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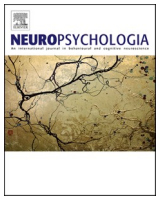

Review article

The neuroanatomy of visuospatial neglect: A systematic review and analysis of lesion-mapping methodology

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ABSTRACT

While visuospatial neglect is commonly associated with damage to the right posterior parietal cortex, neglect is an anatomically heterogenous syndrome. This project presents a systematic review of 34 lesion-mapping studies reporting on the anatomical correlates of neglect. Specifically, the reported correlates of egocentric versus allocentric, acute versus chronic, personal versus extra-personal, and left versus right hemisphere neglect are summarised. The quality of each included lesion-mapping analysis was then evaluated to identify methodological factors which may help account for the reported variance in correlates of neglect.

Overall, the existing literature strongly suggests that egocentric and allocentric neglect represent anatomically dissociable conditions and that the anatomy of these conditions may not be entirely homologous across hemispheres. Studies which have compared the anatomy of acute versus chronic neglect have found that these conditions are associated with distinct lesion loci, while studies comparing the correlates of peripersonal/extrapersonal neglect are split as to whether these neglect subtypes are anatomically dissociable. The included studies employed a wide range of lesion-mapping analysis techniques, each producing results of varying quality and generalisability. This review concludes that the reported underlying anatomical correlates of heterogeneous visuospatial neglect vary considerably. Future, high quality studies are needed to investigate patterns of disconnection associated with clearly defined forms of visuospatial neglect in large and representative samples.

1. Introduction

Visuospatial neglect is a common post-stroke cognitive deficit characterised by consistently lateralised spatial inattention (Parton et al., 2004). This impairment is traditionally associated with damage to right hemisphere posterior-parietal cortex, but modern lesion-mapping investigations have suggested that neglect is an anatomically diverse syndrome (Chechlacz et al., 2012a). Critically, however, specific methodological choices and inherent differences in patient samples in lesion-mapping investigations have the potential to dramatically impact results (de Haan and Karnath, 2018; Sperber and Karnath, 2017). It is therefore important to determine what portion of the variance within the reported anatomy of neglect can be linked back to different lesion-mapping analysis designs and how much can be attributed to true, underlying anatomical heterogeneity within the neglect syndrome.

Lesion-symptom mapping is a popular methodology used to identify specific brain regions which are significantly associated with behavioural impairments (Bates et al., 2003). Traditional lesion-mapping employs mass-univariate analyses to identify specific voxels that, when damaged, are associated with behavioural impairments (Bates et al., 2003). Many studies have employed lesion-mapping techniques to study the anatomy of visuospatial neglect, but no consensus has arisen from this work. For example, left egocentric neglect has been associated with structural damage to right hemisphere temporo-parietal areas (Chechlacz et al., 2012a; Molenberghs et al., 2012), but the exact areas implicated vary widely between studies. Neglect has also been documented following lesions to a wide range of areas, including temporo-parietal cortex (Chechlacz et al., 2012a), frontal cortex (Antoniello and Khazaei, 2019; Husain and Kennard, 1996, 1997), occipital cortex (Bird, 2006), and cerebellum (Hildebrandt et al., 2002; Silveri, 2001; Kim et al., 2008). Neglect has also been identified in patients with lesions exclusively impacting subcortical regions (Karnath et al., 2002) and has been associated with disconnection of white matter tracts including the superior longitudinal, inferior

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longitudinal, and inferior fronto-occipital fasciculi (Chechlacz et al., 2012a; Bird, 2006; Urbanski et al., 2011). Studies of the anatomical correlates of neglect following left hemisphere damage have yielded similarly disparate findings (Beume et al., 2017; Suchan and Karnath, 2011; Moore et al., 2021a). Against this backdrop, a systematic cumulatively analysis of the results of past investigations to identify factors which may help account for the reported variance in correlates associated with the neglect syndrome.

A portion of the reported variance may be accounted for by considering neglect as a behaviourally heterogenous syndrome rather than a unitary deficit. Past research has strongly suggested that neglect is a behaviourally diverse syndrome. Patients can exhibit neglect within a self-centred (egocentric) or object-centred (allocentric) frame of reference (Demeyere and Gillebert, 2019; Farah et al., 1990). Alternatively, neglect can impact either extra-personal (far) space or peri-personal (near) space (Beschin and Robertson, 1997). These neglect subtypes have been demonstrated to be doubly dissociated and differentially predictive of long-term recovery outcomes (Moore et al., 2021b). Previous research which has considered these behavioural dissociations has generally linked different neglect subtypes to distinct neural correlates (Chechlacz et al., 2012a; Ten Brink et al., 2019). However, these findings have not yet been comparatively evaluated to determine whether similar variance exists within the reported correlates of neglect subtypes.

Additionally, some of the variance within reported correlates of neglect may be related to the specific analysis design choices employed by individual studies. There are many potential analysis factors which may dramatically impact the results of lesion-mapping analyses. First, many investigations employ strict patient inclusion criteria which may limit the generalisability of their results. For example, it is unclear whether the results of a study identifying neglect correlates in only right-hemisphere middle cerebral artery strokes (e.g. Carson et al. (2019)) can be generalised to a more diverse and representative sample of stroke survivors. Similarly, it is unclear whether findings from studies involving relatively small numbers of patients (e.g. Toba et al. (2017), N = 25) should be weighted equally with those derived from larger-scale investigations (e.g. Moore et al. (Moore and Demeyere, 2022), N = 573). Furthermore, data collection methods can impact the conclusions of lesion-mapping analyses. For example, previous research has suggested that combining behavioural and neuroimaging data obtained at different timepoints from the same patients can confound the results of lesion-mapping investigations (de Haan and Karnath, 2018), yet this practice has been used in many past neglect studies (Aiello et al., 2012; Golay et al., 2008; Ptak and Schnider, 2011). Finally, specific lesion-mapping analysis parameters can dramatically alter the location and size of significant voxel clusters. For example, investigations which fail to control for lesion volume risk reporting correlates which are likely to be damaged in larger strokes rather than areas associated with the behaviour of interest (Sperber and Karnath, 2017). Similarly, analyses which do not restrict analysis to voxels impacted in a minimum number of patients from an overall sample risk violating the assumptions of lesion-mapping's statistical tests (Sperber and Karnath, 2017). Overall, it is critically important to cumulatively analyse the results and methodologies of past neglect lesion-mapping investigations to further fundamental understanding of the neuroanatomy of this syndrome.

The present investigation aims to summarise the findings of past research using lesion-mapping techniques to investigate the neural correlates of visuospatial neglect. First, a systematic literature review was conducted to identify all regions reportedly associated with neglect impairment. Subsequent analyses were then conducted to compare the reported correlates of egocentric versus allocentric, acute versus chronic, personal versus extra-personal, and left versus right hemisphere neglect. The quality of the reported lesion-mapping analysis was then evaluated in the context of specific methodological decisions, which as highlighted above can introduce biases to lesion-mapping results.

2. Methods

2.1. Systematic review

First, a systematic literature review was conducted to identify reported neural correlates associated with neglect impairment. In line with PRISMA systematic review guidelines (Moher et al., 2015), this project was registered in the PROSPERO (Booth et al., 2012) database prior to formal manuscript screening (CRD4202019612). No part of the study procedures or analyses was pre-registered prior to the research being conducted. We report all data exclusions (if any), all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, and all measures in the study.

Pubmed, Embase, PsychInfo, Scopus, and Web of Science online bibliographic databases were searched from inception to March 2022 using a combination of MeSH terms and keywords related to neglect, voxel-based lesion-symptom mapping, and stroke. A full list of the employed terms is included within supplementary materials. Manuscripts were considered for inclusion if they reported cross-sectional, observational, cohort, case-control, or randomised control trials which included human participants over the age of 18 years, employed quantitative lesion-mapping, and identified specific regions of interest or MNI coordinates implicated in neglect impairment. Additionally, studies were considered for inclusion if they reported data from patients who had suffered any type of cerebrovascular accident resulting in visible lesions on neuroimaging (e.g. ischemic/haemorrhagic stroke and/or traumatic brain injury). Studies were considered for inclusion if patients had completed quantitative neglect assessment (e.g. a neuropsychological test). Studies were not excluded based on any particular type of brain injury in their patient population. Notably, while traumatic brain injury cases were not explicitly excluded, no studies employing this sample was identified in our systematic search.

Studies were excluded from consideration if they were not written in English or reported animal or child (<18 years) data. All studies that included fewer than 10 patients with visuospatial neglect impairment or exclusively employed non-statistical, lesion-mapping methodologies (e.g. lesion subtraction plots, descriptive lesion analyses) were also excluded. All conference abstracts, review articles, book abstracts, and published theses were excluded. Papers which did not report significant correlates associated with either egocentric (including extra/peri-personal neglect) or allocentric neglect were excluded. Notably, egocentric and allocentric neglect are not the only documented neglect subtypes. Previous studies have reported neural correlates of auditory neglect (BLAETTNER et al., 1989; Gutschalk and Dykstra, 2015), motivational neglect (Lecce et al., 2015), and motor neglect (Mattingley et al., 1998; Rossit et al., 2009). However, data from studies reporting exclusively on these other neglect subtypes was not included in this study as this topic was outside the scope of the pre-registered systematic review protocol. Similarly, neuropsychological case and small group lesion studies can provide important insight into the correlates of neglect. However, data from case studies was not included in this investigation as this study aims to evaluate quantitative lesion-mapping techniques which require data from larger groups of impaired patients (de Haan and Karnath, 2018; Bates et al., 2003).

The search criteria yielded 1050 unique manuscripts which were subsequently screened by two independent reviewers (MJM & EM). First, manuscripts were screened to remove all irrelevant studies from consideration based on study title (N = 823) then study abstracts (N = 156). The surviving full-text articles were then screened to identify manuscripts which provided sufficient data and analyses to address the questions posed within this systematic review. Any inclusion/exclusion disagreements were considered and resolved by a third independent reviewer (ND). Both the initial and secondary reviews were conducted by independent reviewers.

Notably, three papers met inclusion criteria, but were subsequently excluded due to lack of useable findings: (1) Balslev et al. (2013)

reported significant correlates associated with less severe neglect rather than more severe neglect; (2) Machner et al. (2018) reported anatomy associated with neglect, but found that no voxels survived correction for lesion volume; (3) Eschenbeck et al. (2010) reported a neglect lesion-mapping analysis, but did not provide sufficient detail for the impacted ROIs to be effectively identified. This screening process resulted in 34 manuscripts meeting all inclusion criteria (Fig. 1). Details of specific manuscripts included/excluded at each stage, raw extracted data, and all other relevant data have been made openly available on the open science framework (https://osf.io/up79e/).

Information pertaining to each of these included article's publication details, patient group demographics, study design, and qualitative results summary was then extracted for analysis. Specifically, brain regions of interest (ROIs) reported to be associated with neglect impairment were extracted. If a study reported MNI coordinates of significant voxels rather than regions of interest, the implicated ROIs were defined via comparison to the Harvard-Oxford Cortical Areas Atlas and the Johns Hopkins white matter atlas. These extracted data were then descriptively synthesized to summarise the different neural correlates of egocentric and allocentric visuospatial neglect deficits. Secondary analyses investigating peri-personal versus extra-personal, left versus right hemisphere, acute versus chronic, and grey versus white matter neglect anatomy were also performed.

2.2. Lesion-mapping quality analysis

Previous research has identified a number of factors related to patient inclusion criteria, data collection, and analysis structure, all of which can impact the quality of results yielded by lesion-mapping analyses (de Haan and Karnath, 2018; Sperber and Karnath, 2017; Bates et al., 2003; Thiebaut de Schotten et al., 2014). We aimed to convert these factors into broad quality criteria to assess the quality of the lesion-mapping studies identified within the systematic search. Quality criteria were considered met if the study manuscript explicitly stated each criterion employed, and were considered *not to be met* if studies did not provide sufficient information to evaluate the criterion. The quality assessment system considered 13 independent criteria which were grouped into patient inclusion, data collection, and analysis structure categories, as described in detail below.

2.3. Patient group factors

The specific patient inclusion and exclusion criteria employed play a key role in determining the quality of any lesion-mapping study. Excluding patients with a particular lesion pattern precludes all inferences about potential (possibly critical) contributions of any regions outside the established inclusion space (de Haan and Karnath, 2018; Bates et al., 2003). Given the established anatomical diversity of the neglect syndrome, lesion mapping studies which do not accurately represent this diversity within their patient groups risk drawing conclusions which are not generalisable outside of their chosen sample. Specifically, limiting analyses to one hemisphere (*Criterion 1*) or a specific within-hemisphere lesion location (e.g. vascular territory) (*Criterion 2*) precludes detection of any contributions from areas outside this selected space, introducing bias into results. Notably, studies explicitly aiming to quantify the anatomy of neglect within a specific region or vascular territory can provide key clues for teasing apart the anatomical complexity of neglect (Bird, 2006; Sperber et al., 2020). For this reason, a summary and comparison of studies which have focused analyses on a specific vascular territory is included.

Similarly, studies which pre-select patients according to a specific behavioural profile risk producing results of limited generalisability. For example, several of the identified studies only considered patients for inclusion if they had been noted as demonstrating neglect within observational clinical assessments (Aiello et al., 2012; Gandola et al., 2013). Previous research has demonstrated that observational neglect

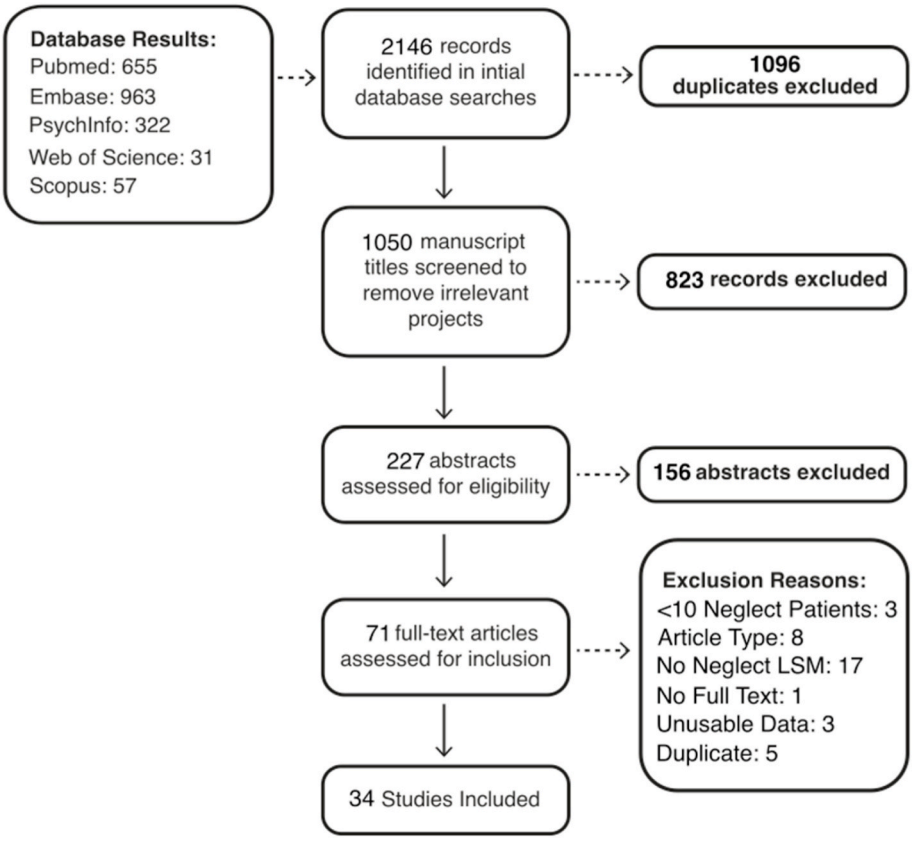

Fig. 1. A PRISMA flow diagram illustrating the inclusion/exclusion of all manuscripts considered in this study.

assessments lack sensitivity, are subject to expectation biases, and commonly misdiagnose early visual field impairment as neglect (Colwell et al., 2021; Moore et al., 2019). Therefore, patients diagnosed with neglect based on observational assessments may not be representative of neglect patients more generally (Balslev et al., 2013). Conversely, studies which include a consecutively recruited sample of patients who complete identical behavioural assessments, and are not pre-selected based on a specific behavioural profile (*Criterion 3*) have a lower risk of producing biased results.

Studies with larger sample sizes tend to produce higher-quality results (Cohen, 1992; Maxwell, 2004; Power et al., 2013). Broadly, a sample of 50 participants is generally considered to be the minimum size necessary to produce a high-quality lesion-mapping analysis (*Criterion 4*) (Bates et al., 2003; Wilson, 2017). Finally, previous studies have found that the neuroanatomy of neglect significantly differs depending on the time of behavioural assessment (Chechlacz et al., 2012b; Karnath et al., 2011). In order to control for this diversity, it is important for lesion-mapping studies to include only patients who were recruited within the same time-window post-stroke (*Criterion 5*) (de Haan and Karnath, 2018). For studies including acute/subacute populations (<3 months following stroke), any investigation that recruited all patients within the same 30-day window post-stroke was considered to have met this criterion. For studies using chronic patients (>6 months following stroke), this criterion was considered met only if all included patients were assessed in the chronic phase. Studies which conducted separate acute and chronic analyses were considered to have met Criterion 5 only if both populations met the above time-window criterion. Studies which did not report sufficient detail for this criterion to be evaluated (n = 1) were classed as unmet on *Criterion 5*.

2.4. Behavioural and neuroimaging data factors

Previous research has demonstrated that neglect impairment is most reliably quantified by considering performance on multiple, independent, standardised neglect assessments (Azouvi, 2006; Ferber and Karnath, 2001; Halligan et al., 1989; Molenberghs and Sale, 2011; Moore et al., 2019; Sperber and Karnath, 2016; Huygelier et al., 2020). Studies that defined neglect diagnostic category or quantified impairment severity using information from multiple (or repeated) assessments were therefore considered to have met *Criterion 6*. Dichotomising behavioural performance (e.g. unimpaired versus impaired) results in a significant loss of information and a corresponding decrease in statistical power (Cohen, 1992; de Haan and Karnath, 2018). Therefore, high-quality lesion-mapping analyses should aim to include continuous behavioural metrics (e.g. severity of neglect) rather than binarized impairment categories (*Criterion 7*).

As noted earlier, it is important that lesion-mapping studies employ behavioural and neuroimaging data that were collected at the same time point post-stroke (de Haan and Karnath, 2018; Bates et al., 2003). Mixing acute/chronic scans and behavioural assessments introduces recovery and cortical reorganisation confounds which can preclude valid inferences of brain-behaviour relationships (de Haan and Karnath, 2018; Bates et al., 2003). For example, a patient with damage to an area critically related to neglect on an acute scan may initially exhibit neglect but recover by the time of a later behavioural assessment. Alternatively, a patient who completes acute behavioural assessment might suffer age-related atrophy or secondary (undiagnosed) stroke events before receiving a brain scan. Acute/chronic data mixing violates the assumptions of lesion-mapping and weakens statistical brain-behaviour relationships (de Haan and Karnath, 2018; Bates et al., 2003). For this reason, high quality lesion-mapping studies should aim to include behavioural and neuroimaging data from the same time point (*Criterion 8*).

Notably, here we do not include type of neuroimaging as a quality criterion. Although MR is commonly thought to be superior to CT imaging for lesion delineation, there is no evidence that this resolution difference significantly impacts the results of lesion mapping studies (de Haan and Karnath, 2018). There are several reasons why CT and MR-derived lesion masks may not result in significantly different lesion mapping results. First, hyper-acute CT scans may not visualize the full extent of stroke lesions, but stroke damage is generally clearly visible on later CT scans (which are generally the scans used in lesion mapping) (Bryan et al., 1991). Second, lesion analysis requires pre-processing employing non-linear transformations to warp native-space lesion masks into standard space templates (de Haan and Karnath, 2018; Brett et al., 2001; Rorden et al., 2012). These essential steps result in a significant loss of detail, which could negate differences between CT and MR-derived lesions (Brett et al., 2001). Finally, all univariate lesion-mapping results are subject to a substantial degree of spatial misallocation due to non-random spatial variation patterns caused by the brain's vasculature structure and the inherent network structure of many behaviors of interest (Mah et al., 2014). Overall, it is unclear whether any variation due to input imaging modality is significant relative to these established factors. Only one quantitative comparison of CT and MR data in lesion-mapping analyses has been conducted, and this study concluded that MR- and CT-based lesion-mapping studies produce comparable results (Moore et al., 2021a, Moore et al., 2021b).

Specifically, Moore et al. (Parton et al., 2004) conducted a large-scale simulation study comparing the performance of matched CT and MR-derived lesion masks in 83 stroke patients. In both ROI-level and voxel-level simulations, CT-derived lesion masks consistently either outperformed or yielded comparable results to MR analyses in terms of degree of displacement and Dice similarity coefficient with targets (Parton et al., 2004). This suggests that despite differences in image resolution at acquisition, there is no evidence that MR-derived lesions outperform CT-derived lesions within large-group lesion mapping analyses. This is in line with established guidelines to lesion mapping methodologies which assert that both CT and MR modalities can and should be used in lesion mapping analyses (Parton et al., 2004).

Additionally, a non-trivial proportion of the stroke population cannot safely undergo MR imaging. Singer et al. (Parton et al., 2004) found that 19.9% of acute stroke patients are not eligible for MR scanning due to safety contraindications (such as metallic implants), diminished consciousness, vomiting, agitation, and hemodynamic compromise. This means that any study including exclusively MR imaging risks drawing conclusions based on an inherently biased and thus potentially non-representative sample of the stroke population. CT is also far more widely available than MR. For example, in their database of routinely collected clinical stroke imaging, Moore et al. (Parton et al., 2004) found that 55.8% of 1517 consecutively recruited stroke patients had CT imaging which could be used for lesion mapping (visible lesions, able to be normalized) whereas only 9.7% had MR scans which could be used. This means that studies incorporating CT scans offer increased lesion coverage and statistical power relative to MR-only analyses. Overall, both CT and MR imaging have strengths and weaknesses in the context of lesion-mapping analyses. Given this complexity and the lack of evidence that MR outperforms CT in large-group lesion-mapping analyses, the modality of neuroimaging was not included as a quality criterion in this study.

2.5. Lesion-mapping analysis factors

Lesion-mapping analyses aiming to produce unbiased results should include theory-blind, voxel-wise analyses (*Criterion 9*) (de Haan and Karnath, 2018). Given that patients with larger lesions are more likely to show a behavioural deficit, high-quality studies should reduce this potential bias by including lesion volume as a covariate (*Criterion 10*) (de Haan and Karnath, 2018; Sperber and Karnath, 2017). Studies which do not employ a minimum-overlap voxel-inclusion threshold risk violating the assumptions of voxel-wise statistical tests (Sperber and Karnath, 2017). In a simulation lesion-mapping study, Sperber and Karnath (2017) found that employing a lesion size covariate (*Criterion 10*) and

minimum overlap threshold (*Criterion 11*) markedly reduced the misplacement of lesion-mapping results compared with uncorrected analyses.

In cases where lesion-mapping analyses are employed with multi-focal behavioural deficits, these analyses are biased to report a single "average" location rather than the actual underlying network of spatially distinct correlates. Given that previous research has suggested that neglect can arise from functional disconnection of distant brain areas, high-quality lesion-mapping studies should account for neural connectivity within lesion-mapping analyses to avoid averaging effects (*Criterion 12*) (Thiebaut de Schotten et al., 2008; Bartolomeo et al., 2007). Similarly, neglect is not a unitary syndrome but is instead composed of several dissociable behavioural phenotypes (Chechlacz et al., 2012a; Demeyere and Gillebert, 2019; Hillis and Caramazza, 1995). Previous research has suggested that egocentric/allocentric and extrapersonal/peripersonal neglect deficits are associated with damage to distinct areas (Chechlacz et al., 2010, 2012a). Therefore, high-quality lesion-mapping studies should aim to include behavioural assessments and analysis designs which can detect and control for this behavioural heterogeneity (*Criterion 13*).

2.6. Quality analysis

To facilitate quality comparisons, each included study was scored based on the total number of quality criteria met. These total scores were used to group study results into category 1 (scores >8, n = 11), category 2 (scores <9 & > 6, n = 12), and category 3 (scores <7, n = 10) quality categories. The reported correlates of neglect were then compared across these quality categories to help distinguish between correlates supported by high-quality evidence and anatomical findings which may be less reliable.

3. Systematic review results

3.1. General summary

A total of 34 studies published between 2007 and 2022 met all criteria for inclusion. These studies included data from 2713 stroke survivors (Age = 63.67 years, (sd = 4.45), Sex = 47.0% female) with a median study sample size of 60 (IQR = 46.4, range = 25–573). The median number of included patients classified as exhibiting significant neglect per study was 38 (IQR = 28.1, range = 11–227). Data from 1891 right hemisphere, 574 left hemisphere, 109 bilateral and 139 unreported patients was included in these studies. The majority of studies (n = 28) considered behavioural data from multiple neuropsychological assessments, whilst 6 investigations included only a single neglect test. Cancellation tests were used to quantify neglect impairment in 97.1% (33/34) of studies. Line bisection (61.8%, 21/34) and drawing/copy (32.4%, 11/34) were also common. All 34 studies reported correlates associated with egocentric neglect (31 right hemisphere, 5 left hemisphere) and 4 studies investigated the correlates of allocentric neglect (4 right hemisphere, 1 left hemisphere).

Of the studies reporting right hemisphere correlates of egocentric neglect within the right hemisphere (n = 31), the most commonly identified significant ROIs were in the superior longitudinal fasciculus (14/31 relevant studies; see Table 1, Fig. 2). The superior temporal gyrus (posterior division) and supramarginal gyrus (posterior division) were each identified in 13/31 relevant studies. Finally, the postcentral, angular, and precentral gyri were also commonly implicated (12/31, 11/31, 11/31 studies respectively). Left-lateralised allocentric neglect was most commonly associated with damage to the right hemisphere middle temporal gyrus (reported in 4/4 studies) (see Fig. 3).

Within the left hemisphere, the insular cortex was most frequently reported as a significant correlate of egocentric neglect (4/5 studies). Brodmann's Area 6, the frontal operculum, and the angular gyrus were also found to be related to left hemisphere egocentric neglect in 3/5

Table 1
Results of the systematic qualitative analysis. Percentages are calculated as the number of studies which identified the relevant ROI as significant divided by the total number of studies which reported correlates of the deficit. The most commonly identified significant ROI for each deficit is highlighted in bold. Details of which studies reported each listed neural correlate are available at https://osf.io/up79e/.

Lobe/Area Name:	Right Hemisphere		Left Hemisphere	
	Ego	Allo	Ego	Allo
Frontal Lobe:				
BA6			3 (60%)	
BA4	1 (3.2%)			
Cingulate Gyrus (Anterior Division)	1 (3.2%)			
Frontal Opercular Cortex	3 (9.7%)		3 (60%)	
Frontal Orbital Cortex	2 (6.4%)			
Frontal Pole	1 (3.2%)			
Inferior Frontal Gyrus (Pars Opercularis)	7 (22.6%)	1 (25%)	1 (20%)	
Inferior Frontal Gyrus (Pars Triangularus)	7 (22.6%)	1 (25%)	1 (20%)	
Middle Frontal Gyrus	10 (32.3%)	1 (25%)		
Precentral Gyrus	11 (35.5%)	1 (25%)	1 (20%)	
Temporal Lobe:				
Anterior Temporal Lobe			1 (20%)	
Heschl's Gyrus	3 (9.7%)			
Inferior Temporal Gyrus (Anterior Division)	4 (12.9%)	2 (50%)		
Inferior Temporal Gyrus (Posterior Division)	4 (12.9%)	2 (50%)	1 (20%)	
Inferior Temporal Gyrus (Temporo-occipital Part)	4 (12.9%)	2 (50%)		
Insular Cortex	10 (32.3%)	1 (25%)	**4 (80%)***	
Middle Temporal Gyrus (Anterior Division)	6 (19.4%)	3 (75%)	2 (40%)	
Middle Temporal Gyrus (Posterior Division)	6 (19.4%)	**4 (100%)***	2 (40%)	
Middle Temporal Gyrus (Temporo-occipital Part)	7 (22.6%)	3 (75%)	2 (40%)	
Middle Temporal Lobe			2 (40%)	
Parahippocampal Gyrus (Anterior Division)	2 (6.4%)	1 (25%)		
Parahippocampal Gyrus (Posterior Division)	2 (6.4%)			
Planum Polare		1 (25%)		
Planum Temporale	4 (12.9%)	1 (25%)		
Superior Temporal Gyrus (Anterior Division)	12 (38.7%)	2 (50%)	2 (40%)	
Superior Temporal Gyrus (Posterior Division)	**13 (41.9%)***	2 (50%)	2 (40%)	
Superior Temporal Lobe			2 (40%)	
Superior Temporal Sulcus		2 (50%)		
Temporal Fusiform Cortex (Posterior Division)		1 (25%)		
Temporal Pole	4 (12.9%)		1 (20%)	
Parietal Lobe:				
Angular Gyrus	11 (35.5%)	1 (25%)	3 (60%)	
BA1	1 (3.2%)			
BA2	1 (3.2%)			
BA3	1 (3.2%)			
BA7	1 (3.2%)			
BA40	1 (3.2%)			
Cingulate Gyrus (Posterior Division)	1 (3.2%)			
Central Opercular Cortex	4 (12.9%)			
Inferior Parietal Lobule	6 (19.4%)	1 (25%)		

(*continued on next page*)

Table 1 (*continued*)

Lobe/Area Name:	Right Hemisphere		Left Hemisphere	
	Ego	Allo	Ego	Allo
			1 (20%)	**1 (100%)***
Parietal Operculum Cortex	4 (12.9%)			
Postcentral Gyrus	12 (38.7%)	2 (50%)	1 (20%)	
Posterior Intraparietal Sulcus	2 (6.4%)			
Posterior Parietal Cortex	2 (6.4%)	1 (25%)		
Precuneus Cortex	1 (3.2%)	1 (25%)		
Rolandic Operculum	4 (12.9%)		1 (20%)	
Superior Parietal Lobule	2 (6.4%)			
Supramarginal Gyrus (Anterior Division)	1 (3.2%)	1 (25%)		
Supramarginal Gyrus (Posterior Division)	**13 (41.9%)***	1 (25%)		
Temporal Parietal Junction	4 (12.9%)	1 (25%)		
Occipital Lobe:				
BA19	1 (3.2%)			
Cuneal Cortex			1 (20%)	
Inferior Occipital Gyrus	1 (3.2%)			
Intracalcarine Cortex			1 (20%)	
Lateral Occipital Cortex (Inferior Division)	3 (9.7%)			
Lateral Occipital Cortex (Superior Division)	4 (12.9%)	1 (25%)	1 (20%)	
Lingual Gyrus			1 (20%)	
Middle Occipital Gyrus		1 (25%)		
Occipital Fusiform Gyrus			1 (20%)	
Superior Occipital Gyrus		2 (50%)		
Supracalcarine Cortex			1 (20%)	
Subcortical:				
Acoustic Radiation			1 (20%)	
Amygdala	2 (6.4%)			
Anterior Commisure	1 (3.2%)			
Arcuate Fasciculus	2 (6.4%)			
Caudate Nucleus	4 (12.9%)			
Corona Radiata (Posterior)	2 (6.4%)			
Corona Radiata (Superior)	2 (6.4%)			
Corpus Callosum (Body)	3 (9.7%)			
Corpus Callosum (Splenium)	1 (3.2%)		1 (20%)	
Corticospinal Tract			1 (20%)	
External Capsule	3 (9.7%)	1 (25%)		**1 (100%)***
Fornix	2 (6.4%)			
Hippocampus	1 (3.2%)	2 (50%)		
Inferior Fronto-Occipital Fasciculus	4 (12.9%)	1 (25%)	1 (20%)	
Inferior Longitudinal Fasiculus	3 (9.7%)			
Internal Capsule (Anterior Limb)	2 (6.4%)			
Internal Capsule (Posterior Limb)	2 (6.4%)			
Internal Capsule (Retrolenticular Part)	2 (6.4%)			
Optic Radiation	2 (6.4%)		1 (20%)	
Pallidium	3 (9.7%)			
Posterior Thalamic Radiation	4 (12.9%)		1 (20%)	
Putamen	5 (16.1%)			
Saggital Stratum	1 (3.2%)			
Superior Fronto-Occipiral Fasciculus	4 (12.9%)	2	1 (20%)	
Superior Longitudinal Fasciculus	**14 (45.2%)***		1 (20%)	
Tapetum	1 (3.2%)			
Thalamus	1 (3.2%)			
Uncinate Fasciculus	5 (16.1%)	1 (25%)		

studies (Table 1, Fig. 2). Finally, right hemisphere allocentric neglect was most commonly associated with damage to the middle temporal gyrus (4/4 studies) while left hemisphere allocentric neglect was found to be related to the external capsule and anterior limb of the internal capsule. Notably, only one previous study investigated left hemisphere correlates of allocentric neglect (Moore et al., 2021a).

3.2. Anatomical dissociations between egocentric/allocentric neglect

In total, 4 studies aimed to compare the correlates of egocentric and allocentric neglect (Moore et al., 2021a; Chechlacz et al., 2010, 2012b; Kenzie et al., 2015). All 4 investigations concluded that egocentric neglect and allocentric neglect represent anatomically dissociable conditions. Kenzie et al. (2015) found that left egocentric neglect was associated with damage to the right precentral gyrus, middle frontal gyrus, insula, and putamen while allocentric neglect was associated with lesions within the right superior/inferior parietal cortex and superior/-inferior middle temporal gyri. Chechlacz et al. (2010) determined that left allocentric neglect was predicted by damage to right posterior cortical regions including the posterior superior temporal sulcus, angular, middle temporal and middle occipital gyri. Conversely, this study found that egocentric neglect was associated with damage to more anterior right hemisphere cortical structures such as the middle frontal, post-central, supramarginal, and superior temporal gyri (Chechlacz et al., 2010). A similar study by Chechlacz et al. (2012b) concluded that persistent left allocentric neglect was associated with lesions to the right angular gyrus and that persistent egocentric neglect was related to damage to the right superior temporal gyrus, supramarginal gyrus, basal ganglia, and insula.

Most recently, Moore et al. (2021a) investigated the correlates of both right- and left-lateralised egocentric and allocentric neglect in a large (n = 446) and representative sample of stroke survivors. This study found that, in the right hemisphere, egocentric and allocentric neglect were related to damage to distinct clusters of voxels within the posterior parietal and temporo-parietal junction areas (Moore et al., 2021a). This anatomical dissociation was also present within left hemisphere, with egocentric neglect being associated with posterior voxels within left occipital cortical areas and allocentric neglect with damage to the anterior limb of the left internal capsule (Moore et al., 2021a). Notably, previous studies have agreed that a degree of overlap does exist between the ROIs associated with egocentric and allocentric neglect (Chechlacz et al., 2012a). For example, lesions to the temporo-parietal junction, intraparietal sulcus, and various white matter tracts (superior/inferior longitudinal fasciculus, superior/inferior fronto-occipital fasciculus), corona radiata, and thalamic radiation have been associated with both egocentric impairment (Moore et al., 2021a; Chechlacz et al., 2010, 2012b). In summary, the existing lesion-mapping literature strongly suggests that egocentric and allocentric neglect are associated with distinct but overlapping neural areas within the right hemisphere.

This conclusion has been supported by subsequent meta-analytic, anatomical likelihood estimation analyses (Chechlacz et al., 2012a; Molenberghs et al., 2012). Chechlacz et al. (2012a) conducted an anatomical likelihood estimate meta-analysis of 1306 neglect patients from 32 different lesion-symptom mapping studies which concluded that left egocentric symptoms are associated with damage to the right hemisphere perisylvian network (e.g. pre- and post-central, supra-marginal, and superior temporal gyri) while allocentric symptoms are associated with more posterior lesions impacting the angular, middle

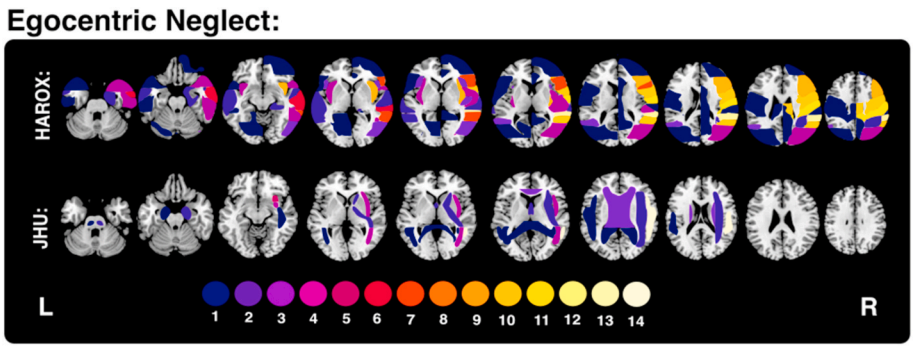

Fig. 2. A visualisation of the frequency with which specific ROIs from the Harvard-Oxford Cortical Atlas (Upper) and Johns Hopkins White Matter Atlas (Lower) were significantly associated with egocentric neglect impairment. Colours denote the number of studies identifying the area as significant. Only reported regions that correspond with atlas-defined ROIs are included in this visualisation. All left hemisphere areas have been associated with right-lateralised neglect impairment and all right hemisphere areas have been associated with left-lateralised neglect impairment. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

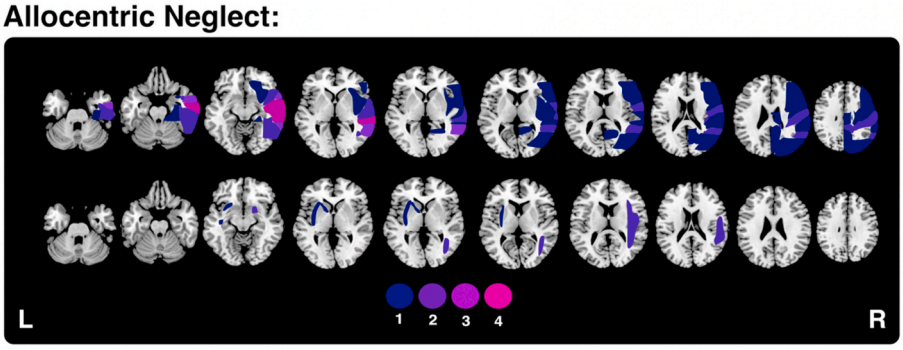

Fig. 3. A visualisation of the frequency with which specific ROIs from the Harvard-Oxford Cortical Atlas (Upper) and Johns Hopkins White Matter Atlas (Lower) ROIs were found to be significantly associated with allocentric neglect impairment. Colours denote the number of studies identifying the area as significant. Only reported regions that correspond with atlas-defined ROIs are included in this visualisation. All left hemisphere areas have been associated with right-lateralised neglect impairment while all right hemisphere areas have been associated with left-lateralised neglect impairment. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

temporal, and middle occipital gyri. These findings support the characterisation of egocentric and allocentric neglect as distinct impairments rather than a unitary syndrome.

3.3. Anatomical correlates of extra-personal versus personal neglect

Two of the included studies conducted separate lesion-mapping analyses aiming to distinguish the correlates of personal and extra-personal neglect deficits (Ten Brink et al., 2019; Committeri et al., 2007). Committeri et al. (2007) concluded that extra-personal neglect is linked to damage to a circuit of right frontal and superior temporal regions and that personal neglect is related to more inferior right parietal regions including the supramarginal gyrus, post-central gyrus, and underlying white matter. Based on these results, Committeri et al. (2007) posit that extra-personal spatial attention depends on a ventral network and personal spatial awareness is supported by a more dorsal network responsible for coding proprioceptive and somatosensory input. By contrast, Ten Brink et al.'s (Ten Brink et al., 2019) more recent analysis of neural correlates of neglect in near and far space yielded conflicting results. They found that personal and extra-personal neglect were associated with largely overlapping neural correlates within the right parietal, temporal, and frontal areas. Extra-personal, but not personal neglect, was linked to damage to right temporo-parietal areas including the superior parietal lobule, angular gyrus, and supramarginal gyrus. Critically, Ten Brink et al. did not find distinct regions associated with personal neglect, suggesting that personal and extra-personal neglect may not be dependent on dissociable networks as proposed by Committeri et al. (2007). Additional research is therefore needed to clarify the relationship between the correlates of personal and extra-personal neglect impairment.

3.4. Neglect anatomy in the right versus left hemisphere

Previous studies have asserted that the neural correlates of egocentric neglect following left and right hemisphere lesions are anatomical homologues (Suchan and Karnath, 2011). However, the existing lesion-mapping data do not clearly support this assertion. There is a degree of similarity between the left and right hemisphere correlates found to be significantly associated with egocentric neglect. For example, Karnath et al. (Suchan and Karnath, 2011) found that left-hemisphere egocentric neglect was associated with damage to the superior/middle temporal gyri, inferior parietal lobule, and insula. Based on these findings, the authors concluded that the correlates of spatial orienting in the left hemisphere are the same as those in the right hemisphere (Suchan and Karnath, 2011). However, this study included a relatively small sample of patients with neglect (n = 11), limiting the generalisability of these findings.

Beume et al. (2017) conducted a larger-scale analysis of the correlates of egocentric neglect following left-hemisphere lesions (n = 121, including 21 neglect patients), which found that this deficit was linked to damage within the superior/middle temporal gyrus, temporal pole, frontal operculum, and insula. The authors concluded that the left-hemisphere correlates of neglect 'partially mirror' areas of the right hemisphere associated with egocentric neglect (Beume et al., 2017). A subsequent study by Beume et al. (2020) (n = 165, 33 neglect patients) found that neglect occurred following damage to the superior/middle temporal lobe, anterior temporal pole, ventral pre-motor cortex, frontal operculum, angular gyrus, and insula. Notably, these three studies each included only patients with left hemisphere damage. It is unclear whether studies that investigated neglect within a single hemisphere can adequately compare their results with those from other studies that included patients with lesions of the opposite hemisphere. Previous studies employing different patient samples, analysis types, and neglect quantification measures have varied widely in their reported neural correlates (see Table 1). For this reason, it is more appropriate for analyses aiming to compare correlates across hemispheres to test and identify correlates in *both* hemispheres in a *single* study, and then to compare results across hemispheres.

Two previous studies have employed this technique. Moore et al. (Moore and Demeyere, 2022) assessed the correlates of neglect

impairment within both the right and left hemispheres in a sample of 573 stroke survivors (including 227 neglect patients). They found that left neglect was associated with a large cluster of voxels centred within the right parietal operculum and underlying white matter (e.g. external capsule, internal capsule, superior longitudinal fasciculus) whereas right neglect was not associated with any significant neural correlates (Moore and Demeyere, 2022). This null result is likely due to the study's failure to distinguish between egocentric and allocentric neglect deficits (Moore and Demeyere, 2022). However, the results clearly imply that the correlates of left and right neglect may not be identical across hemispheres. In another study, Moore et al. (2021a) directly compared the correlates of left and right egocentric/allocentric neglect across hemispheres in a large sample of stroke patients (n = 446, 250 patients with neglect). This study found no overlap between areas associated with neglect in the left and right hemispheres (Moore et al., 2021a).

Overall, the literature on whether left and right neglect involve anatomical homologues is somewhat divided. However, much of the evidence for homologous correlates across hemispheres has come from small-scale studies which have not adequately considered the anatomical variability associated with neglect in the right hemisphere. Conversely, larger-scale studies employing full-brain analyses have concluded that the correlates of neglect deficits are not homologous across hemispheres.

3.5. Neglect anatomy within different territories/lesion sites

8/34 included studies pre-selected participants based on the territory/area impacted by lesions. As neglect is behaviourally heterogeneous and previous studies have suggested that lesions to different stroke territories produce different behavioural symptoms (Husain and Kennard, 1996; Binder et al., 1992; Park et al., 2006), focusing analyses on specific vascular territories/stroke types can potentially help explain this behavioural diversity. However, to help investigate these issues, studies must specifically aim to address these questions.

Of the 8 studies which restricted analyses based on lesion territory, 5 included only MCA patients (Beume et al., 2017, 2020; Carson et al., 2019; Thiebaut de Schotten et al., 2014; Dressing et al., 2020), 2 excluded all patients with basal ganglia or thalamic lesions (Karnath et al., 2004, 2009), and one study excluded patients with cerebellar or brain stem damage (Kenzie et al., 2015). 6/8 of these studies reported no theoretical justification for restricting analyses to a specific territory other than one study which reported focusing on parietal lesions due to the comparatively high prevalence of visuo-constructive deficits following damage to this area. Importantly, none of these studies aimed to link specific behavioural deficits to lesions in a specific territory. Within the 5 studies investigating the correlates of neglect within MCA stroke territory, 21 ROIs were reported to be associated with left egocentric neglect and 10 ROIs were associated with right egocentric neglect. Within the right hemisphere, the superior temporal gyrus and angular gyrus were the most reported neglect correlates (2 studies each), while the frontal operculum, angular gyrus, BA 6, and insula were the most frequently reported left hemisphere neglect correlates (2 studies each).

Two studies aimed to characterise the neuroanatomy of visuospatial neglect following cortical lesions (Karnath et al., 2004, 2009). Karnath et al. (2004) investigated the cortical anatomy of egocentric neglect in a sample of 78 patients with lesions sparing the basal ganglia and thalamus. This study found that the right superior temporal cortex, insula, putamen, and caudate nucleus were damaged more in patients with versus without neglect impairment (Karnath et al., 2004). In a subsequent study, Karnath et al. (2009) employed this same patient sample to quantify patterns of white matter damage associated with neglect, concluding that damage to the right superior longitudinal and inferior/superior occipitofrontal fasciculus was associated with neglect impairment (Karnath et al., 2009). Overall, the majority of studies which focused analysis within a specific territory/region did so for convenience rather than to address a specific theoretical question. The results of these studies exhibited a similar degree of variance (and limited consensus) as is present within the overall sample of included studies.

3.6. The anatomy of acute versus chronic neglect impairment

Three of the identified previous lesion-mapping studies specifically aimed to differentiate the correlates of acute (or subacute) versus chronic neglect impairment (Chechlacz et al., 2012b; Karnath et al., 2011; Lunven et al., 2015). In these studies, the acute stage is generally considered to be < 30 days post stroke, subacute is defined as between 31 days and 3 months post-infarct, and chronic stage refers to >3 months post-stroke (Chechlacz et al., 2012b; Karnath et al., 2011; Lunven et al., 2015). The findings of these studies suggest that the neuroanatomy of neglect may vary slightly depending on the time interval post-stroke at which patients are assessed. For example, Chechlacz et al. (2012b) demonstrated that subacute egocentric and allocentric neglect were associated with damage to the frontal lobe (amongst other, more posterior regions), but these frontal lesions were not significantly associated with either type of neglect at the chronic stage. Karnath et al. (2011) found that damage to the uncinate fasciculus was specifically associated with neglect that persisted into the chronic stage of stroke recovery. Similarly, Lunven et al. (2015) found that acute neglect was associated with damage to the superior longitudinal fasciculus whereas chronic neglect was only associated with damage to the splenium. Each of these studies concluded that lesion location alone can act as an informative predictor of neglect recovery prognosis (Chechlacz et al., 2012b). Overall, these findings suggest that a degree of anatomical variability associated with neglect is likely due to differences in the interval post-stroke at which patients were assessed. These findings highlight the importance of ensuring that patients within individual studies are recruited and assessed at similar timepoints to avoid introducing potentially confounding anatomical variation.

3.7. White matter anatomy of visuospatial neglect

Recent literature has suggested that visuospatial neglect might be more accurately conceptualised as a disconnection syndrome rather than as a deficit linked to a single, spatially contiguous neural region (Thiebaut de Schotten et al., 2008; Bartolomeo et al., 2007). A total of 22/34 included studies conducted lesion-mapping analyses explicitly exploring patterns of dysconnectivity in neglect. These studies investigated the role of white matter disconnection in neglect by overlaying lesion-mapping results on white matter atlases (Suchan and Karnath, 2011; Aiello et al., 2012; Karnath et al., 2011; Committeri et al., 2007; Kaufmann et al., 2020; Wiesen et al., 2019) or conducting separate connectivity-based lesion-mapping analyses (Toba et al., 2017; Machner et al., 2018; Thiebaut de Schotten et al., 2014; Chechlacz et al., 2010, 2012b; Lunven et al., 2015; Ten Brink et al., 2019; Committeri et al., 2007; Karnath et al., 2009; Pedrazzini and Ptak, 2020). These connectivity-based lesion-mapping analyses include approaches which segment and analyse voxel-wise grey and white matter relationships independently (Chechlacz et al., 2010, 2012b), employ hodological lesion-mapping techniques (Toba et al., 2017; Lunven et al., 2015), or otherwise incorporate dysconnectivity metrics in to lesion-mapping analyses (Machner et al., 2018; Thiebaut de Schotten et al., 2014).

For studies reporting white matter ROIs associated with neglect impairment, voxels within the superior longitudinal fasciculus were commonly found to be associated with neglect impairment. Specifically, the right superior longitudinal fasciculus was significantly associated with left egocentric neglect in 9/31 studies and with left allocentric neglect in 1/3 studies. The left superior longitudinal fasciculus was also significantly associated with right neglect in 1/3 studies. Other white matter tracts, including the inferior fronto-occipital fasciculus and uncinate fasciculus, were commonly found to be associated with neglect

impairment (Table 1). It is important to note, however, that not all dysconnectivity analysis designs are of equal quality. Analyses using traditional, univariate lesion-mapping that interpret significant voxel clusters relative to white-matter atlases (e.g. Moore et al. (Moore et al., 2021a; Moore and Demeyere, 2022)) may be susceptible to cluster displacement due to connectivity effects. This is because lesions can cause tract disconnection at multiple, spatially distinct points, and traditional lesion-mapping analyses tend to 'average' across these distinct spatial locations rather than identifying common anatomical loci (Thiebaut de Schotten et al., 2014). This potential displacement can be largely avoided by conducting separate tract-based ROI analyses.

Of the included studies, 11 conducted separate white-matter analyses and 11 evaluated lesion-mapping results relative to white matter atlases. These analyses reported 19 distinct white matter correlates of neglect, 9 of which were identified in both analysis type groups. For example, the superior longitudinal fasciculus was identified as a significant correlate in 4/11 analyses with separate white matter analyses, and in 8/11 studies which did not use this approach. However, there were 8 white matter ROIs which were only found in studies that did not employ separate white matter analyses (sagittal striatum, splenium, optic radiation, internal capsule, tapetum, corpus callosum, superior fronto-occipital fasciculus, and anterior commissure). Most notably, the internal capsule was identified in 4/11 studies that interpreted results relative to white mater atlases, and 0/11 that conducted separate analyses. This finding is likely due to the internal capsule's proximity to commonly affected vascular territories and to the specific cortical anatomy most frequently associated with neglect (Mah et al., 2014). Studies employing separate white matter analyses should more effectively disambiguate between tracts which are commonly damaged rather than tracts which are causally associated with neglect (Lunven et al., 2015).

Together, relevant studies of the white matter anatomy of neglect have achieved a higher degree of consensus than those focused only on grey matter correlates. The variability within reported white matter correlates can be partially accounted for by differences in analysis design.

4. Quality assessment results

The studies included in this systematic review were found to have an average quality score of 7.65 (range = 4–12, SD = 2.00). Studies averaged 2.85 out of 5 available patient group quality criteria (SD = 1.02, range = 2–5). Similarly, studies averaged 1.97 out of 3 available behavioural/neuroimaging data quality factors (SD = 0.74, range = 1–3). Finally, studies averaged 2.81 of 5 for the considered lesion-mapping analysis quality criteria (SD = 1.13 range = 1–5). Criterion 9 (theory-blind, voxel-wise analysis) was the most frequently met (n = 34/34), whereas Criterion 1 (not pre-selected based on lesion side) and

Table 2
A summary of each included study relative to the 13-point quality assessment scale employed in this investigation. In cases where insufficient information was provided to evaluate whether the study met a given criterion, that criterion was considered unmet. Horizontal lines denote boundaries between category 1, category 2, and category 3 quality study groupings (Cojan et al., 2021; de Groot, 2016; Rousseaux et al., 2015; Singer et al., 2004; Spanò, 2022; Takamura, 2021; Verdon et al., 2010; Vossel, 2011).

Criterion Number:	1	2	3	4	5	6	7	8	9	10	11	12	13	
Authors	Unselected Based on Lesion Size	Unselected Based on Lesion Location	Unselected Based on Behaviour	Sample Size > 50	Recruited at Same Time	Multiple Tests Considered	Continuous Neglect Metric Used	Scan/Test at Same Timepoint	Theory-Blind Analyses	Controls for Lesion Volume	Minimum Overlap Threshold Used	Considered Disconnection Effects	Considers Neglect Subtypes	
Golay et al.[28]	Unmet	Met	Unmet	Met	Unmet	Met	Unmet	Unmet	Met	Unmet	Unmet	Unmet	Unmet	4
Gandola et al.[42]	Unmet	Met	Unmet	Unmet	Met	Met	Met	Unmet	Met	Unmet	Unmet	Unmet	Unmet	5
Ptak and Schnider[29]	Unmet	Met	Unmet	Unmet	Met	Met	Unmet	Met	Met	Unmet	Unmet	Unmet	Unmet	5
Karnarth et al.[73]	Unmet	Unmet	Met	Met	Unmet	Met	Unmet	Unmet	Met	Met	Unmet	Unmet	Unmet	5
Dressing et al.[72]	Unmet	Unmet	Met	Met	Met	Met	Unmet	Unmet	Met	Unmet	Met	Unmet	Unmet	6
Kaufmann et al.[76]	Unmet	Met	Met	Met	Unmet	Unmet	Met	Unmet	Met	Unmet	Met	Unmet	Unmet	6
Cojan et al.[79]	Unmet	Met	Met	Unmet	Unmet	Met	Met	Unmet	Met	Unmet	Met	Unmet	Unmet	6
Beume et al.[69]	Unmet	Unmet	Unmet	Met	Met	Met	Unmet	Met	Met	Unmet	Met	Unmet	Unmet	6
Thiebault de Schotten et al.[40]	Unmet	Unmet	Met	Met	Unmet	Met	Met	Unmet	Met	Unmet	Unmet	Met	Unmet	6
Karnarth et al.[74]	Unmet	Unmet	Met	Met	Unmet	Met	Unmet	Unmet	Met	Met	Unmet	Met	Unmet	6
Carson et al.[24]	Met	Unmet	Met	Unmet	Unmet	Met	Unmet	Unmet	Met	Unmet	Met	Met	Unmet	6
Molenberghs and Sale[80]	Met	Met	Met	Unmet	Unmet	Met	Met	Unmet	Met	Unmet	Met	Unmet	Unmet	7
Vossel et al.[81]	Unmet	Met	Met	Met	Unmet	Met	Met	Unmet	Met	Unmet	Met	Unmet	Unmet	7
Suchan and Karnarth[17]	Unmet	Met	Unmet	Unmet	Met	Met	Met	Met	Met	Unmet	Unmet	Met	Unmet	7
Lunven et al.[75]	Unmet	Met	Met	Unmet	Unmet	Met	Met	Unmet	Met	Unmet	Met	Met	Unmet	7
Toba et al.[25]	Unmet	Met	Met	Unmet	Unmet	Met	Met	Unmet	Met	Unmet	Met	Met	Unmet	7
Takamura et al.[82]	Unmet	Met	Met	Unmet	Unmet	Met	Met	Unmet	Met	Unmet	Met	Met	Unmet	7
Pedrazzini and Ptak[78]	Unmet	Met	Unmet	Met	Unmet	Met	Met	Unmet	Met	Unmet	Met	Met	Unmet	7
Aiello et al.[27]	Unmet	Met	Met	Unmet	Met	Met	Unmet	Unmet	Met	Met	Met	Met	Unmet	7
Chechlacz et al.	Met	Met	Unmet	Unmet	Met	Unmet	Met	Met	Met	Unmet	Unmet	Met	Met	8
Beume et al.[16]	Unmet	Unmet	Met	Met	Met	Met	Unmet	Met	Met	Met	Met	Unmet	Unmet	8
Karnarth et al.[50]	Unmet	Met	Met	Met	Unmet	Met	Met	Met	Met	Unmet	Unmet	Met	Unmet	8
Spano et al.[83]	Unmet	Met	Met	Met	Unmet	Unmet	Met	Unmet	Met	Unmet	Met	Met	Met	8
Machner et al.[38]	Unmet	Met	Met	Unmet	Met	Met	Met	Met	Met	Unmet	Met	Met	Unmet	9
Kenzie et al.[67]	Unmet	Unmet	Met	Met	Met	Met	Met	Met	Met	Unmet	Met	Unmet	Met	9
Committeri et al.[68]	Unmet	Met	Met	Met	Unmet	Met	Met	Met	Met	Met	Unmet	Met	Met	10
Verdon et al.[84]	Met	Met	Met	Met	Met	Met	Met	Met	Met	Unmet	Unmet	Met	Unmet	10
Wiesen et al.[85]	Unmet	Met	Met	Met	Met	Met	Met	Met	Met	Unmet	Met	Met	Unmet	10
Moore et al.[26]	Met	Met	Met	Met	Met	Unmet	Unmet	Met	Met	Met	Met	Met	Unmet	10
Chechlacz et al.[49]	Met	Met	Met	Met	Met	Unmet	Met	Unmet	Met	Met	Unmet	Met	Met	10
Rousseaux et al.[86]	Unmet	Met	Met	Unmet	Unmet	Met	Met	Met	Met	Met	Met	Met	Met	10
Wiesen et al. [77]	Unmet	Met	Met	Met	Met	Met	Met	Met	Met	Met	Met	Met	Unmet	11
Ten Brink et al.[23]	Met	Met	Met	Met	Unmet	Met	Met	Unmet	Met	Met	Met	Met	Met	11
Moore et al.[18]	Met	Met	Met	Met	Met	Unmet	Met	Met	Met	Met	Met	Met	Met	12

Criterion 13 (account for neglect subtypes in analysis) were the most frequently unmet (N = 8/34 respectively). In terms of overall analysis quality, 11 studies were classed as category 1 (scores >8), 12 studies were category 2 (scores <9 & > 6), and 10 were category 3 (scores <7). Full quality assessment scores for each of the considered studies are reported in Table 2.

The neural correlates of neglect as reported by quality category are reported within Table 3. As only 4 studies reported correlates of allocentric neglect and 3/4 of these studies were rated as category 1, this information is reported in supplementary materials. Overall, high variability was present within each of the considered quality categories. Within right hemisphere egocentric neglect, 71 distinct ROIs were reported within category 1 quality studies, with the highest degree of agreement between 8 studies identifying the posterior division of the supramarginal gyrus (Fig. 4). Within category 2 studies, 36 ROIs were reported, with the superior longitudinal fasciculus being reported within the most (n = 6) studies. In category 3 studies, 40 ROIs were reported with the highest degree of agreement being 5 studies, all reporting the insular cortex, postcentral gyrus, and supramarginal gyrus (posterior division).

Similar variance was present within studies of varying quality investigating the correlates of left-hemisphere egocentric neglect. Only one category 1 and one category 3 study identifying correlates of left-hemisphere neglect were identified. Within the 2 category 2 investigations, 14 ROIs were reported with the frontal operculum, insular cortex, angular gyrus and BA6 being reported in both studies. The majority of reported areas were identified within analyses in different quality groups. All ROIs with three or more references were never restricted to a single quality category (e.g. high only) but were spread across multiple quality groups.

Notably, our quality ranking scheme weights each individual ranking criterion equally. It is also important to identify whether systematic differences are present across studies which did and did not meet each considered individual Criterion. A series of 12 chi-squared tests were conducted to compare the distribution of reported ROIs between studies which did and did not meet each of the employed quality criteria (Bonferroni-corrected alpha = 0.004). Studies that employed multiple neglect tests reported a different distribution of ROIs than studies that employed only one test (X^2 (116) = 172.64, $p < 0.001$). However, no proportion differences between individual ROIs reported in studies which met and failed to meet this Criterion survived false discovery rate correction in post-hoc tests. Full statistics and visualisations for all conducted comparisons are available in supplementary materials. Although no other quality criteria resulted in a statistically significant difference in reported ROI, this should not be considered as evidence that these criteria do not impact the results of the studies. The chi-squared analyses are likely underpowered, especially considering that 116 different ROIs were included, with most of these areas being identified in less than 3 studies.

Overall, the existing literature has reported that neglect is associated with a wide range of neural correlates. A portion of this variance can be accounted for by considering differences between neglect subtypes, analysis types, and overall study quality. However, a large amount of variance was present even in high-quality studies employing similar methodologies. It is important that future investigations account for this anatomical variance to plan studies which effectively elucidate the neural correlates of the neglect syndrome.

5. Discussion

A total of 34 studies which employed lesion-mapping methodologies to explore the neural correlates of the neglect syndrome were examined. Cumulatively, these studies associated a wide range of cortical and subcortical ROIs with the neglect syndrome, with no consensus emerging. Despite this variance, comparing the findings previous investigations provides novel insight into the anatomy of the neglect syndrome and highlights important considerations that impact both clinical practice and future neglect research.

Despite the lack of obvious consensus, the existing literature does provide some level of agreement as to which areas are associated with neglect impairments. Within the right hemisphere, egocentric neglect was most commonly associated with damage to the superior longitudinal fasciculus and the supramarginal, postcentral, precentral, and angular gyri. In the left hemisphere, egocentric neglect was most frequently linked to damage impacting the insular cortex, Brodmann's area six, the frontal operculum, and the angular gyrus. Allocentric neglect was most commonly associated with lesions to the posterior division of the left middle temporal gyrus, whereas right-lateralised allocentric neglect was linked to lesions of the external capsule and anterior limb of the internal capsule. Previous studies that investigated the anatomy of both egocentric and allocentric neglect concluded that these deficits represent anatomically dissociable deficits (Moore et al., 2021a; Chechlacz et al., 2010). Similar findings have been produced by papers aiming to compare the anatomy of extra-personal versus peri-personal neglect (Ten Brink et al., 2019; Committeri et al., 2007). Chronic visuospatial neglect has been associated with different neural correlates than acute visuospatial neglect (Chechlacz et al., 2012b; Karnath et al., 2011), and the anatomy of right-hemisphere neglect does not appear to entirely mirror that of left-hemisphere neglect (Moore et al., 2021a). This variance has critical implications for both future research and clinical practice.

In terms of future research, modern studies have strongly suggested that neglect is more accurately characterised as a disconnection syndrome than a deficit that results from damage to a single, spatially contiguous neural correlate (Bartolomeo et al., 2007; Chechlacz et al., 2010). Traditional univariate lesion-mapping methodologies may not be entirely appropriate for identifying the correlates underlying disconnection syndromes (Mah et al., 2014; Wiesen et al., 2020; Zhang et al., 2014; Moore, 2022a,Moore, 2022c). This is because univariate lesion-mapping considers each voxel independently. In cases where deficits are related to multiple, spatially distinct cortical areas or a single white matter tract that can be disconnected at many different points, univariate lesion-mapping tends to calculate a spatial average of these distinct areas. This spatial averaging can lead to false negative results and/or critical voxel misallocation in disconnection syndromes (Mah et al., 2014). For this reason, future investigations should aim to employ analyses which more adequately account for disconnection effects in neglect. For example, a recent study by Saxena et al. (2022) quantified lesion-related disruptions to the human connectome to identify specific patterns of disconnection associated with neglect impairment in right hemisphere stroke patients. This study found that left egocentric neglect was associated with damage to tracts connecting the right putamen to other regions and to tracts connecting frontal regions to other brain regions, but did not identify any patterns of disconnection which were significantly associated with allocentric neglect (Saxena et al., 2022).

Similarly, some recent investigations have employed multivariate lesion analysis techniques to identify the correlates of visuospatial neglect. Malherbe et al. (2018) employed multi-perturbation Shapely value analysis to identify the correlates of left egocentric neglect. This multivariate approach helps compensate for potential spatial bias due to stroke vasculature (Mah et al., 2014) and helps eliminate potential confounds due to dysconnectivity effects. This study concluded that neglect impairment was associated with damage to the superior temporal gyrus (Malherbe et al., 2018). Toba et al. (2020) employed a similar approach to identify white matter bundles involved with neglect and concluded that damage to the optic radiations inferior fronto-occipital fasciculus and anterior cingulum was associated with neglect impairment. Notably, the ROIs associated with neglect in these multivariate studies have also been associated with neglect within many of the univariate analyses summarised in this study. While these two studies did not meet inclusion criteria for this study's review, they offer key insight into the correlates of neglect and describe novel

Table 3
Results of the systematic qualitative analysis grouped according to the quality of each individual study. Each cell denotes the number of studies in which the ROI was reported and the percentage of these reports in each quality category group.

Lobe/Area Name:	Right Hemisphere			Left Hemisphere		
	High	Average	Lower	High	Average	Lower
Frontal Lobe:						
BA6					2 (66.7%)	1 (33.3%)
BA4	1 (100%)					
Cingulate Gyrus (Anterior Division)	1 (100%)					
Frontal Opercular Cortex	1 (33.3%)		2 (66.7%)		2 (66.7%)	1 (33.3%)
Frontal Orbital Cortex	1 (50%)		1 (50%)			
Frontal Pole	1 (100%)					
Inferior Frontal Gyrus (Pars Opercularis)	3 (42.9%)	1 (14.2%)	3 (42.9%)	1 (100%)		
Inferior Frontal Gyrus (Pars Triangularus)	3 (42.9%)	1 (14.2%)	3 (42.9%)	1 (100%)		
Middle Frontal Gyrus	3 (30%)	3 (30%)	4 (40%)			
Precentral Gyrus	3 (27.2%)	4 (36.4%)	4 (36.4%)	1 (100%)		
Temporal Lobe:						
Anterior Temporal Lobe					1 (100%)	
Heschl's Gyrus	2 (66.7%)		1 (33.3%)			
Inferior Temporal Gyrus (Anterior Division)	2 (50%)	1 (25%)	1 (25%)			
Inferior Temporal Gyrus (Posterior Division)	2 (50%)	1 (25%)	1 (25%)	1 (100%)		
Inferior Temporal Gyrus (Temporo-occipital Part)	2 (50%)	1 (25%)	1 (25%)			
Insular Cortex	3 (30%)	2 (20%)	5 (50%)	1 (25%)	2 (50%)	1 (25%)
Middle Temporal Gyrus (Anterior Division)	2 (33.3%)	2 (33.3%)	2 (33.3%)	1 (50%)	1 (50%)	
Middle Temporal Gyrus (Posterior Division)	2 (33.3%)	2 (33.3%)	2 (33.3%)	1 (50%)	1 (50%)	
Middle Temporal Gyrus (Temporo-occipital Part)	3 (42.8%)	2 (28.6%)	2 (28.6%)	1 (50%)	1 (50%)	
Middle Temporal Lobe					1 (50%)	1 (50%)
Parahippocampal Gyrus (Anterior Division)	1 (50%)		1 (50%)			
Parahippocampal Gyrus (Posterior Division)	1 (50%)		1 (50%)			
Planum Polare						
Planum Temporale	3 (75%)		1 (25%)			
Superior Temporal Gyrus (Anterior Division)	4 (40%)	2 (20%)	4 (40%)	1 (50%)	1 (50%)	
Superior Temporal Gyrus (Posterior Division)	6 (46.2%)	2 (15.4%)	5 (38.4%)	1 (50%)	1 (50%)	
Superior Temporal Lobe					1 (50%)	1 (50%)
Superior Temporal Sulcus				1 (100%)		
Temporal Fusiform Cortex (Posterior Division)						
Temporal Pole	1 (25%)	1 (25%)	2 (50%)			1 (100%)
Parietal Lobe:						
Angular Gyrus	5 (45.6%)	3 (27.2%)	3 (27.2%)		2 (66.7%)	1 (33.3%)
BA1	1 (100%)					
BA2	1 (100%)					
BA3	1 (100%)					
BA7	1 (100%)					
Central Opercular Cortex	2 (50%)		2 (50%)			
Cingulate Gyrus (Posterior Division)	1 (100%)					
Inferior Parietal Lobule	3 (50%)	2 (33.3%)	1 (16.7%)	1 (100%)		
Parietal Operculum Cortex	2 (50%)	1 (25%)	1 (25%)			
Postcentral Gyrus	4 (33.3%)	3 (25%)	5 (41.7%)	1 (100%)		
Posterior Intraparietal Sulcus		1 (50%)	1 (50%)			
Posterior Parietal Cortex	1 (50%)	1 (50%)				
Precuneus Cortex	1 (100%)					
Rolandic Operculum	1 (25%)	1 (25%)	2 (50%)	1 (100%)		
Superior Parietal Lobule	1 (50%)	1 (50%)				
Supramarginal Gyrus (Anterior Division)		1 (100%)				
Supramarginal Gyrus (Posterior Division)	8 (61.5%)	2 (15.4%)	3 (23.1%)			
Temporal Parietal Junction	1 (25%)	1 (25%)	2 (50%)			
Occipital Lobe:						
BA19	1 (100%)					
Cuneal Cortex	1 (100%)					
Inferior Occipital Gyrus	1 (100%)					
Intracalcarine Cortex				1 (100%)		
Lateral Occipital Cortex (Inferior Division)	2 (66.7%)	1 (33.3%)				
Lateral Occipital Cortex (Superior Division)	3 (75%)	1 (25%)			1 (100%)	
Lingual Gyrus				1 (100%)		
Middle Occipital Gyrus				1 (50%)	1 (50%)	
Occipital Fusiform Gyrus				1 (100%)		
Superior Occipital Gyrus						
Supracalcarine Cortex				1 (100%)		
Subcortical:						
Acoustic Radiation				1 (100%)		
Amygdala	1 (50%)		1 (50%)			
Anterior Commissure	1 (100%)					
Arcuate Fasciculus	2 (66.7%)	1 (33.3%)		1 (100%)		
Caudate Nucleus	1 (25%)	1 (25%)	2 (50%)	1 (100%)		
Corona Radiata (Posterior)	2 (100%)					
Corona Radiata (Superior)	1 (50%)		1 (50%)			
Corpus Callosum (Body)	3 (100%)					

(*continued on next page*)

Table 3 (*continued*)

Lobe/Area Name:	Right Hemisphere			Left Hemisphere		
	High	Average	Lower	High	Average	Lower
Corpus Callosum (Splenium)	1 (100%)			1 (100%)		
Corticospinal Tract	2 (100%)			1 (100%)		
External Capsule	2 (50%)	1 (25%)	1 (25%)			
Fornix	2 (100%)					
Hippocampus	1 (50%)		1 (50%)			
Inferior Fronto-Occipital Fasciculus	1 (25%)	2 (50%)	1 (25%)	1 (100%)		
Inferior Longitudinal Fasciculus	3 (100%)					
Internal Capsule (Anterior Limb)	2 (100%)					
Internal Capsule (Posterior Limb)	2 (100%)					
Internal Capsule (Retrolenticular Part)	2 (100%)					
Optic Radiation	1 (50%)	1 (50%)		1 (100%)		
Pallidium	2 (66.7%)	1 (33.3%)				
Posterior Thalamic Radiation	3 (75%)		1 (25%)	1 (100%)		
Putamen	2 (50%)	1 (25%)	2 (50%)			
Saggital Stratum	1 (100%)					
Superior Fronto-Occipiral Fasciculus	3 (75%)		1 (25%)	1 (100%)		
Superior Longitudinal Fasciculus	7 (50%)	6 (42.9%)	1 (7.1%)	1 (100%)		
Thalamus	1 (100%)					
Tapetum	1 (100%)					
Uncinate Fasciculus	3 (60%)	1 (20%)	1 (20%)			

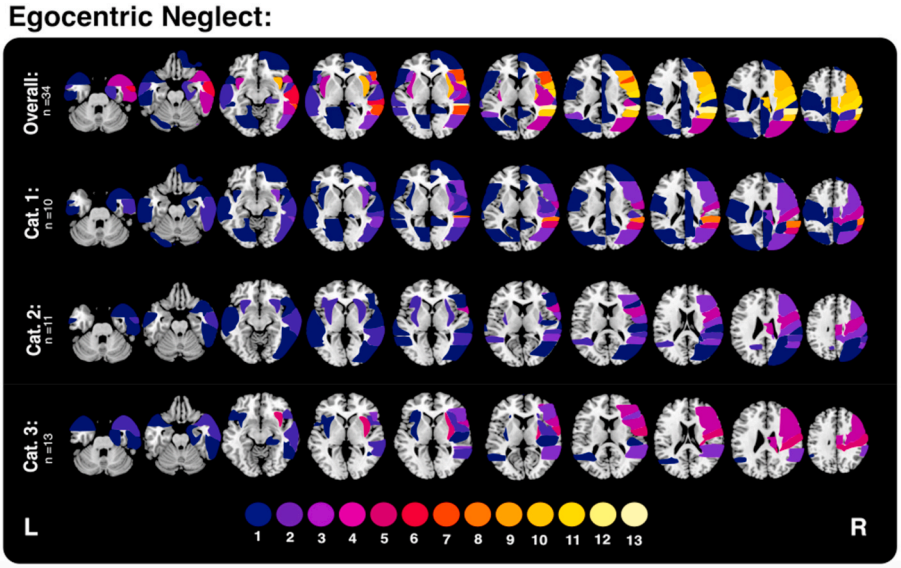

Fig. 4. Visualisation of how the cortical anatomy associated with egocentric neglect varies across the three study quality groups. Only results which correspond to a region of interest defined in the Harvard-Oxford Cortical Atlas are displayed in this figure. For a visualisation of how reported anatomy varies across all considered quality criteria, see Supplementary Materials.

methodologies which can be applied to greatly further understanding of this syndrome. Future studies should employ similar network-level and multivariate analysis techniques in larger, unselected stroke cohorts to further understanding of the left and right hemisphere structures underlying egocentric and allocentric spatial attention.

In terms of clinical practice, it is important for neglect to be effectively diagnosed after stroke as the occurrence of this deficit acts as a key predictor of long-term functional recovery outcomes (Moore et al., 2021b; Nys et al., 2006; Moore and Demeyere, 2021). However, a recent survey of neglect diagnosis techniques found that 20% of included healthcare professionals employ neuroimaging-based methods for detecting and diagnosing neglect impairment (Checketts et al., 2020). The existing literature investigating the anatomy of neglect clearly demonstrates that this approach cannot be expected to be effective, given the large range of lesions and reported critical lesion sites that have been associated with neglect. This anatomical variance has similar implications for studies aiming to develop lesion-location based cognitive diagnostic tools (e.g. Weaver et al. (2021)). Neuroimaging-based diagnostic approaches are often used in conjunction with other neglect screens (Checketts et al., 2020), but this does not necessarily correct the underlying issue. Moore et al. (2019) found that neglect patients with left hemisphere lesions were less likely to be diagnosed with neglect than patients with right hemisphere lesions, even though there were no differences in the severity of neglect between these patient groups. This suggests that expectation biases due to lesion location may reduce diagnostic sensitivity and highlights the importance of using neuropsychological neglect screens which prevent these biases from impacting neglect diagnosis (Moore et al., 2019, Moore et al., 2022b). Overall, it is important for the anatomical heterogeneity of neglect to be adequately acknowledged in clinical environments to improve neglect diagnostic practices.

The existing literature strongly suggests that specific patient groups, behavioural/neuroimaging data, and analysis parameters can dramatically impact the quality of lesion-mapping analyses (de Haan and Karnath, 2018; Sperber and Karnath, 2017; Bates et al., 2003). We found that reported areas associated with neglect were significantly different

between studies which did and did not consider performance across multiple independent neglect assessments. No other individual analysis choice was found to result in significant differences in outcomes. Importantly, this does not imply that other analysis choices do not impact results, but instead suggests that the choices are not linked to systematic differences. For example, failing to employ minimum overlap thresholds can potentially introduce noise into samples, but the spatial biases caused by this noise will depend on the exact lesion-overlay analysed and would not be expected to lead to systematic differences (Sperber and Karnath, 2017). Furthermore, the statistical tests conducted to identify differences between studies which met and did not meet quality criteria were largely underpowered. This is because the number of studies in each group was often low ($n < 10$) and each of the considered ROIs ($n = 114$) were reported in only a subset of included studies. It therefore remains crucial for future lesion mapping studies to employ high-quality designs to continue furthering understanding of the neural correlates of the neglect syndrome.

Importantly, lesion-mapping, like any other statistical approach, is not a perfect methodology and can produce results which are affected by many external factors (Parton et al., 2004; Chechlacz et al., 2012a; de Haan and Karnath, 2018). The significant correlates identified in any analysis ultimately depend on the sample employed, and any individual sample is not necessarily representative of the overall population (Parton et al., 2004). Similarly, the specifics of brain-behaviour relationships may vary across individuals, especially in older participants who are more likely to have cortical atrophy, underlying neurodegenerative disease, and white matter degeneration (Parton et al., 2004; Chechlacz et al., 2012a; Hobden et al., 2021). Finally, the neuroanatomical foci yielded by univariate lesion mapping analyses may be displaced due to the inherently non-random distribution of vascular lesions (Parton et al., 2004). These and other factors probably contribute to the wide degree of variation found across previous neglect lesion-mapping studies. Future work should take this variation into account through all stages of design, analysis, and interpretation to support a more reliable understanding of brain-behaviour relationships.

Overall, the results of this review suggest that neglect anatomy is complex and that reported correlates of this disorder have varied considerably across previous studies. This finding highlights the need for future studies to establish a more unified anatomical framework of this disorder, rather than adding to the extensive list of correlates associated with the neglect syndrome. Specifically, there is a clear need for future studies to investigate patterns of disconnection associated with different neglect subtypes in large and representative samples of stroke survivors.

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Author contributions

In line with CRediT guidelines, MJM was responsible for study conceptualisation, methodology, formal analysis, data curation, visualisation, and writing – original draft. EM was responsible for methodology, data curation, and writing – review and editing. JM was responsible for writing – review & editing. ND was responsible for writing – review & editing, supervision, and funding acquisition.

Declaration of competing interest

The authors report no conflicts of interest.

Data availability

All data is available on the open science framework (https://osf.io/up79e/).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuropsychologia.2023.108470.

References

Aiello, M., et al., 2012. No inherent left and right side in human 'mental number line': evidence from right brain damage. Brain: J. Neurol. 135, 2492–2505.
Antoniello, D., Khazaei, S., 2019. Frontal cortical networks in hemineglect. Neurology 92.
Azouvi, P., et al., 2006. A battery of tests for the quantitative assessment of unilateral neglect. Restor. Neurol. Neurosci. 24, 273–285.
Balslev, D., Odoj, B., Karnath, H.-O., 2013. Role of somatosensory cortex in visuospatial attention. J. Neurosci.: The Official Journal of the Society for Neuroscience 33, 18311–18318.
Bartolomeo, P., Thiebaut de Schotten, M., Doricchi, F., 2007. Left unilateral neglect as a disconnection syndrome. Cerebr. Cortex 17, 2479–2490.
Bates, E., et al., 2003. Voxel-based lesion–symptom mapping. Nat. Neurosci. 6, 448–450.
Beschin, N., Robertson, I.H., 1997. Personal versus extrapersonal neglect: a group study of their dissociation using a reliable clinical test. Cortex; a Journal Devoted to the Study of the Nervous System and Behavior 33, 379–384.
Beume, L.-A., et al., 2017. Visual neglect after left-hemispheric lesions: a voxel-based lesion-symptom mapping study in 121 acute stroke patients. Exp. Brain Res. 235, 83–95.
Beume, L.-A., et al., 2020. Dissociation of visual extinction and neglect in the left hemisphere. Cortex; a Journal Devoted to the Study of the Nervous System and Behavior 129, 211–222.
Binder, J., Marshall, R., Lazar, R., Benjamin, J., Mohr, J.P., 1992. Distinct syndromes of hemineglect. Arch. Neurol. 49, 1187–1194.
Bird, C.M., 2006. Visual neglect after right posterior cerebral artery infarction. J. Neurol. Neurosurg. Psychiatr. 77, 1008–1012.
Blaettner, U., Scherg, M., Von Cramon, D., 1989. Diagnosis of unilateral telencephalic hearing disorders: evaluation of a simple psychoacoustic pattern discrimination test. Brain 112, 177–195.
Booth, A., et al., 2012. The nuts and bolts of PROSPERO: an international prospective register of systematic reviews. Syst. Rev. 1, 1–9.
Brett, M., Leff, A.P., Rorden, C., Ashburner, J., 2001. Spatial normalization of brain images with focal lesions using cost function masking. Neuroimage 14, 486–500.
Ten Brink, A.F., Biesbroek, J.M., Oort, Q., Visser-Meily, J.M.A., Nijboer, T.C.W., 2019. Peripersonal and extrapersonal visuospatial neglect in different frames of reference: a brain lesion-symptom mapping study. Behav. Brain Res. 356, 504–515.
Bryan, R.N., et al., 1991. Diagnosis of acute cerebral infarction: comparison of CT and MR imaging. Am. J. Neuroradiol. 12, 611–620.
Carson, L., Filipowicz, A., Anderson, B., Danckert, J., 2019. Representational drawing following brain injury. Neuropsychologia 133, 107154.
Chechlacz, M., et al., 2010. Separating neural correlates of allocentric and egocentric neglect: distinct cortical sites and common white matter disconnections. Cogn. Neuropsychol. 27, 277–303.
Chechlacz, M., Rotshtein, P., Humphreys, G.W., 2012a. Neuroanatomical dissections of unilateral visual neglect symptoms: ALE meta-analysis of lesion-symptom mapping. Front. Hum. Neurosci. 6.
Chechlacz, M., et al., 2012b. The prognosis of allocentric and egocentric neglect: evidence from clinical scans. PLoS One 7.
Checketts, M., et al., 2020. Current clinical practice in the screening and diagnosis of spatial neglect post-stroke: findings from a multidisciplinary international survey. Neuropsychol. Rehabil. 1–32.
Cohen, J., 1992. A power primer. Psychol. Bull. 112, 155.
Cojan, Y., Saj, A., Vuilleumier, P., 2021. Brain substrates for distinct spatial processing components contributing to hemineglect in humans. Brain Sci. 11.
Colwell, M., Demeyere, N., Vancleef, K., 2021. Visual Perceptual Deficit Screening in Stroke Survivors: Evaluation of Current Practice in the United Kingdom and Republic of Ireland.
Committeri, G., et al., 2007. Neural bases of personal and extrapersonal neglect in humans. Brain: J. Neurol. 130, 431–441.
Demeyere, N., Gillebert, C.R., 2019. Ego-and allocentric visuospatial neglect: dissociations, prevalence, and laterality in acute stroke. Neuropsychology 33, 490.
Dressing, A., et al., 2020. The correlation between apraxia and neglect in the right hemisphere: a voxel-based lesion-symptom mapping study in 138 acute stroke patients. Cortex 132, 166–179.
Eschenbeck, P., et al., 2010. Testing for neglect in right-hemispheric stroke patients using a new assessment battery based upon standardized activities of daily living (ADL). Neuropsychologia 48, 3488–3496.
Farah, M.J., Brunn, J.L., Wong, A.B., Wallace, M.A., Carpenter, P.A., 1990. Frames of reference for allocating attention to space: evidence from the neglect syndrome. Neuropsychologia 28, 335–347.

Ferber, S., Karnath, H.-O., 2001. How to assess spatial neglect - line bisection or cancellation tasks? J. Clin. Exp. Neuropsychol. 23, 599–607.
2020, Game Theoretical Mapping of White Matter Contributions to Visuospatial Attention in Stroke Patients with Hemineglect - Toba - 2020 - Human Brain Mapping - Wiley Online Library. https://onlinelibrary.wiley.com/doi/full/10.1002/hbm.24987.
Gandola, M., et al., 2013. How many forms of perseveration? Evidence from cancellation tasks in right hemisphere patients. Neuropsychologia 51, 2960–2975.
Golay, L., Schnider, A., Ptak, R., 2008. Cortical and subcortical anatomy of chronic spatial neglect following vascular damage. Behav. Brain Funct.: BBF 4, 43.
de Groot, M., et al., 2016. White matter degeneration with aging: longitudinal diffusion MR imaging analysis. Radiology 279, 532–541.
Gutschalk, A., Dykstra, A., 2015. Auditory neglect and related disorders. Handb. Clin. Neurol. 129, 557–571.
de Haan, B., Karnath, H.-O., 2018. A hitchhiker's guide to lesion-behaviour mapping. Neuropsychologia 115, 5–16.
Halligan, P.W., Marshall, J.C., Wade, D.T., 1989. Visuospatial neglect: underlying factors and test sensitivity. Lancet 334, 908–911.
Hildebrandt, H., Spang, K., Ebke, M., 2002. Visuospatial hemi-inattention following cerebellar/brain stem bleeding. Neurocase 8, 7.
Hillis, A.E., Caramazza, A., 1995. A framework for interpreting distinct patterns of hemispatial neglect. Neurocase 1, 189–207.
Hobden, G., Moore, M., Mair, G., Pendlebury, S., Demeyere, N., 2021. Post-Stroke Executive Function in Relation to White Matter Damage on Clinically Acquired CT Brain Imaging. https://doi.org/10.1101/2021.11.12.21266247(2022), 11.12.21266247 Preprint at.
Husain, M., Kennard, C., 1996. Visual neglect associated with frontal lobe infarction. J. Neurol. 243, 652–657.
Husain, M., Kennard, C., 1997. Distractor-dependent frontal neglect. Neuropsychologia 35, 829–841.
Huygelier, H., Moore, M.J., Demeyere, N., Gillebert, C.R., 2020. Non-spatial impairments affect false-positive neglect diagnosis based on cancellation tasks. J. Int. Neuropsychol. Soc. 26, 668–678.
Karnath, H.-O., Himmelbach, M., Rorden, C., 2002. The subcortical anatomy of human spatial neglect: putamen, caudate nucleus and pulvinar. Brain 125, 350–360.
Karnath, H.-O., Fruhmann Berger, M., Küker, W., Rorden, C., 2004. The anatomy of spatial neglect based on voxelwise statistical analysis: a study of 140 patients. Cerebr. Cortex 14, 1164–1172.
Karnath, H.-O., Rorden, C., Ticini, L.F., 2009. Damage to white matter fiber tracts in acute spatial neglect. Cerebr. Cortex 19, 2331–2337.
Karnath, H.-O., Rennig, J., Johannsen, L., Rorden, C., 2011. The anatomy underlying acute versus chronic spatial neglect: a longitudinal study. Brain 134, 903–912.
Kaufmann, B.C., et al., 2020. Eyetracking during free visual exploration detects neglect more reliably than paper-pencil tests. Cortex; a Journal Devoted to the Study of the Nervous System and Behavior 129, 223–235.
Kenzie, J.M., et al., 2015. Lesion sites associated with allocentric and egocentric visuospatial neglect in acute stroke. Brain Connect. 5, 413–422.
Kim, E.J., et al., 2008. Hemispatial neglect in cerebellar stroke. J. Neurol. Sci. 275, 133–138.
Lecce, F., et al., 2015. Cingulate neglect in humans: disruption of contralesional reward learning in right brain damage. Cortex 62, 73–88.
Lunven, M., et al., 2015. White matter lesional predictors of chronic visual neglect: a longitudinal study. Brain: J. Neurol. 138, 746–760.
Machner, B., Könemund, I., von der Gablentz, J., Bays, P.M., Sprenger, A., 2018. The ipsilesional attention bias in right-hemisphere stroke patients as revealed by a realistic visual search task: neuroanatomical correlates and functional relevance. Neuropsychology 32, 850–865.
Mah, Y.-H., Husain, M., Rees, G., Nachev, P., 2014. Human brain lesion-deficit inference remapped. Brain 137, 2522–2531.
Malherbe, C., et al., 2018. Neural correlates of visuospatial bias in patients with left hemisphere stroke: a causal functional contribution analysis based on game theory. Neuropsychologia 115, 142–153.
Mattingley, J.B., Husain, M., Rorden, C., Kennard, C., Driver, J., 1998. Motor role of human inferior parietal lobe revealed in unilateral neglect patients. Nature 392, 179–182.
Maxwell, S.E., 2004. The persistence of underpowered studies in psychological research: causes, consequences, and remedies. Psychol. Methods 9, 147–163.
Moher, D., et al., 2015. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst. Rev. 4, 1–9.
Molenberghs, P., Sale, M.V., 2011. Testing for spatial neglect with line bisection and target cancellation: are both tasks really unrelated? PLoS One 6.
Molenberghs, P., Sale, M.V., Mattingley, J.B., 2012. Is there a critical lesion site for unilateral spatial neglect? A meta-analysis using activation likelihood estimation. Front. Hum. Neurosci. 6.
Moore, M.J.A., 2022c. Practical Guide to Lesion Symptom Mapping. https://doi.org/10.31234/osf.io/2jxr9. Preprint at.
Moore, M.J., Demeyere, N., 2021. Multiverse to inform neurological research: an example using recovery outcome of neglect. J. Neurol. https://doi.org/10.1007/s00415-021-10612-8.
Moore, M.J., Demeyere, N., 2022. Lesion symptom mapping of domain-specific cognitive impairments using routine imaging in stroke. Neuropsychologia 167, 108159.
Moore, M.J., Vancleef, K., Shalev, N., Husain, M., Demeyere, N., 2019. When neglect is neglected: NIHSS observational measure lacks sensitivity in identifying post-stroke unilateral neglect. *J Neurol Neurosurg Psychiatry* jnnp- 2018–319668. https://doi.org/10.1136/jnnp-2018-319668.
Moore, M.J., Gillebert, C.R., Demeyere, N., 2021a. Right and left neglect are not anatomically homologous: a voxel-lesion symptom mapping study. Neuropsychologia 162, 108024.
Moore, M.J., Vancleef, K., Riddoch, M.J., Gillebert, C.R., Demeyere, N., 2021b. Recovery of visuospatial neglect subtypes and relationship to functional outcome six months after stroke. Neurorehabilitation Neural Repair, 15459683211032976. https://doi.org/10.1177/15459683211032977.
Moore, M.J., et al., 2022a. Rapid Screening for Neglect Following Stroke: A Systematic Search and European Academy of Neurology Recommendations.
Moore, M.J., Jenkinson, M., Griffanti, L., Gillebert, C., Demeyere, N., 2022b. A comparison of lesion mapping analyses based on CT versus MR imaging in stroke. Review.
Nys, G.M.S., et al., 2006. Early cognitive impairment predicts long-term depressive symptoms and quality of life after stroke. J. Neurol. Sci. 247, 149–156.
Park, K.C., et al., 2006. Deafferentation–disconnection neglect induced by posterior cerebral artery infarction. Neurology 66, 56–61.
Parton, A., Malhotra, P., Husain, M., 2004. Hemispatial neglect. J. Neurol. Neurosurg. Psychiatr. 75, 13–21.
Pedrazzini, E., Ptak, R., 2020. The neuroanatomy of spatial awareness: a large-scale region-of-interest and voxel-based anatomical study. Brain Imaging and Behavior 14, 615–626.
Power, M., Fell, G., Wright, M., 2013. Principles for high-quality, high-value testing. BMJ Evidence-Based Medicine 18, 5–10.
Ptak, R., Schnider, A., 2011. The attention network of the human brain: relating structural damage associated with spatial neglect to functional imaging correlates of spatial attention. Neuropsychologia 49, 3063–3070.
Rorden, C., Bonilha, L., Fridriksson, J., Bender, B., Karnath, H.-O., 2012. Age-specific CT and MRI templates for spatial normalization. Neuroimage 61, 957–965.
Rossit, S., et al., 2009. The neural basis of visuomotor deficits in hemispatial neglect. Neuropsychologia 47, 2149–2153.
Rousseaux, M., Allart, E., Bernati, T., Saj, A., 2015. Anatomical and psychometric relationships of behavioral neglect in daily living. Neuropsychologia 70, 64–70.
Saxena, S., et al., 2022. Disruptions of the human connectome associated with hemispatial neglect. Neurology 98, e107–e114.
Silveri, M.C., 2001. Right side neglect in right cerebellar lesion. J. Neurol. Neurosurg. Psychiatr. 71, 114–117.
Singer, O.C., Sitzer, M., , de Rochemont, R. du M., Neumann-Haefelin, T., 2004. Practical limitations of acute stroke MRI due to patient-related problems. Neurology 62, 1848–1849.
Spanò, B., et al., 2022. Left egocentric neglect in early subacute right-stroke patients is related to damage of the superior longitudinal fasciculus. Brain Imaging Behav 16, 211–218.
Sperber, C., Karnath, H.-O., 2016. Diagnostic validity of line bisection in the acute phase of stroke. Neuropsychologia 82, 200–204.
Sperber, C., Karnath, H.O., 2017. Impact of correction factors in human brain lesion-behavior inference. Hum. Brain Mapp. 38, 1692–1701.
Sperber, C., Clausen, J., Benke, T., Karnath, H.O., 2020. The anatomy of spatial neglect after posterior cerebral artery stroke. Brain Commun 2, fcaa163.
Suchan, J., Karnath, H.-O., 2011. Spatial orienting by left hemisphere language areas: a relict from the past? Brain 134, 3059–3070.
Takamura, Y., et al., 2021. Interaction between spatial neglect and attention deficit in patients with right hemisphere damage. Cortex 141, 331–346.
Thiebaut de Schotten, M., et al., 2008. Visualization of disconnection syndromes in humans. Cortex 44, 1097–1103.
Thiebaut de Schotten, M., et al., 2014. Damage to white matter pathways in subacute and chronic spatial neglect: a group study and 2 single-case studies with complete virtual 'in vivo' tractography dissection. Cerebr. Cortex 24, 691–706.
Toba, M.N., et al., 2017. Common brain networks for distinct deficits in visual neglect. A combined structural and tractography MRI approach. Neuropsychologia. https://doi.org/10.1016/j.neuropsychologia.2017.10.018.
Urbanski, M., et al., 2011. DTI-MR tractography of white matter damage in stroke patients with neglect. Exp. Brain Res. 208, 491–505.
Verdon, V., Schwartz, S., Lovblad, K.-O., Hauert, C.-A., Vuilleumier, P., 2010. Neuroanatomy of hemispatial neglect and its functional components: a study using voxel-based lesion-symptom mapping. Brain: J. Neurol. 133, 880–894.
Vossel, S., et al., 2011. Visual extinction in relation to visuospatial neglect after right-hemispheric stroke: quantitative assessment and statistical lesion-symptom mapping. J. Neurol. Neurosurg. Psychiatr. 82, 862–868.
Weaver, N.A., et al., 2021. Strategic infarct locations for post-stroke cognitive impairment: a pooled analysis of individual patient data from 12 acute ischaemic stroke cohorts. Lancet Neurol. 20, 448–459.
Wiesen, D., Sperber, C., Yourganov, G., Rorden, C., Karnath, H.-O., 2019. Using machine learning-based lesion behavior mapping to identify anatomical networks of cognitive dysfunction: spatial neglect and attention. Neuroimage 201, 116000.
Wiesen, D., Karnath, H.O., Sperber, C., 2020. Disconnection somewhere down the line: multivariate lesion-symptom mapping of the line bisection error. Cortex 133, 120–132.
Wilson, S.M., 2017. Lesion-symptom mapping in the study of spoken language understanding. Language, Cognition and Neuroscience 32, 891–899.
Zhang, Y., Kimberg, D.Y., Coslett, H.B., Schwartz, M.F., Wang, Z., 2014. Multivariate lesion-symptom mapping using support vector regression. Hum. Brain Mapp. 35, 5861–5876.