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Neuropsychologia 45 (2007) 3346–3350

NEUROPSYCHOLOGIA

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Note

Making the blindsighted see

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Received 20 November 2006; received in revised form 1 June 2007; accepted 4 June 2007
Available online 26 June 2007

Abstract

A lesion of striate cortex, area V1, produces blindness in the retinotopically corresponding part of the visual field, although in some cases visual abilities in the blind field remain that are paradoxically devoid of conscious visual percepts ("blindsight"). Here we demonstrate that the blindsight subject GY can experience visual sensations of phosphenes in his blind field induced by transcranial magnetic stimulation (TMS). Such blind field percepts could only be induced when stimulation was applied bilaterally, i.e. over GY's area V5/MT in both hemispheres. Consistent with an earlier report [Cowey, A., & Walsh, V. (2000). Magnetically induced phosphenes in sighted, blind and blindsighted observers. *Neuroreport*, *11*, 3269–3273], GY never experienced phosphenes when stimulation was restricted to his ipsilesional V5/MT. To the best of our knowledge this is the first time GY has experienced visual qualia in his blind hemifield. The present report characterizes the necessary conditions for such conscious experience in his hemianopic visual field and interprets them as demonstrating that only via a contribution from GY's intact hemisphere can activation in the damaged hemisphere reach visual awareness.

Keywords: Blindsight; Visual qualia

1. Introduction

Destruction of the primary visual cortex (V1) abolishes phenomenal visual awareness in the corresponding part of the visual field. In some cases, however, the ability to detect and localize stimuli in the blind field survives (Pöppel, Held, & Frost, 1973; Weiskranz, Warrington, Sanders, & Marshall, 1974), which unaccompanied by phenomenal visual experience (i.e., blindsight). The dissociation between visual processing and visual awareness is further highlighted by the findings that the blindsight subject GY can detect and discriminate motion in his blind field, usually attributed to intact regions of his ipsilesional extrastriate cortex (Barbur, Watson, Frackowiak, & Zeki, 1993). However, direct stimulation of these regions in GY did not induce conscious visual sensations (Cowey & Walsh, 2000). In contrast, phosphenes could readily be induced from GY's intact hemisphere as well as from the visual cortex of a retinally blind subject with severed optic nerves but an intact V1, indicating that awareness of extrastriate activity is inextricably linked to the integrity of V1.

Even though stimulation of GY's ipsilesional V5/MT does not by itself give rise to a conscious percept, it remains possible that the ipsilesional stimulation can reach awareness via the intact V1 in the normal hemisphere. Activity in GY's ipsilesional V5/MT induced by moving stimuli presented in his blind field is transmitted to his contralesional V5/MT (ffytche, Howseman, Edwards, Sandeman, & Zeki, 2000), and as V5/MT contains a partial representation of the ipsilateral hemifield that extends up to 15° from the vertical meridian (Raiguel, Van Hulle, Xiao, Marcar, & Orban, 1995), it is possible that visual information relating to GY's blind field can influence visual awareness arising in the normal hemisphere. We therefore examined whether visual experiences (qualia) can be induced in the blind field of GY by applying transcranial magnetic stimulation (TMS) over his V5/MT bilaterally at various stimulation onset synchronies.

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doi:10.1016/j.neuropsychologia.2007.06.008

2. Methods

2.1. Subjects

The blindsight subject GY suffered almost total destruction of his left V1 at the age of 8 years by a vascular incident following a traffic accident, with some additional damage to extrastriate areas V2 and V3, and the region of his lesion shows no responsiveness to visual stimulation (Azzopardi & Cowey, 2001; Barbur et al., 1993). He was 51 years old at the time of testing. While structural MRI scans have revealed some spared macular striate cortex, it does not seem to be functional, and it is not activated by stimuli that elicit blindsight in the blind field (Stoerig, Kleinschmidt, & Frahm, 1998). Five neurologically normal subjects acted as controls (three male, two female, 24–34 years old). Subjects gave informed consent before participating in the study, approved by the local ethics committee of University College London. All had previous experience of taking part in phosphene experiments. With the exception of author JS, all subjects were naïve to the aims of the study.

2.2. Transcranial magnetic stimulation

Two Magstim Rapid stimulators (Magstim, Wales) and 70-mm figure-of-eight coils were used. Stimulation was delivered over V5/MT as determined in GY from his structural and functional MRI scans (Cowey et al., unpublished; Goebel, Muckli, Zanella, Singer, & Stoerig, 2001). The skull coordinates with respect to the inion were 3 cm dorsal and 5 cm lateral for the left V5/MT and 3 cm dorsal and 5.3 cm lateral for the right V5/MT. The coil orientation was such that the handle was horizontal and parallel to the midline.

In control subjects, V5/MT was localised using a functional method in which the center of the coil is placed on the surface of the skull such that the stimulation elicits moving phosphenes. This method was first used to identify motion sensitive cortex in a study on motion aftereffects and perceptual learning (Stewart, Battelli, Walsh, & Cowey, 1999) and has since become a standard tool for identifying human V5/MT. Subsequent studies have shown that this functional method yields the same stimulation coordinates as co-registration with Brainsight Trade Mark (Rogue Research, Canada) (cf. Campana, Cowey, & Walsh, 2002; Campana, Cowey, & Walsh, 2006; Sack, Kohler, Linden, Goebel, & Muckli, 2006; Schenk, Ellison, Rice, & Milner, 2005; Silvanto, Cowey, Lavie, & Walsh, 2005; Silvanto, Lavie, & Walsh, 2005). The average coil position was 3.3 cm (±0.4 cm) dorsal and 5.2 cm (±0.7 cm) lateral from the inion. This location was co-registered with the subject's structural brain image. In all subjects this coincided closely with the location of V5/MT in the top of the ascending branch of the middle temporal sulcus as demonstrated by Dumoulin et al. (2000).

TMS was administered over both sites at 33 Hz (i.e., pulse gap of 30 ms). Stimulation onset asynchronies (i.e., the time difference between the start of stimulation over one hemisphere and the start of stimulation over the other hemisphere) were studied from −160 to +160 ms in steps of 20 ms. We used the phosphene studies of Pascual-Leone and Walsh (2001) and Silvanto, Cowey, et al. (2005), in which paired-pulse paradigms were also used as a guide to decide how many SOAs to include.

Trials that included only the contralesional V5/MT pulses were included to provide a comparison with GY's percepts at each SOA condition. The contralesional (right) V5/MT was stimulated at intensities ranging from phosphene threshold to 20% below phosphene threshold and the ipsilesional (left) V5/MT was stimulated at 80% of the maximum output of the stimulator which was the highest intensity at which GY experienced no discomfort. Normal subjects were stimulated with the same parameters. Before the main experimental session we stimulated the ipsilesional V5/MT on its own (with the stimulation parameters described above). Consistent with an earlier report (Cowey & Walsh, 2000), unilateral stimulation of the ipsilesional V5/MT never induced a phosphene.

2.3. Procedure

Initially, the phosphene thresholds in V5/MT of GY's normal hemisphere were determined using a binary search paradigm (Tyrell & Owens, 1988). The phosphene thresholds were re-measured at the end of testing and showed reassuring consistency: the pre- and post-testing values for the single pulse stimulation were 65%/67%. The mean phosphene thresholds of the normal subjects were 57 and 58% for pre- and post-testing, respectively.

Subjects were asked to close their eyes during stimulation, the centre of a sheet of paper directly in front of the subject at a distance of 42 cm served as an imaginary fixation point. Subjects placed a finger on the raised pin-head in the centre of the paper and kept it there for each batch of trials. On each trial the eyes were closed just before the TMS was delivered and the position of the phosphene was then indicated or drawn, with the other hand, either after opening the eyes or while keeping them closed, as the subject preferred. GY usually opened his eyes but kept looking at the finger tip while outlining the phosphene. In all experiments, four trials were given for each SOA condition. There was a two-second gap between trials. The order of the SOA conditions was random. In addition, three contralesional-only TMS trials were conducted prior to each SOA condition to provide a comparison for the phosphenes that were perceived with bilateral stimulation.

3. Results

Whereas pulse trains of TMS administered over V5/MT of either hemisphere of normal subjects induced a phosphene in the contralateral visual field (Fig. 1A), bilateral stimulation induced a single unified phosphene extending bilaterally (see Fig. 1B). In GY, unilateral stimulation of V5/MT in the normal hemisphere induced a phosphene restricted to the contralateral

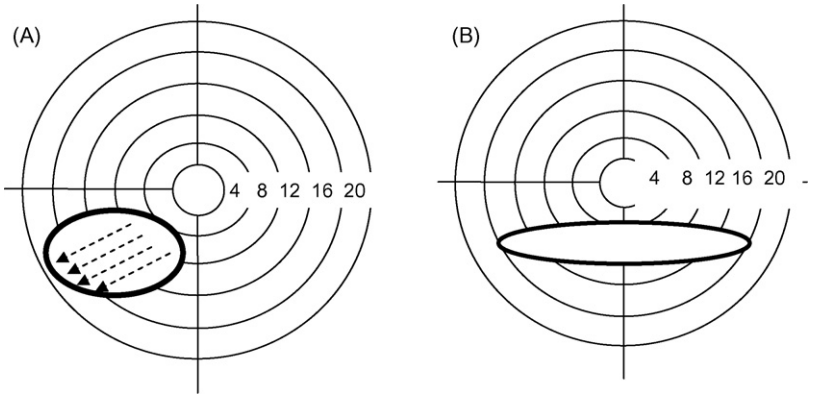

Fig. 1. Schematic examples of phosphene appearance in one representative control subject. The numbers indicate the eccentricity in degrees of visual angle. The figures are based on the subject's drawings. (A) With unilateral stimulation of either hemisphere, the subject perceived a moving phosphene in the contralateral hemifield. The arrows represent the perception of motion. (B) With bilateral stimulation of V5/MT, the subject perceived a unified, static bilateral percept. The static nature of the bilateral phosphene (in both GY and normal subjects) is likely to reflect the summation of two phosphenes moving in opposite directions.

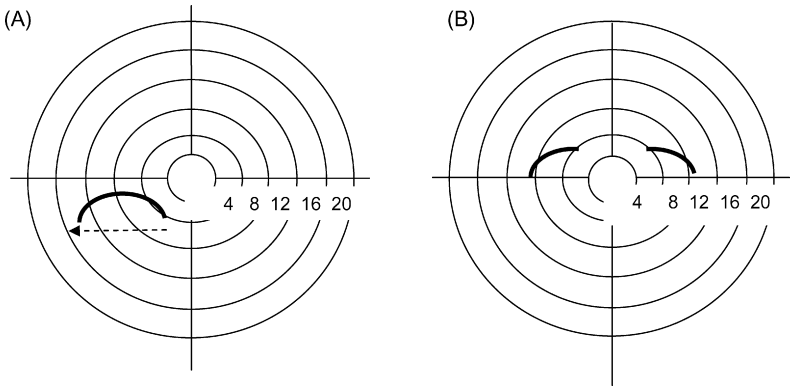

Fig. 2. Phosphene appearance in GY, based on his drawings. (A) Unilateral stimulation of V5/MT in the normal hemisphere induced a contralateral moving phosphene. The shape of phosphenes varies between subjects (and is also dependent on coil orientation), and while most neurologically normal subjects perceive circular or diffuse phosphenes, some do perceive arcs and narrow lines similar to GY's percepts. (B). Bilateral stimulation of GY's V5/MT induced bilateral phosphenes that were not joined.

hemifield, as in normal subjects (Fig. 2A). Consistent with an earlier report (Cowey & Walsh, 2000), unilateral stimulation of the ipsilesional V5/MT, even at high intensities, never induced a phosphene. Nevertheless, bilateral stimulation of V5/MT (with the contralesional V5/MT stimulated at his phosphene threshold, (65%), and the ipsilesional V5/MT at 80% of maximum stimulator output), induced two separate phosphenes, one in the good hemifield and the other in the blind hemifield. These phosphenes, symmetrical in shape, had the appearance of white arcs and they intruded 8–15° into each hemifield (Fig. 2B). Vivid bilateral phosphenes were induced on at least three of the four trials at SOAs ranging from −140 ms (i.e., the first pulse of the ipsilesional pulse train preceding the first pulse of the contralesional pulse train by 140 ms) to +120 ms. In normal observers, bilateral phosphenes were consistently induced at all SOAs.

We also investigated whether GY's blind field can support conscious visual perception when bilateral stimulation is applied but the intact hemisphere is stimulated at an intensity below its phosphene threshold. When the intensity of the normal V5/MT stimulation was 60% (5% below the phosphene threshold) and the stimulus intensity over the ipsilesional V5/MT was 80% of maximum stimulator output, GY still perceived white, bilateral arc-like phosphenes. Bilateral phosphenes were consistently elicited at SOAs ranging from −100 to +100 ms. For control subjects the SOA range at which bilateral phosphenes were induced was, *on average*, from −144 ms + to 96 ms.

When the normal V5/MT was stimulated at 10% below the phosphene threshold and the ipsilesional V5/MT was stimulated at 80% of maximum stimulator output, GY reported the impression of apparent motion in an array of speckles that appeared first in the good field and then in the blind field. With these stimulation parameters he consistently perceived phosphenes with SOAs ranging from −100 to +20 ms. For control subjects the SOA range at which bilateral phosphene was induced was, *on average*, −128 to +60 ms. When V5/MT of his normal hemisphere was stimulated 20% below the phosphene threshold and the ipsilesional V5/MT was stimulated at 80% of maximum stimulator output, he no longer reported phosphenes at any of the SOAs. Similarly to GY, the control subjects also failed to see phosphenes with these stimulation parameters. Fig. 3 shows GY's reports of bilateral phosphenes as a function of SOA.

As the SOA between TMS applied over the two sites was increased, the likelihood of inducing bilateral phosphenes in GY progressively decreased. The likely explanation for this is that at long SOAs the activation originating from the contralateral hemisphere will have faded before the application of the second TMS pulse train.

We also attempted to determine whether it is the TMS intensity over the damaged or the intact hemisphere that is more critical for phosphene perception in GY. To achieve this, we applied single-pulses of TMS bilaterally over the V5/MT instead of pulse trains so that the TMS intensity could be increased to 100% of maximum stimulator output while remaining within published safety parameters. The two sites were stimulated at SOAs ranging from −80 to +80 ms in steps of 10 ms.

When the ipsilesional V5/MT was stimulated at 80% of maximum TMS output and contralesional V5/MT was stimulated at an intensity 10% below the phosphene threshold (that was 69% of maximum TMS output for single-pulse TMS), GY never perceived phosphenes. When the intensity of ipsilesional

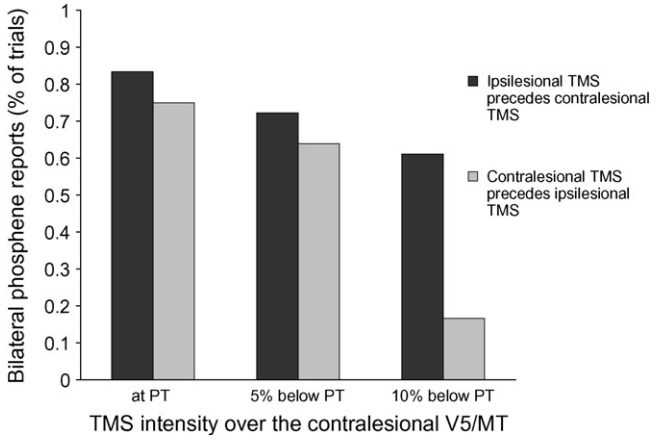

Fig. 3. GY's phosphene report as a function of stimulation onset asynchrony. The ipsilesional V5/MT was stimulated at 80% of maximum stimulator output. The SOAs have been grouped into two categories: (1) ipsilesional TMS preceding contralesional TMS and (2) contralesional TMS preceding ipsilesional TMS.

stimulation was increased from 80 to 100%, (with contralesional V5/MT stimulated 10% below PT) GY still perceived no phosphenes. However, when stimulation intensity of the contralesional hemisphere was increased to phosphene threshold and the ipsilesional V5/MT was stimulated at 80% of maximum TMS output, GY perceived bilateral phosphenes. Strong bilateral phosphenes were consistently induced with stimulation SOAs ranging from 10 to 60 ms (both when the contralesional pulse preceded and followed the ipsilesional pulse), with strongest effects observed at SOAs between 10 and 30 ms.

In summary, with single-pulse TMS, an increase in the intensity of ipsilesional stimulation did not enable phosphene perception in GY if the contralesional V5/MT was stimulated below phosphene threshold. Rather, it was an increase in the TMS intensity over the intact hemisphere that was critical for blind field phosphenes. This pattern of results suggests that the lack of phosphenes when the contralesional hemisphere is stimulated below phosphene threshold is not due to a decrease in overall activation level of the ipsilesional visual cortex. Instead, the data suggest that the activation level of the contralesional visual cortex is critical.

4. Discussion

In agreement with Cowey and Walsh (2000) GY perceived phosphenes in his normal, left, visual hemifield when TMS was applied to his contralesional V5/MT, but he never perceived a phosphene in his blind hemifield when TMS was applied only to V5/MT of his damaged hemisphere. In striking contrast he experienced bilateral phosphenes when V5/MT was stimulated bilaterally. To the best of our knowledge this is the first report of awareness accompanied by visual qualia (as distinct from mere awareness that something happened but with no experience of accompanying visual qualia) (cf. Barbur et al., 1993) in the blind field of a blindsight subject.

Induction of phosphenes in GY's blind field is likely to result from the stimulation of his ipsilesional V5/MT through callosal connections, increasing and/or modulating the activation level of neurons in V5/MT of the normal hemisphere that have a representation of part of the ipsilateral visual field. It was only in this part of the visual field that GY ever experienced phosphenes on his blind side. Furthermore, as the sub-threshold TMS over V5/MT of the normal hemisphere never induced phosphenes when administered without the ipsilesional stimulation, GY's perception of bilateral phosphenes with bilateral TMS must imply that the ipsilesional stimulation increased the activation level or neural coherence of the normal V5/MT. This explanation is also consistent with evidence that activation induced by visually presented moving stimuli in GY's blind field can cross from his ipsi- to the contralesional V5/MT (ffytche et al., 2000). Whether GY can experience visual qualia when real global moving patterns are presented in both hemifields is an open question.

The finding that, with single-pulses of TMS, an increase in the intensity of ipsilesional stimulation does not enable phosphene perception in GY if the contralesional V5/MT is stimulated below phosphene threshold is consistent with this account, as it implies that the TMS intensity over the intact hemisphere is more critical for blind field phosphenes in GY than TMS intensity of the damaged hemisphere. Furthermore, the finding that phosphene perception is more likely when the ipsilesional TMS precedes contralesional TMS rather than vice versa (see Fig. 3) is consistent with the view that the phosphenes are generated through the ipsilateral representation in contralesional V5/MT.

This account is also consistent with neurophysiological evidence, as GY's bilateral phosphenes never extended beyond the limits of the representation in V5/MT of the ipsilateral visual field (up to 15° of visual angle from the vertical meridian (Raiguel et al., 1995). A further aspect of GY's bilateral phosphene also supports this view: in the macaque monkey, nasotemporal overlap of retinal ganglion cell projections can extend 5–9° in the ventral retina and up to 15° in the dorsal retina, whereas it is narrow in the fovea (Fukuyama, Sawai, Wakakuwa, & Morigiwa, 1989), suggesting that the visual cortex contains a crescent-shaped representation of the ipsilateral visual field above and below the fovea. The location of GY's phosphenes mirrors this arrangement: his phosphenes only intruded into the blind field in the lower or upper part of the hemifield, and not along the horizontal retinal meridian.

Alternatively, it is possible that interhemispheric information transfer from the normal hemisphere to V5/MT in the damaged hemisphere is critical in inducing phosphenes in GY's blind field. V5/MT in his damaged hemisphere is itself damaged, as its greatest normal afferent input is from V1 of the same hemisphere and the latter is missing in GY. It is possible that unilateral TMS above his left V5/MT fails to produce a phosphene because V5/MT is not in the appropriate neural condition for TMS to excite it effectively, and that the appropriate conditions can be produced via the callosal connexion from V5/MT of the normal hemisphere.

The most obvious anatomical candidate for any interhemispheric transmission is via the corpus callosum (Maunsell & Van Essen, 1983). However, while GY's corpus callosum has not been sectioned, he does have atrophy of callosal fibres in the fornix major, and it has been argued that a non-callosal pathway mediates this interhemispheric information transfer (Ffytche et al., 1995). A recent study by Leh, Johansen-Berg, and Ptito (2006), using diffusion tensor imaging (DTI) in hemispherectomised subjects who display blindsight, found that the superior colliculus showed both ipsi-and contralateral connectivity with various cortical regions, whereas in normal subjects as well as in hemispherectomised subjects who did not show blindsight these collicular projections were predominantly ipsilateral. As GY sustained his lesion at the age of eight, it is possible that comparable reorganization has taken place in his brain. Future DTI studies already underway, with GY are needed to resolve this issue.

In conclusion, this study provides the first evidence that the blindsight subject GY experiences TMS-induced visual qualia in his blind field, but only when his V5/MT is stimulated bilaterally. While the neural basis of these phosphenes is unproven, our findings are consistent with the view that V1 is necessary for awareness (Pollen, 1999; Lamme, 2001; Pascual-Leone & Walsh, 2001; Silvanto, Lavie, et al., 2005; Silvanto,

Cowey, et al. (2005), as they reinforce the view that GY's ipsilesional hemisphere alone is unable to support conscious visual perception.

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