Collicular Vision Guides Nonconscious Behavior

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Abstract

■ Following destruction or deafferentation of primary visual cortex (area V1, striate cortex), clinical blindness ensues, but residual visual functions may, nevertheless, persist without perceptual consciousness (a condition termed *blindsight*). The study of patients with such lesions thus offers a unique opportunity to investigate what visual capacities are mediated by the extrastriate pathways that bypass V1. Here we provide evidence for a crucial role of the collicular–extrastriate pathway in nonconscious visuomotor integration by showing that, in the absence of V1, the superior colliculus (SC) is essential to translate visual signals that cannot be consciously perceived into motor outputs. We found that a gray stimulus presented in the blind field of a patient with unilateral V1 loss, although not consciously seen, can influence his behavioral and pupillary responses to consciously perceived stimuli in the intact field (implicit bilateral summation). Notably, this effect was accompanied by selective activations in the SC and in occipito-temporal extrastriate areas. However, when instead of gray stimuli we presented purple stimuli, which predominantly draw on S-cones and are thus invisible to the SC, any evidence of implicit visuomotor integration disappeared and activations in the SC dropped significantly. The present findings show that the SC acts as an interface between sensory and motor processing in the human brain, thereby providing a contribution to visually guided behavior that may remain functionally and anatomically segregated from the geniculo-striate pathway and entirely outside conscious visual experience. ■

INTRODUCTION

It is widely assumed that conscious vision is subserved in humans by the retino-geniculo-striate system relaying visual input from the retinal ganglion cells to primary visual cortex (area V1, striate cortex) through the lateral geniculate nucleus (LGN). There is, nevertheless, a multiplicity of parallel pathways that bypass V1 and project to other targets in the brain whose contribution to vision is multifold and not yet ultimately established (Milner & Goodale, 1995). Evidence that residual visual capacities are retained in the absence of awareness by several subjects with cortical blindness ensuing from destruction of V1 (Weiskrantz, 2009; Weiskrantz, Warrington, Sanders, & Marshall, 1974; Pöppel, Held, & Frost, 1973) offers a unique window into the functions mediated by such extrastriate pathways and their subcortical relay centers. Moreover, the study of nonconscious vision following cortical blindness, termed "blindsight" by Weiskrantz et al. (1974), can provide an important contribution to the more general issue of perceptual consciousness.

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The superior colliculus (SC) in the midbrain and its indirect cortical projections to extrastriate visual areas in the occipital and temporal lobes have been suggested as likely candidates in mediating visually guided behavior notwithstanding V1 lesion (de Gelder et al., 2008; Stoerig & Cowey, 2007; Danckert & Rossetti, 2005; Lunenburger, Kleiser, Stuphorn, Miller, & Hoffmann, 2001; Stein, Wallace, & Stanford, 2000; Pöppel et al., 1973). Thus far, however, despite suggestive leads on the role of the collicular–extrastriate pathway in this form of nonconscious visuomotor integration (de Gelder et al., 2008; Leh, Johansen-Berg, & Ptito, 2006; Leh, Mullen, & Ptito, 2006; Schoenfeld et al., 2002; Morland et al., 1999; Sahraie et al., 1997), alternative accounts focusing on the possible contribution of other subcortical structures cannot be safely dismissed. In fact, visual signals may reach extrastriate cortices also through direct connections from the LGN or from the pulvinar nucleus (Bridge, Thomas, Jbabdi, & Cowey, 2008; Leh, Chakravarty, & Ptito, 2008). Convincing evidence on the crucial role of the SC would require two parallel findings: a positive functional demonstration that the SC is involved in implicit visuomotor processing even when V1 is no longer active, along with the concomitant negative evidence that such nonconscious phenomenon disappears when SC's contribution to vision is selectively blocked.

To provide this double evidence here, we draw on the insensitivity of the SC to short wavelength light. Previous

research has shown that the SC does not receive signals from short wavelength (S-) cones in the retina, so that purple stimuli that are predominantly detected by S-cones are invisible to the SC (Bertini, Leo, & Làdavas, 2008; Leo, Bertini, di Pellegrino, & Làdavas, 2008; Savazzi & Marzi, 2004; Sumner, Adamjee, & Mollon, 2002; Marrocco & Li, 1977). Moreover, even if there might be some small S-cones input to the SC, this channel is not chromatically opponent and can be masked using luminance noise (Birch, Barbur, & Harlow, 1992; Mollon, 1982). Conversely, S-cones project through the koniocellular pathway to the LGN as well as to the pulvinar, therefore enabling purple stimuli to be processed by these subcortical structures and their cortical projections (Keller, Lee, & McPeek, 2005; White, Wilder, Goodchild, Sefton, & Martin, 1998; Felsten, Benevento, & Burman, 1983).

Patient G. Y., with right hemianopia and blindsight following selective early damage to his left V1, was tested with an indirect method to assess the influence of stimuli presented to the blind field on the behavioral performance to stimuli presented to the intact field. Luminous squares were briefly projected (200 msec) either singly to the left (intact) visual field (LVF) or right (blind) visual field (RVF), or bilaterally to both fields (BVF), and the patient was asked to respond manually as quickly as possible following stimulus detection. Previous research using achromatic patches has shown that, although hemianopic patients report only the presence of the stimulus shown to the intact field even when the stimuli are flashed to both fields, they actually respond more quickly in this latter condition with respect to stimulation of the seeing field alone, an effect known as implicit bilateral gain (or bilateral summation) (de Gelder, Pourtois, van Raamsdonk, Vroomen, & Weiskrantz, 2001; Tomaiuolo, Ptito, Marzi, Paus, & Ptito, 1997; Corbetta, Marzi, Tassinari, & Aglioti, 1990; Marzi, Tassinari, Aglioti, & Lutzemberger, 1986). This approach to reveal blindsight circumvents methodological limitations related to response bias and does not force the patient to make counterintuitive guesses about unseen events in his blind field, as is the case with direct forced-choice methods (Azzopardi & Cowey, 1997).

In the first experiment, manual response times (RTs) were recorded to provide evidence of implicit bilateral gain in G. Y. Pupillary width was also simultaneously recorded as a second independent psychophysiological measure of nonconscious visual processing. Age-matched control subjects were included in this first experiment to verify the reliability of the color manipulation and to provide direct comparisons with healthy participants who were aware of both stimuli. In the second experiment, RTs and functional magnetic resonance imaging (fMRI) were used conjointly to determine directly the cerebral structures involved in the implicit bilateral gain effect. We found that a gray stimulus projected to the blind field of G. Y., although not consciously seen, speeded up RTs and enhanced pupillary constriction responses to stimuli simultaneously presented to the intact field. Notably, this summation effect was accompanied by a selective activation in the SC and in extrastriate areas, but not in other subcortical sites. However, when the stimulus was colored purple, and was hence invisible to the SC, we no longer found any behavioral or pupillary evidence of bilateral summation, and the fMRI activation in the SC dropped significantly.

EXPERIMENT 1

Experimental Procedures

Patient

G. Y. is a 52-year-old man with right hemianopia and blindsight following selective damage to his left striate cortex suffered at age 8 years as the result of a traumatic brain injury. G. Y.'s visual system has been previously tested with behavioral and psychophysiological experiments, as well as with fMRI and diffusion tensor imaging methods (see Bridge et al., 2008; Goebel, Muckli, Zanella, Singer, & Stoerig, 2001; Baseler, Morland, & Wandell, 1999 for an extensive structural and functional description of G. Y.'s lesion).

A computerized high-resolution visual perimetry was performed before testing. Stimuli consisted of small white circles (1°; stimulus luminance: 95 cd/m^2) presented well above luminance detection threshold against a dark background (2 cd/m^2) on a 21-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; i.e., upper-left, upper-right, lower-left, and lower-right quadrant) with onset and offset signaled by two different sounds. The patient was required to keep steady fixation on a central cross and to report verbally when any stimulus change was detected. This procedure enabled us to map G. Y.'s visual field within an ideal grid spanning 25° of horizontal and 20° of vertical eccentricity. Consistent with the case history, G. Y. showed a right homonymous hemianopia with macular sparing extending ~3° into the otherwise blind hemifield.

G. Y. gave informed consent to participate in the study.

Controls

Eleven age-matched healthy volunteers (all men) participated as control subjects after signing a written informed consent (age: $M = 51.1$ years, $SD = 1.87$, range = 49–54). All subjects reported normal or corrected-to-normal visual acuity and no history of neurological or psychiatric illness.

Stimuli

Stimuli consisted of 5° squares centered vertically at 7° of eccentricity from the innermost edge to the central fixation cross (1.26° × 1.26°) along the horizontal meridian.

There were three types of stimuli: gray (colorimetric values: $x = 0.30$, $y = 0.30$), chromatic purple ($x = 0.183$, $y = 0.087$), and chromatic red ($x = 0.619$, $y = 0.346$); the latter was used only in the behavioral control experiment (see below). The stimuli were calibrated to engage preferentially the achromatic pathway (gray) and the chromatically opponent pathways that predominantly draw on S-cones (purple) or on L- and M-cones (red) (Marzi, Mancini, Metitieri, & Savazzi, 2009; Bertini et al., 2008; Leo et al., 2008; Savazzi et al., 2007; Savazzi & Marzi, 2004; Mullen & Kingdom, 2002; Smithson, Sumner, & Mollon, 2002; Sumner et al., 2002; Hendry & Reid, 2000). With the exception of this color difference, all stimuli were carefully matched for their objective (physical) and subjective attributes; that is, all stimuli had the same luminance (10.6 cd/m^2), were of the same size (5°), and were detectable with the same ease, as shown by similar RTs. All stimulus parameters were verified by direct photometer and colorimeter measurements from the projection screen.

Procedure and Apparatus

The stimuli were projected for 200 msec against a background consisting of achromatic squares (2.5°) changing luminance every 50 msec (20 Hz) (range: 1.1–20.1 cd/m^2). This random luminance noise ensured that color changes could be detected only by chromatically opponent channels, and not also by the rod-generated signals elicited by the onset of the stimulus (Sumner et al., 2002; Barbur, Sahraie, Simmons, Weiskrantz, & Williams, 1998; Birch et al., 1992). This background luminance mask also minimized the possibility of light scatters to the seeing field during the projection of stimuli to the blind field.

The stimuli could be presented either singly to the LVF or RVF, or simultaneously to BVF. G. Y. was required to keep steady fixation on the central cross and to respond manually as quickly as possible following stimulus detection by keypressing on a response button with his index finger. Noteworthy, under these conditions, G. Y. never reported the presence of any stimulus, either gray, purple, or red, in his blind (RVF) field, or any light scatter from the blind to the normal field.

Each stimulus type (gray, purple, red) and each condition (LVF, RVF, and BVF) was equiprobable and was presented in random order. In the main experiment, gray and purple stimuli were used. Four blocks were run, each comprising 42 trials with gray stimuli (14 to the LVF, 14 to the RVF, and 14 to BVF) and 42 trials with purple stimuli. The interstimulus interval (ISI) was 4 sec and there was a short rest of few minutes at the end of every block. Overall, 336 trials were administered with 56 repetitions for each of the six different stimulus conditions. Response hand was alternated between blocks. In the control experiment, gray and red stimuli were used. In all other aspects, the same procedure used in the main experiment was adopted.

Stimulus presentation and response recording were controlled by means of the Presentation 9.3 software (NeuroBehavioral Systems, Albany, CA) installed on an IBM-compatible Pentium PC. Eye movements and pupillary diameter were monitored via an infrared camera (RED-III pan tilt) connected to an eye-tracking system that analyzed on-line monocular pupil and corneal reflection (sampling rate 50 Hz; 20 msec) (iViewX; SensoMotoric Instruments, Teltow, Germany). In case of unsteady fixation, the trial was automatically discarded and replaced by a new one presented at the end of the block.

Pupillometric Data Reduction

Raw pupillary diameter data were first inspected for gross artifacts and discarded in case of major artifacts or excessive blinking. Minor artifacts and normal eye blinks that cause the loss of few data bins were corrected by linear interpolation. A 5-point smoothing filter was then passed over the data. Artifact-free and smoothed pupillary response data were segmented into 4-sec epochs including 1 sec of prestimulus period and 3 sec after stimulus onset for each condition of stimulation separately. A baseline pupil diameter was calculated for each trial by averaging the pupillary diameter samples recorded during the 1-sec preceding stimulus onset. Data were then expressed as differences from baseline by subtracting the mean baseline pupillary diameter from all subsequent samples. A mean pupillary response-from-baseline waveform was finally obtained for each condition simply by averaging across trials the values at each time point. Fewer than 7% of the trials were discarded following this procedure.

Results

Patient G. Y.

Behavioral results. A preliminary analysis, focused only on consciously perceived (LVF) single stimuli, revealed that mean RTs to single gray (355.3 msec) and purple stimuli (350.1 msec) were very similar [$t(55) = 0.68$, $p = .5$ by paired-sample t test], thereby suggesting that the two types of stimuli were equally salient and detectable.

Mean RTs were then analyzed by means of a 2 × 2 repeated measures analysis of variance (ANOVA) with the factors stimulus number (single LVF vs. BVF) and stimulus color (gray vs. purple). There was no significant main effect of stimulus number or color [$F(1, 55) = 2.18$, $p = .145$; $F(1, 55) = 1.65$, $p = .2$; respectively]. However, the interaction was significant [$F(1, 55) = 5.99$, $p = .017$], showing that, with gray stimuli, mean RTs were faster for BVF (333.5 msec) than for single LVF stimuli ($p = .04$ by post hoc Bonferroni test for all comparisons henceforth). In contrast, with purple stimuli, there was no significant difference between BVF (355.2 msec) and single LVF stimuli ($p = 1$) (Figure 1A). The lack of bilateral gain for purple stimuli invisible to the SC is thus in

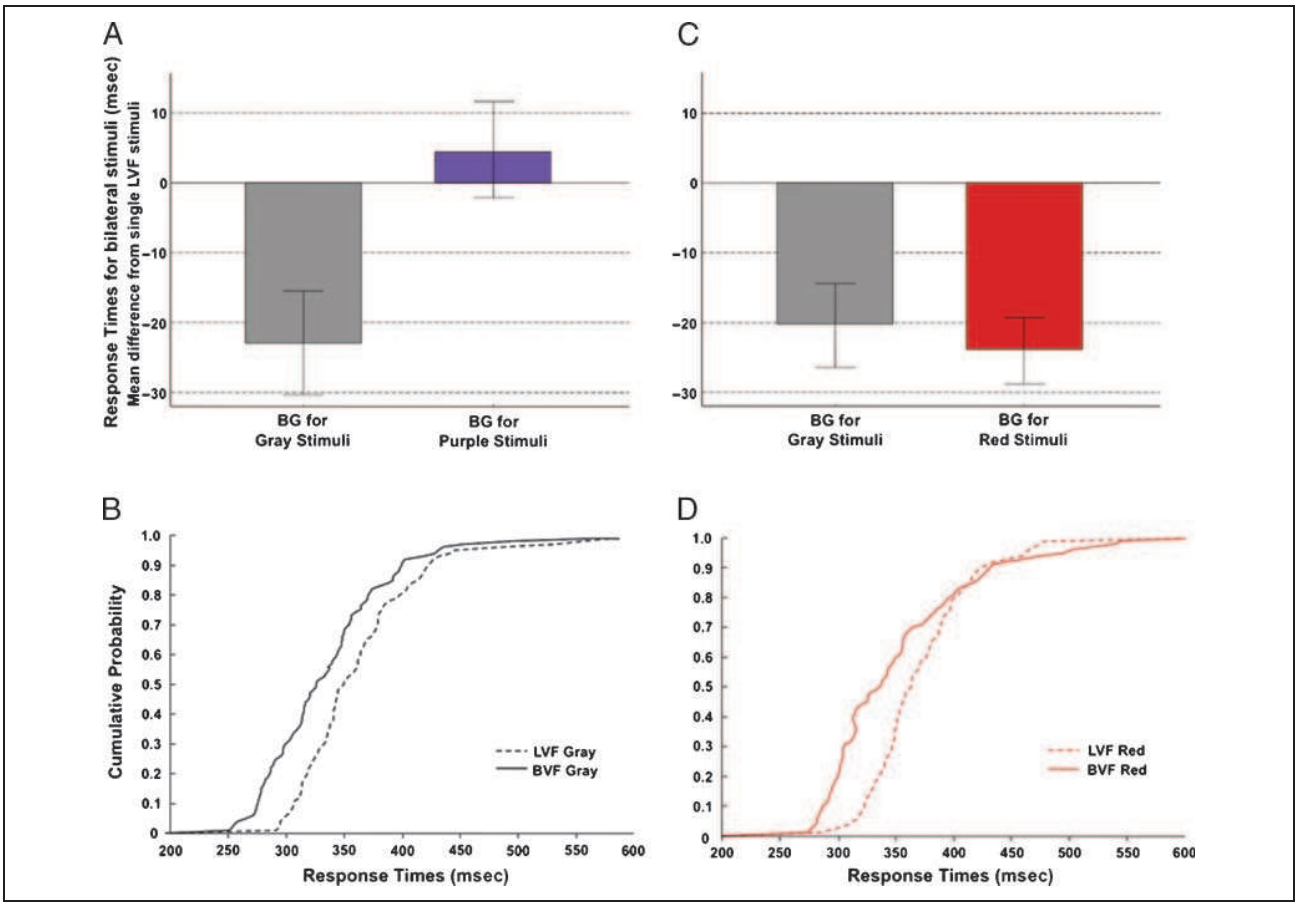

Figure 1. Manual response times. (A) Mean RTs (±*SEM*) differences between BVF and single LVF stimuli as a function of color (gray and purple) in the main experiment. (B) Cumulative distribution functions of RTs for BVF and single LVF gray stimuli showing a significant bilateral gain throughout the entire distribution. (C) Mean RTs (±*SEM*) differences between BVF and single LVF stimuli as a function of color (gray and red) in the control experiment. (D) Cumulative distribution functions of RTs for BVF and single LVF red stimuli showing a significant bilateral gain throughout the entire distribution. BG = bilateral gain; BVF = both visual fields; LVF = left visual field; RTs = manual response times; RVF = right visual field.

keeping with the hypothesis that gray stimuli that are not consciously perceived may affect behavior through SC mediation.

We also plotted the cumulative distribution functions (CDFs) of RTs for single LVF and BVF gray stimuli (Ratcliff, 1979). This detailed graphical description enables to check whether the bilateral gain observed on mean values for gray stimuli occurs throughout the whole distribution of RTs. It also represents a nonparametric version suitable for single-subject analysis of Miller's inequality test, which is a mathematical tool to test whether the bilateral gain is related to probability or neural summation (Maris & Maris, 2003; Miller, 1982). This further analysis is important because only the latter type of bilateral gain postulates the existence of a neural center of summation between seen and unseen stimuli (see Tamietto & de Gelder, 2008; Colonius & Diederich, 2006; Savazzi & Marzi, 2004 for a detailed description of the computations and rationale). As shown in Figure 1B, RTs for BVF gray stimuli were significantly faster than for single LVF stimuli throughout the entire distribution, thereby providing convincing evidence for an interpretation of the bilateral gain effect in terms of neural summation ($p = .025$ by Kolmogorov–Smirnov test).

A behavioral control experiment was also carried out to provide evidence that the absence of bilateral gain was specifically related to chromatic stimuli predominately processed by S-cones, but not to chromatic stimuli that engage L- and M-cones (like red stimuli), which conversely send projections to the SC. This experiment was in all respect identical to the main experiment with the only exception that red, instead of purple, stimuli were used. Mean RTs data were entered into an ANOVA with the same factors and levels considered in the previous analysis (Figure 1C). Only the stimulus number factor turned out significant, indicating a bilateral gain of equivalent magnitude for both gray and red stimuli [$F(1, 55) = 9.03$, $p = .004$] [stimulus color: $F(1, 55) = 0.14$, $p = .71$; interaction: $F(1, 55) = 0.05$, $p = .82$]. This latter result excludes the possibility that the lack of bilateral gain for purple squares was an unspecific effect common to all chromatic stimuli.

CDFs of RTs for single LVF and BVF red stimuli were also plotted, showing a significant bilateral gain throughout the entire distribution, comparable to that reported for gray stimuli ($p < .001$ by Kolmogorov–Smirnov test; Figure 1D).

Pupillometric results. Mean pupillary changes from baseline in response to gray and purple stimuli as a function of LVF, RVF, and BVF stimulation are shown in Figure 2A and B, respectively.

Initially, a 2 × 2 ANOVA with the factors stimulus side (LVF vs. RVF) and stimulus color (gray vs. purple) was carried out to assess the pupillary responses to single stimuli. In keeping with RT results, mean peak of constriction amplitude from baseline was similar for single gray and purple stimuli, thus confirming that the two types of stimuli were matched in terms of detection speed and luminance [stimulus color: $F(1, 55) = 2.22, p = .14$; interaction: $F(1, 55) = 0.11, p = .74$]. The only significant difference between LVF and RVF stimuli was a reduced pupillary constriction in response to stimuli, either gray or purple, projected to the (blind) RVF [$F(1, 55) = 90.3$, $p < .0001$]. This latter result is consistent with recent findings showing an attenuation of the pupillary light reflex to stimuli presented to the blind field of patients with hemianopia following suprageniculate lesions (Papageorgiou et al., 2008). This effect is probably related to a reduced feedback from cortical visual areas to subcortical structures, such as the olivary nucleus of the pretectum, that mediate pupillary constriction.

To assess the presence of a bilateral gain at the pupillary level, mean peak of constriction amplitude data were submitted to a 2 × 2 ANOVA with the same factors applied on RT data (i.e., stimulus number, single LVF vs. BVF; and stimulus color, gray vs. purple). There was a significant main effect of stimulus number and a significant Stimulus number × Stimulus color interaction [$F(1, 55) = 19.3, p < .0001$ and $F(1, 55) = 7.1, p = .01$, respectively;

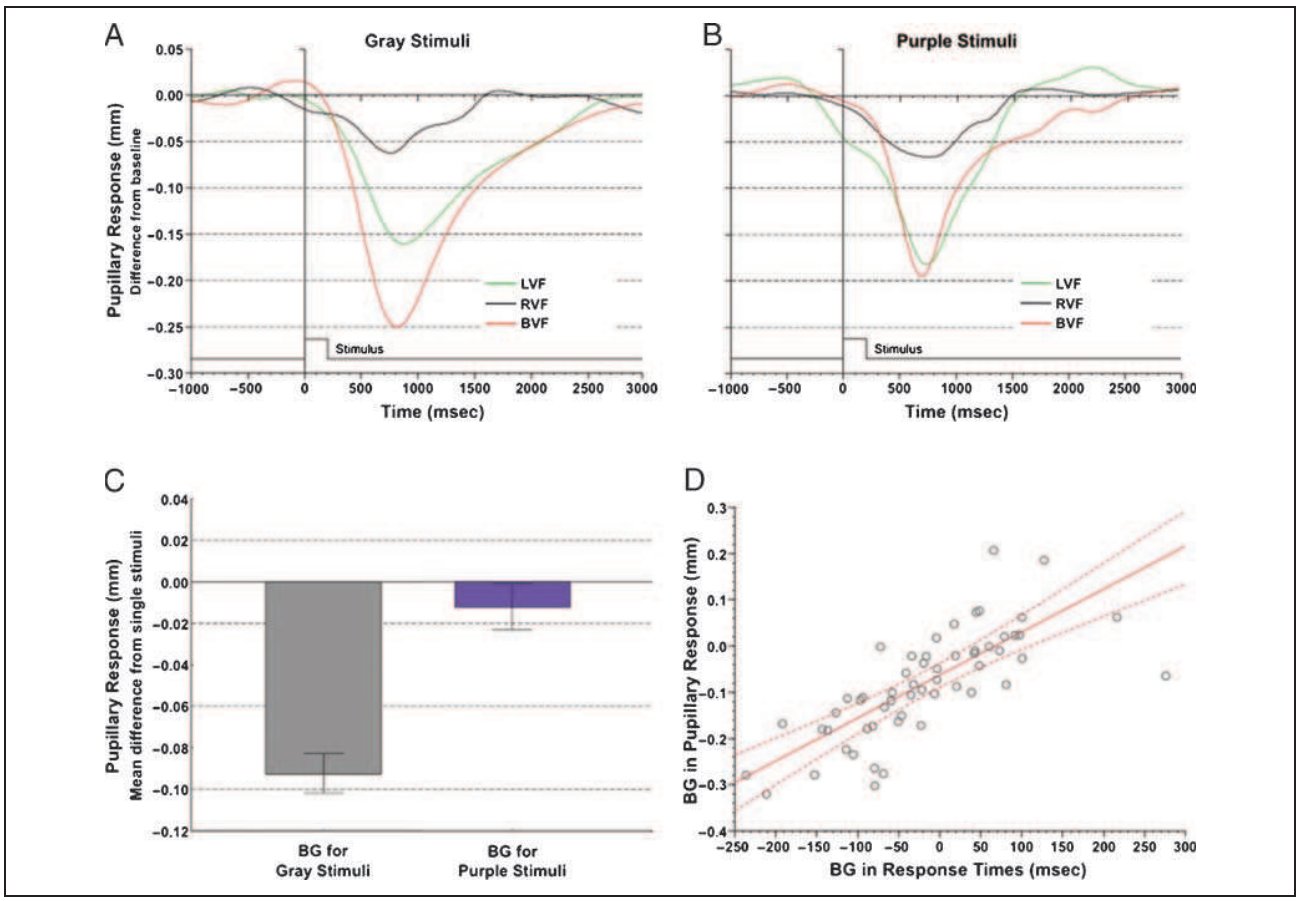

Figure 2. Amplitude and latency of mean pupillary response. (A) Mean pupillary response waveforms during presentation of single LVF, RVF, and BVF gray stimuli. Data are expressed as differences in pupillary diameter from prestimulus baseline. The rectangular pulse trace along the horizontal axis shows the time of stimulus presentation. (B) Mean pupillary response waveforms during presentation of single LVF, RVF, and BVF purple stimuli. (C) Mean differences (±*SEM*) in the amplitude of pupillary response between BVF and single LVF stimuli as a function of color (gray and purple). (D) Correlation between the bilateral gain for gray stimuli in RTs data (BVF gray–LVF gray) and the bilateral gain for the same gray stimuli in the amplitude of pupillary response data. The solid red line represents predicted (i.e., fitted) correlation between behavioral and pupillometric measures. The dashed red lines represent 95% confidence limits. BG = bilateral gain; BVF = both visual fields; LVF = left visual field; RVF = right visual field.

stimulus color: $F(1, 55) = 1.54, p = .22$]. Mean pupillary constriction was enhanced by BVF gray ($p = .0003$) but not by BVF purple stimuli ($p = 1$) with respect to the corresponding single stimuli in the intact LVF, as revealed by post hoc tests on the interaction (Figure 2C).

The pupillometric results thus show a profile remarkably similar to that obtained independently with RTs, as further indicated by the significant correlation between bilateral gain for gray stimuli in RTs and pupillary data (Pearson $r = .63, p < .05$; Figure 2D).

Controls

Mean RTs and mean peak of pupillary constriction amplitude from baseline are shown in Table 1 as a function of the different display types and stimulus colors.

Behavioral results. A first 2 × 2 ANOVA with the factors stimulus side (LVF vs. RVF) and stimulus color (gray vs. purple) was carried out on RTs to single stimuli to verify whether subjective detection was comparable between colors and across hemifields in neurologically intact observers. There was no main effect or interaction, thus confirming results in G. Y.'s seeing hemifield of no difference between colors, and indicating no difference in controls between single LVF and RVF presentation [stimulus side: $F(1, 10) = 0.006, p = .94$; stimulus color: $F(1, 10) = 0.28, p = .61$; interaction: $F(1, 10) = 0.04, p = .85$]. RTs to single stimuli were therefore averaged across visual fields for each color separately.

Evidence of bilateral gain to consciously perceived stimuli was investigated by means of a second 2 × 2 ANOVA with stimulus number (single vs. BVF) and stimulus color (gray vs. purple) as factors. Only the stimulus number main effect turned out to be statistically significant, thereby indicating a bilateral gain for both gray and purple stimuli [$F(1, 10) = 14.7, p = .003$] [stimulus color: $F(1, 10) = 0.009, p = .93$; interaction: $F(1, 10) = 0.58, p = .47$]. Importantly, however, the Miller's inequality test revealed a significant violation only for gray stimuli, whereas purple stimuli never violated the upper limit imposed by the test [$t(36) = 4.1, p < .001$ by single-sample t test]. This means that only gray stimuli produced a bilateral gain explainable in terms of neural summation, whereas the effect observed for purple stimuli was likely the result of probabilistic facilitation induced by the simultaneous presence of two detectable stimuli.

This experiment was repeated by using gray and red stimuli, as previously done with G. Y. The ANOVA with the same factors and levels considered previously showed only the main effect of stimulus number, which indicates a bilateral gain for gray and red stimuli alike [$F(1, 10) = 13.3, p = .004$] [stimulus color: $F(1, 10) = 0.11, p = .75$; interaction: $F(1, 10) = 0, p = .998$]. Noteworthy, in this case the Miller's inequality test was violated by gray as well as red stimuli, thereby suggesting that a neural summation of similar magnitude occurred for both stimulus colors [gray: $t(39) = 3.05, p = .004$; red: $t(34) = 6.93, p < .001$].

Overall, the behavioral responses recorded in healthy subjects to consciously perceived stimuli are closely similar to those obtained in G. Y. when the same stimuli were presented to his intact field. In fact, also in the case of control participants, there was no difference in RTs to single stimuli as a function of color. This further confirms that the color manipulation did not affect subjective stimulus detection or visibility, as measured with RTs, and that G. Y.'s performance to seeing stimuli was, in all respects, similar to that of age-matched control subjects.

Obviously, the bilateral gain effect found in controls should be compared only indirectly to its *implicit* counterpart in G. Y., as healthy subjects were aware of both stimuli in a pair. However, the two phenomena show interesting similarities, and the results in control participants can provide further clues to the interpretation of our main findings in G. Y. Indeed, although a bilateral gain was obtained here with all types of stimulus pairs, the nature of the effect changed depending on stimulus color. With gray or red stimuli we observed a violation of the inequality test indicating a neural mechanism of stimulus summation, whereas with purple stimuli there was no violation and the effect was likely accounted by parallel and independent processing of the two stimuli.

Table 1. Mean RTs and Mean Peak of Pupillary Constriction Amplitude from Baseline (±*SEM*) in Age-matched Controls

	Colors	
Conditions	*Gray*	*Purple*
LVF		
RT	382.4 (±12.7)	380.7 (±11.2)
Pupillary constriction	−0.14 (±0.03)	−0.16 (±0.02)
RVF		
RT	384.8 (±16.1)	381.1 (±20.6)
Pupillary constriction	−0.15 (±0.04)	−0.15 (±0.04)
BVF		
RT	360.4 (±9.1)	362.2 (±11.3)
Pupillary constriction	−0.23 (±0.02)	−0.18 (±0.02)

Pupillometric results. We observed no difference in the pupillary response to single stimuli in a 2 × 2 ANOVA [stimulus side: $F(1, 10) = 0.005, p = .94$; stimulus color: $F(1, 10) = 0.2, p = .66$; interaction: $F(1, 10) = 0.02, p = .88$]. Because of this negative result, we averaged pupillary responses to single stimuli for each color separately.

The assessment of the bilateral gain at the pupillary level showed a significant main effect of the stimulus number factor, indicating an enhancement of pupillary constriction for BVF by reference to single stimuli [$F(1, 10) = 7.81, p = .02$; stimulus color: $F(1, 10) = 2.01, p = .19$]. Although the Stimulus number × Stimulus color interaction was only marginally significant, we, nevertheless, calculated the post hoc tests for theoretical interest [$F(1, 10) = 4.54, p = .059$]. These contrasts revealed that pupillary constriction was more pronounced for BVF than single gray stimuli ($p = .019$), whereas the difference between BVF and single purple stimuli was not significant ($p = 1$).

Also in this case, the present results are in line with those described above in RT data on controls, and are consistent with the pupillary responses shown by G. Y. in terms of (a) reactions to single stimuli projected to the intact field, (b) the presence of the bilateral gain for BVF gray stimuli, and, lastly, (c) the lack of such effect for purple stimuli.

Discussion

The present findings show that a gray stimulus presented to the blind field of a subject with unilateral V1 lesion may affect his behavioral as well as pupillary responses to stimuli simultaneously projected to the intact field. Notably, this bilateral gain effect, due to the implicit neural summation of stimuli across visual fields, disappears when purple stimuli predominantly processed by S-cones are used.

Results collected on neurologically intact age-matched control participants offer interesting analogies with G. Y.'s performance and confirm the results of previous studies that used the same color manipulation and experimental design on normal as well as neuropsychological subjects (Marzi et al., 2009; Savazzi et al., 2007; Savazzi & Marzi, 2004). This enabled us to verify that the behavioral and pupillary responses to single (consciously perceived) stimuli in G. Y., either gray, red, or purple, are closely comparable to those obtained in controls when the same procedure is used, and are not the result of idiosyncratic factors. More interestingly, the common presence of a neural bilateral gain for gray stimuli in both G. Y. and control subjects suggests that a similar mechanism subserves this effect in either cases. This neural mechanism does not appear to depend on the presence of V1 or on visual awareness of both stimuli in a pair. This hypothesis is further supported by evidence that purple stimuli abolish neural summation in G. Y. and controls alike. Conversely, the integrity of the primary visual cortices in both hemispheres and the related perceptual consciousness appear relevant for a probabilistic bilateral gain to take place, as this effect was present for purple stimuli in controls, but absent in G. Y. Although an in-depth investigation of this latter aspect is outside the aims of the present study, it is known that the primary visual cortices are poorly interconnected through the corpus callosum, and only for visual field representations close to the vertical meridian (Marzi, 1986; Pandya & Seltzer, 1986). Therefore, evidence that independent (i.e., parallel) processing of BVF purple stimuli is possible only in control subjects with bilaterally intact V1s fits well with current neurophysiologic data showing that these areas predominantly operate in parallel. This suggests that probability summation may occur at early stages in the central visual system (Miniussi, Girelli, & Marzi, 1998) or, according to other interpretations, at the premotor level in fronto-parietal sites upon modulatory influences from visual cortex (Iacoboni & Zaidel, 2003).

Nonconscious visually guided behavior following cortical blindness, such as the one reported in the present experiment, has been previously associated with the functional integrity of the collicular–extrastriate pathway (Weiskrantz, 2009; de Gelder et al., 2008; Leh, Johansen-Berg, et al., 2006; Leh, Mullen, et al., 2006; Danckert & Rossetti, 2005; Sahraie et al., 1997, 2003). Because the SC is insensitive to purple stimuli, the lack of bilateral summation for such stimuli strongly suggests its critical role in this phenomenon. Nevertheless, a direct investigation of the neural correlates of implicit visuomotor integration, as can be achieved with fMRI methods, is still missing in the literature and possible alternative, although unlikely, accounts of the present results cannot be entirely ruled out. For instance, the influence of the S-cones system on LGN and pulvinar is not known at present. Although both structures receive direct input from all types of color-opponent ganglion cells in the retina, including those connected to S-cones, it is possible that purple stimuli affect these subcortical structures in a different fashion with respect to gray stimuli that preferentially engage the achromatic system. Therefore, the putative weaker or diverse activation induced by purple stimuli on LGN and/or pulvinar may be, in principle, responsible for the lack of bilateral summation, aside from the effect these stimuli exert on the "inactivation" of the SC.

Preliminary clues about the above possibility can be obtained from our RTs and pupillary data, where we systematically found that single gray and purple stimuli were closely similar in terms of detection speed and pupillary constriction in both G. Y. and controls. Hence, there is no evidence in our results supporting the surmise that purple stimuli are generically less salient or detectable than gray ones. However, an fMRI study directly comparing gray and purple stimuli would be timely to clarify how these two different classes of stimuli are processed by subcortical visual structures in the human brain when V1 is damaged, as available evidence is based only on neurophysiologic studies in animal models.

To tackle these unanswered issues and directly determine the neural correlates of the implicit bilateral summation, we used the same design as in the present study in an fMRI experiment.

EXPERIMENT 2

Experimental Procedures

Stimuli and Procedure

The same stimuli and procedure used in Experiment 1 were applied here with the following exceptions: (a) instead of a fixed ISI of 4 sec, the ISI was jittered and varied pseudorandomly from 5800 to 13,800 msec; (b) two runs, instead of four, were administered. A single run lasted 23 min 28 sec and consisted of 144 trials randomly presented and equally subdivided among the six possible conditions (i.e., single LVF, RVF, and BVF, with either gray or purple stimuli), resulting in 24 trials for each condition. G. Y. alternated response hand between runs.

fMRI Acquisition

Data acquisition was performed on a 3-Tesla Siemens Magneton Allegra scanner (Siemens, Erlangen, Germany). We used an imaging protocol optimized for cortical and subcortical visual structures. Multislice T2-weighted fMRI images were acquired using an EPI sequence (TR/TE/flip angle = 2000 msec/35 msec/90°; FoV = 224 mm; acquisition matrix = 128 × 128; 24 contiguous 2-mm axial slices). For each of the two runs, 704 volumes were acquired.

Three-dimensional high-resolution T1-weighted structural images were acquired in the same session using a MDEFT sequence (TR/TE/flip angle = 7.92 msec/2.4 msec/15°; FoV = 256 mm; acquisition matrix = 256 × 256; 176 contiguous 1-mm sagittal slices; isotropic voxel size = 1 × 1 × 1 mm).

fMRI Analysis

Brain Voyager QX was used for image processing and analyses (Brain Innovation, The Netherlands). The first eight volumes of each run were discarded to ensure a steady state. Then, functional volumes were spatially aligned to the first volume by a trilinear interpolation algorithm, and smoothed by a 3-D Gaussian kernel with full width at half maximum (FWHM) of 4 mm. Temporal smoothing with a 2.8-sec FWHM Gaussian kernel was also applied to improve the signal-to-noise ratio by removing high-frequency fluctuations.

Data series were submitted to a single-subject analysis for event-related designs using general linear models. The conditions were modeled by boxcar waveforms and convolved with the hemodynamic response function. Baseline was defined as the average activity during periods of no stimulus presentation, when only the flickering background was visible. Voxelwise inferential testing was constrained to subcortical visual structures (i.e., SC, LGN, and pulvinar) and visual cortices (see fMRI Results for further details). These regions of interest (ROIs) were anatomically defined on T1-weighted images as well as on the base on previous studies that mapped topographic and functional organization of visual areas in the same patient (Schoenfeld et al., 2002; Goebel et al., 2001; Baseler et al., 1999; Sahraie et al., 1997; Barbur, Watson, Frackowiak, & Zeki, 1993). Inclusive mask volumes were then created for each ROI identified with this procedure. A fixed statistical threshold of $p < .05$, corrected for false discovery rate in multiple comparisons, was used to display results and activation maps (Genovese, Lazar, & Nichols, 2002), with a cluster-size threshold >5 contiguous voxels.

For each cluster of active voxels identified in a given contrast, the mean fMRI signal was computed reflecting the mean peak of activity of all voxels in the cluster over an average time course of 14 sec after stimulus onset, and expressed as percentage of BOLD signal change from baseline.

Results

Behavioral Results inside the Scanner

Mean RTs to consciously perceived LVF stimuli were 369.9 msec for gray and 363.7 for purple stimuli, whereas mean responses to BVF displays were 339.2 msec for gray and 364.1 for purple stimuli. A 2 × 2 ANOVA with the same factors and levels considered for the assessment of the bilateral gain outside the scanner was carried out on the present data, showing a significant Stimulus number × Stimulus color interaction [$F(1, 47) = 4.18$, $p = .047$; stimulus number: $F(1, 47) = 2.46$, $p = .12$; stimulus color: $F(1, 47) = 1.9$, $p = .17$]. Post hoc comparisons revealed a bilateral gain for gray stimuli only, as indicated by the significant difference between single LVF and BVF gray conditions ($p = .038$).

A Kolmogorov–Smirnov test carried out on the CDF for single LVF and BVF gray stimuli showed that a neural summation between BVF stimuli occurred even in this case ($p < .01$).

Therefore, aside from an unspecific slowing down of RTs into the scanner, the present results substantially parallel those obtained in Experiment 1 performed outside the scanner and comment on the reliability of the bilateral gain effect observed in G. Y.

fMRI Results

Subcortical response to single stimuli. A first analysis was performed on the pulvinar, LGN, and SC to compare how the subcortical structures receiving direct projections from the retinal ganglion cells process gray and purple stimuli. Responses to single stimuli, projected either to the LVF or to the RVF, were pooled together and contrasted against baseline activity [i.e., (LVF + RVF) > baseline]. This contrast was performed separately for single gray and purple stimuli, and computed on each subcortical ROI mask at a time (e.g., the same contrast was constrained to the left or right pulvinar only, then to the left or right LGN only, and finally to the left or right SC;

overall, this resulted in six different activation maps for gray and six for purple stimuli). This procedure minimized the risk to misleadingly attribute activity resulting from a given contrast to closely neighboring structures, as is the case, for instance, between the LGN and inferior-lateral portions of the pulvinar or between the left and right SC. Activation maps and mean fMRI responses are displayed separately for each structure in Figure 3 as a function of single gray and purple stimulation and of visual field of presentation.

Pulvinar response. Single gray stimuli evoked significant activations in 31 voxels (corresponding to a volume of 31 mm^3) of the left pulvinar and in 255 voxels of the right pulvinar when contrasted against baseline. The same comparison for single purple stimuli activated 167 voxels in the left pulvinar (including all 31 voxels also responsive to gray stimuli) and 213 voxels in the right pulvinar (183 of which—85.9%—were also activated by gray stimuli).

Mean fMRI responses in the left pulvinar were 0.24% and 0.22% of signal change for gray and purple stimuli presented to the LVF, respectively, and 0.31% and 0.33% for gray and purple stimuli to the RVF, respectively. Mean response amplitudes in the right pulvinar were 0.32% for gray and 0.31% for purple stimuli presented to the LVF, and 0.2% for gray and 0.22% for purple stimuli to the RVF (see Figure 3A).

Importantly, there was no significant difference in the mean proportion of signal change evoked by single gray and purple stimuli in the activated areas of both left and right pulvinar ($t \leq 0.22$, $p \geq .82$ for all comparisons). Moreover, although responses in each pulvinar (left or right) were stronger for stimuli presented to the contralateral visual field, this difference was not statistically significant and pulvinar activity was also modulated to a relevant extent by ipsilateral stimuli ($t \leq 0.98$, $p \geq .32$). This is in keeping with recent neuroimaging data in neurologically intact subjects, indicating that activated areas in this portion of the pulvinar may contain visually responsive neurons with large receptive fields extending across the vertical meridian and, perhaps, over the entire visual field (Cotton & Smith, 2007; Kastner et al., 2004).

LGN response. Twelve voxels in the left LGN and 54 voxels in the right LGN were activated by single gray stimuli. Single purple stimuli activated 10 voxels in the left LGN (5–50%—also activated by gray stimuli) and 71 voxels in the right LGN (31–43.7%—also activated by gray stimuli).

Left LGN activity was higher for contralateral (RVF) gray and purple stimuli (0.28% and 0.25% signal change, respectively) than for ipsilateral (LVF) stimuli (0.05% for gray and 0.06% for purple stimuli). Similarly, mean responses in the right LGN to contralateral (LVF) stimuli were 0.26% signal change for gray and 0.28% for purple stimuli, whereas mean responses to ipsilateral (RVF) stimuli were only 0.04% for gray and 0.07% for purple squares (see Figure 3B). The difference between fMRI activity for ipsilateral and contralateral stimuli was marginally significant in both left and right LGN and for gray as well as purple stimuli ($t \geq 1.93$, $p \leq .056$ for all comparisons, with the exception of the t test between LVF and RVF purple stimuli in the left LGN: $t = 1.42$, $p = .159$), consistent with findings of contralateral visual field representation in the LGN (Kastner et al., 2004; Schneider, Richter, & Kastner, 2004).

Notably, analogous to that reported for pulvinar, also in the left and right LGN, there was no significant difference in the mean percent signal change evoked by single gray versus purple stimuli ($t \leq 0.253$, $p \geq .8$).

SC response. Single gray stimuli activated 109 voxels in the left SC and 124 voxels in the right SC. These activations were predominately elicited by stimuli presented to the contralateral field (left SC: 0.06% fMRI response for LVF and 0.26% for RVF gray stimuli; right SC: 0.32% for LVF and 0.07% for RVF gray stimuli; $t \geq 1.69$, $p \leq .09$), supporting previous evidence that neurons sensitive to visual stimulation in this region have receptive fields that do not extend across the vertical meridian (Sylvester, Josephs, Driver, & Rees, 2007; Schneider et al., 2004) (Figure 3C).

No activation in the left or right SC was found in response to single purple stimuli even when a statistical threshold of $p = .3$ was applied. This threshold is far more liberal than any reasonable statistical threshold and was applied to test possible trends of activations evoked by purple stimuli that may go undetected with a conventional statistical approach.

To summarize, the activations produced by single stimuli complement and extend to the human brain prior neurophysiologic findings in animals. The results show that the SC is selectively insensitive to purple stimuli, but responds normally to gray squares. Conversely, the pulvinar and the LGN are activated by gray and purple stimuli to a similar extent in terms of volume, signal amplitude, and spatial location, thereby excluding the possibility that purple stimuli are generically less salient and evoke weaker activations than gray squares across all subcortical visual structures. These findings, also bolstered by simultaneously recorded behavioral results, provide the necessary preconditions to interpret the following analyses and clarify the neural correlates of the implicit bilateral summation for gray stimuli, as well as the reasons of its disappearance with the use of purple stimuli.

A final interesting result refers to the differences in the number of active voxels between subcortical structures in the (right) intact or (left) damaged hemisphere. The largest difference was reported for the LGN, where we found 94 different voxels responsive to visual stimuli in the right LGN, but only 17 in the left LGN (i.e., with a 5.5:1 ratio). This difference was reduced to a 1.7:1 ratio for the pulvinar with 285 different active voxels in the right and 167 in the left pulvinar, and almost absent in the SC, where 124 active voxels were detected in the

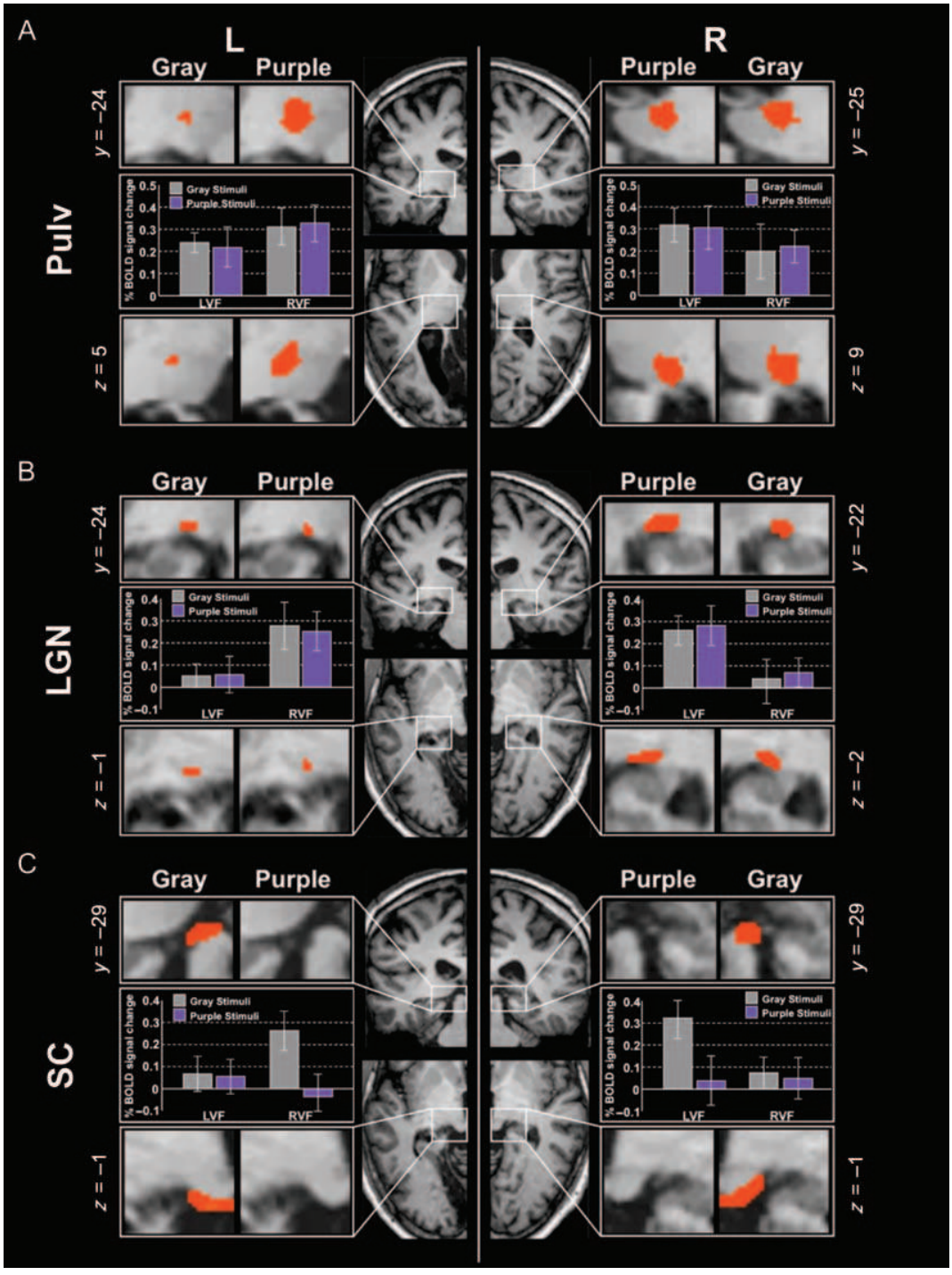

Figure 3. fMRI response to single gray and purple stimuli in subcortical visual structures. Activation maps and mean percentage of BOLD response from baseline evoked by single gray and purple stimuli in the pulvinar (A), LGN (B), and SC (C). Central panels show T1-weighted anatomical images of G. Y.'s brain in the coronal and transversal planes. Boxes indicate the location of the panels to the left (L) and right (R). Each lateral panel shows the voxels activated within the magnified regions by single gray and purple stimuli separately. The histograms represent the mean % of BOLD signal change (±*SEM*) for the voxels in the activated cluster as a function of stimulus color and position. Talairach *z*- and *y*-coordinates are given. Note the lesion to left V1 visible in transversal slices. BOLD = blood oxygen level dependent; L = left side; LGN = lateral geniculate nucleus; LVF = left visual field; Pulv: pulvinar nucleus; R = right side; RVF = right visual field; SC = superior colliculus.

right and 109 in the left SC, leading the difference to a 1.1:1 ratio. These observations provide indirect indications about the impact of striate cortical damage on subcortical visual structures, and support data on monkeys showing that after destruction of V1, retrograde degeneration affects massively the LGN, but produces only mild effects in the SC (Cowey & Stoerig, 1991; Kisvarday, Cowey, Stoerig, & Somogyi, 1991).

Neural correlates of implicit bilateral summation. To reveal the neural correlates of the implicit bilateral summation, inferential testing was extended to all subcortical and cortical ROIs, and all inclusive mask volumes were simultaneously applied. We followed a two-step procedure. First, for each stimulus type (i.e., gray and purple separately), the activity resulting by summing, rather than averaging, the hemodynamic responses associated to single LVF and RVF stimuli was subtracted from that elicited by BVF stimuli [i.e., BVF − (LVF + RVF)]. This approach is the most conservative and appropriate for the present case, as it selectively focuses on those structures sensitive to the spatial summation of two simultaneous stimuli. Second, the activation derived from this comparison computed on gray stimuli was contrasted to the corresponding situation with purple stimuli [i.e., (BVF gray − single gray) > (BVF purple − single purple)]. This contrast highlights only those areas differentially active in the bilateral gain for gray versus purple stimuli, whereas any activity equally present in both conditions (and thus of no interest for our present purposes) is discounted and goes undetected.

Active areas are reported in Figure 4 and full results are given in Table 2.

Consistent with behavioral and pupillometric findings, a significant activation was observed in the SC and in a restricted number of occipito-temporal extrastriate visual areas in both hemispheres, thereby showing a selective modulation of these structures in response to the bilateral summation for gray stimuli. Only the lingual and superior occipital gyrus were more activated by purple than gray stimuli, possibly due to the role of these areas in color processing, most notably in processing blue–purple colors (Murphey, Yoshor, & Beauchamp, 2008).

No significant change in hemodynamic response was observed in the LGN and pulvinar, clearly indicating that these structures are not specifically involved in the bilateral summation effect and cannot account for the difference in the behavioral performance between gray and purple stimuli.

GENERAL DISCUSSION

The present study provides a direct demonstration that, following destruction of V1, the collicular–extrastriate pathway is essential for translating basic visual signals that cannot be consciously perceived into motor outputs. Indeed, we have been able to show a connection between functional activity in this pathway and behavioral as well as pupillometric measures of nonconscious visuomotor integration. Most importantly, we have also been able to supply the parallel negative evidence; namely, that temporary unavailability of the SC due to the use of purple stimuli, as further confirmed by our fMRI data, abolishes the implicit bilateral summation effect observed in the same subject with gray stimuli. Whereas the first (positive) evidence is essentially correlational in nature, the second (negative) one argues for a crucial contribution of the SC and its connections to extrastriate areas in subserving nonconscious visually guided responses following cortical blindness.

This conclusion on the role of the SC is consistent with a number of previous neuroanatomical and neurophysiologic findings. Animal studies have shown that the ipsilateral SC of the monkeys is less liable to neuronal degeneration than the LGN after neonatal hemicorticectomy (Ptito, Herbin, Boire, & Ptito, 1996), a trend that seems in line with our own data about the difference in active voxels between ipsi- and contralesional subcortical structures in G. Y. Moreover, visual functions are restored in cats with unilateral cortical blindness when the inhibitory connections between the two SCs are sectioned (Sprague, 1991), and a similar effect has been recently reported also in humans with hemispatial neglect (Sewards & Sewards, 2000). A bilateral gain in RTs analogous to that reported here has been demonstrated in patients with hemispherectomy, who underwent the removal of the entire cortical mantel of one hemisphere (Leh, Mullen, et al., 2006; Tomaiuolo et al., 1997), and in patients with total section or agenesis of the corpus callosum, which represents the major fiber tract connecting the cortical areas of the two hemispheres (Savazzi & Marzi, 2004; Corballis, 1998; Reuter-Lorenz, Nozawa, Gazzaniga, & Hughes, 1994). These results thus point to a critical contribution of subcortical visual centers, namely, the SC, in the interhemispheric neural summation of two stimuli presented across the vertical meridian. More specifically, Leh, Mullen, et al. (2006), in keeping with the present study, found that visuomotor integration in patients with hemispherectomy disappears for S-cones isolating stimuli, further reinforcing the collicular hypothesis (see Ptito & Leh, 2007 for a recent review).

Previous studies have reported that the pupil is sensitive to the spatio-temporal and physical properties of stimuli in the blind field of patients with V1 lesions (Papageorgiou et al., 2008), and pupillometry has thus proven valid as an indirect measure of nonconscious visual processing (Barbur et al., 1998; Weiskrantz, Cowey, & Le Mare, 1998). There is also evidence that measures of visual acuity or sensitivity to several stimulus properties estimated by pupillometry correlate with that determined by conventional psychophysical methods (Barbur, Harlow, & Sahraie, 1992). Pupillometry has been used here as an additional and independent measure of residual visual

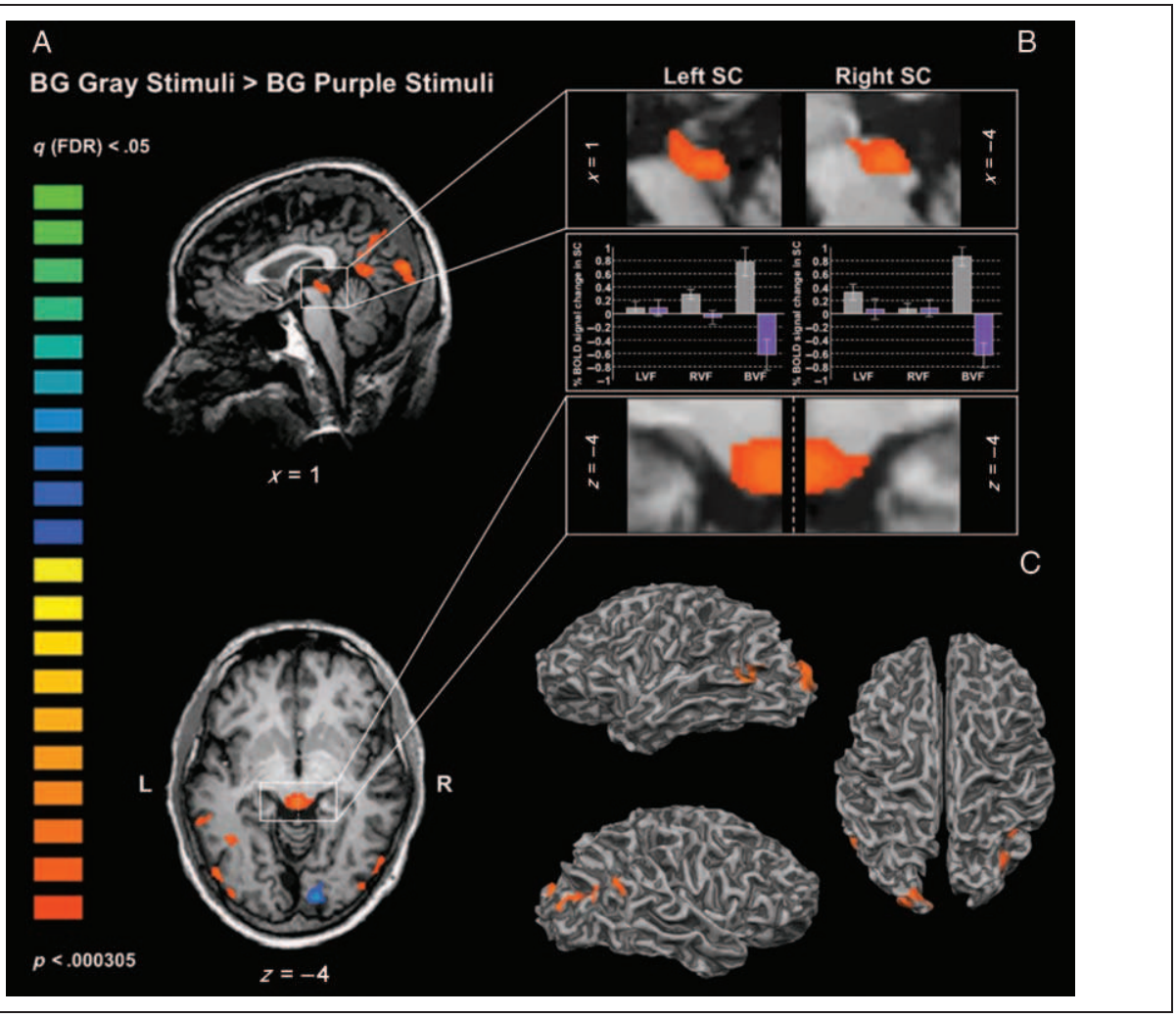

Figure 4. Neural correlates of the bilateral gain. Activation maps and mean percentage of BOLD response in the SC for the contrast between bilateral gain for gray versus purple stimuli. Areas colored from yellow to red are significantly more activated in the bilateral gain for gray stimuli, whereas areas from blue to green are significantly more activated in the bilateral gain for purple stimuli. Talairach *x*- and *z*-coordinates are given. (A) Sagittal and transversal slices of G. Y.'s brain showing significant activations in the left and right SC and in extrastriate visual areas corresponding to higher responses to the condition of bilateral gain for gray stimuli. Boxes indicate magnified regions in the location of the SC shown in panel B. The ventral portion of the lesion to V1 is also visible. (B) Magnified representation of the activations in the SC and mean % of BOLD signal change (±*SEM*) for the voxels in the activated clusters as a function of stimulus color and position. (C) Three-dimensional reconstruction of G. Y.'s brain from lateral and top view showing the occipito-temporal extrastriate areas significantly more activated by the bilateral gain for gray stimuli. The dorsal portion of the lesion to V1 is visible in top view. BG = bilateral gain; BVF = both visual fields; FDR = false discovery rate; LVF = left visual field; RVF = right visual field; SC = superior colliculus.

capacity in the blind field and we have found an effect on pupillary constriction that parallels the bilateral gain on behavioral measures. Moreover, we have shown a close correlation between these two measures, therefore suggesting that the two processes may be mediated by partially overlapping neural mechanisms. Although this issue deserves further investigation, the SC is, even in this case, a strong candidate, given its direct involvement in simple arm movements through connections with the cortical motor system, as far as RT is concerned (Leh, Johansen-Berg, et al., 2006; May, 2005; Lunenburger et al., 2001), and given its connections with the olivary nucleus of the pretectum, as far as pupillary constriction is concerned (Bose, Dhillon, Ross-Cisneros, & Carelli, 2005).

Of course, in addition to the SC, other subcortical structures receive direct projections from the retina and send connections to cortex. Among these, the most prominent and frequently suggested as possible neural substrates of residual visual functions in blindsight are the LGN and the pulvinar, along with their cortical projections. Nevertheless, possible alternative explanations that claim for a pivotal role of these structures in the form of implicit visuomotor integration studied here can be discounted given our negative fMRI, behavioral, and pupillometric evidence alike. Firstly, although a significant bilateral gain

Table 2. Areas of Significant fMRI Activation for the Contrast between Bilateral Summation for Gray versus Purple Stimuli in a Two-sample *t* Test

		Right (Intact) Hemisphere					*Left (Damaged) Hemisphere*				
				Talairach Coordinates					*Talairach Coordinates*		
	Localization (Brodmann's Area)	*No. of Voxels*	*t*	*x*	*y*	*z*	*No. of Voxels*	*t*	*x*	*y*	*z*
+	Middle/Superior temporal gyrus (39/22)	1937	6.0689	50	−59	9	1960	7.1880	−56	−55	10
+	Middle temporal gyrus, posterior part (19)	1680	6.1496	38	−75	18					
+	Fusiform gyrus (20)	342	5.1818	42	−24	−20					
+	Cuneus (30)	1771	6.7362	2	−57	11					
+	Middle occipital gyrus (18)	582	5.008	35	−90	4	2187	5.5581	−17	−93	12
+	Superior colliculus	142	4.6945	2	−28	−4	168	4.8336	−4	−29	−2
−	Lingual gyrus (17)	563	−6.3049	9	−89	−4					
−	Superior occipital gyrus (19)						447	−5.7161	−32	−71	25

Positive activations (+) reflect higher activity for gray stimuli and negative activations (−) higher activity for purple stimuli. All p values $< .05$, corrected for FDR in multiple comparisons.

was observed for gray but not for purple stimuli, we found no sign of differential activation in the LGN or the pulvinar when these two conditions were directly contrasted in fMRI analyses. This clearly indicates that activity in the LGN and the pulvinar is unrelated to the presence/absence of the neural summation effect. Conversely, the same contrast revealed a selective increase of activation in the SC and in occipito-temporal visual cortices of both hemispheres while the bilateral summation was induced by gray stimuli. The latter result is consistent with recent findings showing that these extrastriate areas are heavily interconnected with the SC (Leh, Johansen-Berg, et al., 2006) and are modulated during execution of the same sensory–motor processing involved in the bilateral summation paradigm (Iacoboni, Ptito, Weekes, & Zaidel, 2000; Miniussi et al., 1998). Secondly, both the LGN and the pulvinar receive input from all types of color-opponent cells in the retina, including S-cones (White et al., 1998; Felsten et al., 1983). In addition to this neurophysiologic evidence, we found that gray and purple stimuli were closely matched in their psychophysical properties and evoked highly similar fMRI responses in the LGN and the pulvinar. Thus, had these structures been critical, a bilateral gain should have been reported also for purple stimuli, which clearly was not the case.

Nonconscious processing of other classes of stimulus attributes and in different tasks may, of course, rely on extrastriate pathways that do not depend on the SC. For instance, it has been recently shown that the same patient tested in the present study has aberrant fiber tracts connecting the LGN to ipsilateral as well as to contralateral area MT+/V5 (Leh, Johansen-Berg, et al., 2006). Moreover, G. Y. has a widespread callosal interconnection between areas MT+/V5 of the two hemispheres. Finally, there is initial evidence that G. Y. may correctly guess the presence of S-cones isolating stimuli in his blind field in an alternative forced-choice task, which, however, does not imply visuomotor integration as in the present case (Cowey & Alexander, 2009). Although these important findings can justify some of the residual visual capacities in this patient, such as form or motion discrimination (Morland et al., 1999), they do not probably constitute the neural substrate of the implicit bilateral summation effect found in the present study for the reasons mentioned above.

Hence, the present findings offer a clear demonstration that the SC acts as an interface between sensory and motor processing in the human brain, thereby providing an essential contribution to visually guided behavior that may remain functionally and anatomically segregated from the geniculo-striate pathway, and entirely outside conscious visual experience.

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