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Deficits of Contralesional Awareness: A Case Study on What Paper-and-Pencil Tests Neglect

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Objective: Attentional orienting and awareness for contralesional hemispace were studied longitudinally in a woman (GB) who suffered a right hemispheric stroke without any motor impairment and who presented normal performance on standard paper-and-pencil tests for neglect but manifested difficulties in everyday life. We aimed to test whether computer-based, dual-task paradigms were sufficiently sensitive to detect the presence of subclinical neglect in GB. ***Method:*** We assessed the spatial awareness of GB by means of cued-detection tasks, paper-and-pencil tests, attentionally demanding dual tasks, and in several ecological settings after her discharge from the hospital. A group of right brain–damaged patients and an age-matched healthy participant were also tested with the dual tasks. ***Results:*** Dramatic awareness deficits for the left contralesional hemispace emerged in GB only under dual-task conditions, both in computer-based and in ecological settings, as if her degree of contralesional space awareness impairment was closely dependent on the quantity of available attentional resources. Our dual-task paradigm was also effective in quantifying awareness improvements over time. The absence of motor impairments, uncommon for a postacute patient with severe albeit hidden neglect, allowed us to ascribe her everyday life impairments for contralesional hemispace to awareness deficits. The performance of the group of patients confirmed the detrimental effects of the dual tasks, whereas the performance of the healthy control we tested was not affected by dual-task manipulation. ***Conclusions:*** Our results confirm the well-known lack of sensitivity of standard neuropsychological tests to detect subclinical forms of neglect, which, nonetheless, may result in negative consequences in everyday life. Computer-based, resource-demanding paradigms seem to be a promising solution to uncover subtle awareness deficits that can affect the everyday life of stroke patients.

Keywords: neuropsychological assessment, neglect, attention, extinction, resources, contralesional space awareness

You don't need eyes to see, you need vision.
Maxwell Alexander Frazer

Deficits of contralesional space awareness (i.e., neglect and extinction) index a failure in attending to contralesional space, and they frequently follow a right hemisphere stroke. These deficits result presumably from the disruption of mechanisms subserving the orienting of spatial attention (Driver & Vuilleumier, 2001) and can provide hints about the competitive processes underlying orienting of spatial attention and, thus, awareness of contralesional space (Karnath, 1988; Làdavas, 1990; Làdavas, Menghini & Umiltà, 1994; Mattingley, Bradshaw, Bradshaw, & Nettleton, 1994).

Neglect syndrome is associated with severe impairments in virtually all everyday activities (e.g., eating, dressing, navigating, etc.), thereby constituting a main obstacle to personal autonomy (Barrett et al., 2006). Its presence predicts poor functional outcome in everyday activities better than the overall stroke severity (Buxbaum et al., 2004).

The prevalence estimates for neglect and extinction after a stroke involving the right hemisphere range from 13% to 81% (for review, see Bowen, McKenna, & Tallis, 1999). This variability in reporting neglect may reflect differences in inclusion criteria and assessment procedures (see also Samuelsson, Hjelmquist, Naver, & Bromstrand, 1995). A crucial aspect to consider, however, is that clinical testing for the presence of neglect is based on "paper-and-pencil" tests whose sensitivity is highly variable within and across studies (Halligan, Marshall & Wade, 1989; Azouvi et al., 2002). This fact can be attributable to several factors (Halligan & Marshall, 1992; Azouvi et al., 2002; Sarri, Greenwood, Kalra, &

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Driver, 2009), and one of the most prominent might be the adoption by the patients of compensatory strategies. Indeed, paper-and-pencil tests are not sufficiently sensitive to detect subtle or even mild forms of neglect (Barrett et al., 2006), and, thus, these tests can systematically underestimate the presence and severity of neglect (Buxbaum et al., 2004). A possibility to reveal deficits that do not emerge in paper-and-pencil tests is the adoption of computer-based testing, widely discussed but hardly implemented for diagnosis (Anton, Hershler, Lloyd, & Murray, 1988; Deouell, Sacher, & Soroker, 2005; Rengachary, d'Avossa, Sapir, Shulman, & Corbetta, 2009; Schendel & Robertson, 2002 for review; van Kessel, van Nes, Brouwer, Geurts, & Fasotti, 2010).

The high sensitivity of computerized assessments in detecting attentional orienting deficits seems to be related to the possibility to present patients with stimuli of brief durations and to record response latencies with a millisecond precision. Data from cued detection studies comparing the performance of patients with and without neglect, where the distinction between the two groups is made according to their performance on paper-and-pencil tests, confirm this conjecture (Losier & Klein, 2002). Indeed, very often also the non-neglect group (i.e., the "control" group) show slower responses for targets appearing in the contralesional hemispace than for targets appearing in the ipsilesional hemispace. We highlight that this result is not a consequence of superficial testing and commonly occurs in computer-based (but not in paper and pencil) experimental tasks even when state-of-the-art, paper-and-pencil tests for neglect diagnosis (e.g., the Behavioral Inattention Test, BIT; Wilson, Cockburn, & Halligan, 1987) have been adopted (e.g., Bonato, Priftis, Marenzi, & Zorzi, 2008, 2009).

Another possibility to reveal deficits not detected by paper-and-pencil tests is to implement paradigms sufficiently demanding not to allow patients to compensate for their deficit. Such paradigms could, in turn, allow the clinician to perform a sensitive diagnosis of contralesional awareness deficits. For instance, it has been shown that contralesional space awareness, as measured by a primary task (e.g., cancellation), is affected by the deployment of attentional resources for performing a second, resource-consuming, task (Robertson & Frasca, 1992). However, in the last two decades this approach has been somehow forgotten, because the large majority of clinicians applied only "standard" paper-and-pencil tests and because the issue of what is "task difficulty" is somehow vague. For example, every clinical neuropsychologist knows that simple cancellation tests would detect only moderate-to-severe forms of neglect. Nonetheless, cancellation tests are still the state of the art for the diagnosis of contralesional awareness deficits in the acute phase, because they present several advantages with respect to other paper-and-pencil tests (Rorden & Karnath, 2010), including a higher sensitivity (e.g., Ferber & Karnath, 2001, for a comparison with bisection tasks). The use of large batteries for neglect screening is seldom possible because of time constraints, and this has inspired an enquiry concerning the "most sensitive" single paper-and-pencil test for neglect diagnosis (e.g., Halligan et al., 1989). In some studies patients have been classified as affected by neglect when their performance was pathological on two or more tests. This approach allows to consider as patients with neglect only patients affected by severe neglect. Less clear, instead, is what should be considered as non-neglect. For instance, there is no consensus on whether patients without neglect but with visual extinction should be included in the neglect group, in the non-neglect group, or in a separate category. Moreover, the role of attentional demands as a major determinant of patients' performance is not well established at the moment. With our study we mainly aim to show that a good performance on paper-and-pencil tasks does not fully guarantee for the absence of neglect.

In a recent study, Bonato, Priftis, Marenzi, Umiltà, and Zorzi (2010) coupled the adoption of the two above-mentioned methodologies (computer-based and resource-demanding tasks) for assessing visual extinction and single-target detection in right-hemisphere stroke patients. They showed that the degree of impairment for contralesional space processing depends on the quantity of attentional resources that are available for task performance. Dramatic failures to report left contralesional targets emerged only in dual-task conditions, independently of the nature of the concurrent task (i.e., visual vs. auditory). In contrast, the performance of healthy control participants was unaffected by the dual-task manipulation.

An increase in visual attentional load has been previously described, in right brain–damaged patients, to deeply effect contralesional hemispace processing (Eramudugolla, Boyce, Irvine, & Mattingley, 2010; Russell, Malhotra, & Husain, 2004; Vuilleumier et al., 2008). For instance Vuilleumier et al. (2008) demonstrated, in a fMRI study, that increased attentional load at fixation can reduce or even eliminate brain activations selectively for (ipsilesional) visual areas which process the opposite hemispace.

However, to our knowledge, only Bonato et al. (2010) emphasized the diagnostic potential of load manipulations. In the present study we extend their findings investigating longitudinally the performance of a woman who, after a right-hemispheric stroke, showed unimpaired performance on paper-and-pencil tests for neglect but had neglect-related difficulties in everyday life that severely limited her autonomy. This occurred despite the absence of any motor deficits, which is a condition seldom described in the literature for postacute right brain–damaged patients (Azouvi et al., 2002). We focused our study on her attentional orienting and awareness for contralesional hemispace using computer-based resource-demanding procedures. Classic cued-detection tasks (e.g., Posner, 1980) for the study of attentional orienting were also administered to assess her deficits in exogenous orienting. This allowed us to compare the two procedures in terms of their ability to uncover a subtle, but clinically relevant, deficit of contralesional space awareness. Moreover, longitudinal testing allowed us to test for the sensitiveness of these tasks for tracking spontaneous remission of her deficits over time. Neuropsychological evaluation and computer-based tasks were crucially complemented by repeated ecological observations at the patient's home after her discharge from the hospital. The absence of motor impairments allowed us to rule out potential confounds, such as left motor weakness, and to ascribe to neglect her impaired performance for contralesional hemispace found in everyday life contexts. Finally, the performance of a group of right brain–damaged patients and of an age-matched healthy participant allowed us to replicate the results of Bonato et al. (2010) in showing that performing the dual task induces a bias that is selective for contralesional hemispace, that it emerges in neurologically impaired participants only, and that subclinical neglect in post–acute stroke patients is all but uncommon.

Single Case Study

Method and Results

Participant. The patient, GB, was a right-handed 63-year-old woman. She had five years of education and worked in the quality control section of a jewelry factory. She was admitted to the hospital for sudden loss of movement coordination with largely preserved motor strength, deviation of her mouth, mental confusion, and speech difficulties. She never lost consciousness and underwent trombolisis given the neuroradiological evidence, at hospital admission, of hyperintensity of the M1 tract of the right middle cerebral artery and its branches. The diagnosis of an ischemic stroke was confirmed by CT scans at 2, 24, and 48 hours from the first exam. A CT scan performed three months after her stroke (see Figure 1) showed cortical-subcortical ischemic areas within the territory of the right middle cerebral artery. The brain lesion affected her frontal pars opercolaris, the insula, and the posterior parietal cortex. Neurological examination revealed a mild loss of strength for the left hemibody, completely resolved at discharge. The first testing session (i.e., T1) took place between days 27 and 35 from her stroke onset. Further testing sessions took place on days 47 (T2), 68 (T3), 96 (T4), and 161 (T5) after stroke onset. The patient did not undergo any specific treatment for neglect rehabilitation.

The study was approved by the local Ethics Committee and by an agreement between the University of Padova and the Rehabilitation Centre of Padova Hospital. GB gave informed consent to take part in the study and to have her performance video-taped, according to the Declaration of Helsinki.

T1 Testing Session

T1 Neuropsychological Preliminary Assessment: Method

The patient was administered a set of standardized neuropsychological tests for general cognitive screening and neglect assessment, several cancellation tasks, and a set of computer-based tests. Neuropsychological standardized tests encompassed the Italian version of the Mini Mental State Examination (MMSE, Magni et al., 1996), a comprehensive neuropsychological battery (Esame Neuropsicologico Breve, ENB; Mondini, Mapelli, Vestri, & Bisiacchi, 2003), the conventional part of the BIT for assessing neglect for the within-reaching space (Wilson et al., 1987), the Frontal Assessment Battery (FAB; Dubois, Slachevsky, Litvan, & Pillon, 2000), and the Fluff test for testing neglect for the body (Cocchini, Beschin, & Jehkonen,, 2001). GB's scores on each ENB and BIT (sub)test are shown in Table 3, altogether with tests for motor performance and disability (e.g., Motricity index, Collin & Wade, 1990; the Functional Independence Measure scale, Hamilton et al., 1987; and the Barthel Index, Mahoney & Barthel, 1965).

The second part of the Trail Making Test (TMT-B) from the ENB and the star cancellation subtest of the BIT were readministered to GB, to be fully audio-visually recorded.

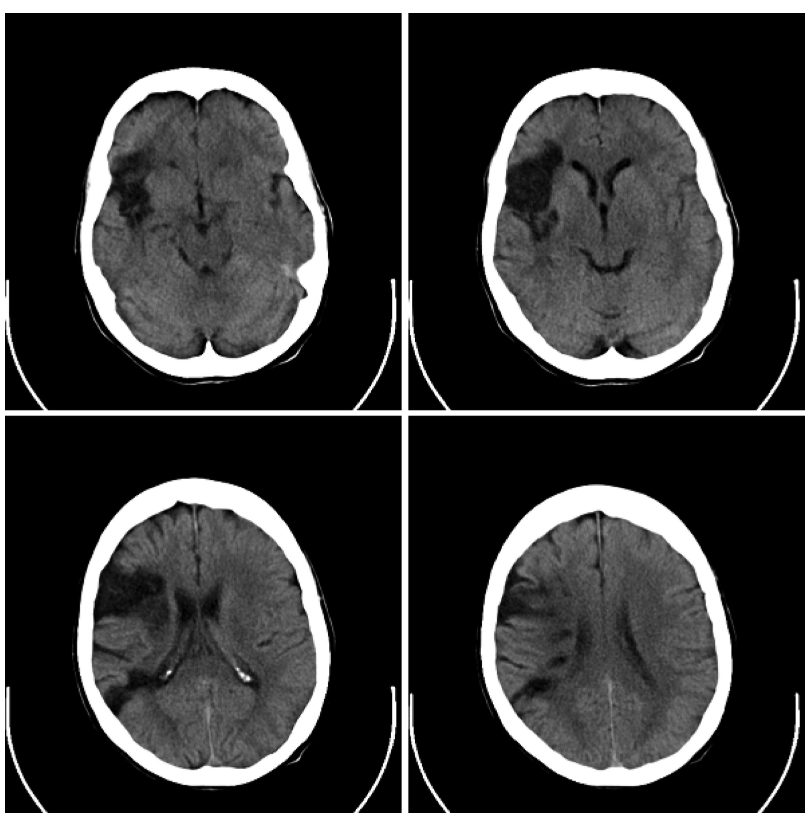

Figure 1. CT scans of GB at three months from stroke onset.

T1 Neuropsychological Preliminary Assessment: Results

GB did not present neglect according to her overall BIT score of 138/146 (cutoff ≤129). In the three cancellation tasks included in the BIT (lines, letters, stars) she did not miss any contralesional item, scoring 65 of 65. Also on the line bisection subtest, her performance did not show any hint of spatial asymmetry (9/9). Across all tasks of the BIT, she showed a unique contralesional omission only in the human figure drawing, where she failed to draw the contralesional eye and ear. While drawing a butterfly and at the copy of a daisy (BIT) she showed signs of left hyperschematia, a distortion in the perception of size in the contralesional hemispace that has been shown to be independent from neglect, at least when assessed by means of paper-and-pencil tests (Rode, Michel, Rossetti, Boisson, & Vallar, 2006).

At the copy of a drawing (ENB) she showed allochiria, that is, she misplaced an item from the contralesional hemispace in the ipsilesional one.

In both the TMT-B and the overlapping figures subtests (ENB) she experienced difficulty in moving toward the contralesional half of the testing sheet. The neuropsychological evaluation was therefore suggestive of a subclinical deficit for contralesional hemispace, which tended to emerge in the case of tasks requiring particularly complex visuospatial abilities (e.g., TMT-B and overlapping figures) but her BIT score was far too high to allow either a diagnosis of neglect or of borderline performance. It might seem paradoxical that two tests intended to measure other cognitive abilities (executive functions in the TMT-B and perceptual integration in the overlapping figures) were more sensitive to spatial biases than specific tests of spatial awareness (cancellation tasks). As we shall discuss later, we maintain that this might have occurred because the former tasks require a greater amount of attentional resources.

On the Fluff test, GB did not remove two markers from her left leg, two from her right leg, and four from her left arm. Her performance was below the cut-off, revealing the presence of left personal neglect (Cocchini, Beschin, & Jehkonen, 2001).

In describing a room, GB showed extrapersonal neglect. In the FAB she scored 12/18, below the cut off according to Appollonio et al. (2005).

With the finger confrontation procedure (Bisiach & Faglioni, 1974) we presented her with 20 bilateral, 32 left, and 32 right stimuli, half for the upper and half for the lower visual field, in a fixed random order (Bisiach, Cappa, & Vallar, 1983). She missed 75% of the left-sided targets on bilateral trials and 47% of left-sided unilateral targets. The finger confrontation technique is known to be one of the most sensitive measures of contralesional attentional impairments because patients are asked to fixate the examiner's face, with a likely attentional capture by the experimenter's gaze (Maravita et al., 2007) in a setting at least in part similar to experiments increasing visual load at fixation.

T1 Dual Task Experiment: Method

GB sat at a distance of about 60 cm from a 15“ computer monitor. We used E-Prime (Psychology Software Tools, Sharpsburg, PA; *http://www.pstnet.com/*) to program and administer the computer-based tasks. A head-and-chin rest was adopted to prevent head movements. There were three experimental conditions: the single-task condition, the visual dual-task condition, and the auditory dual-task condition (see Figure 2).

Each trial started with a blank screen (1000 ms), followed by a black fixation point (1000 ms), which was presented in the center of the screen against a white background. Thereafter, either a single target (left-sided or right-sided) or bilateral targets (left- and right-sided) were presented equiprobably in the periphery, each at a lateral distance of 135 mm (about 12.8°) from the center of the screen. The target was a black disk (diameter: 8 mm) presented against a white background. A letter (a, b, v, or z; font size: 38) was centrally presented synchronously with the target. The duration of the screenshot with the target and the symbol was 50 ms. Along with the central letter and the peripheral target(s) also a spoken number word (i.e., one, two, eight, or nine) was presented by means of earphones. Given that target and letter duration was 50 ms, the auditory stimulus presentation continued across the noisy screenshot that followed the target display until response.

In the single-task condition, GB (and later on all the participants to the study) had to report the position of the target(s) (i.e., "right," "left," or "both" sides) but ignore the centrally presented symbol and the auditory-presented number. By means of a second keyboard, the experimenter coded oral responses to the position of the target ("left," "right," "both" sides, no response).

In the visual dual-task condition, the display and the sequence of events were identical to that of the single-task condition. The task was to name the centrally presented letter and to ignore the auditorily presented number, before reporting the position of the lateral visual target(s). The experimenter checked for GB's letter reading accuracy and coded her oral responses to the position of the target.

In the auditory dual-task condition, the display and the sequence of events were identical to that of the single-task condition. The task was to pay attention to the spoken number word and to ignore the centrally presented letter. GB was asked to count forward twice by two starting from the heard number word, before reporting the position of the lateral visual tar-

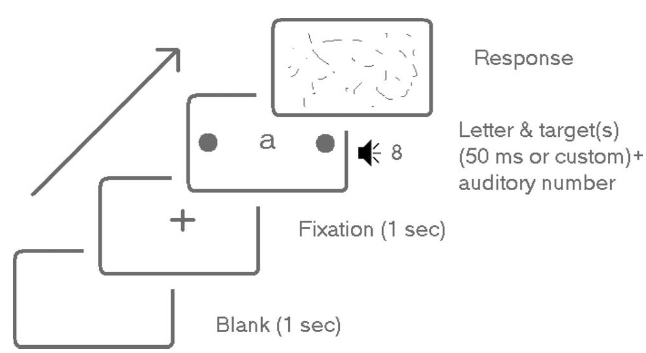

Figure 2. Dual-task paradigm: A schematic outline of the sequence of events. A trial with bilateral targets is shown. There were also trials with unilateral (left or right) single targets, with the same proportion. Altogether with the target(s) a letter and a spoken number word (e.g., eight) were presented. In the last screenshot (response collection) patients reported either the position of the targets (in the Single-task condition) or the identity of the letter and the position of the targets (Visual dual-task) or had to count twice by two from the heard number and then report the position of the targets (Auditory dual-task).

get(s). The experimenter recorded GB's counting accuracy and coded her oral responses to the position of the target.

We highlight two important differences with respect to the study by Bonato et al. (2010), where this paradigm was tested for the first time for the detection of subtle contralesional awareness deficits. The first is that the spoken number words were not only presented in the auditory dual-task condition, in which they had to be processed, but also in the single-task and in the visual dual-task conditions, in which they had to be ignored. This change makes the three conditions exactly the same in terms of stimuli, because for each task, GB was presented with lateralized target(s), a central visual stimulus (letter), and an auditory stimulus (number word). As a consequence, data interpretation is more straightforward because the potential awareness deficits when found under the auditory dual-task condition cannot be ascribed to passive listening to numbers. The second is the use of earphones to present auditory stimuli. This allows us to ensure that the nature of the auditory dual task is not visuospatial, given that loudspeakers occupy a specific position in visual/auditory space.

GB was presented with two blocks of 48 trials each for every experimental condition. She could stop to take a short rest at the end of each trial. A camcorder, zoomed on the patient's eyes, was centrally placed above and behind the computer screen. The experimenter detected and coded eye movements both online and offline.

T1 Dual Task Experiment: Results

Trials affected by eye movements, trials where the central letter was not correctly reported, or trials when counting did not properly occur were discarded from analysis (1.04% of trials) in this as in the next dual-task experiments.

Criteria for extinction and omissions. Extinction rate was calculated for trials with bilateral targets, as the ratio between the number of targets reported as ipsilesional only and the total number of trials with bilateral targets to which a response occurred. The statistical comparisons were made between the number of "right" versus "both" responses to bilateral targets. Omission rate was calculated for trials with unilateral contralesional targets, as the percentage of targets where a response did not occur. The statistical comparisons were made between the number of trials where no response occurred versus the number of trials with "left" responses.

It is worth noting that the term "extinction" can be properly adopted only when a significantly higher number of contralesional omissions emerge for bilateral versus unilateral targets. Before each analysis we, thus, provide a test for this difference, separately for the three conditions.

Contralesional omissions for unilateral versus bilateral targets. GB showed many contralesional omissions under both dual-task conditions, not only for bilateral but also for unilateral targets. The differences between uni- and bilateral targets were not significant (all ps $>$ .05). Thus, we will not adopt the term "extinction" for this testing session.

The patient did not show any omission for single ipsilesional targets in any of the conditions.

Contralesional omissions for bilateral targets. The rate of left omissions for bilateral targets increased dramatically from 29% in the single-task condition to 100% in both the visual, Pearson's $\chi^2(1, n = 62) = 34.1$, $p < .001$, Fisher's exact test and the auditory, $\chi^2(1, n = 63) = 34.9$, $p < .001$ dual-task conditions (see Figure 3).

Contralesional omissions for single targets. GB showed neglect (missed contralesional single targets) only under dual-task conditions, that is when her attentional resources were engaged by a concurrent and demanding task. Her rate of missed responses to single left-sided targets strikingly increased from 9.4% in the single-task condition to 90.3% in the visual dual-task condition, $\chi^2(1, n = 60) = 49.11$, $p < .001$ and to 90.6% in the auditory dual-task condition, $\chi^2(1, n = 61) = 50.1$, $p < .001$ (see Figure 4). The difference of GB's performance in the two dual tasks was nonsignificant.

Although GB's performance was apparently spared on paper-and-pencil tests, she showed a severe awareness deficit for contralesional targets as soon as her attentional resources were engaged in a concurrent task, independently of its nature (i.e., visual vs. auditory), in parallel with the results shown with the finger confrontation procedure.

T1 Cued Detection Experiments

Method

We presented GB with a peripheral nonpredictive cueing paradigm (Posner, 1980), with a target duration of three seconds. Although according to Losier and Klein (2001) previous cued detection studies with right brain–damaged patients have never adopted a target duration shorter than 2 s, we also presented GB with a variant of the task where target duration was reduced to 50 ms (i.e., the same duration as that of the target in the dual-task paradigm). This variant was intended to maximize the possibility to detect contralesional target omissions. In both experiments each trial started with a 500-ms blank screen, then three identical boxes (one central containing a fixation cross, two lateral) were presented until response. After 1 s, a peripheral cue (50-ms-long thickening of one of the two lateral boxes) occurred. Boxes had a side of 1.7 cm, their distance from the center was about 7.2° (center to center), and the diameter of the target (a black disk) was 8 mm.

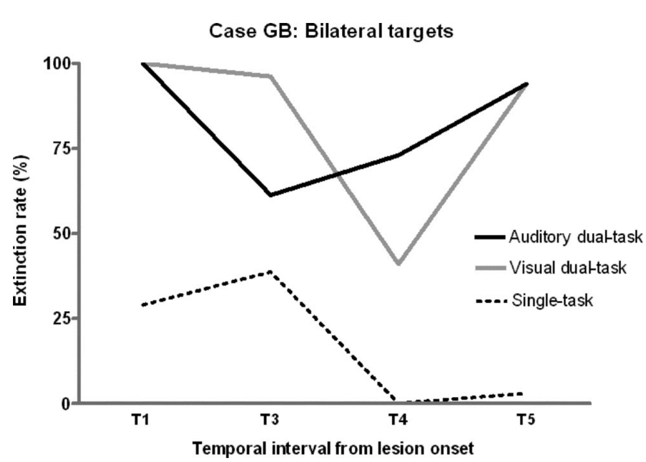

Figure 3. Patient GB: The percentage of bilateral targets reported as ipsilesional at T1, T3, T4, and T5 is shown separately for each condition.

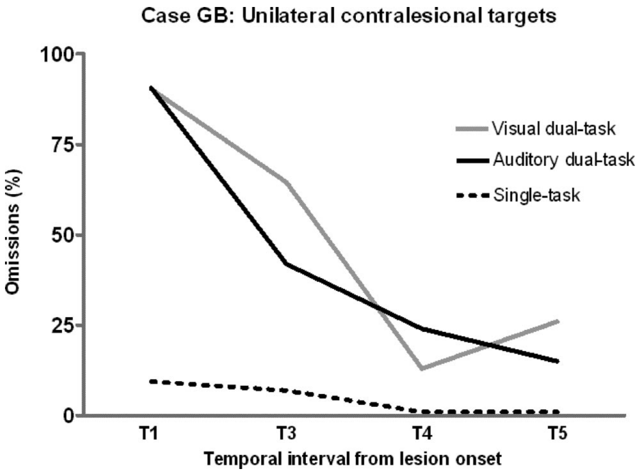

Figure 4. Patient GB. The percentage of contralesional (left-sided) unilateral targets missed at T1, T3, T4, and T5 is shown separately for each condition.

GB was also presented with a central nonpredictive cueing task that has been shown to elicit a disengage deficit in right brain–damaged patients (Bonato et al., 2009). The central cue was either a leftward or a rightward oriented arrow (cue duration: 150 ms) that did not predict target location. The Stimulus Onset Asynchronies (SOAs) were of 100, 300, and 800 ms for peripheral and 200, 500, and 1000 ms for central cueing. There were two blocks of trials for each paradigm. Each block of the peripheral cueing experiments encompassed 60 experimental and 12 catch trials, whereas each block of the central cueing experiments encompassed 72 experimental and 18 catch trials. In both experiments (peripheral and central cueing), GB had to fixate and keep her gaze in the center of the screen and press a centrally aligned key as soon as possible after target presentation.

Results

Median reaction times were calculated on noncatch trials where a response occurred. With target duration fixed at 3000 ms, GB did not miss any contralesional target (accuracy: 100%), in both peripheral and central cueing paradigms. In the variant of the peripheral cueing paradigm where target duration was set to 50 ms, she missed 3.5% of the targets (all misses occurred in contralesional hemispace, resulting in 7% of omissions with respect to all contralesional targets). Despite the temporal reduction of target duration, the number of errors in the contralesional hemispace did not significantly differ from the number of omissions (0%) for targets presented in the ipsilesional hemispace, $\chi^2(1, n = 120) = 4.14$, $p = .12$. No ocular movements were detected during the task.

The three paradigms highlighted a clear slowing of target detection for contralesional with respect to ipsilesional hemispace, across all tasks and SOAs (see Rengachary et al., 2009). The nine values (3 SOAs × 3 tasks) for contra- minus ipsi-RT difference were all positive, thus indexing slower responses in the contralesional with respect to the ipsilesional hemispace, and resulted in a mean value of 105 ms. Slowed processing for the contralesional hemispace is suggestive of subclinical neglect, and it resembles the findings described for some right brain–damaged (RBD) patients (supposedly) without neglect in previous group studies.

The hallmark of disorders for contralesional hemispace processing in cued detection tasks is however considered to be the disengage deficit (DD), that is an increased invalid-valid RT difference for contralesional with respect to ipsilesional targets. The disengage deficit is a measure of the difficulty in reorienting spatial attention toward contralesional hemispace after invalid cueing occurring in the ipsilesional hemispace (Posner, Walker, Friedrich, & Rafal, 1984, see also Olk, Hildebrandt, & Kingstone, 2010 for a more recent account). As expected, GB presented a disengage deficit at the 3000-ms variant of the detection task (see Table 1). The size of her DD was 106, 179, and 53 ms for the SOAs of 100, 300, and 800 ms, respectively (see Table 1). We compared these values with those reported in a previous study, in which chronic brain-damaged patients without neglect and without extinction were presented with a nonpredictive peripheral cueing paradigm with the same target duration of our study (3000 ms, Friedrich, Egly, Rafal, & Beck, 1998; Exp. 1). From this study, we selected only patients with right brain damage ($n = 8$, mean time from lesion onset = 96 months, mean age = 58 years). Beside the absence of neglect on paper-and-pencil tests, we chose this sample for a comparison because a mean time from lesion onset of several years should run counter the presence of subclinical neglect in everyday life. The paradigm encompassed four SOAs (250, 350, 650, and 900 ms). The size of their DD was 60, −8.3, 5, and 5.1 ms, respectively. We compared GB's DD with that of the RBD patients in Friedrich et al.'s (1998) study at the shortest SOA (100 ms for GB vs. 250 ms for the patient group), at two intermediate SOAs (300 ms for GB vs. 250 and 350 ms SOAs for the patient

Table 1
GB's Performance (ms) at the Cued Detection Tasks

				SOA1			SOA2			SOA3		
Experiment	Target duration (ms)	Time	Target position	Invalid	Valid	DD	Invalid	Valid	DD	Invalid	Valid	DD
Peripheral cueing	3000	T1	Left	627	433	106	665	430	179	522	442	53
Peripheral cueing	3000	T1	Right	489	400		453	396		447	421	
Peripheral cueing	50	T1	Left	558	480	47	514	446	17	438	498	−61
Peripheral cueing	50	T1	Right	376	345		418	367		367	366	
Central cueing	4000	T1	Left	642	654	−70	710	602	91	682	538	139
Central cueing	4000	T1	Right	548	490		521	503		544	539	
Peripheral cueing	3000	T4	Left	483	413	−26	472	376	75	433	384	44
Peripheral cueing	3000	T4	Right	438	342		388	367		402	397	

group), and at the longest SOA (800 ms for GB vs. 900 ms for the patient group). By applying a specific method for single case studies (Crawford & Garthwaite, 2002), only the comparison for one of the intermediate SOAs (300 vs. 350 ms) indexed a larger DD in GB compared with the group of chronic right brain–damaged patients, $t = 3.83$, $p < .01$. With the required caution given the differences in the two experimental paradigms, we can suggest that possibly GB presented, at this time of testing, a larger DD with respect to that shown by chronic right brain–damaged patients without neglect at paper-and-pencil tests. We also calculated the valid left-valid right RT difference, following Sieroff et al. (2007), but its size turned out to be modest (33, 34, and 22 ms for the three SOAs, respectively).

When central arrow cueing was adopted, GB showed, at the shortest SOA, positive validity effects only for right- but not for left-sided targets (mean validity for right-side targets = 58 ms, for left-side targets = −12 ms). Thus, she did not present any DD, confirming our previous observation that the size of the DD from central nonpredictive cueing inversely correlates with BIT scores (Bonato et al., 2009). After central cueing, GB showed an increased validity effect for left compared with right targets at the 500 and 1000 ms SOAs (91 and 139 ms).

Although all these paradigms confirm that target detection in contralesional hemispace is slowed in GB, no omissions occurred in both cued detection tasks where target duration was set to three seconds. Even the paradigm with target duration reduced to 50 ms still evoked a rate of omissions (7%) that did not differ significantly from zero and that was much lower than the omission rate elicited by our dual tasks (which was above 90%). If we were to consider contralesional slowing as a reliable index of neglect, the diagnosis would have to be made by reference to a matched control population. Even if an age-matched population were available, one could always question whether the comparison should be made with healthy participants, thus increasing the risk of a type-I error, or with RBD patients, thus incurring in the problem that neglect presence/absence is defined by means of paper-and-pencil tests (i.e., a circularity issue).

Ad Hoc Cancellation Tasks

Method

GB was also administered several ad hoc cancellation tasks to test whether neglect-like performance would emerge without resorting to computer-based paradigms. We used as stimuli the star cancellation subtest of the BIT (Wilson et al., 1987), the Bell test (Gauthier, Dehaut, & Joanette, 1989), four modified versions of the Bell test (Biancardi & Stoppa, 1997), and an ad hoc cancellation task (see Table 2, for details).

We adopted a series of strategies, either known to be highly sensitive for the detection of contralesional awareness deficits or that we considered as potentially useful for exacerbating neglect. First, across all tasks we used materials with a high number of distracters that were very similar to the targets to be cancelled (Sarri, Greenwood, Kalra, & Driver, 2009). Second, we adopted visible-invisible marks because invisible marks lead to worse performance (see Wojciulik, Rorden, Clarke, Husain, & Driver, 2004). Third, the pencil provided to the patient was exchanged with one of different color every 60 seconds. This allowed us to readily monitor her movements across the sheet and to interrupt the patient while performing the task to establish whether she was then able to continue leftward.

Table 2
GB's Performance at the Ad Hoc Cancellation Tasks

Stimulus	Type of mark	Spatial position of the sheet	Left targets	Right targets	CoC[a]	CoC[a] starting point	Time per cancelled item (sec)	Left missed[b]	Right missed
Stars BIT	Standard black	Central	27	27	0.018	0.499	2.02	1	0
Stars BIT	Invisible mark	Central	27	27	0.013	0.499	2.80	1	2
Stars BIT	Standard black	Right	27	27	0.004	1.029	1.56	1	1
Stars BIT	Invisible mark	Left	27	27	0.006	1.029	1.74	1	0
Stars BIT	Standard black	Left	27	27	−0.006	1.029	1.69	1	1
Stars BIT	Invisible mark	Right	27	27	0.063	0.499	2.02	11***	0
Modified Bells Table 2	Color	Right	17	17	−0.014	0.740	3.71	2	4
Modified Bells Table 2	Color	Left	17	17	0.012	0.944	3.55	2	3
Custom made	Standard black	Central	18	18	0.045	0.212	6.10	9	6
Custom made	Color	Central	18	18	−0.004	1.017	6.18	2	1
Custom made	Invisible mark	Central	18	18	0.003	1.017	10.63	1	0
Bells	Invisible mark	Central	17	17	0.103	0.872	4.68	6	3
Bells	Color	Central	17	17	0.142	0.872	4.61	6*	0
Bells	Standard black	Central	17	17	0.267	0.872	4.14	11**	2
Stars BIT	Color	2 sheets	56	56	0.158	0.294	2.50	18***	2
Modified Bells Table 2	Color	2 sheets	35	35	0.001	0.971	4.20	4	6
Modified Bells Table 2[c]	Color	2 sheets	35	35	0.111	0.971	9.02	11	6
Modified Bells Table 1	Standard black	Central	17	17	0.219	0.857	4.28	7	2
Modified Bells Table 2	Standard black	Central	17	17	0.120	0.735	3.40	6	3
Modified Bells Table 3	Standard black	Central	17	17	0.069	0.886	3.96	5	3
Modified Bells Table 4	Standard black	Central	18	16	0.034	1.013	4.50	2	0
Stars BIT	Standard black	Central	27	27	0.016	0.093	1.41	1	0

[a] CoC: Center of Cancellation (Rorden & Karnath, 2010). [b] Significant differences between contra- and ipsilesional omissions are marked with asterisks (* $p < .05$. ** $p < .01$. *** $p < .001$). [c] The patient was asked to count backwards by two while performing the cancellation task.

Fourth, we presented the testing sheets in different spatial positions (e.g., the contralesional position leads to a worse performance). Finally, GB was also asked to count backward while performing one of these tasks (Robertson & Frasca, 1992). Table 2 reports for each testing sheet which combination of the above mentioned strategies was adopted.

The tests were administered on different days, and her performance in all tasks was audio-visually recorded.

Results

Despite our attempts to elicit neglect, GB showed a contralesional deficit only in four of 22 ad hoc cancellation tasks that she was administered. This was indexed by a significant difference (Pearson's Chi Square) between the number of marked and unmarked targets in the contralesional versus the ipsilesional half of the sheet (see Table 2).

Notably, the BIT stars test resulted in contralesional omissions only when invisible marks were adopted and when two testing sheets were horizontally attached one next to the other. Moreover, by reviewing the audio-visual recording, we noticed that GB's omissions in two of the four tasks occurred while she was talking with the experimenter (a dual-task context). In summary, despite the effort to present her with cancellation tasks that are far more complex and challenging than those adopted for clinical assessment of neglect, GB's omissions for contralesional hemispace were sporadic and the statistical comparison with the number of omissions within the ipsilesional hemispace was nonsignificant in almost all variants of the cancellation tasks (18 out of 22). Moreover, we adopted the Center of Cancellation (CoC) method (Rorden & Karnath, 2010) to better quantify the spatial gradient of her performance in a standardized space, where 0 indicates perfect symmetry (i.e., center of the sheet) and 1 cancellation limited to the right-most targets. The mean CoC value across tasks was 0.06 (see Table 2). Even considering only the CoC in the four conditions where a significant number of contralesional omissions emerged, her degree of space neglected was all but severe ($M = 0.16$). Nevertheless, her cancellation performance across tasks was slow (with a mean time per cancelled item of 3.96 seconds, range 1.4–10.6). More importantly, her starting point was always located in the right half of the testing sheet (see Azouvi et al., 2002), in spite of the fact that she was able to move toward the left to perform the cancellation task. We thus decided to apply the CoC method also for her starting point. The mean value of her starting point was 0.77, clearly indexing a rightward bias, in contrast with her close-to-zero CoC for her whole-task cancellation performance.

Longitudinal Testing

GB presented very subtle or no impairments at all on paper-and-pencil tests, whereas she showed severe awareness deficits in our dual-task paradigm, which was designed to divert attentional resources from the visuospatial task. Although the presence of several contralesional omissions in our task might be relevant for classifying the patient as having neglect, one might first question their impact on everyday life.

Second, given that at the visual finger confrontation GB showed both extinction and neglect one might think that this procedure is already sufficiently sensitive to detect subclinical deficits without any need to make use of computer-based, dual-task procedures. To address the first issue, the patient was observed while behaving at home on days 47 (T2), 68 (T3), 96 (T4), and 161 (T5) after stroke onset. To address the second issue we monitored longitudinally her awareness deficits for contralesional hemispace, which is known to ameliorate over time after stroke (Stone et al., 1992), with the dual-task paradigm at T3, T4, and T5 and the peripheral cueing paradigm (3000 ms duration) at T4.

T2 Testing Session

The T2 session occurred 47 days from stroke onset and 12 days after her discharge. GB was able to make coffee, prepare the table, and walk autonomously in her flat, thus allowing us to observe her behavior in an informal and truly ecological setting very close to ethological observation. Strikingly, as soon as the experimenter talked to the patient while she was walking, she collided with her left leg with an obstacle on the left side of a door. Moreover, during the interview, GB showed to the experimenter several wounds on her left arm caused by repeated bumps into an obstacle (a key) protruding from an armchair, thus confirming that neglect was present and constituted a problem in her everyday-life behavior. Object finding in extrapersonal space did not reveal any deficit for contralesional hemispace. She had the tendency to begin reading not from the upper left part of the page but from articles within the ipsilesional hemispace page. The same difficulty was confirmed when the newspaper was turned upside-down, thus suggesting that the effect was not attributable to the presence of more perceptually relevant stimuli in one half of the page.

Questionnaires and Personal Neglect Assessment

The Bergego scale (Deloche et al., 1996) was then administered to the patient, to her husband, and to her daughter. The patient only reported mild difficulties to avoid objects potentially colliding with her left arm–leg. Her husband only reported that GB had a mild difficulty in cleaning the contralesional part of her mouth. Her daughter, instead, reported that GB had several difficulties within more domains. These included mild difficulties in dressing her left arm/foot, in looking toward the left, in avoiding object potentially colliding with her left arm–leg, and a moderate difficulty in paying attention to sounds or people calling for GB's attention on her contralesional hemispace.

Further Tests for Neglect

The performance at the "Comb and compact task" (Beschin & Robertson, 1997), consisting in the request to comb hair/distribute compact all over the face, did not show neglect for the personal space of her face. The Laterality index was 0.33 when calculated according to Beschin and Robertson (mean for patients with neglect 0.25 and mean for patients without neglect 0.37; see McIntosh, Brodie, Beschin, & Robertson, 2000) and -0.05 when calculated according to McIntosh et al. (2000) (mean for patients with neglect -0.36 and mean for patients without neglect -0.14). Four cancellation tasks were administered, and the patient still started from the rightmost part of the sheet, in all of them, in the presence of an accurate performance. Her performance was unimpaired also when she was asked to cancel items with her left arm.

T3 Testing Session

This session took place one month after discharge and 68 days after lesion onset.

Ecological Observation

During an informal interview, her husband did not report that GB had any particular difficulty, beside a slight "decrease of interest" and the fact that she sometimes was not sufficiently accurate in preparing the table (e.g., placing a center-table in the exact center of the table). Neglect in her everyday life was, however, still present: when urging to start a task, GB bumped her left hand on the table while raising it from above the knees (below the table) to the table top.

Finger Confrontation Procedure

At the visual finger confrontation procedure she missed 65% of contralesional targets for bilateral trials (50% for the upper quadrants and 80% for the lower quadrants). In contrast with the results at T1, she did not miss any single target on the left. This finding excludes the presence of any visual deficit, in this as, plausibly, in the previous sessions. The number of left omissions was significantly higher in the bilateral than in the unilateral conditions, $\chi^2(1, n = 52) = 27.73$, $p < .001$, thus allowing for classifying it as "extinction."

We also tested her for tactile extinction, which occurred on 50% of the bilateral targets, again in the absence of any missed unilateral targets. Also this difference was significant, $\chi^2(1, n = 26) = 9.9$, $p < .01$.

Dual-task Experiment: Results

In the dual-task paradigm GB showed a substantially improved performance with respect to T1, but dual-task conditions still induced a severe lack of awareness. The patient did not show any omission for single ipsilesional targets in any of the conditions. The total number of trials excluded from analyses because of ocular movements, errors in reporting the letter, or in counting was 2.43%.

Contralesional omissions for unilateral versus bilateral targets. GB showed again many contralesional omissions, which were particularly high for bilateral targets under dual-task conditions. In contrast, contralesional omissions for unilateral targets were close to zero in the single task condition. The difference between uni- and bilateral trials was significant for the single task, $\chi^2(1, n = 59) = 8.93$, $p < .01$, and the visual dual-task conditions, $\chi^2(1, n = 63) = 10.69$, $p < .01$ but was not significant for the auditory dual task $\chi^2(1, n = 61) = 1.97$, $p = .2$. Thus, the performance shown by the patient allows us to conclude for the presence of both baseline extinction (in the single task) and dual-task extinction (in the visual dual task).

Contralesional omissions (extinction) for bilateral targets. The rate of left extinction increased significantly from 38.7% in the single-task condition to ceiling (96.9% of extinguished targets) in the visual dual-task condition, $\chi^2(1, n= 62) = 23.57$, $p < .001$, whereas the difference with the auditory dual-task condition (61.3% of extinguished targets) was not significant, $\chi^2(1, n = 61) = 2.77$, $p = .13$ (see Figure 3). The difference between the two dual tasks was significant, $\chi^2(1, n = 63) = 12.18$, $p < .001$, indicating a better performance in the auditory than in the visual dual task.

Performance with respect to the same tasks performed at T1 improved significantly for the auditory dual-task, $\chi^2(1, n = 63) = 15.3$, $p < .001$, but it did not change for the visual dual-task, $\chi^2(1, n = 63) = .98$, $p = 1$, and for the single-task conditions, $\chi^2(1, n = 61) = .81$, $p = .43$ (see Figure 3).

Contralesional omissions for single targets. Despite the absence of any contralesional single omission at the visual (and tactile) finger confrontation procedure, GB showed neglect (missed contralesional single targets) under dual-task conditions, that is, when her attentional resources were engaged by a concurrent and demanding task (see Figure 4). Her rate of omitted responses to single left-sided targets increased from 6.9% in the single-task condition to 64.5% in the visual dual-task condition, $\chi^2(1, n = 60) = 21.4$, $p < .001$ and to 41.9% in the auditory dual-task condition, $\chi^2(1, n = 59) = 10.32$, $p < .01$.

GB's performance in the two dual tasks was not statistically different, $\chi^2(1, n = 61) = 2.75$, $p = .13$. Performance with respect to the same tasks performed at T1 significantly improved for both the visual, $\chi^2(1, n = 59) = 12.21$, $p < .001$ and the auditory, $\chi^2(1, n = 59) = 23.09$, $p < .001$ dual-task conditions, but not for the single-task condition, $\chi^2(1, n = 61) = .12$, $p = 1$.

T4 Testing Session

This session took place 96 days after lesion onset. At the Bergego scale neither GB nor her husband reported any difficulty. Her husband reported that GB was able to take the car out from a garage and that she was able to walk alone outside the house without particular difficulties. He reported that GB tended to forget to switch off lights and gas, pointing out that this did not occur selectively for left hemispace items.[1]

Finger Confrontation Procedure

At the visual finger confrontation procedure she did not miss any single left target. She showed, however, extinction on 25% of the trials.

Dual Task: Results

GB showed a substantially improved performance with respect to T1 and T3. Only dual-task conditions induced an awareness deficit, in particular for bilateral targets.

The patient did not show any omission for single ipsilesional targets in any of the conditions. Trials excluded from analyses because of ocular movements, errors in reporting the letter, or in counting were 3.13% of the total.

Contralesional omissions for unilateral versus bilateral targets. GB showed again many contralesional omissions, in particular for bilateral targets under auditory dual-task conditions.

[1] Two weeks after T4 we went with GB to the factory where she used to work before the stroke, for an ethological observation in a different setting. There she proved to us to still be able to check metal jewels and to detect minimal impurities hardly visible to a naïve observer. In striking contrast, when leaving, she entered a wrong car placed on her left and parked to the side of the car that took her there. As in previous occasions, this error occurred while she was talking with other people on her right.

Contralesional omissions for unilateral targets were strikingly reduced. The differences between uni- and bilateral targets were significant for both visual, $\chi^2(1, n = 62) = 5.8$, $p < .05$, and auditory dual-tasks, $\chi^2(1, n = 58) = 13.53$, $p < .01$. She made no contralesional omissions for both uni- and bilateral targets in the single-task. We conclude that, at this time, GB had dual-task extinction in the absence of baseline extinction (single task).

Contralesional omissions (extinction) for bilateral targets. The rate of left extinction increased significantly from 0% in the single-task condition to 40.6% in the visual dual-task condition, $\chi^2(1, n = 64) = 16.3$, $p < .001$ and to 73.3% in the auditory dual-task condition, $\chi^2(1, n = 62) = 36.4$, $p < .001$ (see Figure 3). GB's performance in the two dual-tasks was statistically different, $\chi^2(1, n = 62) = 6.7$, $p < .05$, suggesting that her performance was better in the visual than in the auditory dual-task condition.

GB's performance with respect to the same tasks performed at T3 did not significantly improve for the auditory dual task, $\chi^2(1, n = 61) = 1$, $p = .42$, *ns*, whereas it improved for both the single-task condition, $\chi^2(1, n = 62) = 15.87$, $p < .001$ and the visual dual-task condition, $\chi^2(1, n = 64) = 23.6$, $p < .001$.

Contralesional omissions for single targets. GB again showed neglect (missed contralesional single targets) only under dual-task conditions, that is when her attentional resources were engaged by a concurrent and demanding task (see Figure 4). Her rate of missed responses to single left-sided targets changed from 0% in the single-task condition to 13.3% in the visual dual-task condition, $\chi^2(1, n = 58) = 4$, $p = .11$, *ns*, and to 24.1% in the auditory dual-task condition, $\chi^2(1, n = 56) = 8$, $p < .05$.

The difference in performance between the two dual tasks was not significant, $\chi^2(1, n = 58) = 1.28$, $p = .33$. GB's performance with respect to the same tasks performed at T3 improved significantly for the visual, $\chi^2(1, n = 61) = 16.74$, $p < .001$ but not for the auditory dual-task condition, $\chi^2(1, n = 58) = 2.16$, $p = .17$ or for the single-task condition, $\chi^2(1, n = 57) = 2$, $p = .49$, because at T3 her performance was already close to ceiling (two missed contralesional targets only). These impairments for unilateral targets are in contrast with her perfect performance at the visual finger confrontation and confirm the high(er) sensitivity of dual tasks.

Cued Detection Experiment: Results

The version with target duration of 3000 ms was readministered to GB. At this time the DD for the shortest SOA disappeared (−26 ms), whereas this invalid–valid difference was still larger for left than for right targets at the intermediate SOA (75 ms) and at the longest SOA (44 ms) (see Table 2). No significant differences between GB and the group of right brain–damaged patients reported by Friedrich et al. (1998) emerged. The mean difference between left and right targets was 38 ms in favor of targets presented within the ipsilesional hemispace.

T5 Testing Session

This session took place 161 days after lesion onset.

Ecological Observation

During the testing session the patient did not report any residual difficulty related to contralesional awareness. However, in a subsequent communication that occurred after two months from T5 (about 220 days from stroke), she reported that in some occasions she was not able to "find things" when these were placed on her left.

Finger Confrontation Procedure

At the visual finger confrontation procedure she did not miss any single left target. She showed contralesional omissions on 10% of the bilateral trials for both visual and tactile finger confrontation procedure.

Dual-Task Paradigm: Results

The pattern found at T4 persisted at T5. GB showed many contralesional omissions for bilateral targets under both dual-task conditions, whereas her performance was very good (or perfect) for the single targets and the single-task conditions. A single ipsilesional target was omitted. Trials excluded from analyses because of ocular movements or errors in reporting the letter or in counting were 5.6% of the total.

Contralesional omissions for unilateral versus bilateral targets. The difference between uni- and bilateral targets was significant for both visual, $\chi^2(1, n = 58) = 28.03$, $p < .001$, and auditory dual-task conditions, $\chi^2(1, n = 58) = 36.48$, $p < .001$. For the single-task, there were few contralesional omissions for bilateral targets (3.1%) and no contralesional omissions for unilateral targets. Dual-task extinction but not baseline extinction (single task) found at T4 thus persisted at T5.

Contralesional omissions (extinction) for bilateral targets. The rate of left extinction increased significantly from 3.1% in the single-task condition to 93.5% in both the visual and the auditory dual-task conditions, $\chi^2(1, n = 63) = 51.62$, $p < .001$ (see Figure 3).

Contralesional omissions for single targets. GB again showed neglect (missed contralesional single targets) only under dual-task (see Figure 4). Her rate of missed responses to single left-sided targets increased from 0% in the single-task condition to 25.9% in the visual dual-task condition, $\chi^2(1, n = 56) = 8.6$, $p < .01$. Also the difference with the auditory dual-task condition (14.8% of omissions) was significant $\chi^2(1, n = 56) = 4.63$, $p < .05$. The difference between the two dual tasks was instead not significant, $\chi^2(1, n = 54) = 1.03$, $p = .5$.

Discussion

The persisting contralesional awareness bias found at T5 gives us three important hints.

First, It confirms that dual-task paradigms are suitable for test–retest because they cannot be easily circumvented by the recruitment of additional resources. This characteristic is particularly relevant for rehabilitation purposes, where it is crucial that potential performance improvements found on the tests be not attributable to increased familiarity with testing materials and procedures. The second hint is that our paradigm can induce dramatically extinction also when the double finger confrontation procedure does not. The third hint is that paradigms like the one we propose might show, in the future, that neglect, although weakened, might be much more persistent over time than what it was previously thought.

Summary of case GB results. At the visual finger confrontation procedure GB showed neglect at T1, extinction at T3 and at T4, in the absence of any single contralesional missed trials from T3 through T5. In striking parallel, our single-task condition also elicited neglect at T1, extinction at T3, and no single contralesional omissions at T4 and T5. Crucially, our dual-task manipulations succeeded to induce both neglect and extinction in all testing sessions. At T5 the dual task induced an extinction rate of 90%, when the finger confrontation procedure induced only a 10% of missed contralesional stimuli at double confrontation. It is worth reiterating that the only impairment for contralesional awareness GB that did present according to standard paper-and-pencil tests occurred one month after her stroke in a single condition of a drawing subtest, and that her performance was well above the BIT diagnostic cut-off, in the absence of any contralesional omission in the standard cancellation tasks. Our approach thus seems to be a flexible and sensitive index for detecting and quantifying deficits in the postacute phase and allows to precisely monitor performance improvements over time in the chronic phase. The presence of both single and dual tasks and of unilateral and bilateral target(s) allows to focus on the more suitable index (e.g., unilateral targets under single task in the acute phase vs. bilateral targets under dual task in the more chronic phases). This also allows to circumvent floor and ceiling effects, a major obstacle for a correct and sensitive measurement of patient's performance, to date resolved in part only by the use of RT-based paradigms (e.g., cued detection).

Control Participant

The improvements of GB's awareness found with increasing time from stroke suggest that her awareness deficits are attributable to her brain damage (i.e., are a contralesional bias) and are not attributable to a rightward attentional bias induced by increased task demands (Peers, Cusack, & Duncan, 2007). One might, however, claim that her amelioration with increasing time from stroke might be attributable not to awareness improvements but to a general effect on cognitive performance, and that a moderate number of left omission under attentional load can characterize also a healthy participant. To further address this issue we tested with the same dual-task paradigm a matched control (62-year-old female) with no history of neurological disorders. Target duration (50 ms) and order of tasks were identical to those of GB.

Results

The performance of the control participant was perfect (100% accuracy) in both the single and the visual dual task. In the auditory dual task she mislocated one right target as left. This was the only error she made.

Discussion

The absence of any hint of omissions (and in particular of left omissions) in the control participant supports our interpretation that GB's deficits were attributable to contralesional awareness impairments deriving from her right hemisphere stroke. Indeed, if GB deficits were attributable to a rightward attentional bias emerging under increased demands also the matched control should have shown some deterioration for left hemispace processing.

The absence, in a matched control participant, of awareness deficits under dual-task conditions replicates our previous study (Bonato et al., 2010), where a similar attentional manipulation was implemented and further suggests that providing auditory stimuli across all conditions does not affect awareness. We do not a priori exclude the possibility to induce awareness deficits by increasing task demands also in healthy participants, but this would require, at the very least, a visual masking procedure to bring target perception near threshold.

Right Brain–Damaged Patients Group

We finally tested also a group of right brain–damaged patients, to provide a comparison with GB's performance in the postacute phase and to show that contralesional awareness deficits, as the one she presented, are common after right hemisphere strokes, whenever demanding testing procedures are adopted.

Method

Participants. We tested five patients who had a right hemisphere stroke within the last three months. None of them had visual field deficits. Four patients did not show neglect according to their BIT score, whereas one (Case 3) was below the cut-off (he scored 124). Case 3 presented several contralesional (vs. some ipsilesional) omissions in the letter cancellation task but an almost perfect performance at the finger confrontation procedure. The characteristics of the sample are reported in Table 3. All of them had moderate-to-severe motor deficits for the left hemibody[2] (see Table 3).

Testing materials and procedure. Patients were administered several paper-and-pencil neuropsychological tests. Scores at the MMSE, on each subtest of the BIT, and on each test of the ENB are shown in Table 3. Finger confrontation procedure was also implemented to check for extinction, contralesional omissions, and visual field deficits according to classic neurological examination.

Then the single and dual-task experiments were administered. Patients were tested both with individually calibrated and with fixed (i.e., the shortest, 50 ms as that of GB) target presentation time. Calibration procedure was aimed at avoiding floor and ceiling effects in extinction rate at single task. Lower and upper bounds were 50 ms and 600 ms, respectively (See Bonato et al., 2010 for a more detailed description). Individual target durations as determined by the calibration procedure are shown in Table 3. Task order was counterbalanced between participants.

[2] We managed also to test a second patient (MR, male, 71 years) who suffered an hemorrhagic right parietal stroke without any residual motor deficit. His performance at BIT was two points below the cut-off with good performance at cancellation sub tests. After 39 days from stroke he showed 100% of extinguished items across all conditions (both in the single and dual tasks). We followed him up with the dual-task experiment at 138 days from stroke and his performance did not show any extinguished double nor missed single item (accuracy 100%). We did not observe awareness impairments for contralesional hemispace. In his case neglect was spontaneously remitted.

Table 3
Summary of Demographical and Neuropsychological Characteristics for Case GB and for the Group of Patients

Case	Case GB	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	F	F	F	M	M	M
Age	63	73	73	77	85	53
Education	5	5	2	5	13	8
Days from lesion	27–161	54	24	76	40	75
Lesion site	F, I, P	BG, Th, C	Th, C	T, I, P	I, F, P	T, P
Etiology	I	H	H	I	I	H
MMSE	26	28	19	26	26	27
Double finger confrontation: Missed contralesional stimuli	75%, 65%, 25%, 10%	35%	30%	5%	95%	30%
Finger confrontation: Missed contralesional single stimuli	47%, 0%, 0%, 0%	12.5%	0%	0%	28%	18.8%
Target duration after calibration procedure (in ms)	50	600	50	600	500	500
BIT Total (cutoff = 129)	138	133	127[f]	124	130	131
BIT subtests						
Line cancellation (18–18)[a]	18–18	18–18	18–18	18–18	18–18	18–18
Letter cancellation (20–20)[a]	20–15	18–18	15–19	9–13	17–19	17–18
Star cancellation (27–27)[a]	27–27	22–24	25–26	26–27	26–26	24–27
Copying (4)[b]	3	3	3	3	2	3
Line bisection (9)[c]	9	9	ne	8	3	4
Drawing (3)[b]	1	3	3	2	1	2
ENB tests						
Digit span	5	6	4	6	6	5
Memory: immediate recall	8/28	na	2/28[d]	10/28	14/28	8/28
Memory: delayed recall	11/28	na	7/28[d]	19/28	18/28	12/28
Memory with interference (10 sec)	5/9	8/9	0/9[d]	4/9	7/9	4/9[d]
Memory with interference (30 sec)	4/9	9/9	0/9[d]	3/9	6/9	4/9
TMT[e] version A (sec)	64	125	118	180[d]	105[d]	68
TMT[e] version B (sec)	>420[d]	390[d]	ne[d]	ne[d]	295[d]	ne[d]
Token Test	5/5	5/5	5/5	5/5	4/5[d]	4/5[d]
Fluency (phonemic)	10.3	11.3	2[d]	7[d]	10	na
Abstract reasoning	6/6	2/6[d]	1/6[d]	4/6	6/6	0/6[d]
Cognitive estimation	4/5	4/5	2/5[d]	4/5	5/5	5/5
Overlapping figures	23[d]	14[d]	10[d]	25	31	11[d]
Copy of drawing	0[d] (115 sec)	0[d]	0[d]	1[d]	2	1[d]
Spontaneous drawing	2/2	2/2	1/2[d]	2/2	1/2[d]	1/2[d]
Clock drawing	1/10[d]	10/10	6/10	9.5/10	8/10	5/10[d]
Ideomotor praxis	5/6[d]	6/6	6/6	5/6[d]	5/6[d]	6/6
Motricity index (max 100, 100)[g]	100, 100	35, 48	84, 76	35, 53	73, 76	19, 43
Functional Independence Measure	124/126	62/126	98/126	50/126	71/126	81/126
Barthel Index	95/100	45/100	70/100	5/100	50/100	50/100

Note. Lesion site: F = Frontal; P = Parietal; T = Temporal; I = Insula, BG = Basal Ganglia, C = Capsula, Th = Thalamus. Etiology: I = Ischemic; H = Hemorrhagic. Finger confrontation: For GB the four values refer to performance at T1, T3, T4, and T5, respectively. For the other neuropsychological tests GB scores at T1 are reported. BIT (Behavioral Inattention Test) subtests: maximum scores are shown in brackets. ne: Not executed; na: Not administered.
[a] The two numbers refer to the scores (items marked) on each cancellation task for left and right hemispace, respectively (i.e., left–right). [b] One point is given for each task (four copying and three drawing tasks) if performance does not reveal important asymmetries. [c] Bisection of each of the three lines in the subtest is scored from 0 to 3 according to the accuracy of performance. [d] Altered performance (score < 5th percentile with respect to healthy matched controls). [e] TMT: Trail Making Test. [f] The patient did not follow the instructions in the line bisection task and thus her global performance is missing nine points for that task (adjusted global cut-off: <123). [g] Scores for upper and lower contralesional limb, respectively. Motricity index, FIM, and Barthel Index refer to performance at discharge, except for Case 3 whose scores refer to admission.

Results

Neuropsychological testing. All patients showed impaired performance at the TMT-B, and three of five patients showed impaired performance at the overlapping figures subtest of the ENB. Patients' performance at the ENB was thus compatible with the presence of subclinical neglect, emerging under difficult tasks with an important visuospatial component.

Finger confrontation procedure. Their performance at visual finger confrontation (see Table 3) showed contralesional omissions for bilateral (range 5–35%, except Case 4 at 95%) and unilateral (range 0–19%, except Case 4 at 28%) target presentation.

Dual-task experiment. Group performance was influenced by dual-task manipulations, allowing us to replicate the pattern found for GB. Below, we report the group analyses separately for the 50-ms and the custom target duration, whereas the individual performances are reported in Table 4. Case 2 data are only reported in the custom duration and not in the 50-ms group because individual calibration procedure yielded, for her, the minimal target duration (50 ms).

Contralesional omissions for unilateral versus bilateral targets. Patient group showed extinction across all tasks and target durations, as indexed by significantly higher number of contralesional omissions for bilateral than for unilateral targets (all *p*s < .05).

Contralesional omissions (extinction) for bilateral targets. For trials with *custom duration* the rate of left extinction increased significantly from 29.2% in the single-task condition to 53.2% in the visual dual-task condition, $\chi^2(1, n = 266) = 16.17$, $p < .001$

Table 4
The Individual Omission Rates for Bilateral and Unilateral Targets Presentation Are Shown Separately for Custom and Fixed (50 ms) Target Durations

Case	1		2		3		4		5	
Bilateral targets (extinction rate in %) custom duration										
Single Task vs. Visual Dual Task	0.0	6.7	**31.0**	**100**	90.9	100	**6.5**	**96.9**	**36.7**	**6.5**
Single Task vs. Auditory Dual Task	0.0	3.3	**31.0**	**100**	90.9	93.3	**6.5**	**100**	**36.7**	**100**
Visual Dual Task vs. Auditory Dual Task	6.7	3.3	100	100	100	93.3	96.9	100	**6.5**	**100**
Bilateral targets (extinction rate in %) 50-ms duration										
Single Task vs. Visual Dual Task	**3.4**	**48.3**			100	100	83.9	100	93.8	100
Single Task vs. Auditory Dual Task	**3.4**	**51.6**			100	100	83.9	96.7	93.8	100
Visual Dual Task vs. Auditory Dual Task	48.3	51.6			100	100	100.0	96.7	100	100
Single contralesional targets (omission rate in %) custom duration										
Single Task vs. Visual Dual Task	4.0	0.0	**33.3**	**100**	**6.3**	**71.9**	6.5	0.0	**39.3**	**6.5**
Single Task vs. Auditory Dual Task	4.0	10.3	**33.3**	**87.5**	**6.3**	**54.8**	6.5	15.6	39.3	58.1
Visual Dual Task vs. Auditory Dual Task	0.0	10.3	100	87.5	**71.9**	**54.8**	0.0	15.6	**6.5**	**58.1**
Single contralesional targets (omission rate in %) 50-ms duration										
Single Task vs. Visual Dual Task	**9.7**	**35.7**			90.6	35.0	54.8	14.8	84.4	95.2
Single Task vs. Auditory Dual Task	**9.7**	**37.5**			90.6	65.6	**54.8**	**20.0**	84.4	84.4
Visual Dual Task vs. Auditory Dual Task	35.7	37.5			35.0	65.6	14.8	20.0	95.2	84.4

Note. Values reported in bold index that the difference between the two conditions reported on the left is significant at $p < .05$.

(see Figure 5) and to 78.6% in the auditory dual-task condition, $\chi^2(1, n = 288) = 70.34$, $p < .001$. The difference between performance in the two dual-tasks was significant, $\chi^2(1, n = 268) = 18.8$, $p < .001$.

For the *50 ms target duration* the extinction rate increased significantly from 71.8% in the single-task condition to 84.5% in the visual dual-task condition, $\chi^2(1, n = 217) = 4.51$, $p < .05$, and to 86.7% in the auditory dual-task condition, $\chi^2(1, n = 241) = 6.5$, $p < .05$ (see Figure 5). The difference between performance in the two dual tasks was not significant, $\chi^2(1, n = 216) = .07$, $p = .84$, indicating that group performance was similar under auditory and visual dual-tasks.

Contralesional omissions for single targets. For *customized target duration* the difference between single (17.8% of omissions) and visual dual task (29.5% of omissions) was significant, $\chi^2(1, n = 278) = 6.31$, $p < .05$ (Figure 5). Also the difference between single and auditory dual-task (45.8% of omissions) was significant, $\chi^2(1, n = 293) = 29.85$, $p < .001$. The rate of omitted contralesional stimuli was higher in the auditory than in the visual dual-task condition, $\chi^2(1, n = 281) = 8.59$, $p < .01$.

For the *50 ms target duration* the group of patients did not show any difference in omissions for unilateral contralesional stimuli between the single (60.3%) and the visual dual-task conditions (42.7%), $\chi^2(1, n = 187) = .26$, $p = .64$ nor between single and

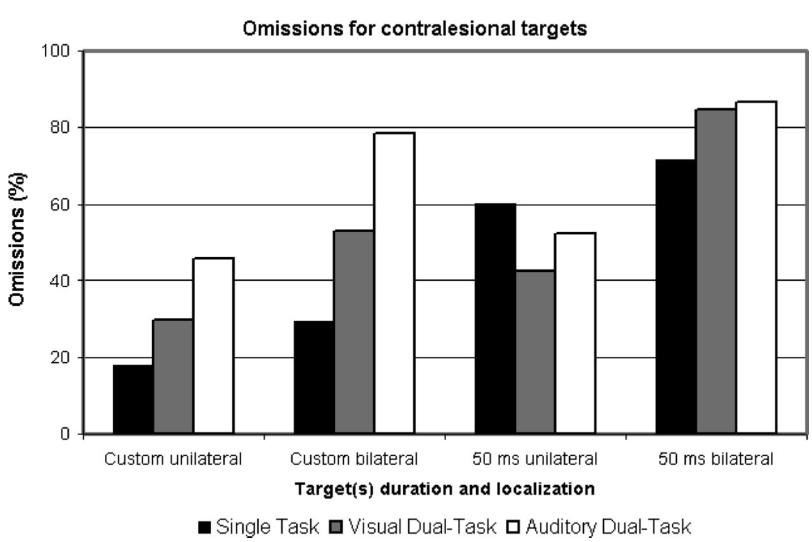

Figure 5. Right hemisphere–damaged patients group. The mean performance for the custom and the fixed (50 ms) target duration for unilateral and bilateral targets is shown.

auditory dual-tasks conditions (52.4% of omissions), $\chi^2(1, n = 228) = .11, p = .79$. Also the difference between the two dual-task conditions was not significant, $\chi^2(1, n = 167) = .045, p = .87$. Under dual task conditions "right" responses to single left targets (allochiria-like) emerged with increased task demands (1.6% in the single task, 33.3% in the visual dual-task, and 17.5% in the auditory dual-task). Although we preferred not to consider these as "proper" omissions the sum of "zero" and "right" responses for unilateral left targets was 61.9% for single task, 76% in the visual dual task and 69.8% in the auditory dual task.

Patients Group Discussion

Group performance showed a clear detrimental effect of dual tasks on contralesional awareness. These results closely resemble those found in GB, in the form of significant impairments under dual-task conditions. The version with fixed (50 ms) target duration induced even more dramatic contralesional impairments, modulated by task demands for bilateral targets only.

Inspection of individual data, however, (reported in Table 4) highlights a great individual variability in the task effect. Most of this variability seems to be related to individual baseline performance (at single task) and seems to derive from the chosen target duration.

For instance, Cases 3, 4, and 5 did not show any significant task modulation at the 50-ms duration for bilateral targets (supposedly the most sensitive condition) because their omission rate was already above 80 or 90% on the single task. However, Cases 4 and 5 showed a striking awareness impairment for auditory dual task when the target duration was calibrated for their individual threshold. Case 3 had instead severe extinction (above 90% in all conditions) even in the custom target duration version, despite a target duration as long as 600 ms and despite the absence of contralesional deficits at the finger confrontation. Quite obviously the effects of the increased task demands cannot emerge when the performance on the single task is so impaired. Bilateral target presentation seems to be by far the most sensitive condition to detect the detrimental effects of increased task demands: all patients not showing severely impaired performance on the single task (Cases 1 for the 50 ms and Cases 2, 4, and 5 for the custom duration procedure) showed a significant increase in extinction rate at individual level. Again, group data are particularly striking in showing a demand-induced modulation for the custom duration because the paradigm, when calibrated, achieved a higher sensitivity to dual-task manipulations.

We reiterate that these results, suggestive of severe albeit hidden difficulty-related contralesional awareness deficits, were obtained in four right brain–damaged patients with mild or no contralesional deficits at paper-and-pencil testing and at finger confrontation procedure. Only one patient (Case 4), although above the BIT cut-off, showed consistent extinction and neglect already at the visual finger confrontation procedure. In no cases either the BIT or the finger confrontation procedure were more sensitive than our dual-task for the detection of contralesional awareness deficits. In contrast, also in the group of patients, our dual task succeeded in eliciting a severe awareness deficit, with an average contralesional omission rate for bilateral targets above 80% in both dual-task conditions, when target duration was as short as 50 ms.

General Discussion

Increased attentional demands, generated by resource-demanding computerized dual-tasks, induced severe unawareness for the left hemispace in a right hemisphere stroke patient, GB, who showed no awareness deficits on standard cancellation tasks for neglect diagnosis, on which the patient showed errorless performance. We maintain that awareness deficits for contralesional hemispace dramatically emerge when attentionally demanding tasks are performed and compensatory strategies cannot be implemented. This occurred in GB when assessed with our dual-task paradigm and, crucially, also when she performed everyday life activities requiring parallel processing. Our study confirms that apparently spared contralesional awareness may simply reflect the general availability of attentional resources that just suffice to perform single tasks (Bonato et al., 2010). It has been suggested that a restricted general attentional capacity, which is a common finding after a large neurological lesion, might be a prerequisite for contralesional extinction (Marzi, Girelli, Natale, & Miniussi, 2001). Accordingly, it seems that our paradigm highlights a deficit of contralesional spatial awareness that emerges within a context of limited attentional resources (Husain & Rorden, 2003).

It is known that patients' performance reflects not only a failure of contralesional orienting mechanisms but also a reduction of resources that has been shown to be crucial in modulating patients' contralesional space awareness (Robertson, Mattingley, Rorden, & Driver, 1998). This robust finding, however, has not yet developed into more sensitive clinical testing or into models of awareness-attention, which should include specific attentional resources as a gate for awareness. Similarly, also the robust load-dependent contralesional impairments described in right brain–damaged patients (Eramudugolla et al., 2010; Russell et al., 2004; Vuilleumier et al., 2008; see also Ptak, Schnider, Golay, & Muri, 2007) did not result, so far, in diagnostic implementations.

Crucially here, in addition to Bonato et al. (2010), we have shown the following:

1. Impaired performance of patients in our test may parallel a deficit for contralesional hemispace in everyday life emerging under demanding (e.g., dual-task) conditions. The absence of motor impairments allowed us to ascribe GB's contralesional behavioural impairments to her neglect (i.e., without the hemiplegia confound).
2. The dual-task method is reliable for monitoring the decrease of awareness deficits over time from lesion onset. It is suitable for test–retest because it cannot be easily circumvented by compensatory strategies and it allows a precise monitoring of the symptoms evolution in time.
3. After three months from stroke a peripheral nonpredictive cued detection paradigm showed a full remission of the disengage deficit, whereas the patient was still suffering from severe awareness deficits both in everyday life and under dual-task conditions (bilateral targets).
4. Even if one would try to make cancellation tasks more demanding their diagnostic potential for peripersonal hemispace is not as high as the one showed, at least in GB, by our computer-based dual-task paradigm.
5. The attentional demands of the concurrent auditory task can be effective even when devoided of any visuospatial

nature, as was shown by the auditory dual-task condition, in which stimuli were delivered by means of earphones.

6. The presence of subclinical neglect and extinction in the post acute phase is confirmed to be all but uncommon after a right hemisphere stroke.

Paper-and-pencil tests (and sometimes only a single test) are very often adopted also to infer patients' performance in everyday life situations. We suggest that this inference might be misleading because everyday life situations are typically more demanding than these tests are and often require visuospatial orienting to occur in parallel with other tasks. Accordingly, some stroke patients may perform within normal limits on paper-and-pencil tests, while showing deficits in everyday activities (Azouvi et al., 2002), where distracters are numerous (e.g., driving) and parallel processing is often required (e.g., driving and conversing). This is a crucial point, because patients' full autonomy and proper recovery crucially imply the achievement of a good performance also in complex activities that everyday modern life requires. When, as in the case of GB, no concurrent motor deficits are present, the risk not to receive a proper diagnosis of neglect is even increased.

Resource-demanding paradigms might also be effective for a more sensitive assessment of any change occurred in patients' performance after rehabilitation of contralesional spatial awareness.

It is, indeed, possible that contradictory evidence with respect to the effectiveness of neuropsychological rehabilitation of neglect (Rousseaux, Bernati, Saj, & Kozlowski, 2006 vs. Frassinetti, Angeli, Meneghello, Avanzi, & Làdavas, 2002) derives from the use of excessively rough measures of outcome. We should strive to develop new ways to perform neuropsychological testing, aiming at being both theoretically based and clinically sensitive.

Indeed, despite the advances in imaging techniques and in knowledge about brain functioning, most of the clinical neuropsychological practice has remained unchanged within the last decades, making the disconnection between neuropsychological theories and clinical practice even more evident.

What we have shown here is that, as soon as one month after the stroke, compensatory strategies might be so effective to successfully hide neglect in cancellation and bisection tasks, that is in the two most common, and often only, tests adopted for neglect diagnosis. Case GB is both paradigmatic and paradoxical for showing the limits of current neuropsychological testing for neglect. In the absence of a resource-demanding testing paradigm, standard paper-and-pencil neuropsychological assessment would have denied the presence of clinically relevant neglect (i.e., BIT score well above the cut-off) despite the advice of the neurologist (e.g., presence of extinction at the finger confrontation) and despite the reports of the family (e.g., presence of deficits in everyday life).

The resource-demanding paradigm we are validating seems to be more sensitive than classical paper-and-pencil testing for the investigation of neglect in peripersonal space. It also seems to be more informative than the classic finger confrontation procedure, which we confirm as being a very sensitive methodology but which, although to a lesser extent with respect to paper-and-pencil tests failed to detect contralesional omissions when GB was entering in the chronic phase, where compensatory strategies are better implemented. Also the group study data are suggestive of more severe contralesional awareness deficits emerging under dual tasks with respect to the finger confrontation procedure.

The group of right hemisphere–damaged patients showed a high degree of individual variability in response to the dual-task manipulation. A larger sample study might in the future better characterize whether some patients are more sensitive to specific dual task manipulations, whether these deficits are more related to damage to specific brain areas, and, finally, how/when these deficits resolve in chronic stages after stroke.

One caveat to the eco(etho)logical approach we adopted to quantify GB's deficits in everyday life is that it does not allow to isolate what spatial components (e.g., extrapersonal vs. peripersonal vs. personal) are impaired in GB's everyday performance. These components in every day life are integrated, and most daily activities reflect the interaction of more than one of these. In summary, the use of resource-demanding paradigms (e.g., using both spatial and nonspatial tasks) can potentially play two key roles within the domain of contralesional awareness deficits. The first role relates to the study of cognitive components involved in attentional orienting: we have shown that contralesional awareness is hindered when resource-demanding tasks are performed. It would be interesting, in light of these findings, to reconsider as heterogeneous groups the samples of RBD patients without neglect described in the literature. Indeed, some of these patients can be affected by mild but disabling forms of neglect. The paradigm described here highlights the importance of unspecific cognitive resources to succeed in a visuospatial task, as if awareness would need a sufficient amount of attentional resources to operate. We suggest that it might be useful to readopt the old and somehow forgotten unspecific term "attentional resources" or even the more general "task difficulty" to account for deficits that do not allow us to use a more precise, and possibly more appropriate, definition of executive functions. This does not exclude that in the future we will be able to better characterize the "increased attentional demands" as more related, for instance, to executive functions or to multimodal attention. The "attentional resources" approach in visuospatial processing has been intensively studied in the past (e.g., Laberge & Brown, 1989; Laberge, Brown, Carter, Bash, & Hartley, 1991) but has been somehow forgotten by recent studies and, despite its high potential, dramatically lacks of clinical implementations.

The second role is more clinical and relates to the potential of these paradigms in highlighting disorders of contralesional space awareness, thus accounting for that category of patients who perform reasonably well on bedside testing but show, nonetheless, contralesional space unawareness in everyday life. Many clinical neuropsychologists know that the most difficult everyday life activities are more demanding than the paper-and-pencil tests adopted for the diagnosis of space awareness disorders. Some clinicians have proposed ecological approaches to circumvent this problem, whereas some others have proposed the use of large batteries of tests for the diagnosis of neglect syndrome in all its possible manifestations and dissociations. Although both suggestions are highly valuable, it might also be useful to adopt more demanding testing procedures.

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