ANATOMICAL AND NEUROLOGICAL CORRELATES OF ACUTE AND CHRONIC VISUOSPATIAL NEGLECT FOLLOWING RIGHT HEMISPHERE STROKE*

Hans Samuelsson[1], Christer Jensen[2], Sven Ekholm[2], Hans Naver[3] and Christian Blomstrand[3]

([1]Dept. of Psychology, University of Göteborg, Göteborg, Sweden; [2]Dept. of Radiology, Sahlgrenska University Hospital, Göteborg; [3]Dept. of Neurology, Sahlgrenska University Hospital, Göteborg)

Abstract

Anatomical and neurological correlates of visuospatial neglect were studied in 53 patients with a CT-documented right hemisphere stroke. Evidence of neglect at the acute stage poststroke was strongly related to large lesions involving the middle temporal gyrus and/or the temporo-parietal paraventricular white matter. Thus, out of 18 patients with evidence of visuospatial neglect at the acute stage, 12 showed a lesion in the middle temporal gyrus and/or the deep temporo-parietal white matter. Among the 35 patients that failed to show visuospatial neglect, only one patient had a lesion within these areas. Comparing those patients who recovered from neglect with those that did not, a high correlation was found between persisting neglect and a lesion involving the paraventricular white matter in the temporal lobe. On the basis of above findings, it was suggested that a simultaneous damage to the cortico-thalamic system for regulation of arousal and to the neural systems mediating visual orienting, is likely to be followed by persisting neglect symptoms.

Introduction

Evidence of visuospatial neglect is often found in patients showing lesions including the temporoparietal-occipital junction in the right hemisphere (Bisiach, Capitani, Luzzati et al., 1981; Hécaen, Penfield, Bertrand et al., 1956; Heilman, Watson, Valenstein et al., 1983). Within this brain area, damage to the parietal lobe is a most frequent observation in patients showing neglect (Vallar and Perani, 1986). Evidence of spatial neglect has, however, also been reported in patients with lesions located outside this brain area, such as the dorsolateral or medial frontal lobe (Heilman and Valenstein, 1972), the thalamus (Motomura, Yamadori, Mori et al., 1986), and the basal ganglia (Ferro, Kertesz and Black, 1987).

Some studies have failed to uncover a relation between damage to the parietal lobe and neglect (Egelko, Gordon, Hibbard et al., 1988; Kertesz and Dobrowolski, 1981; Vilkki, 1989). Thus, Egelko et al. (1988) failed to find a relationship between the degree of parietal lobe damage and the degree of neglect

* Some of the results of this study were presented at: The 5th Nordic Meeting in Neuropsychology, Uppsala, Sweden, August 17-19, 1995.

in a group of 57 right-hemisphere stroke patients, all of which showing evidence of neglect. This study was conducted at a rehabilitation centre and the interval between the onset of the disease and testing was at least one month. Egelko et al. (1988) suggested that the relatively long interval between the stroke and the examination of the patients might have weakened the relationship between neglect and damage of the parietal lobe, that is, such a relationship may be stronger at the acute stage than at the postacute stage. This would explain why a relationship between neglect and damage to the parietal lobe or the temporo-parietal junction often have been reported in studies conducted within the first weeks following the stroke (Bisiach et al., 1981; Hier, Mandlock and Caplan, 1983; Vallar and Perani, 1986).

The assumption that the length of interval between the induction of the brain damage and testing might influence the results obtained, raises the question whether the structural and neurological correlates of visuospatial neglect may differ at the acute stage compared to the chronic stage after stroke. If this is the case, it might allow us to make predictions about those anatomical systems that are critical for the ability to recover from neglect. Although important for the clinical evaluation of the prognosis and the planning of the rehabilitation, only few studies have been reported on the neural mechanisms of recovery from neglect (see Vallar, 1993). The present investigation was undertaken to study these problems in a prospective study on the basis of right hemisphere stroke patients with and without visuospatial neglect.

Materials and Methods

Subjects

All patients with a right hemisphere stroke consecutively admitted to the stroke unit at the Department of Neurology, Sahlgrenska Hospital, Göteborg, during the period of March 1989 to June 1992, were screened for inclusion in this study. Of 181 patients, 53 were selected. The patients excluded met the following criteria: (1) no identifiable lesion on the CT-images; (2) a prior clinically manifested cerebrovascular accident or other cerebral disorder; (3) a return to normal or virtually normal neurological functions within 24 hours; (4) older than 77 years of age; (5) a history of mental retardation, serious abuse, or hospitalisation for psychiatric treatment; (6) not right-handed; (7) severely ill and not able to co-operate; (8) not Swedish speaking; (9) a severely defective vision on both eyes.

Procedure

Patients showing remaining neurological symptoms three weeks after the stroke onset were defined as major stroke patients (N = 40) and those showing normal functions symptoms or nondisabling subtle neurological within 3 weeks were defined as minor stroke patients (N = 13). The Behavioural Inattention Test (BIT) was introduced by Wilson, Cockburn and Halligan (1987) as a valid test of unilateral visual neglect. Seven slightly modified subtests from BIT (Line crossing, Letter cancellation, Star cancellation, Figure copying, Representational drawing, Article reading, and Sentence copying) were used to identify patients showing visuospatial neglect. The patients were tested at 1-4 weeks poststroke except for four patients who were examined during the second month poststroke. A follow-up examination was carried out 6-7 months postonset of stroke. The criteria for visuospatial neglect included a defective number of omissions and a higher incidence of omissions on the left side than on the right side of the test sheet or figure (see Samuelsson, Hjelmquist, Naver et al., 1995). The normative ranges for the test scores were obtained from

TABLE I
Subject Characteristics and Type of Brain Lesion

	Neglect group N = 18	Major group N = 22	Minor group N = 13
Age (years)			
Mean	62.11	59.45	58.15
Range	45-75	21-77	30-74
SD	9.49	15.56	12.15
Sex			
M/F	8/10	15/7	8/5
Type of lesion			
Haem/lnf/Laclnf*	2/16/0	4/14/4	1/4/8

* Haemorrhage/Infarction/Clinically verified lacunar infarction.

34 non-braindamaged controls. Of 40 patients with major stroke, 18 exhibited visuospatial neglect on at least one of the subtests at the first assessment (the *neglect group*), and the remaining 22 patients showed no neglect (the *major group*). None of the patients in the minor stroke group showed visuospatial neglect (the *minor group*). No differences were found between the groups with respect to age or sex (Table I).

Neurological Examination

In addition to routine neurological examinations at the ward, a standardised clinical examination for motor and sensory deficits, muscular tone, cranial nerves and extinction phenomena was conducted by H.N. or C.B. during the acute phase poststroke.

Motor Deficit: At the examination of the contralesional side of the body, one score was given for each of the following findings: defect mobility of the hand or arm, defect mobility of the lower extremity (max. score = 2).

Sensory Deficit: One score was given for each of the following findings: defect sensation of light touch on the palm of the hand; defect judgement of joint position of the thumb or elbow (max. score = 2).

Hemianopic Visual Field Deficit: The clinical confrontation technique was employed and the patients were rated on a three-point scale of severity as follows: (0) no visual field deficits on single stimulation; (1) partial visual field deficit, that is, defect ability, but not a total inability, to detect stimuli on single stimulation in the contralesional field; (2) a total inability to detect stimuli in the contralesional field on single stimulation.

Sensory Extinction: Extinction of stimuli from the contralateral side on double simultaneous stimulation was tested in the tactile, visual, and auditory modality. Light touch on the palm of the hands, finger movements within the visual fields, and sound of rubbing fingers at different distance from the ears served as stimuli. First unilateral sensation was tested by using single stimulations and then extinction was tested by using bilateral simultaneous stimulations randomly intermixed with single stimulations. At least six double stimulations were presented for each sense modality. Omissions of contralesional stimuli on double stimulations but not on single stimulations were used as criteria for sensory extinction. Patients with a partial tactile or visual defect on single stimulation were defined as showing extinction only if all contralesional stimuli were omitted on the double stimulations. Sensory extinction was not measured when a total deficit was found on the single stimulations. Auditory extinction was only measured when the sound of the rubbing fingers was recognised at a distance of at least 10 cm from the ear on single stimulations. Patients with missing data from more than one modality were excluded. Sensory extinction was rated on a three-

point scale of severity as follows: (0) no extinction was found, (1) extinction was found in one modality, (2) extinction was found in at least two modalities.

Defective Conjugate Eye Movement: Fast saccadic and slow smooth-pursuit eye movements were tested horizontally and vertically by instructing the patient to focus on the examiner's moving index finger. Pathological conjugate eye movements towards the contralesional side were particularly noted and scored. One score was given for each of the following findings; a spontaneous conjugate deviation of the eyes towards the ipsilesional side, defective smooth-pursuit eye movements, and defective saccadic eye movements (max. score = 3).

Neuroradiological Examination

The CT scans were performed routinely with canthomeatal parallel planes; i.e. about plus 10°-15° gantry tilt from Reid's baseline and with 5-10 mm slice thickness. CT scans were performed acutely within 2 days after onset of neurological symptoms as well as 4 weeks or later after onset. The latter to get optimal conditions to make a fair judgement of the localisation and extent of the lesions, which then should be well demarcated. The evaluation of the CT examinations were carried out by two trained neuroradiologists without knowledge of clinical data. With guidance of the atlas of Kretschmann and Weinrich (1986), 58 anatomical structures were defined and all images were judged corresponding to the localisation, extent, and vascular supply of the area damaged. Suspected and definite lesions were plotted in a standardized record for each patient. Also, the substructures were grouped into six main brain areas (frontal, central grey, insula, temporal, parietal, and occipital) and the incidence of a lesion within each area was computed.

A conservative rating format was applied at the statistical analysis, that is, only lesions judged as definite in the record were rated as a positive CT-finding. Of the 58 substructures identified, the following 10 were excluded from the analysis due to absence of a registered brain damage: orbital gyri, paracentral lobule, uncus, precuneus, fornix, septum verum, hypothalamus, and corpus callosum. Substructures with a low incidence (≤ 3) of registered lesions and with adjoining anatomic sites were combined and treated as a single subarea. Furthermore, paraventricular white matter at the level of and immediately above the collateral trigone within the temporal and parietal lobes were considered as representing one subarea (temporo-parietal paraventricular white matter), since these structures were difficult to separate on the images. The same type of pooling of data was made for the extreme capsule, the claustrum, and the external capsule. Thus, the number of individual substructures analysed for incidence of a lesion was reduced from 58 to 38 structures (see Table III).

The size of the lesion(s) was defined by using sagittal and transversal measurements (rounded off to the closest 1/2 cm) on the scan where the lesion had its greatest extent. In addition, the size was indicated by the number of main brain areas damaged. By judging the non-affected hemisphere, the degree of atrophy (sulcal width and ventricular size) as well as the degree of deep white matter disease, were ranked into three categories (major = 2, moderate-minor = 1, and none = 0). An estimation of the supraventricular size was made using a ventricular index (a ventricle-brain matter ratio) modified from Hughs and Gado (1981). The method used was described in detail by Larsson, Jensen, Bilting et al. (1992). The size of the right temporal horn of the lateral ventricle was evaluated by comparing the right temporal horn with the left temporal horn (smaller = – 1, same = 0, mildly larger = 1, moderately larger = 2, marked larger = 3).

Statistical Analyses

Univariate group comparisons were made for the nominal variables by the Chisquare test or the Fisher exact test and for the ordinal or continuous variables by the Mann-Whitney U test. Individual correlation was computed using the Phi coefficient (Siegel and Castellan, 1988). $p < .01$ was used as cut-off for significant univariate findings. This restrictive p-level was chosen considering the exploratory nature of the investigation and the high number of group comparisons presently used.

Multivariate comparisons were made using multiple logistic regression (Hosmer and Lemeshow, 1989) in order to examine the effect of each anatomical variable on the occurrence of neglect, while adjusting for the effect of the other variables. All variables showing a p-value of <.05 at the univariate comparison were included. An interactive forward stepwise selection procedure was used with the alpha-to-enter set to .05 and alpha-to-remove set to .10. The dependent variable was presence or absence of visuospatial neglect.

Odds ratios and 95% confidence intervals were estimated for the variables selected by the regression analysis. Unadjusted and adjusted odds ratios were given. The adjusted version was estimated with the variables transversal size of the lesion and sagittal size of the lesion forced into the model, while no variables were forced into the model at the unadjusted estimation.

RESULTS

The First Assessment

The minor stroke patients differed from those suffering from major stroke by absence of visuospatial neglect. Further, the minor group differed with respect to the extension of the lesion; most of the patients in this group showed very small lesions (≤1 cm in the transversal and sagittal plane) restricted to the central grey and adjoining white matter. A lacunar syndrome (Bamford, Sandercock, Dennis et al., 1991) was observed in more than half of the patients in this group, but only in four patients in the major stroke patients (Table I). At this stage of the data analysis, the minor stroke group was excluded since this group did not seem to provide any further information on the neuroanatomical correlates to neglect. The remaining analyses involved a comparison between the neglect group and the major group.

As shown in the Table II, an infarction involving the vascular territories of the middle cerebral artery was a finding common for the two groups, while lesions within the territories of the other cerebral arteries were less common. The neglect group showed more extensive lesions involving more lobes or main areas compared to the major group (Mann-Whitney U test; p = .00l). Also, in the transversal plane, the lesions of the neglect group were more extensive (Mann-Whitney U test; p <.00l). The width of the temporal horn within the right hemisphere was more extensive (relative to the left temporal horn) in the neglect group (Mann-Whitney U test; p <.01).

A comparison was performed of the number of patients showing injury to the six main brain areas subjected to analysis (Table II). The number of patients with a lesion involving the temporal lobe was significantly higher in the neglect group than in the major group (Fisher exact test; p =.001). Table III shows the incidence of positive CT-findings for 38 anatomical substructures. The number of patients showing positive CT-findings in the neglect group and in the major group was compared for each structure. The table indicates that the neglect group showed a higher incidence of lesions for five of the structures, located in the superior and middle temporal lobe, insula, and the deep temporo-parietal area (p <.0l). The same holds true of six substructures located in frontal, parietal, temporal, and occipital brain areas, and in central grey areas, tested at the p-level of <.05.

A further statistical analysis was undertaken using a stepwise logistic

TABLE II

Neuroradiological Characteristics of Patients in the Major Group and the Neglect Group (only p-values below .05 are given)

	Major group N = 22		Neglect group N = 18		p-level*
Damaged area: N, %					
Frontal lobe	8	36%	11	61%	
Central gray†	7	32%	11	61%	
Insula and adjoining matter	4	18%	10	56%	.021
Temporal lobe	4	18%	13	72%	.002
Parietal lobe	7	32%	10	56%	
Occipital lobe	6	27%	4	22%	
Number of damaged areas: median, range	1	1-4	4	1-5	.001
Vascular territories / cerebral artery					
Anterior	4	18%	1	6%	
Penetrating anterior	1	4%	3	17%	
Middle	15	68%	15	83%	
Penetrating middle	3	14%	8	44%	.04
Posterior	6	27%	4	22%	
Penetrating posterior‡	0	0%	1	6%	
Anterior choroid artery	1	4%	2	11%	
Left hemisphere: median, range					
Atrophy	0	0-1	0	0-2	
White metter disease	0	0-2	0	0-2	
Ventricular					
Right temporal horn	0	0-2	1	0-3	.008
Index: median, IQR	65,5	19	73,5	9	.041
Max size of lesion: median, IQR					
Sagittal (cm)	2,5	2	4,3	4	.041
Transversal (cm)	1	1	3,3	2	.001

IQR= interquartile range.
* Fisher exact test or Mann-Whitney U test.
† Central gray and adjoining white matter.
‡ Penetrating posterior and posterior communicating artery.

regression method. This analysis included the 11 substructures found to be statistically significant at least on the p-level of <.05 as indicated in Table III. In addition, the following six variables from Tables I and II were included in this analysis: age, number of main areas involved, transversal size of lesion, sagittal size of lesion, ventricular index, and size of the right temporal horn. An interactive forward stepwise selection procedure was applied using presence or absence of visuospatial neglect as dependent variable.

In the above analysis a methodological difficulty arose in that all patients of the major group showed negative CT-findings for the occipital gyri, the inferior temporal gyrus, and the middle temporal gyrus (Table III). Since the logistic regression method does not allow analysis of variables including groups with altogether negative findings, substructures with negative findings have to be either excluded or pooled with other variables (Hosmer and Lemeshow, 1989). The occipital gyri and the inferior temporal gyrus were excluded from the analysis, since only few patients showed lesions involving these structures and since all patients with positive CT-findings showed additional damage to adjoining substructures already included in the regression analysis. The middle

TABLE III

Proportion of Patients in the Major Group and the Neglect Group Showing Lesions in 38 Substructures, Compared with the Fisher Exact Test (only p-values below .05 are given)

	Major group (N = 22)		Neglect group (N = 18)		
	N	%	N	%	p-level
Frontal lobe					
Superior g/fro pool/g rectus	3	14	1	6	
Subventricular w m	3	14	2	11	
G. cinguli and adjoining w m	2	9	1	6	
Middle g	3	14	0	0	
Inferior g	1	5	3	17	
Precentral g	3	14	4	22	
Preventricular w m	2	9	4	22	
Paraventricular w m	2	9	6	33	
Semioval centre ACM	3	14	9	50	.018
Central grey and adjoining white matter					
Putamen	4	18	10	56	.021
Pallidus	4	18	6	33	
Caudate nucleus	2	9	5	28	
Internal capsule anterior	3	14	7	39	
Internal capsule genu	2	9	4	22	
Internal capsule posterior	3	14	4	22	
Corona radiata	6	27	8	44	
Thalamus	0	0	1	6	
Insula and adjoining grey and white matter					
Insula	3	14	10	56	.007
Ext capsule/claustrum	3	14	6	33	
Temporal lobe					
Temporal paraventricular w m	3	14	8	44	.04
Tem-par paraventricular w m	1	5	10	56	.001
Transverse g	l	5	9	50	.002
Superior g	3	14	11	61	.003
Middle g	0	0	10	56	<.001
Inferior g	0	0	4	22	.034
Mesial aspect	1	5	2	11	
Parietal lobe					
Postcentral g	3	14	2	11	
Superior lobule	1	5	4	22	
Semioval centre ACM	3	14	7	39	
Supramarginal g	1	5	6	33	.033
Angular g	4	18	8	44	
G. cinguli and adjoining w m	1	5	0	0	
Occipital lobe					
Mesial occ-tem junction	2	9	2	11	
Central w m	4	18	4	22	
Occipital pole	3	14	3	17	
Visual cortex	6	27	3	17	
Occipital g	0	0	4	22	.034
Cuneus	3	14	2	11	

g = gyru; w m = white matter; ACM = the territory of the middle cerebral artery; Ext. capsule/claustrum = Extreme capsule, Claustrum and External capsule; Tem-par = Temporo-parietal; Occ-tem = Occipito-temporal; Occipital g = gyri on the lateral convexity of prestriate cortex which borders on the parietal and temporal lobes.

TABLE IV

Estimated Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Variables in the Multivariate Model for Neglect Selected by Stepwise Logistic Regression

	Neglect			
Variable	OR	95% Cl	$OR_{adjusted*}$	95% Cl
Temporo-parietal paraventricular white matter	26,3	2,9 239,6	13,8	1,0 196,0
Pooled variable: middle temporal gyrus and temporo-parietal paraventricular white matter	42,1	4,5 391,7	21,4	1,2 369,4

* Odds values adjusted for the size of the lesion by the inclusion of transversal and sagittal size of lesion to the model.

temporal gyrus was included in the analysis by pooling the values for this structure with the temporo-parietal paraventricular white matter. The pooling of these structures into one variable was motivated by the fact that, of the substructures adjoining the middle temporal gyrus, the temporo-parietal paraventricular white matter showed the highest correlation (Phi = .68) and agreement (88%) with respect to damage to the middle temporal gyrus. A second version of the logistic regression analysis was made without any pooled variables, that is, after exclusion of the middle temporal gyrus, the occipital gyri, and the inferior temporal gyrus. Thus, in both versions of the logistic regression analysis, the number of individual brain areas included in the analysis was reduced from 11 to 9 substructures. The first version of the analysis resulted in a selection of the pooled variable consisting of the middle temporal gyrus and the temporo-parietal paraventricular white matter as the variable showing the strongest connection with neglect ($G = 19.40$; $p < .001$). According to the second version of the analysis, the temporo-parietal paraventricular white matter and the maximal transversal size of the lesion were selected as the variables showing strongest association with neglect ($G = 20.48$, d.f. = 2, $p < .001$).

Additional support for a high association between the occurrence of visuospatial neglect and lesions involving the middle temporal gyrus and the temporo-parietal paraventricular white matter was obtained by the odds ratios of the occurrence of neglect shown in Table IV. The table reveals high odds ratios of occurrence of neglect following damage to the middle temporal gyrus and the temporo-parietal paraventricular white matter. Of 12 out of 18 patients with neglect, 8 showed a lesion involving both the middle temporal gyrus and the temporo-parietal paraventricular white matter, 2 patients showed a lesion that involved the middle temporal gyrus, and 2 patients showed a lesion involving the temporo-parietal paraventricular white matter. Only 1 out of 22 patients in the major group showed a lesion in these area.

The Neurological Assessment

Table V shows the relationship between visuospatial neglect and five neurological variables. At the first examination, patients in the neglect group exhibited more sensory deficits (Mann-Whitney U test; $p < .005$), and sensory

TABLE V

Neurological Characteristics Compared to the Presence of Neglect at the Initial Examination (N = 40) and at the Follow-up (N = 15) in the Major Stroke Paxients

	Acute neglect			Recovered*		
Score	No N	Yes N	p†	No N	Yes N	p†
Motor			.014			.227
0	12	4		1	2	
1	5	3		0	3	
2	5	11		5	4	
Sensory			.002			.590
0	16	5		1	3	
l	4	3		1	1	
2	2	10		4	5	
Visual field			.218			.001
0	16	9		0	8	
l	2	5		4	1	
2	4	4		2	0	
Eye movements			.044			.029
0	14	7		0	6	
1	5	4		1	1	
2	3	2		2	0	
3	0	5		3	2	
Extinction‡			.001			.156
0	16	3		0	3	
1	3	3		1	2	
2	1	9		4	4	

Note: High score = severe deficit.
* Three patients with no follow-up.
† Mann-Whitney U test.
‡ Five patients excluded due to missing data.

extinction ($p < .001$) compared to the major group. No group difference was found for visual field deficits.

Figure 1 shows the site of the brain lesion in the patients in the neglect and major groups. The two groups were cross-classified for the presence of visual field deficits. The figure shows that patients with homonymous visual field deficits but with no neglect differed from the other three subgroups by showing lesions confined to the occipital lobe. The only exception was one patient with a lesion also involving the temporal lobe.

The Follow-up Assessment

In the follow-up study, only the data obtained from the neglect group were analysed. The patients in this group were divided into two subgroups; patients still showing visuospatial neglect (N = 6) and patients who had recovered from neglect (N = 9). A follow-up assessment was missing for three patients; two patients had experienced a second stroke, and one patient was inaccessible because he had moved to another part of the country. Univariate analyses was made, comparing those patients who had recovered from neglect with those still showing neglect; no statistically significant differences were obtained between the two groups regarding age, sex, number of main areas involved, transversal size of the lesion, or sagittal size of the lesion. The severity of the visuospatial

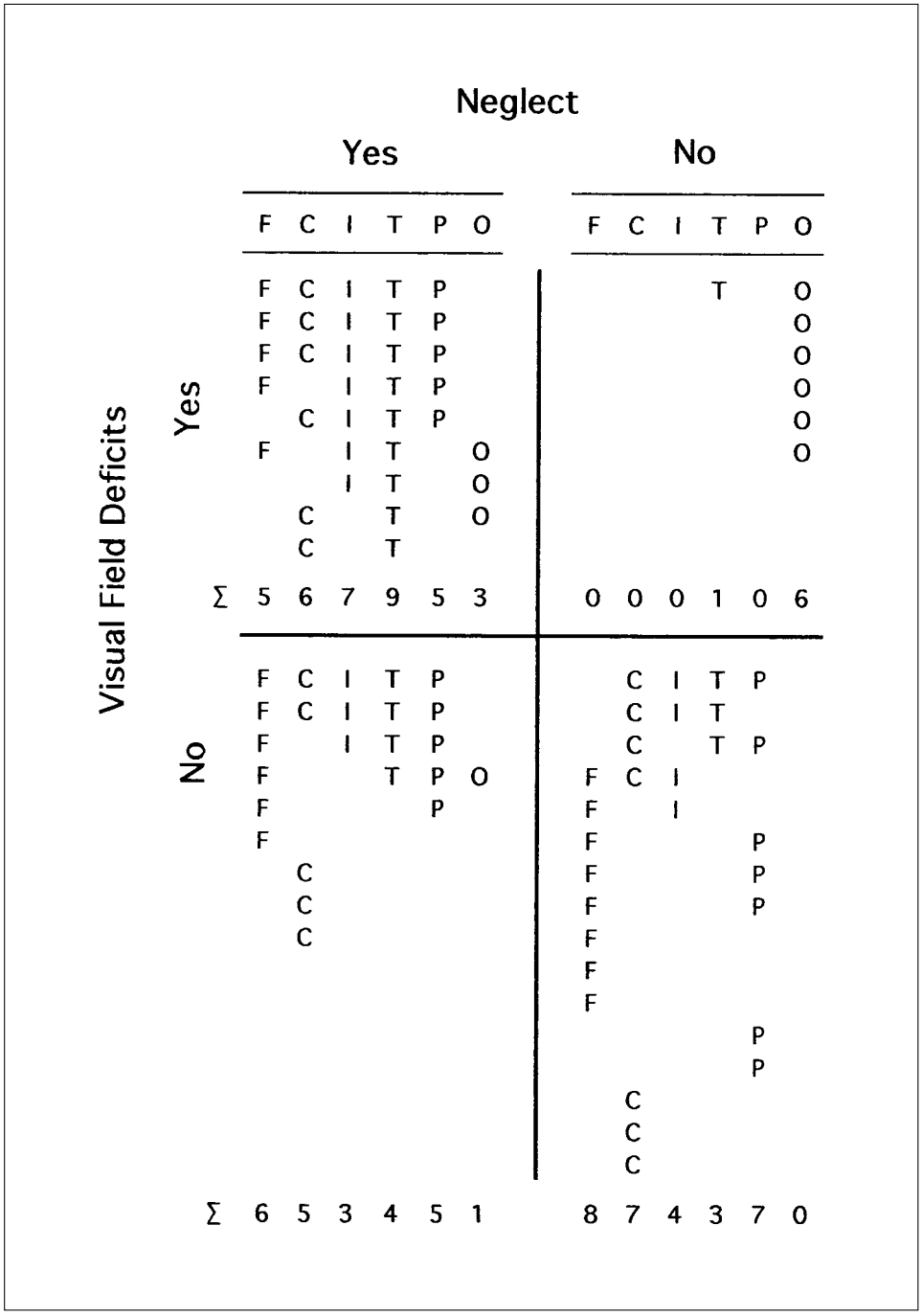

Fig. 1 – *The location of the lesion in patients with and without neglect divided into four groups based on the presence or absence of a visual field deficit. F = frontal lobe, C = central gray and adjoining white matter, I = insula and adjoining matter, T = temporal lobe, P = parietal lobe, O = occipital lobe. Each line of letters in the four fields represents a patient.*

neglect observed at the first assessment was found to be associated with remaining symptoms of neglect. Thus, patients still showing neglect exhibited neglect in a higher number of tests at the first assessment compared to the patients recovered from neglect (Mann-Whitney U test; $p < .005$). No differences were found for left hemisphere atrophy or white matter disease.

A lesion involving the central white matter below the collateral trigone in the temporal lobe showed a high correlation with persisting symptoms of visuospatial neglect at the follow-up (Phi = .76, Fisher exact test; $p < .01$). Additional support for a high association between lesion involving the white matter within the temporal lobe and persisting neglect was obtained by a statistically verified increase of the size of the right temporal horn (relative to the left horn) of the ventricular system in the patients with persisting symptoms of neglect (Mann-Whitney U test; $p = .01$). No other substructures showed a significant relationship between incidence of lesions and remaining symptoms of visuospatial neglect.

No statistically significant differences were found between the two groups for motor deficits, sensory deficits, and for sensory extinction (Table V), while visual field deficits (measured at the first assessment) were more common in those patients that still had not recovered from visuospatial neglect (Mann-Whitney U test; $p = .001$). Also, defective conjugate eye movements tended to be more common for these patients, although this findings was not statistically confirmed at the p-level chosen ($p < .05$). The low number of patients in the no-recovery group prevented the performance of a multivariate regression analyses of the follow-up data.

Subgroups of Patients

On the basis of the Cl7-scan inspections and the statistical analysis, the patients in the neglect group may be divided into a number of subgroups. The largest group (N = 11) consisted of patients who showed large lesions clustering in the posterior part of the middle temporal lobe and/or in the temporo-parietal paraventricular white matter at the level of the collateral trigone. Patients with severe symptoms of visuospatial neglect (neglect in ≥ 4 subtests, N = 7) and persistent symptoms of neglect in the follow-up study (N = 6) were only found in this group of patients (a follow-up was missing for two of the patients). The group may be divided into two subgroups; patients with lesions mainly involving the vascular territory of the middle cerebral artery (N = 8), and patients with lesions mainly involving the vascular territory of the posterior cerebral artery (N = 3).

Of the remaining 7 patients in the neglect group, 6 showed lesions mainly involving the anterior part of the brain. Of these patients, 3 showed rather small lesions confined to the basal ganglia and adjoining white matter, 1 patients showed a lesion confined to the frontal lobe (inferior frontal gyrus, supraventricular white matter, and white matter in front of the horn of the lateral ventricle), and another two patients showed lesions involving the frontal lobe and the basal ganglia. Also, the anterior parts of the temporal lobe were involved in the damage shown by the last two patients. In a single patient the lesion extended into the paraventricular white matter in the parietal lobe. All of these patients exhibited mild to moderate neglect at the acute stage and a complete

recovery from visuospatial neglect at the follow-up examination (a follow-up was missing for one of the patient).

One of the patients in the neglect group, with moderate symptoms of visuospatial neglect and complete recovery at the follow-up, did not fit with any of the descriptions of the lesion given above. This single patient had a lesion confined almost entirely to structures in the parietal lobe.

DISCUSSION

Three main findings were made regarding anatomical correlates of visuospatial neglect following acute right hemisphere stroke. Firstly, visuospatial neglect was highly associated with large lesions, converging on the middle temporal lobe and/or the temporo-parietal paraventricular white matter. Secondly, lesions confined to the basal ganglia and adjoining white matter, and lesions mainly confined to the inferior frontal lobe, may produce visuospatial neglect at the early stage poststroke. However, absence of neglect symptoms was a common observation following lesions in these brain structures, indicating a rather weak association between the phenomenon of visuospatial neglect and damage to these structures. Thirdly, lesions confined to the occipital lobe are probably not primarily associated with visuospatial neglect; none of the patients with lesions restricted to this lobe showed visuospatial neglect, although most of the patients with occipital lesions extending into the temporal or parietal lobes showed neglect.

Although present findings agree with currently reported observations of anatomical correlates of neglect (Vallar, 1993), our observations do not support the hypothesis of an exclusive role of the parietal lobe for the appearance of neglect. While the connection between inferior parietal lobe damage and unilateral neglect of visual information often is emphasised (see Vallar and Perani, 1986), our observations indicate that the involvement of the temporal lobe may be just as important as the involvement of the parietal lobe.

Two main systems of visual information processing have been described by Ungerleider and Mishkin (1982) in non-human primates, and by Corbetta, Miezin, Dobmeyer et al. (1990), Haxby, Grady, Ungerleider et al. (1991), and Zeki, Watson, Lueck et al. (1991) in humans. A dorsal occipito-parietal complex seems to be critical for the processing of spatial relationships (the dorsal "where" system) and a ventral occipito-temporal complex is primarily involved in the recognition of visual patterns (the ventral "what" system). These systems may be of great importance in mediating attention and awareness of visual information (Posner and Dehaene, 1994; Watson, Valenstein, Day et al., 1994). In fact, several recent authors have stressed the importance of an interaction between the processing of information in the two systems (Farah, 1990; Humphreys and Riddoch, 1993; Milner, 1995; Van der Heiden, 1992). Consequently, the high association observed in the present study between the presence of neglect and the injury to temporal and temporo-parietal areas may not only be related to defect functions within the dorsal "where" system, but also to defect functions within the ventral "what" system and to defective interaction between the two systems.

Recovery of Visuospatial Neglect

A significant association was revealed between persistent symptoms of visuospatial neglect and damage to the deep white matter of the temporal lobe. Thus, it appears that sparing of subcortical structures in the temporal lobe may be critical for the recovery of neglect following a right hemisphere stroke, whereas damage to the middle temporal gyrus and/or the deep temporo-parietal white matter seems to be related to the occurrence of neglect at the acute poststroke phase.

In the present study the strongest association between brain damage and visuospatial neglect involved the posterior areas of the brain. At least two cortical networks for attention have been described for the posterior part of the brain with respect to visuospatial neglect. One of these systems is supposed to mediate arousal (Heilman, 1979; Watson, Valenstein and Heilman, 1981) and the other visual orienting (Posner and Petersen, 1990; Posner, Petersen, Fox et al., 1988).

Posterior areas of association cortex, structures within diencephalon and mesencephalon, and pathways connecting these structures are considered critical for the functions mediated by these two networks. Circuits involving unimodal and polymodal association areas, nucleus reticularis thalami, and the mesencephalic reticular formation were considered as playing an important role in the mediation of arousal and alertness (Heilman, 1979), while a network consisting of the posterior parietal lobe, the superior colliculus, and the pulvinar nucleus of the thalamus were believed to be involved in the disengaging, orienting, and engaging of visual attention (Posner and Petersen, 1990).

Adhering to this conceptualisation, we suggest that a concomitant damage to these networks for arousal and orientation of visual attention may cause severe and persisting neglect following a right hemisphere stroke. In the present study, these two networks seem to have been severely damaged by the lesions observed in those patients that showed persisting neglect. These lesions include the deep white matter of the temporal lobe combined with damage to the posterior middle temporal gyrus and damage to the deep temporo-parietal white matter.

In addition to asymmetric defects in the orientation of attention, the damage to the subcortical components of the networks may have led to a general disturbance in the attention capacity. A combination of a general deficit in the attentional capacity and a directional-specific attentional deficit, may be important for the occurrence of persistent and severe visuospatial neglect (for review, see Robertson, 1993). The relationship found between effects produced by lesions involving the deep white matter in the temporal lobe and the persistence of unilateral neglect, may correspond to a disturbed regulation of alertness. The disturbed regulation of alertness may have led to a general deficit in the attentional capacity and it may be a result of damage to the fibres that connect the cortical part with the diencephalic and mesencepalic parts of the network described by Heilman (1979).

Persisting symptoms of visuospatial neglect at the follow-up assessment showed a high association with evidence of a visual field deficit measured at first assessment. All patients with persisting neglect at the follow-up showed a visual field deficit as well as a lesion involving subcortical white matter in the

temporal lobe. Consequently, a combination of damage to the subcortical structures in the temporal lobe and early evidence of a visual field deficit may represent an important indicator of persisting symptoms of neglect in patients showing visuospatial neglect at the acute stage following a right hemisphere stroke.

In the present study, the severity of visuospatial neglect at the first assessment was a strong predictor of symptoms of neglect still remaining at the follow-up assessment. Similar findings have been reported in some recent studies of recovery from neglect (Levine, Warach, Benowitz et al., 1986; Stone, Patel, Greenwood et al., 1992).

Further longitudinal studies of the anatomical correlates of recovery of visuospatial neglect could usefully focus on a more detailed mapping of the cortical and subcortical structures in the temporal, parietal, and temporo-parieto-occipital border area of the brain. Further research along these lines will probably help to clarify the relationships between location of brain damage and the time course of visuospatial neglect. Also, the relation between general arousal effects and hemispatial dysfunction is of interest to specify with respect to prognosis clinical implications.

Acknowledgements. This work was supported in part by grants from the Delegation for Social Research (No. 90-0176), The 1987 year's Foundation of Stroke Research, Greta and Einar Asker's Foundation, Per-Olof Ahl's Foundation of Cerebrovascular Disease Research and John and Brit Wennerström's Foundation of Neurological Research. We thank Elisabeth Hjelmquist for her assistance in data collection and analysis. We also thank Knut Larsson for his helpful comments.

References

BAMFORD, J., SANDERCOCK, P., DENNIS, M., BURN, J., and WARLOW, C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet, 337:* 1521-1526, 1991.

BISIACH, E., CAPITANI, E., LUZZATTI, C., and PERANI, D. Brain and conscious representation of outside reality. *Neuropsychologia, 19:* 543-551, 1981.

CORBETTA, M., MIEZIN, F.M., DOBMEYER, S., SHULMAN, G.L., and PETERSEN, S.E. Attentional modulation of neural processing of shape, color, and velocity in humans. *Science, 248:* 1556-1559, 1990.

EGELKO, S., GORDON, W.A., HIBBARD, M.R., DILLER L., LIEBERMAN, A., HOLLIDAY, R., RAGNARSSON, K., SHAVER, M.S., and ORAZEM J. Relationship among CT scans, neurological exam, and neuropsychological test performance in right-brain-damaged stroke patients. *Journal of Clinical and Experienced Neuropsychology, 10:* 539-564, 1988.

FARAH M.J. *Visual Agnosia.* Cambridge: MIT Press, 1990.

FERRO J.M., KERTESZ, A., and BLACK, S.E. Subcortical neglect: Quantitation, anatomy, and recovery. *Neurology, 37:* 1487-1492, 1987.

HAXBY, J.V., GRADY, C.L., UNGERLEIDER, L.G., and HORWITZ, B. Mapping the functional neuroanatomy of the intact human brain with brain work imaging. *Neuropsychologia, 29:* 539-555, 1991.

HÉCAEN, H., PENFIELD, W., BERTRAND, C., and MALMO, R. The syndrome of apractognosia due to lesions of the minor cerebral hemisphere. *Archives of Neurology and Psychiatry, 75:* 400-434, 1956.

HEILMAN, K.M. Neglect and related disorders. In K.M. Heilman and E. Valenstein (Eds.), *Clinical Neuropsychology.* New York: Oxford University Press, 1979, pp. 268-307.

HEILMAN, K.M., and VALENSTEIN, E. Frontal lobe neglect in man. *Neurology, 22:* 660-664, 1972.

HEILMAN, K.M., WATSON, R.T., VALENSTEIN, E., and DAMASIO, A.R. Localization of lesions in neglect. In A. Kertesz (Ed.), *Localization in Neuropsychology.* New York: Academic Press, 1983, pp. 471-492.

HIER, D.B. , MONDLOCK, J. , and CAPLAN, L.R. Behavioral abnormalities after right hemisphere stroke. *Neurology, 33:* 337-344, 1983.

HOSMER, D.S., and LEMESHOW, S. *Applied Logistic Regression.* New York: John Wiley and Sons, 1989.

HUGHES, C.P., and GADO, M. Computed tomography and aging of the brain. *Neuroradiology, 139:* 391-396, 1981.

HUMPHREYS, G.W., and RIDDOCH, M.J. Interactions between object and space systems revealed through neuropsychology. In D.E. Meyer and S. Kornblum (Eds.), *Attention and Performance, XIV.* Hillsdale, NJ: Lawrence Erlbaum Associates, 1993.

KERTESZ, A., and DOBROWOLSKI, S. Right-hemisphere deficits, lesion size and location. *Journal of Clinical Neuropsychology, 3:* 283-299, 1981.

KRETSCHMANN, H.-J., and WEINRICH, W. *Neuroanatomy and Cranial Computed Tomography.* Stuttgart: Georg Thieme Verlag, 1986.

LARSSON, A., JENSEN, C., BILTING, M., EKHOLM, S., STEPHENSEN, H., and WIKKELSÖ, C. Does the shunt opening pressure influence the effect of shunt surgery in normal pressure hydrocephalus? *Acta Neurochirurgica (Wien), 117:* 15-21, 1992.

LEVINE, D.N., WARACH, J.D., BENOWITZ, L., and CALVANIO, R. Left spatial neglect: effects of lesion size and premorbid brain atrophy on severity and recovery following right cerebral infarction. *Neurology, 36:* 362-366, 1986.

MILNER, A.D. Cerebral correlates of visual awareness. *Neuropsychologia, 33:* 1117-1130, 1995.

MOTOMURA, N., YAMADORI, A., MORI, E., OGURA, J., SAKAI, T., and SAWADA, T. Unilateral spatial neglect due to hemorrhage in the thalamic region. *Acta Neurologica Scandinavica, 74:* 190-194, 1986.

POSNER, M.I., and DEHAENE, S. Attentional networks. *Trends in Neuroscience, 17:* 75-79, 1994.

POSNER, M.I., and PETERSEN, S.E. The attention system of the human brain. *Annual Review of Neuroscience, 13:* 25-42, 1990.

POSNER, M.I., PETERSEN, S.E., FOX, P.T., and RAICHLE, M.E. Localization of cognitive operations in the human brain. *Science, 240:* 1627-1631, 1988.

ROBERTSON, I.H. The relationship between lateralised and non-lateralised attentional deficits in unilateral neglect. In I.H. Robertson and J.C. Marshall (Eds.), *Unilateral Neglect: Clinical and Experimental Studies.* Hove: Lawrence Erlbaum Associates, 1993, pp. 257-275.

SAMUELSSON, H., HJELMQUIST, E., NAVER, H., and BLOMSTRAND, C. Different criteria in the assessment of visuospatial neglect. *Journal of Neurology, Neurosurgery and Psychiatry, 58:* 114-115, 1995.

SIEGEL, S., and CASTELLAN, N.J. *Nonparametric Statistics for the Behavioral Sciences.* New York: McGraw-Hill, 1988.

STONE, S.P., PATEL, P., GREENWOOD R.J., and HALLIGAN, P.W. Measuring visual neglect in acute stroke and predicting its recovery: the visual neglect recovery index. *Journal of Neurology, Neurosurgery, and Psychiatry, 55:* 431-436, 1992.

UNGERLEIDER, L.G., and MISHKIN, M. Two cortical visual systems. In D. Ingle, M.A. Goodale and R.J.W. Mansfield (Eds.), *Analysis of Visual Behaviour.* Cambridge, MA: MIT Press, 1982.

VALLAR, G. The anatomical basis of spatial hemineglect in humans. In I.H. Robertson and J.C. Marshall (Eds.), *Unilateral Neglect: Clinical and Experimental Studies.* Hove: Lawrence Erlbaum Associates, 1993, pp. 27-59.

VALLAR, G., and PERANI, D. The anatomy of unilateral neglect after right-hemisphere stroke lesions. A clinical/CT-scan correlation study in man. *Neuropsychologia, 24:* 609-622, 1986.

VAN DER HEIDEN, A.H.C. *Selective Attention in Vision.* London: Routledge, 1992.

VILKKI, J. Hemi-inattention in visual search for parallel lines after local cerebral lesions. *Journal of Clinical and Experimental Neuropsychology, 11:* 319-331, 1989.

WATSON, R.T., VALENSTEIN, E., and HEILMAN, K.M. Thalamic neglect. Possible role of the medial thalamus and nucleus reticularis in behavior. *Archives of Neurology, 38:* 501-506, 1981.

WATSON, R.T., VALENSTEIN, E., DAY, A., and HEILMAN, K.M. Posterior neocortical systems subserving awareness and neglect. *Archives of Neurology, 51:* 1014-1021, 1994.

WILSON, B., COCKBURN, J., and HALLIGAN, P. *Behavioural Inattention Test; Manual.* Fareham: Thames Valley Test Company, 1987.

ZEKI, S., WATSON, J.P.G., LUECK, C.J., FRISTON, K., KENNARD, C., and FRANCKOWIAK, R.S.J. A direct demonstration of functional specialization in human visual cortex. *Journal of Neuroscience, 11:* 641-649, 1991.

H. Samuelsson, Dept. of Psychology, University of Göteborg, Haraldsgatan 1, 413 14 Göteborg, Sweden.

(Received 11 March 1996; accepted 11 July 1996)