



## Letter to the Editor

# Bilateral neglect after bihemispheric strokes

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Spatial neglect is the failure to attend, explore, and act upon the contralesional hemispace after unilateral brain lesion. Lesions associated with neglect are most commonly localised in the territory of the right middle cerebral artery (MCA), but neglect may also occur after left MCA stroke (Parton et al., 2004; Ringman et al., 2004). A previous report described unilateral neglect remission after two sequential MCA strokes involving the right parietal cortex and the left frontal eye field within 10 days (Vuilleumier et al., 1996). Here we describe the case of a patient displaying bilateral neglect for the excentric space after a right MCA stroke involving subcortical structures with the inferior fronto-occipital fasciculus and a subsequent left MCA stroke involving the posterior parietal cortex within 24 h. These observations are consistent with animal models of neglect and underline the importance of both chronological factors and lesion location for the behavioural outcome after subsequent, bilateral brain lesions within an extended attentional network.

## 1. Case report

The 67 years old, right-handed patient was hospitalised following sudden weakness of the left side. Clinical examination on the stroke unit revealed left-sided neglect, rightward conjugate eye deviation and a left sensory-motor hemisindrome. Magnetic resonance imaging (MRI) revealed acute ischaemia of the right insula, crus anterior of the internal capsule, anterior part of the putamen, head of the nucleus

caudatus, and precentral gyrus. Diffusion tensor imaging (DTI) (Basser et al., 2000) revealed a clear-cut disruption of the right inferior fronto-occipital fasciculus (IFOF). Conversely, neither the left nor the right superior longitudinal fasciculi (SLF) were disconnected. The next day, the patient was found in agitated state and presented with aphasia. Moreover, he displayed right-sided neglect with difficulty to orient gaze and head towards the right space and respond to right-sided stimuli. A second MRI confirmed new ischaemic lesions in the left angular and postcentral gyrus (Fig. 1A and B).

Eleven days later, the patient was transferred to the neuro-rehabilitation unit and neuropsychological evaluation became possible (see Section 2, *Neuropsychological assessment*). Clinical investigation on the neurorehabilitation unit revealed left sensory-motor hemisindrome, mild aphasia (non-fluent aphasia with anomia and initially speech apraxia, but well conserved comprehension for simple everyday speech), and spatial neglect for both left and right space with difficulties to orient, act upon, and respond to stimuli presented in the horizontal peripheral visual field. The patient was unaware of his deficits, bumped into objects, and ignored people in both left and right excentric space. Unlike previous case reports describing simultaneous, extensive lesions of parietal or occipito-parietal areas of both hemispheres (Kase et al., 1977; Wilson et al., 2005), the patient did not show a Balint's syndrome or important spatial orientation impairments.

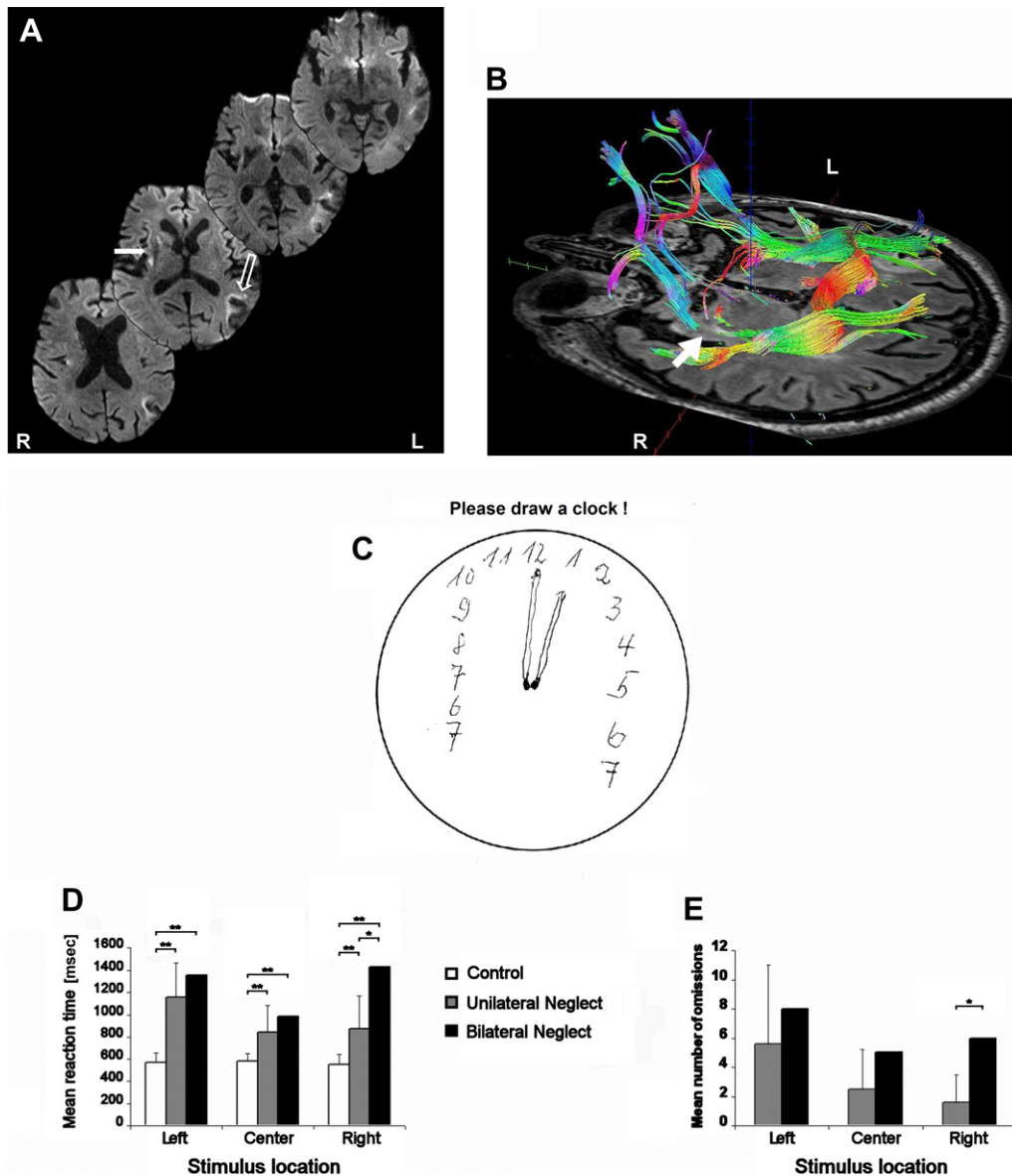
Neglect resolved within 2 months and visual field perimetry (Octopus Perimetry, G2 program, and Goldman Kinetic Perimetry with marker III/3e; Octopus Perimeter 101,

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**Fig. 1** – (A, B) MRI (T2) (A) and DTI (B) of the patient with bilateral neglect. Filled arrows indicate the right-hemispheric subcortical damage, disrupting the IFOF. The empty arrow indicates the left-hemispheric cortical lesion. R = right, L = left. (C) Graphical production of the patient in the Clock Drawing Task, demonstrating bilateral spatial compression. (D, E) Mean reaction times (D) and mean number of omissions (E) in the TAP-Neglect test – over three equal, vertical subdivisions of the screen – of the patient with bilateral neglect, the group of patients with unilateral left neglect, and the group of healthy controls (no omissions). Error bars depict SD. Significant differences ( $*p < .05$ ;  $**p < .01$ ) were assessed by single-case adapted t-tests (between the patient and the two groups) (Crawford and Howell, 1998), or by Mann–Whitney U tests (between the two groups).

Haag-Streit International, Koeniz, Switzerland) revealed no visual field deficits. There was no visual extinction.

## 2. Neuropsychological assessment

In the Clock Drawing Task, the patient demonstrated bilateral spatial compression (Fig. 1C). In the Bells Test (Gauthier et al., 1989), he omitted three targets on each side (three bells in columns one and two; three bells in columns six and seven).

The pattern of omissions was symmetric, the Centre of Cancellation (CoC) score being equal to .006 (Rorden and Karnath, 2010). In the PVT (subtask of the Vienna Test System, Schuhfried GmbH, Mödling, Austria), the patient had to react to left- and right-sided light bands moving from the periphery to the centre of the visual field, simultaneously performing a central tracking task. He demonstrated considerably slowed reaction times to both right- and left-sided stimuli (left:  $m = 3.96$  sec, percentile 4; right:  $m = 4.90$  sec, percentile 2). Reaction times and omissions in the TAP-Neglect test (subtask

of the Test for Attentional Performance, Zimmermann & Fimm, Psytest, Herzogenrath, Germany) were evaluated over three equal, vertical subdivisions of the screen. The patient had to react to flickering stimuli appearing at random positions among steady distractors, while keeping central fixation. Since the patient suffered from a left-sided sensory-motor hemisindrome, only testing with the right hand was possible. Results of the patient, 10 patients of comparable age with left neglect after unilateral, right-sided brain lesion [four men, m age = 66 years, standard deviation (SD) = 7.53 years], and 10 healthy controls of comparable age (four men, m age = 71 years, SD = 3.44 years) are depicted in Fig. 1D and E. Demographic and clinical data of the 10 patients with left-sided unilateral neglect are provided in Table 1. The patient had a comparably poor performance for left-sided and central stimuli as patients with left-sided neglect. However, he additionally had a significantly poorer performance for right-sided stimuli than patients with left-sided neglect.

The performance in the Line Bisection Task<sup>1</sup> was normal (m relative deviation = .4%).

### 3. Discussion

We describe a patient who displayed excentric bilateral neglect following a right MCA stroke involving subcortical structures with the IFOF and a subsequent left MCA stroke involving the posterior parietal cortex. Until now, only unilateral neglect has been described after a lesion of the above-mentioned regions (Buxbaum et al., 2004; Karnath et al., 2009; Urbanski et al., 2008).

Pathological horizontal shifts of visual attention after brain lesions may be interpreted within the interhemispheric rivalry model (Kinsbourne, 1987). This states that both hemispheres compete to direct visual attention towards the contralateral space exerting reciprocal interhemispheric inhibition. A lesion of one hemisphere results in interhemispheric imbalance with a pathological hyperactivity of the undamaged hemisphere and an ipsilesional shift of visual attention. Subsequent damage of the other hemisphere should result in a restoration of interhemispheric balance and in a reorientation of visual attention towards the centre. Evidence for this model in humans comes from a clinical observation in a patient who suffered two sequential, bihemispheric strokes (Vuilleumier et al., 1996). The first stroke occurred in the region of the right parietal cortex and provoked severe left hemispacial neglect. After a second, left-hemispheric stroke in the region of the frontal eye field, the neglect completely remitted.

In the present report, we show that bihemispheric strokes may not only result in a new interhemispheric balance with reorientation of visual attention towards the centre, but also

<sup>1</sup> Twenty lines with lengths varying between 12.2 cm and 21.6 cm were presented on a landscape DIN A4 paper sheet, with the centre aligned with the patient's sagittal body axis. Lines 1 and 20 (uppermost and lowermost) were used as practice trials. The lines were 1 mm thick, were separated to each other by 1 cm on the vertical axis, and were pseudo-randomly located on the horizontal axis over the whole width of the paper sheet.

**Table 1 – Demographic and clinical data of the patients with left-sided unilateral neglect.**

Sex	Age	Aetiology	Lesion <sup>a</sup> (only right-hemispheric lesions)	CoC Score Bells Test <sup>b</sup>	Relative bisection bias [%]	Clock Drawing Task – Score <sup>c</sup>	PVT			
							Omitted targets left	Mean RT left [s] <sup>d</sup>	Omitted targets right	Mean RT right [s] <sup>d</sup>
w	67	Ischaemia	front, op, temp	.089	9.21	0	5.26**	0	1.6	
m	68	Ischaemia	BG	.019	n/a	1L	n/a	n/a	n/a	
w	67	Ischaemia	front, op, temp	.015	13.44	2	3.86**	0	1.9	
w	68	Haemorrhage	par, temp	.115	14.65	1L	n/a	n/a	n/a	
w	70	Ischaemia	par, temp	.037	14.4	0	5.94**	0	1.89	
m	68	Ischaemia	par, temp	.219	-6.38	0	7.8**	2	3.68*	
m	71	Haemorrhage	par, temp	.404	10.32	0	6.11**	0	1.74	
w	72	Haemorrhage	BG	.704	64.92	2L	n/a	n/a	n/a	
m	46	Ischaemia	temp	n/a	n/a	1L	2.92*	0	2.32	
w	68	Haemorrhage	BG	n/a	-2.7	0	6.93**	0	1.05	

n/a = not available.

a Lesion location (areas involved): BG = basal ganglia; front = frontal cortex; op = operculum; par = parietal cortex; temp = temporal cortex.

b CoC Score according to Rorden and Karnath (2010) in the Bells Test (Gauthier et al., 1989).

c Performance in the Clock Drawing Task was scored as: 0 = intact; 1L = distorted left side; 2L = distorted right side; 1R = flagrant omission(s) on the left side; 2R = flagrant omission(s) on the right side.

d PVT, mean reaction time: \*borderline performance; \*\*impaired performance (based on percent ranges, cut-off value of 15, according to Heaton et al., 2004).

in neglect of excentric bilateral space. The attentional reorientation towards the visual field centre after two sequential, bihemispheric strokes was indeed similar in both our case report and in the one by Vuilleumier et al. (1996). However, in the latter case no bilateral neglect for excentric stimuli was described. Two possible mechanisms may account – alone or in conjunction – for this disparity. The first mechanism may involve chronological factors. In our case, both left- and right-hemispheric strokes occurred within 24 h. In the case described by Vuilleumier et al. (1996), the interval between both strokes was 10 days. Hence, the evolution of neuronal plastic changes due to the interhemispheric imbalance postulated by Kinsbourne (1987) may be different in our and Vuilleumier et al.'s (1996) case. The second mechanism may concern the localisation of the two strokes. In the present case, the first, right-hemispheric stroke was mainly subcortical, resulting in a disconnection of the IFOF. The subsequent, left-hemispheric stroke involved the parietal cortex, i.e., angular and post-central gyrus. In the case described by Vuilleumier et al. (1996), the right parietal and left frontal cortex were involved. One could thus hypothesize that the consequences of interhemispheric imbalance are different whether cortical or subcortical structures including fibre tracts are damaged. This hypothesis is supported by the functional–anatomical model of attention developed in neglect patients by Corbetta et al. (2005), postulating both a ventral and a dorsal system with different attentional properties. In our case, the location of the right-hemispheric lesion is relatively ventral and the location of the left-hemispheric lesion is rather dorsal. Thus, different dorsal and ventral attentional mechanisms may have been implicated.

The findings described here – to the best of our knowledge – for the first time in humans have been previously observed in an animal model of neglect. In the cat, the deactivation of the right visuoparietal cortex leads to a rightward shift of visual attention. However, the simultaneous deactivation of both the right and the left visuoparietal cortex provokes an attentional orientation towards the visual field centre with a bilateral attentional impairment in both the left and the right visual field periphery (see for a review Payne and Rushmore, 2004; Lomber and Payne, 1996; Payne et al., 1996). The findings in the cat model support the significance of both chronological factors and lesion localisation, as previously discussed. For instance, a sequential deactivation of the posterior-middle suprasylvian sulcal cortex after a lesion of the contralateral homologue area led to an attentional reorientation towards the visual field centre with recovery of neglect in peripheral visual locations. Interestingly, the patterns of compensation after bilateral deactivation seem to be different for static and moving stimuli, the detection of the latter being better remitted than the former (Payne and Rushmore, 2004). This may explain why the performance of our patient was not homogeneous over the administered tests, which had partly static and partly dynamic stimuli. However, the parallels between the cat model and the data obtained in humans must be regarded with some caution. In fact, the excentricities of the stimuli used to test the animals in the above-mentioned experiments are larger than the ones usually applied in clinical settings for the assessment of spatial neglect in humans.

As an alternative interpretation, one might claim that a widespread, bilateral disorder of spatial attention is responsible for our observations, in accordance with the predictions of other models of spatial attention distribution after bilateral brain damage (e.g., Bisiach and Vallar, 2000; Mesulam, 2002). The patient with bilateral brain damage shows slower latencies and more errors than patients with unilateral neglect in all three subdivisions of the screen. However, these differences are statistically significant only for right-sided stimuli, i.e., left-sided and central stimuli were similarly processed by the patient with bilateral brain lesions and the patients with unilateral neglect. This speaks against a general breakdown of spatial attention distribution and underlines the bilateral neglect characteristics. The same can be stated for the clinical clock drawing performance.

The present report shows that bilateral lesions of the cortical and subcortical network guiding visuospatial attention may not only result in neglect remission (Vuilleumier et al., 1996), widespread impairment of spatial attention (Bisiach and Vallar, 2000; Mesulam, 2002), left neglect (Heilman et al., 1993), right neglect (Weintraub et al., 1996), or vertical neglect (Rapcsak et al., 1988; Shelton et al., 1990), but also in bilateral neglect. Chronological factors (i.e., the interval between strokes) and lesion location may play a major role in the behavioural outcome.

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