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Neural correlates of somatosensory processing in patients with neglect

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Abstract. *Purpose*: Recent evidence from neuroimaging studies using visual tasks suggests that the right superior parietal cortex plays a pivotal role for the recovery of neglect. Importantly, neglect-related deficits are not limited to the visual system and have a rather multimodal nature. We employed somatosensory stimulation in patients with neglect in order to analyze activity changes in networks that are presumably associated with this condition.

Methods: Eleven chronic neglect patients with right hemispherical stroke were investigated with a fMRI paradigm in which the affected and unaffected hands were passively moved.

Results: Brain activation was correlated with the performance in clinical neglect tests. Significant positive correlations with brain activation were found for the lesion duration, the performance in bells and letter cancellation tests and the line bisection test. These activated areas formed a distributed pattern in the right superior parietal cortex.

Conclusions: The results suggest a shared representation of visual and somatosensory networks in the right superior parietal cortex in patients with right hemispherical strokes and neglect. The spatial pattern of activity in the superior parietal cortex points out to a different representation of changes related to lesion duration and neglect.

Keywords: Neglect, fMRI, recovery of function, somatosensory processing, passive movement, superior parietal lobe

1. Introduction

Patients exhibiting neglect demonstrate a variety of symptoms associated with reduced attention or perception within the contralesional space and side of the body. These deficits can result from lesions in different cerebral regions. In fact, neglect symptoms were documented after lesions in ventral frontal and inferior parietal cortical areas as well as the basal ganglia (Damasio et al., 1980; Caplan et al., 1990; Husain and Kennard, 1996; Weiller et al., 1996). Previous work tried to identify a "core region" responsible for neglect. The inferior parietal lobe (Heilman et al., 1985; Mort et al., 2003) or the neighboring superior temporal gyrus (Karnath et al., 2004) have been suggested to be a good candidate. Nevertheless, the fact that lesions at different locations can cause neglect symptoms rather suggests that a dysfunction of a broad fronto-parietal network including the basal ganglia might underlie neglect. Several studies showed that

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subcortical infarctions can cause hypometabolism in these regions (Fiorelli et al., 1991; von Giesen et al., 1994). It has therefore recently been suggested that neglect symptoms are associated to activity and connectivity changes within this fronto-parietal attention network (Corbetta et al., 2005).

Furthermore, within the framework of the fronto-parietal attention network a ventral and a dorsal part have been described (Corbetta et al., 2005). The bilateral dorsal part including the superior parietal lobule and the frontal eye field is active during goal-directed stimulus- and responses selection, in spatial attention and visuomotor control of eye-hand movements (Astafiev et al., 2003; Kincade et al., 2005). The ventral frontal cortex and the temporo-parietal junction form the ventral part that redirects the dorsal network to novel and behaviorally relevant stimuli (Thiebaut de Schotten et al., 2005). The attention deficits observed in neglect could arise from structural or functional dysfunction of either part or both parts of the attention network.

Importantly, neglect symptoms are subject to changes across time, in most of the cases leading to an improvement of function from the acute to the chronic stage. Only few imaging studies so far have investigated the neural basis of recovery in neglect. Pizzamiglio and colleagues showed in a PET study that after recovery the activation during a visual search task in the right superior parietal cortex and precuneus was considerably higher (Pizzamiglio et al., 1998). Consistent with this finding Corbetta and colleagues described in a longitudinal study an initial increased activation in early stages after stroke in the left superior parietal cortex (SPL) during a Posner-type (Posner et al., 1984) visual attention task and a shift of the increased activation to the right SPL after recovery (Corbetta et al., 2005). Thus, the connectivity between left and right SPL appears to play an important role.

Most studies typically employed visual tasks to investigate the neural basis of neglect. However, not only visual but multisensory input processing is disturbed in neglect. Recently, evidence has been provided that the entire spatial representation is shifted (mostly to the right) regardless of the type of input (Driver and Vuilleumier, 2001; Karnath and Dieterich, 2006; Grandjean et al., 2008). In neglect patients the processing of multisensory input appears to have a systematical error that leads to an ipsilesional shift of orientation and also of spontaneous explorative movements to the ipsilesional side (Himmelbach and Karnath, 2003). Several studies made therapeutical use of the multisensory nature of neglect and showed a substantial reduction of neglect symptoms by employing different sensory stimulations of peripheral pathways contributing to higher-order representations of space, such as proprioceptive-kinaesthetic stimuli (Ladavas et al., 1997; Frassinetti et al., 2001; Eskes et al., 2003), visual stimuli (Harvey et al., 2003; Thimm et al., 2009), vestibular stimuli (Bisiach et al., 1991) and somatosensory input (Lafosse et al., 2003). However, it is still unclear, weather the previously shown pattern of recovery from neglect (Corbetta et al., 2005) is specific for visual tasks, or also applies to other modalities such as somatosensory input.

To test this hypothesis we used the passive movement of the hand as a sensorymotor task, which presents a strong proprioceptive-kinaesthetic stimulus that is mostly independent of the concurrent paresis. Furthermore, passive movement activates the inferior parietal lobe (Weiller et al., 1996; Nelles et al., 1999; Leonhardt et al., 2001) and the superior parietal lobe (Reddy et al., 2002), which also enables us to investigate neglect specific changes in the dorsal or ventral part of the attention network.

2. Methods

2.1. Subjects

Thirteen patients aged between 53 and 71 years (mean $\pm$ SD: 65.1 ± 5.2; five female, eight male) were included. The study was performed in a rehabilitation hospital where all patients underwent standard rehabilitation therapy. All participants had given their written informed consent before the experiments, and the Ethical Committee of the University of Konstanz had approved the study. The fMRI experiment was performed following the principles and guidelines of the Declaration of Helsinki (1975).

All patients showed evidence of a rightward attentional bias and consequent left inattention and were positive in standard neuropsychological testing concerning visual neglect. Due to intolerable artifact in fMRI data 2 patients were excluded from analysis (P05 and P12). All residual eleven patients had right cerebral lesions; seven had suffered an ischemic, four patients an hemorrhagic stroke. Mean duration between the stroke onset and the examination date was 21.3 ± 34.9 (mean $\pm$ SD) weeks, minimum 2 weeks and maximum 115 weeks. All patients were right-handed according the *Oldfield Handedness* Inventory (Oldfield, 1971).

Table 1
Clinical data

	Age	Sex	Time since lesion (weeks)	Ethiology	Lesion location	Visual field defect	Extinction	Sensory deficit score
P1	64	M	8	Infarct	F,T,P,I,BG	left lower quadrant	v,t,a	2
P2	65	F	4	Infarct	F,T,P,I,BG	No	t	3
P3	67	M	4	Infarct	T,O,I,BG	No	v	0
P4	71	F	115	Infarct	T,O,F,I,BG	left lower quadrant	v,t,a	4
P6	68	M	4	Hemorrhage	F,P	No	t	0
P7	53	F	7	Infarct	F,I	No	No	1
P8	68	M	6	Hemorrhage	BG,I,F	No	v	2
P9	70	F	2	Hemorrhage	F,P,CC,TH	No	t	3
P10	68	M	58	Infarct	F, BG	No	No	1
P11	69	M	11	Hemorrhage	F,P,BG,TH,I	No	v,t,a	2
P13	58	M	15	Infarct	T,F,BG,TH,I	No	v,t,a	4

Note: F: frontal; I: insula; P: parietal; T: temporal; O: occipital; BG: basalganglia; TH: thalamus; CC: corpus callosum; v: visual; a: auditory; t: tactile. Sensory deficit score: 0: no deficit; 1: minimal deficit of a small part of the body (e.g., finger or hand); 2: minor deficit of the whole side; 3: severe hypaesthesia but residual sensibility; 4: anesthesia.

Clinical data for each patient are presented in Table 1. The structural MRI slices presenting the most extensive lesion size for each patient are shown in Fig. 1. All patients underwent standard rehabilitation treatments including physical and occupational therapy directing attention to the left side of body and space by sensory and visual stimuli.

2.1.1. Clinical investigation

Visual fields, sensory deficits and extinction were investigated by standard neurological examination. Patients were tested using a battery of standard neglect tests:

2.1.1.1. Bells test This test consists of seven columns each containing five targets (bells) and 40 distractors (Gauthier et al., 1989). Three of the seven columns are on the left side of the DIN A4 sheet (15 targets), one is in the middle and three are on the right (15 targets). The patient was asked to crossout all the bells; the maximum score was 15 for omissions on the left side.

2.1.1.2. Letter cancellation and line bisection test These tests are subtests of the German adaptation (Fels and Geissner, 1997) of the Behavioral Inattention Test (Wilson et al., 1987). The letter cancellation test contains of 5 lines letters containing 20 targets ("E" and "R") on the left-side and twenty targets on the right-side of the sheet. The patient had to cross out all the targets; the maximum score was 20 for omissions on the left side. In the line bisection test the patients were asked to mark 3 lines at the point which divided each line into two equally long halves. The deviation of the bisection mark from the true center of the line was measured; the score was 3 for a bisection mark within an interval of $\pm$ 1.3 cm; 2 for a more distant mark within an interval of $\pm$ 1.95 cm; 1 for a even more distant mark within an interval of $\pm$ 2.6 cm and 0 for a mark more distant than 2.6 cm; the maximum score was 9.

The motor testing included the Rivermead motor assessment (gross function/leg and trunk), action research arm test (ARAT) and 9 hole peg test (9 HP-Test); the 9 HP-Test was executed three times with the affected left hand; the mean time in seconds for three repetitions was recorded (Wade, 1992; Lincoln and Leadbitter, 1979). The handedness was assigned by the *Oldfield Handedness* Inventory (Oldfield, 1971).

2.1.2. Experimental stimuli

Subjects lay supine on the coach of the MRI scanner with their head fixed in the head-holder; the eyes were closed and the ears plugged. The patient's forearms were placed on cushions in comfortable positions-lightly flexed at the elbow. By fixing the distal forearm of the patient and moving his hand repeatedly, the investigator could perform passive flexion-extension movements of the wrist. Patients were instructed to relax completely and not to interfere voluntarily with the passive movements. This was trained outside the scanner before the experiment. Passive flexion-extension wrist movements of 70–90° were executed at a fixed rate of 1 Hz for 25 seconds. This rate was given to the operator projected on an only from the operator's perspective visible screen inside the scanner. For stimulus presentation and MR scanner synchronization the 'Presentation' software (http://www.neurobs.com, Albany, CA, USA) was used. A block of resting of 25 seconds followed every movement block. The pas-

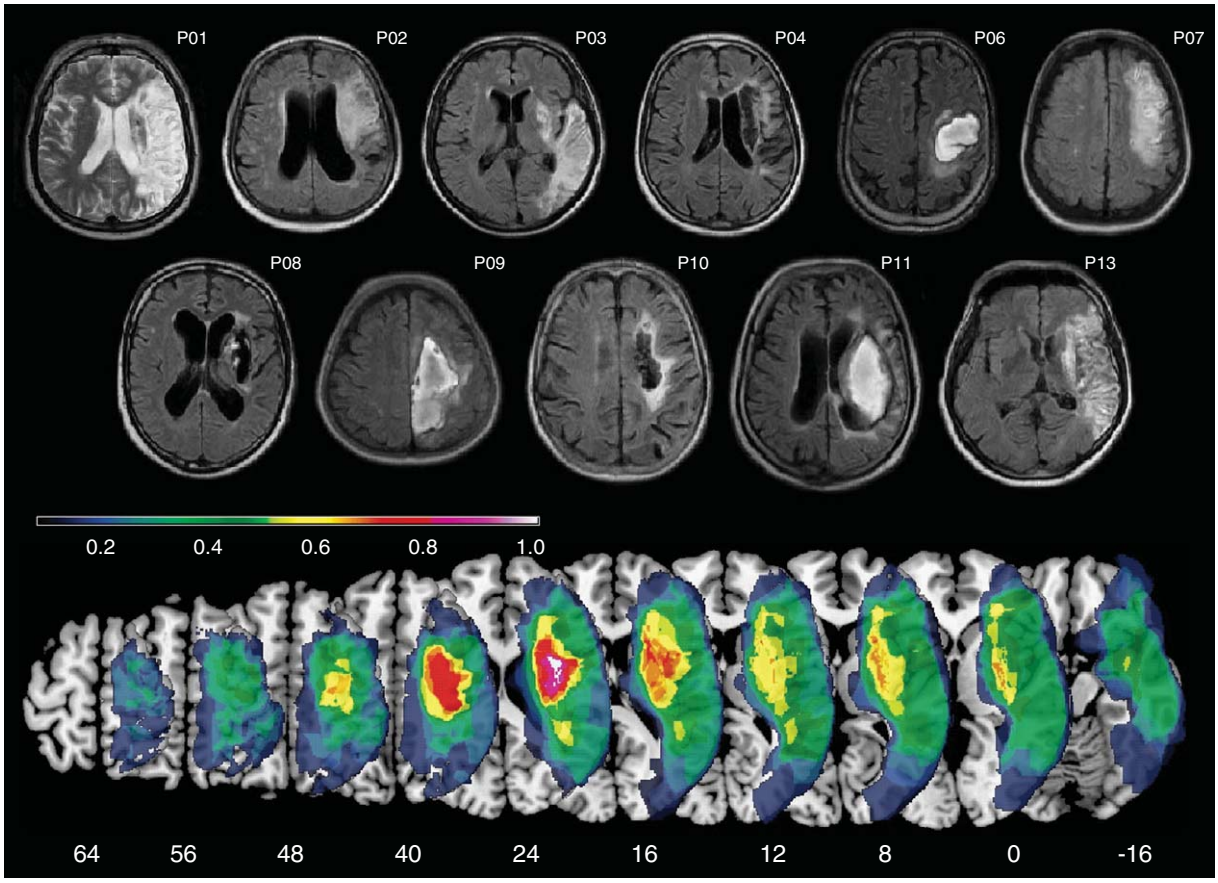

Fig. 1. Upper panel: slices of Flair sequences showing the most extensive lesion size for each patient. Lower panel: Superimposed lesion plots of the patients brains ($n = 11$). The different colors are coding the frequency of number of overlapping lesions in each voxel from dark blue ($n = 1$) to bright pink ($n = 11$), bright pink indicating regions damaged in all patients. The numbers below the axial slices indicate the position on z-axis correspondent to MNI-space.

sive flexion-extension wrist movements were executed alternating on both sides and the sides were intermixed in a pseudorandomized order. Four blocks of passive movements of the right wrist and four blocks of the left wrist were delivered per run, resulting in a run duration of 6.6 min. The experiment was performed in three runs with total duration of 20 minutes.

2.1.3. MRI data acquisition

For fMRI, whole brain acquisition using T2*-sensitive gradient-echo echoplanar imaging (EPI) was performed on 1.5 Tesla Philips Gyroscan (Philips Medical, Hamburg). A total of 185 scans were acquired per session (32 axial slices of 3.1 mm thickness with 1 mm gap, FOV of 230×230 mm, 80×80 matrix TR 2.392 ms, TE 40 ms, flip angle 90°). The first five scans were discarded in order to account for T1 saturation effects resulting in 185 scans per session. A FLAIR sequence (21 axial slices of 5 mm thickness with 1 mm gap, FOV 250×250 mm, 512×512 matrix, TR 11000 ms, TE 140 ms, flip angle 90°) was acquired to assess lesion dimension.

2.1.4. Lesion mapping

Lesions were mapped with the ROI tool of SPM5 (Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm/; (Friston et al., 1995). The Flair images of the subjects were normalized to a template based on Montreal Neurological Institute (MNI) brain for SPM. On slices of the normalized FLAIR images the lesions were manually localized with the polygon slice tool (SPM5); all slices were saved to a 3-dimensional map of the lesion. The individual maps of the subjects were used to decide if

a region of interest (ROI) was affected by the lesion corresponding to the MNI coordinates of the ROI. For superimposing of the individual brain lesions the 11 individual lesion maps were added up in a common stereotactic space with the imcalc tool of SPM5; the voxels of this group map contained values on a scale from 0 to 1 corresponding to the lesion density in this particular voxel. To illustrate the common regions of involvement this overlap image was plotted on a template with the MRIcron software (Rorden et al., 2007), http://www.sph.sc.edu/rorden/mricron/.

2.1.5. FMRI data analysis

Statistical parametric mapping software (SPM5; Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm/; (Friston et al., 1995) was used for fMRI data analysis. Images were preprocessed using spatial realignment of all images to the first image for motion correction, spatial normalization to a template based on Montreal Neurological Institute (MNI) brain as adopted for SPM and spatial isotropic smoothing with 8 mm FWHM Gaussian kernel. BOLD effect was modeled with a box-car function and convoluted with the standard SPM5 hemodynamic response function. The regressor's coefficients for this voxel-based general linear model were estimated using least squares (Friston et al., 1995) and correction for non-sphericity. Confounding factors from head movement (6 parameters obtained from realignment) were also included in the model. Specific contrasts were set for passive movement of the right hand (PMR) and passive movement of the left hand (PML) over all three sessions in this 'first level analysis'.

Random effects over subjects were assessed in an ANOVA design ('full factorial') with two groups (PMR; PML, see results section) using the computed contrasts ('second level analysis') and the duration since the lesion occurred as well as behavioral score built of the sum of mean values of the behavioral neglect tests (bells and letter cancellation and line bisection) and the motor deficit as covariates. In addition voxelwise correlations with clinical and behavioral scores (time duration since lesion, scores of neglect) were assessed in a multiple regression model. The statistical parametric maps were thresholded at $p < 0.01$, uncorrected with an extent threshold of 10 voxels and the motor deficit was integrated in the regression model as a non weighted covariate.

3. Results

3.1. Behavioral data

In the Bells Test mean score of omissions on the neglected left side was 8.91 ± 5.99 (mean $\pm$ SD) of 15 possible items. The corresponding omission score in the letter cancellation test was 10.27 ± 7.6 (mean $\pm$ SD; 20 possible items). In the line bisection test the mean score of 9 possible points was 5.18 ± 2.82 (mean $\pm$ SD).

The mean score in the Rivermead motor assessment (testing gross function of leg (max 13 points)/ trunk (max 10 points) was $6.82/4.8 \pm 4.62/4.1$ (mean $\pm$ SD); the mean of the total of the two parts was 11.6 ± 8.5 (mean $\pm$ SD).

Nine of the eleven patients had a complete hemiplegic left arm and could not perform in the ARAT and 9 hole peg test; patients 2 and 3 were able to perform in the tests and performed the 9 hole peg test in 28/53.9 sec and had 55/57 points in ARAT (see Table 2).

3.2. Location of the lesions

Most patients had lesions in the right putamen in 73% (8 of 11) and the insula in 73% (8 of 11) of the cases. All patients had lesions in the periventricular white matter. We also observed lesions in the vicinity of the temporo-parietal junction / angular gyrus in 27% (3 of 11) and in the superior temporal cortex in 36% (4 of 11). 73% (8 of 11) of the patients had no structural lesion in the primary motor cortex. No lesions were observed in the superior parietal cortex, however one patient had a lesion that was just adjacent to the right intraparietal sulcus. The overlap of the lesion maps is shown in Fig. 1.

3.3. Brain activation during passive movement

3.3.1. Unaffected hand (right hand)

To reveal those regions that were activated during the passive movement of the hand periods with passive movement of the right hand were contrasted against periods of rest. This contrast revealed that passive movement of the right unaffected hand elicited hemodynamic activity in a number of areas that belong to the motor network. In particular including a cluster comprising the left primary somatosensory and motor cortex (S1/M1), furthermore the supplementary motor area (SMA), the left supramarginal gyrus and

Table 2
Behavioral data

	Bells test omissions left side	Letter cane omissions left side	line bisection	RMA gross	RMA leg/trunk	sum	ARAT	9 hole peg test
P1	15	20	0	3	3	6	0	0
P2	5	5	8	10	9	19	55	28
P3	6	3	6	11	10	21	57	53.9
P4	4	1	8	5	2	7	0	0
P6	2	5	8	13	10	23	0	0
P7	1	3	6	12	10	22	0	0
PS	15	10	6	3	0	3	0	0
P9	15	20	1	0	1	1	0	0
P10	15	17	3	10	5	15	0	0
P11	15	20	4	1	1	2	0	0
P13	5	9	7	7	2	9	0	0

Note: Bells test: left side: omissions of 15 possible targets on the neglected left side; Letter Cancellation test: left side: omissions of 20 possible targets on the neglected left side. Line Bisection: 0–9 points; a low score indicates severe neglect. RMA gross: Rivermead motor assessment (gross function). RMA leg/trunk: Rivermead motor assessment (leg and trunk); a low score indicates severe paresis. 9 Hole Peg test: the score 0 indicate subjects with hemiplegia.

the right rostral cerebellum responded to this type of stimulation. Within this network the most prominent activations were in S/M1 and in the cerebellum (see Fig. 2; according to the high level of activation in this specific contrast the threshold was set in this figure at $p < 0.05$, family-wise-error corrected, 5 voxel extent threshhold; for MNI coordinates and T value see Table 3).

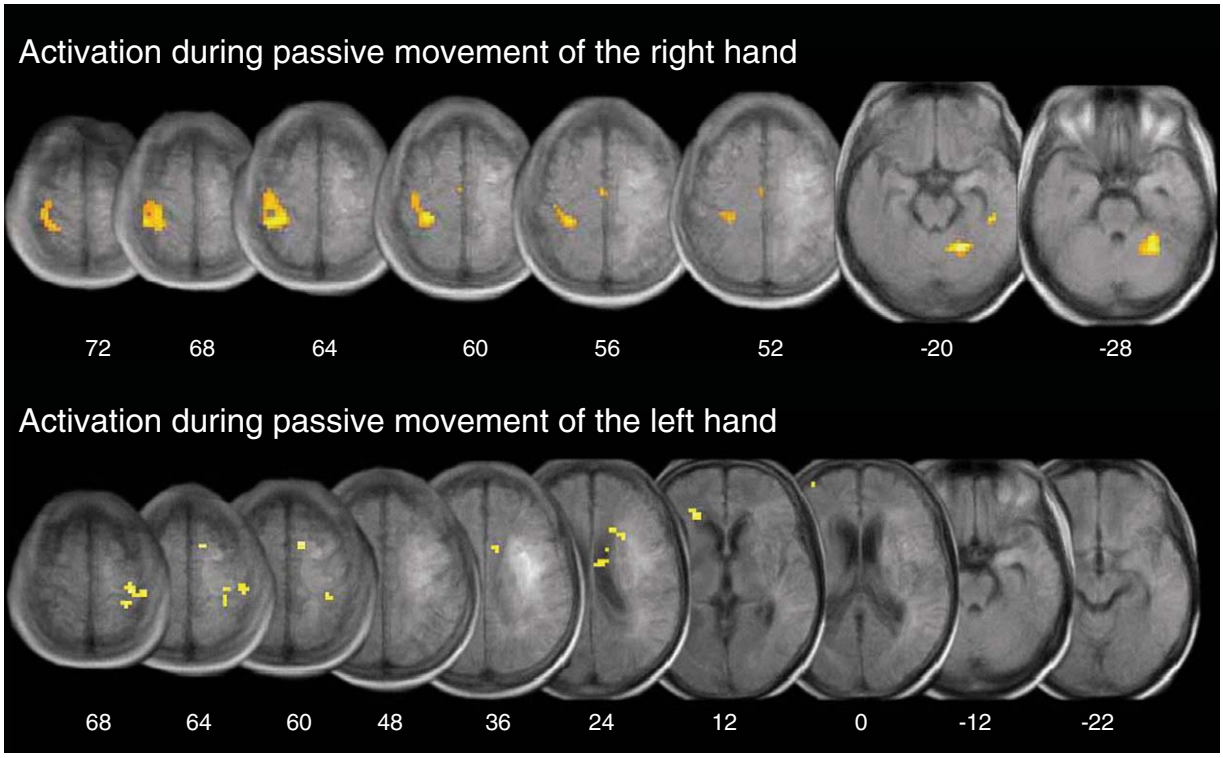

Fig. 2. Activation during passive movement of the right unaffected hand and the left affected hand. Note that the activation level was considerably smaller in the lesioned compared to non-lesioned hemisphere. Note that different thresholds were employed for illustration (passive movement right: $p < 0.05$, FWE corrected and passive movement left: $p < 0.001$ uncorrected both with a 5 voxel extent threshold). The activation is displayed on a template of superimposed FLAIR sequences of the 11 patients.

Table 3
Brain activation during passive movement of the right unaffected hand and the left affected hand vs. rest

Right hand				Left hand			
Region	MNI (x, y, z)	*T* values	*p* values (FWE)	Region	MNI (x, y, z)	*T* values	*p* values (FWE, SVC)
$p < 0.05$ (FEW), 5 voxel ext. thr.	maximum			$p < 0.001$ (cluster), 5 voxel ext. thr.	maximum		
Left Precentral Gyrus/BA 6	−39 −24 64	8.52	0.001	Thalamus	−18 −21 16	5.22	0.000
Left Postcentral Gyrus /BA 4p	−27 −33 60	11.31	0.000	Right Middle Cingulate Cortex	9 6 32	4.63	0.001
Right Cerebelum (VI)	24 −51 −24	14.49	0.000	Right SMA	9 6 60	4.56	0.001
Right Cerebelum (IV-V)	9 −57 −16	9.20	0.001	Anterior cingulate cortex	18 21 28	4.30	0.001
CerebellarVermis (4/5)	3 −60 −12	8.14	0.004	Right Postcentral Gyrus/BA 6	30 −30 68	4.28	0.001
Left SupraMarginal Gyrus	−51 −24 20	7.81	0.004	Right Postcentral Gyrus	42 −30 68	4.06	0.002
Right Fusiform Gyrus	42 −30 −20	8.77	0.001	Right Postcentral Gyrus/BA 1	27 −42 68	4.12	0.002
Left SMA	−3 −12 56	7.76	0.004	Right Postcentral Gyrus/BA 4p	30 −33 60	4.05	0.002
				Left Middle Frontal Gyrus	−36 54 16	4.25	0.001

BA: Brodmann area. FEW: family wise error. SCV: small volume corrected.

3.3.2. *Affected hand (left hand)*

The passive movement of the left hand contrasted against periods of rest also revealed hemodynamic activity in a number of areas of the motor network. These were in particular primary somatosensory and motor cortex (S/M1), the supplementary motor area (SMA) and the anterior and middle cingulate cortex, the thalamus and the left middle frontal gyrus. No activity was observable in the cerebellum (see Fig. 2 and Table 3). In comparison to the network activated by passive movement of the right hand the magnitude of the activations by passive movement of the left hand was decreased.

3.4. *Correlations with clinical and behavioral data*

Brain activation during passive movement of the affected hand was correlated to clinical and behavioral data. A multivariate analysis revealed that the posterior part of the SPL was associated to the duration since the lesion occurred. In the more anterior and lateral part of the SPL activity was associated with the behavioral deficits revealed by the behavioral score built out of the neglect tests (see Fig. 3a). Additional analyses were performed to disentangle the activation associated with behavioral deficits. These analyses revealed a distributed pattern of areas in which the activity correlated positively with the duration since the lesion occurred and positively with the performance in the cancellation and line bisection tasks (i.e., good performance is equivalent to minor neglect symptoms). The location of these areas formed a distributed pattern in the right superior parietal cortex (see Fig. 3b). The posterior medial portion of SPL correlated positively with the duration since the lesion occurred. A more lateral and dorsal located portion of the SPL correlated positively with better performance in the line bisection task. Better performance in the letter and Bells cancellation tests correlated positively with anterior-lateral portion of the SPL. Importantly, both tests exploring space-based aspects of neglect correlated with areas which were adjacent to each other; in contrast to the correlating area of the object-based line bisection which was located more distant (see Table 4 for details).

4. Discussion

Several studies have investigated the neural basis of neglect (Caplan et al., 1990; Husain and Kennard, 1996; Mort et al., 2003; Karnath et al., 2004). Recent work suggested a dysfunction in a network of areas that largely overlaps with the fronto-parietal attention net-

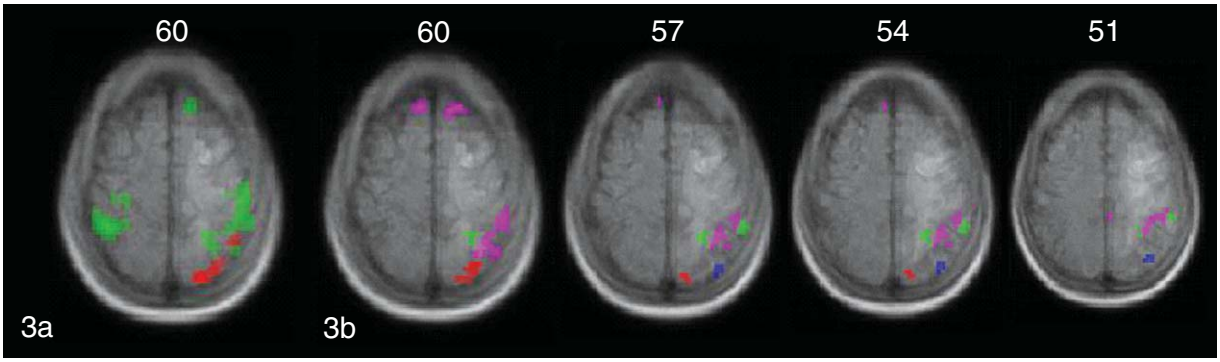

Fig. 3. a) Results of the multivariate analysis. Note that the maximum of the activity associated with the duration since the lesion occurred (in red) is located in the posterior part of the SPL while activations related to the behavioral deficits were less prominent and located more anterior and lateral (in green) in the SPL. Note that different thresholds ($p < 0.05$ unc, and $p < 0.05$, FEW) were used to illustrate the difference between the activation maxima. b) Results of the regression analysis with clinical and behavioral data. As observed in the multivariate analysis the activity during passive movement of the affected left hand was positively correlated to the time since lesion (red) and to the behavioral performance in neglect tests: letter cancellation test (green), bells cancellation test (magenta) and line bisection test (blue). All correlation analyses were thresholded at $p < 0.01$ unc. with 10 voxel extent threshold. The position on z-axis in the MNI-space is indicated above each slice.

Table 4

Correlation analysis of fMRI to clinical and behavioral data. Activation during passive movement of the affected left hand was positively correlated to the time since the lesion occurred (PML-InsultDur); positive correlations to the performance in behavioral tests were calculated for letter cancellation test (PML-LetterCanc), bells cancellation test (PML-BellsCanc) and line bisection test (PML-LineBis)

	MNI (x, y, z)	maxima *T* values	*p* values (FWE, SVC)	Region
PML-LineBis	33 −69 52	4.56	0.001	right superior parietal lobule
PML-BellsCanc	30 −54 60	6.41	0.000	right superior parietal lobule
	45 −36 64	4.49	0.001	right postcentral gyrus
PML-LetterCanc	27 −54 60	4.38	0.001	right superior parietal lobule
PML-lnsultDur	27 −66 64	5.82	0.000	right superior parietal lobule

work (Mesulam, 1981) to underlie neglect (Corbetta et al., 2005). In this network the right SPL plays a pivotal role. Its dysfunction, although not directly lesioned, results from missing input. As a consequence a dysbalance between the left and right SPL with disinhibition of the left SPL is believed to be at the core of the attentional reference frame shift to the right (Karnath et al., 1998; Vallar et al., 2003) in the acute phase of neglect. The recovery of function at the chronic stage is associated with increased activation in the right SPL (Corbetta et al., 2005) that leads to the restoration of the competitive balance between left and right SPL.

Most studies that investigated the neural basis of neglect employed visual tasks. This is not surprising given that the visual system is by large the most investigated sensory system and the existence of a large expertise with attentional tasks in the visual modality. Nevertheless, it has to be noted that the deficits during neglect also involve auditory, somatosensory and motor processing for stimuli delivered to the neglected side (Farne et al., 1998; Berti et al., 1999; Grandjean et al., 2008). Although a multimodal deficit in neglect patients can be assumed, investigations have rarely been performed through other modalities than visual. In the current study we employed passive movement of the hand as a somatosensory stimulus in order to investigate attentional control structures involved in neglect through the somatosensory modality with bathyesthetic stimulation in chronic neglect patients. It should be noted that even though the patients were at the chronic stage numerous deficits were still observable (see Table 1).

Passive movement of the contralateral hand elicited in general much less activity in the lesioned right hemisphere than in the left (see Fig. 2). While passive movement of the unaffected right hand evoked activity in the left primary somatosensory and motor cortex, the SMA, parietal cortex and in the right cerebellum,

left hand movement only activated the right primary sensory and motor cortex, the SMA and the cingulate cortex. These findings are well in line with studies, in which ipsilesional regions were shown to be less activated than their non-lesioned contralesional homologues during similar tasks (Loubinoux et al., 2003; Tombari et al., 2004). In the currently studied patient group this is most likely caused by missing input from lesioned homolateral areas. In addition S1/M1 was touched itself by the lesion in three of our patients.

In the correlation analysis of brain activation during passive movement of the affected hand with clinical and behavioral data we found changes in different portions of the right parietal cortex. A distributed pattern of areas was found, in which the activity was positively correlated with the duration since the lesion occurred and with the performance in the cancellation and line bisection tasks (see Fig. 3). The performance in cancellation tests depends on spatial processing and the ability to analyze the entire visual field. Line bisection tasks require local processing of a distinct shape and have a different neural representation (Fink et al., 2001; Rorden et al., 2006; Sarri et al., 2009). It is well known (Driver and Vuilleumier, 2001; Scholl, 2001) that both (space-based and object-based) cognitive processes can be disturbed during neglect. The distributed pattern of parietal activations correlating with the performance in the different tasks provides a neural basis for the distinction of space- and object-based neglect. The proximity of the cortical representations in the right parietal cortex provide a good explanation why depending of the type of disconnection both neglect types can appear at the same time but also independently from each other. In addition, the positive correlation of right parietal activity with the duration since the lesion occurred underlines the role of this region during the recovery from neglect and replicates the results of previous studies that employed visual stimulation (Corbetta et al., 2005; Umarova et al., 2010) to investigate the neural correlates of neglect.

It should however also be noted that the correlation of the activity in the right superior parietal cortex and the duration since the lesion occurred could be interpreted differently. The changes observed in the current study could also be caused by changes in network processing that are strongly dependent on the duration since the lesion occurred. The different spatial distribution in the right superior parietal cortex of activity correlating with the duration since the lesion occurred being located more posterior while activations correlating with the outcome of behavioral neglect tests being located more lateral and anterior argues against simple changes in network processing but does not exclude this possibility entirely. Therefore the current results need to be interpreted with care.

The convergence of the present results with studies that employed visual stimulation points out to the multimodal nature of neglect and provides support to the idea that the activity in the right parietal cortex is associated to the behavioral performance during neglect. More importantly the present results support the model proposed by Corbetta (Corbetta et al., 2005) also for the somatosensory modality. The positive correlation between the time since the lesion occurred and the activity in the parietal cortex supports the idea that activity in the right superior parietal cortex is closely associated with the process of restoration. The observed correlations between the clinical performance in visual tasks and the activity elicited in the right parietal cortex during somatosensory bathyesthetic stimulation in neglect patients suggest a shared representation of visual and somatosensory networks in this region.

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