Blindsight after Optic Nerve Injury Indicates Functionality of Spared Fibers

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Abstract

■ Some patients with lesions in the geniculostriate pathway (GSP) can respond to visual stimuli in the blind field without conscious acknowledgement. The substrate for this ''blindsight'' is controversial: whether it is the uninjured extrastriate pathway (EXP), which bypasses the lesion site, or residual fibers within damaged visual cortex (''islands of vision''). Using stimulus detection, localization, and spatial summation tasks, we have found blindsight in patients with damage both in the optic nerve (ON) and EXP. The prevalence and functional characteristics of their blindsight are indistinguishable from that in patients with GSP lesions, so blindsight does not require a completely intact EXP. The present findings support the view that a few surviving ON axons within an area of primary damage are sufficient to mediate blindsight: Several combinations of partially intact pathways can transmit information to the extrastriate cortex and the sum of activation of all visual fibers surviving the injury determines if and to what extent blindsight occurs. ■

INTRODUCTION

Damage to the geniculostriate pathway (GSP) results in phenomenal blindness, but some patients have spared function within the deprived area, or scotoma, in the visual field, such as stimulus localization (Pöppel, Held, & Frost, 1973) or stimulus detection (Stoerig, Hübner, & Pöppel, 1985), even though they have no conscious awareness of the stimulus. Despite numerous studies (Schärli, Harman, & Hogben, 1999a; Weiskrantz, 1986; Weiskrantz, Cowey, & Barbur, 1999; Stoerig, Kleinschmidt, & Frahm, 1998; Azzopardi & Cowey, 1997; Sahraie et al., 1997; Ptito, Lepore, Ptito, & Lassonde, 1991; Corbetta, Marzi, Tassinari, & Aglioti, 1990; Blythe, Kennard, & Ruddock, 1987; Zihl & Werth, 1984b; Bridgeman & Staggs, 1982; Perenin & Jeannerod, 1978), the neurobiological basis of this ''blindsight'' (Sanders, Warrington, Marshall, & Weiskrantz, 1974; Weiskrantz, Warrington, Sanders, & Marshall, 1974) is controversial. One theory is that visual information reaches the extrastriate cortex through secondary, extrastriate visual pathways (EXP) that bypass the primary lesion site and are presumed to remain uninjured after GSP damage; one such route is through the superior colliculus and inferior pulvinar (Weiskrantz, 1986; Stoerig et al., 1985; Pasik & Pasik, 1982; Perenin & Jeannerod, 1978; Mohler & Wurtz, 1977). Because this theory requires that EXP remain intact, blindsight should not be possible if they are damaged [as in patients with partial optic nerve (ON) injury; see Figure 1].

The opposing view is that blindsight is mediated by small amounts of spared, partially injured tissue (''islands'') in the primary GSP (Campion, Latto, & Smith, 1983). Supporting evidence comes from patients who have one or more small isolated areas of residual tissue in the striate cortex (V1), with nonconscious residual vision (Wessinger, Fendrich, & Gazzaniga, 1997, 1999; Fendrich, Wessinger, & Gazzaniga, 1992, 1993). However, the observation that at least some patients show blindsight at several positions along the horizontal meridian within the damaged visual field rather than in isolated ''islands'' (Stoerig et al., 1985; Stoerig & Pöppel, 1986) is at variance with this proposal. Indeed, contrary to this view, two recent observations generally support the concept that residual neurons of the injured system itself might provide a substrate for residual vision. Firstly, in rats after recovery from diffuse ON injury, 10–15% of the retinofugal fibers are sufficient for brightness and pattern discrimination (Sabel, Kasten, & Kreutz, 1997; Sautter & Sabel, 1993). Secondly, patients with injury to the ON or posterior to the optic chiasma display areas of partial visual function, or ''transition zones'' (Kasten, Wüst, & Sabel, 1998), in which lost visual function can be restored by regular training (Kasten, Wüst, Behrens-Baumann, & Sabel, 1998). This points towards the existence of diffusely surviving residual fibers within or near the scotoma, raising the possibility that a few spared fibers in an area of diffuse injury could be sufficient to mediate blindsight. Using stimulus detection, localization, and spatial summation tasks, this research is the first to show blindsight responses in ''blind'' regions of patients with partial ON

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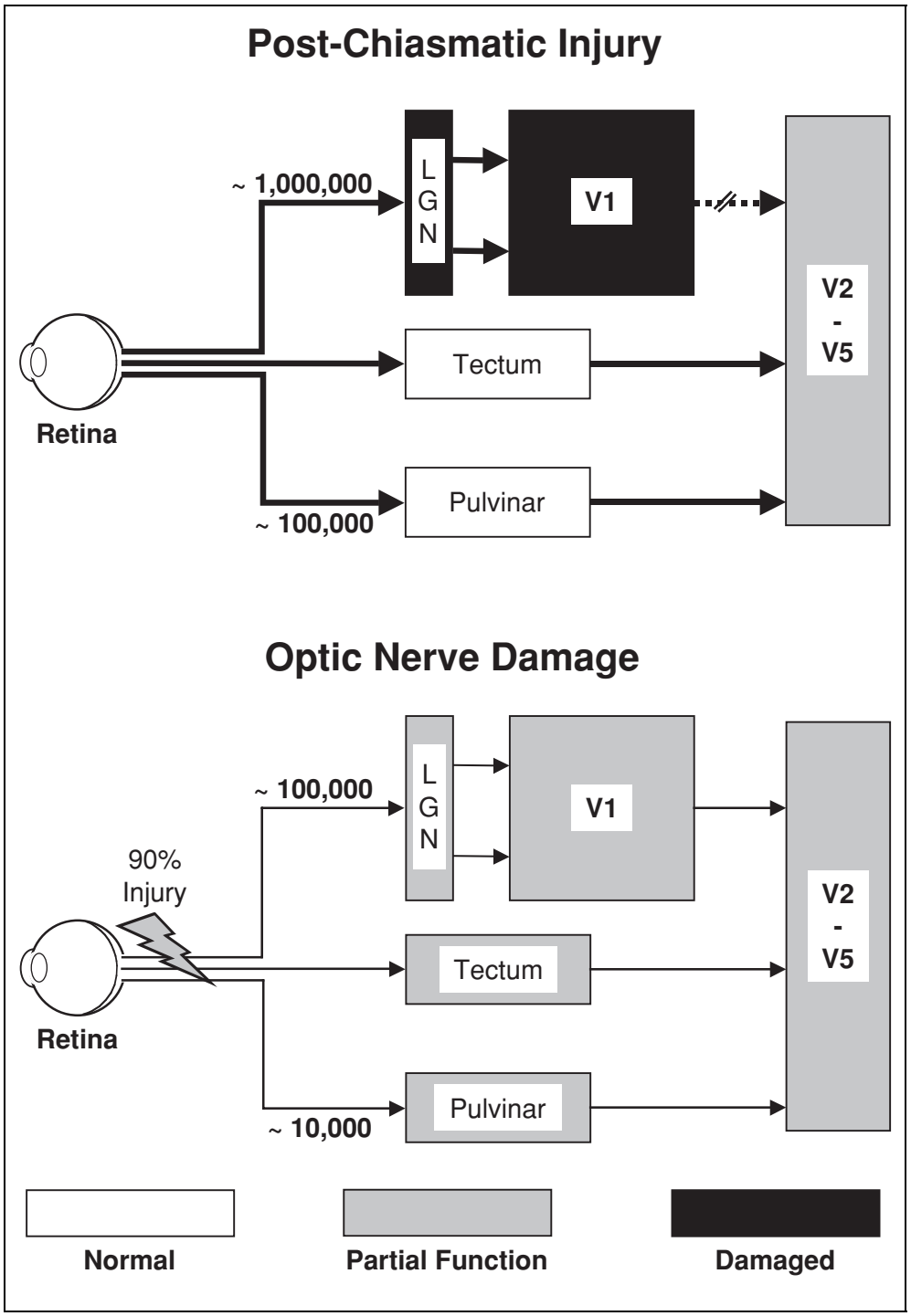

Figure 1. Schematic diagram of blindsight after postchiasmatic (upper panel) or ON injury (lower panel). According to the EXP hypothesis, blindsight is mediated by higher cortical areas (V2–V5), which receive inputs from uninjured, extrastriate areas of the brain (for clarity only tectum and pulvinar are shown). A rough estimate of fiber number is also shown. Gray indicates partial function, white intact function, and black a complete loss. According to the EXP hypothesis, there are no residual fibers in V1, whereas the ''Island'' hypothesis proposes that a few surviving fibers in V1 survive (not shown here). Because the retina sends only about 100,000 fibers to the extrastriate, subcortical regions, direct retinal input to higher cortical regions will probably not exceed this value. After ON injury, many fibers are lost at the ON level, producing a diffuse deafferentation of all visual areas, including V1 and higher cortical regions (V2–V5) that are excited through all visual pathways. If we exemplary assume that 90% of the optic fibers are lost, only about 110,000 inputs would survive to produce blindsight in higher cortical regions. Note that the ON in patients is usually only partially injured, with some intact sectors, some blind regions and some regions of diffuse injury with residual functions.

injury in which the EXP is also damaged, documenting the functionality of a few surviving fibers.

RESULTS

Analysis of ''level-of-consciousness'' values revealed that all 16 patients rated each response in the two forced-choice paradigms (detection and localization) as a complete guess. Furthermore, all subjects expressed at least once the opinion that they definitely performed at chance level.

In the ''stimulus detection task,'' above-chance performance was observed in 3 out of 16 patients. Patient 3 from the ''postchiasmatic group'' detected the visual stimuli significantly better than expected by guessing at 5 out of 9 test locations (after alpha adjustment for 9 tests). The distance between the test location and either the fixation point or the border of the intact part of the

visual field, respectively, was not associated with detection performance (for details, see Figure 2B). The two other subjects showing above-chance performance in the detection paradigm were from the ON lesions group (''ON''). Patient ON1 yielded a significant hit rate at 8 out of 9 test positions. The highest detection rate was observed at the location with the largest distance to the fixation point (Position 9, 71.62% correctness, $p < .001$). The performance of the third patient with above-chance correct guessing without awareness, Subject ON7, was clearly below that of Patients POST3 and ON1. Here, significant blindsight responses could be observed only at one test location (Figure 2B).

In the stimulus detection task, subjects were neither instructed to respond as quickly as possible nor was there an a priori hypothesis regarding response times (RET). However, we noted that some of the patients responded in a more confident manner and possibly faster in trials with correct responses (i.e., a key press when a stimulus was presented, or a ''hit'') compared to trials with incorrect responses (i.e., a key press when no stimulus was presented, or a ''false alarm''). To substantiate this chance observation, all trials of all patients were grouped into ''hit trials'' and ''false alarm trials'' and the respective RET were compared (Figure 3). The mean RET in false alarm trials (723.95 ± 30.05 msec) was significantly longer than in hit trials (693.57 ± 31.15, $p < .001$). In order to analyze which specific test sessions accounted for the difference of means, the trials were compared further as follows: (a) hit trials versus false alarm trials from sessions ''with'' significant detection performance (i.e., only the corresponding sessions from Subjects POST3, ON1, and ON7) and (b) hit trials versus false alarm trials from sessions ''without'' significant detection performance. In the latter group, the reported RET difference vanished almost completely (false alarm: 741.76 ± 32.41; hit: 736.35 ± 32.18, *ns*). On the other hand, analysis of sessions with significant detection performance revealed an entirely different result with a mean RET in false alarm trials of 654.38 ± 84.84 msec compared to 556.30 ± 96.29 msec in hit trials. This unexpected and significant difference of 98.08 msec ($p < .001$) shows that subjects made significantly faster decisions only in sessions with an above-chance detection performance. Furthermore, this RET difference could not only be observed between groups but also

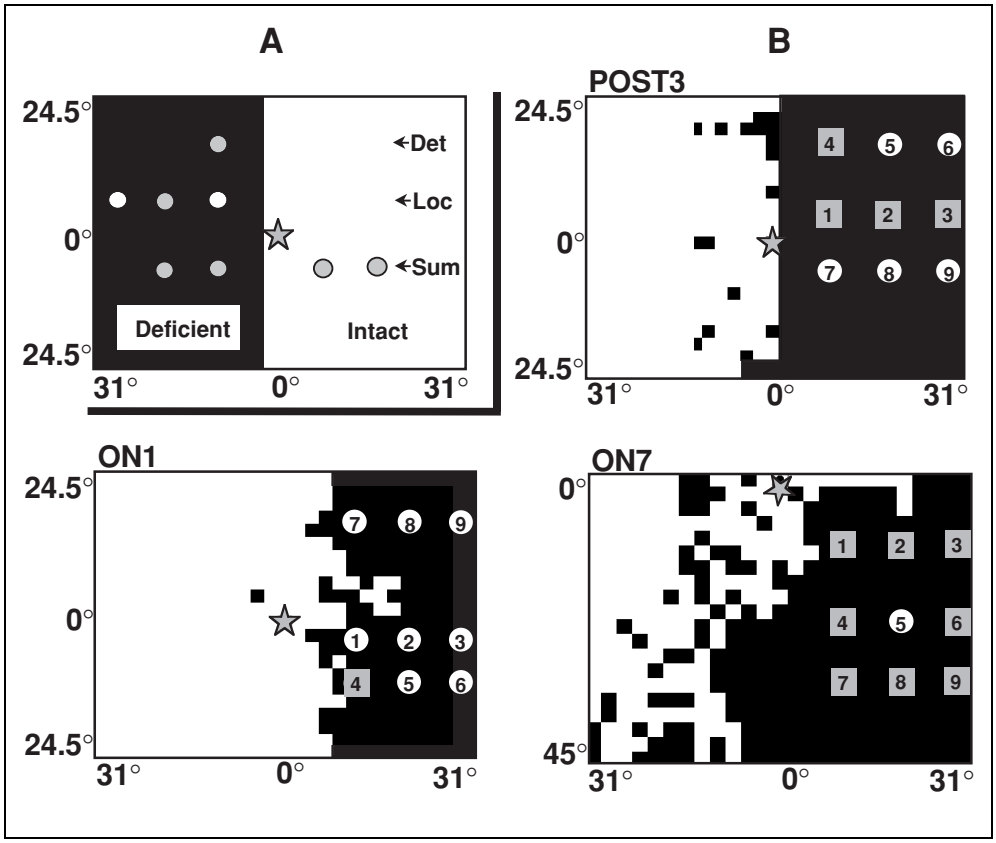

Figure 2. (A) The three tests for blindsight capacities. The star indicates the position of the fixation point; examples of stimulus positions are given by ''Det'' in the detection task, ''Loc'' in the stimulus localization task, and ''Sum'' in the spatial summation task (see text for more detail). (B) Results of the detection task in three patients with above-chance performance. Black represents clinically blind and white, intact areas, of the visual field as assessed with the ''PeriMa'' program. The position of the fixation point, as well as the test locations, was selected for each individual based on several predefined criteria (see text). Symbol sizes and distances between symbols (also in Figures 4 and 5) do not accurately represent the sizes of and distances between the test stimuli. For instance, the distance between test locations and the fixation point or the transition zone was always at least 4° of the visual angle. White circles show test locations with above-chance performance (after alpha adjustment, ''blindsight''); gray squares indicate test locations where detection was not significant. The distance between the test location and either the fixation point or the border of the intact part of the visual field showed no correlation with detection. For instance, in Patient POST3, Position 1 (66.67% correct, *ns* after alpha adjustment) was located at 10°/4° horizontal/vertical eccentricity whereas the best detection occurred at Position 6 (85.71%, $p < .01$), which was located at 30°/14°.

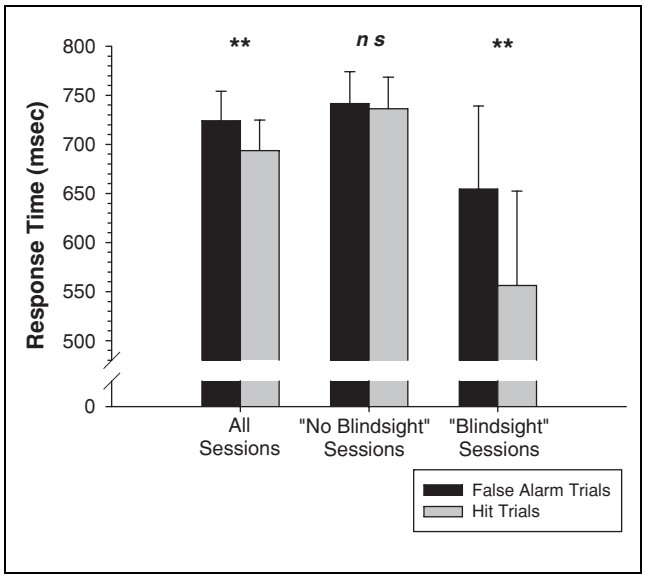

Figure 3. Response times (RET) in the detection task (mean ± *SE*). Black bars show RET in trials where a subject pressed the key although no stimulus was presented (''false alarm''), gray bars show RET in trials when a stimulus was presented (''hit''). Bars on the left: RET in all nine test sessions from all patients (''all sessions''); bars in the middle: RET in all test sessions without significant detection rate from all subjects (''no blindsight sessions''); bars on the right: RET in all sessions with significant detection rate (''blindsight sessions'') only from patients showing blindsight in the direction task (Subjects POST3, ON1, and ON7) (**p < .001).

in a case-by-case analysis. All three patients with an above-chance detection performance (and no other subject) showed this effect in the corresponding sessions (POST3: false alarm: 373.42 ± 22.48; hit: 351.99 ± 19.81, $p < .05$/ON1: false alarm: 891.78 ± 77.59; hit: 749.05 ± 69.34, $p < .001$/ON7: false alarm: 653.74 ± 50.33; hit: 599.50 ± 42.76, $p < .05$).

In the ''stimulus localization task,'' above-chance performance was noted in six subjects (four POST, two ON), and in some of the patients, the ability to localize visual targets above-chance was remarkably pronounced (see Figure 4). POST1 localized the visual stimuli better than expected by guessing at six out of nine locations. Subject POST2 achieved a blindsight response only at one test position and POST3 as well as POST6 performed significantly better than expected by guessing at 4 out of 9 locations. Finally, Subjects ON1 and ON5 achieved an above-chance localization accuracy at 8 out of 9 test locations. Only one subject (ON7) showed blindsight responses (though rather weak) in the detection task and not in the localization paradigm (Figure 4).

The justification for using the ''spatial summation paradigm'' to test for nonconscious, residual vision depends on two requirements. Firstly, when test locations are selected properly, subjects should never respond when stimuli are presented only in the perimetrically blind part of the visual field, because they cannot consciously see them. As this requirement was fulfilled, neither the results of the double stimulation in the deficient area nor the single stimulation will be discussed further. Secondly, when either one stimulus or two simultaneous stimuli are presented in ''intact''

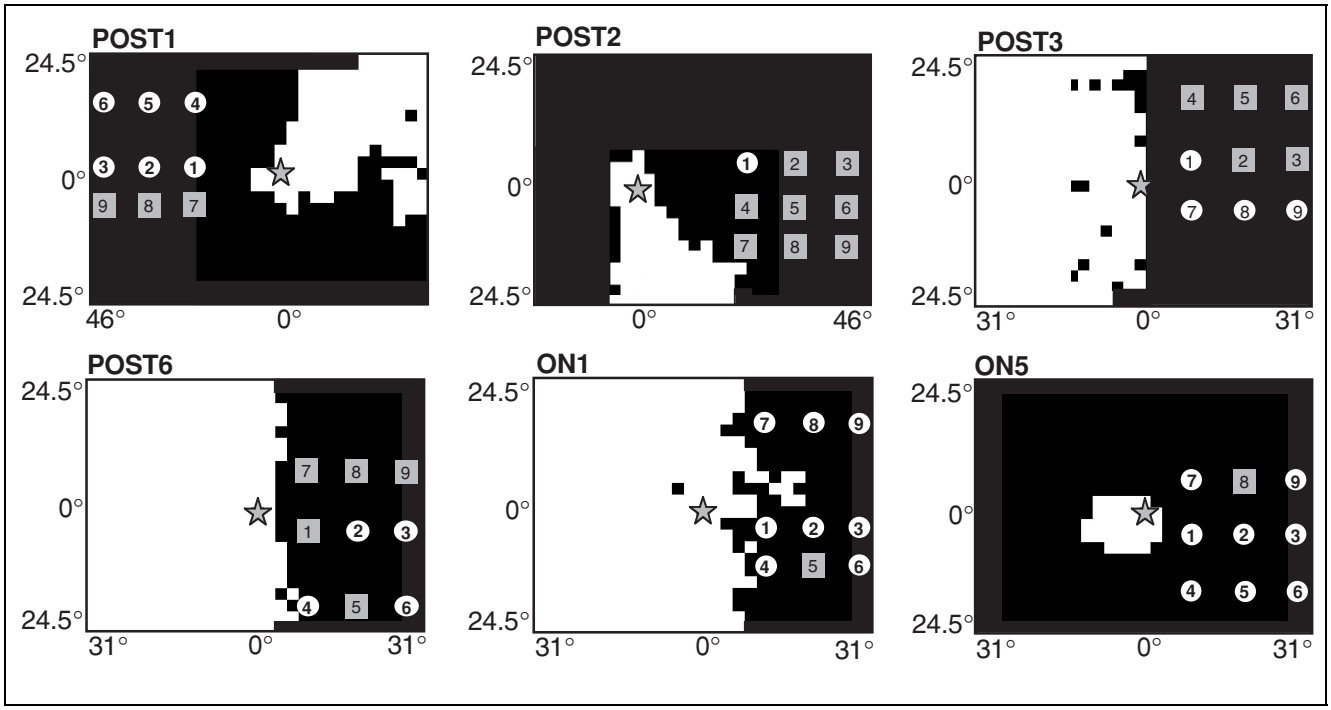

Figure 4. Results of the localization task of the six patients with above-chance performance. The symbols are identical to Figure 2. As in the detection paradigm, there was no association between localization performance and the distance between test locations and either the fixation point or the border of the intact part of the visual field. The highest localization accuracy was achieved by Patient POST1 (67.7%, $p < .01$) at Position 1, which was located at −26°/4°.

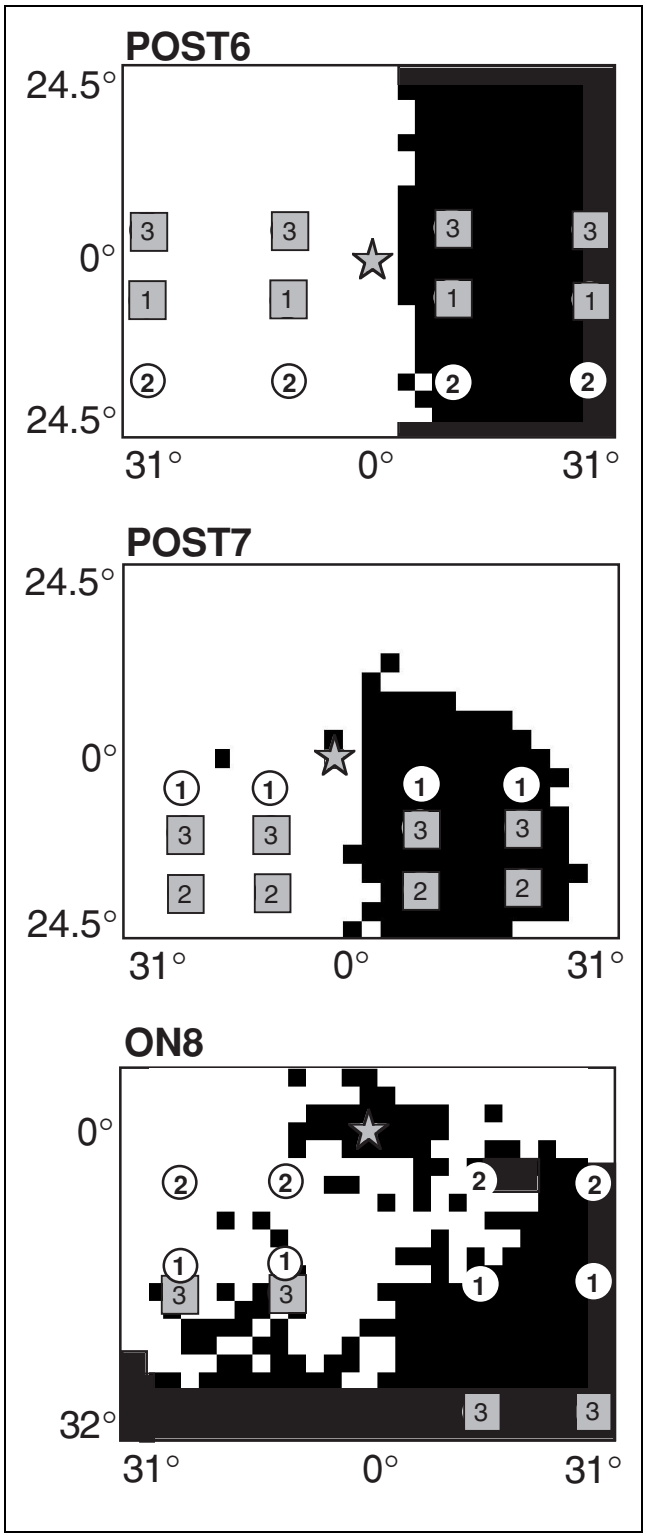

Figure 5. Results of the spatial summation task in the three patients with significant performance (same symbols as in Figure 2). This task required slightly different test locations. A significant RT advantage of the summation condition (sc) over the single stimulus condition (ss) occurred at location set 2 in Patient POST6 (−14° vertical eccentricity; sc: 321.27 msec, ss: 330.25 msec, Δ 8.98 msec, $p < .05$), at set 1 in Subject POST7 (−4° vert. ecc.; sc: 353.95, ss: 367.55, Δ 13.6, $p < .05$), and at two location sets in Subject ON8 (set 1: −16° vert. ecc.; sc: 349.53, ss: 376.22, Δ 26.69, $p < .01$/set 2: −7° vert. ecc.; sc: 348.25, ss: 360.93, Δ 12.68, $p < .05$).

areas of the visual field, the mean reaction time (RT) in the double stimulus condition has to be significantly shorter than in the single stimulus condition (the RT advantage). This mandatory effect was clearly observed in a pilot study with healthy volunteers but could not be detected in the intact field when data from all our brain-damaged patients were pooled: In Group POST the mean RT to a single stimulus presentation was 388.88 msec and was almost identical in the double stimulus condition (388.34 msec). A similar result was observed in Group ON. RT in the single and double stimulus conditions was on average 377.12 and 374.45 msec, respectively (*ns*).

A case-by-case analysis, however, revealed the mandatory RT advantage in the intact field in 3/16 patients, varying between 11.43 msec ($p < .05$) and 46.54 msec ($p < .001$; one-way ANOVA and subsequent Scheffé post hoc tests). Interestingly, exclusively these three patients showing the RT advantage in the intact field also showed evidence for blindsight, defined as a significant mean RT advantage of the ''summation condition'' (one stimulus in the intact area and one in the deficient part of the patient's visual field) over the single stimulus condition. A significant RT advantage of the summation condition occurred at one out of three sets of test locations in Patients POST6 and POST7 and at two location sets in Subject ON8, respectively (see Figure 5). Out of these three patients, only Patient POST6 performed above-chance in the forced-choice tasks.

A summary of the results for the three blindsight paradigms shows that the pattern of performance is variable between patients, and that performance in one blindsight paradigm is not a reliable predictor for performance in another paradigm (Table 1B). Rather, blindsight seems to be a heterogeneous capacity that can express itself in different ways. In 9 out of the 16 patients studied, blindsight capacities were found in at least one test procedure but none had blindsight capabilities in all three paradigms.

DISCUSSION

The most intriguing finding of the present study is the demonstration of blindsight in patients with ON damage using three blindsight paradigms: detection, localization, and summation. In its prevalence and functional characteristics, blindsight after ON injury was indistinguishable from that we observed after GSP lesions.

We also documented blindsight with a novel, objective parameter that is independent of the decisional criterion. Namely, blindsight was associated with a significantly shorter RET, which is consistent with previous findings in monkeys with striate cortex lesions (Cowey, Stoerig, & Le Mare, 1998; Stoerig & Cowey, 1996). As we did not predict this in humans, we specifically avoided instructing patients to make their decisions in the detection task as quickly as possible.

Table 1. Patient Characteristics and Performance Overview

		A		B		
Patient	*Sex*	*Age/age of lesion (years)*	*Cause of lesion*	*Detection*	*Localization*	*Summation*
POST1	m	74/42	S		++	
POST2	f	44/12	S		+	
POST3	m	61/6	S	++	++	
POST4	m	65/10	S			
POST5	f	46/6	T			
POST6	f	40/2	S		++	+
POST7	m	50/2	IS			+
POST8	f	61/2.5	S			
ON1	m	68/15	PA	++	++	
ON2	m	58/1.5	ION			
ON3	m	61/1	T			
ON4	f	28/1	ON			
ON5	m	67/1.5	ION		++	
ON6	f	66/25	PA			
ON7	m	61/3	ION	+		
ON8	m	64/1	ION			++
				3/16	6/16	3/16

(A) Patient characteristics. Mean age of Group ''POST'' was 55.1 years (40–74 years, *SD* = 10.12) and patients had postchiasmatic injuries. Subjects from Group ''ON'' had partial ON lesions and the average age was 59.1 years (28–68 years, *SD* = 11.34). Abbreviations: f = female, m = male, S = stroke, T = trauma, IS = ischemia after strangulation, PA = pituitary adenoma, ION = ischemic optic neuropathy, ON = optic neuritis.
(B) Overview of the performance of all subjects in the three test procedures. ''+'' indicates evidence for blindsight at one test location or one location set; ''++'' indicates evidence for blindsight at numerous test locations or two location sets. Evidence for blindsight was obtained from five patients in the POST group and four patients in the ON group. No patient showed blindsight in all three tasks, three patients showed blindsight in two paradigms, and six patients showed blindsight in only one.

Because of methodological problems, blindsight is sometimes regarded with skepticism. Therefore, we took particular care to control for methodological artifacts such as improper fixation, the perception of scattered light, or changes in the subject's decisional criterion. There are two reasons for excluding the possibility that improper fixation caused above-chance performance in the present investigation: (1) The method employed to control proper fixation detected eye movements larger than 2°, but the distance between the test location and the fixation point or the border to the intact sector of the visual field, respectively, was always >4° (in the majority of the test locations this distance was much larger); (2) Improper fixation would—at least in the detection task—cause significant visual perception at test locations that are located close to the fixation point or the intact field, respectively. However, such an association was not observed. The perception of scattered light (Campion et al., 1983) also cannot explain the observed blindsight responses. Zihl and Werth (1984a) clearly showed that the minimal amount of stray light that emerges in a low target–background luminance ratio condition could not account for the patient's above-chance performance; in the present study, the same target–background luminance ratio was employed. Again, the stray light hypothesis also would predict above-chance performance at test locations that are positioned close to the border of the intact field, which was clearly not the case. A third source of potential artifact, correctly identified by Campion et al. (1983), is a possible shift in the subject's decisional criterion as he or she turns from clinical perimetry to a forced-choice procedure. For several reasons, it is very unlikely that such shifts had a considerable impact on the outcome of the present study: (1) The identification of areas of the subject's visual field as ''blind'' was based on measurements with the ''PeriMa'' program. The employed target–background luminance ratio (50: <1 cd/m^2) was by far higher than in tests for blindsight capacities (40: 4 cd/m^2). (2) Our ''level-of-

consciousness'' values argue against shifts in response criteria. None of the subjects ever reported that they had a conscious perception or any feeling that ''something was there'' although they were explicitly encouraged to report even subtle light sensations. (3) Since the spatial summation paradigm avoids the problem of changed response criteria altogether, at least the evidence for blindsight from this task cannot be explained by such shifts.

Due to the relatively large patient number, we are also able to contribute to the important question of prevalence of blindsight. Only a few previous reports permit conclusions on the prevalence of blindsight (Schärli et al., 1999a; Blythe et al., 1987; Marzi, Tassinari, Aglioti, & Lutzemberger, 1986); in most other studies either a selected group of patients was investigated or, commonly, only single cases were investigated. Taking all indicators of blindsight in the present study into consideration (detection, localization, and summation), the overall prevalence of blindsight was between 50% (ON patients) and 60% (POST patients), with some patients showing blindsight in two of the three paradigms. The 20% prevalence reported by Marzi et al. (1986) for the summation paradigm is similar to our values (3/16 patients). However, our prevalence is higher than that found by Schärli et al. (1999) and Blythe et al. (1987), but this may reflect methodological differences. For instance, the saccadic localization task employed by Blythe et al. was rather difficult and, in this study as well as in the study by Schärli et al., relatively few trials were performed. Furthermore, in most investigations, only locations along the horizontal meridian were tested, whereas the nine test points used in the present study were distributed over a larger area of the blind visual field sector, thus increasing the odds of detecting blindsight responses.

In the Wessinger et al. (1999) study of patients with occipital cortex lesions, small areas of residual vision could be identified in 4 out of 7 patients. Within these islands, one or more additional indicators of blindsight (localization, motion detection, wavelength, and shape discrimination) were found with considerable between-subject variability. This finding is consistent with both the prevalence and the variability of blindsight abilities that could be observed in the present study.

Our demonstration of blindsight after ON injury has several implications. Firstly, it is generally assumed that no axons remain in the ON sector corresponding to the visual field deficit, but our study indicates for the first time that at least some axons in the clinically blind field have escaped injury and are able to transmit visual information. Secondly, unconscious visual responses can be achieved without a completely intact EXP, because all visual structures, including the EXP, are diffusely deafferented by ON injury: In primates, the 10% of retinal ganglion cells that project to the superior colliculus and pretectum (Perry & Cowey, 1984) are distributed throughout the retina and crush of the ON leads to anterograde degeneration and metabolic depression in all structures of the visual system, including the tectum (Schmitt, Cross, Pazdernik, & Sabel, 1996; Sautter & Sabel, 1993). In fact, only about 10% of retinofugal fibers in intact rats are capable of considerable brightness and pattern discrimination (Schmitt et al., 1996; Sautter & Sabel, 1993), emphasizing the functional potential of a few residual fibers in the ON.

Thus, the presence of unconscious residual vision in patients with ON and EXP damage indicates that an intact EXP is not necessary for blindsight to occur. This argues against the theory that the EXP has an exclusive and prominent role in mediating blindsight (Stoerig et al., 1985, 1998; Weiskrantz, 1986; Pasik & Pasik, 1982; Perenin & Jeannerod, 1978; Mohler & Wurtz, 1977), though surviving EXP fibers may well contribute to blindsight.

Our findings are therefore consistent with the fundamental assumption of the alternative ''island of vision'' hypothesis that fibers of the primary GSP surviving the injury can mediate blindsight (Wessinger et al., 1997; Fendrich et al., 1992, 1993; Campion et al., 1983). As recently demonstrated (Wessinger et al., 1999), patients can possess two ''islands'' or ''clusters'' of residual vision with a patchy distribution in the blind field. This is compatible with our assumption, but we rarely observed blindsight in such isolated areas. Only two subjects (ON7, POST2) had blindsight restricted to one test location, suggesting an ''island''-like distribution of residual tissue to be the exception rather than the rule.

In place of both hypotheses, our study in human subjects strongly supports a ''summation'' hypothesis to explain blindsight, which, based on animal data, was previously suggested by Pasik and Pasik (1982): Whether blindsight occurs depends on the sum of residual, neuronal activation in all pathways reaching the extrastriate cortex. The precise functional characteristics of blindsight depend, in turn, on which combination of pathways is still active and to what extent. The functional contribution of each of the pathways—the retinocollicular projections, the direct route from the geniculate to the extrastriate cortex, the ventral lateral geniculate nucleus, the three accessory optic nuclei, and the nucleus of the optic tract (Cowey & Stoerig, 1991)—still needs to be characterized.

Both our experiments and the summation hypothesis leave some important questions unanswered. For instance, neither the extent to which different brain areas are deafferented by an ON lesion nor the amount of extrastriate cortex activation, which is necessary for blindsight to occur, can be precisely determined with the techniques employed in this study. Even though the prevalence of blindsight and the magnitude of the effect are comparable whether the EXP is injured or not, the extent to which each pathway contributes to blindsight cannot be determined. A few retinocollicular fibers, for

instance, presumably also survive the injury and contribute to residual visual capacities.

Despite these limitations, the summation hypothesis integrates several findings. For instance, results emphasizing the relevance of the superior colliculus for residual vision (Mohler & Wurtz, 1977), as well as demonstrations of residual vision in the absence of the superior colliculus (Pasik & Pasik, 1982), are compatible with the summation hypothesis. Similarly, the hypothesis accommodates the opposing proposals that extrastriate, subcortical pathways may contribute to blindsight (e.g., Danckert, Maruff, Kinsella, de Graaff, & Currie, 1998; Stoerig et al., 1985) and that surviving remnants of the primary visual system are involved (Fendrich et al., 1992), because both assume residual activation of the extrastriate cortex. Rather than being mutually exclusive, these two explanations may therefore represent different forms of blindsight, with functional characteristics that mirror the specific nature and distribution of residual visual fibers.

The summation hypothesis also indicates why not all patients with cortical blindness have blindsight: They may simply lack enough functional neurons within the area of injury. The observation that blindsight can be seen in large parts but not all of the defective visual field is also compatible with the summation hypothesis, as is the individual blindsight pattern that emerges when several blindsight tests are combined. If and how blindsight occurs in a given patient thus depends on the relative size of the lesion—that is, on a minimum of residual fibers—and on the location of the lesion—that is, which combination of preserved pathways transmit information to the neurons of the extrastriate cortex.

METHODS

Patient Characteristics

Six women and ten men (mean age of 57.1 years, *SD* = 14.48) with both a visual field defect and morphological evidence of visual system injury (as documented by CT, MRI, surgical records, or ophthalmoscopic documentation of ON atrophy) were studied. Patients were not entered if any one of the following exclusion criteria applied: lesion occurred less than 1 year before or presence of concomitant visual disorders, such as retinal lesions, cataract, glaucoma, nystagmus, color blindness, visual neglect, or other cognitive deficits (e.g., impaired ability to sustain attention or impaired memory). Subjects were divided into two groups based on the location of the brain lesion (see Table 1A): postchiasmatic injury (''POST,'' n = 8, 4 women, 4 men) and ON damage (''ON,'' n = 8, 2 women, 6 men).

Diagnostic Procedures

Visual impairments were determined using perimetry, campimetry (see below), visual acuity, and contrast sensitivity measurements (Landolt acuity test charts, Haase & Hohmann, 1982; Vision Contrast Test System, Ginsburg, 1984). After preliminary examination using both eyes, one eye was selected for further testing based on visual field size, visual acuity, and standard ocular dominance tests. To assure test reliability, all diagnostic procedures were conducted four times with the test eye alone. Perimetry and campimetry, as well as the tests for residual unconscious vision, were carried out in a darkened room. The head position was controlled with a chin rest such that the tested eye was continuously located at the same height as the fixation point while the other eye was occluded. Prior to each measurement, the participants received detailed, standardized instructions.

Static threshold-oriented perimetry of the visual field up to 80° eccentricity (performed with 104 stimuli) as well as of the 30° visual field (with 191 stimuli) was conducted repeatedly with a Tübinger automatic perimeter (TAP; Lachenmayr & Vivell, 1992), while stable fixation was assured by continuous video monitoring. TAP has a relatively low spatial resolution with stimuli at near-threshold luminance, which is a disadvantage because an important prerequisite for determining blindsight is the unequivocal identification of perimetrically ''blind'' areas in the visual field. Therefore, campimetry was also performed repeatedly using the PeriMa computer program. PeriMa allows the assessment of the patient's light detection ability in the central area of the visual field with high spatial resolution (Kasten & Sabel, 1995; Kasten, Strasburger, & Sabel, 1997; Kasten, Wüst, Behrens-Baumann, et al., 1998). Briefly, in PeriMa, small light stimuli of 150-msec duration are randomly presented in a 20 × 25 matrix (a total of 500 stimuli) on a computer screen viewed at a distance of 30 cm. The stimuli are gray and have a diameter of 0.08°, with a luminance clearly above detection threshold (50 cd/m^2, background <1 cd/m^2). The subjects had to indicate detection of the stimulus by pressing a key within 0.5 sec. The position of the fixation point was adapted to the patient's individual visual defect. With the fixation point at the center of the screen, the test area had a horizontal eccentricity of ±31.2° and a vertical eccentricity of ±24.4° (on a 21-in. monitor).

Tests for Blindsight Capacities

Blindsight tests were carried out with an adaptation of the PeriMa software. Test stimuli were gray circles with a luminance of 40 cd/m^2 on dark background (4 cd/m^2). In contrast to randomized stimulus presentation in perimetry or campimetry, in blindsight test paradigms the patients often know roughly in which part of their damaged visual field a target stimulus may occur and performance might be improved by eye movements in that direction. Therefore, proper fixation was carefully controlled in two ways: First, the patients had to

respond to a slight change of the fixation point's color from light green to light yellow which occurred randomly throughout the session. The second procedure consisted of an adjustable mirror system installed below the computer monitor that allowed the continuous observation of the patient's eye by the experimenter. Fixation control had been validated in prior pilot tests and eye movements >2° were detected with 100% reliability.

A stimulus detection paradigm was used to test the ability to discriminate between blank trials and trials in which a visual target was presented within the scotoma. A tone signal indicated the start of a random presentation of target or blank; the ratio of target to nontarget presentations was 1:1 and was known to the patients. The target was a round visual stimulus (diameter of 1°) presented for 100 msec during each session at one predetermined location of the scotoma. The total number of trials, sessions, and test locations, as well as the criteria for test point selection, is described below. After each tone signal the patients were required to press a key on the computer keyboard when they guessed that a visual stimulus was presented. Patient responses were regarded as valid when they occurred within 2 sec after the tone and the intertrial interval (ITI) was 3 sec (Figure 2A).

In the stimulus localization task, the patients used hand/arm movements to localize visual stimuli in a forced-choice situation. After an initial tone signal and a randomly selected time interval between 1 and 3 sec, a visual target was presented randomly at one of three predetermined test locations. One second after the presentation, a second tone indicated that the patients could make an eye movement from the fixation point to the respective test location and touch the position on the screen where they ''guessed'' that the target stimulus had been presented. In order to receive unambiguous patient decisions, at all three test positions a small cue (a thin light gray circle filled with background color) was permanently present. Following the response, the patient was required to fixate the fixation point again and the next trial started after an ITI of 3 sec (stimulus diameter of 1°; presentation time of 100 msec; see Figure 2A).

The spatial summation paradigm was introduced by Marzi et al. (1986), who demonstrated that RTs were faster when two stimuli were presented simultaneously compared to a single stimulus, even if one of the targets in the double stimulus condition was presented in the clinically blind area of hemianopic subjects. They concluded that an unconscious percept (blindsight) of the stimulus in the affected field facilitates the response to the second stimulus. This implicit procedure for testing blindsight capacities has the advantage that it avoids the problem of a possible shift in the subject's decisional criterion as they turn from clinical perimetry to a forced-choice experimental procedure (Campion et al., 1983). Using a test based on this paradigm, in each session, two possible test locations in the deficient area (D) and two locations in the intact part of the patient's visual field (I) were first selected and a brief acoustic tone was given prior to the visual stimulus presentation. In each trial, 1 of 5 stimulus patterns were presented randomly: one stimulus in either I (1) or D (2); two stimuli in either I (3) or D (4); one stimulus in I and one in D (5, the summation condition). The subject's task was to constantly fixate the fixation point and to press a key as fast as possible following presentation of either one or two flashes in any of the 4 possible locations. The target stimuli were presented for 20 msec. The interval between the warning stimulus and the visual targets was randomly chosen within 1–3 sec and the ITI was 3 sec. RTs faster than 150 msec and longer than 900 msec were excluded from subsequent analysis. Due to the short presentation time, a larger stimulus of 1.5° was employed; pretests revealed that some patients were not reliably able to detect a stimulus with a diameter of 1° even in their intact area of the visual field (Figure 2A). In contrast to forced-choice procedures, the employment of this paradigm as a blindsight test is dependent on an important prerequisite. When stimuli are presented in ''intact'' areas of the visual field, the mean RT in the double stimulus condition has to be significantly shorter than in the single stimulus condition. A pilot study revealed that our test procedure is able to induce this summation effect. A consistent and significant RT advantage of about 17 msec could be observed in normal subjects.

Experimental Procedure

All subjects attended 9 separate experimental days and performed all 3 paradigms once during each visit. Each test included 150 trials per session. In both the detection and localization tasks, 9 locations were each tested with 150 trials; 3 ''location sets'' (consisting of 2 locations in the intact area and 2 locations in the clinically blind part of the visual field) with 450 trials each were studied with the summation paradigm. Before testing, the patients received detailed information and an explanation of the objectives of the study, then they were pretrained until they learned to master the tasks. They received no feedback about test performance until all 9 sessions were completed.

A conservative criterion for defining an area of a patient's visual field as ''blind'' was based on the PeriMa results. Because of the large interindividual differences in the size, form, and location of visual field defects, test points based on several predefined criteria were determined for each individual before the formal test sessions (see Figures 2B, 4, and 5). Selection criteria were, for instance, that stimuli were never presented in the natural blind spot and the distance between test locations and the transition zone, which was determined

prior to the assessment as previously described (Kasten, Wüst, & Sabel, 1998) was at least 4°. Coordinates of test points in the detection and localization task were identical, whereas due to the nature of the spatial summation paradigm, in this task slightly different test locations had to be selected. This selection procedure revealed that test locations had a maximal horizontal eccentricity of ±44° and a maximal vertical eccentricity of ±40° in the stimulus detection and localization tasks. In the spatial summation paradigm, test points were placed in a matrix of ±31° horizontal and ±40° vertical eccentricity.

Rating "Level of Consciousness"

During testing, patients were repeatedly asked if they were conscious of seeing the visual targets. However, because patients with visual field defects often report difficulties in answering unambiguously whether or not they consciously saw a visual stimulus, subjective awareness was assessed as accurately as possible by testing all 9 locations in the patients' visual fields in additional sessions with both the detection and localization paradigm. Each session consisted of 50 trials, after each of which subjective consciousness values were rated on a 5-point scale. Subjects were instructed to report: a"1" when their response was a complete guess; a"2" when they had an intuition that something had influenced their response; a"3" when they felt that they had seen something; a"4" when they saw a portion of the stimulus; and a"5" when they clearly saw a stimulus. Consciousness ratings have been previously assessed with slightly different techniques (Schärli, Harman, & Hogben, 1999a, 1999b; Kolb, Braun, & Kölmel, 1995; Weiskrantz, Barbur, & Sahraie, 1995).

Statistical significance of performance in the forced-choice procedures was assessed with binomial tests (with normal approximation). When more than one binomial test was included in a given analysis, an alpha adjustment according to Bonferroni was applied. RT data in the spatial summation paradigm were tested for statistical difference with one-way analyses of variance (ANOVAs) followed by Scheffé post hoc tests.

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