

Functional MRI exploration of visuospatial attention in acute neglect and non-neglect stroke patients

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Introduction. Neglect (NGL) is an intriguing brain lesion syndrome, which manifests with the failure to respond to stimuli of the contralesional side. Usually it occurs after right hemisphere lesion. It is proposed that NGL is deficit of the spatial attention, which is provided by the function of bilateral intraparietal sulcus (IPS), frontal eye field (FEF), lateral occipital complex (V5/MT+) and right temporoparietal junction (supramarinal gyrus, SMG and superior temporal gyrus), anterior insula (INS) and ventral frontal cortex (1). In spite of the long history of NGL investigation, it is still unclear why some patients have NGL after stroke and others do not. We aimed to explore visuospatial attention in acute stroke patients with and without neglect.

Methods. We examined 23 patients with acute ischemic stroke in the territory of the right middle cerebral artery. Additional to the ordinal neurological examination, all patients were examined for neglect using 5 standardized tests (2). Neglect was diagnosed if patients failed to perform at least two of them. We diagnosed neglect in 13 patients (NGL group), other 10 patients without neglect formed the non-neglect (NonNGL) group (Table 1). All patients and 26 healthy control subjects were examined with fMRI. We used a Posner-like paradigm in a mixed-design. Task blocks contained 12 trials, which were separated from each other by crosshair. First, the valid cue (800 msec) was presented pointing equally to the right and left. Then in two thirds of trials the target appeared (400 msec) in the pointed direction, and one third of trials were without target ('null-events'). The patients were asked to detect the targets as fast as possible by pressing a button. The fMRI examination consisted of two sessions (each ~6 minutes) with 196 trials. Altogether 64 left and 64 right targets were presented. Behavioral performance during fMRI examination was controlled by target detection in events with target and non-response in "null events". Additionally, MPRAGE and DWI images were acquired. The images processing of the fMRI data was performed with SPM5. At the single-subject level the visuospatial attention task blocks were modelled as one main regressor ('VisAtt'). To capture the extra variance introduced by the motor response, it was modelled as the second regressor ('MotResp') orthogonalised with respect to the main regressor of interest. The group data were analysed using a flexible factorial design, which contained 3 groups (healthy subjects, NonNGL, NGL) and 2 conditions ('VisAtt' and 'MotResp'). The volume of infarct was determined from normalized DWI images using MRIcron.

Results. The clinical and behavioural data are shown in the Table 1. All subjects completed the fMRI experiment successfully. Healthy subjects detected all targets, the NonNGL patients most of them. NGL patients detected most of right targets, while the performance for left targets among NGL patients was different (Table 1). The 'MotResp' caused activation of common motor-associated areas in all groups, though in patients the size of effect was significantly smaller (Fig. 1, primary motor cortex M1). The activation to 'VisAtt' was different among groups. In healthy subjects the fMRI paradigm activated all key attentional centers in both hemispheres. In NonNGL patients, the pattern of activation was the same as in healthy subjects except the involvement of right frontal structures. The size of effect in some regions even corresponded to the level of normals (Fig. 1). In NGL patients, the visuospatial attention task modulated neither structures of the right hemisphere nor FEF of the left hemisphere. NGL patients had activation only in the structures of the left hemisphere (left INS, SMG, V5/MT+ and V1), which was significantly lower than in NonNGL and with a very low modulation of right primary and association visual areas (Fig. 2). Since the task performance differed among subjects, we used their target detection score as a covariate. The detection of the left targets by NGL patients correlated with activation of the attention relevant areas in the left hemisphere and partly of the right hemisphere (Fig. 2). The contrast [NonNGL-NGL] showed the difference in recruiting attentional centers in both hemispheres with the maximum in the right V5/MT+ area (Fig. 3).

Table 1. Groups characteristics.

	healthy subjects	NonNGL	NGL
n	26	10	13
age	30.3 ± 7.3	65.1 ± 8.5	67.2 ± 12.6
initial NIHSS	-	7.0 ± 4.5	9.0 ± 4.4
infarct volume, ml	-	29.22 ± 15.47	55.2 ± 28.2
fMRI ex. (hours from stroke)	-	52.4 ± 38.0	49.7 ± 29.6
detected left targets (max. 64)	64	57.8 ± 10.7	21.6 ± 21.8
detected right targets (max. 64)	64	59.2 ± 10.4	51.6 ± 8.5
reaction time left targets	325.8 ± 93.3	497.7 ± 127.7	824.0 ± 394.4
reaction time right targets	320.8 ± 89.6	457.0 ± 126.2	648.9 ± 171.0

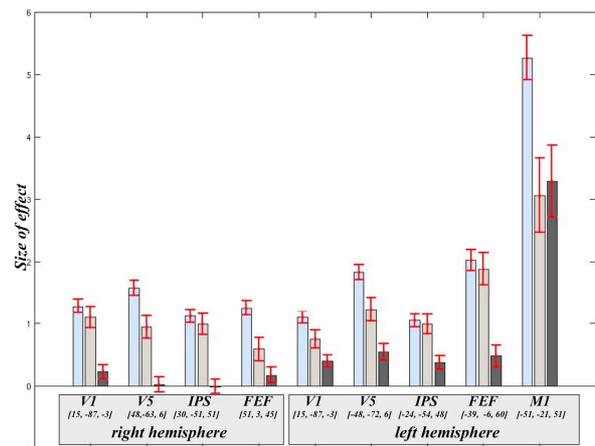


Fig. 1. Size of effect in attention relevant cortical areas and primary motor cortex.

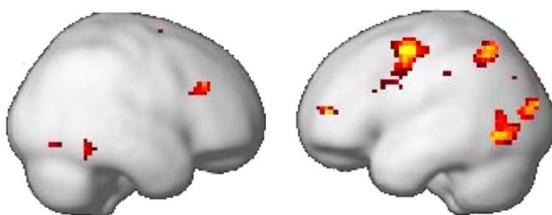


Fig. 2. Correlation of brain activation with left target detection in neglect patients, $p < 0.001$ uncorr.

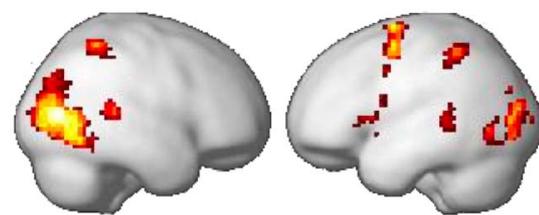


Fig. 3. Contrast of non-neglect vs. neglect patients activation on a visuospatial attention task [NonNGL-NGL], $p < 0.001$ uncorr.

Discussion. Present study is the first to our knowledge that investigated neglect in acute stroke using fMRI. Since in acute stroke the BOLD response could be changed due to cerebrovascular disease, we compared NonNGL and NGL stroke patients and also used the epoch designed paradigm with a 'MotResp' as a control condition. The 'MotResp' associated BOLD signal was smaller in all patients, but qualitatively the activation pattern was the same in all groups. However, 'VisAtt' modulated the patients' cortex differently. NonNGL patients demonstrated the spared function of the attention relevant areas in the left hemisphere and post-Rolandic regions of the right hemisphere. While their 'MotResp' activation was lower, 'VisAtt' response corresponded to the level of healthy subjects, showing the functional compensation after structural lesion. NGL patients showed a down-regulation in most of attentional centers. Thus, in NGL patients the structural lesion broke entirely the function of attention system, which was not compensated or unable to recruit the intact left attentional centers and right V5/MT+. In contrast, partly spared function of some attention relevant regions in NonNGL patients enabled the attentional modulation of the primary and association visual areas with a subsequent left targets detection.

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