J Rehabil Med 2002; 34: 215–220

Taylor&Francis healthsciences

NEGLECT AND ANOSOGNOSIA AFTER FIRST-EVER STROKE: INCIDENCE AND RELATIONSHIP TO DISABILITY

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Neglect and anosognosia are serious consequences of stroke. Authors have found great variations in their incidence and their relationship to disability has been unclear. We studied the incidence of neglect and anosognosia within the scope of a population-based stroke-incidence study, and also evaluated their impact on disability. Four tests of visuo-spatial neglect, four tests of personal neglect, and an anosognosia questionnaire were used. Sixty-two patients (23%) of the study group had visuo-spatial neglect according to our definition, 21 patients (8%) had personal neglect, and 48 (17%) showed signs of anosognosia. Using a multiple logistic regression model, we found that both neglect and anosognosia influenced disability. To ascertain the true incidence of neglect and anosognosia after stroke, it is necessary to use a community-based study design, where cases treated outside the hospital are included. Some of the variability found in previous incidence studies is likely to be explained by not using such a design.

Key words: cerebrovascular disorders, epidemiology, perceptual disorders.

J Rehabil Med 2002; 34: 215–220

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Submitted October 23, 2001; Accepted March 15, 2002

INTRODUCTION

Neglect in its various forms and anosognosia are serious companions of primarily right-sided stroke with lesions in the parieto-temporo-occipital area. According to Heilman (1), neglect may be spatial or personal, and can be defined as "a 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". Anosognosia is the lack of awareness of the effects of a brain lesion, including hemiplegia and hemianopia (2). Previous studies have reported an incidence of neglect due to stroke varying between 12% and 95%. For a comprehensive summary see Robertson & Halligan (3).

Several studies indicate that neglect implies a worse prognosis after stroke in terms of functional outcome (4, 5), length of hospital stay (6), and discharge to home than for stroke patients lacking this symptom (7). Furthermore, patients with neglect seem susceptible to falls and wheelchair collisions (8). On the other hand, results from a well-designed study state that neglect *per se* has no influence on the functional outcome (9). Contradictory results therefore exist on how to interpret the poor functional outcome seen in patients with neglect, as to whether the deteriorated outcome is an effect of neglect itself, or if it should be attributed to overall functional deterioration.

To bring further light to these issues, we decided to determine the incidence of neglect and anosognosia, and their impact on disability, within the scope of a population-based stroke-incidence study. To our knowledge, the incidence of neglect has never been examined within the frames of a community-based stroke incidence study design (10). By adopting such an approach, bias due to incomplete case ascertainment, ill-defined denominator (i.e. population at risk), and imbalance of stroke severity between in- and out-patients could be minimized.

MATERIAL AND METHODS

Definitions

Stroke was defined as "rapidly developing clinical symptoms and/or focal, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin", according to the World Health Organization (WHO) criteria (11). Patients with intracerebral hemorrhage and cerebral infarction were included. Cases of recurrent stroke, subarachnoidal hemorrhage (SAH), subdural or epidural hemorrhage, and TIA were excluded, as were cases associated with intracranial malignancy.

Subjects

A stroke-incidence study was carried out in Örebro, Sweden, from February 1, 1999, through January 31, 2000. The total number of inhabitants, which also constitutes the study population, was 123503 as of December 31, 1999 (59759 males and 63744 females). The study was community based, and cases were included prospectively according to the "hot pursuit" method (10), i.e. cases were pursued as they occurred. Cases were identified in several overlapping ways: (1) daily checks with the admission data system; (2) daily visits to the emergency room, the admission department and relevant hospital wards; (3) reports from about 70 GPs at 14 health centres, and 25 nursing homes; (4) all CT scans of the skull taken at the hospital were reported; (5) discharge records from the hospital (with ICD-10 codes G46, G81, and I60 to I69); (6) patient register from the nearest neurosurgery department; (7) protocols from autopsies performed at the pathology department in Örebro and at the nearest forensic department; and (8) examination of death certificates for a stroke diagnosis either as a main or as a contributing cause of death. Data collection in patients $<$18 years of age was performed retrospectively according to methods 5–7 above. Collaborators were instructed to report not only definite first-ever stroke cases, but also cases with recurrent stroke, stroke-like symptoms, acute vertigo, disturbances of consciousness, and TIA, to let the study doctor decide on the possible presence of inclusion criteria.

Nineteen of the 377 patients were discovered retrospectively, when

 ISSN 1650–1977

Table I. *Visuospatial neglect as assessed on individual subtests in the Behavioural inattention test (reducd version (r-BIT) and the Baking tray task (BTT)*

Line crossing	27/260 (10.4%)	r-BIT total 41/263 (15.6%)	Visuospatial tot. 62/270 (23.0%)
Letter cancellation	22/244 (9.0%)		
Line bisection	30/247 (12.1%)		
BTT	51/254 (20.1%)		

the hospital discharge records and death certificates were scrutinized. Nine other patients denied consent. Therefore, 349 patients were accessible for our investigations. Sixty-four patients could not complete any of the tests during the test period. The various reasons for this were early death, low level of consciousness, confusion, aphasia, and/or apraxia. Three patients were missed because tests could not be performed within the correct time window. (They did not, however, have neglect at a later date.) Consequently, 282 patients could complete at least one of all the tests for neglect and/or anosognosia. Owing to low level of conciousness, 14 of them could not complete their tests within the first 4 days, but were tested successfully within the first month.

Compared with the total 377 stroke patients, those included somewhat more often males (48% compared with 45%), had a somewhat lower mean age (75 years compared with 77 years), a clearly lower 28-day fatality rate (3% compared with 18%), had a little more often right-sided brain damage (45% compared with 43%), and had less neurological impairment as measured with the NIH stroke scale (6 compared with 9 points).

Assessment

There is no "pure" test of neglect (3). Neglect may be task-specific (12, 13). In assessing neglect, therefore, it is crucial to use several tests (14), in order to reveal different modalities of the disorder.

Visuospatial neglect was assessed using a reduced version (15) of the Behavioural inattention test (BIT) (16), and a recently developed test, the Baking tray task (BTT) (17). The reduced version of the BIT-test (r-BIT) consists of three sub-tests: the Line crossing test (Albert's test), the Letter cancellation test, and the Line bisection test. Personal neglect was assessed with a test developed by Zoccolotti & Judica (18), which consists of three subtests: the Comb test, the Razor/compact test, and the Eyeglass test. Personal neglect was also assessed using the test procedure described by Bisiach and coworkers (13). Anosognosia was assessed using a questionnaire developed by Starkstein and coworkers (2). The degree of impairment was assessed with the National Institute of Health Stroke Scale (NIHSS) (19) and disability was assessed with the Katz ADL Index (KADLI) (20). It should be noted that data are limited regarding validity and reliability for many of the test instruments used here (with the exception of NIHSS and KADLI). The KADLI, neglect and anosognosia tests, as well as the scoring and cut-off scores, are described in more detail in the Appendix.

Suspected stroke cases were reported to the study doctor (who in 99% of cases was the principal investigator, PA). He performed a detailed neurological examination within the interval 24 hours to 48 hours after the event. If the diagnosis first-ever stroke could be confirmed, the occupational therapist proceeded with assessments of neglect, anosognosia and ADL capacity during days 1–4 after the event. Some patients were not able to go through the neglect and anosognosia tests in this early phase of the disease. If a patient initially was too ill, the occupational therapist would try the tests at weekly intervals up to one month after the event.

In addition to the cut-off scores, we included a demand of asymmetry in the r-BIT tests, so that patients with decreased general attention would not be mixed up with patients showing the typical pattern of visuospatial neglect (21, 22). The number of detected targets at the contralesional side was divided by the total number of detected targets and then represented by a percentage measure. The procedure and cut-off levels were adopted from Samuelsson and coworkers as $<$44% or $>$56% (22).

Statistics

Assuming the binomial distribution, confidence intervals for proportions were calculated using the STATA package, version 7.0. Multiple logistic regression was calculated using the SPSS package, version 10.0.

Ethics

Before entering the study, patients were asked orally for consent. They also received an information letter. In some cases, when a patient's ability to communicate was restricted, consent by next of kin was obtained. The Human Ethics Committee of the Örebro County Council approved the study. The local Data Inspection Board approved the data register.

RESULTS

Between February 1, 1999 and January 31, 2000, 377 patients were found having a first-ever stroke in Örebro of the types brain infarction (BI), intracerebral hemorrhage (ICH), or stroke of undetermined type (UND). Nineteen were included retrospectively when hospital discharge records and death certificates were scrutinized. Of the 377 patients, 208 were female, and 169 male. The mean age for all cases was 76.6 years, for females 78.9 years and for males 73.9 years. The distribution of stroke types was as follows: BI 73% (95% CI, 68 to 77), ICH 12% (95% CI, 9 to 15), and UND 15% (95% CI, 12 to 20). A computerized tomography scan was performed in 84% of patients. The proportion of different stroke types in the neglect and anosognosia groups did not differ much from that of the whole stroke cohort, except that the lacunar type of BI was less common in the above-mentioned groups (6% compared with 21%). Lesions in the posterior circulation were less common in

Table II. *Personal neglect as assessed on individual subtests*

PNT Comb test	14/270 (5.2%)	PNT total 19/274 (6.9%)	Personal tot. 21/276 (7.6%)
PNT Razor/compact	11/268 (4.1%)		
PNT Eyeglasses	13/273 (4.8%)		
THT	13/272 (4.8%)		

18 of the patients reached cut-off by having 2 or more points on at least one of the three subtests of the PNT. One patient reached cut-off by having 1 point on each of the three subtests.
PNT = personal neglect test; THT = touching hand test.

Table III. *Distribution of right and left hemisphere damage in the whole patient sample versus the neglect group*

	All assessable patients (*n*)	Neglect patients (*n*)	Neglect frequency (%; with 95% CIs)
Right hemisphere damage	126	40	32; 24–41
Left hemisphere damage	146	25	17; 11–24
Unknown or bilateral	7	0	
Total	279	65	23; 18–29

the neglect and anosognosia groups than in the whole stroke cohort (3% compared to 21%).

Visuo-spatial neglect

Two hundred and seventy of the 349 patients (77%) were able to complete at least one of the four tests for visuo-spatial neglect, which was our minimum requirement for assessibility; 263 patients were able to complete at least one of the three subtests of the r-BIT, and 238 completed them all; 254 patients completed the BTT; 233 patients (67%) completed all four tests.

Sixty-two of our patients (23%; 95% CI, 18 to 28) reached cut-off on at least one of the four subtests, *and* showed lateralization of performance. The results are shown in detail in Table I.

Personal neglect

Two hundred and seventy-six of the 349 patients (79%) were able to complete at least one of the three subtests of the Personal neglect test battery (PNT) or the Touching hand test (THT), which was our minimum requirement for assessibility; 273 patients were able to complete at least one of the three subtests of the PNT, and 267 completed them all; 272 patients completed the THT; 264 patients (76%) completed all four tests.

Twenty-one patients (8%; 95% CI, 5 to 11) had personal neglect according to our cut-off limits. The results on the individual tests are shown in detail in Table II.

Total incidence of neglect (visuo-spatial and/or personal)

Two hundred and seventy-nine patients were able to complete at least one of the neglect tests. Signs of neglect (visuospatial and/or personal) were present in 65 of those (23%; 95% CI, 18 to 29). Three patients showed signs of personal neglect only, but they were not evaluated regarding visuospatial neglect.

Incidence of anosognosia

Two hundred and seventy-six of the 349 patients (79%) were able to complete the anosognosia questionnaire. Forty-eight of those (17%; 95% CI, 13 to 22) showed signs of anosognosia. Fifteen had one point (weakest form of anosognosia), 8 had two points, and 25 had three points.

Re-test after six months

After six months, we tried to re-test 36 surviving patients that were not initially testable. At this time, it was possible to test 7 of them with regard to neglect and 6 with regard to anosognosia. One of them had visuo-spatial neglect, but none had personal neglect or anosognosia.

Right versus left hemisphere damage

The distribution between right hemisphere damage (RHD) and left hemisphere damage (LHD) with CIs is shown in Table III. Of the 22 patients with personal neglect 18 had RHD, and 4 had LHD. Of the 48 patients with anosognosia, 26 had RHD, 19 had LHD, and 3 had unknown or bilateral damage.

Impairment and disability

The median NIHSS score for testable patients without neglect was 4 (inter-quartile range 2 to 6), and for the 65 neglect patients the median score was 9 (inter-quartile range 4 to 14). The KADLI scores are shown in Table IV.

In order to evaluate whether neglect and anosognosia are predictors of the ADL level at the acute stage, we analyzed the data using a logistic regression model. The result of the KADLI

Table IV. *Katz ADL Index (KADLI) scores for all assessable patients, for neglect patients, and for anosognosia patients*

KADLI score	Neglect patients versus all assessable patients (*n*)	Neglect frequency (%)	Anosognosia patients versus all assessable patients (*n*)	Anosognosia frequency (%)
A	14/133	11	2/132	2
B	3/10	30	1/10	10
C	1/10	10	0/9	0
D	2/7	29	1/7	14
E	8/39	21	7/36	19
F	17/50	34	19/51	37
G	20/30	67	18/31	58
Total	65/279	23	48/276	17

Table V. *Final multiple logistic regression model: odds ratios for being dependent in Activities of Daily Life (Katz ADL Index level B or worse)*

Variable	Odds ratio	95% CI	*p* value
Anosognosia	19.9	4.1 to 96.5	<0.001
Level of consciousnes s	5.3	2.7 to 10.2	<0.001
Leg paresis	3.5	1.6 to 7.4	0.001
Neglect	2.5	1.1 to 6.0	0.037
Arm paresis	2.4	1.0 to 5.4	0.041

assessment was used as the dependent variable. The following explanatory variables were used: (1) level of consciousness as measured with NIHSS items 1a, 1b, and 1c, (2) visual fields as measured with NIHSS item 3, (3) paresis of arm as measured with NIHSS item 5, (4) paresis of leg as measured with NIHSS item 6, (5) sensory function as measured with NIHSS item 8, (6) language as measured with NIHSS item 9, (7) presence of neglect, (8) presence of anosognosia, (9) presence of diabetes mellitus, and (10) presence of cardiovascular disease (other than stroke).

All variables were dichotomized. The outcome variable was dichotomized to either independent (KADLI level A), or dependent (other KADLI levels). The result of the individual NIHSS items was dichotomized as normal (0 point), or not normal (1 point or more). One point on any of the subtests in NIHSS items 1, 5, and 6 led to coding "not normal". Neglect, anosognosia, diabetes mellitus and cardiovascular disease were coded as either present or not present.

The 10 explanatory variables were first tested one by one against the dependent variable for the presence of significant association. The language (aphasia), diabetes mellitus and cardiovascular disease variables were removed from the model because of lack of significant association. Thereafter, the remaining variables were cross-tabulated (according to Pearson), to assess for multicolinearity. No two variables were correlated at more than 0.60, which was acceptable for the subsequent analysis. The logistic regression analysis was then performed. The following combination was identified as the best predictor variables: anosognosia, level of consciousness (NIHSS items 1a, 1b, and 1c), leg paresis (NIHSS item 6), neglect, and arm paresis (NIHSS item 5). The visual field and the sensory variables were excluded, because of lack of significant contribution to the regression model. The individual *p* values, and odds ratios with 95% CIs are shown in Table V. There is no widely accepted direct analogue to the r^2 in multiple linear regression. When using the Nagelkerke *R* Square, which is a part of the SPSS output, the resulting model accounted for 48% of variance in outcome. Finally, the model was examined for goodness-of-fit. Deviance values were calculated to analyze how well the model fitted each case. The relative influence of individual observations was analyzed by Cook's influence statistic. To validate the model, we experimentally excluded cases that had extreme standardized residuals, and influential observations. The removal of these ($n = 8$) did not violate the model, and therefore it was concluded that model fit was adequate.

DISCUSSION

We found that neglect and anosognosia are relatively common companions to first-ever stroke in the acute phase. The visuo-spatial type of neglect is more common than the personal type. We also found that neglect and anosognosia are predictors of the ADL level at the acute stage, as measured with KADLI early after the event.

Regarding the selection of test instruments, there were on the one hand reasons to use a rather compact test battery. The number of patients was large. Many stroke patients quickly got tired in the early phase of the disease, and it was desirable that most patients completed all the tests. On the other hand, there were reasons to use a more comprehensive test battery because tests should cover different modalities of neglect. This was emphasized by discrepancy between individual tests. In our study, it is possible that additional neglect patients would have been revealed had we used a still broader test battery, covering also for example motor neglect and neglect of far space. Some authors have shown that traditional tests, such as paper-and-pen tests, are insensitive for determining the presence of neglect (23, 24), and that more demanding assessment methods have to be used to reveal subtle signs of neglect. It has also been shown in some subjects that carrying out an attention-demanding task temporarily aggravates neglect symptoms (25). The documentation regarding the validity for some of the tests used, notably the personal neglect and anosognosia tests, is quite scarce, especially for the acute phase of the disease. However, to our knowledge these were the best available tests at the time the study started.

The reasons for including a measure of asymmetry may be controversial, as one of the mechanisms behind neglect may be a non-directional attention deficit (26). In our study, the general alertness and cognitive function of the patients were very variable, correlating to the individual stroke severity and pre-existing conditions. It was considered that the risk of encountering false-positive neglect cases, as a result of low level of general consciousness or low cognitive capacity, rather than neglect, outweighed the disadvantages in favour of using the condition of lateralization.

Since double dissociation between visuo-spatial and personal neglect has been described (13, 27), we included a test of personal neglect in our battery. Even though visuo-spatial neglect without personal neglect was often found, no example of the reverse was identified, and therefore we failed to confirm the existence of such a double dissociation.

Few instruments exist for evaluating anosognosia. As a result of development over several years, the questions in the present test (2) are now more specific, and consequently less is left to the judgement of the investigator. However, there are still some questions regarding the overall validity of the test procedure.

Obviously, the instrument cannot be used when a patient's level of consciousness is reduced, or in cases of confusion or dementia. However, borderline cases may have both anosognosia and a low-grade level of confusion, which adds some degree of uncertainty to our results.

The fact that 64 patients were not able to complete any of the tests adds uncertainty to the estimate of neglect incidence. In order to minimize this uncertainty, we tried to re-test at 6 months patients who initially were untestable. Of the seven patients who were testable at 6 months, one had neglect (14%), which implies that this problem may not be so great. Inevitably, a large proportion of the patients was still not able to complete any of the tests at 6 months. The reason for this is first and foremost cognitive difficulties, which overshadow the possible presence of neglect.

No previous neglect incidence study has been based on a community-based stroke incidence study design. Closest came a study performed as a part of the Copenhagen Stroke Study (9). It was hospital-based, even though as many as 88% of stroke patients were admitted to the hospital. Of the 602 patients who were able to cooperate, hemineglect was found in 138, or 23%. The test procedures described by Bisiach and coworkers (28) were used. Although the study basis was somewhat different, and the test material was not the same, the Copenhagen study and our study gave similar results regarding incidence of neglect.

Although a number of studies exist on neglect incidence after stroke, interpretation is complicated because of methodological differences (29). Subject selection affects the denominator when incidence rates are calculated. Hospital admission rate varies widely between centers, and may affect incidence, if only in-patients are studied. Neglect after LHD may be less common and have more favourable prognosis, which affects incidence if only RHD patients are studied. The timing of assessment is important, because neglect often shows a regressive tendency. In the present study, our goal has been to minimize variability by a carefully prepared study design. Inevitably, some design elements are open for discussion. It is no axiom that neglect should be assessed 1–4 days after the stroke event, and the choice of test battery can be disputed. Our study design aims to capture symptoms of acute neglect in patients with first-ever stroke. However, neglect symptoms often disappear after some time. Furthermore, neglect may be more common after a second or third stroke. This design is therefore not suitable for estimating the prevalence of chronic neglect in a stroke cohort.

Even regarding anosognosia, this is the first incidence study based on a community-based stroke incidence study design. An incidence study of anosognosia was performed as part of the Copenhagen Stroke Study (30). A procedure described by Bisiach and co-workers (28) was used. Pedersen and co-workers (30) found that anosognosia was present in 21% (95% CI, 17 to 25) of their patients compared with 17% (95% CI, 13 to 23) in our study. In the Copenhagen study, 44% of patients were excluded compared with 27% of ours.

It has often been pointed out that stroke patients with neglect carry a greater burden of disability than patients without this symptom (4, 5, 9). Our data in Table V support this thesis, as well as that anosognosia is a still stronger predictor of disability. Our data also show that neglect and anosognosia do not only affect disability through co-variation with other impairment variables.

Based on a community-based stroke incidence study design, this investigation has shown the occurrence of neglect and anosognosia after first-ever stroke. We have also shown that those symptoms affect disability. This finding justifies further research efforts on how to treat, rehabilitate, or compensate for neglect and anosognosia.

ACKNOWLEDGEMENTS

This study was supported by a grant from Örebro County Council. The authors thank Anders Magnusson, BSc, for statistical advice.

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APPENDIX

Katz's ADL Index (KADLI) is used for ADL assessments. KADLI is an ordinal, cumulative scale with well-defined steps. It summarizes an individual's dependence or independence of another person in performing six primary activities, namely eating, continence, transferring, going to toilet, dressing and bathing. Grade A stands for independence in all functions, grades B–F for gradually increasing dependence and grade G for total dependence. When recovering from an illness, the functional abilities are usually regained in order from G to A. The index has been shown to have high reliability and validity in acute care.

The Line crossing test (16), or Albert's test, consists of a page containing 40 × 25 mm long lines. The patient is asked to cross out all the lines on the paper. The tester illustrates this by crossing out central lines. The total number of lines crossed is noted. The maximum point is 36. Cut-off is 34 or less.

The Letter cancellation test (16) consists of a paper containing five lines of letters (34 per line). The examiner asks the patient to cross out the letters E and R. The total number of crossed Es and Rs is scored. The maximum point is 40. Cut-off is 32 or less.

The Line bisection test (16) consists of a paper containing three horizontal 204 mm lines spread in a staircase fashion across the page. The patient is asked to divide each line at its center. A scoring template is used to measure deviations from the mid-point. The maximum score is three for each line, and is achieved if the patient's mark lies within 12.75 mm to the left or right of the center. The maximum point is 9 for all three lines. Cut-off is 7 or less.

In the Baking Tray Task (17), patients are asked to spread out 16 cubes as evenly as possible over a 75 × 100 cm board "as if they were buns on a baking tray". The number of cubes in each half field is counted. Normal is eight cubes in each field. Cut-off is an asymmetry of 10 to 6 or worse.

Personal neglect was evaluated according to the following procedure (18): The patient is presented with three objects, one at a time (comb, razor for man, powder for woman, eyeglasses), and is asked: "Show me how you use ____?" Each item is scored as normal (0), slight deficit (1), medium deficit (2), or severe deficit (3), according to scale descriptions. Normal is 0/0/0. Cut-off is 1/1/1 or 2 points on any one of the three tasks.

Personal neglect was also evaluated as follows (13): The examiner, clearly pointing to the patient's hand, instructs: "With this hand, touch your other hand". The test is scored 0–3 points. Zero is normal and means that the patient promptly reaches for the target. Cut-off is one point or higher.

Anosognosia was assessed according to a questionnaire (2), and is scored 0–3 points. Zero is normal, and means that the patient can spontaneously report the disorder following a general question about the patient's complaints. Cut-off is one point or higher.