurons in the superior temporal polysensory area (STP) and area MT continue to respond to visual stimuli even after V1 is chronically removed, reversibly cooled, or acutely ablated (Rodman et al., 1989; Bruce et al., 1986; Girard et al., 1992). By contrast, neurons in the inferotemporal cortex were found to be unresponsive to visual stimuli following ablation of V1 (Rocha-Miranda et al., 1975). Subsequent single-unit studies in the macaque showed that the magnitude of residual responses in extrastriate cortical areas differed between dorsal and ventral stream pathways, with dorsal areas showing a higher fraction of neurons with residual stimulus responses than ventral ones (summarized in (Bullier et al., 1994), see **Figure 5a**). Studies of residual MT responses in other primates are mixed (Rosa et al., 2000; Collins et al., 2003; Kaas and Krubitzer, 1992) with the basis of the discrepancy presently unknown.

Functional imaging has the advantage of being able to simultaneously monitor neural responses in multiple areas. It also has certain disadvantages, such as poor temporal resolution and the uncertain origin of the blood-based response. Positron emission tomography (Barbur et al., 1993) and fMRI studies (Bridge et al., 2010; Baseler et al., 1999; Goebel et al., 2001) of human blindsight patients have reported responses in the extrastriate visual cortex, and particularly in area MT, to stimuli presented to the blind field. Recent fMRI studies in macaques have also shown extrastriate activity in the months following surgical ablation to V1. One study in anesthetized animals used retinotopic mapping to demonstrate preserved responses in regions of V2 and V3 corresponding to the blind field (Schmid et al., 2009). Another study in awake animals found responses in several extrastriate areas to a small stimulus confined entirely to the blind field (Schmid et al., 2010). In that study, V1-independent responses reached on average 20% of the response strength compared to the control condition (**Figure 5b**). There was a pronounced dorsoventral asymmetry within the early extrastriate cortex, with the dorsal components of areas V2/V3 and V4 showing notably higher residual activity than the ventral components, in agreement with a previous human study (Baseler et al., 1999).

Which pathways support blindsight?

A difficult and sometimes frustrating feature of blindsight is that the experimental evidence fails to converge on a single pathway. There are at least three distinct challenges in the study of blindsight. The first challenge is the biological complexity of the brain, including its parallel and redundant projections and the imperfect segregation of pathways. The second challenge is the inherent plasticity of the brain, raising the specter that the various candidate pathways change in their relative strengths over time. The third challenge is the imperfect and indirect nature of most evidence as it pertains to the pathways that support blindsight.

To take a concrete example, consider an electrophysiological study by Bender, which used lesions to investigate potential sources of visual input into the macaque inferior pulvinar (Bender, 1988). In the study, visual responses were recorded in the pulvinar of animals that were intact or had experienced unilateral ablation of either the SC or V1. Bender found that whereas SC ablation had minimal effects, V1 ablation completely abolished visual responses in the pulvinar. This finding suggests that SC inputs alone are unable to drive responses in the pulvinar, which would seem to refute any hypothesis of blindsight based on the colliculopulvinar pathway. However, in reference to the challenges mentioned above, rejecting the pulvinar contribution to blindsight based on this finding alone would be unwise. First, regarding the biological complexity of the pathways, Bender's recordings may not have adequately sampled from the two subregions of the pulvinar now suspected to be the critical visual relays (Berman and Wurtz, 2010; Lyon et al., 2010). Second, regarding the inherent plasticity of the system, Bender found that, after several weeks, a few neurons in the inferior pulvinar did, in fact, start to show modest visual responses. And third, regarding the indirect nature of experimental evidence, the demonstration of a physiological pathway in the anesthetized animal may or may not be related to residual visual performance in blindsight.

With these caveats in mind, a recent study points strongly to the LGN as being a critical relay in blindsight (Schmid et al., 2010). As mentioned earlier, following V1 ablation, fMRI responses to small stimuli in the blind field were observed in multiple extrastriate areas. Behaviorally, the monkeys were also able to respond to visual stimuli well above chance. However, following the additional pharmacological inactivation of the LGN, the residual extrastriate fMRI responses were abolished (**Figure 5b**), as was the monkey's behavioral performance, indicating that the LGN is critical for V1-independent vision. This result is consistent with two previous findings in macaques, where inactivation of all LGN layers

temporarily blocked visual responses in cortical area MT (Maunsell et al., 1990), and chemical lesions to all LGN layers permanently abolished visual detection, with no recovery even after several months (Schiller et al., 1990). It also challenges explanations of blindsight that do not include the LGN. Whether the very sparse direct projections from the LGN to the extrastriate cortex could support residual vision has been addressed by Alan Cowey, who points out that while the absolute number of such neurons is unknown, they are probably at least as numerous as all the retinal ganglion cells in the rat, a species that can exhibit reasonable visually guided behavior (Cowey, 2010).

Finally, any reading of the literature makes it difficult to escape the conclusion that the SC must also be involved in blindsight. Ablation of the SC during blindsight abolishes visual performance mediated by eye movements (Mohler and Wurtz, 1977; Kato et al., 2011) and visually guided reaching (Solomon et al., 1981) and obliterates responses in the extrastriate cortex (Rodman et al., 1990; Bruce et al., 1986). The dependence on the SC has generally been interpreted as evidence for the importance of the colliculopulvinar pathway, although they are also consistent with mediation through the colliculogeniculate pathway (Rodman et al., 1990). These findings, combined with the recent results from Schmid et al. (Schmid et al., 2010), raise the possibility that retinal information reaches the extrastriate visual cortex following V1 lesions via a colliculogeniculate pathway. Whether this pathway is, in fact, the ultimate answer to the blindsight puzzle, or whether the challenges outlined above will continue to keep the answer out of reach, remains to be seen.

WHAT IS THE ROLE OF V1 IN CONSCIOUS PERCEPTION?

We end by considering how these and other findings illuminate the specific contribution of V1 to visual awareness. As this line of inquiry runs the danger of becoming too abstract, we formulate our question in terms of a dichotomy, which may, admittedly, also be a false one: Is V1 an essential and inseparable component of the neural processes that generate perceptual awareness, or is V1 instead primarily a conduit for retinal image information, receiving, processing, and passing it along to higher, “perceptual” centers? Within this framework, we conclude that there is insufficient evidence in support of the former proposition and that the latter is more likely to be correct.

First, the neurophysiological results do not much support the view that V1 activity is a direct contributor to visual awareness. Although V1 neural activity correlates with some aspects of perception (reviewed in (Tong, 2003)), firing rates in V1 are only minimally affected when a stimulus is rendered completely invisible. In general, the responses of V1 neurons appear more closely tied to the sensory afferents arriving from the LGN than to perception-sensitive responses characteristic of some extrastriate visual areas.

Second, the blindness produced by V1 damage and unconscious vision supported by V1-bypassing pathways does not imply that V1 has a generative role in perception. While damage to V1 disrupts many pathways that could contribute to visual awareness, including, for example, feedback to V1 from the extrastriate cortex (Lamme, 2001) or feedback from V1 to the LGN, a more parsimonious explanation for blindness is the deafferentation of the extrastriate cortex and possibly the pulvinar from V1's principal feedforward visual projections. Deprived of all visual information, neither telencephalic nor higher-order thalamic centers can contribute to visual awareness. The fact that vision after V1 damage in blindsight is unconscious is not a compelling argument that V1 activity contributes directly to visual awareness. Residual visual pathways, beyond being sparse in their projections, differ from the geniculostriate pathways in many ways. They are composed mainly of $P\gamma$ and $P\alpha$ channels and may involve a relay in the SC. They may draw on a special category of hypertrophied koniocellular LGN cells that project to layer 5 of extrastriate cortex, or may

be relayed through the pulvinar exclusively to dorsal stream extrastriate cortical areas. These and many other features might help explain why the visual signals carried to the extrastriate cortex through these residual visual channels fail to reach consciousness. However none of these explanations points to a special role for V1 in the generation of visual awareness.

Third, it is not strictly correct to say that V1 damage always leads to blindness, as pointed out frequently in the human blindsight literature (Ffytche and Zeki, 2011). In addition to the difficult task of determining what exactly blindsight patients subjectively perceive, at least two findings demonstrate that they can experience vivid visual percepts in the region of visual space corresponding to the V1 lesion. First, there is “prime-sight”, where blindsight subject D.B. could consciously see an afterimage generated by a visual stimulus in the blind field, but strangely not the adapting stimulus that generated it (Weiskrantz et al., 2002). Second, transcranial magnetic stimulation (TMS) applied bilaterally over area MT of blindsight subject G.Y. produced perceptually visible phosphenes that travelled into his blind field (Silvanto et al., 2008). In both subjects, percepts in the blind field could be induced to take on a color when chromatic visual stimuli were applied. The bases of these phenomena are unknown, as is their generality. However, they do argue that visual awareness can occur in a region of space corresponding to a V1 lesion. Further evidence for V1-independent visual awareness comes from humans, and quite possibly monkeys, who are not blind if their V1 damage is acquired in infancy (for a recent review, see (Silvanto and Rees, 2011)).

In summary, the data accumulated from a wide range of anatomical, physiological, and behavioral studies in monkeys and humans paint a picture of V1 as a critical component of primate vision. Its importance, however, stems not from a direct contribution to visual awareness, but rather from its role as a highly adapted cortical lens through which the cerebral hemispheres, including the extrastriate visual cortex and many other structures thought to participate directly in perception, receive visual information about the world.

Acknowledgments

Thanks to Drs. A. Maier, L. Ungerleider, and R. Wurtz for comments on the manuscript. Thanks to Drs. M. Schmid and M. Mishkin for discussion. This work was supported by the Intramural Research Programs of the National Institute of Mental Health, National Institute for Neurological Disorders and Stroke, and the National Eye Institute.

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Figure 1.

Paradigms to study unconscious vision in monkeys. (a) During perceptual suppression a target stimulus is continuously presented on a video monitor, but disappears because of a visual illusion. Depicted here is generalized flash suppression (Wilke et al, 2003), where the presentation of a bright red patch at time t_1 is followed by the appearance of dynamic surrounding white dots at time t_2 , causing the red patch to perceptually disappear for up to several seconds. (b) Cortical blindness following V1 lesion leads to the inability to perceive stimuli in an entire region of visual space corresponding to the retinotopic position of the lesion. Following such lesions, blindsight allows for some residual visual responses to stimuli presented to the scotoma (blind portion of the visual field).

Figure 2.

Sensory and spontaneous physiology across V1 layers. (a) The basic pathways projecting from the LGN to the different layers of V1, including the magnocellular (M), parvocellular (P) and koniocellular (K). (b) Current source density (CSD) response to flashed stimuli in V1. The horizontal line is drawn through the initial current sink in layer 4C (Maier et al., 2011). (c) Spontaneous spiking responses in different cortical layers of monkeys sitting in a dark room (Snodderly and Gur, 1995). (d) Sustained CSD power that persists in the infragranular layers during the presentation of a simple stimulus (Maier et al., 2011). (e) Pattern of coherence of spontaneous high-frequency (gamma) local field potential (LFP) activity. Pairwise coherence is computed between a reference position (arrows) and all other laminar positions (Maier et al., 2010).

Figure 3.

Neural correlates of perceptual suppression in V1. (a) Spiking modulation in V1 and V4 of visual responses associated with perceptual suppression vs. physical removal of a stimulus (Wilke et al., 2006). (b) Local field potential (LFP) modulation in V1 associated with perceptual suppression vs. physical removal of a stimulus (Maier et al., 2008). (c) Comparison of the effects of perceptual suppression on the blood oxygenation level-dependent (BOLD) vs. spiking signals in V1 (Maier et al., 2008).

Figure 4.

Visual pathways through the dorsal thalamus to the cortex. (a) Targets of retinal ganglion cells in the diencephalon and mesencephalon. Projections are depicted on an embryonic brain to emphasize the relative positions of the retinal projection targets with respect to the neuraxis. Note that this depiction is for schematic purposes only, as the neural connections have not been formed at this stage of development. The strongest projections are to the lateral geniculate nucleus, followed by the superficial layers of the superior colliculus. (b) Schematic illustration of pathways to the cortex. There are two direct pathways from the retina to the dorsal thalamus, a retinogeniculate pathway (1) and a retinopulvinar pathway (2), along with two indirect pathways that pass through the midbrain, the retinocolliculogeniculate pathway (3) and the retinocolliculopulvinar pathway (4). Both the inferior pulvinar and the lateral geniculate nucleus project to both V1 and extrastriate visual cortex (A-D), with the former projecting predominantly to V1 (A) and the latter projecting predominantly to the extrastriate cortex (D). Of particular interest for understanding blindsight are the direct extrastriate projections, (C) and (D). DT, dorsal thalamus; H, hypothalamus; P, pons; LGN, lateral geniculate nucleus; M, medulla oblongata; Pim, medial division of the inferior pulvinar; PT, pretectum; SC, superior colliculus; VC, visual cortex.

Figure 5.

Extrastriate visual activation following V1 lesion and LGN inactivation. (a) Residual responses of single-units in multiple extrastriate visual areas following the destruction or cooling of V1 in the macaque (Bullier et al., 1994) (b) Functional magnetic resonance imaging (fMRI) responses in a range of extrastriate cortical areas in a normal hemisphere (blue), following V1 damage (red), and following V1 damage combined with acute inactivation of the LGN (green) (Schmid et al., 2010).