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Review

Prevalence of spatial neglect post-stroke: A systematic review

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ABSTRACT

Objective: Spatial neglect (SN) impedes stroke rehabilitation progress, slows functional recovery, and increases caregiver stress and burden. The estimation of SN prevalence varies widely across studies. *Background:* We aimed to establish the prevalence of SN based on the injured cerebral hemisphere, recovery stage post-stroke, and diagnostic methodology.

Materials and methods: All journal articles published up to February 27, 2019 from CINAHL, PsycINFO, PubMed and Web of Science were searched. We selected original research articles that described observational studies, included both individuals with left brain damage (LBD) and those with right brain damage (RBD) post-stroke, and reported specific diagnostic methods for SN. All authors reached consensus for the final selection of 41 articles. Time post-stroke, patient selection criteria, study setting, SN diagnostic methods were extracted.

Results: A total of 6324 participants were included: 3411 (54%) with RBD and 2913 (46%) with LBD. Without considering time post-stroke or diagnostic methods, the occurrence rate of SN was 29% (38% after RBD and 18% after LBD). Using ecological assessments resulted in higher prevalence than using tests not directly related to daily life activities (53% vs. 24%). Using methods based on a single-cutoff criterion led to lower occurrence of SN than using multi-test methods (27% vs. 33%). The prevalence decreased from the acute to chronic stage post-stroke.

Conclusions: The estimated prevalence of SN after unilateral stroke is 30%. SN is more common after RBD than after LBD, but SN after LBD is still quite common. Using ecological assessments and multi-test methods to detect SN is preferred to using a single-cutoff criterion of a test that is not directly related to daily function. The decrease in SN prevalence over time is evident, but the exact prevalence in later stages cannot be estimated. More research is needed to better understand chronic SN.

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1. Introduction

Spatial neglect (SN) is a syndrome resulting from damage to the neural networks critical to spatial attention and related cognitive and motor functions [1–3]. The neural networks involve all the major cortices, subcortical areas and structures, and whitematter fibres [4–10]. The syndrome typically renders abnormal bias toward the side of space ipsilateral to the injured cerebral hemisphere. Thus, affected individuals "neglect" (i.e., pay insufficient or no attention toward) the contralesional side of

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space, in a way that cannot be attributed to primary sensory or motor defects [11,12] That is, individuals with SN after right brain damage (RBD) typically neglect the left side of space, and those with SN after left brain damage (LBD) neglect the right side of space. The space can be close or on the body (personal space), within arm's reach (peripersonal space; near space), beyond arm's reach (extra-personal space; far space), or in one's mind (mental space) [13–15] The side of space can be classified based on the egocentric frame of reference (i.e., body-centered or viewer-centered) or an allocentric frame of reference (i.e., stimulus-centered or object-centered) [16–18]. Because SN research examines these many differing facets of SN, it advances not only the clinical fields of neuropsychology and neurology, but also the broad field of cognitive psychology and neuroscience in terms of

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understanding spatial processing and attention control and understanding the roles played by these mechanisms in different cognitive and motor functions.

SN is typically presented as a failure to respond to or report to stimuli presented in the contralesional side of space, a failure to initiate or complete movement in or toward the contralesional side of space, a failure to report, manipulate, or produce information stored mentally, or a failure to keep the gaze or body posture centered but deviating toward the ipsilesional [12,13,19,20]. The deficits created by SN disrupt basic self-care activities (e.g., dressing, grooming) [21,22], impair postural balance [23,24], interfere with reading ability [25–27], and impede navigation (e.g., avoiding furniture or walls when walking or using a wheelchair) [28-30]. SN also increases the risk of falls [31] and body injuries [32] and puts the affected individuals in danger of being struck by a vehicle when crossing the street [33,34]. Importantly, many individuals with SN are unaware of their own symptoms or the consequences of their deficits [35–39], which delays their seeking appropriate treatment or learning compensatory strategies. The disabling consequences of SN may last for a number of years after stroke [40-43], and family caregivers of affected individuals report greater burden and stress than family caregivers of stroke survivors without SN [44,45]. The profound impact of SN on stroke survivors and their families underscores the need for clinical implementation of research-informed assessments and evidence-based treatments. However, the prevalence of SN is undetermined, which impedes knowledge translation and further slows down research progress in seeking effective

The occurrence of SN varies across studies, from 20% to 80% [47–56], depending on brain lesion locations, time post-stroke, and assessment methods [21,46]. Overall, SN after RBD is more prevalent than SN after LBD [46,47,57], and left-sided SN is more severe than right-side SN. This situation may be related to the neural networks critical to spatial attention being predominately located in the right hemisphere [2,58]. Assessment directly related to daily functions (i.e., ecological assessment) [59] has shown greater sensitivity than conventional neuropsychological tests in detecting SN [60,61]. However, which test has greater specificity is difficult to determine, given that there is no gold standard for SN screening or diagnostic methods. SN is not a unitary disorder and presents a great variety of symptoms because spatial attention is essential to many perceptual, cognitive, and motor functions. SN impairs visual perception, auditory localisation, tactile spatial perception, proprioception, visuospatial memory, visuomotor control, and movement planning and initiation [2,12,62-65]. In studies aiming to establish SN prevalence, completing a comprehensive battery that covers every domain that may be affected by SN is challenging. For example, Ringman et al. [53] conducted an observational study in an acute care setting and determined the presence of SN based on one item on the National Institutes of Health Stroke Scale, which screens for extinction (i.e., a failure to detect a contralesional stimulus in the presence of an ipsilesional stimulus), one of many symptoms of SN. Extinction screening is quick and easy, requiring no device or equipment, and can be done in visual, auditory, and tactile modalities. However, whether the extinction test is as sensitive or representative as other tests for SN is unknown. Even in studies that used a popular battery, such as the Behavioural Inattention Test (BIT) [66], how SN is evaluated, varied. Some used the standard cut-off score [67], and others classified an individual as having SN as long as they demonstrated abnormal left-right asymmetry [68] in any one (or any number) of the multiple tests within the battery. Whether using the singlecutoff criterion or the multi-test methods is a better practice is unknown.

The purpose of the present study was to estimate the prevalence of SN post-stroke by a systematic review of the literature. To do so, we cast a wide net over all definitions, diagnostic methods, and criteria of SN. In this context, we define SN operationally as an abnormal left-right asymmetry presented in a specified assessment, or a test score below a pre-determined cutoff criterion. The latter does not necessarily indicate a left-right asymmetry, especially in a target cancellation test. However, using cut-off criteria on test scores is a common practice. Because of this. the present study did not distinguish subtypes of SN and thus included all of them (egocentric, allocentric, personal, peripersonal, extrapersonal, visual, tactile, auditory, representational, and motor neglect, etc.). Importantly, our objective was to establish the prevalence of SN post-stroke rather than post-right-brain stroke. Thus, we specifically selected studies that included both RBD and LBD individuals and excluded studies that did not include LBD or RBD individuals. This selection ensured that both LBD and RBD individuals included in a given study were assessed the same way. Our a priori questions were:

- What is the prevalence of SN among individuals with unilateral stroke?
- Does the prevalence of SN differ depending on the lesioned hemisphere, time post-stroke, or SN diagnosis methods?

2. Methods

2.1. Review procedures

We searched CINAHL, PsycInfo, PubMed and Web of Science for articles published from inception to February 27, 2019, by using the following search terms for the title or abstract: "spatial neglect" OR "visual neglect" OR "hemineglect" OR "visuospatial neglect" OR "unilateral neglect" OR "spatial inattention." Two authors (EE and GS) independently removed replicates, screened the titles and abstracts to identify those that were potentially eligible for full-text reviews, reviewed the full texts, and determined whether an article was included for analysis based on information extracted. This procedure created 2 sets of articles, which then were further reviewed and discussed by all 3 authors for the final decision. Any discrepancies were resolved by discussion.

2.2. Eligibility criteria and selection of studies

Once a full-text article was obtained, the article was evaluated according to the eligibility criteria:

- original research articles published in peer-reviewed journals;
- observational studies;
- including both RBD and LBD stroke survivors;
- reporting the number of patients with SN after RBD and the number of patients with SN after LBD;
- specifying the methods determining the presence of SN;
- written in English.

If the exact numbers of patients with SN after RBD or LBD were not reported but could be calculated based on the information available in a given article, the article was considered eligible. If the same cohort was reported in different articles but assessed at different times (e.g., acute and chronic), the articles were included; otherwise, studies of the same cohort were excluded. We excluded case studies, controlled or clinical trials, and reviews of the literature. We also excluded studies that specifically selected

individuals based on the presence or absence of SN, used computer models, or focused on clinical populations unrelated to stroke as well as editorials and comments, replies and corrections.

2.3. Data synthesis

We extracted participant characteristics, time post-stroke, setting, and diagnostic methods (assessment and criteria used for determining the presence of SN), and number of individuals with RBD, LBD, SN after RBD and SN after LBD from the selected studies.

2.3.1. Diagnostic methods

Two authors (GS and PC) independently classified the types of assessment used in each study as "ecological" (e.g., text reading, Baking Tray Test [69], Catherine Bergego Scale) [70] or "nonecological" (e.g., extinction screening, conventional subtests of the Behavioural Inattention Test [67], observation of basic limb movement in the contralesional and ipsilesional sides of space) [71] following similar criteria used in published reviews [59,72]. Studies were also classified as "single-cutoff criterion" or "multi-test methods" based on criteria specification for SN diagnosis. For example, Stone et al. [54] identified SN if abnormality was demonstrated in any one of the tests administered to their participants, so the study was classified as using "multi-test methods". Furthermore, a given study could use

multiple tests on the same cohort, and some participants were able to be tested on all or some of the tests. In such case, each test resulted in different occurrence rates of SN, and we considered them as different data entry for prevalence analysis.

2.3.2. Time post-stroke

The classification on time post-stroke was based on the review of participants' time post-stroke and the setting in which a given study was conducted because of unspecified time information provided in some articles as well as the differences in healthcare facility across countries and regions. Four categories regarding time post-stroke emerged:

- acute: first week post-stroke in acute care and general hospital settings;
- subacute: 1 week to 3 months post-stroke in inpatient rehabilitation and general hospital settings;
- post-acute: 6 months to 1 year post-stroke in inpatient rehabilitation and general hospital settings;
- chronic: > 1 year post-stroke in community and outpatient settings.

Studies, that did not specifically select participants based on time post-stroke or did not provide information on time post-stroke or study setting, were not classified. Any discrepancies were resolved by discussion among the 3 authors.

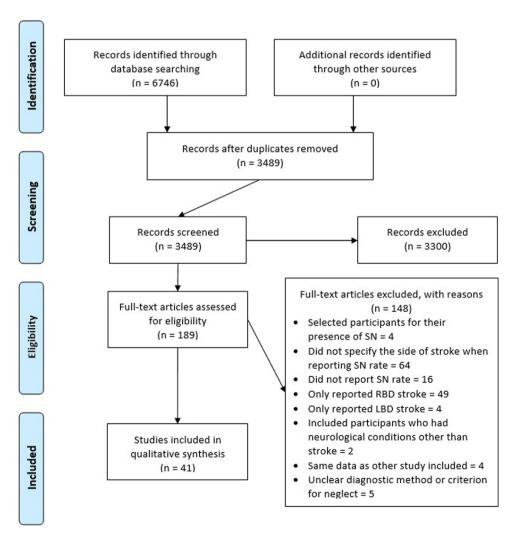


Fig. 1. PRISMA flow diagram. LBD: left brain damage; RBD: right brain damage; SN: spatial neglect.

(54%)

"subacute"

Using our classification for "time post-stroke" as described in

Methods, 11 (27%) studies were classified as "acute"

95,98,100,101], 1 (2%) "post-acute" [48], and one (2%) "chronic"

[88]; 7 (17%) could not be classified [50,75,78,81,83,90,96]. For one

of the studies, participants were assessed at 2 time points that fell into 2 categories, so the results were classified as both subacute

and post-acute, based on the time point [48]. The prevalence of SN

The studies reviewed dated back in 1972 (Table 1). With almost

decreased from acute (34%) to chronic (17%) stage (Fig. 3).

[53,54,71,73,74,79,80,86,92,97,99], 22

[41,43,47,48,51,52,55,69,76,77,82,84,85,87,89,91,93-

3. Results

The two independent reviewers selected 50 articles, and all authors reached consensus for the final selection of 41 (82%) articles to be included in the analysis (Fig. 1). The studies were conducted in 15 countries, with one study each from Australia, France, Georgia, Japan, New Zealand, Switzerland, and Turkey; 2 studies from Belgium; 3 were from Germany and the United States; 4 from Sweden; 5 from Canada and Italy; and 6 from The Netherlands and the United Kingdom. A total of 6324 participants were included: 3411 (54%) with RBD and 2913 (46%) with LBD. Across all the 41 studies, SN was more prevalent after RBD than after LBD (Table 1). Without considering diagnostic methods or time post-stroke, the overall occurrence rate of SN was 29%. Specifically, it was 38% after RBD and 18% after LBD.

Fig. 2 summarises the results based on diagnostic methodology. Fewer studies used ecological than non-ecological assessments (7 vs. 35), but studies using ecological assessments resulted in a higher prevalence of SN (53%) [47,54,69,73–76] than studies using non-ecological assessments (24%) [41,43,48,50–55,71,77–101]. One study was counted for both ecological and non-ecological assessments because it included both types [54]. For the diagnostic criteria, one study was excluded because the information was unclear [86], and 2 studies were classified in both types of diagnostic criteria because they used them to detect different SN subtypes [54,78]. Thus, 24 (59%) studies used a single-cutoff criterion to determine the presence of SN, and 18 (44%) used multi-test methods. Overall, we found lower occurrence rate of SN for studies using a single-cutoff criterion than multi-test methods (27% vs. 33%).

half a century between the oldest and latest studies, we acknowledged the potential changes in diagnostic methods over time. Thus, we conducted a post-hoc analysis to examine whether the SN occurrence rate differed in the literature by classifying 21 (51%) articles published before 2000 as "old" and 20 (49%) articles published in 2000 and later as "recent." Without considering diagnostic methods or time post-stroke, the overall occurrence rate of SN was 27% in the old studies (35% vs. 19% after RBD vs. LBD) and 32% in the recent literature (42% vs. 18% after RBD vs. LBD).

We repeated the same analyses described in the ad hoc analysis for each group. Fig. 4 summarises the prevalence change as a function of time post-stroke. Many of the old studies (13/21; 62%) were conducted during the subacute stage, and none focused on the chronic stage. The trend of decreasing SN occurrence rate was apparent, consistent with the trend shown in Fig. 3. In the recent group, no study focused on the post-acute stage, and the occurrence rate appeared higher in the subacute than acute stage. Fig. 5 presents the results based on diagnostic methodology. The patterns were consistent with those in Fig. 2, showing higher SN

Table 1Studies included in the systematic review of special neglect (SN).

Study	Setting	Country	Criteria	Time post-stroke	Diagnostic methods and criteria for SN	Rate of SN
Acute (with the first we Appelros et al. (2002) ^c	ek post-stroke in acut University hospital		l hospital settings) First stroke, able to complete all	1-4 davs	Line crossing, letter	RBD: 40/126 (31.7%)
,	omversity nospital		the assessments in the right	J	cancellation and	, , ,
			time period, and no recurrent stroke, stroke-like symptoms, acute vertigo, disturbances of consciousness or transient ischemic attack		line bisection (from the BIT), Baking Tray Task and two personal neglect tests (comb test, razor/compact test and eyeglasses test	LBD: 25/146 (17.1%)
					and hand touching)	
Becker and Karnath (2007)	University centre of neurology	Germany	First stroke, unilateral stroke and no other neurological	2.9 days (average)	Bells test	RBD: 11/42 (26.2%)
(2007)	neurology		disorders, tumours or history of lesions			LBD: 1/41 (2.4%)
Becker and Karnath (2010)	University centre of neurology	Germany	First stroke, unilateral stroke, and no diffuse or brain stem	48.3 hrs (average)	Letter cancellation, bells test, Albert's	RBD: 30/71 (42.3%)
			strokes		test, copying test	LBD: 6/53 (11.3%)
Kumral et al. (2002)	University stroke unit	Turkey	Anterior ACA infarction, first stroke and no border-zone ACA/	Within 1 week	Line bisection and line cancellation	RBD: 3/16 (18.8%)
			MCA/PCA stroke			LBD: 1/30 (3.3%)
Motomura et al. (1986)	Brain and heart centre, cardio-	Japan	Thalamic hemorrhage, testing within 7 days of onset, and no	Within 7 days	Line bisection, line cancellation, draw	RBD: 11/20 (55.0%)
	vascular centre and department of neuro-psychiatry in a medical college		more than minimal disturbance of consciousness from the onset		a man, copy a cube	LBD: 0/13 (0.0%)
Ringman et al. (2004)	Hospital	US	Between 18 and 85 years old, stroke symptoms lasting 1 to	Within 7 days	NIH Stroke Scale neglect subscore	RBD: 165/386 (42.7%)
			24 hrs, ischemic stroke, independent prior to stroke on the Barthel Index and no resolution of neurologic symptoms or an isolated mild neurologic deficit		(Cookie Theft Picture)	LBD: 77/394 (19.5%)

Table 1 (Continued)						
Study	Setting	Country	Criteria	Time post-stroke	Diagnostic methods and criteria for SN	Rate of SN
Siekierka-Kleiser et al. (2006)	Stroke unit	Germany	First stroke, middle cerebral artery stroke, acute motor hemi-syndrome with upper limb, full consciousness, ability to comply with tasks, symptoms within 72 hr of hospital admission and no aphasia	Within 7 days	Castaigne et al.'s methods (1970, 1972) for motor neglect	RBD: 14/30 (46.7%) LBD: 5/22 (22.7%)
Stone et al. (1991) ^c	Hospital	UK	Acute hemispheric stroke	3 days	Neglect battery	RBD: 13/18 (72.2%)
Stone, Halligan and Greenwood (1993) ^c	Hospital	UK	First stroke and acute stroke	2-3 days	Modified BIT, "hemi- inattention," tactile extinction, allaesthesia, visual extinction	LBD: 16/26 (61.5%) RBD Modified BIT: 50/61 (82.0%) Hemi-Inattention: 44/ 63 (69.8%) Tactile Extinction: 34/ 52 (65.4%) Allaesthesia: 32/56 (57.1%) Visual Extinction: 14/ 60 (23.3%)
						LBD Modified BIT: 48/74 (64.9%) Hemi-Inattention: 43/87 (49.4%) Tactile Extinction: 15/43 (34.9%) Allaesthesia: 5/46 (10.9%) Visual Extinction: 2/81 (2.5%)
Tatuene et al. (2016)	Stroke unit of a hospital	Switzerland	First stroke, acute stroke, admission within 15 days of stroke onset and no pre- existing alterations of visual or cognitive functions	Within 15 days, 3.7 days (average)	Ota's cancellation task and line bisection task (5 cm and 20 cm)	RBD: 9/36 (25.0%)
Van Nes et al. (2009)	Neurology wards of hospitals	The Netherlands	First stroke, supratentorial stroke, within two weeks of the stroke, and no diminished level of consciousness, primary visual deficits, aphasia, nonstroke related sensory or motor impairments or concomitant cognitive problems that impair ability to follow simple verbal instructions	5.5 days (average)	Star cancellation and letter cancellation (BIT subtests)	RBD: 15/44 (34.1%) LBD: 2/34 (5.9%)
Subacute (1 week to 3 r Albert (1973)	nonths post-stroke in Neuropsychology research unit	inpatient rehabilit US	cation and general hospital setting Unilateral cerebral lesion and right-handedness	gs) At least 3 weeks	Line cancellation	RBD: 11/30 (36.7%)
Azouvi et al. (2006) ^c	Subacute facility	France	Subacute stroke	11.02 days (average)	Bells test, figure copying, clock drawing, line bisection, overlapping figures test, reading, and writing	LBD: 11/36 (30.6%) RBD: 175/206 (85.0%) LBD: 34/78 (43.6%)
Chen et al. (2015) ^c	Inpatient rehabilitation facility	US	First stroke, able to complete assessments within 72 hr of admission, unilateral stroke, and 18–99 years old	Admission 6 days (median) Discharge 26 days (median)	Catherine Bergego Scale via Kessler Foundation Neglect Assessment Process	•

Table 1 (Continued)						
Study	Setting	Country	Criteria	Time post-stroke	Diagnostic methods and criteria for SN	Rate of SN
Denes et al. (1982) ^a	Department of physical therapy in a geriatric hospital	Italy	Motor deficit after stroke, unilateral stroke, right handedness and no history of motor deficit or neurological disease	Admission 53.5 days (average) Follow-Up 6 months later	Copying Crosses Test	RBD Admission: 8/24 (33.3%) Follow-Up: 7/24 (29.2%)
Edmans and Lincoln	Hospitals	UK	First stroke, unilateral stroke,	4 weeks	Cancellation,	LBD Admission: 5/24 (20.8%) Follow-up: 2/24 (8.3%) RBD
(1987) ^b	·		understand English, hemiplegia, able to sit during assessment, and no previous stroke, head injury or dementia		copying words and copying shapes from the Rivermead Perceptual	Cancellation Contralateral: 23/75 (30.7%) Ipsilateral: 4/75 (5.3%)
					Assessment Battery	Copying Words Contralateral: 7/75 (9.3%) Ipsilateral: 21/75 (28.0%)
					Copying Shapes Contralateral: 14/75 (18.7%) Ipsilateral: 6/75 (8.0%)	
						LBD Cancellation Contralateral: 6/75 (8.0%) Ipsilateral: 11/75 (14.7%)
						Copying Words Contralateral: 24/75 (32.0%) Ipsilateral: 2/75 (2.7%)
						Copying Shapes Contralateral: 9/75 (12.0%) Ipsilateral: 2/75 (2.7%)
Gauthier, Dehaut, and Joanette (1989)	Hospital	Canada	Right handedness, first stroke, unilateral lesions	Within 3 months	Bells Test	RBD: 10/19 (52.6%) LBD: 3/20 (15.0%)
Halligan, Marshall and Wade (1989)	Rehabilitation centre	UK	Right handedness, unilateral stroke and able to understand	85.5 days (average)	BIT	RBD: 26/54 (48.1%)
Kalra et al. (1997)	Stroke unit	UK	tasks Partial anterior circulation infarction, between a 3 and 5 on	1 to 2 weeks	Rivermead	LBD: 4/26 (15.4%) RBD: 32/75 (42.7%)
			an impairment scale (so-called "middle group") at 1 to 2 weeks post-stroke, and no hemianopsia and severe dysphasia		Perceptual Assessment Battery	LBD: 15/71 (21.1%)
Korner-Bitensky, Mayo and Kaizer (1990)	Stroke unit of a rehabilitation	ehabilitation	First stroke and no confusion, primary visual impairment,	59.8 days (average)	Computerised REACT program	RBD: 25/70 (35.7%)
	hospital		homonymous hemianopsia, neurological condition, severe comprehension disorder, temporary discharge over 10 days, or bilateral motor or sensory loss			LBD: 11/89 (12.4%)
Lafosse et al. (2005)	Rehabilitation centre	e	First stroke, between 35 and 80 years old, unilateral	52.29 days (average)	Line cancellation test	RBD: 15/55 (27.3%)
			ischemic MCA stroke, and no severe cognitive disorientation, or history of dementia, neurological, or psychiatric disorders			LBD: 4/50 (8.0%)

Table 1 (Continued)						
Study	Setting	Country	Criteria	Time post-stroke	Diagnostic methods and criteria for SN	Rate of SN
Marsh and Kersel (1993)	Stroke rehabilitation unit of a hospital	New Zealand	60 years or older, not blind, at least one functional hand, infarction, and no illness precluding rehab, pre-stroke physical or mental disorder, too	Between 15 and 20 days, with a mean of 17.15 days	Line crossing test, star cancellation test, indented paragraph reading test, line bisection	RBD: 10/17 (58.8%) LBD: 1/8 (12.5%)
McGlone, Losier and Black (1997)	Hospital	Canada	disabled to participate Acute, unilateral stroke, able to sit up, cooperate and complete the protocol	Within 2 months	test Sunnybrook Battery for Hemispatial Neglect (drawing and copying, line bisection, line cancellation, figure cancellation)	RBD: 43/71 (60.6%) LBD: 21/67 (31.3%)
Mosidze, Mkheidze and Makashvili (1994)	Hospital	Georgia	Right handedness, unilateral ischemic stroke, and no hemianopsia, oculomotor disorders, aphasia, bilateral damage or significant differences between patients in treatment procedures or education level	3 weeks	Figure copying	RBD: 39/290 (13.4%) LBD: 1/100 (1.0%)
Nijboer, Kollen and Kwakkel (2013)	Rehabilitation hospital	The Netherlands	Between 30–80 years old, first stroke, MCA or ACA region stroke, unable to walk at first assessment, no complicating medical history, and able to give informed consent	8.13 days (average)	Line bisection	RBD: 42/59 (71.2%) LBD: 9/42 (21.4%)
Nijboer and Van Der Stigchel (2019)	Inpatient rehabilitation hospital	The Netherlands	At least 18 years old, normal or corrected-to-normal visual activity and no severe deficits in communication and/or understanding	34.3 days (average)	Computer-based shape cancellation test	RBD: 27/106 (25.5%) LBD: 12/101 (11.9%)
Nijboer et al. (2013)	Rehabilitation hospitals	The Netherlands	First stroke, one-sided supratentorial lesion, above 18 years old, written or verbal consent, premorbid ability to speak Dutch, and no disabling comorbidity or SAH	50.0 days (average)	Letter cancellation test	RBD: 47/115 (40.9%) LBD: 6/69 (8.7%)
Plourde et al. (1993)	Hospital	Canada	First stroke, unilateral stroke and no neurological disease	Between 1 to 2 months, 46 days (average)	Line cancellation test (Albert's test)	RBD: 19/41 (46.3%) LBD: 5/36 (13.9%)
Rose et al. (1994)	Acute care	Canada	Independent prior to stroke, stroke within 3 weeks, adequate basic touch sensation, first stroke, no history of alcohol or substance abuse, dementia, or psychosis and not extremely frail or visually impaired	1 month	Face-Hand Test of tactile extinction	RBD: 5/14 (35.7%) LBD: 0/5 (0.0%)
Ten Brink et al. (2019)	Inpatient rehabilitation centre	The Netherlands	Assessed on neglect assessment within two weeks of admission and ischemic stroke or delayed cerebral ischemia after SAH	Part 1 25.8 days (average) Part 2 24.4 days (average)	Part 1 Computerised shape cancellation test Part 2 Computerised line bisection	RBD Part 1: 19/51 (37.3%) Part 2: 13/61(21.3%) LBD Part 1: 9/37 (24.3%) Part 2: 5/42 (11.9%)
Ten Brink et al. (2017) ^b	Inpatient rehabilitation centre	The Netherlands	Screened for SN, able to perform the object cancellation task completely, data on hemisphere of lesion and no discrepancy between side of SN between peripersonal and extrapersonal space	24.7 days (average)	Digital object cancellation task, line bisection and Catherine Bergego Scale	RBD Contralateral SN: 41/ 171 (24.0%) Ipsilateral SN: 11/171 (6.4%) LBD Contralateral SN: 19/ 146 (13.0%) Ipsilateral SN: 9/146 (6.2%)
Tham and Tegner (1996) ^c	Neurology department of a hospital	Sweden	No requirements	Between 3 and 30 days	Baking Tray Task	RBD: 13/28 (46.4%) LBD: 6/24 (25.0%)

Table 1 (Continued)						
Study	Setting	Country	Criteria	Time post-stroke	Diagnostic methods and criteria for SN	Rate of SN
Viken et al. (2012)	Neurological department of a university hospital	Sweden	Acute onset of clinical symptoms suggestive of stroke, under 70 years old, ischemic stroke, and no etiology other than ischemic stroke or diagnosis of cancer at an advanced stage, infectious hepatitis or human immunodeficiency viruses	Between 1 and 51 days, 8 days (median)	Star cancellation test	RBD: 46/168 (27.4%) LBD: 33/189 (17.5%)
Denes et al. (1982) ^a	Department of physical therapy in a geriatric hospital	Italy	tation and general hospital settin Motor deficit after stroke, unilateral stroke, right handedness and no history of motor deficit or neurological disease	gs) Admission 53.5 days (average) Follow-Up 6 months later	Copying Crosses Test	RBD Admission: 8/24 (33.3%) Follow-Up: 7/24 (29.2%) LBD Admission: 5/24 (20.8%) Follow-Up: 2/24 (8.3%)
Chronic (>1 year post-s Linden et al. (2005)	troke in community a University hospital		ic settings) 70 years or older, able to consent and no severe disorders that required specialized care at other units	19.9 months (average)	Star cancellation test	RBD: 15/75 (20.0%) LBD: 7/56 (12.5%)
Other (time post-stroke Barbieri and Renzi (1989)	unspecified or not lir Neurological wards	•	ic time frame above, in mixed set Right handedness, able to complete testing and unilateral stroke	ttings) Not specified	Picking up circular wells from a wooden board while blindfolded (tactile neglect) and visual, tactile and auditory extinction	RBD Tactile Neglect: 3/38 (7.9%) Extinction: 12/30 (40.0%) LBD Tactile Neglect: 2/46 (4.3%) Extinction: 8/39
Colombo, De Renzi and Faglioni (1976)	University centre for psychiatric and neurological diseases	Italy	Right handedness, unilateral stroke and able to complete the tests	Not specified	Copying drawings and Raven's CPM	(20.5%) RBD Copying Drawings: 21/ 53 (39.6%) Raven's CPM: 17/53 (32.1%)
Colorati Caltarina	Not are if od	Italia	Right handedness, unilateral	Not an arifold	Pausala CDM	LBD Copying Drawings: 16/50 (32.0%) Raven's CPM: 16/50 (32.0%)
Gainotti, Caltagirone and Miceli (1977)	Not specified	Italy	stroke, able to complete the tasks and no impaired consciousness, history of diffuse or bilateral cerebral damage	Not specified	Raven's CPM	RBD: 96/173 (55.5%) LBD: 37/170 (21.8%)
Gainotti, Messerli and Tissot (1972)	Clinic of mental diseases at a university and neuro- psychological unit of the department of neurology	Italy	Unilateral stroke and able to complete the tasks	Not specified	Copying designs (omissions of small lateral figure, omission of large lateral figure or unfinished figures)	RBD Small Lateral Figure: 32/114 (28.6%) Large Lateral Figure: 19/114 (16.7%) Unfinished Figures: 27/ 114 (23.7%)
						LBD Small Lateral Figure: 22/108 (20.4%) Large Lateral Figure: 3/ 108 (2.8%) Unfinished Figures: 1/ 108 (0.9%)

Table	1	(Cont	innod	n

Study	Setting	Country	Criteria	Time post-stroke	Diagnostic methods and criteria for SN	Rate of SN
Meyer et al. (2016)	Neuro- rehabilitation centres	Belgium	First stroke, assessed within 6 months, motor and/or somatosensory impairment in upper limb, 18 years old or older, substantial cooperation to perform assessment, functionally independent prestrike, and no other neurological impairments, SAH, tumour, encephalitis, TBI, or serious communication or language impairments	Between 12 days and 6 months, with a median 82 days	Star cancellation test	RBD: 22/73 (30.1%) LBD: 5/48 (10.4%)
Paolucci, McKenna and Cooke (2009) ^c	Multiple hospitals, inpatient and outpatient	Australia	18 years or older, medically stable, able to speak, read, understand English, able to complete tasks, participating in OT and allowed by their OT, not too low consciousness, able to use hand for assessment tasks, and no receptive aphasia or disorder of cognitive function	Between 2 and 451 days; 43.5 days (average)	The Occupational Therapist Adult Perceptual Screening Test	RBD; 57/107 (53.3%) LBD: 31/90 (34.4%)
Sunderland, Wade and Langton Hewer (1987)	Stroke registry from general practitioners	UK	First stroke, unilateral stroke and alive at 3 weeks post- stroke	3 weeks, 6 months and 1 year	Raven's CPM	RBD 3 Weeks: 7/67 (10.4%) 6 Months: 2/63 (3.2%) 1 Year: 1/56 (1.8%) LBD 3 Weeks: 4/88 (4.5%) 6 Months: 0/71 (0.0%) 1 Year: 1/67 (1.5%)

ACA: anterior cerebral artery; BIT: Behavioural Inattention Test; LBD: left brain damage; MCA: middle cerebral artery; NIH: National Institutes of Health; OT: occupational therapy; PCA: posterior cerebral artery; Raven's CPM: Raven's Coloured Progressive Matrices; RBD: right brain damage; SAH: subarachnoid hemorrhage; TBI: traumatic brain injury.

- ^a Denes et al. (1982) assessed patients at subacute and post-acute stages.
- ^b Ten Brink et al. (2017) and Edmans and Lincoln (1987) report both ispi- and contra-lateral neglect rates.
- ^c Studies that used ecological assessments.

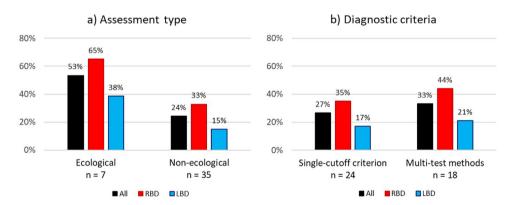


Fig. 2. Prevalence of spatial neglect based on diagnostic methodology. The number of studies is indicated for each category. A total of 41 studies were reviewed, but the total number of studies in (a) is 42 because one study was counted in both categories. The total number of studies in (b) is 42, because one study was excluded and 2 studies were counted in both categories. LBD: left brain damage; RBD: right brain damage.

occurrence rates with ecological assessment and multi-test methods than non-ecological assessment and single-cutoff criterion methods.

4. Discussion

The present systematic review aimed to establish the prevalence of SN after unilateral stroke. For the 41 articles reviewed and a total of 6324 individuals with unilateral stroke, the general

occurrence rate of SN was 29%, with greater prevalence after RBD than after LBD (38% vs. 18%). The overall rates were similar in studies published before and after the year 2000, 27% and 32%, respectively. Thus, the estimated prevalence of SN was close to 30% regardless of lesion location, diagnostic methods, or time post-stroke.

SN is indeed more prevalent after RBD than after LBD, and this is true across all 41 studies we reviewed. This result supports that attention networks involve both cerebral hemispheres, but are predominantly located in the right hemisphere [2,58]. From the

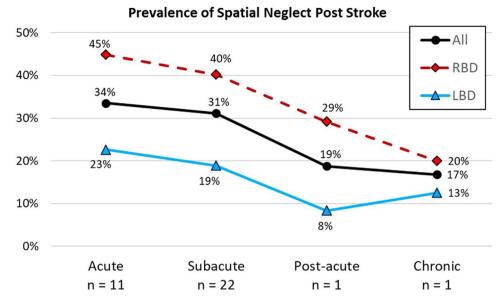


Fig. 3. Prevalence of spatial neglect over time post-stroke. The number of studies is indicated for each category. LBD: left brain damage; RBD: right brain damage.

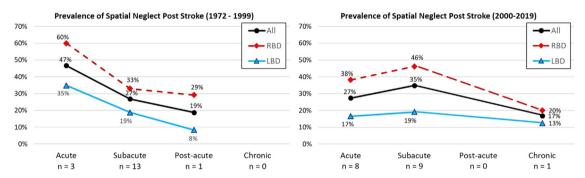


Fig. 4. Prevalence of spatial neglect over time post-stroke before and after year 2000 in the literature. The number of studies is indicated for each category. LBD: left brain damage; RBD: right brain damage.

perspective of clinical care, the prevalence of SN after LBD is lower than that after RBD, but cannot be considered rare. SN post-LBD is usually less severe than SN post-RBD [31,55,102], but the impact of SN on rehabilitation outcomes does not differ between individuals with LBD or RBD stroke [32,103]. We suggest that clinicians screen all stroke patients for SN regardless of the injured hemisphere.

The occurrence rate of SN changes, based on diagnosis methodology. We found that using ecological assessments increased the prevalence as compared with using tests that are not directly related to daily functions. This finding is consistent with the literature demonstrating that ecological assessments are more sensitive to detecting SN than are conventional neuropsychological tests [60,61]. Unlike neuropsychological tests, ecological assessments are often not specific to a perceptual modality, a cognitive domain, or a motor function; rather, ecological assessments evaluate the ability to perform a task that requires all the necessary perceptual, cognitive, and motor elements (e.g., the Baking Tray Test [69] and reading tasks) [104]. If one of the elements is impaired, the task cannot be completed or cannot be completed effectively. Thus, ecological assessments may not lead to an impairment-specific diagnosis (e.g., visual neglect, tactile neglect, representational neglect, or motor neglect), but they are useful in revealing SN symptoms efficiently. The number of studies using ecological assessment was much smaller than that of studies using non-ecological tests (7 vs. 35), but we found a great variety of ecological assessments as well as non-ecological tests for SN. However, we do not have evidence to suggest that using a

particular ecological assessment is sufficient to identify all patients with SN.

A comprehensive evaluation with multiple tests and assessments is recommended. As mentioned above. SN is multimodal and can be manifested across domains. One test or single-cutoff criterion is not likely to adequately capture SN impairments, symptoms, or related dysfunctions in a way that multiple tests or a single test performance evaluated multiple ways can. For example, the Bells Test can evaluate SN based on the accurate response, lateralised omission difference, and starting location [60], which is more sensitive to capturing SN than using a single evaluation method [76]. Lindell et al. [105] showed that at least 10 tests were needed to capture all 24 SN patients in their sample of 34 stroke patients with RBD. Consistently, the present review demonstrated that using multi-test methods led to a higher occurrence rate than using a single-cutoff criterion, in both RBD and LBD patients. However, one must keep in mind the risk of false discovery by using multiple screening tests and assessment methods, given the great variety of assessments and tests used in research studies, as revealed by the present review. There is a critical need to determine which tests to include in a battery and how many ways to evaluate performance on a given test. Only then can the "gold standard" of the SN diagnosis be specified.

From the present review, we estimate that one third of stroke survivors at the acute stage have SN. This is alarming because the presence of SN at early stages is associated with poor long-term recovery [41,106,107]. However, SN may be under-detected and

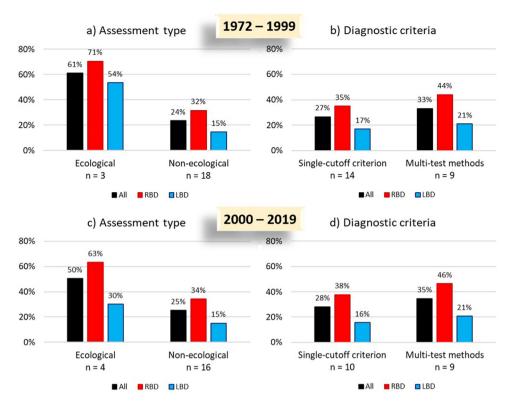


Fig. 5. Prevalence of spatial neglect based on diagnostic methodology before (a,b) and after year 2000 (c,d) in the literature. The number of studies is indicated for each category. LBD: left brain damage; RBD: right brain damage.

thus under-treated clinically [108,109]. Only when SN is detected can the stroke survivor be evaluated in detail and treated properly. The gap between current and best practices with respect to patient assessment prevents people with SN from getting the services they need and contributes to suboptimal patient outcomes [108–112]. Many clinicians misunderstand SN as a visual dysfunction rather than acknowledge it as a cognitive disorder that leads to a wide range of symptoms that are not limited to the visual modality. Some consider SN a "parietal problem" or "right brain problem", and immediately skip SN screening for patients who have subcortical or left-brain lesions [110]. This belief is simply not true; as the present review showed, approximately 20% of people with LBD stroke have SN at the acute and subacute stages.

Our review revealed that the occurrence rate of SN decreased over time, but we acknowledge that the estimated prevalence of SN at post-acute and chronic stages may not be as generalisable as that at acute and sub-acute stages. In addition, when evaluating studies before and after year 2000, the SN occurrence rate appeared to be higher at the subacute than acute stage. This finding could be a result of many factors, such as the changed environment of clinical research and the development of new assessments. Most studies reviewed were conducted at the acute (first week post-stroke in acute-care and general hospital settings) and subacute stages (1 week to 3 months post-stroke in inpatient rehabilitation and general hospital settings). Only one study involved the post-acute category (6 months to one year post-stroke in inpatient rehabilitation and general hospital settings) [48] and one study in the chronic category (> 1 year post-stroke in community and outpatient settings) [88]. Our review criterion mandated that our selected studies include both stroke patients with RBD and those with LBD, which may have reduced the number of usable studies that investigated later stages post-stroke. Although left-sided SN is studied relatively extensively at different stages post-RBD stroke [7,106,113-116], as evidenced by the low number of studies in our review, few studies have focused on

chronic SN after LBD. This is a knowledge gap that needs to be addressed by future studies that incorporate comprehensive assessments and follow both LBD and RBD patients from acute to chronic stages.

Although we are unable to estimate the prevalence of SN in later stages post-stroke, the trend of decreasing SN prevalence over time is evident [106,113]. This decrease may be attributed to the effectiveness of rehabilitation care [47] or spontaneous recovery [114]. However, SN can still persist for a long time in some individuals, especially those with brain damage in the ventral frontal cortex [115], superior and middle temporal gyri [116], or basal ganglia [7,116], or a fasciculus connecting occipital, temporal, parietal and frontal cortices [116,117]. It is important to continue seeking effective treatment or tailored neurorehabilitative interventions for patients whose SN symptoms persist long after they have completed all the standard rehabilitation therapies.

4.1. Study limitations

There are several limitations of this review. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [118] were followed for the present systematic review study, but the study was not registered at the international prospective register of systematic reviews (PROS-PERO) [119]. This oversight may have misled other researchers to perform the same or similar review studies. At the time this study was completed, no systematic review on the same topic of the present study was registered. Therefore, the risk of duplicated efforts is low. Despite having systematically searched 4 electronic databases, we may have missed some relevant studies. Studies may have been published in journals that were not covered by the databases. In addition, this review only included published studies; therefore, studies that were submitted and not accepted for publication or were accepted for publication only recently

would be excluded. Only English-written articles were included, so this systematic review may not be a complete representation of the evidence available worldwide. Finally, studies may not have been identified with the search strategy we used, especially considering that SN is a notorious syndrome with various names and definitions. Although we cast a wide net in trying to identify all the published articles focused on all types of SN and lateralised inattention, some articles might not have been considered in the review.

5. Conclusion

The estimated prevalence of SN after unilateral stroke is 30%, regardless of brain lesion location, diagnostic methodology, or time post-stroke. SN is more common after RBD than after LBD, but SN after LBD is still quite common (almost 20%). Using ecological assessments and multi-test methods to detect and diagnose SN is preferred to using a single-cutoff criterion of a test that is not directly related to daily function. We found decreased SN prevalence over time, but the number of studies focused on later stages was not comparable to those focused on earlier stages. More research is needed to better understand chronic SN.

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Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.rehab.2020.10.010.

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