Dissociation between Goal-directed and Discrete Response Localization in a Patient with Bilateral Cortical Blindness

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Abstract

We investigated localization performance of simple targets in patient TN, who suffered bilateral damage of his primary visual cortex and shows complete cortical blindness. Using a two-alternative forced-choice paradigm, TN was asked to guess the position of left–right targets with goal-directed and discrete manual responses. The results indicate a clear dissociation between goal-directed and discrete responses. TN pointed toward the correct target location in approximately 75% of the trials but was at chance level with discrete responses. This indicates that the residual ability to localize an unseen stimulus depends critically on the possibility to translate a visual signal into a goal-directed motor output at least in certain forms of blindsight.

INTRODUCTION

Destruction of the primary visual cortex leads to clinical blindness in the corresponding portion of the visual field. However, some patients with cortical blindness can correctly localize unseen targets presented in their blind visual field, a phenomenon described as “blindsight” (Weiskrantz, Warrington, Sanders, & Marshall, 1974). Prior studies have shown that this residual localization ability is sensitive to the response modality used. Indeed, localization of objects in space is often above chance when patients are required to respond with a goal-directed action toward the target, such as reaching, grasping, or making eye movements (Danckert & Rossetti, 2005; Zihl & von Cramon, 1980; Weiskrantz et al., 1974) but drops significantly when verbal responses are required. However, it should be pointed out that there is considerable variability among different blindsight patients as a function of lesion site and extension. Moreover, the nature of the task used to explore residual visual functions, as well as the specific stimulus properties investigated, determine to a large extent the patient’s performance (Danckert & Rossetti, 2005). For example, patient DB was considerably better at localizing targets presented to his blind (left) hemifield when pointing at them with his finger than when making saccades toward them (Weiskrantz et al., 1974). Lastly, the type of response is known to influence not only localization but also nonconscious processing of size and orientation (Rossetti, 1998; Perenin & Rossetti, 1996). Similar observations have been made in other sensory modalities, such as, for example, haptic perception where dissociations between stimulus identification and object-oriented actions have been found (referred to as numb sense or blind touch; e.g., Rossetti, Rode, & Boisson, 1995).

However, it is unclear whether the above-chance localization capacity for unseen targets requires the execution of a goal-directed manual action (requiring on-line visuomotor interaction with the target) or whether it can also be observed when a discrete manual motor response is performed (e.g., key-press or finger-lift response). Indeed, in the visuomotor domain, dissociations between an arbitrary response and a goal-directed action have only been demonstrated for intrinsic (e.g., size) and extrinsic (e.g., orientation, motion) properties of the visual target (e.g., Perenin & Rossetti, 1996; Perenin, 1991) but not for localization itself. For instance, Perenin and Rossetti (1996) showed that two blindsight patients were able to grasp objects between their thumb and index finger and adjust their hand to the orientation of a slot. However, the same patients were at chance level when they had to guess the size of the stimulus and its orientation using verbal or visual matching responses. Overall, this indicates that goal-directed actions can promote the processing of properties such as size and orientation. There is a wealth of evidence indicating that coding of visual properties relevant for action, such as size, orientation, or motion, is carried out by a complex cortico-subcortical network involving the superior colliculus,
motor areas, and posterior dorsal areas, which are sensitive to the egocentric features of objects and mediate the nonconscious control of visually guided actions (Milner & Goodale, 2006). Conversely, the visual processing carried out by the ventral system enables the formation of perceptual and cognitive representations that embody the invariant characteristics of objects, their significance and conscious representation. Therefore, if one considers that localization of objects in space is possibly the most typically action-related “dorsal” attribute, then one may also expect a difference between goal-directed and discrete responses for object localization.

In addition, localization of visual stimuli outside awareness has been reported only in patients with unilateral destruction of the visual cortex, therefore leaving open the possibility that cortical visual areas in the intact hemisphere mediate this residual function through a mechanism of interhemispheric cross talk (Tettamanti et al., 2002). In the present investigation, we studied patient TN, the only currently available case in the literature with complete cortical blindness following bilateral destruction of the visual cortex (de Gelder et al., 2008; Pegna, Khateb, Lazeyras, & Seghier, 2005), and we compared his ability to localize left- versus right-sided targets nonconsciously using goal-directed and discrete manual actions. Thus, TN had to guess the location of a visual stimulus by moving his arm in the direction of the stimulus and touching it with his right index finger (goal-directed response) or by raising his left or right index finger while his hands lay on the screen just below the boxes where stimuli were displayed (discrete manual response).

METHODS
Case Report
Patient TN suffered two strokes in rapid successions (36 days apart). His first stroke occurred in the left parieto-temporo-occipital area, producing right hemiplegia and transcortical sensory aphasia, which receded rapidly, in addition to a dense and persistent right homonymous hemianopia. The second hemorrhage subsequently occurred in the right occipital lobe causing the loss of his left visual field with no other signs of neuropsychological deficit (and in particular no behavioural signs of spatial neglect). Detailed descriptions of TN’s lesions can be found in de Gelder et al. (2008) and Pegna et al. (2005).

Behavioral Assessment of Clinical Blindness with a Computerized Visual Field Mapping
A high-resolution visual perimetry was administered the day before the present experiment with stimuli consisting of small white circles (1°; stimulus luminance 95 cd/m²) presented against a dark background (2 cd/m²) on a 17-in. computer monitor. The stimuli were presented one at a time for 300 msec at each of 64 different positions (16 stimuli for each visual quadrant) with onset and offset signaled by two different sounds. The ISI was 3 sec. TN was required to report verbally when he consciously detected the appearance of a stimulus. Emphasis was placed on the requirement to report “normal” conscious perception of a visual stimulus, as opposed to a “feeling” that a stimulus occurred without any definable and conscious visual perception. This procedure enabled us to map TN’s visual field within an ideal grid spanning 25° of horizontal and 20° of vertical eccentricity. A visual perimetry was also performed with flickering, instead of static, stimuli. The same procedure as before was used, with the only exception that white circles were presented for 300 msec with a flickering rate of 20 Hz.

fMRI Assessment of Functional Activity in the Visual Cortex
The fMRI session was administered 2 days before the present experiment. The BOLD response to visual stimulation was tested by presenting alternating black and white checkerboard patterns (10.5° × 10.5°). The checkerboards were presented for 20-sec periods, at three different rates: 2, 10, and 20 Hz. After each block of checkerboard presentation, a black screen (baseline) was presented for a randomly jittered period, between 11 and 16 sec. Four blocks were presented per condition, resulting in 40 EPI volumes per condition.

The patient was asked to look directly ahead, and gaze direction was monitored using an infrared MR-compatible eye tracker. On-line visual inspection of gaze direction allowed the experimenters to verify that the patient behaved as instructed.

Scanning took place in a 3T Siemens Trio MRI scanner, using a 12-channel head coil. Two hundred seventeen functional volumes were acquired in one single session, lasting approximately 7 min (T2*-weighted EPI, 32 × 3 mm slices, 15% interslice gap, 2.56 × 2.56 mm in-plane resolution) angled away from the eyes to prevent ghost artifacts from aliasing of eye movements, acquisition time = 2 sec, repetition time = 2 sec, echo time = 30 msec). A high-resolution (0.43 mm × 0.43 mm × 1 mm voxels) T1-weighted anatomical image was also acquired.

Data were processed and analyzed using the SPM8 software package (www.fil.ion.ucl.ac.uk/spm/). Data pre-processing consisted of (1) rigid realignment of each EPI volume to the first volume in the session, (2) coregistration of the structural volume to the mean EPI image, and (3) spatial smoothing using a gaussian kernel of 8 mm FWHM height. Analysis was carried out using a general linear model, in which every scan was coded for condition (2, 10, and 20 Hz) and null events were not modeled. Each block was modeled using the canonical hemodynamic response function in SPM8. Eighteen parameters were appended to code for the effects of movement (x, y, and z translations and x, y, and z rotations derived from...
the rigid realignment step of the preprocessing, as well as the first and second derivatives of these). A high-pass filter (cutoff 128 sec) and AR1 correction for serial autocorrelation were applied.

The data were examined for a low-level stimulation versus baseline contrast to reveal any activity induced by the flickering checkerboards. An F test was performed, interrogating the parameter estimates of the general linear model to determine whether any voxels showed increased BOLD responses relative to baseline for any of the conditions.

We first carried out a whole-brain analysis to establish possible islands of residual functional activity in cortical visual areas that could support coarse detection or localization of visual targets and could therefore account for the observed performance in the main behavioral experiment. A standard statistical threshold of \( p < .05 \) family-wise error corrected for multiple comparisons was initially applied. Then, a more liberal statistical threshold of \( p < .0001 \), uncorrected for multiple comparisons, was applied to the same contrast to test possible trends of activations evoked by visual stimuli that may go undetected with a conventional statistical approach. Finally, an ROI analysis was carried out to determine whether any activation was observed in primary visual cortices or in peristriate regions of the occipital cortex. ROIs were defined anatomically in the calcarine sulcus, lingual gyrus, and cuneus using the automated anatomical labeling template (Tzourio-Mazoyer et al., 2002) supplied with the MRIcron software package (Rorden & Brett, 2000). The patient’s anatomical scan was normalized to the single-subject Montreal Neurological Institute template supplied with SPM8, using the unified segmentation procedure, which is relatively robust in the face of lesions (Crinion et al., 2007; Ashburner & Friston, 2005). The inverse normalization parameters generated by this process were applied to the anatomical ROIs to bring them into the patient’s native anatomical space. The ROIs projected upon the patient’s anatomical scan are shown in Figure 2.

Main Experiment: Goal Directed versus Discrete Response Localization

The current experiment was performed 7.5 years after the infarcts. The study was approved by the local ethics committee.

Task and Stimuli

Manual responses were performed on a flat screen that was attached to the edge of a table at an angle of about 38°. The 3-D coordinates of manual movements were recorded at a sampling frequency of 150 Hz using a marker positioned on the nail(s) of the finger(s) used to perform the task (CMS20S, Zebris Medical GmbH, Isny in Allgäu, Germany).

To assess left–right localization, we asked TN to respond with two different actions that were implemented in a two-alternative forced-choice paradigm. In the first task (Experiment 1), TN reported the target location by means of a goal-directed pointing action (Figure 1A). He was asked to lift his hand from the screen when performing the reaching movement. An adhesive patch was placed at the center of the screen to allow him to find the starting position more easily. In the second task (Experiment 2), TN responded with a discrete finger-lift action. His hands lay on the screen, just below the boxes where stimuli were displayed (Figure 1B). This finger-lift action was shown to be comparable with more common button-press responses (Buetti & Kerzel, 2010; see also Buetti & Kerzel, 2009).

In Experiment 1, TN responded either to a 25-Hz flickering 4° white dot (Experiment 1A) or to a static dot (75 Hz) of the same size and luminance (Experiment 1B). In Experiment 2, only the 25-Hz flickering dots were displayed because no difference was found between flickering and static dots in Experiment 1.

The stimuli could appear randomly at one of two empty place-holder boxes, which were displayed 10° to the left and right of the center of the screen. A white fixation cross was displayed at the center of the screen. A 200-msec duration, 1000-Hz tone was used as an auditory go signal. The tone was delivered synchronously with the onset of the visual target.

Experimental Procedure

The participant’s eyes were at a distance of approximately 42 cm from the flat panel screen, and his head was stabilized with a chin rest. TN was required to place his finger(s) on the starting position(s) on the screen at the beginning of each trial. When the finger(s) touched the correct starting positions, the fixation cross and the two placeholder boxes with white outlines were displayed on the screen. Once these stimuli appeared on the screen, the experimenter pressed a key to start the trial. At 300–800 msecs later, the tone and the visual target were presented. TN was told that, upon hearing the tone, he had to provide the required response even if he experienced no conscious percept of the visual target. The visual target stayed on the screen until the response was given. In Experiment 1, TN had to guess the side on which the target appeared by reaching to it with his right index finger (see Figure 1A). In Experiment 2, he had to guess the target side by lifting his left or right index finger (see Figure 1B).

The experiments took place in a single session, in a dimly lit room, and with 10-min breaks between the tasks. TN did not receive any information about the stimuli’s characteristics nor did he receive any feedback regarding his performance. Each task was carried out in one block of 80 trials long (half in the left visual field and...
half in the right visual field, randomly intermingled) and included about 30 practice trials at the beginning.

Data Analysis

First, we calculated the hit rate and performed a two-tailed binomial test to determine whether performance differed from chance level. Hit rates equal or higher than 61% were at the .05 level of significance and were considered to be above chance. Binomial tests were performed after excluding trials in which TN did not respond within 3 sec following the auditory go signal (i.e., one, three, and six trials were excluded in Experiments 1A, 1B, and 2, respectively).

Second, to verify whether the proportion of correct responses depended on the target location, we calculated the percentage correct separately for left and right targets. On these percentages we then computed the Z-score of the difference between left and right proportions correct. At the 0.05 level of significance, we considered the two proportions as different if \( z < -1.96 \) or \( z > 1.96 \).

We opted for Z-scores rather than for the more common \( \chi^2 \) test because expected frequencies in the four possible combinations composing the cross-tabulation between target position (left vs. right) and response localization (correct vs. incorrect) were at risk of falling below the minimum criterion for computing the \( \chi^2 \) test, because of TN’s response bias tendency toward right-side responses (see below in the Results section).

Third, we reported the mean RT for left and right targets separately and ran independent \( t \) tests to assess differences between the two RT distributions.

Finally, we performed a signal detection analysis since in Experiment 2 discrimination of left targets was below chance, indicating that TN presented a right-response bias in this condition. To verify that performance observed for right targets did not result solely from this right-response bias, we calculated the \( d’ \) signal detection measure for right targets. Hits were trials in which a target was displayed on the right and a right response was given. False alarms where trials in which there was no signal on the right (i.e., the target was on the left) and a right response
was given. Notice that a $d'\!$ of 0 indicates an inability to distinguish signal from noise, whereas higher values indicate better signal sensitivity.

**RESULTS**

**Computerized Visual Field Mapping**

Consistent with the case history, TN was unable to report the presence of any visual stimulus, showing clinical blindness in all regions of the visual field tested, both with static and flickering stimuli.

**Functional Activity in the Visual Cortex**

The whole-brain analysis showed no significant increase of BOLD activity in response to visual stimulation in any extrastriate area. Instead, significant activity was observed in the right inferior sensorimotor cortices, right inferior parietal lobule, and right posterior insula. Even at a more liberal threshold, there was no evidence of functional activity in extrastriate visual areas, whereas increased activation was observed in cortical and subcortical areas related to motor control and action executions, such as the left primary motor cortex, bilateral BG, right cerebellum, right OFC, bilateral insula, and bilateral mid pons.

Lastly, ROI analyses showed no significant change in activation relative to baseline in any of the three regions analyzed and in any of the voxels belonging to these regions (see Figure 2) [lingual gyrus: $F(3, 189) = 0.98, p = .79$; calcarine sulcus: $F(3, 189) = 0.92, p = .82$; cuneus: $F(3, 189) = 1.16, p = .70$]. Therefore, no significant BOLD activity was observed in any of the analyses performed, in tissue that might be considered as striate or extrastriate visual areas.

**Goal-directed versus Discrete Responses Localization**

In Experiment 1, TN pointed toward the correct location of flickering targets on 74% of the trials and on 75% of the trials when presented with static targets, a performance that was clearly above chance ($ps < .001$; Figure 1C). The localization of the flickering target was above chance level for both left and right targets, although the performance was better for right than left targets (86% vs. 64%; $z = -3.59, p < .05$; Figure 1D). With static stimuli, the performance was at chance for left targets.

![Figure 2](image-url). Coronal and axial slices showing TN’s bilateral occipital lesion. AAL templates of the lingual gyrus (blue), calcarine sulcus (green), and cuneus (red), projected into the patient’s native space are superposed on the anatomical images showing the residual tissue of the main occipital subdivisions. The bar charts show the activation within each anatomically defined region in response to a checkerboard flickering at 2, 10, and 20 Hz, averaged across the voxels in the anatomical subdivision. Error bars represent 90% confidence intervals. No voxel within any of the ROIs reached significance of $p < .05$, corrected for multiple comparisons at the whole-brain level or within their respective ROI.
targets but was significantly above chance level for right targets (54% vs. 94%; $z = -6.45, p < .05$; Figure 1D). Finally, RTs were longer for left than right targets with both flickering [837 vs. 610 msec; $t(57) = -6.01, p < .001$, Figure 1E], and static targets [699 vs. 579 msec; $t(55) = -3.20, p < .01$].

Importantly, the comparison between flickering and static targets in Experiments 1A and 1B, respectively, showed no significant difference for left (hit rate: 64% and 54%; $z = 1.44, ns$) and right side targets (hit rate: 86% and 94%; $z = 1.89, ns$).

In Experiment 2, TN’s localization performance with finger-lift responses was at chance level (53%; $p = .73$; Figure 1C), indicating that left–right localization in TN critically depends on the possibility to perform a goal-directed pointing action toward the stimuli. Analysis of localization accuracy for left and right targets separately showed a greater hit rate for right targets, whereas performance was significantly below chance level for left targets (68% vs. 38%; $z = -4.25, p < .05$; Figure 1D). Signal detection analyses showed that the above chance performance for right targets in Experiment 2 was because of a right-sided response bias and not to a real increase of sensitivity for the detection of targets on the right ($d' = 0.16$). It is noteworthy, however, that this right-side response bias cannot account for the higher hit rate observed when pointing to right-side targets in Experiments 1A and 1B ($d' = 1.44$ and 1.66), indicating an actual increase of detection sensitivity in these latter cases. Finally, RTs were slower for left than right targets [852 vs. 542 msec; $t(37) = -4.44, p < .001$; Figure 1E].

**DISCUSSION**

In this study, a patient with bilateral cortical blindness underwent a series of experiments that required left–right localization of unseen targets using goal-directed and discrete manual responses. TN was remarkably efficient in localizing targets when required to point directly toward them but showed chance performance when asked to indicate their position using a finger-lift response. This indicates that the residual ability to localize correctly an unseen stimulus critically depends on the requirement to convert a visual signal into a goal-directed motor output and not simply on the performance of a manual motor response per se. The present finding provides compelling evidence that even a very basic parameter such as location in space may be more readily encoded in the action (dorsal) system than in the perceptual/categorical (ventral) system (Danckert & Rossetti, 2005; Rossetti, 1998). Furthermore, the bilateral destruction of visual cortices in patient TN rules out the possibility that localization without awareness relies on the contribution of cortical visual areas in the intact hemisphere.

To our knowledge, this is the first demonstration in blindsight of a dissociation in localization that depends on whether a goal-directed or a discrete manual motor response is required. In contrast to previous studies in which goal-directed actions were compared with verbal responses or perceptual decisions (Danckert & Rossetti, 2005; Weiskrantz et al., 1974), our current investigation directly compared two different types of responses involving the manual motor system, allowing us to focus on the critical contribution of visuomotor integration and goal-directed interaction in the localization of unconsciously seen targets. To what extent the present findings generalize to other blindsight patients with unilateral or bilateral lesions remains open to further investigation. Nevertheless, our findings are in keeping with neurophysiological and neuropsychological evidence pointing to a pivotal role of dorsal frontoparietal regions, as detailed below.

The specificity of goal-directed motor responses for the localization of unseen stimuli is consistent with neurophysiological evidence suggesting the existence of a neural system that mediates visually guided motor outputs in the absence of awareness and encompasses the superior colliculus, posterior dorsal areas including the parietal cortex, and anterior motor areas (Milner & Goodale, 2006). In fact, the proximity of the hand with an invisible target improves its detection and visuomotor processing (Roseboom & Arnold, 2011; Brown, Kroliczak, Demonet, & Goodale, 2008), an effect likely mediated by visuotactile bimodal neurons. These bimodal neurons have been found in the premotor cortex and in the ventral intraparietal sulcus and their firing rate in response to a visual stimulus decays as the distance between the stimulus and the spatial extent of the tactile receptive field increases (Graziano, Yap, & Gross, 1994). They are thus ideally placed along the dorsal visual stream known to support “vision for action.” Moreover, these areas can receive direct visual input bypassing VI from the superior colliculus, which also contains bimodal neurons and is directly involved in the control of goal-directed hand movements through monosynaptic connections with cortical and subcortical motor areas as well as with posterior parietal regions (Tamietto, Pellens, de Gelder, Weiskrantz, & Goebel, 2012; Tamietto et al., 2010; Tamietto & de Gelder, 2008). More specifically, there is neuropsychological evidence suggesting a causal role of the posterior parietal cortex in visuomotor localization of targets presented in the hemianopic field of blindsight participants (Danckert et al., 2003). In fact, target localization by pointing seems preserved only in blindsight patients in whom the posterior parietal cortex is spared. It is worth mentioning that most of these areas composing the frontoparietal dorsal system seem functionally and anatomically spared in TN and responded to visual stimulation during the fMRI testing. Our fMRI findings thus provide further support, although indirect, to the possible pivotal role of the dorsal system in nonconscious visuomotor localization. Nevertheless, because neuroimaging was not performed on TN during the behavioral experiment, these neurofunctional considerations remain speculative at
present, notwithstanding the fact that a significant amount of functional and anatomical reorganization may have occurred subsequently to the infarcts. Finally, it is noteworthy that the intention to perform a goal-directed hand movement facilitates the allocation of attention toward the target location before the manual response is executed (Reed, Grubb, & Steele, 2006).

The present finding suggests that rehabilitation training protocols for cortically blind patients could prove more efficient providing they focus on the execution of goal-directed movements, rather than discrete movements or verbal responses. Also, our method of contrasting different types of actions within an identical paradigm is well suited for further investigations of the neural pathways mediating perception and action in the absence of awareness. This can be applied in the same way to different neurological conditions (e.g., visual extinction, neglect), as well as to healthy participants in whom stimuli are rendered invisible through experimental manipulations such as flash suppression or masking.

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