Journal of Clinical and Experimental Neuropsychology

ISSN: 1380-3395 (Print) 1744-411X (Online) Journal homepage: https://www.tandfonline.com/loi/ncen20

Differences between left- and right-sided neglect revisited: A large cohort study across multiple domains

Antonia F. Ten Brink, Jurre H. Verwer, J. Matthijs Biesbroek, Johanna M. A. Visser-Meily & Tanja C. W. Nijboer

To cite this article: Antonia F. Ten Brink, Jurre H. Verwer, J. Matthijs Biesbroek, Johanna M. A. Visser-Meily & Tanja C. W. Nijboer (2017) Differences between left- and right-sided neglect revisited: A large cohort study across multiple domains, Journal of Clinical and Experimental Neuropsychology, 39:7, 707-723, DOI: 10.1080/13803395.2016.1262333

To link to this article: https://doi.org/10.1080/13803395.2016.1262333

Published online: 12 Dec 2016.

JOURNAL OF CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY, 2017
VOL. 39, NO. 7, 707–723
https://doi.org/10.1080/13803395.2016.1262333

Differences between left- and right-sided neglect revisited: A large cohort study across multiple domains

Antonia F. Ten Brink [a], Jurre H. Verwer [b], J. Matthijs Biesbroek [b], Johanna M. A. Visser-Meily [a,c] and Tanja C. W. Nijboer [a,c,d]

[a]Center of Excellence in Rehabilitation Medicine, Brain Center Rudolf Magnus, University Medical Center Utrecht, and De Hoogstraat Rehabilitation, Utrecht, The Netherlands; [b]Department of Neurology, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands; [c]Department of Rehabilitation, Physical Therapy Science & Sports, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands; [d]Department of Experimental Psychology, Helmholtz Institute, Utrecht University, Utrecht, The Netherlands

ABSTRACT

Unilateral spatial neglect (USN) is a syndrome that can occur after right- and left-hemisphere damage. It is generally accepted that left-sided USN is more severe than right-sided USN. Evidence for such a difference in other domains is lacking. Primary aims were to compare frequency, severity, region specificity, cognition, physical functioning, and physical independence between left and right USN. Secondary aims were to compare lesion characteristics. A total of 335 stroke patients admitted for inpatient rehabilitation were included. The severity of the lateralized attentional deficit was measured with a shape cancellation and line bisection test (in peripersonal and extrapersonal space) and the Catherine Bergego scale. The Mini-Mental State Examination, Stichting Afasie Nederland score, search organization (i.e., best *R* and intersections rate), Motricity Index, balance, mobility, and self-care were assessed. Measures were statistically compared between left, right, and no USN patients. Lesion overlay plots were compared with lesion subtraction analyses. *Results*: Left USN (15.82%) was more frequent than right USN (9.25%). Demographic and stroke characteristics were comparable between groups. The lateralized attentional deficit was most severe in left USN. USN in both peripersonal and extrapersonal space was more frequently left-sided in nature. Search efficiency was lower in left USN. Balance was poorer in right USN. No differences between left and right USN were found for cognitive ability, communication, motor strength, mobility, and self-care. Most patients with left USN had right-hemispheric lesions, whereas patients with right USN could have lesions in either the left or the right hemisphere. To conclude, left and right USN are both common after stroke. Although the lateralized attention deficit is worse in left than in right USN, consequences at the level of physical functioning and physical independence are largely comparable. From a clinical perspective, it is important to systematically screen for USN, both after right- and after left-hemisphere damage.

ARTICLE HISTORY
Received 18 July 2016
Accepted 11 November 2016

KEYWORDS
Cognition; Functional impairment; Lateralized attentional deficit; Stroke; Unilateral spatial neglect

Unilateral spatial neglect (USN) is a syndrome that occurs frequently after stroke (Appelros, Karlsson, Seiger, & Nydevik, 2002; Buxbaum et al., 2004). The core cognitive deficit of USN is a deficit in *lateralized attention*, resulting in *involuntary* impairments in detecting or responding to contralesional stimuli (Appelros et al., 2002; Buxbaum et al., 2004). Even though it is generally the lateralized inattention that is measured during, for example, a neuropsychological assessment, the most widely used term for this cognitive disorder is neglect, both in scientific studies and in clinical practice. In this paper, the honored term "neglect" is therefore used for sake of clarity, but one should be aware that the core deficit that we measure, and that is the basis for categorizing patients, is the lateralized attention deficit. Neglect may vary in sensory modality (i.e., visual, auditory, haptic, and tactile; Jacobs, Brozzoli, & Farnè, 2012), region of space (i.e., peripersonal and extrapersonal; Van der Stoep et al., 2013), and frame of reference (i.e., egocentric and allocentric; Chechlacz et al., 2010). Spontaneous recovery of USN takes place within the first 3 months post stroke onset, leaving about 40% of neglect patients with chronic USN after 1 year post stroke onset (Nijboer, Kollen, & Kwakkel, 2013; Ringman, Saver, Woolson, Clarke, & Adams, 2004).

CONTACT Tanja C. W. Nijboer t.c.w.nijboer@uu.nl Department of Experimental Psychology, Utrecht University, Heidelberglaan 1, 3584 CS, Utrecht, The Netherlands.
The supplemental data for this article can be accessed here

Estimations are that USN occurs in approximately 50% of stroke patients with right-sided hemisphere damage and in 30% of stroke patients with left-sided hemisphere damage (Chen, Chen, Hreha, Goedert, & Barrett, 2015). Some studies reported that USN is more severe and more persistent after right-hemisphere damage than after left-hemisphere damage (Chen, Hreha, Kong, & Barrett, 2015; Gainotti, Messerli, & Tissot, 1972; Ogden, 1985; Ringman et al., 2004), whereas others indicate that USN severity does not differ between left and right USN (Chen, Chen, et al., 2015; Suchan, Rorden, & Karnath, 2012). This right-hemispheric dominance of USN has not yet been completely elucidated. A widely accepted theory of USN states that the right hemisphere controls shifts of attention to both the left and right side of space, while the left hemisphere only controls attention to the right side (Mesulam, 1981). Another theory proposes that both hemispheres have a role in orienting to the contralesional side, but this bias is larger in the left than in the right hemisphere (Kinsbourne, 1987). Corbetta and Shulman (2011) propose that lesions in right-hemisphere ventral regions would result in a disturbed balance between hemispheres regarding physiological activity, resulting in a left-hemispheric dominance. Both theories, however, have received limited empirical support from neuroimaging studies. The nonspatial functions of the ventral attention network, such as reorienting, target detection, visual search, and arousal, are strongly right-hemisphere dominant (Bartolomeo, Thiebaut de Schotten, & Chica, 2012; Ten Brink, Biesbroek, et al., 2016).

In general, USN is linked to poor motor recovery (Nijboer, Kollen, & Kwakkel, 2014), higher disability (Appelros et al., 2002; Buxbaum et al., 2004; Chen, Chen, et al., 2015; Nijboer, van de Port, Schepers, Post, & Visser-Meily, 2013), poor responses to rehabilitation services (Chen, Chen, et al., 2015; Chen, Hreha, et al., 2015; Nys et al., 2005), and a reduced likelihood to being discharged home (Wee & Hopman, 2008). More severe USN is associated with more suppression on the (pattern of) recovery in other domains (Nijboer, Kollen, et al., 2014); however, it is unknown whether a difference between the left and right networks exist. In none of the studies was a dissociation between left- and right-brain-damaged patients, or left and right USN, made (Appelros et al., 2002; Buxbaum et al., 2004; Chen, Chen, et al., 2015, Chen, Hreha, et al., 2015; Nijboer, Kollen, et al., 2014, Nijboer, van de Port, et al., 2013; Nys et al., 2005). Since USN severity is thought to be more severe after right- than after left-hemispherical damage, possibly, motor, functional or cognitive differences exist too between left and right USN patients.

The primary aim of the current study was to investigate the distinctions and similarities between patients with left and right USN in a large cohort of stroke patients, regarding frequency, severity, and region-specific USN (i.e., peripersonal, extrapersonal), cognition, physical functioning, and physical independence. The secondary aim was to compare lesion characteristics between patients with left versus right USN. To our knowledge, we are the first to assess all these different domains to compare performance between left, right, and no USN groups.

1. Method

1.1. Patients

Stroke patients were included from a patient population admitted for inpatient rehabilitation to De Hoogstraat Rehabilitation center, from October 2011 to August 2014. In the Netherlands, a patient is admitted to a rehabilitation center if: (a) discharge to home is expected in view of the prognosis and availability of the caregivers, but not from the hospital within 5 days; (b) the patient is capable of participating in therapy; (c) the patient is vital enough; (d) a multidisciplinary approach is essential to reach the complex rehabilitation goals; and (e) discharge to home is expected to be within <3 months. Older patients (75 years or older) are more likely to be admitted to geriatric rehabilitation.

All stroke patients were screened for USN as part of standard care, within 2 weeks after admission. From the resulting database, the following exclusion criteria were used for the current study: (a) not screened for USN (due to being sick, being absent, or a lack of motivation); (b) not able to perform the object cancellation task (i.e., unable to understand instructions, unable to use a computer mouse, or severe alterations in vision); (c) performed the object cancellation task in only one region of space (due to fatigue, lack of motivation, or lack of time); (d) absence of data on hemisphere of lesion; and (e) discrepancy regarding side of USN between peripersonal and extrapersonal space.

Patients were grouped based on the presence of a deficit in lateralized attention. Performance at the object cancellation was used to group patients (see *2.3.1 Severity of the lateralized attentional deficit*). An omission difference score (left versus right) of at least 2 was used as the criterion for USN (Van der Stoep et al., 2013). Subsequently, patients with a lateralized attentional deficit were allocated to the “left USN” or “right USN” group, exclusively based on the laterality of omissions on the object cancellation task. Patients with a lateralized attentional deficit in peripersonal and/or extrapersonal space were classified as either left or right USN. Patients without a lateralized attentional deficit formed the third group (i.e., no USN). Lesion side was not taken into account in the allocation procedure.

1.2. Procedure

The data were collected from existing databases (Supplementary Table 1). We collected demographic and stroke characteristics from patient files, lesion characteristics from magnetic resonance imaging (MRI) or computed tomography (CT) scans, measures of communication, overall cognition, and physical independence. Within 2 weeks after admission, a neuropsychologist conducted a USN screening (consisting of the object cancellation task and line bisection task) and administered measurements of balance for all stroke patients. Within the same week, the nurse observed the presence and severity of USN during activities of daily living (ADL) with the Catherine Bergego Scale (CBS). The research and consent procedures were in accordance with the standards of the Declaration of Helsinki.

1.3. Outcome measures

Outcomes split for left and right USN are presented per domain. The domains are severity of the lateralized attentional deficit, other cognitive measures, and physical functioning and physical independence for the primary aims, and lesion characteristics for the secondary aims.

1.3.1. Severity of the lateralized attentional deficit

A digitized object cancellation task was performed both in peripersonal and in extrapersonal space (Van Der Stoep et al., 2013). Object cancellation tasks are the most widely used and most valid task to assess USN (Machner, Mah, Gorgoraptis, & Husain, 2012; Sperber & Karnath, 2016). The object cancellation task consisted of 54 small objects (0.6° × 0.6°) among 75 distractors (identical, yet larger objects 0.95° × 0.95°) and letters and letter combinations (0.45° × 2.1°). Patients were seated in front of a monitor and used a computer mouse to click the targets presented on a computer monitor. Patients were instructed to indicate when they were finished. After each click, a blue circle appeared on the clicked location and remained visible throughout the task. There was no time limit. The monitor was placed at a distance of 30 cm for assessing peripersonal USN, and at a distance of 120 cm for assessing extrapersonal USN. Stimuli in extrapersonal space were presented enlarged to control for visual angle. The order of the region-specific measurements (peripersonal and extrapersonal) was randomized across patients.

The following outcome measures were derived: omission difference score, center of cancellation (CoC), consistency of the search direction (best *R*), and intersections rate. Best *R* and the intersections rate are measures of search organization, and are described in 1.3.2 "Other cognitive measures." The horizontal normalized CoC (CoC-x) reflects both the location and the amount of the cancelled targets (Rorden & Karnath, 2010). The CoC-x ranges from −1 to 1. For example, a missed target at the most left side of the stimulus field results in a shift of the CoC-x towards 1, reflecting a CoC towards the right side. A CoC-x of zero indicates an absence of a spatial bias regarding the cancelled targets. The CoC-x outcome was used to determine the severity of deficit in lateralized attention. Since left USN would result in a positive CoC-x, and right USN would result in a negative CoC-x, differences between relative CoC-x values would not be informative. Therefore, in order to compare the left and right USN group, the absolute values of the CoC-x were used.

A digitized line bisection task was administered in peripersonal and extrapersonal space, in which the same distances were used as in the object cancellation task (Van der Stoep et al., 2013). Three horizontal lines (22° long and 0.2° thick) were presented at different horizontal positions. From upper to lower lines, the horizontal shift was always 15% of the line length to the left. The lines were vertically evenly distributed: The vertical shift was 28% of the line length. Patients were asked to mark the subjective midpoint of each line by clicking on it with a computer mouse. Patients were instructed to start with the upper line. The task was conducted four times, resulting in bisecting a total of 12 lines. Scoring was conducted according the method of Van der Stoep et al. (2013): A negative value reflects a shift of the subjective midpoint to the left, and a positive value vice versa. The normal range (mean ±3 *SD*s) was −0.74° to 0.48° for the presented lines in peripersonal space and −0.86° to 0.56° for the presented lines in extrapersonal space (Van der Stoep et al., 2013). For each region of space the average deviation for all lines (upper, middle, and bottom) was used as an outcome measure of the severity of deficit in lateralized attention. For evaluation of both the direction of deviation (i.e., side of USN) and the degree of deviation (i.e., severity of deficit in lateralized attention) both relative and absolute values of the averaged deviation scores were used.

The CBS is an observation scale for functional assessment of USN (Azouvi et al., 2003; Dutch version: Ten Brink et al., 2013). It assesses performance in personal (body parts and body surface), peripersonal, and extrapersonal space, as well as in perceptual, representational, and motor domains. Nurses rated the severity of USN resulting in a range of 0 (no USN) to 30 (severe USN). The CBS total score was used as an outcome measure of the severity of deficit in lateralized attention.

1.3.2 Other cognitive measures

The Mini-Mental State Examination (MMSE) task is a cognitive screening instrument (Folstein, Folstein, & McHugh, 1975). It is an 11-point questionnaire assessing orientation, memory, attention, calculation, language, and constructive functions. The score ranges from 0 to 30; a score of less than 24 is regarded to reflect cognitive impairment.

The Stichting Afasie Nederland (SAN) task is a screening instrument for communication deficits, which focuses on verbal and auditory language and is filled out by the rehabilitation physician (Deelman, Koning-Haanstra, Liebrand, & van den Burg, 1981). The score ranges from 1 (no communication possible via language) to 7 (normal speech and understanding of language).

The measure best *R* was derived from the object cancellation task, and depicts whether one searched in the same direction throughout the whole task, for example in a columnar fashion or row after row. In order to derive best *R*, we computed the Pearson correlation coefficient (r) from the linear regression of the x-values and y-values of all marked locations relative to the order in which they were marked. The highest absolute correlation of these two (best *R*) represent the degree to which calculations were pursued orthogonally (Mark, Woods, Ball, Roth, & Mennemeier, 2004). The best *R* value can range from 0 to 1, in which a higher value depicts a more efficient search.

The measure intersections rate indicates the amount of crossings with paths between previously cancelled targets. It has been shown that few intersections occur during efficient search (Woods & Mark, 2007). Further, the intersections rate differentiates between groups of stroke patients (Ten Brink, Van der Stigchel, Visser-Meily, & Nijboer, 2016). To compute the intersections rate, the total amount of path intersections was divided by the amount of cancellations that were not immediate revisits (Dalmaijer, Van der Stigchel, Nijboer, Cornelissen, & Husain, 2015). Thus, a high intersections rate indicates less organized search. Both best *R* and the intersections rate were computed using CancellationToolbox (Dalmaijer et al., 2015). Only data from the object cancellation in extrapersonal space were used to compute best *R* and the intersections rate, because clicks in the peripersonal task were located too close to each other in order to reliably compute these measures.

1.3.3. Physical functioning and physical independence

The Motricity Index (Collin & Wade, 1990) assesses the severity of motor impairment after stroke. There are three items for the arm (pinch grip, elbow flexion, and shoulder abduction) as well as three for the legs (ankle dorsiflexion, knee extension, and hip flexion). Scores range from 0 (very severe motor impairment) to 100 (full motor function) per extremity (arm and leg).

Since a negative relation has been reported between USN and postural balance (Nijboer, Ten Brink, Van Der Stoep, & Visser-Meily, 2014; van Nes et al., 2009), and disturbances in balance are related to problems in daily-life functioning (Suzuki, Ohyama, Yamada, & Kanamori, 2002), the measure of postural balance was included in the current study. During the balance task, the average sitting position and postural sway of the patient were measured in two conditions: with eyes open and with eyes closed (Nijboer, Olthoff, Van der Stigchel, & Visser-Meily, 2014). The patient sat with their hands in their lap, on a Nintendo Wii Balance Board placed on a stool in front of a white wall. For each condition (eyes open and closed), four outcomes were taken into analysis. First, the center of pressure (CoP) reflects the average sitting position on the Wii balance board. The mediolateral CoP represents the "side-to-side position" (horizontal axis), and the anteroposterior CoP represents the "front-to-back position" (vertical axis). In order to compare the left and right USN group, both the relative and the absolute values of the average mediolateral CoP were used, in order to evaluate both the direction and the degree of deviation, respectively.

Shifts in CoP from the ideal weight distribution (i.e., a 50–50% weight distribution between the left and right and the front and back sensors) were seen as a measure of postural sway, or the ability to maintain balance (i.e., a large shift indicates poor balance). Mediolateral and anteroposterior postural sway (i.e., the mean variance of displacement) were calculated. The Wii Balance Board has shown good test–retest reliability of CoP path length and between devices, in validity and reliability comparisons with a force plate by Clark et al. (2010).

The Barthel Index (Collin, Wade, Davies, & Horne, 1988) measures the level of independent functioning in activities in daily living. Scores range from 0 (completely dependent) up to 20 (completely independent).

The Utrecht Scale for Evaluation of Rehabilitation (USER) covers physical independence (mobility and self-care; Post, van de Port, Kap, & Berdenis van Berlekom, 2009). The USER Mobility subscale consists of 7 items including sitting, standing, transfers, and several forms of mobility, whereas the Self-Care subscale consists of 7 items including basic activities of daily living. Total scores of each subscale range from 0 to 35, with higher scores reflecting better performance. The USER has been proven reliable, valid, and responsive (Post et al., 2009). Compared with the Barthel Index, the USER is more sensitive for improvement in patients with relatively good recovery, which can be attributed to the extended response categories used (Post et al., 2009). However, since the Barthel Index is more widely known, we additionally derived Barthel Index scores from the USER.

1.3.4. Lesion characteristics

The following lesion characteristics were retrieved from the medical charts: lesion side (left, right, or bilateral) and lesion focality (focal, diffuse, or bilateral).

For a subset of 81 ischaemic stroke patients, CT or MRI scans were available for lesion segmentation. Infarcts were manually segmented on transversal slices of follow-up CT scans, or on T2 FLAIR sequences of MRI scans by a trained rater (J.M.B.) who was blinded to clinical data. Infarct segmentations were transformed to the Montreal Neurological Institute (MNI)-152 template (Fonov, Evans, McKinstry, Almli, & Collins, 2009; Klein, Staring, Murphy, Viergever, & Pluim, 2010; Kuijf, Biesbroek, Viergever, Biessels, & Vincken, 2013), with an intermediate registration step using an age-specific CT and MRI template (Rorden, Bonilha, Fridriksson, Bender, & Karnath, 2012), which served to improve the quality of the registrations. A more detailed description of the procedures for lesion segmentation and registration are provided elsewhere (Biesbroek et al., 2014, 2016). Quality checks of the registration results were performed by comparing the native scan to the lesion map in MNI space. For 45 patients, the coregistered lesion maps were manually adjusted to correct for slight registration errors using MRIcron (http://www.mccauslandcenter.sc.edu/crnl/mricron) by J.M.B.

In order to determine which brain regions were most strongly related to left and right USN, we performed a qualitative lesion overlay and subtraction analysis. In this analysis, lesion overlay and subtraction plots were generated for patients with left USN versus no USN, and right USN versus no USN using MRIcron. The registered lesion maps were additionally used to compute normalized lesion volumes for these patients (Rorden, Karnath, & Bonilha, 2007).

Thus, the variables lesion side and lesion focality were retrieved from the medical charts for all patients, whereas lesion subtraction analyses and computation of lesion volumes were performed for a subset of 81 patients with lesion segmentations.

1.4. Data preprocessing and analysis

Since group sizes were unequal, and data were not normally distributed, differences between left, right, and no USN groups were tested with Mann–Whitney tests. Dichotomized variables were analyzed with a chi-square test. In case of 5 expected count in less than 80% of cells, or a cell with zero expected count, the Fisher exact test was used.

For Mann–Whitney tests, effect sizes were calculated [with the formula: $r = Z/\sqrt{(N)}$]. For chi-square tests, phi (with a data table of 2 × 2) or Cramer's V (with a data table of >2 × 2) was calculated (with the formula: φ or $V = \sqrt{[\chi^2/N(k - 1)]}$. Effect sizes of .1, .3, and .5 were interpreted as small, medium, and large, respectively.

In order to answer our main question regarding differences between patients with left and right USN, all outcome measures were compared between patients with left and right USN in separate Mann–Whitney tests with a level of significance of $p = .05$.

Performance of patients with left and right USN was compared with performance of patients with no USN, in order to evaluate whether patients with USN differed from patients without USN. We used Mann–Whitney tests with a Bonferroni correction to avoid a family-wise error rate (adjusted level of significance $p = .025$).

2. Results

2.1. Inclusion

A flowchart of the included patients for this study is depicted in Figure 1. Of the 426 stroke patients admitted to the rehabilitation center, 335 patients were included in behavioral analyses. Of these patients, 251 were classified as no USN, 53 as left USN, and 31 as right USN.[1] Left USN was more frequent than right USN (see Table 1 for statistics). In Table 1 the

[1]Patients with left-sided USN omitted on average 6.34 targets on the left (SD = 6.31) and 1.27 targets on the right (SD = 1.75); patients with right-sided USN omitted on average 0.27 targets on the left (SD = 0.63) and 2.48 targets on the right (SD = 2.52).

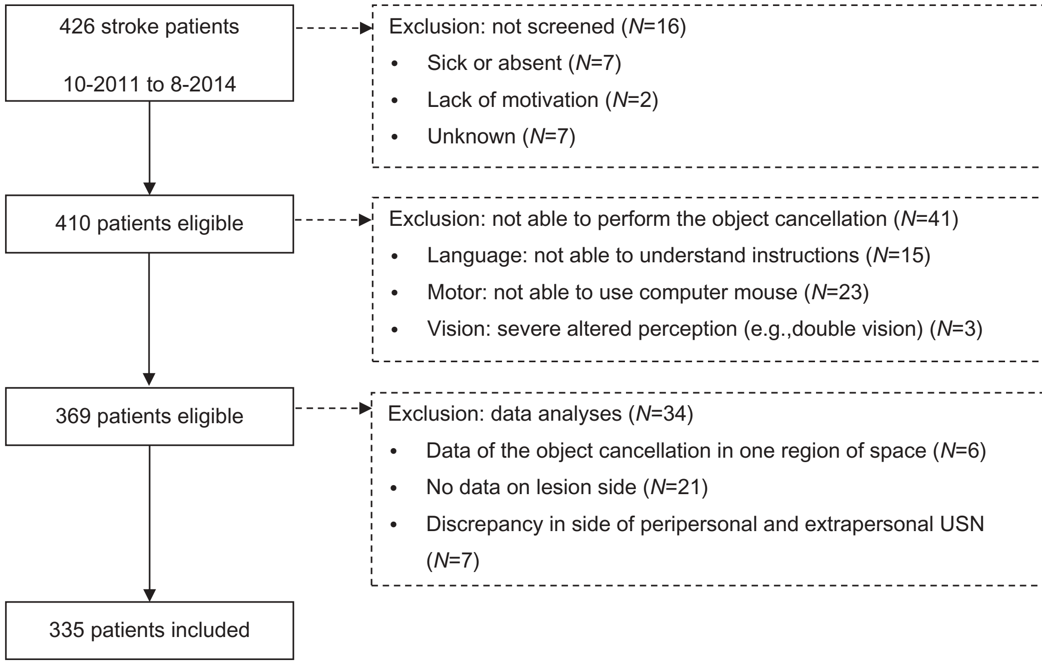

Figure 1. Flowchart of patient inclusion.

Table 1. Amount of patients per group.

	Left USN	Right USN	Left vs. right USN
Group size	53	31	$\chi^2(1, N = 2) = 5.76; p = .016^*$
Region of space, %			$\chi^2(2, N = 84) = 15.80; p < .001^{*a}, V = 0.43$
Peripersonal	32.1	51.6	
Extrapersonal	9.4	32.3	
Both	58.5	16.1	

Note. USN = unilateral spatial neglect.
[a]Post hoc comparisons showed that only the group size of the "both" group differed significantly between left and right USN patients.

occurrence of region-specific USN is depicted for patients with left and right USN. These frequencies differed significantly between patients with left and right USN. Left USN patients had USN in both regions of space more often than right USN patients (see Table 1 for statistics).

2.2. Demographic and stroke characteristics

Distribution of demographic and stroke characteristics are listed in Table 2. No differences in age, gender, handedness, stroke history, and etiology were found between patients with left and right USN, left and no USN, or right and no USN. No difference was seen in time post stroke onset at the moment of the USN screening between patients with left and right USN. Patients with left USN were screened at a later time post stroke onset (5 days) than patients without USN.

2.3. Outcome measures

2.3.1. Severity of the lateralized attentional deficit

In Table 3 the results of the measures of lateralized attention are presented. A larger deficit in lateralized attention (absolute CoC-x) was found for patients with left than with right USN, in both peripersonal and extrapersonal space.

Regarding the line bisection, a deviation to the right was seen in patients with left USN compared to patients without USN, in both peripersonal and extrapersonal space. The deviation in patients in right USN did not differ from that in patients without USN, in neither peripersonal nor extrapersonal space. The magnitude of the deviation was larger for patients with left USN than for those with right USN in peripersonal and extrapersonal space, indicating larger deficit in lateralized attention.

With respect to observations of USN in daily life, no discrepancies were found between patients with left and right USN, and between patients with right and no USN. Higher scores on the CBS were found, however, for patients with left USN than for patients without USN, indicating a deficit in lateralized attention in daily-life activities.

2.3.2. Other cognitive measures

Boxplots with scores on all four cognitive measures are depicted in Figure 2. Patients with left USN showed comparable general cognitive functioning (MMSE) to that of patients with right or no USN. Patients with

Table 2. Demographic and stroke characteristics.

Measure	Left USN	Right USN	No USN	Left vs. right USN	Left vs. no USN	Right vs. no USN
Age in years, median (IQR)	62 (16)	57 (18)	61 (16)	$U = 744.5; Z = -0.714; p = .475, r = -.08$	$U = 6382.5; Z = -0.463; p = .643, r = -.03$	$U = 3620.0; Z = -0.632; p = .528, r = -.04$
Sex, % male	60.4	61.3	63.3	$\chi^2(1, N = 84) = 0.01; p = .934, \varphi = .01$	$\chi^2(1, N = 304) = 0.17; p = .684, \varphi = .02$	$\chi^2(1, N = 282) = 0.05; p = .823, \varphi = .01$
Handedness, %				$p = 1.00$	$p = .776$	$p = 1.00$
Left	12.5	9.7	10.2			
Right	87.5	90.3	88.5			
Ambidexter	0.0	0.0	1.2			
Time post stroke onset in days, median (IQR)	28 (22)	33 (28)	23 (15)	$U = 788.5; Z = -0.306; p = .760, r = -.03$	$U = 4981.0; Z = -2.804; p = .005^*, r = -.16$	$U = 2932.0; Z = -2.183; p = .029, r = -.13$
Stroke history, % first	89.1	88.9	90.9	$p = 1.00$	$p = .780$	$p = .726$
Etiology, % ischemic	79.5	82.1	82.0	$\chi^2(1, N = 72) = 0.07; p = .786, \varphi = .03$	$\chi^2(1, N = 250) = 0.15; p = .698, \varphi = .02$	$\chi^2(1, N = 234) = 0.00; p = .989, \varphi = .00$

Note. USN = unilateral spatial neglect; IQR = interquartile range. Ranges of group size: left USN = 44–53, right USN = 27–31, no USN = 206–251.
*Statistically significant with alpha = .05 (a Bonferroni correction was used for comparisons with the no USN group, alpha = .025).

right USN showed a lower cognitive functioning (2 points lower on the MMSE) than patients without USN (Table 4).

No difference was seen between patients with left and right USN, left and no USN, and right and no USN regarding communication impairments as measured with the SAN.

Regarding search consistency at the object cancellation task, no differences were seen between patients with left and right USN, left and no USN, and right and no USN. Search organization differed between patients with left and right USN, and left and no USN, with higher intersection rates for patients with left USN, indicating less organized search. No differences were seen between patients with right and no USN.

2.3.3. Physical functioning and physical independence

Table 5 shows the outcomes of the physical functioning and physical independence domain. With respect to motor strength (Motricity Index arm and leg), no differences were obtained between patients with left, right, and no USN.

Data of two patients (2.8%) were considered outliers in multiple balance outcomes and were excluded from all balance analyses; both patients were part of the left USN group. Patients with right USN were shifted more to one side of the balance board (either the left or right, as measured with the absolute CoP mediolateral deviation) than patients with left USN, only with eyes closed (see Figure 3). Neither the relative CoP mediolateral and anteroposterior deviation (i.e., the average deviation) nor the postural sway differed between patients with left and right USN. Patients without USN did not differ from patients with left and right USN on any of the balance measures.

Physical independence at admission, as measured with the Barthel Index, did not differ between patients with left, right, and no USN. Physical independence (Barthel Index) in the first week did not differ between patients with left and right USN. Compared to patients without USN, physical independence in the first week was lower for patients with right or left USN. At discharge, no difference was seen regarding physical independence between patients with left and right USN. Patients with left and right USN had lower physical independence scores than patients without USN.

In the first week, mobility (as measured with the USER) did not differ between patients with left and right USN. However, it was worse for patients with right and left USN than for patients without USN (see Figure 4). At discharge, no differences were seen regarding mobility between patients with left, right, and no USN.

Table 3. Severity of the lateralized attentional deficit: Median and IQR per outcome measure.

Measure	Left USN	Right USN	No USN	Left vs. right USN	Left vs. no USN	Right vs. no USN
Peripersonal space[a]						
OC CoC-x	0.054 (0.13)	0.020 (0.03)	0 (0)	U = 408.0; Z = −3.835; p < .001*; r = −.42		
LB deviation	0.09 (1.08)	−0.26 (0.40)	−0.19 (0.51)	U = 498.0; Z = −2.715; p = .007*; r = −.30	U = 4434.0; Z = −3.508; p < .001*; r = −.20	U = 3351.0; Z = −0.854; p = .393; r = −.05
LB absolute deviation	0.74 (0.68)	0.45 (0.35)	0.34 (0.35)	U = 548.5; Z = −2.229; p = .026*; r = −.25	U = 3795.0; Z = −4.636; p < .001*; r = −.27	U = 3221.0; Z = −1.168; p = .243; r = −.07
Extrapersonal space[a]						
OC CoC-x	0.037 (0.07)	0.013 (0.03)	0 (0)	U = 490.5; Z = −3.077; p = .002*; r = −.34		
LB deviation	0.27 (1.74)	−0.23 (0.68)	−0.22 (0.55)	U = 413.0; Z = −3.621; p < .001*; r = −.40	U = 3921.0; Z = −4.461; p < .001*; r = −.26	U = 3163.5; Z = −1.180; p = .238; r = −.07
LB absolute deviation	0.81 (1.09)	0.51 (0.52)	0.42 (0.37)	U = 481.5; Z = −2.972; p = .003*; r = −.33	U = 3176.0; Z = −5.780; p < .001*; r = −.34	U = 3086.5; Z = −1.369; p = .171; r = −.08
Both distances[b]						
CBS	8.0 (15.9)	3.2 (7.1)	1.1 (4.0)	U = 141.5; Z = −1.454; p = .146; r = −.22	U = 1332.5; Z = −4.336; p < .001*; r = −.32	U = 674.5; Z = −1.566; p = .117; r = −.12

Note. CBS = Catherine Bergego Scale; CoC = center of cancellation; IQR = interquartile range; LB = line bisection; OC = object cancellation; USN = unilateral spatial neglect.
[a]Group size ranges: left USN = 52–53, right USN = 30–31, no USN = 243–251. [b]Group sizes: left USN = 33, right USN = 12, no USN = 153.
*Statistically significant with alpha = .05 (a Bonferroni correction was used for comparisons with the no USN group, alpha = .025).

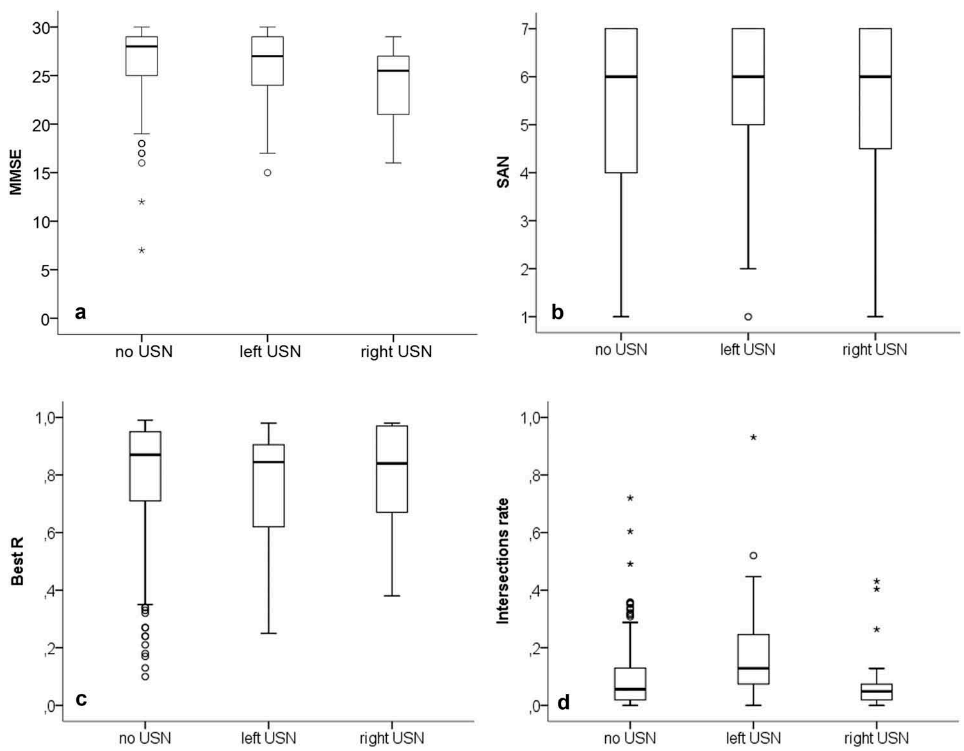

Figure 2. Boxplots of the (a) Mini-Mental State Examination (MMSE), (b) Stichting Afasie Nederland (SAN), (c) best *R*, and (d) intersection rate scores for the no, left, and right unilateral spatial neglect (USN) groups.

Regarding self-care (as measured with the USER) in the first week, patients with left USN did not differ from patients with right and no USN. However, self-care was worse for patients with right or left USN than for patients without USN. At discharge, patients with left USN had worse self-care than patients without USN at discharge; this was a trend for patients with right USN.

2.3.4. Lesion characteristics

The side of the lesion differed significantly between patients with left and right USN and between patients with left and no USN (Table 6), with more right-hemisphere damage in patients with left USN (77.4%) than in those with right (35.5%) and no USN (47.4%). No difference was seen between patients with right and no USN regarding lesion side. Note that 17% to 35.5% of patients

Table 4. Other cognitive measures: Median and IQR per measure.

Measure	Left USN	Right USN	No USN	Left vs. right USN	Left vs. no USN	Right vs. no USN
MMSE	27 (5)	26 (6)	28 (4)	U = 249.0; Z = −1.519; p = .129; r = −.20	U = 2651.0; Z = −1.362; p = .173; r = −.10	U = 940.5; Z = −2.629; p = .009*; r = −.19
SAN	6 (2)	6 (3)	6 (3)	U = 466.0; Z = −0.524; p = .600; r = −.06	U = 4234.0; Z = −0.124; p = .901; r = −.01	U = 2295.5; Z = −0.519; p = .604; r = −.03
OC best R	.85 (.29)	.84 (.30)	.87 (.24)	U = 686.0; Z = −0.907; p = .364; r = −.10	U = 5673.5; Z = −1.239; p = .215; r = −.07	U = 3527.0; Z = −0.360; p = .719; r = −.02
OC intersection rate	0.13 (0.17)	0.05 (0.06)	0.06 (0.11)	U = 391.5; Z = −3.742; p < .001*; r = −.41	U = 3572.5; Z = −4.985; p < .001*; r = −.29	U = 3466.5; Z = −0.509; p = .611; r = −.03

Note. IQR = interquartile range; MMSE = Mini-Mental State Examination; OC = object cancellation; SAN = Stichting Afasie Nederland; USN = unilateral spatial neglect. Group size ranges: left USN = 37–53, right USN = 18–30, no USN = 167–245.
*Statistically significant with alpha = .05 (a Bonferroni correction was used for comparisons with the no USN group, alpha = .025).

Table 5. Physical functioning and physical independence: Median and IQR per measure.

Measure	Left USN	Right USN	No USN	Left vs. right USN	Left vs. no USN	Right vs. no USN
Motricity Index						
arm[a]	72 (100)	76 (75)	76 (61)	U = 381.5; Z = −0.996; p = .319; r = −.13	U = 3058.0; Z = −1.808; p = .071; r = −.12	U = 2154.0; Z = −0.156; p = .876; r = −.01
leg[a]	75 (86)	83 (45)	91 (50)	U = 351.5; Z = −1.438; p = .151; r = −.18	U = 2908.5; Z = −2.132; p = .033; r = −.14	U = 2146.5; Z = −0.100; p = .920; r = −.01
Barthel Index						
admission[a]	11 (10)	11 (7)	14 (9)	U = 482.0; Z = −0.318; p = .751; r = −.04	U = 3388.0; Z = −1.778; p = .075; r = −.12	U = 1682.5; Z = −1.673; p = .094; r = −.12
first week[a]	13 (9)	12 (8)	17 (8)	U = 662.5; Z = −0.354; p = .724; r = −.04	U = 3966.0; Z = −2.576; p = .010*; r = −.16	U = 2140.5; Z = −2.798; p = .005*; r = −.18
discharge[a]	20 (2)	20 (2)	20 (0)	U = 550.0; Z = −0.177; p = .859; r = −.02	U = 3864.5; Z = −2.809; p = .005*; r = −.18	U = 2041.0; Z = −2.677; p = .007*; r = −.17
USER Mobility						
first week[a]	12 (19)	10 (11)	17 (18)	U = 693.0; Z = −0.181; p = .856; r = −.02	U = 4163.0; Z = −2.293; p = .022*; r = −.14	U = 2235.0; Z = −2.477; p = .013*; r = −.16
discharge[a]	29 (16)	26 (16)	31 (9)	U = 551.0; Z = −0.143; p = .886; r = −.02	U = 3869.5; Z = −1.809; p = .071; r = −.11	U = 2045.5; Z = −1.741; p = .082; r = −.11
USER Self-care						
first week[a]	18 (13)	18 (12)	24 (14)	U = 681.5; Z = −0.153; p = .879; r = −.02	U = 3906.0; Z = −2.717; p = .007*; r = −.17	U = 2315.5; Z = −2.315; p = .021*; r = −.15
discharge[a]	28 (9)	32 (9)	35 (4)	U = 506.5; Z = −0.698; p = .485; r = −.08	U = 3269.5; Z = −3.651; p < .001*; r = −.23	U = 2028.0; Z = −2.166; p = .030; r = −.14
Balance eyes open[b]						
CoP anteroposterior	−0.64 (2.05)	0.37 (4.58)	0.37 (1.64)	U = 25.0; Z = −1.228; p = .219; r = −.28	U = 231.0; Z = −1.597; p = .110; r = −.20	U = 142.0; Z = −0.212; p = .832; r = −.03
CoP mediolateral	0.64 (3.55)	−2.62 (6.66)	0.10 (3.88)	U = 22.0; Z = −1.491; p = .136; r = −.34	U = 321.0; Z = −0.068; p = .946; r = −.01	U = 93.0; Z = −1.510; p = .131; r = −.20
CoP mediolateral absolute	1.61 (1.93)	2.69 (2.06)	2.09 (2.63)	U = 17.0; Z = −1.930; p = .054; r = −.44	U = 308.0; Z = −0.289; p = .773; r = −.04	U = 96.0; Z = −1.430; p = .153; r = −.19
Sway anteroposterior	0.009 (0.009)	0.002 (0.010)	0.005 (0.011)	U = 22.0; Z = −1.491; p = .136; r = −.34	U = 259.0; Z = −1.121; p = .262; r = −.14	U = 93.0; Z = −1.510; p = .131; r = −.20
Sway mediolateral	0.009 (0.028)	0.002 (0.021)	0.006 (0.009)	U = 20.0; Z = −1.666; p = .096; r = −.38	U = 213.0; Z = −1.902; p = .057; r = −.24	U = 117.0; Z = −0.874; p = .382; r = −.12
Balance eyes closed[b]						
CoP anteroposterior	−0.21 (1.94)	0.41 (4.40)	0.41 (1.73)	U = 29.0; Z = −0.877; p = .380; r = −.20	U = 251.0; Z = −1.257; p = .209; r = −.16	U = 134.0; Z = −0.424; p = .672; r = −.06
CoP mediolateral	0.49 (3.44)	−2.75 (6.69)	−0.03 (3.90)	U = 24.0; Z = −1.316; p = .188; r = −.30	U = 323.0; Z = −0.034; p = .973; r = .00	U = 96.0; Z = −1.430; p = .153; r = −.19
CoP mediolateral absolute	1.71 (1.62)	2.75 (2.33)	2.06 (2.57)	U = 15.0; Z = −2.105; p = .035*; r = −.48	U = 318.0; Z = −0.119; p = .905; r = −.01	U = 94.0; Z = −1.483; p = .138; r = −.20
Sway anteroposterior	0.006 (0.011)	0.005 (0.011)	0.005 (0.006)	U = 28.0; Z = −0.965; p = .335; r = −.22	U = 248.0; Z = −1.308; p = .191; r = −.16	U = 132.0; Z = −0.477; p = .633; r = −.06
Sway mediolateral	0.006 (0.010)	0.005 (0.015)	0.006 (0.013)	U = 30.0; Z = −0.789; p = .430; r = −.18	U = 294.0; Z = −0.527; p = .599; r = −.07	U = 127.0; Z = −0.609; p = .542; r = −.08

Note. CoP = center of pressure; IQR = interquartile range; USER = Utrecht Scale for Evaluation of Rehabilitation; USN = unilateral spatial neglect.
[a]Group size ranges: left USN = 39–49, right USN = 23–29, no USN = 186–217. [b]Group sizes: left USN = 13, right USN = 6, no USN = 50.
*Statistically significant with alpha = .05 (a Bonferroni correction was used for comparisons with the no USN group, alpha = .025).

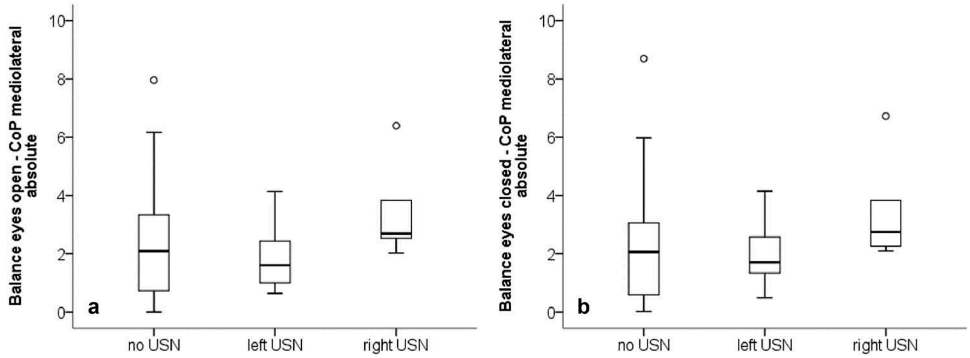

Figure 3. Boxplots with the absolute balance center of pressure (CoP) mediolateral value for (a) eyes open and (b) eyes closed, for the no, left, and right unilateral spatial neglect (USN) groups.

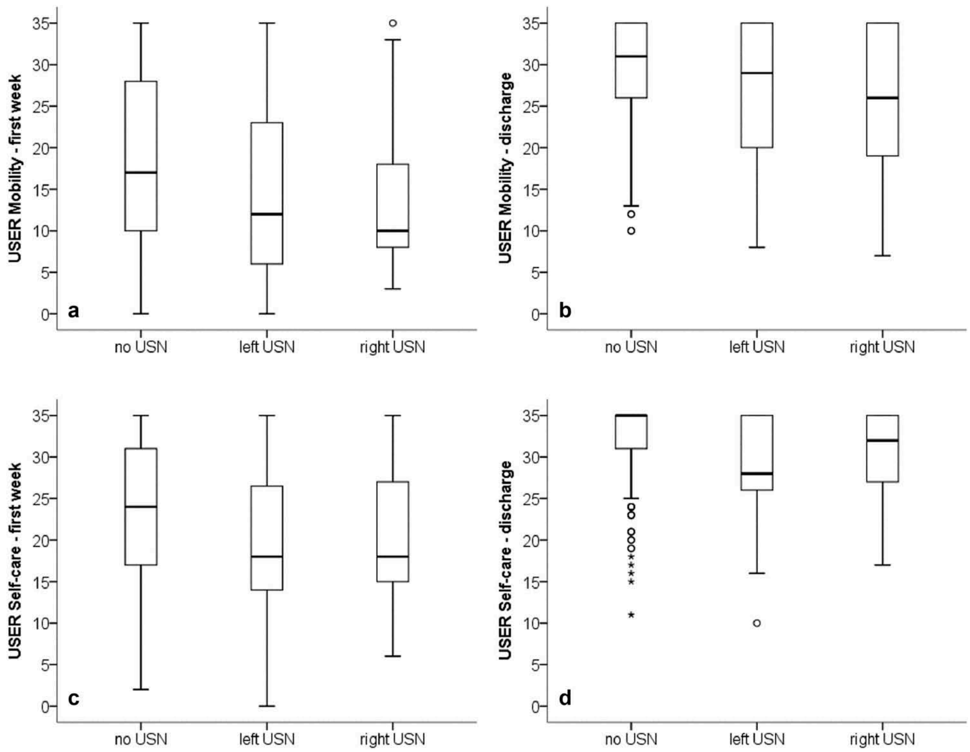

Figure 4. Boxplots of the Utrecht Scale for Evaluation of Rehabilitation (USER) Mobility scale (a) in the first week and (b) at discharge, and boxplots of the USER Self-Care (c) in the first week and (d) at discharge, for the no, left, and right unilateral spatial neglect (USN) groups.

Table 6. Lesion characteristics.

Measure	Left USN	Right USN	No USN	Left vs. right USN	Left vs. no USN	Right vs. no USN
Retrieved from medical chart[a]						
Lesion side, %				$p < .001$*	$\chi^2(2, N = 304) = 16.90$; $p < .001$*, $V = 0.24$	$\chi^2(2, N = 282) = 2.30$; $p = .317$, $V = 0.09$
Left	17.0	61.3	47.0			
Right	77.4	35.5	47.4			
Bilateral	5.7	3.2	5.6			
Lesion focality, %				$p = .799$	$p = .269$	$p = .092$
Focal	75.6	70.0	85.1			
Diffuse	17.1	25.0	9.4			
Bilateral	7.3	5.0	5.5			
Retrieved from CT or MRI scan[b]						
Lesion volume in ml, median (IQR)	95 (218)	85 (182)	30 (82)	$U = 63.0$; $Z = -1.107$; $p = .268$; $r = -.21$	$U = 239.0$; $Z = -3.379$; $p = .001$*; $r = -.40$	$U = 190.0$; $Z = -0.969$; $p = .332$; $r = -.12$

Note. USN = unilateral spatial neglect; MRI = magnetic resonance imaging; CT = computed tomography.
[a]Group size ranges: left USN = 41–53, right USN = 20–31, no USN = 181–251. [b]Group sizes: left USN = 19, right USN = 9, no USN = 53.
*Statistically significant with alpha = .05 (a Bonferroni correction was used for comparisons with the no USN group, alpha = .025).

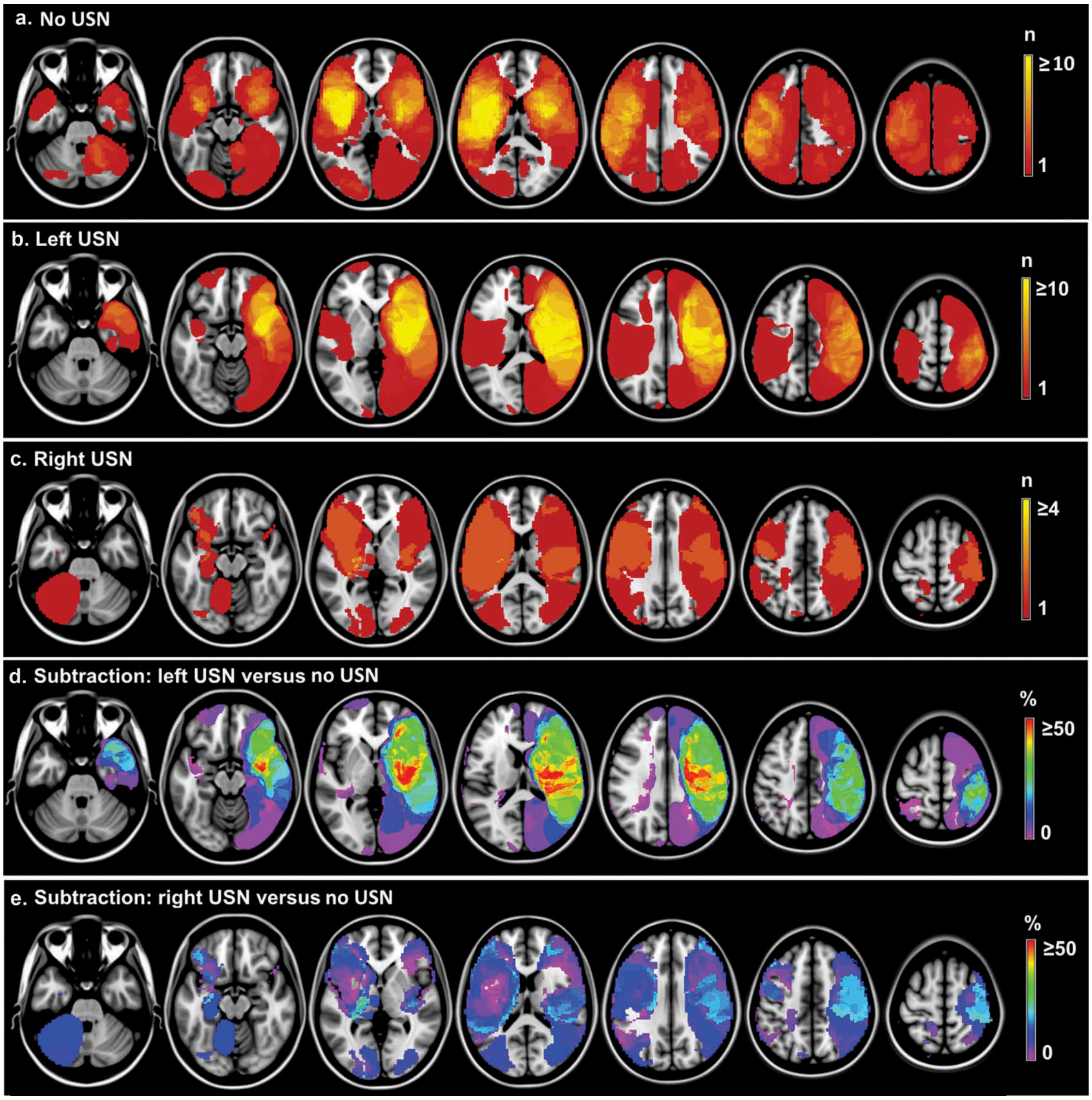

Figure 5. Lesion overlay plots and subtraction plots. Damaged voxels are depicted for patients with (a) no unilateral spatial neglect (USN; N = 53), (b) left USN (N = 19), and (c) right USN (N = 9). The colored bar indicates the number of patients with a lesion for each voxel. The final two panels show subtraction plots of no USN patients versus patients with (d) left USN, and (e) right USN. Voxels in the lesion subtraction plot that are more often damaged in the USN group than in the no USN group are shown on a scale ranging from pink (1% absolute difference in lesion frequency) to red (>50% absolute difference). Results are projected on the Montreal Neurological Institute (MNI) 1-mm template (z coordinates: −30, −15, 0, 15, 30, 45, 60). The right hemisphere is depicted on the right.

showed ipsilesional USN. Lesion focality did not differ between patients with left, right, and no USN.

Figures 5(a)–5(c) show the overlay plots of patients with no USN (N = 53), left USN (N = 19), and right USN (N = 9), and Figures 5(d)–5(e) show the qualitative lesion subtraction plots of patients with and without USN. Left USN was predominantly associated with lesions in the postcentral gyrus, supramarginal gyrus, angular gyrus, parietal operculum cortex, central operculum cortex, insula, Heschl's gyrus, and frontal operculum cortex of the right cerebral hemisphere. In contrast, regions that were more frequently lesioned in patients with right USN were not clearly lateralized and included left- and right-hemispheric temporo-parietal regions. Lesion volume did not differ between patients with left and right USN. Patients with left USN had significantly higher lesion volume than patients with no USN, whereas patients with right and no USN did not differ regarding lesion volume.

3. Discussion

In this study, data were collected in cognitive and physical domains for a large cohort of stroke patients. The primary aim was to investigate distinctions and similarities between patients with left and right USN regarding frequency, severity, region specificity (i.e., peripersonal, extrapersonal), general cognition, physical functioning, and physical independence. The secondary aim was to compare lesion characteristics between patients with left versus right USN. This study is one of the first to provide an extensive overview of different outcomes in multiple domains.

To be able to adequately pinpoint and thus interpret the current results and its impact, it is important to note that the sample of stroke patients were admitted to inpatient rehabilitation, in the subacute phase post stroke onset. In the Netherlands, this patient population is general relatively young and moderately impaired. As a direct result, the current results might not generalize to an older and/or more severely impaired population. However, the current results are still of major importance for diagnostics and treatment in the subacute phase post stroke, as treatment in this phase is most intensive.

3.1. Frequency, severity, and region-specific USN

Overall, left, right, and no USN patients were comparable regarding age, sex, handedness, time post stroke onset, stroke etiology, and stroke history. Of the total sample of 335 patients, 86 patients showed USN. Of the USN patients, 63.09% showed left-sided and 36.90% showed right-sided USN. This ratio is in line with other studies who included patients in the subacute phase after stroke; left USN is more frequent than right USN after 3 months post stroke onset (Stone et al., 1991; Wee & Hopman, 2008). Overall percentages of USN (15.82% left USN and 9.25% right USN) were somewhat lower than those in other studies (Ringman et al., 2004; Stone, Halligan, & Greenwood, 1993; Wee & Hopman, 2008). This might be the result of the number of tests that were used to assess USN.

Although USN is commonly known as a contralesional symptom, the current results confirm previous studies (Kim et al., 1999; Kwon & Heilman, 1991) that ipsilateral neglect also exists, with a prevalence of 17% to 35.5% for left and right USN, respectively. While previous studies have detected ipsilateral neglect with the line bisection task, the current study shows that the object cancellation task is also sensitive to detect this symptom. It has been hypothesized that ipsilateral USN particularly results from fronto-subcortical brain damage (Kim et al., 1999).

With respect to the severity of the lateralized attentional deficit, as measured with the shape cancellation and line bisection task, the magnitude of lateralized inattention was larger in patients with left USN (i.e., more omissions, a larger asymmetry of omissions, and a larger deviation on the line bisection) than in patients with right USN. Contrary, left, and right USN had a comparable negative impact on behavior of USN (i.e., comparable scores on the CBS). When compared to patients without USN, left USN—but not right USN—appeared to have a larger negative impact on behavior of USN in ADL.

Last, with respect to region specificity, left peripersonal and extrapersonal USN occurred as frequently as right peripersonal and extrapersonal USN. However, USN for both peripersonal and extrapersonal regions of space was more frequent in patients with left than in those with right USN. This could relate to the specific brain areas that were damaged. Possibly, lesions were larger in patients with left USN, resulting in both peripersonal and extrapersonal USN and a larger deficit in lateralized attention. Several overlapping brain structures (i.e., the middle temporal and frontal cortex as well as the anterior cingulate cortex) are possibly involved in both peripersonal as extrapersonal USN (Aimola, Schindler, Simone, & Venneri, 2012). In prior research, lesion size and the severity of the deficit in lateralized attention correlated (Leibovitch et al., 1998).

In the current study, 3.52% of patients (N = 15) were excluded due to problems with understanding task instructions. Excluding patients with (mild) difficulties in understanding task instructions might lead to underdetection of especially right USN (i.e., left-hemisphere lesions; Bowen, McKenna, & Tallis, 1999; Suchan et al., 2012; Wee & Hopman, 2008). However, in several studies the assessment of USN was feasible in patients with aphasia (Chen, Chen, et al., 2015; Wee & Hopman, 2008), and those studies reported that the occurrence of left USN was still higher than that of right USN. In addition, Ringman et al. (2004) corrected for the possibility of a selection bias, by considering patients with left-hemisphere damage with severe aphasia as USN patients. Even with this strict correction, the differences between hemispheres with regard to incidence and severity remained in their study.

3.2. Cognitive measures

General cognitive status, as measured with the MMSE, was found to be marginally lower in patients with right USN than in those with no USN. One explanation might be that language is a key component in the MMSE. In our sample, patients with severe language deficits (especially understanding) were excluded from the neglect screening, yet left-hemisphere damage might also result in very subtle language deficits that are likely to be picked up with the MMSE. Overall, MMSE scores were fairly high in our sample, and no difference was seen between patients with left and right USN, and left and no USN. Both findings are in line with those of another comparable study (Nijboer, Van de Port, et al., 2013).

Search efficiency was found to be poorer in patients with left USN than in those with right and no USN, which suggests that patients with left USN might have poorer visual overview or spatial working memory (see also Ten Brink, Van der Stigchel, et al., 2016). As the right hemisphere has been suggested to be dominant for visuospatial processing and representation (Pisella et al., 2011), spatial working memory problems (which are a subcomponent of USN) presumably result more often following right-hemisphere damage.

3.3. Physical functioning and physical independence

No differences in motor impairment of the arm and leg were found between patients with left, right, and no USN, which is in contrast with prior studies (Meyer et al., 2016; Nijboer, Kollen, et al., 2014). In, for example, the study by Nijboer et al. (2014), a hampering effect of USN on motor functioning and motor recovery was described. However, in the Nijboer et al. study (2014), only patients with motor impairment in the first week post stroke onset were included, and recovery trajectories were calculated for the first year post stroke. In the current study, only a very limited time-window was tested in a different class of patients (namely, patients relatively young and fit enough for inpatient rehabilitation), which might explain the apparent difference in impact of USN on motor impairment.

Patients with left and right USN did not differ from each other regarding Barthel Index at admission, nor mobility and self-care in the first week and at discharge. However, in the first week, patients with USN had lower mobility and self-care scores than patients without USN. At discharge, patients with left USN had lower self-care scores than patients without USN. This is in line with prior studies, showing that USN is negatively associated with performance in other domains (Wee & Hopman, 2008).

With respect to sitting balance with eyes closed, right USN patients showed a larger absolute deviation from left to right than left USN patients. This effect was not seen in the eyes-open situation. This implies that patients with left and right USN differ in other sensory modalities beside visual information, at least in the current sample. Figure 5 shows that right USN patients are proportionally more often subject to lesions in the cerebellum. As the cerebellum plays a major role in maintaining balance and posture, this may explain the difference found in the current study. There was no difference with respect to the direction of this deviation. Regarding the other balance outcomes, left and right USN patients showed comparable deviations from front to back, as well as comparable postural sway. Additionally, no differences were found between either USN group and the non-USN group. Due to task demands (i.e., being able to sit unaided for 30 s), patients with severe balance problems were excluded.

3.4. Lesion characteristics

A lateralization of right-hemisphere damage in patients with left USN was seen (77.4% right brain damage). However, no clear lateralization regarding lesion location was seen in patients with right USN: Only 61.3% of patients had left brain damage. Lesion focality did not differ between patients with left, right, and no USN.

Our lesion subtraction analyses demonstrated that left USN was associated with right-hemispheric temporo-parietal and frontal lesions, predominantly involving the postcentral gyrus, supramarginal gyrus, angular gyrus, parietal operculum cortex, central operculum cortex, insula, Heschl's gyrus, and frontal operculum cortex of the right cerebral hemisphere, which is in line with earlier findings (Danckert & Ferber, 2006; Karnath, Berger, Küker, & Rorden, 2004). In contrast, regions that were more frequently lesioned in patients with right USN were not clearly lateralized and included left- and right-hemispheric temporo-parietal regions. This is in line with prior research (Mesulam, 1981). Lesion volume did not differ between patients with left and right USN. For patients with left USN—but not for patients with right USN—lesion volume was larger than that for patients without USN. It is important to note that these results were based a relatively small sample (9 right and 19 left USN); especially, potential differences in volumes between no USN and right USN could have been missed due to limited statistical power. The modest sample size precluded the option of voxel-based lesion symptom-mapping analyses. Nevertheless, these findings suggest that the differences found at the behavioral level (mainly severity of the lateralized attentional deficit and its consequences in basic ADL) are not a mere consequence of larger lesions or different focality for left versus right USN. In a prior study, comparable brain areas (e.g., posterior cortical lesions) were associated with both left and right USN (Beis et al., 2004), whereas in another study right-hemisphere-damaged USN patients had mostly posterior lesions, and left-hemisphere damaged USN patients had mostly anterior lesions (Ogden, 1985). Larger numbers of stroke patients are needed in order to fully unravel neuronal correlates of left and right USN.

3.5. USN versus lateralized inattention

As already mentioned in the introduction, there is an ongoing debate about proper terminology for the neuropsychological disorder that is central in our paper: unilateral spatial neglect. For example, another term that is also used in science as well as clinical practice is visuospatial neglect, stressing the sensory modality, although the visual domain is by no means central to this disorder. In our view, neglect is a complex and heterogeneous *syndrome*. The core cognitive deficit, however, is *lateralized inattention*, yet nonlateralized cognitive deficits have also been associated with the neglect syndrome, such as impairments in arousal and more general awareness. In clinical practice (the magnitude of) lateralized inattention is measured with a neuropsychological assessment, and patients who fail such tests are generally diagnosed with neglect. The same is true for many scientific studies. Consensus on better use of proper terminology for either the syndrome or the specific lateralized inattention would therefore not only enhance clarity on the specificity of impairments in patients (both in science and in clinical practice), but also improve assessment and treatment of patients.

3.6. Limitations

The retrospective nature is a limitation of the current study. Data quality was dependent on the consistency of the individual nurses, physical therapists, and neuropsychologists. For some of the measures (i.e., balance) the group sizes were small, reducing statistical power. A limitation of the overlay and subtraction analyses is that it can only be applied to voxels that are damaged in a certain amount of patients. As a consequence, we cannot draw any conclusions regarding regions that were not affected in any of the patients. In the current study, no data on visual field deficits, such as hemianopia, were present, and effects of hemianopia on our outcome measures could not be evaluated. However, hemianopia would have affected both groups, as the disorder is not specifically related to one of the hemispheres. In addition, anosognosia (i.e., a deficit in self-awareness where the patient seems unaware of the existence of the deficit) and anosodiaphoria (i.e., acquired indifference to the presence of the deficit, specifically paralysis) are two disorders more commonly observed in patients with right-hemisphere lesions than in those with left-hemisphere lesions (Pia, Neppi-Modona, Ricci, & Berti, 2004). Systematic screening for these disorders was not part of standard clinical care. It might be that patients with anosognosia and/or especially anosodiaphoria are less likely to be admitted to a rehabilitation center for inpatient rehabilitation as a certain amount of motivation and endurance is mandatory for keeping up with the intense schedules and pace, resulting in a underrepresentation of USN patients with right-hemispheric damage. Due to the design of this study—a retrospective cohort study—and the lack of systematic information from the patient files with respect to these disorders, we cannot report frequencies of these disorders in our current samples.

The allocation of the patients in the three groups was based on a single test that was administered in two regions of space. No distinction was made between patients with USN in peripersonal, extrapersonal, or both regions of space. Furthermore, seven patients were excluded based on discrepant results between regions of space. Since consequences of peripersonal and extrapersonal USN on the level of activities differ (Nijboer, Ten Brink, Kouwenhoven, & Visser-Meily, 2014; Nijboer, Ten Brink, Van Der Stoep, et al., 2014), it would have been of great value to separately analyze these groups. Unfortunately we were unable to do so due to a lack of statistical power. To prevent underdetection, one might consider using a test-battery and composed score of 3 (types of) tests: one traditional neglect-test (e.g., a cancellation task), one functional test such as the CBS (Azouvi et al., 1996), and one test that is insensitive to aphasia, like the Albert's Test (Suchan et al., 2012). For the current study, this was not feasible as not enough patients were tested with three tests for neglect. In addition, other types of USN, such as personal or motor neglect, were not thoroughly investigated as no specific measures were used to determine these types of neglect.

As mentioned above, the current study was performed in a distinct class of patients—namely, patients relatively young and fit enough for inpatient rehabilitation. Therefore, it remains to be seen whether differences between left and right USN patients exist in the acute and/or chronic phase post stroke onset and whether differences in the timing of recovery of left versus right USN patients exist.

3.7. Conclusion

Left and right USN are both common after stroke. The current study shows that left USN is more frequent, and the deficit in lateralized attention is more severe with respect to the neuropsychological outcomes and observations of USN in ADL. Patients with right USN showed poorer overall cognition than those with no USN, whereas patients with left USN showed problems with search organization. Patients with right USN had poorer balance, while no differences were seen on other motor functions or physical independence in ADL. Left USN was associated with lesions in the right hemisphere predominantly involving temporo-parietal and frontal regions, whereas no clear lateralization was observed for right USN.

With respect to several aspects of cognition, physical functioning, and physical independence, left and right USN were associated with poorer performance than no USN. From a clinical perspective, it is good to systematically screen for USN, both after right- and after left-hemisphere damage.

Acknowledgments

Antonia F. Ten Brink and Jurre H. Verwer contributed equally to this work.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by the Netherlands Organization for Scientific Research (NWO) [grant number 451-10-013] to T.C.W.N.; and by the Revalidatiefonds [grant number R2012134] to T.C.W.N. and J.M.A.V.M. None of the funders had any role in study design, in the collection, analysis and interpretation of data, in the writing of the report, or in the decision to submit the article for publication.

ORCID

Antonia F. Ten Brink http://orcid.org/0000-0001-7634-0819
Jurre H. Verwer http://orcid.org/0000-0002-6842-8586
J. Matthijs Biesbroek http://orcid.org/0000-0001-7017-2148
Tanja C. W. Nijboer http://orcid.org/0000-0001-6683-0267

References

Aimola, L., Schindler, I., Simone, A. M., & Venneri, A. (2012). Near and far space neglect: Task sensitivity and anatomical substrates. *Neuropsychologia*, *50*(6), 1115–1123. doi:10.1016/j.neuropsychologia.2012.01.022

Appelros, P., Karlsson, G. M., Seiger, A., & Nydevik, I. (2002). Neglect and anosognosia after first-ever stroke: Incidence and relationship to disability. *Journal of Rehabilitation Medicine*, *34*(5), 215–220. doi:10.1080/165019702760279206

Azouvi, P., Marchal, F., Samuel, C., Morin, L., Renard, C., Louis-Dreyfus, A., … Bergego, C. (1996). Functional consequences and awareness of unilateral neglect: Study of an evaluation scale. *Neuropsychological Rehabilitation*, *6*(2), 133–150. doi:10.1080/713755501

Azouvi, P., Olivier, S., de Montety, G., Samuel, C., Louis-Dreyfus, A., & Tesio, L. (2003). Behavioral assessment of unilateral neglect: Study of the psychometric properties of the Catherine Bergego Scale. *Archives of Physical Medicine and Rehabilitation*, *84*(1), 51–57. doi:10.1053/apmr.2003.50062

Bartolomeo, P., Thiebaut de Schotten, M., & Chica, A. B. (2012). Brain networks of visuospatial attention and their disruption in visual neglect. *Frontiers in Human Neuroscience*, *6*(May), 110. doi:10.3389/fnhum.2012.00110

Beis, J.-M., Keller, C., Morin, N., Bartolomeo, P., Bernati, T., Chokron, S., … Azouvi, P. (2004). Right spatial neglect after left hemisphere stroke: Qualitative and quantitative study. *Neurology*, *63*(9), 1600–1605. doi:10.1212/01.WNL.0000142967.60579.32

Biesbroek, J. M., van Zandvoort, M. J., Kappelle, L. J., Velthuis, B. K., Biessels, G., & Postma, A. (2016). Shared and distinct anatomical correlates of semantic and phonemic fluency revealed by lesion-symptom mapping in patients with ischemic stroke. *Brain Structure and Function*, *221*(4), 2123–2134. doi:10.1007/s00429-015-1033-8

Biesbroek, J. M., van Zandvoort, M. J. E., Kappelle, L. J., Schoo, L., Kuijf, H. J., Velthuis, B. K., … Postma, A. (2014). Distinct anatomical correlates of discriminability and criterion setting in verbal recognition memory revealed by lesion-symptom mapping. *Human Brain Mapping*, *36*(4), 1292–1303. doi:10.1002/hbm.22702

Bowen, A., McKenna, K., & Tallis, R. C. (1999). Reasons for variability in the reported rate of occurrence of unilateral spatial neglect after stroke. *Stroke*, *30*(6), 1196–1202. doi:10.1161/01.STR.30.6.1196

Buxbaum, L. J., Ferraro, M. K., Veramonti, T., Farne, A., Whyte, J., Ladavas, E., … Coslett, H. B. (2004). Hemispatial neglect: Subtypes, neuroanatomy, and disability. *Neurology*, *62*(5), 749–756. doi:10.1212/01.WNL.0000113730.73031.F4

Chechlacz, M., Rotshtein, P., Bickerton, W.-L., Hansen, P. C., Deb, S., & Humphreys, G. W. (2010). Separating neural correlates of allocentric and egocentric neglect: Distinct cortical sites and common white matter disconnections. *Cognitive Neuropsychology*, *27*(3), 277–303. doi:10.1080/02643294.2010.519699

Chen, P., Chen, C. C., Hreha, K., Goedert, K. M., & Barrett, A. M. (2015). Kessler soundation neglect assessment process uniquely measures spatial neglect during activities of daily living. *Archives of Physical Medicine and Rehabilitation*, *96*(5), 869–876.e1. doi:10.1016/j.apmr.2014.10.023

Chen, P., Hreha, K., Kong, Y., & Barrett, A. M. (2015). Impact of spatial neglect on stroke rehabilitation: Evidence from the setting of an inpatient rehabilitation facility. *Archives of Physical Medicine and Rehabilitation*, *96*(8), 1458–1466. doi:10.1016/j.apmr.2015.03.019

Clark, R. A., Bryant, A. L., Pua, Y., McCrory, P., Bennell, K., & Hunt, M. (2010). Validity and reliability of the Nintendo Wii Balance Board for assessment of standing balance. *Gait & Posture*, *31*(3), 307–310. doi:10.1016/j.gaitpost.2009.11.012

Collin, C., & Wade, D. (1990). Assessing motor impairment after stroke: A pilot reliability study. *Journal of Neurology, Neurosurgery & Psychiatry*, *53*(7), 576–579. doi:10.1136/jnnp.53.7.576

Collin, C., Wade, D., Davies, S., & Horne, V. (1988). The Barthel ADL Index: A reliability study. *Disability & Rehabilitation*, *10*(2), 61–63. doi:10.3109/09638288809164103

Corbetta, M., & Shulman, G. L. (2011). Spatial neglect and attention networks. *Annual Review of Neuroscience*, *34*(1), 569–599. doi:10.1146/annurev-neuro-061010-113731

Dalmaijer, E. S., Van der Stigchel, S., Nijboer, T. C. W., Cornelissen, T. H. W., & Husain, M. (2015). CancellationTools: All-in-one software for administration and analysis of cancellation tasks. *Behavior Research Methods*, *47*(4), 1065–1075. doi:10.3758/s13428-014-0522-7

Danckert, J., & Ferber, S. (2006). Revisiting unilateral neglect. *Neuropsychologia*, *44*(6), 987–1006. doi:10.1016/j.neuropsychologia.2005.09.004

Deelman, B., Koning-Haanstra, M., Liebrand, W., & van den Burg, W. (1981). *Stichting Afasie Nederland - de SAN-test*. Lisse: Swets & Zeitlinger.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*(3), 189–198. doi:10.1016/0022-3956(75)90026-6

Fonov, V. S., Evans, A. C., McKinstry, R. C., Almli, C. R., & Collins, D. L. (2009). Unbiased nonlinear average age-appropriate brain templates from birth to adulthood. *NeuroImage*, *47*, S102. doi:10.1016/S1053-8119(09)70884-5

Gainotti, G., Messerli, P., & Tissot, R. (1972). Qualitative analysis of unilateral spatial neglect in relation to laterality of cerebral lesions. *Journal of Neurology, Neurosurgery & Psychiatry*, *35*(4), 545–550. doi:10.1136/jnnp.35.4.545

Jacobs, S., Brozzoli, C., & Farnè, A. (2012). Neglect: A multisensory deficit? *Neuropsychologia*, *50*(6), 1029–1044. doi:10.1016/j.neuropsychologia.2012.03.018

Karnath, H.-O., Berger, M. F., Küker, W., & Rorden, C. (2004). The anatomy of spatial neglect based on voxelwise statistical analysis: A study of 140 patients. *Cerebral Cortex*, *14*(10), 1164–1172. doi:10.1093/cercor/bhh076

Kim, M., Na, D. L., Kim, G. M., Adair, J. C., Lee, K. H., & Heilman, K. M. (1999). Ipsilesional neglect: Behavioural and anatomical features. *Journal of Neurology, Neurosurgery & Psychiatry*, *67*(1), 35–38. doi:10.1136/jnnp.67.1.35

Kinsbourne, M. (1987). Mechanisms of unilateral neglect. In M. Jeannerod (Ed.), *Neurophysiological and neuropsychological aspects of spatial neglect* (pp. 69–86). Amsterdam: Elsevier Science.

Klein, S., Staring, M., Murphy, K., Viergever, M. A., & Pluim, J. P. W. (2010). Elastix: A toolbox for intensity-based medical image registration. *IEEE Transactions on Medical Imaging*, *29*(1), 196–205. doi:10.1109/TMI.2009.2035616

Kuijf, H., Biesbroek, J., Viergever, M., Biessels, G., & Vincken, K. (2013). Registration of brain CT images to an MRI template for the purpose of lesion-symptom mapping. In *Multimodal brain image analysis, lecture notes in computer science* (Vol. 8159, pp. 119–128). Springer International Publishing. doi:10.1007/978-3-319-02126-3_12

Kwon, S. E., & Heilman, K. M. (1991). Ipsilateral neglect in a patient following a unilateral frontal lesion. *Neurology*, *41*(12), 2001–2004. doi:10.1212/WNL.41.12.2001

Leibovitch, F. S, Black, S. E, Caldwell, C. B, Ebert, P. L, Ehrlich, L. E, & Szalai, J. P. (1998). Brain-behavior correlations in hemispatial neglect using ct and spect: the sunnybrook stroke study. *Neurology*, *50*, 901–908. doi:10.1212/WNL.50.4.901

Machner, B., Mah, Y.-H., Gorgoraptis, N., & Husain, M. (2012). How reliable is repeated testing for hemispatial neglect? Implications for clinical follow-up and treatment trials. *Journal of Neurology, Neurosurgery & Psychiatry*, *83*(10), 1032–1034. doi:10.1136/jnnp-2012-303296

Mark, V., Woods, A., Ball, K., Roth, D., & Mennemeier, M. (2004). Disorganized search on cancellation is not a consequence of neglect. *Neurology*, *63*(1), 78–84. doi:10.1212/01.WNL.0000131947.08670.D4

Mesulam, M. (1981). A cortical network for directed attention and unilateral neglect. *Annals of Neurology*, *10*(4), 309–325. doi:10.1002/(ISSN)1531-8249

Meyer, S., De Bruyn, N., Lafosse, C., Van Dijk, M., Michielsen, M., Thijs, L., … Verheyden, G. (2016). Somatosensory impairments in the upper limb poststroke: distribution and association with motor function and visuospatial neglect. *Neurorehabilitation and Neural Repair*, *30*(8), 731–742. doi:10.1177/1545968315624779

MRIcron. (n.d.). Retrieved from http://www.mccauslandcenter.sc.edu/crnl/mricron

Nijboer, T. C. W., Kollen, B. J., & Kwakkel, G. (2013). Time course of visuospatial neglect early after stroke: A longitudinal cohort study. *Cortex*, *49*(8), 2021–2027. doi:10.1016/j.cortex.2012.11.006

Nijboer, T. C. W., Kollen, B. J., & Kwakkel, G. (2014). The impact of recovery of visuo-spatial neglect on motor recovery of the upper paretic limb after stroke. *PloS One*, *9*(6), e100584. doi:10.1371/journal.pone.0100584

Nijboer, T. C. W., Olthoff, L., Van der Stigchel, S., & Visser-Meily, J. M. A. (2014). Prism adaptation improves postural imbalance in neglect patients. *NeuroReport*, *25*(5), 307–311. doi:10.1097/WNR.0000000000000088

Nijboer, T. C. W., Ten Brink, A. F., Kouwenhoven, M., & Visser-Meily, J. M. A. (2014). Functional assessment of region-specific neglect: Are there differential behavioural consequences of peripersonal versus extrapersonal neglect? *Behavioural Neurology*, *2014*, 526407. doi:10.1155/2014/526407

Nijboer, T. C. W., Ten Brink, A. F., Van Der Stoep, N., & Visser-Meily, J. M. A. (2014). Neglecting posture: Differences in balance impairments between peripersonal and extrapersonal neglect. *NeuroReport*, *25*(17), 1381–1385. doi:10.1097/WNR.0000000000000277

Nijboer, T. C. W., van de Port, I., Schepers, V., Post, M., & Visser-Meily, J. M. A. (2013). Predicting functional outcome after stroke: The influence of neglect on basic activities in daily living. *Frontiers in Human Neuroscience*, *7* (182), 1–6. doi:10.3389/fnhum.2013.00182

Nys, G. M. S., van Zandvoort, M. J. E., de Kort, P. L. M., van der Worp, H. B., Jansen, B. P. W., Algra, A., … Kappelle, L. J. (2005). The prognostic value of domain-specific cognitive abilities in acute first-ever stroke. *Neurology*, *64*(5), 821–827. doi:10.1212/01.WNL.0000152984.28420.5A

Ogden, J. A. (1985). Anterior-posterior interhemispheric differences in the loci of lesions producing visual hemineglect. *Brain and Cognition*, *4*(1), 59–75. doi:10.1016/0278-2626(85)90054-5

Pia, L., Neppi-Modona, M., Ricci, R., & Berti, A. (2004). The anatomy of anosognosia for hemiplegia: A meta-analysis. *Cortex*, *40*(2), 367–377. doi:10.1016/S0010-9452(08)70131-X

Pisella, L., Alahyane, N., Blangero, A., Thery, F., Blanc, S., & Pelisson, D. (2011). Right-hemispheric dominance for visual remapping in humans. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *366*(1564), 572–585. doi:10.1098/rstb.2010.0258

Post, M. W., van de Port, I. G., Kap, B., & Berdenis van Berlekom, S. H. (2009). Development and validation of the Utrecht Scale for Evaluation of Clinical Rehabilitation (USER). *Clinical Rehabilitation*, *23*(10), 909–917. doi:10.1177/0269215509341524

Ringman, J. M., Saver, J. L., Woolson, R. F., Clarke, W. R., & Adams, H. P. (2004). Frequency, risk factors, anatomy, and course of unilateral neglect in an acute stroke cohort. *Neurology*, *63*(3), 468–474. doi:10.1212/01.WNL.0000133011.10689.CE

Rorden, C., Bonilha, L., Fridriksson, J., Bender, B., & Karnath, H.-O. (2012). Age-specific CT and MRI templates for spatial normalization. *NeuroImage*, *61*(4), 957–965. doi:10.1016/j.neuroimage.2012.03.020

Rorden, C., & Karnath, H. (2010). A simple measure of neglect severity. *Neuropsychologia*, *48*(9), 2758–2763. doi:10.1016/j.neuropsychologia.2010.04.018

Rorden, C., Karnath, H., & Bonilha, L. (2007). Improving lesion-symptom mapping. *Journal of Cognitive Neuroscience*, *19*(7), 1081–1088. doi:10.1162/jocn.2007.19.7.1081

Sperber, C., & Karnath, H.-O. (2016). Diagnostic validity of line bisection in the acute phase of stroke. *Neuropsychologia*, *82*, 200–204. doi:10.1016/j.neuropsychologia.2016.01.026

Stone, S., Halligan, P., & Greenwood, R. (1993). The incidence of neglect phenomena and related disorders in patients with an acute right or left hemisphere stroke. *Age and Ageing*, *22*(1), 46–52. doi:10.1093/ageing/22.1.46

Stone, S., Wilson, B., Wroot, A., Halligan, P., Lange, L., Marshall, J., & Greenwood, R. (1991). The assessment of visuo-spatial neglect after acute stroke. *Journal of Neurology, Neurosurgery & Psychiatry*, *54*, 345–350. doi:10.1136/jnnp.54.4.345

Suchan, J., Rorden, C., & Karnath, H.-O. (2012). Neglect severity after left and right brain damage. *Neuropsychologia*, *50*(6), 1136–1141. doi:10.1016/j.neuropsychologia.2011.12.018

Suzuki, M., Ohyama, N., Yamada, K., & Kanamori, M. (2002). The relationship between fear of falling, activities of daily living and quality of life among elderly individuals. *Nursing and Health Sciences*, *4*(4), 155–161. doi:10.1046/j.1442-2018.2002.00123.x

Ten Brink, A. F., Biesbroek, M. J., Kuijf, H. J., Van der Stigchel, S., Oort, Q., Visser-Meily, J. M. A., & Nijboer, T. C. W. (2016). The right hemisphere is dominant in organization of visual search—A study in stroke patients. *Behavioural Brain Research*, *304*, 71–79. doi:10.1016/j.bbr.2016.02.004

Ten Brink, A. F., Nijboer, T. C. W., Van Beekum, L., Van Dijk, J., Peeters, R., Post, M. W. M., & Visser-Meily, J. M. A. (2013). De Nederlandse Catherine Bergego schaal: een bruikbaar en valide instrument in de CVA zorg. *Wetenschappelijk Tijdschrift Voor Ergotherapie*, *6*, 27–36.

Ten Brink, A. F., Van der Stigchel, S., Visser-Meily, J. M. A., & Nijboer, T. C. W. (2016). You never know where you are going until you know where you have been: Disorganized search after stroke. *Journal of Neuropsychology*, *10*(2), 256–275. doi:10.1111/jnp.12068

Van der Stoep, N., Visser-Meily, J., Kappelle, L., de Kort, P., Huisman, K., Eijsackers, A., … Nijboer, T. (2013). Exploring near and far regions of space: Distance-specific visuospatial neglect after stroke. *Journal of Clinical and Experimental Neuropsychology*, *35*(8), 799–811. doi:10.1080/13803395.2013.824555

van Nes, I. J. W., van Kessel, M. E., Schils, F., Fasotti, L., Geurts, A. C. H., & Kwakkel, G. (2009). Is visuospatial hemineglect longitudinally associated with postural imbalance in the postacute phase of stroke? *Neurorehabilitation and Neural Repair*, *23*(8), 819–824. doi:10.1177/1545968309336148

Wee, J. Y. M., & Hopman, W. M. (2008). Comparing consequences of right and left unilateral neglect in a stroke rehabilitation population. *American Journal of Physical Medicine & Rehabilitation*, *87*(11), 910–920. doi:10.1097/PHM.0b013e31818a58bd

Woods, A. J., & Mark, V. W. (2007). Convergent validity of executive organization measures on cancellation. *Journal of Clinical and Experimental Neuropsychology*, *29*(7), 719–723. doi:10.1080/13825580600954264