

Neuroimaging Patterns Associated with Motor Control in Traumatic Brain Injury

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Objective. To determine if patients with traumatic brain injury (TBI) and motor deficits show differences in functional activation maps during repetitive hand movements relative to healthy controls. Are there predictors for motor outcome in the functional maps of these patients? **Methods.** In an exploratory cross-sectional study, functional magnetic resonance imaging (fMRI) was used to study the blood-oxygenation-level-dependent (BOLD) response in cortical motor areas of 34 patients suffering from moderate motor deficits after TBI as they performed unilateral fist-clenching motions. Twelve of these patients with unilateral motor deficits were studied 3 months after TBI and a 2nd time approximately 4 months later. **Results.** Compared to age-matched, healthy controls performing the same task, TBI patients showed diminished fMRI-signal change in the primary sensorimotor cortex contralateral to the moving hand (cSM1), the contralateral dorsal premotor cortex, and bilaterally in the supplementary motor areas (SMAs). Clinical impairment and the magnitude of the fMRI-signal change in cSM1 and SMA were negatively correlated. Patients with poor and good motor recovery showed comparable motor impairment at baseline. Only patients who evolved to “poor clinical outcome” had decreased fMRI-signal change in the cSM1 during baseline. **Conclusions.** These observations raise the hypothe-

sis that the magnitude of the fMRI-signal change in the cSM1 region could have prognostic value in the evaluation of patients with TBI.

Key Words: TBI—fMRI—Primary motor cortex—Outcome.

Functional magnetic resonance imaging (fMRI) techniques may contribute to the understanding of the neural substrates underlying functional recovery after traumatic brain injury (TBI). Problems in carrying out such studies include the heterogeneous nature of this condition and the logistical difficulties of testing patients often marginally able to cooperate with instructions. The initial Glasgow coma scale (GCS) score of these patients appears to have limited prognostic value.¹ For patients suffering from mild to moderate TBI, evaluation of posttraumatic amnesia and proton MR spectroscopic investigations provide prognostic information on neuropsychological outcome a year later.^{2,3} Especially for the prognosis of motor outcome in TBI patients, it could be theoretically advantageous to use functional imaging methods in addition to anatomical investigations of lesion location and size.

In the absence of functional imaging data from TBI patients, prognostic hypotheses on the neural substrates of motor recovery might be based on the substantial amount of knowledge gained from motor recovery observed in patients suffering from stroke.⁴ A simple extrapolation of expectations from one of these collectives to the other would, however, seem of only limited value, owing to 1) the substantially different patterns of lesions, 2) the fundamentally different incidence

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Lotze M, Grodd W, Rodden FA, Gut E, Schönle PW, Kardatzki B, Cohen LG. Neuroimaging patterns associated with motor control in traumatic brain injury. *Neurorehabil Neural Repair* 2006;20:14–23.

DOI: 10.1177/1545968305282919

of comorbidity between patient populations, and 3) differences in demographic parameters (particularly age and sex). On the other hand, patients with both stroke and TBI experienced damage to the central nervous system leading to motor deficits and subsequent motor recovery based on principles of neuroplasticity.

Within a 5-year period, we carried out fMRI investigations on 42 patients with TBI and unilateral or bilateral motor deficits. We compared activation maps in patients and controls, and within the patient group, we compared fMRI maps in patients with different motor outcomes. The earliest investigation was usually done as soon as the patient was able to cooperate with simple instructions, although in some cases, other factors (i.e., acute anxiety conditions) delayed testing. Thirty-four patients were able to follow the experimental protocol, and 6 had to be excluded because of lack of compliance. The fMRI data were assessed in the anatomical regions most active⁵ during fist clenching including the primary sensorimotor (precentral and postcentral gyrus, SM1, Brodmann area [BA] 4, 1-3) and dorsal premotor (dPMC contralateral and ipsilateral to the movement; dorsolateral part of BA 6) cortices, the supplementary motor area (medial part of BA 6), and the superior parietal lobes (BAS 5 and 7).

METHODS

Subjects

Forty-two right-handed patients (Edinburgh handedness inventory⁶) were recruited from a neurorehabilitation clinic while being treated for moderate to severe TBI. The patients were selected according to the following inclusion criteria: they had to 1) exhibit motor impairment to one or both hands due to the recent TBI; 2) fulfill the general conditions necessary for an fMRI investigation; and 3) possess the ability to cooperate with instructions, in particular, to squeeze a softball upon command.

For the cross-sectional study, we were interested in possible correlates of clinical and demographic data with the MRI and fMRI results. Therefore, patients with a high range after the accident (from 0.25 to 288 months) were included. Patients were clinically examined and subjected to structural and functional MRI investigations on the same day, on average, $60.51 \pm$ (=standard error) 15.15 months after TBI. Eight patients had to be

excluded because they could not control mirror movements of the (relatively) unimpaired hand during scanning or because they could not control task-associated head movements that were too large to be corrected by the data-evaluation program used in the study (SPM, see below). The remaining 34 patients (20 men, 14 women; age = 37.64 ± 2.17 years; range = 18-63 years) were included in the study. Clinical data are shown in Table 1.

Fourteen of them showed right (median of inverted DWW-scale in these patients = 1.0), 15 showed left (median of inverted DWW-scale = 1.0), and 5 showed bilateral hand paresis. Twelve patients showed unilateral direct lesions, and 22 showed bilateral lesions (10 restricted to the cortex and adjacent white matter and 12 with additional deeper lesions) (Table 1). Lesions were located in the precentral or postcentral gyrus ($n = 14$), PMC or SMA ($n = 24$), prefrontal areas ($n = 9$), superior parietal lobe ($n = 6$), and cerebellar hemispheres ($n = 5$). Axonal ruptures and tiny bleeding, as observed after shearing injury, were located in the SMA, the prefrontal lobe, but also in the basal ganglia ($n = 9$) and/or in the midencephalon and mesencephalon ($n = 8$). Median of vigilance impairment was 1 (slight). Medians of memory and orientation impairment were 0 (absent).

An age-matched group of healthy right-handers ($n = 6$; 3 women; age = 35.66 ± 3.59 ; range = 25-51 years) served as the control. In the longitudinal study, we were interested in possible predictors of motor outcome and therefore selected patients with predominantly unilateral paresis (3 right sided and 9 left sided) who had the 1st investigation early enough (3.12 ± 0.87 months after TBI) to allow a subsequent investigation after additional rehabilitation training (6.91 ± 1.55 months after TBI; $n = 12$, 8 of them men, age = 34.29 ± 3.94 years) (see Table 1). Routine inpatient rehabilitative treatment between the 2 determinations (51.88 ± 13.58 days) included physical (43.11 ± 13.96 sessions of Bobath therapy⁷) and occupational (42.33 ± 13.28 sessions) therapy (along with logotherapy and psychotherapy according to individual needs).

Clinical and MRI Measurements

Each patient received a complete neurological examination including the Adams score⁸ (assessment of motor function, tendon reflexes, tactile discrimination, visual acuity, eye movements,

Table 1. Clinical Data and Individual cSMI-Activation Maxima

Patient	Gender ^c	Age	Months Since TBI	Damaged ^d Area	Lesion Type ^e Group	Lesion Size (mm ³)	Adams Score ^f	Paresis ^a		cSMI ^b	
								Right	Left	Right	Left
1	m	37	2	1-4,6,8,9	1	81,116	30	0	2	1.6	2.8
2	m	49	3	3-7,PCB	poor	21,000	28	0	2	1.5	3.9
3	f	37	4	1-4,5,7	1	90,040	21	0	2	1.8	1.7
4	m	40	10.5	4,6	poor	900	17	0	2	3.5	2.2
5	m	40	7	6,44,46,22,37,39	1	7800	20	2	0	3.0	1.8
6	m	57	2.50	6,11,12,44	1	2700	7	1	0	2	3.1
7	m	21	2	1-4,6,7	1	80,100	17	1	0	1.4	4.0
8	m	46	5	6,8,9,44-46,BG	poor	39,900	27	0	3	3.5	4.2
9	f	42	26	1-4,6,7	1	27,200	13	0	1	6.4	5.3
10	f	35	178	1-4,6,22	1	7000	8	1	0	2.0	1.8
11	m	48	84	1,3,5,7,39	1	143,100	5	0.5	0	4.9	4.8
12	f	60	3	4,6,9	1	6700	4	0	1	5.8	3.8
13	m	31	2	4,6	2	2700	20	0	1	2.5	1.9
14	f	19	6.5	6,8,9,22,44	good	26,215	12	0	0	4.3	5.1
15	m	20	21	4,6,8,9	2	1400	10	1	0	4.5	5.4
16	f	18	0.25	6	2	800	15	0.5	0	2.1	4.4
17	f	26	186	6,22	2	2850	9	0	1	4.0	5.6
18	f	37	168	4,6	2	1200	2	0	0	3.5	3.2
19	f	52	30	6,8,9	2	800	9	0	1	5.7	5.3
20	m	18	12	6,8	2	5520	10	0	1	6.9	6.7
21	f	65	15	6	2	700	2	0	0	4.8	4.4
22	m	30	4	4,6	2	9000	4	1	0	2.6	3.7
23	m	61	8	4,6,PT,MO	good	805	2	0	1	5.4	5.2
24	m	32	17.5	6,BG,ME,Thal	3	1600	0	0	0	7.0	3.1
25	m	31	5.5	BG,ME	3	2500	38	0	3	2.5	3.8
26	m	33	66	BG	3	1300	11	0	1	4.0	3.7
27	m	33	70	caps. int,BG,CB	3	5400	31	1	1	3.8	3.8
28	m	35	31	6,BG,ME	3	1500	24	2	0	3.0	2.1
29	f	57	3	5,7,BG,CB	3	3953	21	1	0	2.4	1.3
30	m	34	9	6,BG	good	2600	19	0	0	3.0	3.2
31	f	37	1.5	ME,CB,MO	3	3100	18	0	1	3.5	1.8
32	m	32	2	4,6,BG	3	3529	12	0	2	5.2	4.2
33	f	27	6	BG,MO	3	3200	11	1	1	2.4	0.8
34	f	38	204	9-10,BG,CB	3	1300	7	0	2	1.6	2.1
							10	0	2	4.7	5.0
							6	0	0	3.8	5.9
							10	2	1	2.0	5.1
							6	1	1	1.6	3.2

cSMI = primary sensorimotor cortex contralateral to the moving hand; TBI = traumatic brain injury.

a. Inverse neurologic paresis 5-point scale for the upper extremity, ranging from 0 (no paresis), 3 (elevation against gravity possible) to 5 (plegic).

b. Activation intensity in the highest activated voxel in the contralateral SM1 in z value.

c. Gender: f = female; m = male.

d. Damaged area indicated in approximating Brodmann and anatomical areas: PT = pyramidal tract; BG = basal ganglia; ME = mesencephalon; P = pons; CB = cerebellum; MO = medulla oblongata; temp = temporal; no = no visible lesion.

e. Lesion type: 1 = unilateral fronto-parietal; 2 = shearing lesion restricted to neocerebrum; 3 = shearing lesion with inferior damage; group in follow-up study: good or poor.

f. Adams score: 100 point scale, ranging from 0 (healthy) to 100 (dead).

inverted Glasgow coma scale, and language and speech function); the inverted Daniels, Williams and Worthingam (DWW) muscle strength scale⁹ of finger flexion/extension; and evaluation of attention, orientation, and memory (scaled from 0 = no impairment to 2 = severely impaired).

MRI data were acquired with a commercial 1.5-T tomograph (Philips Gyroscan, Philips, Best, the Netherlands). Anatomical MRIs included a T1 (192 sagittal slices, 1.5 mm thickness, FOV = 250 mm, 256 matrix, TR = 26.4 ms, TE = 4.6 ms), a T2-weighted (18 transversal slices, 6 mm thickness, 1 mm gap, FOV = 190 mm, 256 matrix, TR = 500 ms, TE = 20 ms), and a T2*-weighted (18 transversal slices, 6 mm thickness, 1 mm gap, FOV = 190 mm, 256 matrix, TR = 600 ms, TE = 15 ms) dataset. These measurements allowed for adequate identification of the lesion sites and size, even in patients with the tiny vascular ruptures associated with shearing lesions.¹⁰

The lesion size was evaluated in the transversal T2-weighted and sagittal T1-weighted images by using a manual region of damage selection and a volume of lesion calculation with the MRicro-software (Nottingham University; <http://www.psychology.nottingham.ac.uk/staff/cr1/mricro.html>). Very tiny bleedings as detected in the T2*-weighted images were additionally segmented and used for the assessment of the lesion size. For the specification of lesion location (see Table 1), Brodmann areas were assigned according to the atlas of Talairach and Tournoux.¹¹

Functional MRI measurements were obtained using a multislice echo planar imaging sequence (EPI; 18 slices, 6 mm slice thickness, 1 mm gap, FOV = 230 mm, 128 matrix, voxel size = 2*2*6 mm, TR = 250 ms, TE = 35 ms; flip angle = 35°, acquisition time = 4.5 s, interscan interval = 5 s). Subjects lay in a supine position with their eyes closed. Head position was kept stable by a plastic shell with tightly fitting foam rubber padding.

Task

fMRI examinations were performed in a block design alternating a simple fist-clenching task around a soft sponge rubber sphere of the size of a tennis ball with rest (5 scans each). Each block was repeated 4 times. The more nearly normal hand was investigated first, followed by the more paretic hand. Subjects were instructed to perform mild right or left fist contractions at 0.7 to 1 Hz, as cued by a metronome. The same protocol was used for

the follow-up study as was used for the 1st study. This motor task was selected simply because it is easier for patients suffering from TBI to perform than the often-used sequential finger-tapping task would have been. Some of the patients with TBI would have had cognitive difficulties with the finger-tapping task (memory, sequential thinking) that would have created artifacts confounding to this study of simple motor performance control.¹² All 34 patients were able to perform the task as instructed (monitored by a physician standing by the examination table during scanning).^{13,14} Patients with significant movements other than the ball-squeezing were discarded from further analysis.

fMRI Data Analysis

Analysis of the functional imaging data was performed with SPM99 (Wellcome Department of Imaging Neuroscience, London, UK) implemented in Matlab5 (Mathworks, Natick, MA). The fMRI scans of each individual were realigned to the 1st scan to correct for movement. Realigned images were coregistered onto the structural T1-weighted MRIs.¹⁵ To allow a standardized, fully automatic anatomical labeling, the anatomical and functional maps of each patient were normalized using the SPM template brain. To take into account incorrect normalization procedures in patients with circumscribed lesions, we used the MRicro software to mask the lesion of each patient. This mask was then incorporated into the normalization step.¹⁶

To differentiate between the hemispheres contralateral and ipsilateral to the impaired hand during the normalization process, we flipped the sides (right to left) of the functional maps of the patients with predominantly right-sided paresis included in the longitudinal study ($n = 3$).

Normalized images were smoothed with a Gaussian filter of 8 mm (full width at half maximum).

Statistical Tests

We relied on 2 different statistical approaches. The voxel-based approach was only used for visualization. Because the somatotopic representation maps in these patients were distorted, a voxel-based group analysis results in artificially low activation magnitude in SM1. Therefore, most emphasis was laid on the region of interest (ROI) analysis.

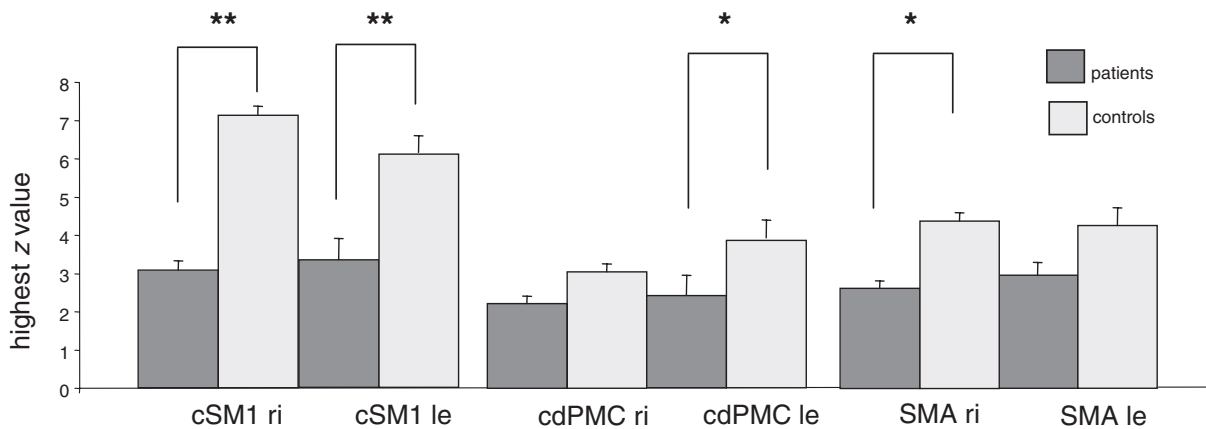


Figure 1. Cross-sectional study. Highest z value in the cSM1 after movement of both the right and the left hands; the cdPMC during left-hand movement and the SMA during right-hand movement were significantly decreased in the patient measures in comparison to the control group. Bars indicate standard errors. cSM1 = primary sensorimotor cortex contralateral to the moving hand; cdPMC = contralateral dorsal premotor cortex; SMA = supplementary motor area; ri = right; le = left. * $P < 0.05$; ** $P < 0.01$.

The voxel-based analysis was performed with SPM99 random effects t tests within or between groups. Individual T1-weighted images of patients were segmented, and functional maps were shown on the group averaged, rendered brains using a statistical threshold of $P < 0.01$ uncorrected for multiple comparisons. This lenient threshold was only used for visualization purposes but not for demonstration and discussion of the results. Maps of controls or contrast controls minus patients were projected on the segmented MNI-template brain (Figure 2).

The main analysis, ROI, was performed to allow correlations of highest signal change per ROI and clinical data. Because activation amplitudes as absolute values are not reasonably scored and vary largely between measurement,¹⁷ we used transformed values as an endpoint measure: all parameter estimates for each single subject were normalized to zero mean and standard deviation of unity per measurement and subject (z score). This measure has been successfully utilized before¹⁸ to compare differences in activation across patient groups and healthy controls and will hereafter be referred to as “fMRI-signal change.” A low threshold cutoff ($P < 0.05$) was utilized to identify global activation areas within each specific ROI. All regions of interest without the dPMC could be automatically defined by the “Automated Anatomical Labeling” software (AAL¹⁹). The dorsal premotor cortex—which is not provided in the AAL toolbox—was spatially defined from the precentral sulcus reaching 2.2 cm anterior, an inferior

border of $z = 50$ extending superior to the SMA (up to $z = 78$) as included in the mask, as provided by Tzourio-Mazoyer and others.¹⁹ Nonparametric demographic data were compared with Mann-Whitney U tests between lesion groups. Comparisons between signal change within regions of interest of each hand movement were performed with a repeated measurements ANOVA (factor region; 7 levels), based on the general linear model (GLM) as implemented in the Statistical Package for the Social Sciences (SPSS 10.05). This analysis was followed by post hoc t tests corrected for multiple comparisons (corrected P value [P_c]; for 7 different comparisons/regions per hand side). The outcome of patients, who participated in the longitudinal study, was stratified according to improvements in the DWW muscle-strength scale during the rehabilitative treatment. Over time, patients in the “good” outcome group improved 2 levels or completely, whereas those in the “poor” outcome group did not change their paresis more than 1 score.

RESULTS

Cross-Sectional Study

The signal change within the 7 regions of interest differed between patients and controls during all initial measurements (ANOVA: left hand: $F[1,37] = 6.52$; $P < 0.05$; right hand: $F[1,37] = 9.77$; $P < 0.005$). Post hoc t tests demonstrated a

Table 2. Cross-Sectional Study: Functional Magnetic Resonance Imaging Group Data

Group Lesion Type	1 Unilateral Lesion Sub- & Cortical		2 Bilateral Lesion Sub- & Cortical		3 Shearing Lesion and Inferior		5 Controls	
	Not affected	Affected	Right	Left	Right	Left	Right	Left
Patients	<i>n</i> = 12		<i>n</i> = 10		<i>n</i> = 12		<i>n</i> = 6	
Lesion size, mm ³	48,671		4538		2548		0	
Adams score ^a	13.8		11.1		19.8		0	
Hand used	Not affected		Affected					
Paresis ^b	0	1	0	1	1	1	0	0
cSMI ^c	3.2	2.8	3.7	4.2	2.6	3.0	6.7	6.0
iSMI ^c	2.3	2.2	3.0	2.8	2.0	2.7	3.4	3.3
cPMC ^d	1.9	2.1	2.9	2.5	1.9	2.6	3.0	4.2
iPMC ^d	1.9	2.0	1.7	1.8	1.7	2.6	2.5	2.4
SMA ^e	2.9	2.8	3.0	2.7	2.2	3.2	4.4	4.3
c. parietal ^f	1.8	1.9	2.5	2.1	1.9	2.6	2.9	3.2
i. parietal ^f	1.8	1.6	2.0	1.6	1.7	2.5	2.8	2.4

a. Mean of the Adams score: 100 point scale, ranging from 0 (healthy) to 100 (dead).

b. Median of the inverted DWV muscle strength scale ranging from 0 (no paresis) to 3 (elevation against gravity possible) to 5 (plegic).

c. Mean of highest *z* value in the contralateral (cSMI) or ipsilateral (iSMI) primary sensorimotor cortex.

d. Mean of highest *z* value in the dorsal premotor cortex (PMC); c = contralateral; i = ipsilateral.

e. Mean of highest *z* value in the supplementary motor area (SMA).

f. Mean of highest *z* value in the superior parietal lobe; c = contralateral; i = ipsilateral.

Table 3. Longitudinal Study: Functional Magnetic Resonance Imaging Group Data

Group	HC		GOODpre		POORpre		HC minus GOOD		HC minus POOR	
	Right	Left	Less ^a	Impaired ^a	Less	Impaired	Less	Impaired	Less	Impaired
<i>z</i> value	3.37	4.27	2.96	3.77	—	2.53	—	3.03	3.51	3.63
Cluster size	159	224	49	142	—	2	—	28	119	51
Significant after SVC ^b (cM1)	0.002**	0.001**	0.05*	0.003**	—	0.63 ns	—	0.37 ns	0.05*	0.08 ns
Coordinates x, y, z	-48,-21,54	33,-27,66	-57,-27,51	48,-21,63	—	36,-18,54	—	48,-21,54	-33,-24,57	42,-30,66

HC = healthy controls.

a. Less = less impaired side; Impaired = more impaired side.

b. SVC = small volume correction for the contralateral precentral gyrus (cM1).

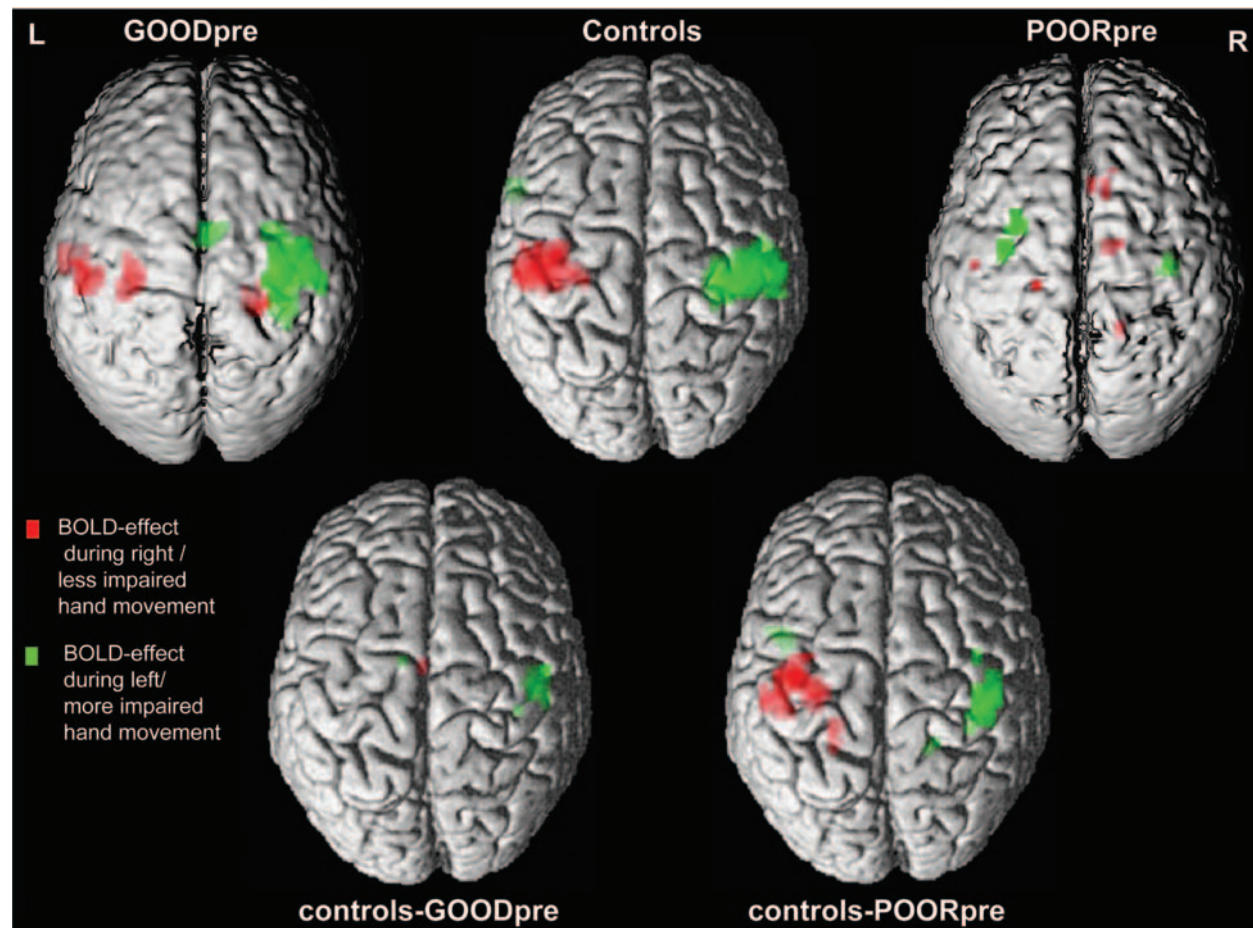


Figure 2. Follow-up study. Functional maps (random effects) of each group (baseline measurement) thresholded at $P < 0.01$ (uncorrected) and masked for regions of interest (ROIs). Top row: Within-group effect; t test. Left: TBI-patients who later developed a “good” outcome showed predominantly cSM1 activation during the baseline measurement. Middle: The controls showed only activation within cSM1 during simple, unilateral, repetitive 1 Hz fist movements. Right: TBI-patients who later developed a “poor” outcome demonstrated almost no relevant fMRI-signal change during movement of the more and less impaired hand. Bottom row: Between-group effect; t test. Left: Comparison between controls minus baseline measurement of the good group (GOODpre) revealed no relevant additional activation. Right: Comparison between controls minus baseline measurement of the poor group (POORpre) showed decreased fMRI-signal change for the poor group in cSM1 during both hand movements. BOLD = blood-oxygenation-level-dependent.

significant decrease of fMRI-signal change within cSM1 ($t(38) = 4.90$; $P < 0.01$) and contralateral dorsal premotor cortex (cdPMC) ($t(38) = 2.88$; $P <$

0.05) for the left-hand movement and cSM1 ($t(38) = 6.45$; $P < 0.01$) and SMA ($t(38) = 3.14$; $P < 0.05$) for the right-hand movement (see Figure 1).

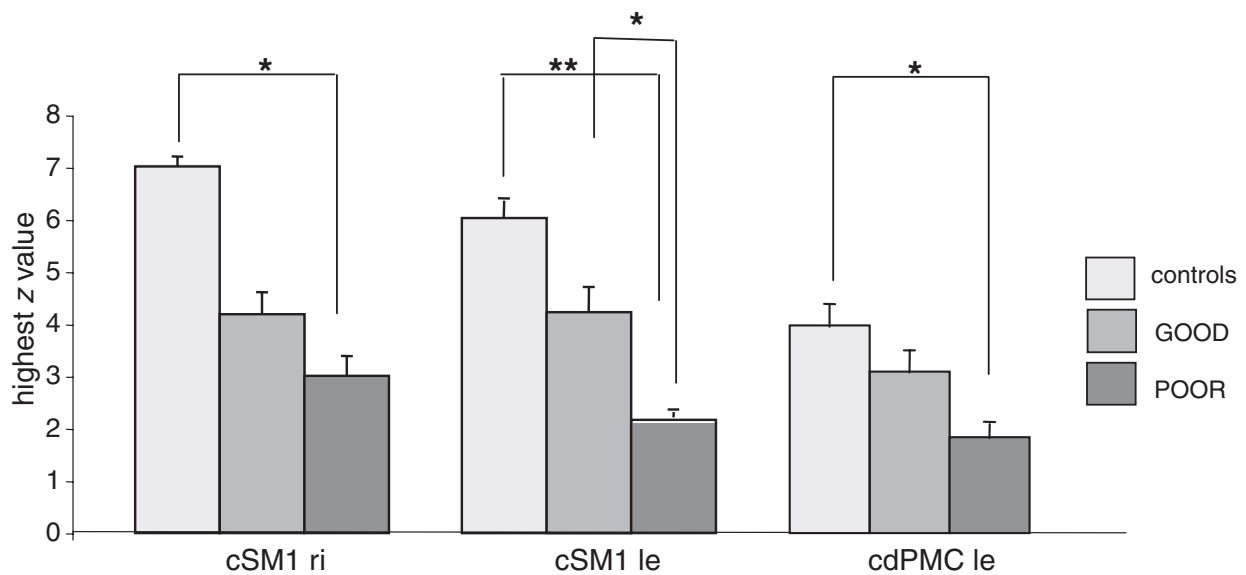


Figure 3. Follow-up study. During the baseline measurement, the fMRI-signal change within cSM1 for the impaired hand differed significantly between the patients who later developed a “good” and those who developed a “poor” outcome. During the impaired hand movement, fMRI-signal change within cSM1 and cdPMC differed between the poor patient group and the controls. The less impaired hand also demonstrated differences of the fMRI-signal change within cSM1 if the poor outcome group was compared to the healthy controls. Patients with good outcome showed no significant differences in comparison to controls. Bars indicate standard errors. cSM1 = primary sensorimotor cortex contralateral to the moving hand; cdPMC = contralateral dorsal premotor cortex; ri = right; le = left. * $P < 0.05$; ** $P < 0.01$.

Clinical impairment correlated negatively with signal change in cSM1 (left hand and Adams score: $r = -0.31$; $P < 0.05$; right-hand movement and paresis right: $r = -0.34$; $P < 0.05$) and in SMA (left-hand movement and Adams score: $r = -0.41$; $P < 0.05$). Age, lesion size, and time after lesion did not show significant correlations with fMRI-signal change. Demographic data between unilateral lesions, bilateral lesions restricted to the cortex and the adjacent white matter, and shearing lesions with additional inferior damage did not differ (age, time since TBI, gender). Bilateral lesions with additional inferior damage were smaller than unilateral lesions (unilateral: $48,671 \text{ mm}^3$; bilateral inferior shearing: 2548 mm^3 ; Wilcoxon $z = -3.39$; $P < 0.005$), but they showed comparable impairment and fMRI-signal change (see Table 2).

Longitudinal Measures

Demographic parameters and clinical data (age, time since lesion, Adams score, neuropsychological ratings, paresis right and left, and lesion size) were similar at the baseline measurements between the group of patients that later developed a good outcome to the group that developed a

poor outcome. Interestingly, no characteristic patterns concerning lesion size and location for the outcome were observed.

Voxel-based group statistics, performed only for visualization of the data, of each outcome group and time illustrated that the baseline measures of the patients who later developed a good outcome showed a comparable activation pattern if compared to the controls. Furthermore, the direct contrast between controls and the good baseline group revealed no relevant activation differences even with the lenient threshold used (see Table 3). fMRI activation maps of patients who later developed a poor outcome exhibited less activation within cSM1 of both hand sides (as demonstrated in the contrast controls minus poor in Figure 2).

Only the ROI-based analysis enabled a statistically relevant approach. This analysis revealed that the larger the lesion, the less improvement of the Adams score ($r = -0.65$; $P < 0.05$). Analysis of variance (GLM) revealed a significant effect for signal change within all tested regions between baseline measurements of patient groups for the more impaired hand side ($F[1,10] = 5.41$; $P < 0.05$) but not for the less impaired hand side ($F[1,10] = 1.79$; ns). The effect was increased if the control group was added ($F[1,15] = 7.09$; $P < 0.01$). The follow-up

measurements revealed no significant results (e.g., impaired hand: $F[2,15] = 1.53$; ns). Post hoc t tests for the baseline measurement demonstrated a significant decrease of fMRI-signal change for the poor versus the good outcome group within the cSM1 during movement of the more impaired hand ($t(10) = 3.61$; $P_c < 0.05$). Poor versus controls differed for the more impaired/left-hand movement within cSM1 ($t(10) = 7.32$; $P_c < 0.01$) and cdPMC ($t(10) = 3.52$; $P_c < 0.05$) and for the less impaired/right hand for cSM1 ($t(10) = 6.00$; $P_c < 0.05$) (see Figure 3).

The main finding of the study was a significant decrease of fMRI-signal change in cSM1 of the poor-outcome group in comparison to the good-outcome group during the baseline measurement.

DISCUSSION

One of the purposes of this experiment was to determine whether patients suffering from hand pareses due to TBI exhibited differences in the magnitude of fMRI-signal changes in motor-relevant ROIs compared to controls. To this end, we examined 34 TBI patients using fMRI, as they executed a simple repetitive motor task, and structural imaging for careful evaluation of lesion sites.

The magnitude of fMRI-signal change in the motor cortical network (cSM1, cdPMC, and SMA) was significantly smaller in patients than controls. The fMRI-signal change within cSM1, in particular, was negatively correlated with motor deficits. This was observed bilaterally.

Activation patterns across lesion types did not show convincing differences either because of bilateral damage or small sample size. The finding that the deeper shearing lesions result in especially severe motor impairment is consistent with a previous report.²⁰ Lesions in the descending motor pathway also showed the least favorable outcome in patients suffering from motor impairment after stroke.²¹

A 2nd purpose of this study was to acquire preliminary evidence to assess the prognostic value of fMRI in TBI. To this end, we selected 12 patients with predominantly unilateral hand pareses who (aside from 2 chronic patients) were tested as early as possible after the TBI and a 2nd time after roughly 7 months of rehabilitative treatment. We found that for patients who later developed poor outcomes, fMRI signal in cSM1 during movement of the paretic limb was especially low. These findings clearly differ from those reported after stroke.

Ward et al.¹³ documented a negative correlation between task-related increases in brain activation and recovery. Moreover, stroke patients with good outcome continued to show linear decreases in the magnitude of the fMRI-signal change in the primary sensorimotor cortex. In addition to the differences in etiology, it is of note that most of our patients had cortical lesions, many involving area BA4, whereas those of the Ward et al. study had predominantly subcortical lesions (see Table 1). With a lesion in the primary motor area, a decrease of fMRI-signal change can be expected because there is a decrease of intact neuronal assemblies for motor execution rather than damage of the descending tract. Additionally, we found a weaker effect for cSM1 also for the less impaired hand. Consistent with other authors,²² we found a poor predictive value for clinical and demographic features.

Our findings suggest that the magnitude of fMRI-signal change in cSM1 after TBI might have predictive value in terms of recovery of motor function, as previously demonstrated after stroke.^{4,23,24} This notion is in line with the previous finding that when the physiological integrity of corticomotoneuronal connections originating in the cM1 after stroke is preserved, as measured using transcranial magnetic stimulation, the chances of motor recovery increase substantially.²⁵

Although differences in the fMRI-signal change between patient groups were significant only for cSM1, we cannot exclude an overall decrease of fMRI-signal change in patients with poor outcome because signal change correlated highly within ROIs. A depressed cerebral oxidative metabolism for the 1st 2 weeks after severe head injury has been shown to correlate with poor long-term outcome.²⁶

It should be kept in mind that the associations demonstrated in this study do not document a causal link between activation in cSM1 and motor recovery; this would be a different issue to be addressed in future studies. Furthermore, our experimental design, although controlling for movement rate and the presence or absence of associated movements, cannot rule out changes in the imposed pressure around the ball between baseline and the follow-up experiments or differences in the frequency of the movement as being partially responsible for these results. Movements, paced acoustically at 1 Hz, were slower in some individuals (approximately 0.7). Because a magnitude of this difference might have some impact on the fMRI signal,²⁷ we cannot rule out performance

as a cofactor in this investigation. This confound has to be carefully controlled in future studies.

Overall, the results described above underline the importance of an intact cSM1 for the process of recovery of motor function after TBI. These results also suggest that fMRI-signal change in primary sensorimotor regions might have prognostic value in attempts at predicting the motor outcome of patients after TBI.

ACKNOWLEDGMENTS

We thank Marlies Koestlinger and Sabine Belz for their excellent management of data acquisition, Ralf Veit and Kai Müller for help in data evaluation, and Silke Anders and Reinhard Vontheim for help in the biometrical statistical design. This study was supported by the Bundesministerium für Bildung und Forschung. L. G. Cohen was partially supported by a Humboldt Foundation award. We declare that there is no financial or commercial interest in our work.

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