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Visual neglect as a predictor of functional outcome one year after stroke

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Objectives – The aim was to study the role of visual neglect in acute right hemisphere brain infarct as a predictor of poor functional outcome during the first year after stroke. In particular, we were interested in the additional value of neglect measures besides hemiparesis, hemianopia, cognitive deficits and age. *Patients and methods* – A consecutive series of 57 patients with a neuroradiologically verified right hemisphere infarct was examined within 10 days of the stroke. Fifty patients were followed up for 1 year. Neglect was measured with the Conventional and the Behavioural subtests of the Behavioural Inattention Test (BITC and BITB, respectively). The predictors were determined at the 10-day examination. Functional outcome was assessed 3, 6 and 12 months after the onset with the Frenchay Activities Index. *Results* – Neglect in BITB was the best single predictor, which together with high age formed the best combination of predictors for poor functional outcome at each follow-up. Hemiparesis was also included in this prediction model at the 3-month follow-up, but hemianopia, BITC, or visuoconstructional and memory deficits showed no additional predictive value. However, neglect usually recovered soon. When neurological and cognitive deficits were assessed at the same time as the outcome, hemiparesis rather than neglect was the strongest correlate of poor outcome. *Conclusion* – Neglect in acute stroke is an important predictor of poor functional recovery. Residual neglect, which could be compensated in the follow-up tests, may nevertheless restrict patients' real-life activities and hobbies.

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Patients with neglect syndrome due to a unilateral cerebral lesion ignore relevant stimuli on the side contralateral to the lesion when performing everyday tasks (1). Several studies suggest that neglect at the acute stage after stroke might be an important predictor of patients' functional recovery. Fullerton et al. (2) found that the score in Albert's visual neglect test, leg and arm power, level of consciousness, weighted mental score (a sum score of questions measuring orientation and vigilance) and electrocardiographic changes were significantly and independently related to stroke outcome at 6 months. Wade et al. (3) reported that age, hemianopia, visual inattention, urinary incontinence, motor deficit of the arm and sitting balance were the best predictors of poor outcome 6 months after stroke. Denes et al. (4) observed that the presence of neglect in patients with acute haemorrhagic or ischaemic right or left hemisphere lesions was the only significant predictor of poor activities of daily living (ADL) score after a 6-month follow-up, whereas the severity of lesion (an index involving motor, sensory and visual field defects), dysphasia and intellectual impairments all failed to show a significant relationship to ADL. According to Kinsella & Ford (5) the presence of hemi-inattention in the acute stage is an important predictor of poor functional ability 18 months after onset of either left- or right-sided stroke. Kalra et al. (6) examined the functional outcome of stroke patients with or without visual neglect, with comparable stroke pathology (partial anterior circulation infarction) and severity of motor defects. They found that visual neglect patients managed on a stroke unit had similar discharge destinations but lower Barthel Index scores than patients with equal stroke severity but no neglect. Paolucci et al. (7) found in their series of 273 consecutive patients that the severity of stroke at admission (as measured by the Canadian Neurological Scale) and hemineglect were the strongest predictors of poor inpatient rehabilitation outcome. Especially patients with hemineglect and global aphasia had a high risk of poor autonomy and impaired mobility, thus underlining the crucial role of cognitive disorders in this prediction. Another study of Paolucci et al. (8) confirmed that absence of hemineglect is a prerequisite for excellent prognosis on both ADL (Barthel Index) and mobility. However, Pedersen et al. (9) observed in their series of 602 acute stroke patients that anosognosia for limb weakness and visual field defect rather than hemineglect had negative prognostic value on functional outcome (Barthel Index, length of rehabilitation, mortality and rate of discharge to independent living). Hemineglect was associated with poor outcome in univariate analyses, but it had no independent contribution when other influences were taken into account in multivariate analyses.

Given the contradictory findings of the influence of neglect on functional outcome and the fact that neglect usually recovers completely after the acute phase (10), we decided to determine the predictive value of acute neglect for functional outcome at 3, 6 and 12 months after stroke in a consecutive series of 57 patients with right hemisphere infarct. Neglect was assessed with two measures, conventional and behavioural subtests of the Behavioural Inattention test (11–13). In several earlier studies (2–4, 9), neglect was evaluated with only a few subtests, which may have undermined diagnostic accuracy. Our aim was to find out whether neglect in acute stroke has any additional role besides hemiparesis, hemianopia, cognitive deficits and age in the prediction of functional outcome during the first year after stroke. Moreover, it might be speculated, why acute neglect that usually recovers rather quickly could be an important predictor of poor long-term outcome. Evidently, neglect that has disappeared does not disturb functional ability. Therefore, we wanted to clarify whether neglect, besides being an early prognostic sign of poor functional recovery, is also a persistent deficit associated with poor functioning during the follow-up and its plausible cause.

Patients and methods

Patients

Fifty-seven consecutive patients with acute right hemisphere brain infarct admitted to Tampere University Hospital as emergency cases were examined between February, 1994 and March, 1998. Brain infarct was verified by computerized tomography and magnetic resonance imaging. Exclusion criteria were history of neurological disorders, insufficient cooperation due to decreased level of consciousness, severe primary visual impairment, left-handedness and age over 75 years. Neuropsychological and neurological examinations were carried out within 10 days of onset (mean = 6.1; SD = 1.97; range = 2–10). Follow-up studies were conducted 3, 6 and 12 months after onset. None of the patients had recurrent stroke events during the 1-year follow-up. All patients volunteered to take part and gave their informed consent. The study was approved by the Ethical Committee of Tampere University Hospital. The patients were treated and rehabilitated during their hospital stay and the 1-year follow-up period in accordance with the standard procedures for stroke patients at our department. No specific rehabilitation programme was included in this study.

One patient had developmental dyslexia that clearly disturbed his performance in the BIT subtests involving reading, but he did not show signs of neglect at the 10-day examination and his Frenchay Activities Index was high (>45) at each follow-up. He was excluded from the further analyses. We had 53 patients at the 3-month, 52 at the 6-month and 50 at the 12-month examination. Table 1 presents the characteristics of the patients who dropped out during the follow-up.

Table 1. Description of the patients with incomplete follow-up: neglect (BITB and BITC) and severity of hemiparesis at the 10-day examination and available Frenchay Activities Index (FAI)

Case number	Missing data	BITB	BITC	Hemiparesis	FAI: 3 months	FAI: 6 months
1	3, 12 months[1]	Absent	Absent	5	–	39
20	12 months[2]	Absent	Absent	0	37	34
30	6, 12 months[3]	Present	Present	7	14	–
33	6, 12 months[3]	Present	Absent	8	27	–
41	3, 6, 12 months[2]	Present	Present	7	16	–
42	3, 6, 12 months[2]	Present	Present	8	16	–

Abbreviations:
[1] = poor test motivation; [2] = died; [3] = refused to participate.
Hemiparesis: range 0–8 (0 = no hemiparesis; 8 = severe hemiparesis).
BITB = the dichotomy of the behavioural subtests of the Behavioural Inattention Test.
BITC = the dichotomy of the conventional subtests of the Behavioural Inattention Test.

Table 2. Patients' demographical and clinical characteristics at each examination

	Follow-up times			
Descriptive variables	10 days	3 months	6 months	12 months
Number of patients	56	53	52	50
Sex (F/M)	20/36	18/35	19/33	18/32
Hemianopia: present	13 (23%)	7 (13%)	7 (13%)	7 (14%)
Hemiparesis: present	19 (34%)	12 (23%)	11 (21%)	12 (24%)*
BITB: N+	15 (27%)	6 (11%)	4 (8%)	3 (6%)
BITC: N+	16 (29%)	5 (9%)	6 (12%)	4 (8%)
Age: mean (SD)	63.23 (10.21)	62.89 (10.18)	63.23 (10.23)	63.54 (10.38)
Visual memory: mean (SD)	4.70 (3.52)	8.17 (3.47)	8.38 (3.42)	8.68 (3.53)
Verbal memory: mean (SD)	19.77 (6.35)	18.73 (6.64)	20.46 (6.41)	19.62 (5.95)
Block Design: mean (SD)	12.41 (10.61) **$n=55$	18.08 (10.11)	19.58 (10.18)	19.20 (5.95)

Abbreviations:
BITB = the dichotomy of the behavioural subtests of the Behavioural Inattention Test.
BITC = the dichotomy of the conventional subtests of the Behavioural Inattention Test.
SD = standard deviation.
N+ = neglect patients.
* Fluctuation in the number of hemiparetic patients between the 6- and 12-month follow-up is due to 1 patient's score which changed from 0 (= normal motor functioning; 0 for hand and 0 for leg function) to 2 (= mild motor dysfunction; 1 for hand function and 1 for leg function) without any recurrent stroke event.
** One case (42) missing due to poor test cooperation.

Neuropsychological examination

Presence of neglect was determined with the Behavioural Inattention Test (BIT) (11–13). It has 9 behavioural subtests considered to assess neglect in an ecologically valid way and 6 conventional subtests (11). The behavioural subtests are picture scanning, telephone dialling, menu reading, article reading, telling and setting the time, coin sorting, address and sentence copying, map navigation and card sorting. The 6 conventional subtests are line crossing, letter cancellation, star cancellation, figure and shape copying, line bisection and representational drawing. The patients were divided into a neglect and a non-neglect group on the basis of the original cutoff scores of BITB and BITC (11). Visuospatial abilities were evaluated using the Block Design subtest of the Wechsler Adult Intelligence Scale (14). Visual memory was assessed with the Visual Reproduction subtest and verbal memory with the Logical Memory subtest of the Wechsler Memory Scale (15). Raw scores of the Wechsler (14, 15) subtests were used.

Functional outcome was studied in each follow-up examination, 3, 6 and 12 months after the stroke, using the Frenchay Activities Index (FAI) (16, 17). It consists of 15 items assessing three major factors, domestic chores, leisure and work, and outdoor activities (16), which measure independence and "social survival" at a higher level than activities of daily living (ADL) scales at the basic level of self-care (bathing, dressing, walking, etc.) (17). The FAI is a homogenous scale showing substantial validity with stroke patients and with nonstroke elderly patients (18–20).

Our outcome variable was the sum score of the 14 FAI items. Item 12 (gardening) was irrelevant for many patients and was deleted. The possible range of the original FAI is from 15 (poor functional ability) to 60 (good functional ability) points. In our reduced scale it was from 14 to 56. The neuropsychologist read the questions to the patient and filled in the form according to the patient's evaluations.

In the original FAI participants evaluate how frequently (1 = not at all; 2 = less than once a week; 3 = one or two times in a week; or 4 = almost daily). They performed each of the 10 activities during the last 3 months and each of the 5 other activities during the last 6 months. In our study the patients estimated the frequency of each activity during the time from the stroke to the first follow-up examination and thereafter from the previous to the present follow-up.

Neurological examination

A complete neurological examination including confrontational assessment of visual fields was performed on the same day as the neuropsychological assessment or not more than 1 day before or after that assessment. The neurologist evaluated the degree of motor defect and hemianopia according to the NIH Stroke Scale (21) at the acute stage (2–10 days after the infarct).

Neuroradiological examinations

The neuroradiological studies were done on average 6 days after onset (SD = 2.6; range: 0–12). Right hemisphere infarct was verified in all patients by computerized tomography of the brain. Fifty-three patients had also magnetic resonance imaging of the brain.

Statistical analyses

The outcome (dependent) variable was the sum score of the FAI at each follow-up: 3, 6 and 12 months after the stroke. The predictor variables from the 10-day examination and the independent variables from the 3 follow-up examinations were patient's age, hemiparesis, hemianopia, visuoconstructional ability, visual memory, verbal memory and 2 measures of neglect (BITB and BITC). Hemiparesis was scored using a scale of 0 (=normal motor functioning) to 4 (=severe hemiparesis) for leg and arm, and these scores were summed thus having a range from 0 to 8. Hemianopia was scored as absent (=0) or present (=1). The other independent variables were age (range: 25–75), and the raw scores of the Logical Memory (range: 0–56), Visual Reproduction (range: 0–14) and Block Design (range: 0–51). The 2 measures of neglect were scored using the original scoring procedure (11).

The best combination of predictors (determined at the 10-day examination) of functional ability (FAI) at each follow-up examination was computed using forward stepwise linear regression analyses (probability of F to enter = 0.05 and probability of F to remove = 0.10). This method was also used to compute the best combination of independent variables, measured at the same follow-up examination as functional ability (FAI). The neglect and hemiparesis scores had so skewed distributions that these variables had to be dichotomized for the linear regression analyses. Using the original cutoff scores (11) the presence of neglect in BITC (sum score ≤129) and in BITB (sum score ≤67) was 1 and the absence of neglect was 0. The presence of hemiparesis (cutoff score: 1) or hemianopia was 1 and the absence of these defects was 0. The statistical analyses were performed using the SPSS for Windows 8.0 statistical package.

Results

Table 2 gives the patients' demographical and clinical characteristics. The actual ranges of the FAI sum scores of the total patient group at each follow-up were: 14–54 (mean: 35.6; SD = 9.09) at 3 months, 17–54 (mean: 37.8; SD = 8.29) at 6 months, and 21–54 (mean: 36.2; SD = 8.12) at 1 year. Five patients were classified differently by BITB and BITC into the neglect and non-neglect groups: 2 patients had neglect only according to BITB, and 3 patients only according to BITC.

Acute neglect in BITB predicted poor functional outcome (FAI) better than any other predictor variable. It explained 73% of the total variance of the FAI at the 3-month, 64% at the 6-month and 61% at the 12-month examination. Eight variables from the 10-day examination, namely hemiparesis, hemianopia, age, visual memory, verbal memory, visuoconstructional ability, and BITC and BITB were included in forward stepwise linear regression analyses to predict the FAI at each follow-up examination. Table 3 presents the best combinations of predictors. BITB, age and hemiparesis were the best predictors of the 3-month FAI, and only BITB and age remained in the model at the 6- and 12-month examinations. When hemiparesis was forced into the forward stepwise linear regression model to predict 6- and 12-month outcome and

Table 3. Best combinations of predictors in the acute stage of right hemisphere infarct for functional outcome 3, 6 and 12 months after stroke

Follow-up time	Independent variables	R	F	*P*-value for the model	β	*t*	*P*-value for the predictors
3 months	BITB	0.83	36.06	<0.001	−0.57	−5.29	<0.001
(*n* = 53)	Age				−0.36	−4.40	<0.001
	Hemiparesis				−0.33	−3.01	0.004
6 months	BITB	0.75	30.73	<0.001	−0.73	−7.47	<0.001
(*n* = 52)	Age				−0.40	−4.07	<0.001
12 months	BITB	0.75	29.47	<0.001	−0.71	−7.11	<0.001
(*n* = 50)	Age				−0.44	−4.45	<0.001

Abbreviations:
BITB = the dichotomy of the behavioural subtests of the Behavioural Inattention Test.
n = number of patients.
β = regression coefficient.
R = coefficient of determination.

Table 4. Multiple regression analyses of deficits measured in the same examination as the functional outcome (Frenchay Activities Index)

Follow-up time	Independent variables	R	F	*P*-value for the model	β	*t*	*P*-value for the correlates
3 months	Hemiparesis	0.67	20.44	<0.001	−0.44	−3.89	<0.001
(*n* = 52*)	Block Design				0.38	3.36	0.001
6 months	Hemiparesis	0.70	15.70	<0.001	−0.43	−3.85	<0.001
(*n* = 52)	BITC				−0.36	−3.17	0.003
	Age				−0.31	−3.01	0.004
12 months	Hemiparesis	0.75	20.14	<0.001	−0.49	−4.68	<0.001
(*n* = 50)	BITC				−0.36	−3.42	0.001
	Age				−0.30	−3.03	0.004

Abbreviations:
BITC = the dichotomy of the conventional subtests of the Behavioural Inattention test.
n = number of patients.
β = regression coefficient.
R = coefficient of determination.
* = case number 30: missing data in BITB.

each independent variable was allowed to enter simultaneously into the model, only BITB and age improved the prediction. Hemiparesis was a significant predictor alone, but when BITB and age were included in the model, hemiparesis became non-significant.

Acute neglect observed in BITB was the best predictor of later outcome, but during the follow-up the number of neglect patients declined (Table 2) and BITB was replaced by hemiparesis as the strongest correlate of poor outcome. Table 4 presents the results of the stepwise linear regression analyses, when the independent variables were measured in the same examination as the FAI. At the 3-month follow-up, the best combination of correlates of the FAI was hemiparesis and Block Design. At 6- and 12-month examinations this combination was hemiparesis, BITC and age. Thus, visuoconstructional deficit or neglect in BITC had significant independent correlation with functional outcome besides hemiparesis and age during the 1-year follow-up.

Discussion

Many previous studies suggest that visual neglect is a strong predictor of poor functional recovery after stroke (2–5, 7, 8). However, contradictory evidence has recently been presented (9). We assessed 8 prognostic factors (hemiparesis, hemianopia, age, visuoconstructional ability, 2 neglect measures and 2 memory measures) in a consecutive series of patients with acute right hemisphere infarct. The aim was to find out whether neglect has any independent additional role along with other deficits as a predictor and possible cause of poor functional recovery during the 1-year follow-up. To obtain a precise and accurate evaluation of neglect, we used a comprehensive and standardized measure of visual neglect, namely the complete Behavioural Inattention Test (BIT).

Acute neglect in BITB was the best predictor of functional outcome at each follow-up examination, and it was included with age in the best combinations of predictors. Hemiparesis was also included in the linear regression model predicting the outcome after the 3-month follow-up, but not in those predicting the outcome 6 or 12 months after infarct. The other indices of acute defects did not have additional value in these predictions.These results confirmed the previous findings that visual neglect at the acute stage after infarction is a strong predictor of poor functional recovery during the first year after stroke.

On the other hand, neglect usually disappeared. The number of patients with neglect detected with BITB diminished from 15 to 3 during the follow-up (Table 2). When the deficits were measured at the same time as the functional outcome (FAI), BITB did not significantly increase the multiple correlation obtained at the 3-month follow-up examination, where hemiparesis was the strongest correlate of poor functional outcome. The multiple correlation was significantly increased with the inclusion of visuoconstructional deficits measured with the Block Design at the 3-month examination, and neglect determined with BITC together with age at the 6- and 12-month examinations. Why acute neglect in BITB was the strongest predictor of functional outcome, but alleviated and became so weak a correlate of functional outcome that it seemed not to be the principal reason for poor functional recovery?

Robertson (10) has hypothesized that for neglect to be manifest in the acute phase, damage to the posterior orientation system is sufficient. Most neglect patients learn spontaneously to compensate for this deficit, if their damage is restricted to the posterior orientation system. However, patients with large right hemisphere lesions tend to have deficits in the arousal or vigilance system, which impairs their learning of compensatory strategies. A likely explanation for our somewhat paradoxical result could be that most of the patients who had visual neglect at the first examination were normally aroused or alert and learned quickly during the follow-up to be careful in situations where they tended to fail due to their neglect. In other words, they were able to anticipate their skewed spatial orientation and to compensate for neglect in structured and predictable circumstances. Consequently, their BITB performances improved. Nevertheless, daily situations were diverse and novel enough to result in failures and accidents caused by their residual neglect. Therefore, these patients restricted their activities and hobbies. This was evidently the most effective strategy to avoid harmful occurrences. Our results indicate that hemiparesis causes persistent functional difficulties. However, the important role of acute neglect in the prediction of functional impairment suggests that even slight residual neglect, which could not be detected with BITB after the 3-month follow-up, restricts activities and hobbies during the follow-up.

Neglect is almost always associated with other deficits. Pedersen et al. (9) observed anosognosia for limb weakness or visual field defect in 73% of their neglect patients. Note that anosognosia was by definition observed only in patients with obvious motor and/or visual defect. Half of the anosognosic patients were disoriented (22). According to multivariate analyses anosognosia was a more important predictor of poor functional recovery than hemineglect. The authors concluded that patients with anosognosia had much worse overall outcomes than patients with hemineglect and suggested that anosognosia rather than hemineglect decreased functional recovery because of a decreased use of compensatory strategies and increased rate of complications with immobility. They thought that the negative prognostic significance of anosognosia could erroneously be ascribed to hemineglect due to the frequent co-occurrence of these defects.

These notions certainly deserve further investigation. Poor awareness of deficits and lack of insight may coincide with acute neglect and persist after obvious neglect has disappeared. This may partly explain poor functional recovery after the alleviation of acute neglect. On the other hand, it is difficult or perhaps impossible to confirm this hypothesis or to demonstrate direct causes of poor functional recovery with correlational studies searching statistically valid prognostic deficits or syndromes at the acute stage. The role of neglect in the prediction of functional outcome after stroke depends on how these variables are measured, what other predictors are included in multivariate analyses and how patients are selected. Slight differences in these respects could cause apparently conflicting results.

We were not able to assess all patients at each follow-up examination. However, an inspection of Table 1 reveals that acute neglect and hemiparesis were strongly associated with poor FAI scores in these patients and the 2 patients who did not have neglect had rather high FAI scores. This indicates that the incomplete follow-up of the 6 patients decreased rather than enhanced the relationship between acute neglect and poor functional outcome. Because our functional outcome (FAI) was based only on the patients' own evaluation of their activities, it is possible that especially patients with neglect tended to underestimate their deficits and overestimate their functional competence and activity. If persisting unawareness of deficits was associated with acute neglect in our patients, then the role of neglect in the prediction of poor functional outcome was underestimated in our results. Consequently, our failure to follow-up all the patients and the possible bias in the functional outcome measure, did not invalidate our main result.

In conclusion, this study confirmed the findings of previous studies that neglect is a powerful predictor of poor functional recovery. Acute neglect and high age were associated with poor outcome during the 1-year follow-up. However, the number of patients with neglect diminished considerably during the follow-up and when neuropsychological deficits were measured at the same time as the outcome, neglect was not as strongly associated with functional outcome as hemiparesis. Our findings suggest that assessment of neglect should be included in the acute neuropsychological examination after stroke to obtain an adequate prognosis of functional recovery. During the follow-up, latent residual neglect that is not detectable in repeated neuropsychological tests of neglect may continue to cause real-life difficulties and to restrict activities and hobbies. This may indicate that the available measures of neglect are not sensitive enough to detect latent but practically significant neglect.

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