

NEURAL CORRELATES OF CONSCIOUSNESS IN HUMANS

Geraint Rees^{*‡}, Gabriel Kreiman[§] and Christof Koch^{¶||}

The directness and vivid quality of conscious experience belies the complexity of the underlying neural mechanisms, which remain incompletely understood. Recent work has focused on identifying the brain structures and patterns of neural activity within the primate visual system that are correlated with the content of visual consciousness. Functional neuroimaging in humans and electrophysiology in awake mokeys indicate that there are important differences between striate and extrastriate visual cortex in how well neural activity correlates with consciousness. Moreover, recent neuroimaging studies indicate that, in addition to these ventral areas of visual cortex, dorsal prefrontal and parietal areas might contribute to conscious visual experience.

ASCENDING RETICULAR ACTIVATING SYSTEM

A loosely organized core of neurons that extends from the midbrain to the thalamus. These neurons project widely to the cerebral hemispheres and are thought to be involved in maintaining the alert state.

^{*}*Institute of Cognitive Neuroscience, University College London, Alexandra House, 17 Queen Square, London WC1N 3AR, UK.*

[‡]*Wellcome Department of Cognitive Neurology, Institute of Neurology, 12 Queen Square, London WC1N 3BG, UK.*

[§]*Division of Biology and*
^{||}*Division of Engineering and Applied Science, 139-74, California Institute of Technology, Pasadena, California 91125, USA.*

Correspondence to G.R. e-mail: g.rees@fil.ion.ucl.ac.uk

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The search for the neural correlate (or correlates) of consciousness¹ has resulted in two important distinctions being made. The first is that the neural correlates of the level of consciousness (for example, awake, asleep, attentive or drowsy) should be distinguished from the neural correlates of specific phenomenal content (such as a green apple versus an orange). This distinction reflects our everyday experience of the phenomenal distinction between being conscious (as opposed to being unconscious) and being conscious of X (as opposed to not being conscious of X). The level of consciousness can be thought of as an enabling factor (like neuronal arousal mediated by the ASCENDING RETICULAR ACTIVATING SYSTEM², or even heartbeat) that is required for awareness but does not directly reflect specific conscious experiences.

The second distinction is between neural activity that correlates directly with a single conscious experience and activity that reflects unconscious perception (or action) associated with that experience. This reflects the common observation that many of the cognitive processes that underpin our conscious experience are inaccessible to introspection. Similarly, stimuli that bypass awareness can influence behaviour not only in pathological conditions (such as NEGLECT³), but also in normal subjects⁴. To identify neural correlates of consciousness, investigators must use experimental designs that dissociate the contributions of conscious and

unconscious processes to sensory experience, typically by manipulating them independently⁵.

A neural correlate of consciousness is a specific pattern of brain activity that correlates with particular conscious experiences. It is not clear how any physical process, such as neural activity, can give rise to a subjective phenomenon such as awareness. Indeed, even the possibility of such a causal relationship remains controversial among philosophers^{6–8}. The search for the neural correlates of consciousness is therefore an empirical investigation that remains initially neutral on issues of causality, seeking instead to identify and characterize patterns of neural activity that specifically correlate with conscious experience, rather than with unconscious perception or action.

In this review, we focus on the neural correlates of awareness of specific phenomenal content in the human visual system^{9,10}. The visual system is the best-studied sensory system, and a wealth of anatomical and physiological data from non-human primates complements psychophysical, electrophysiological and functional neuroimaging investigations in humans.

Awareness and primary visual cortex

When a stimulus is presented visually, successive hierarchical levels of the visual system are rapidly activated through a cascade of feedforward connections (see below for a discussion of feedback connections).

Box 1 | Measuring neural correlates of consciousness

Recording the activity of single neurons in humans and non-human primates is invasive: it requires electrodes to be inserted through the skull and into the brain, which can put subjects at risk of injury and infection. Such electrodes can be used to record extracellular single-neuron activity, multi-unit activity and local field potentials (LFPs). Single- and multi-unit activity reflects the action potentials that are produced by local processing in, and output from, a cortical area. Recording the spiking activity of neurons is considered to be the gold standard that is necessary for a quantitative and reductionist explanation of perception and behaviour in terms of its underlying constitutive elements. By contrast, LFPs represent the aggregate activity of a population of neurons located close to the electrode, and are thought to reflect mainly synaptic activity localized to dendrites and somata. Such activity is associated with both input to, and processing within, a cortical area.

An important issue in understanding the neural correlates of consciousness is how such invasive electrophysiological measures of neuronal activity relate to non-invasive measures of brain activity, such as the scalp electroencephalogram (EEG) or functional neuroimaging. The most popular form of functional neuroimaging, blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI), measures a component of the haemodynamic response that is associated with local neural activity¹⁰⁵. Several studies have shown an essentially linear relationship between non-simultaneous measures of multi-unit activity and the fMRI bold signal^{106–109}. Recent evidence¹¹⁰ using simultaneous extracellular recording and BOLD contrast fMRI in anaesthetized monkeys indicates that both multi-unit activity and LFPs are correlated with BOLD contrast in the visual cortex. In this study, LFPs were a slightly better predictor of BOLD contrast than multi-unit activity and, indeed, for some recording sites, BOLD remains elevated at a time when multi-unit activity returns to baseline. This indicates that, in certain circumstances¹¹¹, BOLD contrast might reflect pre- and postsynaptic dendritic activity (and hence input processing in an area) more closely than multi-unit activity (output or intracortical processing from an area) owing to the presence of inhibition. Taken together, this evidence indicates that the firing activity of a neuronal population will, in general, be proportional to the BOLD response. However, there could also be cases in which there is no correlation between BOLD contrast and spiking activity. For example, feedback activity from higher cortical areas to lower ones will give rise to metabolic demand in the lower area due to the associated synaptic activity, and so result in enhanced BOLD contrast, but might not give rise to spiking activity in the affected neurons. Another popular non-invasive technique, the scalp EEG/event-related potential (ERP), is also thought to reflect the summed electrical effects of excitatory synaptic neurotransmission in large populations of neurons¹¹². Consistent with the association of BOLD contrast fMRI and LFPs, there is an essentially linear relationship between ERP amplitude and BOLD signal in visual¹¹³ and primary somatosensory cortex¹¹⁴. Despite this good agreement between population measures of neural activity and single-cell measures, it is important to bear in mind that changes in the distribution of neural activity in a population of neurons might cause large changes in single-cell firing rates without altering the overall summed population activity^{111,115}.

NEGLECT

A neurological syndrome (often involving damage to the right parietal cortex) in which patients show a marked difficulty in detecting or responding to information in the contralesional field.

BLINDSIGHT

The ability of a person with a lesion in the primary visual cortex to reach towards or guess at the orientation of objects projected on the part of the visual field that corresponds to this lesion, even though they report that they can see nothing in that part of their visual field.

Anatomically, the primary visual cortex, V1, is the lowest cortical visual area. Patients with damage to V1 typically report no conscious visual experience in their blind visual field, even though some residual capacity for unconscious visual discrimination might remain — a phenomenon known as blindsight^{11,12}. This shows that V1 is necessary for normal visual perception. However, by itself, it does not reveal whether activity in V1 gives rise directly to conscious visual experience, or whether further processing in extrastriate areas is necessary. This situation is similar to that of the retina. Activity in retinal ganglion cells is necessary for normal vision. But most observers would agree that the receptive field properties of these cells are too different from the properties of visual perception for them to give rise directly to conscious vision.

In 1995, Crick and Koch¹³ proposed that a key function of consciousness is to produce the best current interpretation of the visual scene in a compact form and to make this information available to the planning stages of the brain. As the cognitive processes involved are associated with the frontal lobes¹⁴, and as V1 does not project directly to premotor or prefrontal areas, Crick and Koch surmised that the activity of V1 neurons, although necessary for most forms of normal vision, does not constitute part of the neural correlates of consciousness.

Psychophysical evidence is broadly consistent with the proposal that information represented in V1 is not available to consciousness. For example, we cannot perform utricular discrimination (identifying the eye to which a stimulus is presented), even though V1 contains neurons that receive input from one eye only, and so represent this information¹⁵. Similarly, orientation-dependent aftereffects, which are thought to arise from the activity of cells in the primary visual cortex, can be induced by stimuli that cannot be consciously perceived. For example, the orientation of a grating is rendered invisible and indiscriminable by crowding when it is presented with four similar gratings positioned above and below it. However, adaptation to such a grating results in an orientation-dependent aftereffect that is indistinguishable from that produced when it is presented alone with its orientation clearly (and consciously) perceived¹⁶. In addition, very high-frequency gratings that are perceptually indistinguishable from a uniform field nevertheless produce robust orientation-dependent aftereffects¹⁷. The presence of aftereffects from stimuli that are not consciously perceived¹⁸ indicates that stimulus properties must be represented outside awareness. So, activity in V1 often does not correlate with awareness.

These inferences are complemented by direct electrophysiological measurements of neuronal activity in V1 in macaque monkeys that show that perceptual report (presumably reflecting awareness) and neuronal activity can change completely independently. For example, disparity-selective cells in V1 differentiate between local depth cues even when these do not give rise to an overall depth percept¹⁹. Similarly, V1 cells can respond in an identical manner to two depth cues that yield very different global depth percepts¹⁹. This indicates that single V1 cells that are sensitive to binocular disparity might represent a first crucial stage for generation of stereo cues, but that conscious perception of depth is probably generated further upstream. A similar lack of correlation between perceptual experience and the response properties of V1 cells can be seen during blinks. Blinking produces profound and frequent interruptions in retinal stimulation, but barely impinges on our visual experience (which remains continuous). The responses of cells in the supragranular layers of V1 to visual stimulation decrease substantially during reflex blinks²⁰, and this reduction is significantly more pronounced than when there is an equally long gap in visual stimulation. Similarly, microsaccades, which occur continually, do not alter our impression of the world, but are reflected in the

Box 2 | Dreaming and neural correlates of consciousness

Although dreams are intensely visual experiences, and often seem to be as vivid as life itself, dream consciousness differs from that in the waking state, most importantly in the absence of insight and self-awareness. However, the neural processes that occur during awake seeing seem to be closely related to those that occur during visual dreaming. Sleep is conventionally divided into several distinct phases on the basis of the scalp electroencephalogram (EEG)^{116,117}. During slow-wave sleep (SWS), dreaming typically does not occur and the scalp EEG is dominated by high-amplitude, low-frequency oscillations. Most vivid visual dreams take place during the rapid eye movement (REM) phase of sleep¹¹⁸, when the scalp EEG shows similar patterns of activity to the waking state, being characterized by high-frequency, low-amplitude signals.

In humans, brain activity measured with functional magnetic resonance imaging (fMRI) during REM sleep is suppressed in primary visual cortex and directly adjacent areas (compared with non-REM phases of sleep), whereas intermediate visual areas in the fusiform gyrus and medial temporal lobe are highly activated¹¹⁹ (for reviews, see REFS 120,121). By contrast, during SWS, activation of the primary auditory¹²² and visual^{119,123} cortices is observed, but medial temporal areas are deactivated. Suppression of activity in V1 during REM sleep is consistent with the finding that patients who have lost part or all of V1 continue to dream visually. Global cessation of dreaming is associated with unilateral damage to either frontal or parietal cortex¹²⁴. However, specific loss of visual dreams is associated with bilateral lesions in the medial occipitotemporal region. Interestingly, patients who describe exclusively non-visual dreaming also show complete deficits in visual reminiscence and some form of visual agnosia such as prosopagnosia or TOPOGRAPHICAL AGNOSIA¹²⁴.

Together, these data indicate that there is an important dissociation in brain activity during dream and non-dream sleep. Visual sensations can be experienced during dreams in the absence of input to, or activity in, primary cortical areas; this is consistent with the idea that activity in higher visual areas is better correlated with the contents of consciousness.

MICROSACCADES

Small, abrupt eye movements that occur constantly during normal vision.

TOPOGRAPHICAL AGNOSIA

A condition in which patients become disorientated because they can no longer recognize their environment.

VISUAL EXTINCTION

This is often associated with damage to the parietal cortex. The patient can see a stimulus presented alone in the contralateral visual field, but cannot see it if it is presented at the same time as a stimulus in the ipsilateral visual field.

AKINETOPSIA

The inability to perceive moving stimuli.

ACHROMATOPSIA

The inability to perceive colours.

PROSOPAGNOSIA

Classically, a type of visual defect in which the patient cannot identify a familiar face, even though they know that a face is a face and can point out the features.

activity of neurons in V1 (REF 21). Finally, activity in striate cortex neurons faithfully follows rapid chromatic flickering of a coloured grating even when the flickering is too fast for humans to resolve the individual colours²². So, individual cells in primary visual cortex show response patterns that are quite unlike conscious visual experience.

Changes in conscious perception can also occur in the absence of concomitant variations in neuronal activity in V1. Binocular rivalry has proved to be a powerful paradigm with which to study the neural correlates of conscious visual experience²³. When two dissimilar images are presented to corresponding areas of the two eyes, they compete for perceptual dominance. Each image is visible in turn for a few seconds, while the other is suppressed. Perceptual transitions between each monocular view occur without any corresponding change in the physical stimulus, allowing experimental dissociation of the neural correlates of consciousness from changes that are attributable to stimulus characteristics. Monkeys can be trained to report their percept during rivalry, and their behaviour is similar to that of humans²⁴. In monkeys, the firing of most cells in and around V1 primarily reflects stimulus properties rather than the conscious percept reported by the animal²⁵, which is consistent with the evidence presented above. However, several neuroimaging studies in humans have presented evidence that argues for a stronger role of V1 in binocular rivalry and hence, by implication, visual awareness. Averaged over the whole of human V1, there are reliable fluctuations in blood oxygen level dependent

(BOLD) contrast activity when the conscious percept changes²⁶. These fluctuations are about half the size of those evoked by non-rivalrous stimuli, and even larger in the part of V1 that is associated with the blind-spot representation²⁷ (which contains cells that receive only monocular input from the other eye). The reasons for the discrepancy between human and monkey data (and between the blind-spot representation and the rest of V1) are not yet clear. Areas of human V1 such as the blind-spot representation might have special properties or, alternatively, the discrepancy might lie in the relationship between single-cell activity and BOLD contrast measurements (BOX 1).

Other studies in humans show a poor correlation between V1 activity and visual awareness. During dreaming, intensely visual experiences are associated with suppression of activity in V1 (BOX 2). Activity in V1 in the absence of awareness is observed in patients with damage to the right parietal cortex and VISUAL EXTINCTION^{28–30}. Patients with visual extinction show deficient awareness for contralesional visual stimuli, particularly when a competing stimulus is also present ipsilesionally³. An extinguished left visual field stimulus of which the patient is unaware nevertheless evokes activity in V1 that is very similar to that evoked by a stimulus in the left visual field that is seen^{28,29,31} (FIG. 1). This indicates that the presence of activity in primary visual cortex *per se* is insufficient to support visual awareness, at least after damage to the right parietal cortex.

We conclude that the current data are compatible with the hypothesis that neurons in V1, although necessary for normal visual experience, do not give rise, by themselves, to conscious visual perception — in other words, activity in V1 cells is not sufficient to explain conscious perception.

Awareness and ventral visual cortex

Beyond V1, the primate visual system is organized in a distributed fashion, with different aspects of the visual scene being analysed in different cortical areas³⁰. These areas are densely interconnected in non-human primates, although in humans the equivalent anatomical connectivity is less well established (FIG. 2). On the basis of anatomical criteria, different areas form a rough hierarchy that fits well with the physiological hierarchy in receptive field size and complexity of tuning properties in these areas. Damage to cortical areas that contain neurons that are tuned to specific features of the visual environment leads to a corresponding deficit in consciousness of these features. So, bilateral damage to the human homologue of area V5/MT (middle temporal area), which contains neurons that respond specifically to moving visual stimuli, leads to AKINETOPSIA³². Similarly, damage to colour-selective areas in human ventral occipitotemporal cortex³³ can result in ACHROMATOPSIA³⁴. Finally, damage to areas of the fusiform gyrus that contain face-responsive neurons (the ‘fusiform face area’ or FFA^{35,36}) can cause PROSOPAGNOSIA³⁷. In contrast to damage to V1, which gives rise to a general deficit in awareness for all stimuli presented in a particular region of space, damage to ventral visual cortex causes specific deficits

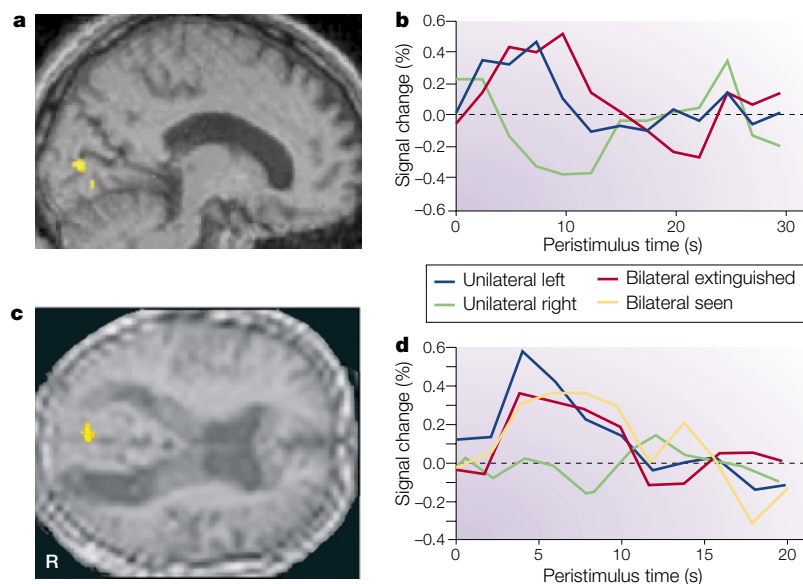


Figure 1 | Activity in V1 does not correlate with awareness. **a** | A sagittal slice through the right hemisphere including the calcarine sulcus of patient G.K., who suffered a right parietal stroke that caused visual extinction. The image shows the locus in V1 that is activated by an unseen and extinguished left visual field stimulus (as measured by blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI), superimposed). **b** | Peristimulus time histogram of BOLD contrast activity evoked by three different types of visual stimulus, taken from the activated right V1 locus in panel **a**. Left visual field stimuli that are either seen (unilateral left trials) or unseen (bilateral extinguished trials) evoke similar patterns of activity, whereas a right visual field stimulus that is seen (unilateral right) results in little positive response in right V1. **c** | An axial image through V1 of another patient with right parietal stroke and visual extinction. Superimposed on the image is the BOLD contrast activity evoked in right V1 by an unseen extinguished left visual field stimulus. **d** | Peristimulus time histogram of BOLD contrast activity evoked by four types of visual stimulation, taken from the activated right V1 locus in **c**. Seen bilateral, unseen and extinguished bilateral, and seen left unilateral stimulation all produce similar patterns of activity, whereas seen right unilateral stimulation evokes little response in ipsilateral visual cortex. Parts **a** and **b** modified with permission from REF. 31 © 2000 Oxford University Press. Parts **c** and **d** modified with permission from REF. 29 © 2001 National Academy of Sciences, USA.

in awareness for particular types of stimulus or object feature. These findings indicate that activity in a functionally specialized cortical area — termed an ‘essential node’ by Zeki³⁸ — is required to evoke consciousness of the attribute that is analysed in that area.

Data from neuroimaging studies are consistent with this idea. Patients with **schizophrenia** show activity in modality-specific cortex during visual or auditory hallucinations³⁹, even though no external stimulus is presented. During visual hallucinations that have a specific form, activity in visual cortex reflects the perceived content of the hallucinatory episode⁴⁰. In normal subjects, contingent aftereffects based on colour^{41–43} or motion^{44–46} result in activation of corresponding functionally specialized cortices, and the time course of such activation reflects reported experience⁴⁴. Perception of illusory⁴⁷ or implied⁴⁸ motion in a static visual stimulus results in activation of area V5/MT, whereas perception of illusory contours activates **EXTRASTRIATE CORTEX**^{49–51}. Areas that are associated with processing the meaning of flashed words are activated when the words are consciously perceived at the focus of attention, but not when attention is withdrawn and the words are no longer consciously

perceived⁵². In these experiments, the subjects’ phenomenal experience changes without corresponding changes in the physical stimulus⁵. Concomitant with these changes in perceptual experience, altered activity is observed in areas of the brain that contain neurons with stimulus specificities that encompass the attribute being represented in consciousness.

Binocular rivalry and the related phenomenon of **FLASH SUPPRESSION**⁵³ have also been used to probe the involvement of areas beyond V1 in visual awareness. Classic studies in monkeys have shown that the proportion of neurons with activity that reflects the monkey’s perceptual report (rather than the stimulus properties) increases from V1 along the ventral visual pathway⁵⁴. In monkey inferior temporal cortex, most of the relevant neuronal responses reflect conscious perception rather than the retinal stimulus²⁵. These data are compatible with more recent functional magnetic resonance imaging (fMRI) observations in humans experiencing binocular rivalry^{26,55,56} (FIG. 3). During rivalry, fMRI responses that are recorded in the human FFA to face stimuli (and in the parahippocampal gyrus to images of places) are large and equal in magnitude to responses that are evoked by non-rivalrous stimuli⁵⁶.

The activity of single neurons can be recorded in even more anterior regions of the medial temporal lobe in epileptic patients in whom electrodes have been implanted for presurgical mapping. Such rare electrophysiological investigations in humans have found many neurons that are tuned for specific categories of visual stimulus⁵⁷. Most of these neurons fire selectively when their preferred stimulus is perceived — but not when it is perceptually suppressed (and invisible) — during binocular rivalry or flash suppression⁵⁸. Furthermore, single neurons that show category-specific responses to visual stimulation are activated to a similar degree during visual imagery or passive presentation of a visual stimulus⁵⁹ (FIG. 4). These single-cell findings complement neuroimaging studies that show activation of common brain areas during both visual processing and recall during imagery of specific types of stimulus^{60,61}. Moreover, they indicate that activity at the level of neuronal populations, as seen with fMRI in humans, might be reflected at the level of single neurons (BOX 1).

The evidence reviewed above indicates that the spiking activity of individual neurons in ventral visual cortex, in contrast to those in V1, generally correlates well with the visual contents of consciousness. However, the correlation is not perfect and other studies using fMRI in humans indicate that activity in ventral visual cortex might not always be correlated with visual awareness (FIG. 1). Stimulation of the blind hemifield of patients with damage to V1 results in activation of extrastriate cortex in the ventral visual pathway by the unseen visual stimulus^{62,63}. In visual extinction resulting from damage to the right parietal cortex, an unseen and extinguished face stimulus can evoke face-specific activity in extrastriate visual cortex and more anteriorly in the FFA^{28,29,31}. These studies in patients with cortical damage are complemented by investigations of

EXTRASTRIATE CORTEX
A belt of visually responsive areas of cortex surrounding the primary visual cortex.

FLASH SUPPRESSION
The perceptual suppression of a monocular stimulus on flashing a different stimulus to the opposite eye, while keeping the original stimulus on the other eye.

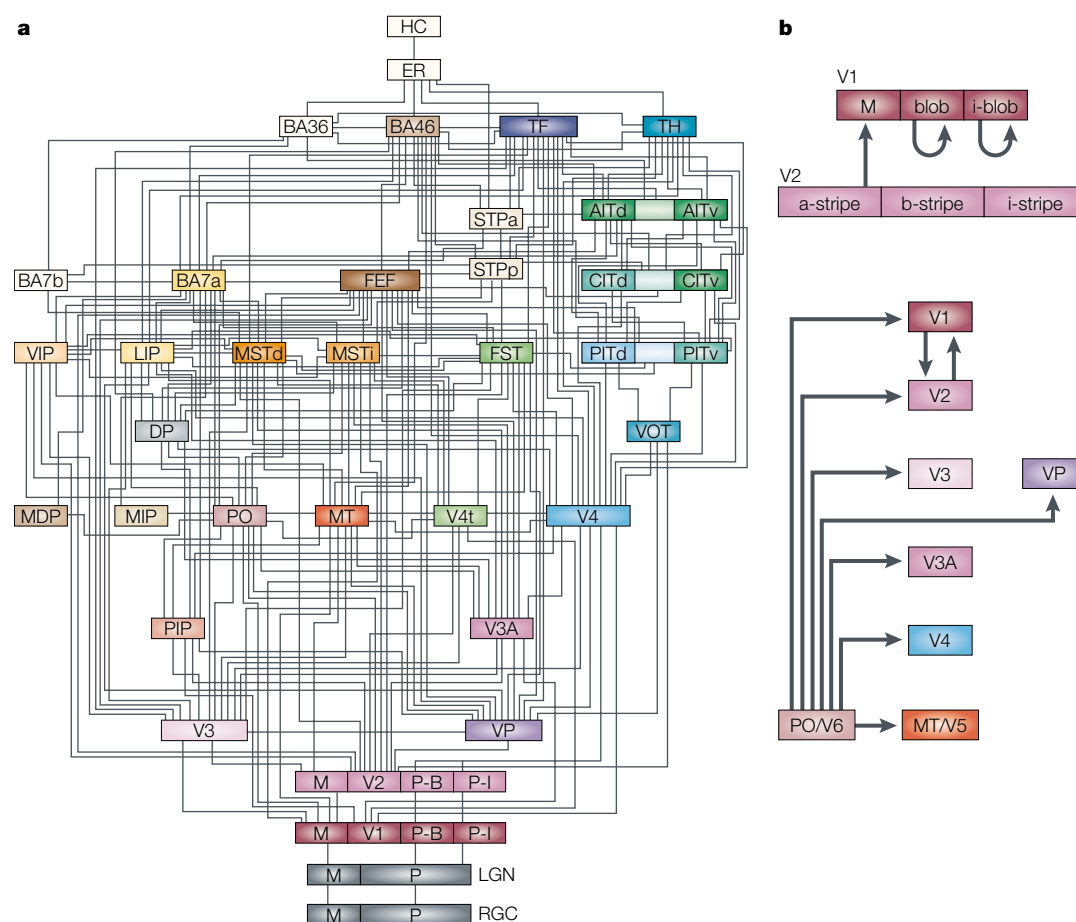


Figure 2 | Anatomical hierarchy of visual areas in human and non-human primate. a | A summary of the layout and demonstrated anatomical connectivity of macaque visual cortex. Thirty-two visual cortical areas, two subcortical visual stages and several non-visual areas are shown, connected by 187 anatomically demonstrated links, most of which are reciprocal. Modified with permission from REF. 30 © 1991 Oxford University Press. **b** | Identified visual areas, demonstrated connectivity and putative hierarchical organization of human visual cortex. There has been little direct study of the pattern of connections between human visual areas, but several characteristics of the macaque model (such as selective connections within V1 and between V1 and V2, plus the range of backprojections from higher-order visual areas) are present. Modified with permission from REF. 125 © 1997 Plenum Press. M, blob and i-blob are subdivisions of V1, characterized by cytochrome oxidase staining. a-stripe and i-stripe are subdivisions of V2, identified using cytochrome oxidase staining. AIT, anterior inferotemporal cortex; BA, Brodmann area; CIT, central inferotemporal cortex; d, dorsal; DP, dorsal prelunate area; ER, entorhinal cortex; FEF, frontal eye fields; FST, floor of superior temporal cortex; HC, hippocampus; LGN, lateral geniculate nucleus; LIP, lateral intraparietal area; M, magnocellular regions; MDP, mediodorsal parietal area; MIP, medial intraparietal area; MSTd, dorsal part of the medial superior parietal area; MSTl, inferior part of the medial superior parietal area; MT, middle temporal cortex (visual area 5); P, parvocellular regions; P-B, parvo-blob; P-I, parvo-interblob; PIP, posterior intraparietal area; PIT, posterior inferotemporal cortex; PO, parieto-occipital area (visual area 6); RGC, retinal ganglion cells; STPa, anterior superior temporal polysensory cortex; STPp, posterior temporal polysensory cortex; TF–TH, temporal areas; v, ventral; V1–V4t, visual areas; VIP, ventral intraparietal area; VOT, visual occipitotemporal cortex; VP, ventroposterior visual area.

stimulus masking in normal subjects. Awareness of a single word is profoundly degraded if it is presented very briefly and followed by a pattern mask. When subjects are unable to report the presence or absence of a masked word, it can nevertheless evoke activity in extrastriate visual cortex and the fusiform gyrus, leading to identity-specific priming, independently of the physical characteristics of the stimulus⁶⁴. Similarly, semantically anomalous words presented during the ATTENTIONAL BLINK produce an N400 EVOKED POTENTIAL (thought to have its basis in processing in the ventral visual pathway⁶⁵), even though they do not reach awareness⁶⁶.

So, although single-cell activity at some levels of the ventral visual pathway correlates strongly with conscious

vision, evidence from fMRI indicates that the presence of some level of BOLD activity by itself might not be sufficient to produce a conscious experience. BOLD contrast activity evoked by unseen stimuli in ventral visual cortex is typically much smaller than for seen stimuli. For example, there is approximately a tenfold difference in the level of activation in ventral visual cortex between masked words that are consciously perceived and those that are not⁶⁴. It is not yet clear whether this is because neural activity has to exceed a certain threshold to reach consciousness, or because consciousness is related in a continually graded way to activation. For example, the observation that object recognition performance correlates strongly with the overall level of

ATTENTIONAL BLINK

The brief time after responding to an attended visual stimulus during which a subsequent visual stimulus cannot be seen or reported accurately.

N400 EVOKED POTENTIAL

A characteristic waveform that appears 400 ms after presentation of a target word and is considered to represent an index of language processing.

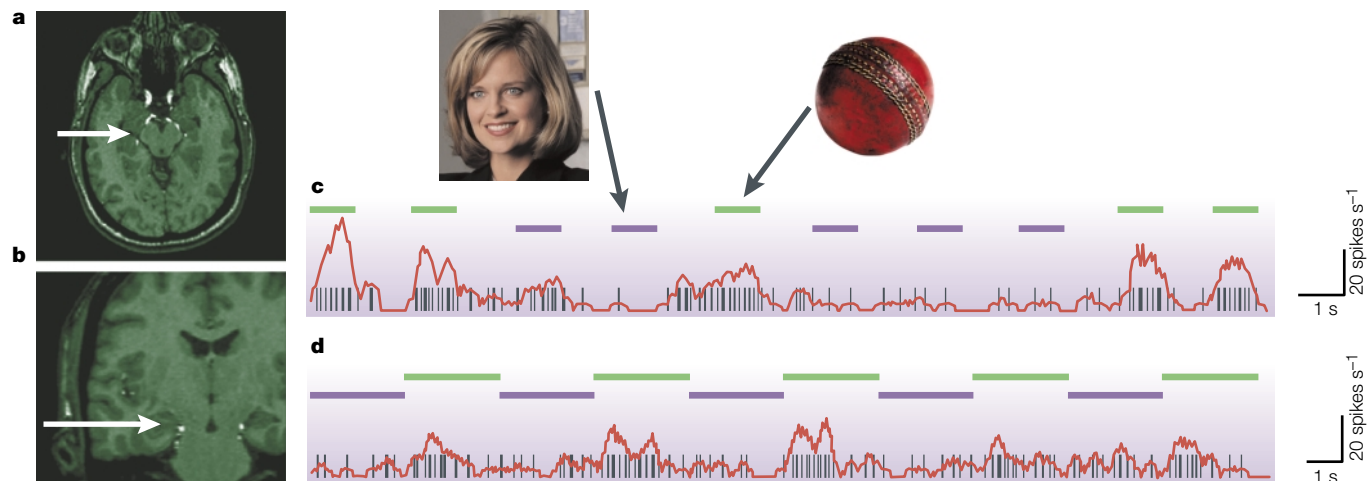


Figure 3 | Single-neuron activity in human temporal cortex correlates with awareness. a, b | Electrode placement. The trajectory of an electrode placed in the hippocampus is depicted in axial (**a**) and coronal (detail, **b**) structural magnetic resonance images. Post-operative computerized tomography (CT) and magnetic resonance imaging (MRI) were used to confirm the location of the electrode. The CT was co-registered with MRI structural information for anatomical verification. The distal end of the electrode included platinum–iridium microwires from which single neurons were recorded. The microwires extended about 4 mm from the tip, lying on a cone with an opening angle of less than 45°. **c** | Individual responses of a single neuron during vision. Two images were shown separately for 1 s each, with five repetitions per image, indicated by horizontal green and blue bars. After each picture, subjects pressed a button to indicate whether or not the picture was a human face. The continuous red line shows the spike density function. **d** | After ten visual presentations, subjects closed their eyes and imagined one picture on hearing a high tone and the other picture on hearing a low tone. Tones were alternated every 3 s. Data shown are from the same neuron during visual imagery. This neuron showed a similar pattern of firing during visual presentation and visual imagery, with increased firing rate in response to the image of the ball, but not that of a human face. Modified with permission from REFS 57,59 © 2000 Macmillan Magazines Ltd.

BINDING PROBLEM

The problem of binding together in a single unified percept the different features of an object, which are represented in different locations in the brain. For multiple objects, binding the correct features of each object to its perceptual representation is a particularly complex problem.

STRABISMIC CATS

Strabismus is a condition in which the eyes are not straight or properly aligned. The misalignment reflects the failure of the eye muscles to work together. One eye might turn in (crossed eyes), turn out (wall eyes), turn up or turn down. Although some cats are congenitally strabismic, strabismus can also be achieved by cutting the tendon of one of the eye muscles.

STEADY-STATE NEUROMAGNETIC RESPONSES

Changes in electrical activity in the brain produce tiny magnetic field perturbations that can be detected as neuromagnetic responses using an array of magnetometers placed on the scalp in a magnetoencephalographic scanner.

activity in occipitotemporal visual cortex⁶⁷ indicates that there is a graded relationship between brain activity and visual awareness. Resolving this issue will be an important focus for future research, and depends in part on understanding the relationship between BOLD contrast and neuronal activity (BOX 1).

We conclude that the current data show that activity in functionally specialized regions of ventral visual cortex is necessary for conscious experience of specific features, and that there is generally a strong correlation between activity in such areas and conscious experience. However, as with V1, although activity in ventral visual cortex is necessary, it might not be sufficient for conscious visual experience.

The timing of neural activity

The data reviewed above have addressed the hypothesis that there might be anatomically localized neurons or neural pathways with a level of spiking activity that mediates awareness. However, the overall level of spiking in a specific area need not be the relevant neural correlate. Another hypothesis is that awareness might be associated with specific types of neural activity, such as oscillatory or synchronized discharges. These two hypotheses are not mutually exclusive, and a combination of synchronous activity and neural spike rates might be an important attribute of the neural correlates of consciousness.

The surface electroencephalogram (EEG) is recorded from the scalp and reflects electrical activity in the human brain. It shows complex patterns of activity in different frequency ranges⁶⁸. The dominant frequency components change according to the level of consciousness (BOX 2). It has been suggested that synchronized oscillations in the high-frequency range (40–150 Hz)

might underlie feature integration (and so be a candidate solution to the so-called BINDING PROBLEM⁶⁹) and form a substrate for visual awareness^{1,70}, although this idea remains controversial⁷¹. In support of this theory, cognitive processes that are thought to be closely associated with awareness⁷² can modulate synchrony. For example, selective attention synchronizes evoked activity in visual⁷³ and somatosensory⁷⁴ cortex. Moreover, spontaneous fluctuations in perceptual state during binocular rivalry are accompanied by changes in synchrony among V1 neurons in STRABISMIC CATS⁷⁵. On a larger spatial scale, STEADY-STATE NEUROMAGNETIC RESPONSES have shown a correlation between perception of a visual stimulus during binocular rivalry and both interhemispheric and intrahemispheric coherence⁷⁶. Viewing ambiguous visual stimuli that can be perceived as either faces or meaningless shapes leads to a long-distance pattern of synchronization in the scalp EEG that is specific for face perception and corresponds to the moment of conscious perception itself⁷⁷. Although these findings are highly suggestive of a role for synchronous processes in conscious vision, a synthesis has not yet emerged. There is no clear evidence in primates that disrupting synchrony causes any perceptual impairment, unlike the situation for the insect olfactory system⁷⁸, so any causal role for synchrony in perceptual awareness remains open to debate. This is a very difficult question to address empirically.

Another possibility is that the specific time at which neural activity occurs (relative to stimulus presentation) might be important. Neurons in V1 change their tuning dynamically over the course of a response to a visual stimulus⁷⁹. Similarly, complex properties of facial stimuli such as facial identity seem to be represented only in the later part of the responses of neurons in inferior temporal

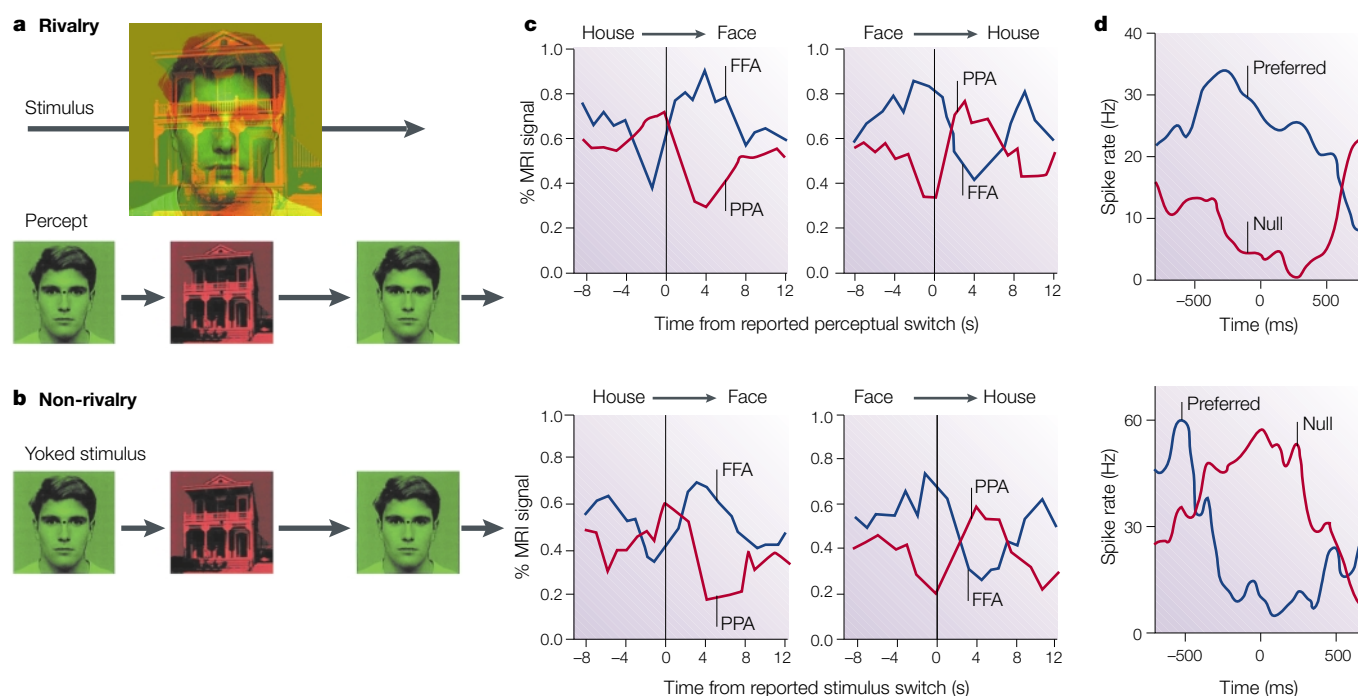


Figure 4 | Neural correlates of awareness during binocular rivalry. **a** | Stimuli that elicit binocular rivalry consist of dissimilar images that are presented separately to each eye (the stimulus shown is used in conjunction with red/green filters to achieve this). Subjects typically report spontaneous perceptual alternations between each monocular view every few seconds, as illustrated below (percept). **b** | Neuroimaging studies of binocular rivalry in humans have typically compared the activity associated with switches between alternate percepts during binocular rivalry with that associated with yoked physical alternations between monocularly presented stimuli, using the temporal sequence derived from the perceptual report of an earlier period of binocular rivalry (yoked stimulus). **c** | Activity, assessed by magnetic resonance imaging (MRI), in the fusiform face area (FFA) and parahippocampal place area (PPA) that is associated with perceptual alternations between the rivalrous house and face stimuli shown in **a**. When a switch occurs during rivalry from house to face, activity in the FFA increases and that in the PPA decreases; the reverse pattern is seen for switches from face to house (top panels). So, activity in these functionally specialized areas of visual cortex closely correlates with the content of reported perceptual experience. The strength of these modulations of activity is very similar to that produced by physical alternation between stimuli (bottom panels). Modified with permission from REF. 56 © 1998 Elsevier Science. **d** | Similar patterns of activity can be seen when activity is recorded from single neurons in monkey area V4 during binocular rivalry in which the rivalrous stimuli have different orientations, one of which is the preferred orientation of the cell. The upper panel shows activity recorded from a cell that responded strongly when the monkey reported perception of the preferred orientation (preferred), but not when the non-preferred orientation was dominant (null). The lower panel shows a neuron that fired strongly when its preferred orientation was suppressed (null), but not when its preferred orientation was perceived (preferred). Modified with permission from REF. 54 © 1996 Macmillan Magazines Ltd.

cortex⁸⁰. Neural responses are also modulated by signals that originate outside their CLASSICAL RECEPTIVE FIELDS. This modulation reflects several properties that are relevant to visual perception, such as texture segregation and grouping⁸¹, as well as higher-order processes such as working memory⁸¹. It has been proposed that these higher-order properties result from feedback connections from higher areas and might be required for awareness^{82,83}. In humans, perception of moving phosphenes caused by stimulation of area V5 with transcranial magnetic stimulation (TMS) can be diminished by stimulation of V1, but only if the stimulation of V1 is applied after the TMS pulse to V5 (REF. 84). This preliminary evidence indicates that conscious perception of moving phosphenes might be contingent on feedback connections to V1 that are disrupted by the second pulse.

Parietal and prefrontal cortex

Recent neuroimaging investigations into the neural correlates of bistable perception have indicated that activity in the parietal and prefrontal cortices might be associated with visual awareness in normal subjects^{85–87}. These studies measured brain activity time-locked to

spontaneous fluctuations in awareness both during binocular rivalry^{85,86} and for other bistable figures⁸⁷. Cortical regions with activity that reflects perceptual transitions include ventral extrastriate cortex, and parietal and frontal regions that have been implicated previously in the control of spatial attention. Although extrastriate areas are equally engaged by non-rivalrous perceptual changes, areas in frontal and parietal cortex show significantly greater activation time-locked to the perceptual alternations during binocular rivalry. During rivalrous fluctuations in perceptual experience, the time course of haemodynamic activity in V1 shows little correlation with that recorded elsewhere in the brain⁸⁶. However, the time course of activity recorded from areas in extrastriate cortex that are thought to be involved in binocular rivalry correlates strongly with activity in areas of frontal and parietal cortex that have been implicated in rivalrous transitions. Similar parietal and frontal regions are active during perceptual transitions that occur while viewing bistable figures⁸⁷ (such as the Necker cube and Rubin's face/vase figure). These data indicate that activity in frontal and parietal cortex might be causally associated with the generation

CLASSICAL RECEPTIVE FIELD
The region of the visual field in which visual stimulation typically causes a response in a particular neuron.

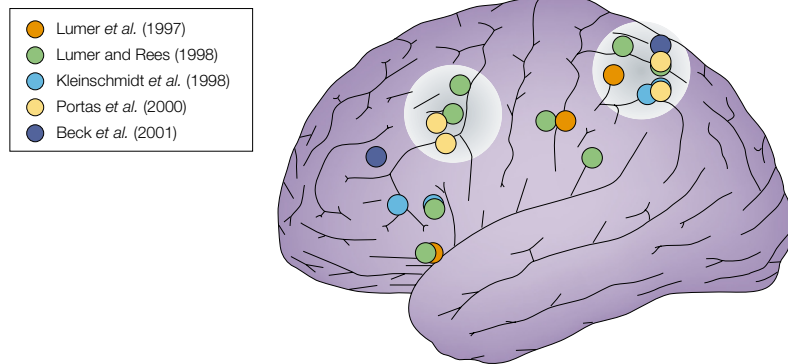


Figure 5 | **Parietal and prefrontal correlates of consciousness.** Areas of parietal and prefrontal cortex that show activation correlated with changes in visual awareness (REFS 85–87,91,92) are plotted on a standardized brain. Each coloured circle is placed at the centre of a cluster of activation, with different colours representing different studies; overlapping loci from the same study are omitted for clarity. There is prominent clustering of activations in superior parietal and dorsolateral prefrontal cortex, highlighted by large, light circles.

of transitions between different percepts. This idea is supported by the clinical observation that patients with prefrontal cortex lesions typically have abnormal transitions in bistable perception^{88–90}. However, the correlation of activity in frontal and parietal cortex with visual awareness is not restricted to bistable perception. When subjects become consciously aware of a change in a visual scene, compared with when they are blind to that change, there is reliable parietal and dorsolateral prefrontal activation⁹¹. Similar cortical loci (FIG. 5) are activated by STEREO POP-OUT but not with stable viewing⁹², and during perceptual binding of colour and motion in object recognition⁹³.

So, although activity in ventral visual cortex is a consistent neural correlate of consciousness, it might be insufficient to produce awareness without an additional contribution from parietal and prefrontal loci. The nature of the cognitive processes involved in such a contribution and the anatomical connectivity that might mediate such interactions (FIG. 2) are not yet clear. The loci of activation in parietal and frontal areas that are associated with visual awareness generally overlap with areas that have been associated with spatial and non-spatial attention^{94–96}. This is consistent with our intuition that awareness and attention are intimately linked, and it is reflected in the common claim that attention helps to modulate visual awareness⁹⁷ by biasing competition within the ventral visual pathway. The anatomical overlap further strengthens the proposed link between attention and awareness by providing evidence that some of the mechanisms that subservise the two processes might share a common neural substrate^{98–100}. Future work should address more precisely the degree of anatomical overlap and the nature of the cognitive relationship between these two processes.

Consistent with these data, disturbances of visual attention and visual awareness in humans are seen not only after damage to ventral visual cortex, but also after damage to the parietal or frontal cortex. For example, visual extinction is a common component of the neglect syndrome that can follow parietal damage, in which

patients show deficient awareness of contralesional visual stimuli (see above)³. In animals, much larger lesions have more profound effects. In monkeys, a massive cortical ablation that spares most of the modality-specific visual cortex, but not parietal and frontal areas, leads to chronic blindness^{101,102}. Similarly, removal of frontoparietal cortex in cats produces as much or more decrement in visual discrimination than does removal of temporal cortex¹⁰³. Such syndromes illustrate that visual awareness for particular regions of visual space can be lost even when visual cortex and its afferent inputs are intact. Nevertheless, awareness of ipsilesional visual stimulation is possible following parietal damage, even with profound spatial neglect. Similarly, although bilateral damage to human parietal cortex can give rise to BALINT'S SYNDROME OF SIMULTANAGNOSIA, patients still see something, even if it is only a single object¹⁰⁴. Therefore, although neglect or extinction reveals a profound inability to process the world beyond the immediate focus of attention, visual awareness (in some form) seems to be present. Activity in the localized cortical areas that are damaged in these syndromes might therefore be crucial in normal vision, but it is not strictly necessary for some conscious visual experiences. Whether the same can be said for activity in prefrontal cortex remains uncertain.

Future directions

The focus on the identification of reliable neural correlates of consciousness in vision has led to a general consensus on the types of experiment that are likely to prove informative, mainly those that explicitly dissociate conscious and unconscious neural processes. Most of the single-cell evidence from monkeys and fMRI data in humans are compatible with the hypothesis that activity in V1, although necessary for many forms of vision, does not correspond to visual perception. Other experiments have been interpreted to suggest that some aspects of V1 activity do relate to conscious perception. Most observers agree that the neural correlates of consciousness are associated with functionally specialized areas in the ventral visual pathway interacting with specific areas of prefrontal and parietal cortex. However, a fully developed empirical synthesis has yet to emerge. In part, this might be due to the present state of theoretical models of consciousness, which offer plausible frameworks for understanding empirical findings, but few specific predictions that can be tested with current technology.

Two areas that might provide fertile ground for future study emerge from this review. For the first challenge, within functionally specialized areas of visual cortex it will be important to characterize more closely the nature of the neural correlates of consciousness. For example, is awareness a function of the intensity of neural activity within such an area, or does it relate more closely to the timing of that activity? Do the neural correlates of consciousness within a visual area represent activity only in a particular fraction of the neuronal population? How are those cells individuated anatomically and physiologically? However, as we have emphasized, understanding

STEREO POP-OUT

Presenting each eye with two slightly different images that create a binocular disparity gives rise to a vivid impression of stereo depth. If the images are intricate patterns of dots (forming a shape) that are embedded in a similar background, then this perception of depth is not instantaneous — the figure 'pops out' after a short period of viewing.

BALINT'S SYNDROME

A neurological disorder caused by bilateral damage to the parieto-occipital region of the brain and characterized by disorders of spatial perception.

SIMULTANAGNOSIA

An impairment in the ability to perceive and attend to all of the features of an object or a scene at the same time. Sufferers perceive the individual parts of a complex visual display better than they do the whole.

the neural correlates of consciousness in functionally specialized visual areas might be insufficient to answer these questions, as activity in prefrontal and/or parietal cortex also correlates with changes in the contents of consciousness. A second challenge is to explore the role and nature of the interactions between these dorsal areas and the ventral visual pathway. Cognitive processes such

as working memory and visual attention are thought to be associated with such dorsal cortical areas. It will therefore be important to characterize how these cognitive processes interact with signals in the visual cortex, exploring the anatomical and physiological substrates that allow such large-scale integration and result in phenomenal awareness in the human brain.

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