HEMINEGLECT IN ACUTE STROKE—INCIDENCE AND PROGNOSTIC IMPLICATIONS

The Copenhagen Stroke Study[1]

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Widely different incidences have been found for hemineglect in acute stroke, and there is no agreement on the consequences of hemineglect for activities of daily living recovery. We assessed acute admission visuo-spatial and personal hemineglect in a prospective, community-based study of 602 consecutive stroke patients. Hemineglect was found in 23%. Functional outcome was assessed with the Barthel Index (BI), length of rehabilitation, mortality, and rate of discharge to independent living. The independent influence of hemineglect on outcome was analyzed with multiple linear and logistic regression analysis also including functional and neurologic scores on admission, age, gender, previous stroke, comorbidity, anosognosia, orientation, and aphasia. Marital status was also included in the analysis of determinants of discharge to independent living. Hemineglect had no independent influence on admission BI, discharge BI, length of hospital stay used for rehabilitation, mortality, or rate of discharge to independent living. It is concluded that hemineglect per se has no negative prognostic influence on functional outcome.

KEY WORDS: Hemineglect, Cerebrovascular Disorders, Activities of Daily Living, Outcome, Risk Factors

Hemineglect has been defined as "the failure to report, respond, or orient to novel or meaningful stimuli presented to the side opposite a brain lesion, when this failure cannot be attributed to either sensory or motor defects."[1] After having been relatively "neglected" in neuropsychology and neurology for many years, research on hemineglect is now a very active field, with new publications every month.[2] Most of these publications are concerned with experimental investigations in small groups of patients, often trying to differentiate among a spectrum of hemineglect symptoms and to discover basic mechanisms.[3-5] There have also been investigations of the incidence of hemineglect in stroke,[6-9] sometimes with very comprehensive batteries,[10] but never in a community-based population and never in the acute stage of stroke. In reports on hemineglect, it is common to refer to the grave consequences for functional prognosis as one reason why it is important to investigate this symptom.[11] Knowledge of the consequences of hemineglect is, however, rather limited and provided by studies in small and selected populations,[12-16] sometimes without control for other potential influences.[17, 18] These studies have revealed contradictory results. The present study reports the incidence of hemineglect in the acute stage of stroke in a large, community-based sample and evaluates the prognostic consequences of hemineglect per se when other potential influences are taken into account.

Objectives: Upon completion of this article, the reader should be able to (1) define hemineglect and to state its frequency and main determinants in acute stroke; (2) consider the disparate sensitivities for hemineglect when in the clinic and when reading the literature; (3) argue against the widespread belief concerning grave consequences of hemineglect for functional outcome by pointing out the confounding variables of general stroke severity and anosognosia. **Level:** Comprehensive.

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MATERIAL AND METHODS

Definition of Stroke

Stroke was defined according to World Health Organization criteria:[19] rapidly developed clinical signs of focal disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin. Subarachnoidal bleeding was not included.

Subjects

A total of 1,014 patients were recruited in the period from January 1, 1992 to September 30, 1993 in the Copenhagen Stroke Study as previously described.[20,21] This sample is community-based, as 88% of all acute stroke patients in a well defined area are known to be admitted to the hospital and were assessed prospectively and consecutively on acute admission to the hospital. We excluded 76 patients who were not admitted to the hospital within the first week of stroke onset, 57 patients who were unconscious on admission, and 279 patients who were unable to cooperate either because of aphasia (202) or general weakening in the acute state (77). The 602 included patients were more often males (48% compared with 39%; $\chi^2 = 8.9$; $P = 0.003$), had a lower mean age (73.7 years with a standard deviation (SD) of 11.1 compared with 75.6 years with a SD of 10.4; $t = 2.8$; $P = 0.006$), a lower mortality (8.6% compared with 38.3%; $\chi^2 = 131.5$; $P < 0.00001$), and less neurologic impairment as measured by the Scandinavian Neurological Stroke Scale (43.4 points (SD, 11.9) compared with 25.5 points (SD, 18.5); $t = -17.2$; $P < 0.001$).

Procedures

Assessment of Anosognosia and Hemineglect

Anosognosia and hemineglect were assessed on admission using the test procedures described by Bisiach et al.[22] According to these procedures visuospatial hemineglect is assessed with a paper and pencil circle cancellation test, and personal hemineglect is assessed by asking the patient to reach out for the upper limb on the affected side. Anosognosia is assessed by questioning the patient about limb weakness and visual field defects. The hemineglect and anosognosia scores were dichotomized to symptom present or absent. The assessment was done by neurologists who had been carefully introduced to the test.

Assessment of Stroke Severity

Initial stroke severity was assessed with the Scandinavian Stroke Scale (SSS)[23,24] on admission. The SSS evaluates level of consciousness, eye movement, motor strength in arm, hand, and leg, orientation, aphasia, facial paresis, and gait. The total score ranges from 0 to 58 (normal) points. A pure score of "neurologic severity" not including aphasia and orientation was also computed from the SSS (ranging from 0 to 42 points). Aphasia was rated with the SSS speech score and orientation with the SSS orientation score. The SSS was done by neurologists who had been carefully introduced to the scale.

Former Stroke and Comorbidity

A history of former stroke was obtained on admission, and former stroke was coded as present or absent. The hospital register containing information on diagnosis from former admissions was also studied. Information concerning comorbidity was obtained on admission and included other disabling disease apart from previous stroke (amputation, multiple sclerosis, heart failure, latent or persistent respiratory insufficiency, parkinsonism, and so forth.). Comorbidity was coded as present or absent.

Computed Tomographic (CT) Scans

Type, size, and localization of the stroke lesion were determined by visual inspection of CT scans. The size of the lesion was measured as the largest diameter. All scans were evaluated by the same radiologist, who were blinded to patient data. CT scans were done by a Siemens Somatom DR scanner.

Assessment of Activities of Daily Living Function

Activities of daily living (ADL) were assessed by the Barthel Index (BI),[25] which evaluates ten different basic abilities and ranges in total score from 0 to 100 points. Patients included in the study were assessed during the first week after admission, subsequently every week during hospital stay, and at discharge by the nursing and training staff, who had been trained in the ratings. Patients who died during hospital stay were assigned a discharge BI score of 0.

Length of Rehabilitation

Length of rehabilitation was computed as the length of hospital stay minus days spent in hospital for nonmedical reasons after completed rehabilitation, e.g., waiting time for nursing-home.

Rehabilitation

Rehabilitation based on the Bobath technique was given daily to all patients by the nursing staff, physiotherapists, and occupational therapists within the neurologic ward. Rehabilitation was completed within the department. Patients were discharged when the rehabilitation team decided that further in-hospital improvement in function was unlikely.

Statistics

Comparisons for continuous data were carried out with Student's nonpaired t test and categorical tables were analyzed with the χ^2 test. Univariate correlations were performed with Pearson's product-moment correlation. To evaluate the relative importance of multiple influences on outcome variables, multiple linear regression and multiple logistic regression analyses were performed. To retain as much information as possible, backward stepwise regression was first performed, and then all independent variables with $P < 0.2$ were entered into forward stepwise regression. The explanatory power of the multiple linear regression models were judged by Adjusted R^2. Additional analyses were performed to determine whether there was interaction or collinearity between anosognosia and hemineglect. The required two-tailed significance level was set at 0.05 for all statistical tests except for univariate correlations for which the required one-tailed significance level was set at 0.001 because of the large number of significance tests. All analyses were carried out using SPSS for Windows 6.0.[26]

Ethics

The study was approved by the Ethics Committee of Copenhagen, approval number V. 100.2263/91.

RESULTS

Incidence and Patient Characteristics

Basic characteristics appear from the first column in Table 1. This table also shows the variables separately for patients with and without hemineglect along with the statistics for differences between these groups. Hemineglect was found in 23% of patients. The incidence of hemineglect in patients with right hemisphere lesions was 42%. In patients with left hemisphere lesions, it was 8%. Anosognosia was present in 73% of patients with hemineglect and in 6% of those without hemineglect ($\chi^2 = 257.9$; $P < 0.00001$).

Determinants of Hemineglect

The presence of hemineglect was associated with severity of the stroke, and patients with hemineglect were older (Table 1). As mentioned, there was a strong association of hemineglect with right hemisphere lesions; 85% of the patients with hemineglect had a right hemisphere lesion, and for patients without hemineglect it was 39% ($\chi^2 = 84.4$; $P < 0.00001$). There was no significant association of hemineglect with gender, prior stroke, comorbidity, or handedness.

A CT scan was performed in 89% of the patients. Median time from stroke onset to the scan was ten days. General CT characteristics are listed in Table 2. There was no significant difference in the percentage of hemorrhages between patients with and without hemineglect, but patients with hemineglect had a larger mean diameter of stroke lesions, and the stroke lesions more often involved the cortex. Patients with the parietal lobe involved in the stroke lesion had hemineglect (61%) more often than patients without parietal involvement (41%; $\chi^2 = 5.3$; $P = 0.021$), whereas significant differences in the frequency of hemineglect were not seen with frontal, temporal, or occipital involvement.

TABLE 1
Basic patient characteristics and association with hemineglect

	All patients	Patients with hemineglect	Patients without hemineglect	Statistics
N	602	138	464	
Age, years (SD)	73.7 (11.1)	76.6 (10.1)	72.8 (11.3)	$t = -3.8$; $P < 0.001$
Sex, male %	48	42	50	NS
Handedness, right (%)	93	91	94	NS
Lesion side, left (%)	49	15	61	$\chi^2 = 84.4$; $P < 0.00001$
Mortality in hospital (%)	9	17	6	$\chi^2 = 17.4$; $P < 0.00003$
Previous stroke (%)	21	24	21	NS
Comorbidity (%)	18	21	17	NS
SSS on admission, mean (SD)	43.4 (11.9)	35.1 (13.7)	45.9 (10.1)	$t = 8.6$; $P < 0.001$
Neurologic score, mean (SD)	29.9 (10.1)	22.6 (11.4)	32.0 (8.6)	$t = 8.93$; $P < 0.001$
Initial BI score, mean (SD)	62.8 (38.2)	34.1 (36.4)	71.0 (34.6)	$t = 10.3$; $P < 0.001$

SSS = Scandinavian Neurological Stroke Scale.
Neurological Score = SSS on admission excluding aphasia and orientation.
Statistics = univariate comparisons of patients with and without hemineglect.

TABLE 2
CT scan characteristics and association with hemineglect

	All patients	Patients with hemineglect	Patients without hemineglect	Statistics
CT performed, N (%)	533 (89)	122 (88)	411 (89)	NS
No focal lesion on CT (%)	192 (36)	20 (16)	172 (42)	$\chi^2 = 26.6$; $P < 0.00001$
Infarct (%)	310 (58)	91 (75)	219 (53)	$\chi^2 = 17.5$; $P = 0.00003$
Hemorrhagic (%)	31 (6)	11 (9)	20 (5)	NS
Lesion size, mm (SD)[a]	36.6 (25.5)	51.7 (29.5)	30.4 (10.6)	$t = -6.6$; $P < 0.001$
Cortical involvement (%)[a]	139 (41)	64 (52)	75 (18)	$\chi^2 = 29.1$; $P < 0.00001$

[a] In patients with visible lesions on CT-scans.
Statistics = univariate comparisons of patients with and without hemineglect.

Prognostic Implications

Hemineglect was associated with a lower initial functional score: BI was 34.1 points (SD, 36.4) with neglect and 71 points (SD, 34.6) without neglect ($t = 10.3$; $P < 0.001$). A multiple linear regression analysis of initial BI score was performed with the following independent variables: neurologic score on admission, aphasia score, orientation score, anosognosia, age, gender, prior stroke, comorbidity, and hemineglect. The resulting model explained 56% of the variance ($F = 159.6$; $P < 0.0001$). Hemineglect was not included in the resulting model.

Hemineglect was associated with a poorer functional outcome in univariate analyses. The mean BI score at discharge was 47.6 points (SD, 42.4) with hemineglect and 82.6 points (SD, 30.8) in those without ($t = 8.7$; $P < 0.001$). Survivors with hemineglect had a longer mean rehabilitation period (35.2 days (SD, 28.3) compared with 25.2 (SD, 25.3); $t = -4$; $P < 0.001$) and a lower rate of discharge to independent living (54% compared with 85%; $\chi^2 = 57.7$; $P < 0.0001$). Because of the association between hemineglect and stroke severity, the influence of hemineglect per se on outcome was further investigated with multiple regression analyses.

A multiple linear regression analysis of functional outcome (with BI score at discharge as the dependent variable) was performed to evaluate the influence of hemineglect per se when other possible influences are taken into account. The analysis included the following independent variables: neurologic score on admission, functional score on admission, aphasia score, orientation score, anosognosia, age, gender, prior stroke, comorbidity, and hemineglect. The resulting model explained 61% of the variance ($F = 259.4$; $P < 0.0001$) and did not include hemineglect. A multiple linear regression analysis of determinants of the length of rehabilitation including the same independent variables (43% explained variance; $F = 77.9$; $P < 0.0001$) showed that hemineglect had no independent influence on the length of rehabilitation. A multiple logistic regression analysis of discharge to independent living was performed, including the above-mentioned independent variables and also marital status. This model correctly classified 91.2% of the cases. Hemineglect was excluded from the model.

Univariately, in-hospital mortality was significantly higher in patients with *v* those without hemineglect (17% v 6%; $\chi^2 = 17.4$; $P = 0.00003$). However, the multiple logistic regression analysis of mortality including the same independent variables as in the previous analyses did not include hemineglect. The model correctly classified 90.5% of the cases.

DISCUSSION

Hemineglect was found in 23% of acute stroke patients. The findings in previous studies range from 8%[18] to 73%.[10] This wide range can, in part, be explained by variation in patient selection criteria and differences in assessment time post-stroke, but the unusually wide range indicates that the choice of test for the assessment is also of importance. Sensitivity differs between tests[11]; therefore, the use of more sensitive tests results in the finding of a higher incidence. Although it is of interest to know that 73% of all stroke patients have deficient performances on visual attention tests,[10] the relation of this finding to what is usually understood as hemineglect behavior remains unclear. The choice of assessment for the present study was limited by the demands of the acute setting and the size of our study population but was also motivated by the wish to detect only behaviorally relevant hemineglect. Thus, in addition to visual hemineglect, we also tested personal hemineglect. This has not been done in previous studies of the incidence of hemineglect in acute stroke, although it is usual to include personal or "body" hemineglect among the manifestations of hemineglect in theoretic reviews.[1]

Variation in the frequency of hemineglect reported between studies is likely because no generally accepted operational definition of hemineglect exists. A cautious assertion based on the incidence found in the present study is that clinically significant hemineglect is present in at least 23% of all acute stroke patients and most frequently in patients with right hemisphere stroke involving the parietal lobe.

We found that hemineglect per se had no influence on the (1) initial functional status of the stroke patients, (2) the functional prognosis, (3) the length of rehabilitation, or (4) the mortality. Adams and Hurwitz[27,28] reported that recovery from stroke could be impeded not only by hemiplegia but also by a range of neuropsychologic deficits including neglect and anosognosia. Poorer functional recovery in left hemiplegia was reported by Marquardsen,[29] and Denes et al.[13] investigated whether this could be explained by unilateral spatial neglect and anosognosia. The prognostic significance of laterality of stroke has been rejected by the vast majority of subsequent studies,[30] whereas the significance of neglect and anosognosia remains controversial. Contradictory results have been reported. Denes et al.[13] and Fullerton et al.[12] found neglect but not anosognosia to be of significance, whereas the opposite result was found by Sundet et al.[14] and by Gialanella and Mattioli.[16] Friedman[15] did not assess anosognosia and reported neglect to have no independent influence on outcome.

In our sample, a large proportion of the patients with hemineglect also had anosognosia. Despite this overlap, there were dramatic differences in the consequences of hemineglect and those of anosognosia, which we reported elsewhere.[31] Anosognosia had an independent influence on discharge BI score and had severe consequences for both mortality and rate of discharge to independent living. The overall outcome of patients with anosognosia was, thus, much worse than that of patients with hemineglect. It is possible that anosognosia increases mortality because of increased rate of complications with immobility and that it decreases functional remission because of a decreased use of compensatory strategies. It could also be that neither of these mechanisms follows from hemineglect. Given the frequent co-occurrence of hemineglect and anosognosia, the negative prognostic significance of anosognosia can easily be erroneously ascribed to the hemineglect.

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