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Distance-mediated spatial neglect

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Abstract

Unilateral spatial neglect (USN) is usually assessed by means of individual stimuli or single arrays of stimuli. Seldom are stimuli presented as multiple objects or in spatially separated blocks, except in some tests for object-based neglect. The distance between individual objects or blocks of stimuli in such stimuli is implicitly considered irrelevant. We report on the case of a patient, EC, who showed severe USN in his everyday behaviour, yet performed normally on standard tests for USN. Presented with stimuli in separate blocks, he performed flawlessly with 4cm gaps between blocks, yet ignored all leftward blocks of stimuli when the gap was larger than this. EC's dissociation between good performance on standard tasks and severe neglect with separate groups of stimuli, and the distance-mediated nature of his USN are novel observations with relevant theoretical and clinical implications.

Keywords: unilateral spatial neglect, distance effect, cancellation tasks, stroke.

Introduction

Unilateral Spatial Neglect (USN) is a common and disabling condition after brain damage. Several tests are used to detect its presence in clinical practice (Parton, Malhorta, & Husain, 2004) and in scientific reports (e.g., Lenggenhager, Loetscher, Kavan, Pallich, Brodtmann, Nicholls & Brugger, 2012; Viggiano, Marzi, Forni, Righi, Franceschini, & Peru, 2012); among these, cancellation tasks are reported to be the most sensitive (Azouvi, et al., 2002; Ferber & Karnath, 2001). However, remarkable differences in performance are often observed in the same patient across different tests (Halligan & Marshall, 1992) and even between different cancellation tests (Sarri, Greenwood, Kalra & Driver, 2009).

Patients with USN may commit errors according to different coordinates: for instance, patients can show either evidence of “space based” neglect with the tendency to ignore the stimuli located on the left of the viewer’s body midline or evidence of “object based” neglect with omission errors involving the left half of each visual stimulus independently of its spatial location (Walker, 1995; see early report of this condition by Gainotti & Tiacci, 1971, who labelled it “piecemeal neglect”). Most clinical tasks do not allow one to distinguish between these two forms of neglect (in both cases patients omit the stimuli on the left side of the visual array). Therefore, it has been proposed to assess patients also presenting them with two items simultaneously as separate figures (Marshall & Halligan, 1993) or in two separate blocks of stimuli (Driver & Halligan, 1991). Patients with USN have been reported who tend to ignore only stimuli of the left block whereas others omit stimuli from the left side of each block (e.g., Neppi-Mòdona et al., 2002).

The pattern of a patient performing flawlessly on standard tasks assessing USN yet neglecting left stimuli when presented as separate groups has never been reported. Moreover, the possible modulation of neglect according to the distance between separate groups of stimuli has not been investigated. Here we report on the case of a patient who was completely accurate in standard clinical tasks but ignored the left block in two-block versions of the task, whenever groups of stimuli were separated by a critical distance. This uncommon pattern of performance revealed a “space based” neglect which is highly sensitive to the distance between stimuli.

Case Report

EC is a right handed man with 5 years of education who at the time of testing was 74 year-old. He was admitted on April 2010 to the Stroke Unit of the Gallarate Hospital following a right hemisphere haemorrhagic stroke resulting in a left hemiparesis coupled with sensory deficits in his left arm and leg. He had no clinically detectable oculomotor disturbances. CT and MRI scans, performed 9 and 24 days post-stroke respectively, demonstrated a large lesion encroaching upon the parietal and temporal lobes and the insula in the right hemisphere (see Figure 1); as it is typical in haemorrhages, the lesion also damaged white matter tracts (Thiebaut de Schotten, et al., 2008) including the Internal capsule and the Arcuate fasciculus (Catani and Thiebaut de Schotten, 2008).

--- Insert Figure 1 about here ---

EC scored 13/36 on the VATAm (Della Sala, Cocchini, Beschin & Cameron, 2009) indicating moderate anosognosia for motor problem and 6/63 on the Beck Depression Inventory score (Beck, Ward, Mendelson, Mock & Erbaugh, 1961) suggesting absence of depression. His speech was fluent and he did not present with detectable language deficits. He could easily recognise familiar names and faces.

General Neuropsychological Evaluation

Fifty-one days after his stroke he underwent a neuropsychological evaluation. At the time of testing, EC had full postural control of his trunk and neck, though his weight was asymmetrically distributed with a tendency to overload the right side of his body, also when sitting. EC had visual extinction in his left visual hemifield measured by means of a clinical confrontation test, but had no sign of hemianopia or quadrantopia (score: right 10/10, left 10/10, right-left 4/10 - Bisiach, Cappa & Vallar, 1983). He performed normally in all measures of memory and executive functions, though his score in the Cognitive Estimation test was borderline (see Table 1).

--- Insert Table 1 about here ---

Assessment of Unilateral Spatial Neglect

EC's close relatives and professional carers reported that he had severe difficulties in acting on his left side of the space, consistent with perceptual and personal neglect. This is testified by scores on the Catherine Bergego Scale (CBS – Azouvi et al., 2006) whereby both his wife and his physiotherapist independently rated EC's neglect as 20/30 (CBS score ranges from 0 = no neglect to 30 = very severe neglect in daily activities). He presented symptoms of personal neglect, as he tended to ignore the left side of his body in grooming, and could not spontaneously reach his left hand with his right. EC also presented with anosognosia for his neglect, being unaware of the problems observed by his carers (CBS own rating: 5/30). EC usually kept his gaze fixed to the right, and frequently bumped into doors with the left part of his wheelchair.

At odds with his daily behaviour, he scored normally on 13 out of 15 clinical tests assessing visual neglect (see Table 2); though in all tests he performed from the right to the left. It is noteworthy that EC performed flawlessly in all the standard cancellation tasks. However, he showed space-based neglect in a two-block version of the "Letter Cancellation" but not in the two-block version of the "Line Cancellation" test. This difference might have been related to the different stimulus material (verbal vs. non-verbal), or simply to the distance between the two blocks in these two tests. In the Line Cancellation, presented on an A4 sheet of paper, the distance between the two blocks was 4 cm, whereas in the Letter Cancellation, presented on an A3 sheet, the distance was 11cm. We aimed at investigating the influence of the inter-block separation more systematically.

---Table 2 about here---

Experimental Tests

To assess whether the distance between blocks could account for the discrepancy observed in the two-block cancellation tasks, we varied the distance between blocks, using separations of 4, 8 and 11cm for each stimulus type (lines and letters). In addition, we presented the material in two or four blocks. The four blocks condition was introduced to assess whether the pattern observed in the two blocks condition was specific to midline crossing. The materials were modified versions of the original tests, presented on white sheets of paper glued together. Blocks were presented with no frame and each block occupied an area of 10x19cm for lines (each line 2.5cm) and 13.5x10cm for letters (each letter 4mm). Figures 2 and 3 incorporate depictions of the spatial layout, for two and four block versions respectively together with the outcome from the assessment.

We aimed additionally to test whether the neglect of the left block of stimuli was driven by spatial separation, or by the perceptual grouping of the blocks as separate objects. To promote stronger perceptual grouping of individual blocks, we adopted a strategy from Driver and Halligan (1991), presenting each of the blocks in a different colour. This was done first by using blocks of stimuli printed in colour, and secondly by presenting the original stimulus materials with each block covered by a coloured overlay (the patient used a black marker pen to complete the task in this condition. The colours used were red and green when two blocks were presented, and red, green, yellow and blue when four blocks were presented.

Overall, each stimulus type (lines or letters) was presented in each of three colour conditions (black print, coloured print, coloured overlays), in each of six spatial configurations (two or four blocks, each with 4, 8 or 11 cm inter-block separation), for a total of 36 cancellation assessments. The assessments were spread over multiple sessions within the same day, and the different conditions were intermingled.

--- Figures 2 and 3 about here---

From Figures 2 and 3, it is clear that EC's region of neglect depended upon the distance between the blocks. When this distance exceeded 4cm, he was unable to heed the items on the left side. Moreover, in the majority of the conditions with four blocks, he appeared anchored to the right-most block, even when the distance between blocks was 4cm. It would appear that EC's neglect is critically dependent upon the separation between stimuli, and that the largest inter-stimulus distance that he can traverse may, if anything, decrease when working in right space.

The distance-dependence of EC's neglect was further supported by additional tests using 10 objects (glue, scissor, rubber, pencil, glasses, watch, stamp, sharpener, and lipstick). Two blocks, each encompassing 67x44cm and containing 5 objects, were presented using five different distances between them (2, 8, 10, 11 and 20 cm). On each occasion, EC was asked to name and reach for all the objects. His reading of two columns of text, and copying of two flowers of 3.3x2cm in size (Halligan & Marshall, 1993) were also tested with blocks at varying distances. The results of these additional assessments are summarised in Table 3.

--- Table 3 about here ---

As Table 3 shows, EC neglected all the left sided objects when blocks were separated by 10cm or more. In the test of prose reading, he ignored the left column of two independent texts even

when the distance between them was only 4 cm. Finally, his copying was flawless when the two flowers were separated by only 3cm (as in the original test from Marshall & Halligan, 1993); but when the separation was increased to 10cm he ignored the left flower entirely.

Conclusions

Across various stimuli, including lines, words, objects, texts and pictures, the distribution of EC's neglect was modulated dramatically by the distance between stimulus blocks. EC presented severe neglect when the left sided stimuli were separated by more than 4cm, with complete inattention to all stimuli except those in the rightmost block. When there was no discontinuity between left and right stimuli, as in standard cancellation tasks, EC succeeded in exploring the whole visual array performing from right to left, across the midline. Similarly, EC's was able to cross the midline only when the two blocks were presented at the closest distance (4cm). In contrast, with larger gaps between the blocks he always failed to attend to stimuli on the left side. This pattern of spared and impaired performances is unique in the copious neglect literature.

This novel pattern is not fully accounted for by the idea that neglect is as egocentric gradient of impairment, with progressively less attention available at increasingly leftward locations (Kinsbourne, 1993; Driver & Pouget, 2000). On the contrary, EC attended or neglected items *in exactly the same egocentric location* under different stimulus conditions (see Figure 3). A modified proposal would be that an egocentric gradient of attention in EC was distributed relative to the task-relevant stimulation, rather than egocentric space *per se* (Driver & Pouget, 2000). In our design, when the spatial separation between blocks was increased, the rightmost block moved further rightward so that the other blocks were *relatively* more leftward, perhaps receiving less attention as a result. However, even a *stimulus-relative* egocentric gradient of attention would not account for the abrupt all-or-nothing nature of EC's attention to each stimulus block. That is, it would not explain the apparent existence of a critical inter-stimulus distance that barred further leftward exploration.

EC performed as if he had a spatially-restricted span of attention, so that, scanning from right to left, he could attend to the next stimulus on the left only when it was close enough, otherwise his exploration ground to a halt. This is compatible with the existence of a "magnetic attraction" to the right-sided stimuli (De Renzi, Gentilini, Faglioni & Barbieri, 1989; Mark, Kooistra & Heilman, 1988), with a residual ability to disengage attention and explore further leftward only when a leftward candidate stimulus is sufficiently close to the current focus of

attention. Thus, with closely adjacent objects, EC could eventually achieve a complete exploration of the display; but when a large enough inter-stimulus gap was interposed, his attention could not bridge the empty space without being recaptured by a right-sided item.

This effect of inter-stimulus distance was, if anything, more evident when EC was tested with four blocks. In four of six instances he only attended to the rightmost block even at the shortest (4cm) distance between the blocks. It appeared as if the more rightwards EC had to search, the less likely he was to move his attention leftwards (Posner, Walker, Friedrich & Rafal, 1984; Bisiach, Geminiani, Berti & Rusconi, 1990), a phenomenon which has been observed before in line bisection tasks. For example, Bisiach, Bulgarelli, Sterzi and Vallar (1983) reported on case RG who behaved as if his deduced left subjective endpoint was progressively misplaced rightwards as the length of the lines increased, as if he was more and more anchored to the right end.

It is not rare in clinical practice to observe patients with USN who learn to compensate for their deficits when performing of-the-shelves paper-and-pencil tests (e.g., Cantagallo & Della Sala, 1998), but who return to show clear signs of neglect once they are presented with novel, unexpected situations. This novelty effect in USN (Bartolomeo, 1997), which is clinically very relevant (Bartolomeo, 2000), has been described (e.g., Campbell & Oxbury, 1976; Mattingley, Bradshaw, Bradshaw & Nettleton, 1994; Bonato, Priftis, Marenzi, Umiltà & Zorzi, 2010) but it still little explored. EC was not tested formally for the presence of USN in the acute stages of his disease, therefore it is well possible that EC is one of these "recovered" patients (Bartolomeo, 1997) who presented with clear signs of USN subsequently fading when tested with standard procedures. A hint supporting this hypothesis comes from the analysis of his performance in cancellation tasks, whereby he tended to start from the right side of the sheet (whereas normal controls typically start from the left side, see Bartolomeo, D'Erme & Gainotti, 1994), showing signs of subclinical USN (Colombo, De Renzi & Faglioni, 1976). However, the fact remains that, when formally assessed, EC presented with an unexpected pattern, and his neglect was exposed only by test material presented in spatially-separated blocks. His behaviour is compatible with a diagnosis of space-based neglect, possibly due to a reduced focus of attention, which requires stimulus continuity or closeness for accurate performance.

This pattern is unusual and theoretically challenging, and also of clinical relevance. EC showed severe left visual neglect in daily activities but almost none in formal assessment. This exposes limitations in the way that neglect is usually assessed. Had EC been tested only with the standard format of the tests, he would have been considered exempt from neglect. Manipulating distance allows us to reconcile the severe neglect observed by his carers and his good performance

on formal tests. It is worth noting that in everyday life items tend to be more distant from one another than in clinical test batteries.

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Table 1
EC's General Neuropsychological Examination scores adjusted for age and education.

Test (score range)	EC's score [adjusted for age and education]	Cut off score
- Verbal abstract reasoning (0-60) ^a	45	32
- Token Test (0-36) ^a	36	29
- Digit Span ^a	4.5	3.5
- Prose Memory (0-28) ^b	15.5	7.5
- Cognitive Estimation Test accuracy (40-0) ^c bizarre (20-0)	18.97* 5*	18 4
- Weigl Test (0-15) ^a	10.25	4.25
- Frontal Assessment Battery (0-18) ^d	15.5	3.4
- Wisconsin Card Sorting Task ^e Total score (128-0) Perseverative answers (128-0) Non perseverative errors (128-0)	62.8 23.6 12.6	90.6 42.7 30.0

Normative data from: a) Spinnler and Tognoni, 1987; b) Novelli et al., 1986; c) Della Sala et al., 2003; d) Apollonio et al., 2005; e) Laiacona et al., 2000. *score below cut off.

Table 2
EC's performance on 16 tests assessing neglect

Space-based tests	Left side		Right side		Neglect
- Star Cancellation ^a	27/27		27/27		-
- Line Cancellation ^a	18/18		18/18		-
- Letter Cancellation ^b	53/53		51/51		-
- OTA test ^c	10/10		9/10		-
- Description of a complex scene ^d	6/10		4/10		-
- Copy of a vase ^e	50/50		50/50		-
- Copy of geometrical pictures ^f	3/3		3/3		-
- Reading words in the centre ^g	33/35		33/35		-
- Reading words in the left ^g	34/35		34/35		-
- Reading words in the right ^g	34/35		34/35		-
- Five-element copy ^h	3/5		4/5		+*
- Lines Bisection ^a	-5 mm		-15 mm		-
Object-based tests					
	Left side		Right side		
	Left	Right	Left	Right	
- Copy two flowers ^e	25/25	25/25	25/25	25/25	-
- Two block Line Cancellation ⁱ	10/10	10/10	10/10	10/10	-
- Two block Letter Cancellation ^g	0/27	0/27	27/27	27/27	+

+ presence of neglect, - absence of neglect

a) Wilson et al., 1987 ; Spinazzola et al., 2010; b) Diller et al., 1974; c) Ota et al., 2001; d) Cocchini et al., 1999 (the figure used was a city traffic scene with ten obvious elements on each side; a performance would be considered as sign of USN if the number of elements reported from the right side compared to those copied from the left would exceed three; e) Halligan and Marshall, 1993; f) Spinnler and Tognoni, 1987; g) Own test; h) Gainotti et al., 1972, scoring according to Mancini et al., 2011, subdivided in L and R; * EC neglected a full item on the left side, and the left half of a right sided item); i) Driver and Halligan, 1991.

Table 3

EC's scores on non-cancellation tasks (correct detection), with varying distances between blocks.

	Left space	Right space
Naming Objects (N=5)		
2cm	5	5
8cm	5	5
10cm	0	5
11cm	0	5
20cm	0	5
Prose reading (1 text, 11 lines)		
4cm	10	10
8cm	0	10
Prose reading (2 texts, 11 lines)		
4cm	0	10
8cm	0	11
Copying two flowers		
3cm	100%	100%
10cm	0	100%

Only the whole target detection is considered, independently of the quality of the response (oral paraphasias, paralexical errors, apraxic reproductions are not taken in account).

Figures Captions

Figure 1. Reconstruction of the area of lesion (MRICro) at 24 days post-stroke.

Figure 2. EC's performance of two-block cancellation of lines and letters. The horizontal extents of the blocks, and the separations between them, are scaled in proportion to the stimuli as presented. Within each stimulus block, the three values represent, from top-to-bottom, the percentage of targets cancelled for the black print, coloured print and coloured overlay versions of the task respectively. For lines, the percentage is from 25 stimuli per block; from letters, it is from 54.

Figure 3. EC's performance of four-block cancellation of lines and letters. The horizontal extents of the blocks, and the separations between them, are scaled in proportion to the stimuli as presented. Within each stimulus block, the three values represent, from top-to-bottom, the percentage of targets cancelled for the black print, coloured print and coloured overlay versions of the task respectively. For lines, the percentage is from 25 stimuli per block; from letters, it is from 54.

Fig. 1



Fig. 2

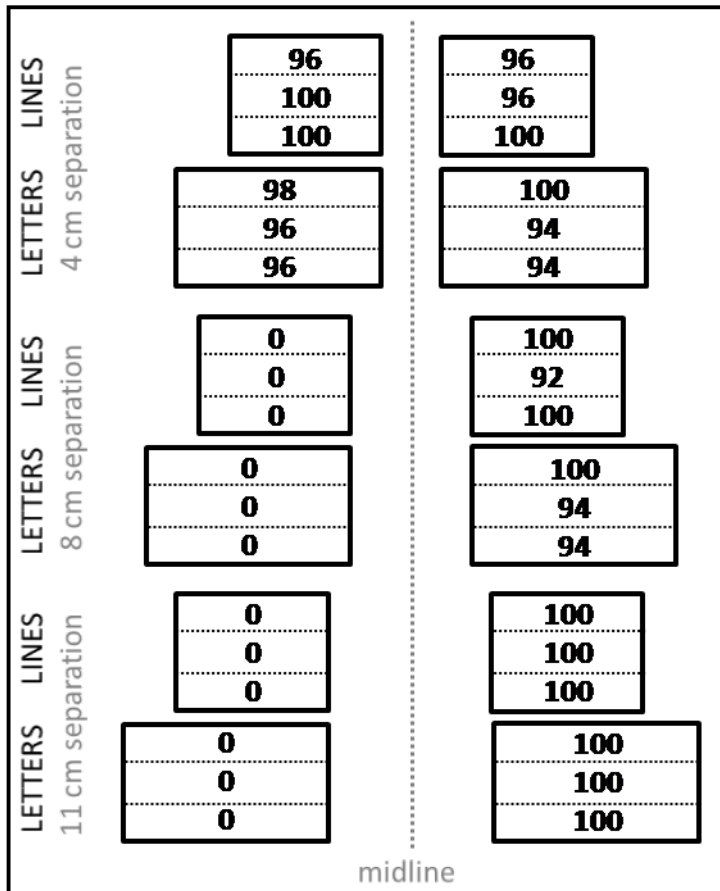


Fig. 3

