Reasons for Variability in the Reported Rate of Occurrence of Unilateral Spatial Neglect After Stroke

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Background and Purpose—We sought to determine the frequency of occurrence of contralesional unilateral spatial neglect (USN) after stroke and to investigate the effect of side of lesion, nature of assessment tool used, and timing of assessment relative to stroke onset.

Methods—We performed a systematic review of published reports, identified by a search of electronic databases (MEDLINE 1966–1997, PSYCHLIT 1974–1996, and CINAHL 1982–1997) and by searching reference lists of the reports selected. Excluded were unpublished, non–English language, and nonhuman studies.

Results—Thirty published reports met the selection criteria, 17 of which directly compared right brain damage (RBD) and left brain damage (LBD). Contralesional USN appeared to occur more frequently after RBD than LBD in 16 of these. Both the assessment tool used and the time of assessment relative to stroke onset affected the reported rate of occurrence, although recovery rate data were inadequate (4 reports).

Conclusions—The clinical belief that USN occurs more frequently after RBD than LBD was apparently supported by a systematic review of published data. However, an accurate estimate of the rates of occurrence and recovery after stroke could not be derived. Four reasons for the variability among studies were discussed, including subject selection, lesion localization, and nature and timing of assessment. Different USN disorders may exist, which may require type-specific rehabilitation approaches. This may have implications for epidemiological studies and for the development of new treatments. Theoretically driven epidemiological studies are required before adequately powered randomized controlled trials of rehabilitation can be conducted. **(*Stroke*. 1999;30:1196-1202.)**

Key Words: neglect ■ rehabilitation ■ spatial behavior ■ stroke

Unilateral spatial neglect (USN) is a neuropsychological disorder or more likely a set of disorders[1] commonly encountered by rehabilitation professionals working with people who have had a stroke. In the early stage after onset, USN is reflected in poor performance of activities of daily living[2] and may hinder response to therapy. In a typical rehabilitation setting, USN may need to be addressed on a daily basis by all members of the multidisciplinary team: nurses, occupational therapists, physiotherapists, speech and language therapists, and psychologists.

Despite the vast research interest in USN, there appears to be no clear evidence for the rehabilitation of this set of disorders. There have been many promising approaches to the amelioration of the symptoms of neglect, but they produce only transient effects and may do so only with certain patients. The lack of a base of evidence may in part be due to the lack of consensus regarding the methods of identifying USN and the measurement of change after treatment. An additional requirement for clinical effectiveness in research with the use of randomized controlled trials is adequate statistical power. A small sample size may be inadequately powered to detect changes between the control and treatment groups and therefore unable to answer the research question. If USN is a heterogeneous condition, this source of "noise" should be taken into account in power calculations. The determination of the statistical power of a study is also dependent on good epidemiological data. Therefore, the rate of occurrence of USN and the extent of spontaneous recovery must be known before effective controlled trials can be performed.

The present study used a systematic review of the literature to determine the reported frequency of occurrence of USN after stroke. The effect of the following factors on the reported frequency of USN was examined: side of stroke, time after onset of assessment, and type of assessment tool used. It is commonly believed that USN occurs more frequently after right- than left-sided stroke, and this has been reported in several textbooks.[3] The present report seeks to verify this by a systematic analysis of the accumulated research findings. We also looked at the subject selection methods and other issues affecting the generalizability of the samples studied.

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Subjects and Methods

Definition of Neglect

USN has been defined as "a failure to report, respond, or orient to stimuli in the contralesional hemispace that cannot be attributed to sensory or motor impairments."[4] Given the wide-ranging types of USN that can occur, it is not surprising that there are a large number of terms used in the literature to refer to USN. The most frequently used terms are *neglect* and *inattention*. These are often preceded by the words *unilateral* or *hemi*, as in unilateral neglect, hemineglect, or hemi-inattention. However, some of the reports reviewed aimed to look specifically at one type of neglect (eg, a disorder of attention) and to distinguish it from another (eg, disorder of the intention to act). For example, reports have used the term *visual inattention/perceptual neglect* to refer to a failure to attend to a part of space and the term *motor neglect* to refer to an intentional failure to perform a movement in that part of space. In an attempt to include all of these studies in our review, we used *neglect* or *inattention* as a starting point for our search strategy, which was refined as described below.

Eligibility of Studies

All English language, published studies reporting data on the frequency of occurrence of neglect after stroke were eligible for inclusion. Studies were included even if their primary aim was not to determine the frequency of occurrence. However, studies whose explicit aim was to recruit individuals known to have USN were not eligible for this review. Studies that investigated USN after etiologies other than stroke were included if the data were described in such a way that the stroke data could be examined independently. Excluded were those in which the data were not reported in sufficient detail to answer the questions addressed by this study. Unpublished work was not included in this review.

Search Strategy

The Cochrane Library database was initially searched to determine whether a review of this nature already existed or was in progress. None was found.

Between August and November 1997, published reports were identified by a search on the electronic databases MEDLINE 1966–1997, PSYCHLIT 1974–1996, and CINAHL 1982–1997. At the time of the search, the 1997 PSYCHLIT database was not available to the authors. As described above, the initial search words used were *neglect* or *inattention*. These were modified to exclude non-English reports and reports whose subjects were not human. We further modified our search using the exclusion terms *mothers*, *elderly abuse*, *alcohol*, and *children* since the term *neglect* appeared in association with these terms.

All remaining abstracts were viewed. The search included books, journal articles, and published letters. Full copies of selected texts were obtained for those likely to contain data on the rate of occurrence of neglect. Reference lists from these articles were also searched. A data extraction form was used to ensure that the same data were extracted from each study. The data collected included subject selection methods and reporting of exclusion rates, timing of assessment of USN, methods used to assess USN, and the frequency of USN reported after left- and right-sided strokes. All studies were independently checked by a second reviewer to increase accuracy. Frequency rates reported are for contralesional neglect. Several studies also reported ipsilesional neglect,[5] but this issue is not considered in the present study.

Results

Studies whose aim was to recruit individuals known to have USN were not eligible for this review (eg, Weintraub et al[6]). Fifty-two reports were initially reviewed. Excluded were 12 studies that recruited subjects with other neurological etiologies (eg, neoplasms) as well as subjects with stroke.[7–18] Although these 12 included some of the key texts cited in the USN literature,[8,14] they could not be included in this review because it was not possible to extract the frequency data specific to stroke. Four other studies were excluded because they did not specify the etiology.[19–22] In addition, apparently eligible studies were excluded if it was not possible to extract the data in the form required for this review[23,24] or to avoid duplication of subsets of data from other included studies by the same research group.[25,26] Two of the 32 studies that investigated USN specifically in stroke patients were based on analyses of case notes from those patients who had previously been given a neuropsychological examination.[27,28] To increase the homogeneity of the data set, only data from the remaining 30 were used in this review.[2,5,29–56]

TABLE 1. Sample Size and Characteristics of the 30 Studies Reviewed

No. of subjects assessed for USN	9–602 (median, 63)
No. of subjects excluded/could not be assessed	1–336 (not specified in 12 studies)
No. of RBD subjects assessed	9–307
No. of LBD subjects assessed	0–295
No. of studies with both LBD and RBD subjects	17
Mean age of subjects assessed, y	54–74 (not specified in 5 studies)
Maximum age of subjects assessed, y	71–100 (not specified in 10 studies)

Subject Selection

The subject selection methods used in these 30 studies were examined to determine whether generalizations could be made from their samples to the wider stroke population. The quality of the information provided on the subject selection methods varied between studies. Eleven of the 30* made explicit mention of the fact that their sample was drawn from consecutive cases of stroke, either from admissions to general hospitals or to rehabilitation facilities.

Information on Exclusions

The number of subjects recruited to the 30 studies varied widely. Data on sample size and characteristics are summarized in Table 1. The numbers excluded ranged from 1 subject[47] to >300.[43] Reasons for excluding patients were as follows: low level of consciousness and inability to cooperate with the assessment, no abnormality detected on CT brain scan, previous history of stroke, left-handed, not admitted within 1 week of onset, unilateral left hemisphere brain damage, and aged >74 years. Clearly these varied depending on the main aim of the study. Twelve of the 30 studies reviewed did not provide any data on the number excluded.

Demographic and Clinical Data

Data reported on the stroke patients in the 30 studies included demographic and clinical information. The mean age of stroke patients was provided for 25 studies and is given in Table 1. As shown, 20 studies also provided the maximum age of recruited subjects.

*References 2, 5, 29, 33, 34, 37, 38, 41, 43–45.

TABLE 2. Number of Times Each USN Test Was Used in the 30 Studies Reviewed

Test Used	No. of Studies Using This Test*
Cancellation	
Line	8
Star	6
Letter	6
Figure Copying	13
Line Bisection	7
Drawing From Memory	7
Raven's Colored Progressive Matrices	2
Others	22
Not specified	1

*This column does not total 30 because several studies used >1 test.

Seventeen studies recruited subjects with both left brain damage (LBD) and right brain damage (RBD).[2,5,29–43] The remaining 13 only investigated USN in the latter group.[44–56] In addition, more RBD than LBD patients were generally recruited. For the 17 studies investigating USN in both LBD and RBD stroke patients, fewer of the former were recruited (median sample size, 40 and 54, respectively). Explanations typically given for this are that patients with LBD are more likely to be dysphasic and have difficulty understanding the assessment instructions.[32]

Timing of Assessment

All but 2 of the 30 studies reviewed provided data on the timing of the assessment of USN relative to the onset of the stroke. The majority of studies were performed during the acute phase, often within 1 week after onset, for example.[40,41] Eighteen were conducted within 4 weeks, and 6 studies were conducted within 6 months of stroke. Four studies had heterogeneous samples, consisting of individuals varying from a few months to several years after onset of stroke.

Method of USN Assessment

Only 1 study did not specify how USN was assessed.[2] The most common assessment procedure was to administer a battery of paper-and-pencil tests.[38] The purpose of some studies was the development or standardization of a test battery.[33] Nineteen studies used a battery of up to 7 different tests. The tests used to detect USN and the number of times each was used in the 30 studies reviewed are listed in Table 2. As shown, the most frequently used single task was a cancellation task. Some of these used structured arrays (eg, Letter Cancellation) and others unstructured arrays (eg, Star Cancellation). Figure Copying was also commonly used; figures included were the Rey Osterreith Complex Figure[57] and shapes from the Behavioral Inattention Test[33] and the Rivermead Perceptual Assessment Battery.[58]

In general, the tests used were traditional paper-and-pencil assessments. Only occasionally did the assessment of USN involve an evaluation of the subjects' performance of everyday activities.[45] Some studies used the Behavioral Inattention Test, which includes 9 subtests intended to be more ecologically valid as well as 6 traditional tests.[37] Several of the studies used tests designed specifically for the study.[53]

TABLE 3. Frequency of Occurrence of Contralesional Neglect After Stroke in the 17 Studies That Compared LBD With RBD Subjects

	RBD		LBD	
	Range	Median	Range	Median
No. of subjects recruited	14–307	54	8–295	40
No. with contralesional neglect	8–129	19	0–48	4
Percentage with contralesional neglect	13–82	43	0–76	21

Control Groups

Nine of the 30 studies compared the stroke patients' performance with that of a control group. These tended to be studies in which the primary aim was the validation of a USN assessment tool, such as the Behavioral Inattention Test[33] and the Random Chinese Word Cancellation Test.[53] Others used unusual assessment tools, such as the LAVA figure[34] and Wundt-Jastrow illusion,[35] which lacked appropriate normative data. The numbers of control subjects recruited varied from 12 to 120. Some studies matched for age[55] or age and level of education.[50] Both healthy[42] and patient control groups[52] were used.

Results of Main Analyses

The following questions, on the rate of occurrence of neglect after stroke, were tested with the use of the data reviewed. It is important to point out that the numbers reported here (ie, sample size and rate of occurrence of neglect) may differ from those reported in certain of the 30 articles reviewed. This is because for the purpose of comparison between studies, the present figures reflect the numbers actually assessed rather than initial sample size reported by the original authors before exclusions or loss to follow-up.

Does Contralateral Neglect Occur More Often in RBD Than LBD?

This review supported the belief that contralateral neglect occurs more often after RBD than LBD. The frequency of contralesional (left-sided) USN after RBD ranged from 12% to 100% in the 30 studies that prospectively recruited RBD stroke patients. The frequency of contralesional neglect after LBD in the 17 studies that recruited LBD stroke patients ranged from 0% to 76%.

To answer the question of whether contralateral neglect occurs more often in RBD than LBD, only those 17 studies that compared both were considered.[2,5,29–43] This information is summarized in Table 3. Comparison of these studies' findings suggests that there is a higher occurrence of neglect in the RBD subjects. In all but 1 of the 17 studies reviewed, the occurrence rate is higher after RBD than LBD. The exception is 1 study[5] that reported almost equivalent rates for both groups of 75 RBD and 75 LBD subjects 1 month after stroke.

TABLE 4. Example of Study Showing Variability of USN by Side of Lesion and Test Used

Test Used	Frequency of Contralesional Neglect	
	RBD (n=75)	LBD (n=75)
Cancellation	23 (31%)	6 (8%)
R/L Copying Shapes	14 (19%)	9 (12%)
R/L Copying Words	7 (9%)	24 (32%)

Data from Edmans and Lincoln (1987).[5]

Because of the methodological differences between studies, a meta-analysis comparing odds ratios was not considered appropriate.

Does the Frequency of Contralateral Neglect Vary With the Nature of the Assessment Used?

This review supported the expectation that the reported frequency of contralateral neglect would vary with the nature of the assessment used. The majority of the 30 studies reviewed used a battery of tests of neglect. Hier et al,[45] studying the same group of subjects, reported a rate of 46% from behavioral observations of neglect and 88% from a paper-and-pencil Figure Copying Test. Another study[35] reported a difference in occurrence of neglect between 2 paper-and-pencil tests, from 49% on a letter cancellation task to 30% on Albert's Test, another cancellation task that involves canceling lines.

The frequency data (reported above and in Table 3) are based on the subtests that detected the highest rate of neglect. The present study's claim of equivalence in frequency of USN between the RBD and LBD groups in the study of Edmans and Lincoln[5] was based on the highest rate reported on different tests. The findings from the latter study are summarized in Table 4 as an example of how the frequency of neglect varies with the test used. Despite this, it remains higher after RBD if comparisons are made on identical subtests. The exception was Copying Words, which was rejected by the original authors as an invalid assessment of neglect because the results of this time-limited test may be contaminated by other cognitive deficits (eg, dysphasia).

Is the Frequency of Occurrence of Contralateral Neglect Affected by the Timing of the Assessment?

This review supported the belief that contralateral neglect was most frequent soon after stroke and that the rate of occurrence decreased with time. However, this statement needs qualification, as discussed below.

Four of the 17 studies comparing RBD and LBD groups were examined to answer this question because they had completed repeated assessments over time. Because they used different tests, between-study comparisons of the frequencies reported cannot be made. However, longitudinal changes within studies can be evaluated (Table 5). After RBD, only 1 of the 4 studies reported an apparent decrease in the proportion of stroke patients with contralateral USN, from 13% to 3% over a 6-month period.[32] A reduction in the frequency of USN appeared more likely after LBD.

Discussion

To provide evidence for neuropsychological rehabilitation, controlled trials are required of the techniques that claim to reduce the disabling effects of USN. Although single-case designs are often used, group studies (particularly randomized controlled trials) are requested more frequently by organizations that fund research grants. Reliable epidemiological data are essential to ensure that these studies have adequate statistical power. These data include the proportion of patients likely to experience contralateral USN after stroke and the extent of natural recovery over time.

The present report systematically reviewed existing data on the frequency of USN after stroke and the effects of various factors on the reported frequency rates. For many of the studies investigated, the frequency data were not reported in sufficient detail for the purposes of the present study. However, no criticism is intended of these studies since the frequency data were often not the main aim of their work.

The main finding was that it was not possible to derive a reliable estimate of the frequency rate from the existing literature. The reported frequency varied widely between studies, largely because of methodological differences. We determined 4 reasons why there is no secure knowledge of the frequency or duration of contralateral USN after stroke. First, different populations of stroke patients have been studied with the use of different sampling methods, selection criteria, and the exclusion of individuals who could not complete certain types of assessments. For example, fewer patients with LBD are typically studied since they are more likely to be dysphasic and have difficulty understanding the assessment instructions. This has important methodological implications for the finding that USN occurs more frequently after

TABLE 5. Four of the 17 Studies Comparing RBD and LBD Groups Reporting Repeated Assessments Over Time

Study	RBD		LBD	
	Assessment 1	Assessment 2	Assessment 1	Assessment 2
Kinsella and Ford[2] (1980)	8/14 (57%)	No change*	0/17 (0%)	No change*
Denes et al[30] (1982)	8/24 (33%)	7/24 (29%)†	5/24 (21%)	2/24 (8%)†
Sunderland et al[32] (1987)	11/82 (13%)	2/75 (3%)†	4/106 (4%)	0/87 (0%)†
Stone et al[37] (1991)	13/16 (81%)	9/11 (82%)*	16/21 (76%)	5/15 (33%)*

*3-month follow-up.
†6-month follow-up.

RBD than LBD since the more severely LBD patients may not have been assessed.

Second, there was often poor definition of lesion site, and the possibility of multiple lesions could not be excluded. Despite the description in the present report of LBD and RBD subjects, it is important to point out that this classification was not always based on neuroradiological evidence of lesion location. Most studies described subjects as having a unilateral stroke from the presence of a hemiplegia and other neurological signs. Only in some cases was this supported by electroencephalographic or neuroradiological evidence. The possibility of multiple lesions, from preexisting possibly silent stroke, could not be excluded. Although this did not prevent examination of the frequency data, it made it difficult to state definitively that the USN behaviorally observed was associated with a contralateral rather than ipsilateral or bilateral lesion(s). Furthermore, although CT scans were used in some studies, the moment when the scan was performed was rarely specified. In those reports that did, it was invariably within the first few days after onset of stroke.[38,41,48] It is well known that early (<24 hours after onset of stroke) CT scans can be misleading because they may show few or no abnormalities.

The third reason for the lack of secure knowledge of the frequency or duration of contralateral USN after stroke was that USN assessments were performed at different times, and there was some evidence that frequency varied according to the timing of the assessment. A reduction in the frequency of USN with time appeared more likely after LBD. However, these longitudinal comparisons must be treated with caution because of the possible effect of subject attrition, which was not accounted for. It may have been that those with USN have a poorer long-term outcome and are less likely to participate at the follow-up assessment.

It is also important to note that interpretations of frequency based on percentages must be made with caution because of the large variability in sample size, with some studies recruiting only small samples. For instance, the finding of neglect in 100% of the RBD subjects studied by one group[47] should be countered by the fact that only 9 RBD subjects were assessed. Five of the 30 studies included in this review had <20 RBD subjects, and 5 of the 17 LBD studies had <20 subjects. In all but 1 of the 17 studies reviewed, the occurrence rate is higher after RBD than LBD. The exception is the study that reported almost equivalent rates for both groups of 75 RBD and 75 LBD subjects 1 month after stroke.[5] This latter study raised the important issue of the influence of the method of assessment on the reported frequency of neglect.

The fourth reason was that differing methods of assessment were used, and the frequency of USN varied with the tool used. Several alternative explanations for this have been proposed. One has been that the tests differ in terms of task difficulty, or that some tests are more precise and can detect milder degrees of neglect.[36] As Sunderland et al[32] commented, "Visual neglect is not an all-or-none phenomenon, but must be considered as a point somewhere along a continuum." There is also the suggestion that neglect is a variable phenomenon that is influenced by extraneous factors (N.B. Lincoln, PhD, unpublished data, 1998). For example, variations in frequency of USN may occur as a result of tiredness, distractions, motivation, and external cues.

However, there is also the compelling explanation that different tests require different abilities and therefore detect different USN disorders. Support for this explanation has been provided in the form of double dissociations.[56,59] A single dissociation, such as neglect on a Line Bisection task but not on a Figure Copying task, could be interpreted as evidence of Line Bisection as a more difficult or precise task. However, McIntosh et al[56] also described a patient with neglect on Figure Copying but not Line Bisection. This double dissociation refutes the possibility of the 2 tasks varying in level of difficulty and points to the heterogeneity of neglect. In fact, in recent years there has been a growing consensus of the concept of a "multiplicity of neglects."[1,60,61] However, caution should be exercised because there are not yet adequate data on the reliability of many of these paper-and-pencil tests.

Whatever the explanation, the implications are that only if the same tests are used can the frequency rates in the literature be compared across studies. Although several studies used a common assessment (eg, Figure Copying), the frequency data were rarely reported separately from the battery of other tests used. Two additional difficulties were encountered. The first was the methodological differences in scoring many of the assessments. Some studies have relied on comparison with the performance of a control group.[52] Others have not used control data but identified USN if subjects made more errors on the contralateral than the ipsilateral side.[30] This variability in scoring further confounded comparisons between studies.

Finally, the validity of the tests used and their relevance for activities of daily living may be questioned. Most studies used paper-and-pencil tests such as cancellation and copying. Only occasionally did the assessment of USN involve an evaluation of the subjects' performance of everyday activities.[45] Some studies used the Behavioral Inattention Test,[37] but none used other recent assessments that emphasize behavioral aspects of USN.[62–64] The use of paper-and-pencil tests alone to elicit and measure USN may be insufficient. They may give false-positive results since individuals may "fail" these tests because of deficits other than the presence of USN. Alternatively, "normal" performance (on structured paper-and-pencil tests that involve an activity in peri-personal space) may mask a disabling USN, for example, neglect of personal space observed when the individual bathes the affected side. Many therapists are placing less trust in the results from paper-and-pencil assessments because these may remove the unpredictable, multitasking demands that occur in everyday activities and mask the real-life difficulties an individual might have outside the artificial testing situation. Given the encouraging growth of interest in ecologically valid functional assessments in recent years, their use may soon become more widespread.

Limitations of the Present Study

The limitations of the present study should also be acknowledged. Only data from published studies were used in this review. Had this been a review of the literature on the

effectiveness of treatment, then a publication bias would be expected, since studies reporting positive findings are more likely to be published. This was considered less likely in a review of observational studies that included some in which very little neglect was detected and others in which the frequency of occurrence was high. However, a publication bias may have resulted from the exclusion of non–English language reports.

There are also limitations to the breadth of this review in that the frequency of ipsilesional USN was not considered. We believed that this puzzling phenomenon required separate consideration. Furthermore, this review only considered contralateral USN rather than the associated neurological signs, such as extinction and anosognosia, known collectively as the "neglect syndrome." However, a recent article has produced evidence of double dissociations among these signs, which the authors suggest argues against a functional syndrome arising from damage to a single underlying mechanism.[59]

Finally, the exclusion of 2 articles from this review on the grounds that they were based on retrospective analyses of case notes[27,28] was possibly not warranted since the assessments were conducted prospectively at a common time after injury. However, inclusion of these data does not change the core conclusions of the present report.

Recommendations for Further Research

From this review, several recommendations can be made for future research. First, prospective studies are required that are representative of the stroke population. The method of assessment should be chosen with the aim of reducing the exclusion of certain individuals on the grounds of inability to perform the assessment task. For example, many existing methods require the manual dexterity to hold a pen. The second recommendation is for longitudinal studies with initial and follow-up assessments at fixed times. This would allow consideration of the magnitude of spontaneous recovery and should make appropriate adjustments for subject attrition. Studies that investigate recovery over time may produce useful data beyond recording quantitative changes in the occurrence of contralesional USN. The longer-term follow-up study of Halligan et al,[26] which assessed nearly 100 cases each of LBD and RBD after 4 years, found interesting qualitative differences between the groups in the rate of occurrence of ipsilesional USN. Ipsilesional USN was not the subject of this review but warrants further investigation.

The third and crucial issue for future research is a recognition that USN may not be a unitary disorder. Epidemiological research needs to take advantage of recent developments regarding the theoretical bases of the different types of USN. Assessments need to be developed that distinguish between the different disorders. This is particularly important if more effective treatments, which would need to be tailored to the underlying impairments, are to be developed. However, it is not the intention of this report to criticize the use of test batteries consisting of subtests that may elicit different types of USN. Their value in detecting the presence of neglect is acknowledged. The point we wish to make is that for epidemiological studies, we need to develop tools that distinguish between the types of neglect and are capable of detecting change over time or after intervention. These should include reliable assessments relevant to behavioral activities of everyday living. The fourth recommendation is for research to include a clear definition of the locus of the lesion since different tests may elicit different deficits related to differing anatomic sites, which may help to unravel the underlying theoretical bases of these disabling disorders.

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