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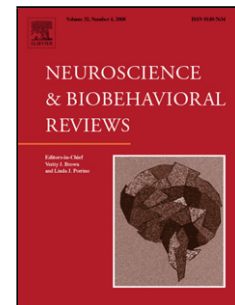
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Classification of navigation impairment: A systematic review of neuropsychological case studies

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Highlights

- Navigation impairment is often investigated in neuropsychological case studies
- Current study provides a systematic inventory and interpretation of 58 case studies
- We identified three main categories of navigation impairment
- These categories are related to landmarks, locations, and paths
- The model has implications for theory and clinical assessment of navigation ability

Abstract

The neurocognitive architecture of navigation ability has been investigated by extensively studying the navigation problems of individual neurological patients. These neuropsychological case reports have applied highly variable approaches to establish navigation impairment in their patients. This review provides a systematic and up-to-date inventory of all relevant case studies and presents an analysis of the types of navigation impairments that have been described. The systematic literature search revealed 58 relevant papers reporting on 67 neurological patients. Close analysis of their patterns of navigation performance suggests three main categories of navigation impairments. These categories are related to three types of representations that are considered highly relevant for accurate navigation: knowledge of landmarks, locations, and paths. The resulting model is intended to serve both clinical and theoretical advances in the study of navigation ability and its neural correlates.

Keywords: spatial navigation, navigation impairment, landmark, location, path

1. Introduction

Many daily activities require humans to be able to adequately navigate from one location to another. This might concern navigating to a particular location in a familiar environment, such as moving from the living room to the kitchen in our own homes. On other occasions, it might be needed to navigate through environments we have never visited before. Such situations can occur when visiting a friend in an unfamiliar, distant city or when going on vacation. Although directions provided by navigation aids or other people can be of assistance when navigating, complete reliance on such aids would clearly reduce our autonomy and mobility.

Given the importance of navigation for daily life, researchers have shown increasing interest in unraveling the neurocognitive mechanisms that support this ability. This research has clearly revealed that navigation ability is dependent on the integration of many cognitive mechanisms (e.g., Brunsdon, Nickels, & Coltheart, 2007; Wiener, Büchner & Hölscher, 2009; Wolbers & Hegarty, 2010). Some have focused on healthy individuals, for example with regard to allocentric and egocentric processing mechanisms for the purpose of navigation (e.g., Burgess, 2006; Klatzky, 1998). Other researchers have studied the types of information that allow for adequate navigation in healthy people, such as the distinction between landmark, route, and survey knowledge (e.g., Latini-Corazzini et al., 2010; Montello, 1998; Wolbers & Büchel, 2005; Wolbers, Weiller & Büchel, 2004). These findings jointly emphasize that navigation ability is supported by a complex interaction between multiple cognitive operations and, thus, heavily depends on the integrity of the brain.

Several group studies on navigation have shown that brain disorders might negatively affect navigation ability. These types of studies represent another approach

to the study of this ability and its neural correlates. Busigny and colleagues (2014), for instance, systematically verified navigation impairment in patients who suffered from ischemic stroke in the territory of the posterior cerebral artery. Several earlier studies have also investigated navigation problems in samples of stroke patients (e.g., Barrash et al., 2008; Van Asselen et al., 2006) and others have focused on other types of acquired brain damage, including traumatic brain injury (e.g., Livingstone & Skelton, 2007), Korsakoff's syndrome (Oudman et al., 2016), and Alzheimer's disease (e.g., Cushman et al., 2008). This line of studies has been helpful in verifying navigation ability in neurological patient groups. But it does not allow for the consideration of individual differences, while these have been found to be highly prominent with regard to navigation (e.g., Hegarty et al., 2006). Neuropsychological assessment of navigation performance at a single cases level is, however, highly suitable to study individual variation in navigation ability.

While the single-case approach is at the historical root of neuropsychology, studies using this methodology are still published on a highly regular basis (McIntosh & Brooks, 2011). This is particularly true for the study of navigation ability, as many extensive case investigations into neurological patients with impaired navigation skills have been published throughout the past decades (e.g., Caglio et al., 2011; Ciaramelli, 2008; Mendez & Chérier, 2003; Rainville et al., 2005; Rusconi et al., 2008; Ruggiero et al., 2014; Turriziani et al., 2003; Van der Ham et al., 2010). The conductance of adequate case studies is essential to gain further knowledge about the neurocognitive architecture of navigation ability. That is, only close investigation and inventory of individual patterns of intact and impaired navigation performances can lead to the identification of distinct types of navigation impairments and their origins.

In 1999, Aguirre and D'Esposito published a seminal review on the patterns of navigation impairment that had been described in single-case studies until then. Their analysis resulted in the taxonomy of “topographical disorientation” identifying four types of navigation impairments: 1) egocentric disorientation, an inability to represent locations of objects in relationship to one's own body, 2) heading disorientation, an inability to derive directional information from landmarks, 3) landmark agnosia, problems with recognizing and using landmarks for navigation, and 4) anterograde disorientation, navigation problems strictly confined to novel environments. Over the past two decades, this taxonomy has proven to be informative for the assessment of navigation impairment.

Navigation researchers have continuously applied the case study method to study navigation impairment in neurological patients. Hence, many new case studies have been added to the literature since the model by Aguirre and D'Esposito was published in 1999. It is therefore high time for an updated inventory of case studies on navigation impairment. In addition, the current review will apply systematic procedures for the identification and selection of relevant case studies. Such an approach improves the quality and replicability of the findings (Gates & March, 2016). The aim of this systematic review is thus to identify all relevant case studies as extensively as possible and to make an inventory of distinct categories of navigation impairments. This approach will allow analysis and subsequent classification of the patterns of intact and impaired navigation performance that have been reported in the literature so far. The resulting classification system will have both clinical and theoretical implications for the field of navigation ability. Clinically, it will provide guidance for the assessment and treatment of navigation problems in neurological patients. This system can also be used to couple distinct categories of navigation impairments to brain diseases and to

identify neuroanatomical associations. As it will be based on the reported dissociations and associations between distinct aspects of navigation ability, it will also contribute to further development of theories and models of navigation ability.

2. Method

A systematic literature search, adhering to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA), was performed using PubMed and Web of Science. Over the past decades, an extensive terminology has been used to indicate problems in navigation ability. The search terms were drafted to cover the range of this terminology as closely as possible and are reported in Appendix A. The result of the database search strategy was a total of 2,901 records (see Figure 1). After duplicates had been removed, titles and abstracts of the remaining records were screened for relevance to the review topic. This procedure resulted in a selection of 87 potentially relevant studies. A manual reference list screening of these studies led to the identification of an additional set of 38 potentially relevant papers. This additional set included ten papers (26%) that used the term “*topographic* disorientation” (instead of “*topographical* disorientation”), which was not included in the search terms. We also analyzed the other 28 papers in the additional set, but no further clues were found that could explain why these papers were not identified in the literature search. Full-texts (if available) were assessed for eligibility in the next stage. Studies had to be written in English and report on a case study of one or more neurological patients with navigation impairment. For inclusion of a case report, it was required that at least one navigation task (representing large-scale space) was used to objectively establish the navigation impairment. Case reports that solely relied on self-report, observational evidence, a single map drawing task or geographical knowledge tasks were considered to be

insufficient to determine a pattern of navigation impairment. Studies were excluded if the case report concerned a patient younger than 18 years of age or if the patient suffered from congenital brain damage; the review is not intended to cover developmental aspects related to navigation ability. Case reports on Developmental Topographical Disorientation were also excluded, given that these individuals are by definition free of any type of acquired brain damage or neurological disorder (e.g., Iaria & Burles, 2016). Author M.C. performed the procedure as described above. Author I.H. was consulted when there was doubt about the inclusion of a paper.

<<Insert Figure 1 around here>>

3. Results

The systematic literature search resulted in the selection of 58 papers with 67 case reports of neurological patients suffering from navigation impairment that fulfilled the inclusion criteria. Their performance patterns on objective neuropsychological, small-scale and large-scale spatial tasks were analyzed in detail. The analysis started with an inventory of all small-scale and large-scale spatial tasks that had been used in the selected case reports. In the next stage, tasks were classified according to the concepts that they are assumed to address. The classification was thus guided by the content of the tasks and not by theoretical considerations. Furthermore, performance on tasks involving environments familiar to the patient was separated from task performance in novel environments as encountered after the neurological event. Then it was established whether a patient's performance within each group of tasks was intact, impaired or unknown. This classification procedure eventually led to the identification of three functional categories of navigation impairments as described below. While these

categories are clearly dissociable, some patients are representative of more than one type of navigation impairment. A fourth category includes cases with navigation problems as a result of other conditions.

3.1 Landmark-based navigation impairment

The navigation problems for a subset of 26 patients reported in 21 papers (see Table 1) are the result of difficulties with the processing of landmarks (mainly buildings) or environmental scenes (landmark configurations or landscapes). Although their impairments might concern various aspects of this ability (perception, encoding, retrieval, and recognition), they have difficulties with landmarks or scenes in common. Further study of similarities and differences in their landmark processing abilities resulted in four subcategories of landmark-based navigation impairment.

<<Insert Table 1 around here>>

Nine cases have been shown to suffer from difficulties with both recognition of famous and familiar landmarks and acquiring knowledge about new landmarks as encountered after the neurological event. Patient F.G. is a comprehensively tested model case for this category (Rainville et al., 2005). F.G. was a 71-year-old male with an inability to recognize faces of family members and friends that had gradually increased over five years. He was, however, completely independent in his daily activities and did not experience problems with navigation in daily life. Formal neuropsychological testing confirmed prosopagnosia and a mild visual agnosia for object recognition. His performance on episodic memory tests was slightly lower than expected based on his high level of intellectual functioning. Assessment of his

navigation abilities revealed a clear impairment in identifying famous world monuments from photographs (such as the Eiffel tower in Paris, France, and the Pyramids in Egypt) while his performance was better when asked to identify these famous monuments from their name. This finding showed that his deficit was confined to visual recognition of the monuments, while his semantic knowledge of these places was preserved. A similar deficit was found for the identification of famous monuments in his hometown *Orange* (France), most of which he had encountered on a daily basis for 30 years. In addition, he was unable to learn a set of sixteen places and buildings as seen during a walk along an unfamiliar route in *Orange*. Despite his problems with landmarks, F.G. was able to provide detailed descriptions of familiar routes. Also, F.G. performed accurately when asked to reach a destination in his hometown when allowed to use only secondary roads. Subsequent retracing of this route was nearly flawless and pointing and distance estimation tasks were performed without difficulty as well. In strong contrast, F.G. was unable to reproduce a new route in an unfamiliar environment. The authors explained his intact performance on tasks in his hometown as a result of the strategy he applied. They found that F.G. compensated for his visuospatial deficit by heavily relying on verbal information such as street names or written signs. He rarely used buildings as landmarks. As the pre-existing internal representations of his hometown were well-preserved, his compensation strategy was successful for familiar but not for unfamiliar environments.

A similar pattern of impairments in the processing of famous/familiar and new landmarks was found in the patient reported by Incisa della Rochetta and colleagues (1996), and cases 2, 3 and 4 by Takahashi and Kawamura (2002). Three other patients might also represent this subcategory given their descriptions, but their assessments are

less convincing given that no formal tests were used to confirm their landmark problems (Landis et al., 1986; Paterson & Zangwill, 1945; Whiteley & Warrington, 1978).

The second subcategory of landmark-based navigation impairment is comprised of patients who have difficulties, exactly like the patients described above, with recognizing famous and familiar landmarks. Convincing and primary evidence for this subcategory is provided by the reports on the patient in Hirayama and colleagues (2003), S.E. (McCarthy et al., 1996), K.C. (Rosenbaum et al., 2000; Herdman et al., 2015) and S.B. (Rosenbaum et al., 2005). Their assessments, however, were not designed to measure their ability to acquire information about new landmarks or scenes. Consequently, it remains unclear whether the landmark problems of these patients would also occur in unfamiliar environments. Given that a pattern of intact landmark recognition for unfamiliar environments along with impaired familiar landmark recognition has never been reported in the literature, it seems unlikely that these cases are able to acquire information about new landmarks. Six other patients also belong to this subcategory, but their reports are less convincing given methodological limitations. This concerns patients R.B. (Bouwmeester et al., 2015), D.G. and D.A. (Herdman et al., 2015), A.R. (Hécaen et al., 1980) and cases 1 and 2 reported by Pai (1997). Patient W.J. was found to be impaired on a recognition test for newly learned scenes (Van der Ham et al., 2010). Her ability to recognize familiar landmarks was, however, not verified in the report. It thus remains unclear whether she would be able to perform accurately on such a task. Given her spatial deficits, it appears more likely that she suffers from broad difficulties with landmark processing like the patients in subcategories 1 and 2.

The third subcategory of landmark-based navigation impairment is represented by four patients who have selective difficulties with processing of landmarks in newly

learned environments (after the neurological event). This includes the reports on R.H. (Bird et al., 2007; Hartley et al., 2007), T.T. (Maguire et al., 2006), R.G. (Rusconi et al., 2008) and case 1 (Takahashi & Kawamura, 2002). This latter case, for example, was found to be able to identify several photographs of his house and the landscapes near his house. Furthermore, his spatial representation of the area around his house was intact given his accurate map drawing for this environment. In contrast, his ability to identify photographs taken in the hospital he was admitted to was impaired. This pattern of results indicates problems with landmarks only in new environments. The case report on R.H. also suggested that problems with landmarks can affect processing of new landmarks alone (Bird et al., 2007). While her ability to name famous buildings was preserved, she performed at an impaired level on a recognition memory task for unfamiliar buildings. Further study suggested that her difficulties with topographical information might also concern the perceptual rather than the mnemonic level alone (Hartley et al., 2007).

The fourth subcategory of landmark-based navigation impairment concerns patients with very specific dissociations in their landmark processing abilities that need to be described in detail. Mendez and Cherrier (2003) have described a patient who had difficulties in finding his way around, also in familiar environments, after having suffered an ischemic stroke event. The authors identified that, despite his problems with navigation in familiar environments, he was accurate at drawing maps and in describing familiar routes. His performance for familiar landmark recognition was also intact. In contrast, he was unable to identify familiar scenes in the absence of major landmarks. This finding was replicated based on a route learning task, in which the patient was able to correctly recognize landmarks but not scenes. Consequently, he had problems reproducing the newly learned route in case a break in landmarks occurred. The authors

thus argue that his navigation problems result from an isolated problem with deriving information from scenes, or visual configurations of the environment, that are composed of individually indefinite features.

An even more specific impairment in scene processing was presented in two detailed case studies reported by Epstein and colleagues (2001). They described two neurological patients, G.R. and C.O., who both reported difficulties with navigation in new environments. G.R. also explicitly complained of a perceptual deficit with complex scenes. Elaborate analyses of their abilities revealed that both of them had an isolated inability to encode novel information from scene-like spatial layouts and use it for later recognition. This task was, however, accurately completed for simple object stimuli. They also performed normally on several other tasks involving scene-like stimuli, such as perceiving spatial information from scenes and matching different views of scenes. No problems were found when the patients were asked to discriminate famous landmarks from closely matched non famous distractors. Assessment of their navigation abilities further indicated that their spatial representations of familiar environments were largely preserved, while they had difficulties with tasks concerning novel environments (e.g., map drawing or retracing of a newly learned route).

All patients mentioned in Table 1 thus share in common a deficit in the processing of landmarks or environmental scenes. Closer analysis of their patterns of performance revealed a clear dissociation in the processing of landmarks in familiar and unfamiliar environments. While defective landmark processing might affect navigation in both familiar and novel environments, some patients have specific difficulties in novel landmark processing alone. The opposite pattern of results has never been reported. Several further case studies have suggested even more specific dissociations. Mendez and Chérrier's patient (2003), for instance, showed intact

landmark processing along with selectively disturbed scene processing. Most case reports have not only focused on landmark processing, but have also addressed other aspects of navigation ability. In nine patients, the problems seemed to be confined to landmark processing alone, while, for example, spatial representations of familiar environments were preserved (G.R. in Epstein et al., 2001; McCarthy et al., 1996; Mendez & Chierri, 2003; case 2 in Pai, 1997; Rainville et al., 2005; Takahashi & Kawamura, 2002). It should, however, be mentioned that in some reports this finding was based on a single task, usually a map drawing of the patient's house. It might be that the sensitivity of such a task is insufficient to identify spatial representational deficits. The remaining cases present with at least subtle difficulties in, for instance, drawing a map of a familiar environment or describing familiar routes. At this point, it remains hard to determine whether or not these problems are directly related to the landmark processing deficit.

Analysis of the neuropsychological characteristics of the 26 patients with landmark-based navigation impairment revealed that visual field defects are relatively common. Fourteen patients (54%) suffered from a left visual field defect (hemianopia or quadrantanopia). Only two patients (8%) had intact visual fields, while this information was not reported for the remaining ten patients. Neglect was reported for four patients (15%), absent in nine patients (35%) and no information regarding neglect was provided for the others. If tested, higher-order visuospatial perception is usually intact. Patients F.G. (Rainville et al., 2005) and W.J. (Van der Ham et al., 2010) are the only exceptions given their (mild) object agnosia. Moreover, a deficit in landmark processing is not necessarily accompanied by problems in facial processing. Six patients (23%) suffered from prosopagnosia or obtained impaired scores on tests of facial processing. Twelve patients had intact facial processing (46%), while this ability

was not assessed in the remaining eight patients. As regards spatial span, ten patients (38%) performed adequately on the Corsi Block-Tapping task or comparable measures. Three patients (12%) had an impaired spatial span, while this ability was not evaluated in the remaining thirteen patients. Fourteen patients (54%) suffered from problems in spatial learning given impaired or borderline scores on tests like the recall condition of the Rey Complex Figure, the Benton Visual Retention Test, the Corsi supraspan, and maze learning tasks. Three patients showed intact spatial learning (12%), while this ability was not assessed in the remaining reports. This analysis shows that landmark-based navigation impairment rarely occurs in strict isolation and can be accompanied by visual field defects, neglect, facial processing deficits and problems in spatial span and spatial learning. Given the variability in the pattern of neuropsychological deficits across patients with landmark-based navigation impairment, however, these deficits appear to be an unlikely explanation for their problems in landmark processing.

As regards the underlying neuroanatomical correlates of landmark-based navigation impairment, the majority of patients suffered from lesions involving the right temporal and occipital lobes. More specifically, the right temporal lobe was affected in twenty patients (77%). The right hippocampus was damaged in fourteen patients (54%) and the right parahippocampal areas in eight patients (31%). Damage to the right occipital lobe was also relatively common (58%). For five patients, it was explicitly reported that the lesion involved the right lingual gyrus. Four studies implicated the right parietal lobe (precuneus). In two studies, researchers were unable to specify the lesion localization. A specific comparison between the patients in subcategory 1 (broad deficit in landmark processing) and subcategory 3 (novel landmark processing alone) revealed a notable difference in lesion localization. Lesions of patients in the latter subcategory appear primarily restricted to right medial temporal

areas such as the hippocampus. Most patients in subcategory 1, however, suffered from lesions also incorporating substantial portions of the right occipital lobe. The etiology of the brain damage was diverse. Ischemic and hemorrhagic stroke were common, but traumatic brain injury (open and closed head), encephalitis and Alzheimer's disease were also reported. In the discussion section, these findings will be interpreted in the light of existing neurocognitive studies on landmark processing in the healthy population.

To summarize, the first category of patients with navigation impairment concerns individuals who have difficulties with the processing of landmarks (mainly buildings) and environmental scenes (landmark configurations and landscapes). Closer analysis has shown that landmark-based navigation impairment might affect landmark processing in a generalized sense (i.e., both familiar and novel landmarks). However, difficulties restricted to novel landmarks or even more specific deficits have also been reported. This type of navigation impairment is not necessarily accompanied by a specific pattern of neuropsychological deficits, however, left visual field defects and spatial learning problems are relatively common. Inventory of lesion areas has suggested that most patients suffered from lesions comprising the right temporo-occipital areas. The involvement of the right occipital lobe is more likely in patients with a broad landmark processing deficit. In contrast, patients who have specific difficulties with novel landmarks mostly have lesions confined to right temporal lobe structures such as the hippocampus.

3.2 Location-based navigation impairment

Patients in this second category of navigation impairment have difficulties with recalling and/or acquiring knowledge of landmark locations and how these places relate

to each other. In contrast, they are usually accurate in visually identifying these landmarks. These patients show impaired performance on tasks that require them to describe the absolute or relative spatial locations of landmarks or to point into their directions when (imagining) standing at a certain location. Consequently, they tend to draw incorrect maps and might have difficulties with providing accurate route descriptions between locations. The patient reported by Caglio and colleagues (2011) is a model case for the seventeen patients (seventeen papers) who fit this category.

<<Insert Table 2 around here>>

Caglio and colleagues' (2011) patient concerned a 68-year-old male who suddenly became unable to navigate while driving in his car. Examination at the hospital revealed an ischemic stroke affecting the right mesial occipito-temporal region of his brain. More specifically, the right parahippocampal and lingual gyri were damaged, while the hippocampus was found to be intact. Four months after the stroke event, his navigation abilities were assessed in detail as he still reported to be unable to find his way around in the city center that was highly familiar to him. Neurological examination showed a left upper quadrantanopia. Visual perception and verbal memory were intact and no indications for neglect were objectified. His spatial span was limited but normal. He was unable to learn the sequence of the spatial supraspan. Analysis of his navigation abilities revealed that he was able to recognize familiar landmarks and to indicate distances between pairs of these landmarks. Route descriptions and descriptions of alternative routes were accurate. His performance on a pointing task between pairs of landmarks was impaired. He was also unable to draw a map of the city center and became confused when asked to indicate the locations of important

landmarks on it. This pattern of results indicates that he was unable to recall landmark locations and their interrelationships. The fact that his (alternative) route descriptions were accurate shows, however, that his knowledge of the paths that connect landmarks is preserved. As such, this case report can be interpreted as providing a dissociation between this category and the one that will be described in 3.3.

Further primary evidence for location-based navigation impairment is provided by ten case reports (Burgess et al., 2006; Descloux et al., 2015; Hirayama et al., 2003; Ino et al., 2007; Luzzi et al., 2000; Ruggiero et al., 2014; R.G. reported in Morganti et al., 2008 and Rusconi et al., 2008; patients 1 and 2 by Takahashi et al., 1997; Tamura et al., 2007). Six additional case reports are also indicative of location-based navigation impairment (Bouwmeester et al., 2015; Davis & Coltheart, 1999; Gardini et al., 2011; Grossi et al., 2007; patient 2 by Habib & Sirigu, 1987; Han et al., 2011). As their testing procedures and/or statistical findings are less convincing than the other reports, these cases are interpreted as yielding probable evidence.

Several reports have attempted to unravel the deficit that underlies location-based navigation impairment by administering (experimental) tasks tapping into more general spatial cognitive abilities. Burgess and colleagues (2006), for instance, verified their patient's ability to recognize object locations from the same or a different viewpoint in a virtual object location task. While her performance was comparable to that of matched controls in the "same" condition (egocentric spatial memory), performance worsened in the condition requiring her to recognize object locations from a shifted viewpoint. These results suggest that a deficit in allocentric spatial memory (or in the processes required to interpret output from the allocentric system) might explain her navigation problems in both familiar and novel environments. Further evidence suggesting that spatial memory problems might underlie location-based

navigation impairment comes from the reports on patients M.S. (Ruggiero et al., 2014) and R.G. (Morganti et al., 2008; Rusconi et al., 2008). Based on an object location task, it was found that they were both able to remember the identity of the presented objects, while they had difficulties with recalling the object locations. Moreover, the patient reported by Ruggiero and colleagues (2014) had problems in associating, or binding, the objects with their positions. When translating these findings based on small-scale spatial tasks to large-scale space, they might well provide a plausible explanation for the problems that these patients experience with recalling and/or acquiring information about the locations of landmarks.

Two case reports have closely evaluated their patients' ability to make spatial judgments either based on categorical (left/right) or coordinate (metric) relationships (Descoux et al., 2015; Ruggiero et al., 2014). Interestingly, the patients were highly similar in their pattern of performance on this type of task. While they performed at the level of healthy controls for categorical relationships, their performance was significantly lower compared to controls for metric spatial judgments. These findings might provide a further explanation for the inability of patients in this category of navigation impairment to recall and/or acquire information about the interrelationships of landmark locations.

Another spatial processing deficit that appears to underlie the navigation problems of the patients in this category comes from two reports (patient 2 by Habib & Sirigu, 1987; Ino et al., 2007). These two patients share a remarkable similarity in terms of their inability to egocentrically update their position relative to an invisible starting point when moving along a route. This process of updating one's position from an egocentric perspective has also been defined as dead reckoning. Ino and colleagues (2007) have argued that adequate dead reckoning is essential to gain reliable knowledge

about locations and their spatial relationships. In this sense, a deficit in egocentric updating or dead reckoning might negatively affect the ability to acquire information concerning locations and their interrelationships in previously unknown environments.

Inventory of neuropsychological deficits of the seventeen patients with location-based navigation impairment revealed that visual field defects were reported for seven patients (41%). For six of them, the defect affected the left visual field and one patient had a right-sided visual field defect. Another patient had been blind for 30 years due to glaucoma. No information about visual fields was mentioned for the other six patients. Neglect was uncommon and objectified in only two patients (12%). Eleven patients (65%) showed no indications of neglect, while neglect was not verified for the other four patients (23%). Evaluation of visuospatial perception showed normal performance in eleven patients (65%) and impaired performance in one patient (6%). For three patients (18%), tests for visuospatial perception revealed inconsistent findings suggesting that this ability might be affected at least to some extent. No information on visuospatial perceptual abilities was provided in two case reports. A deficit in face processing was objectified for three patients (18%), while this ability was normal in eleven patients (65%). Tests addressing facial processing were not administered in the remaining three patients. Nine patients (53%) had a normal spatial span, three patients (18%) had an impaired spatial span and no such information was given in the remaining case reports. Lastly, nine patients (53%) obtained impaired or borderline scores on tests of spatial learning. Intact spatial learning was objectified in only two patients (12%). This function was not evaluated in the other six patients. This analysis indicates that location-based navigation impairment might be accompanied by visual field defects and problematic spatial learning appears to be highly common. In contrast, neglect and

problems regarding visuospatial perception and facial processing are rather uncommon in combination with location-based navigation impairment.

Inventory of the lesion locations of patients with location-based navigation impairment indicated involvement of the right temporal lobe (65%), right parietal lobe (41%) and the right occipital lobe (35%). In comparison to the landmark category, the lesion incorporated the right parietal lobe relatively more often in the location group. Only two patients had lesions strictly confined to the left hemisphere. Two specific brain areas were relatively often mentioned as affected by the lesion: the right retrosplenial cortex (6 patients, 35%) and the right parahippocampal gyrus (5 patients (29%). No brain abnormalities could be objectified in three case reports. Damage due to ischemic or hemorrhagic stroke was the most common etiology in this category. Alzheimer's disease, limbic encephalitis and PCA (posterior cortical atrophy) have also been mentioned as the origin of the lesions.

The second category of navigation impairment concerns patients who show problems in recalling and/or acquiring information about landmark locations and their interrelationships. This type of impairment might affect navigation in familiar and novel environments. The analysis has suggested that location-based navigation impairment might result from deficits in spatial memory, specifically with regard to locations as well as binding objects (e.g., landmarks) to their locations. Some patients have also presented with difficulties in making spatial judgments based on metric relationships, and defective egocentric updating. These impairments might underlie the difficulties that the patients have when asked to indicate the spatial relationships between locations. From a neuropsychological perspective, these patients suffer relatively often from defective spatial learning and visual field defects are also common. Damage is usually located in the posterior portion of the right hemisphere; that is in the temporal, parietal

and occipital areas. More specifically, the right retrosplenial area and the right parahippocampal gyrus might play a specific role in location-based navigation impairment.

3.3 Path-based navigation impairment

The third category of navigation impairment is comprised of thirteen patients (twelve papers) who experience difficulties regarding the paths that connect locations with each other. They have problems with recalling these paths for familiar environments and/or in acquiring this information for new environments and routes. Furthermore, navigation-related problems might occur when these patients have to rely on spatial information alone, as they are unable to use (the metric structure of) paths for orientation purposes. This inability is reflected in their defective use of maps. Like patients with location-based navigation impairment, they usually produce distorted maps and provide inaccurate descriptions of routes between locations or landmarks.

<<Insert Table 3 around here>>

The case report on patient T.T. by Maguire and colleagues (2006) provides a clear example of path-based navigation impairment. T.T. was a 65-year-old male who worked for 37 years as a licensed taxi driver in London. To qualify for the London taxi driver license, candidates have to undergo an extensive training procedure (2-4 years) known as “The Knowledge”. The training requires candidates to learn the full layout of the city which comprises 25,000 streets and thousands of places of interest (Maguire et al., 2006). Passing the difficult series of examinations is only possible if candidates are able to demonstrate highly detailed knowledge of the city’s layout. As a consequence

of limbic encephalitis, it was found that T.T. suffered from selective damage to both of his hippocampi. Neuropsychological evaluation revealed severe anterograde and retrograde memory impairments. Moreover, the authors investigated T.T.'s ability to actively navigate between landmarks in central London using a realistic video game. Elaborate analyses indicated that T.T. relied heavily on main roads to navigate between London landmarks. He tended to become lost when use of non-main roads was inevitable. This pattern of performance shows that T.T.'s navigation impairment results from difficulties with recalling information about the fine-grained structure of the paths that connect London landmarks. Importantly, he performed intact on a London landmark recognition test, which used distractors that were closely matched in their visual appearance to the actual London landmarks.

The case reports on patients A.C. and W.J. (Van der Ham et al., 2010) suggest that even more selective and dissociable impairments in path knowledge can occur. Patient A.C. was a 36-year-old female suffering from an ischemic infarction to the medial occipital, the angular and a small part of the postcentral gyrus. Van der Ham and colleagues (2010) showed that she had a highly selective deficit in acquiring information about the order of decision points along a newly learned virtual route. In contrast, she performed accurately on a task that required her to form associations between places (decision points) and actions (turns). Patient W.J. showed exactly the opposite pattern of performance, that is, intact ordering but impaired at connecting decision points and turns. Similar to patient T.T. described above, the navigation impairments of patients A.C. and W.J. result from problems with knowledge that is associated with paths.

In addition to Maguire and colleagues' patient (2006) and the two patients presented by Van der Ham and colleagues (2010), further primary evidence for path-

based navigation impairment is offered by seven case reports (Bottini et al., 1990; Hécaen et al., 1980; Hublet & Demeurisse, 1992; Katayama et al., 1999; Rusconi et al., 2008; Suzuki et al., 1998; Turriziani et al., 2003). Given that only very limited information was available about the navigation assessments of three further patients (Alemdar et al., 2008; patient 1 in Habib & Sirigu, 1987; Osawa et al., 2006), these reports are interpreted as probable evidence for path-based navigation impairment.

A commonality between patients with path-based navigation impairment lies in their problematic use of maps and/or in transferring map representations to the real-world. This indicates that the navigation impairment of these patients does not only affect route knowledge, but also aspects of survey knowledge, such as the metric features of paths. For many patients in the category, this inability is evidenced by impaired performance on tasks that were introduced by Semmes and colleagues (1963) and Hécaen and colleagues (1972). In these tasks, participants are given maps depicting a particular path between landmarks placed in rows on the floor (Hécaen et al., 1972) or taped on the wall (Hécaen et al., 1972). Participants are required to walk the indicated path between the landmarks. A critical manipulation usually lies in the type of landmarks. Landmarks can be distinct (various geometrical shapes or concrete objects) or identical (plain papers). Many patients produce correct paths when distinct landmarks are present. In contrast, they fail when the landmarks are identical. Hence, difficulties with this type of task occur when the patients have to rely solely on spatial information or the structure of paths as depicted on the map (Alemdar et al., 2008; Bottini et al., 1990; Hécaen et al., 1980; Hublet & Demeurisse, 1992; Katayama et al., 1999; Turriziani et al., 2003). An illustration of defective transfer of map representations to the real-world is provided by the patient described by Suzuki and

colleagues (1998). Due to an inability to trace her actual position on a map, it took her very long to follow a route indicated on a map.

As regards the neuropsychological characteristics of the thirteen patients in this category, it was found that seven patients (54%) suffered from a visual field defect. The defect was located on the left side in four patients and on the right side in two patients. Two other patients (15%) had normal visual fields and information about visual fields was absent in the remaining four case reports. The presence of neglect was objectified in only one patient (8%), explicitly absent in eight patients (62%) and not assessed in four patients. Visuospatial perception was intact, if tested, and only two patients (15%) showed borderline performance. Face processing was found to be intact if tested and only one patient had temporary difficulties with face recognition. Normal spatial spans were found for seven patients (54%), impaired in two patients (15%) and untested in the other four cases. Lastly, spatial learning problems were highly common in this group. Ten patients (77%) showed impaired spatial learning, one patient had intact spatial learning skills (8%). No assessment of spatial learning was reported in two case studies. This analysis shows that path-based navigation impairment is likely to be accompanied by impaired spatial learning and visual field defects are relatively common. Neglect and problems with visuospatial perception and facial processing hardly occur in combination with path-based navigation impairment.

Analysis of lesion locations revealed that damage to the right occipital lobe (46%), the right temporal lobe (38%) and the right parietal (31%) was relatively often reported for the patients in the path-based category. For only two patients, the brain damage was found to be primarily confined to the left hemisphere. Further inventory of more specific brain areas revealed that the right hippocampus was the only structure that was damaged in more than a single patient (i.e., four patients, 31%). Interestingly,

this category of navigation impairment includes some patients who have suffered from highly focal brain lesions. For example, Hublet and Demeurisse's (1992) patient had a lesion confined to the posterior limb of the right internal capsule and the patient described by Katayama and colleagues (1999) had a lesion in the isthmus of the right posterior cingulum and the right lateral thalamus. Stroke was a common origin of brain damage (62%); however, brain tumor, limbic encephalitis, heroin overdose, and closed head TBI were also mentioned.

Path-based navigation impairment concerns patients who have difficulties with recalling and/or acquiring information about the paths that connect locations. Many patients have been shown to be unable to use spatial information for navigation purposes. This inability is clearly reflected in their defective performance on tasks that require them to find paths based on maps. In many cases, this type of navigation impairment has affected navigation in both familiar and novel environments. Inventory of neuropsychological profiles showed that path-based navigation impairment can be accompanied by visual field defects and spatial learning problems. In contrast, neglect and impairments in visuospatial perception and facial processing are rather uncommon in combination with this type of navigation impairment. Neurologically, it is primarily associated with right-sided brain damage, in particular to the temporal, parietal and occipital areas. Further specification of the brain structures involved was hindered by limited lesion descriptions, but it could be speculated that the right hippocampus plays some role in path-based impairment in navigation ability.

3.4 Navigation impairment secondary to other conditions

Twelve patients reported in eleven papers also suffer from navigation problems. Their navigation impairment should, however, be interpreted as secondary to other severe conditions. These case reports will be discussed briefly below.

<<Insert Table 4 around here>>

3.4.1. General spatial disorders

Eleven case reports concern patients who are, in addition to their navigation problems in large-scale spaces, more generally impaired in their spatial cognition abilities. Such spatial disorders result from conditions like unilateral neglect, deficits in visuospatial perception, disorientation for place or an impaired egocentric reference frame.

3.4.1.1. Unilateral neglect

Two papers have described patients with navigation difficulties as a direct consequence of unilateral neglect. Two patients investigated by Bisiach and colleagues (1993) showed problems with providing accurate route descriptions in case left turns were involved. For example, patient A.S. (Bisiach et al., 1993) provided accurate route descriptions, but she tended to become confused and to perform less accurately when left turns were needed. The paper by Bisiach and colleagues (1993) is suggestive of a preference for right turns being the origin of the navigation problems in their patients. A similar pattern of results has been found for case 5 reported by Brain (1941).

3.4.1.2. Deficits in (visuospatial) perception

Reports on two patients indicate that severe deficits in (visuospatial) perception can lead to navigation impairment. Lin and Pai (2000) have described a patient who, after

a stroke in the territory of the right posterior cerebral artery, felt unfamiliar in surroundings that should have evoked familiarity and he was unable to find his way around in the hospital ward during his hospitalization. Also, he could not provide an accurate description of a highly familiar route. His navigation problems were suggested to result from severe associative visual agnosia, which hindered him in recognizing his surroundings.

The second report concerns a 28-year-old male who suffered from a brain abscess in the right occipito-parietal region (Whitty & Newcombe, 1973). Although draining and removal of the abscess led to successful treatment, the patient reported difficulties regarding visuospatial perception and navigation. Formal testing of spatial perception revealed a strong emphasis on details and a lack of holistic perception. The patient used a similar approach for navigational purposes. He learned to use small detailed landmarks (instead of salient cues such as buildings) to find his way around. Ten years after the initial assessment, the patient recognized the ward and his previous room by way of highly detailed features like a particular clock. Despite a lack of objective evidence, this case history might still be informative given that impaired global perception played a prominent role in the defective use of landmarks.

3.4.1.3. Disorientation for place

Fisher (1982) has described a 72-year-old man (case 1) who suffered from an ischemic lesion in the right inferior parieto-occipital region. Initially, he was unaware of his current place during his stay in the hospital (Boston). He changed his answer to the question of his whereabouts nearly every day, which varied from places such as Paris, China, and Africa. He thus had the erroneous belief of being located in another place. In addition, he suffered from more general visuospatial deficits. Testing of his

environmental representations revealed that he could not draw an accurate map of his house and he was unable to trace a familiar route on a map. In contrast, the directions he provided to his daughter to find some documents in his home were correct. Hence, the primary problem of this patient appears to be a disturbance in orientation for place rather than navigation impairment.

3.4.1.4. Global spatial disorientation

Five patients, reported in five papers, showed difficulties with spatial processing notably extending the level of navigation in large-scale spaces (Hanley & Davies, 1995; Kase et al., 1977; patient 2 in Levine et al., 1985; Stark et al., 1996; Wilson et al., 2005). All of these patients showed, at least to some extent, difficulties with locating objects in space, while being able to name the objects correctly. When asked to reach for an object or to describe the spatial relationships between two objects, they failed to do so. Patient M.U., for example, could not complete any of the WAIS performance tasks, as he was unable to adequately reach for or point to the test materials (Wilson et al., 2005). The defective visuospatial behavior of two patients was also demonstrated by the observation that, when they moved through space, they acted as if they were blind (Kase et al., 1977; Levine et al., 1985). They walked around with their arms stretched out to detect obstacles and, despite that, still bumped into objects on a regular basis. Lastly, patients M.V.V. (Kase et al., 1997) and G.W. (Stark et al., 1996) showed severe difficulties with positioning their body in space. When asked to lie down on a bed, for instance, they were hardly able to position themselves in the correct orientation.

Given their severe global spatial disorientation, it is rather self-evident that these five patients also experience serious difficulties with finding their way around. Four patients were only cursorily assessed in their navigation abilities (Hanley & Davies,

1995; Kase et al., 1977; Levine et al., 1985; Stark et al., 1996). In general, their performance on tasks requiring them to describe familiar routes or draw maps of familiar environments was very poor. A more elaborate and systematic investigation of patient M.U. was undertaken by Wilson and colleagues (2005). They established that the pattern of performance of M.U. could be explained by an impaired egocentric reference frame. His inability to represent the locations of the landmarks in egocentric coordinates hindered him in providing accurate directional information and route descriptions, as these tasks rely heavily on an intact egocentric reference frame.

The five patients described above showed many similarities in their defective spatial behavior and, based on the report by Wilson and colleagues (2005), it appears that their navigation problems result from an impaired egocentric reference frame. A further similarity is that four patients suffered from bilateral parietal lobe damage; no lesion information was provided for Mr. Smith (Hanley & Davies, 1995).

3.4.2. Working memory impairment

The report on patient L.G. is unique in underlining the importance of working memory for navigation (Ciaramelli, 2008). L.G., a 56-year-old male, suffered from a bilateral lesion to the ventromedial prefrontal and rostral anterior cingulate cortices following a subarachnoid hemorrhagic stroke. After a few years of recovery, the only residual problem concerned serious difficulty in finding his way around in his hometown. Neuropsychological evaluation, however, revealed largely intact cognitive functions except for low or impaired performances on working memory and cognitive flexibility tasks. In addition, Ciaramelli observed L.G. while navigating between landmarks in his hometown. She found that most of his failures were the result of going to a location other than the intended goal destination. Upon arriving at the wrong location, though,

L.G. was able to mention the goal location and felt embarrassed. Further systematic investigation of his navigation abilities revealed that L.G.'s navigation problems resulted from an inability to actively maintain (the intention to reach) the goal location in working memory. Interestingly, L.G.'s ability to process familiar landmarks was intact and he was also accurate in providing directional information for these landmarks. The case of L.G. thus shows that navigation ability can (indirectly) be affected by deficits in cognitive functions such as working memory, despite the fact that landmark processing is intact and spatial representations are preserved.

3.5 Remaining cases

The systematic literature search was designed to include all relevant case reports as extensively as possible by requiring only a single objective navigation test for inclusion. This liberal criterion led to the identification of five case reports (five papers), which do not clearly fit into one or more of the categories described above. All five of these reports have only used unspecific navigation tasks like map drawings and/or route descriptions and no clear indications for the underlying nature of the navigation impairment were provided. Hence, the case reports by Greene and colleagues (2006), Maeshima and colleagues (2001), Nyffeler and colleagues (2005), and Teng and Squire (1999) could not be classified according to the model reported in this paper. Also, no classification was possible based on the performance pattern of patient 3 reported by Takahashi and colleagues (1997). Lastly, the report by Carelli and colleagues (2009) only provided limited information about the administered tasks and the performance of the patient, which also hindered classification.

4. Discussion

Neuropsychological case studies on patients with navigation problems provide a powerful approach to studying the neurocognitive architecture of navigation ability. These individual patterns of intact and impaired navigation performance can be analyzed to identify whether distinct types of navigation impairments exist. The most recent publication providing such an interpretation and synthesis of types of navigation impairments was published in 1999 by Aguirre and D'Esposito. Since many case studies on individuals with navigation problems have been added to the literature in the meantime, it appears high time for an update. The current review thus made an up-to-date inventory of all relevant case studies on navigation ability published to date (last literature search: October 2015). To improve quality and replicability of this inventory, a systematic literature search was applied. Individual patterns of navigation impairment were carefully analyzed to give an interpretation of the distinct types of navigation impairments that have been reported so far.

4.1 Three main categories of navigation impairment

This review reveals three main categories of navigation impairments as summarized in Figure 2. “Landmark-based navigation impairment” relates to difficulties with recognizing landmarks in familiar environments and/or in acquiring information about landmarks in novel environments. Patients with “location-based navigation impairment” show problems with recall of location knowledge for familiar environments and/or in learning this information for novel environments. Lastly, “path-based navigation impairment” concerns navigation problems resulting from defective recall of paths in familiar environments and/or in acquiring information about paths in novel environments. These main categories of navigation impairments represent the ‘what’, ‘where’, and ‘how’ of navigational knowledge, that is, landmark, location, and

path knowledge respectively. These categories are clearly dissociable, but not necessarily exclusive as some patients suffer from more than one type of navigation impairment.

<<Insert Figure 2 around here>>

4.1.1. Landmark-based navigation impairment

Patients with landmark-based navigation impairment have problems with landmark processing in common. A further subdivision shows that a deficit in landmark processing can broadly affect navigation in both familiar and novel environments or can be confined to novel environments. Inventory of neuropsychological profiles revealed that landmark-based navigation impairment is likely to be accompanied by visual field cuts and defective spatial learning. Higher visuospatial perception is usually intact and problems in facial processing do not necessarily accompany this type of navigation impairment. Many patients suffered from damage to the right temporal and/or occipital lobe regularly involving the hippocampus. A comparison between lesion locations of patients with a broad landmark processing deficit and patients with landmark problems in novel environments alone reveals an interesting finding. Lesions of many patients in the latter group were restricted to areas in the right medial temporal lobe. The lesions in patients with a broad deficit often extend into the right occipital lobe, for instance damaging the lingual gyrus.

The above findings are in line with neurocognitive studies into landmark and scene processing. The parahippocampal place area (PPA), a functionally defined area encompassing the posterior parahippocampal cortex and the anterior lingual gyrus, has been associated with the processing of complex visual scenes (Epstein & Kanwisher,

1998) and the encoding of landmarks (i.e. objects with navigational relevance; Janzen & Jansen, 2010; Janzen & Van Turenout, 2004). Epstein (2008; 2014) has recently suggested that the PPA consists of two functionally distinct areas. While its posterior part might be mainly engaged in the encoding of the visual properties of scenes, the anterior PPA appears to play an important role in the processing of the spatial layout of scenes and spatial memory more generally (e.g., Buffalo, Bellgowan & Martin, 2006). This functional distinction is further supported by anatomical evidence (Baldassano, Beck & Fei-Fei, 2013), that is, the posterior PPA holds strong connections with visual areas, whereas the anterior PPA is strongly connected to the retrosplenial complex and the parietal lobe. This leads to the speculation that damage to the posterior PPA would cause difficulties with landmarks in general, whereas damage to the anterior part of the PPA would result in difficulties with unfamiliar landmarks (Epstein, 2014). This speculation accords with our subdivision of broad landmark problems and landmark problems in novel environments alone, as well as the associated lesion locations.

4.1.2. Location-based navigation impairment

Patients with location-based navigation impairment suffer from defective recall or acquisition of location knowledge. They are unable to indicate the correct direction from one location to another. It has implicitly been suggested that defective egocentric (Morganti et al., 2008; Ruggiero et al., 2014) or allocentric spatial memory (Burgess et al., 2006) underlie this type of navigation impairment. Two reports have implicated a role for egocentric updating in the acquisition of location knowledge (patient 2 by Habib & Sirigu, 1987; Ino et al., 2007). That is, the ability to adequately integrate paths might be vital for building a representation of the interrelationships between locations. Patients with location-based navigation impairment can suffer from visual field defects

and impaired spatial learning is common. Inventory of lesion locations indicated that the right temporal, parietal or occipital areas were often damaged. In contrast to the landmark-based category, there is more involvement of right parietal areas in location-based problems. The lesion location analysis further tentatively suggests that the right retrosplenial area and parahippocampal gyrus might play a role in this category of navigation impairment.

Based on the case reports of patients with location-based navigation impairment as described in this review, it thus appears that both egocentric and allocentric spatial memory contribute to knowledge of locations. This might lead to the speculation that the underlying deficit in location-based navigation impairment relates to the translation processes between egocentric and allocentric representations, rather than one or the other type of representation. From a neurocognitive perspective, allocentric processing has been associated with the right medial temporal lobe and the hippocampus in particular, while egocentric processing has been coupled to the right parietal areas and, more specifically, the precuneus (Ciaramelli, Rosenbaum, Solcz, Levine & Moscovitch, 2010; Vogeley & Fink, 2003). In addition, it has been argued that the right retrosplenial cortex is responsible for the processes that allow egocentric representations to be translated into allocentric representations (Byrne, Becker & Burgess, 2007). Thus, there appears to be an overlap in the brain areas associated with egocentric and allocentric processing and their interaction, on the one hand, and the brain areas that have been implicated in location-based navigation impairment, on the other hand. Future research is, however, needed to verify this speculation.

4.1.3. Path-based navigation impairment

The category of path-based navigation impairment is comprised of patients who have problems related to the paths that connect locations. This concerns the recall of these paths in familiar environments and/or acquisition of this type of knowledge for new environments. It should be emphasized that their deficits encompass aspects of both route and survey knowledge (Montello, 1998) related to these paths. Their problems might, for example, concern the fine-grained structure of paths (Maguire et al., 2006) or affect selective aspects of route knowledge, such as the order in which landmarks occur along a route (Morganti et al., 2008; Van der Ham et al., 2010). Many of the patients in this category further share difficulties with using maps. This results from an inability to interpret the metric structure of paths, which is clearly related to survey knowledge. This type of navigation impairment is regularly accompanied by visual field defects and impaired spatial learning. Analysis of lesion locations implicates the right-side of the brain and the temporal, parietal or occipital lobes in particular in path-based navigation impairment. As regards specific brain structures, only the right hippocampus was found to be damaged in more than one patient. This unspecific pattern of neural correlates is most likely related to the fact that path-based navigation impairment includes various types of selective deficits. As mentioned, this type of navigation impairment can result from problems with regard to concrete information related to paths, such as place-actions associations and order knowledge, as well as more abstract information, such as the length of paths or its metrical structure. Further research is clearly needed to unravel the lesion locations associated with these possible subcategories.

From a conceptual viewpoint, this category of navigation impairment is clearly the most complex one. That is, many types of path characteristics can be linked to path knowledge: among many other things, sequences of landmarks or locations,

associations between places and actions, and the metrical structure of paths. The complex nature of the concept of path knowledge is also reflected in the fMRI literature on this topic showing widespread involvement of brain networks in the temporal, parietal, and occipital areas. Knowledge of landmark order, for instance, has been coupled to activation in the (para)hippocampus (e.g., Ekstrom, Copara, Isham, Wang & Yonelinas, 2011; Maguire, Frackowiak & Firth, 1997), but more widespread activation in an occipito-temporal network in a landmark ordering task has also been reported (Nemmi et al., 2013). As another example, response learning (i.e., learning to perform a particular action at a particular location) has been linked to activation of the caudate nucleus (Doeller, King & Burgess, 2008; Iaria, Petrides, Dagher, Pike & Bohbot, 2003; Marchette, Bakker & Shelton, 2011) and the parietal cortex might be involved as well. Hence, the complexity of path knowledge is clearly reflected in both neuropsychological studies and in the fMRI literature.

4.2 Implications

The current model describes three main categories of navigation impairments directly related to three types of representations that support adequate navigation behavior. Navigation requires knowledge of landmarks ('what'), locations ('where'), and paths ('how'). As such, the model has important implications for the assessment of navigation impairment. Assessment of navigation ability should at least include tests for landmark, location, and path knowledge. Equivalent tests for each representation type should be administered based on both familiar and novel environments. This allows one to verify what type(s) of representation is/are affected and to establish whether these problems arise from difficulties in recall and/or encoding of a particular type of navigational

knowledge. Impaired navigation ability confined to familiar environments alone has never been reported.

This review also gives rise to methodological improvements for enhancing the quality of neuropsychological case reports into navigation impairment. Case reports were included in the review when at least one large-scale navigation task was used to objectively establish the navigation impairment. This criterion was applied in a liberal manner. Ad-hoc tests, for instance, were considered sufficient to allow inclusion. Nonetheless, some well-known and very recent case reports that only rely on anecdotal information were not taken into account. As this review shows, navigation impairment is frequently but not invariably accompanied by impaired performance on spatial learning tasks. This finding clearly underlines that navigation ability is a unique cognitive domain, which calls for use of large-scale navigation tasks. In several case reports, navigation problems could only be established based on large-scale navigation tasks as opposed to standard neuropsychological small-scale spatial tasks (see e.g., Incisa della Rochetta et al., 1996; Van der Ham et al., 2010; Whiteley & Warrington, 1978). This clearly accords with studies indicating that small-scale spatial tasks, such as the Corsi Block-Tapping Task and the Rey Complex Figure Test, are no reliable predictors of navigation performance (e.g., Nadolne & Stringer, 2001; Van der Ham et al., 2010). In fact, it has been shown that performance on small-scale and large-scale spatial learning tasks can be dissociated in brain-damaged patients (Piccardi et al., 2010; Piccardi, Iaria, Bianchini, Zompanti & Guariglia, 2011), and rely on neural circuits that are partly independent (Nemmi, Boccia, Piccardi, Galati & Guariglia, 2013). All of these findings clearly highlight the necessity of using large-scale spatial tasks to assess navigation ability.

Inclusion of a case report in the current review, on the other hand, should not be interpreted as a direct indication of high methodological quality. First, many case studies did not systematically verify the navigation abilities of their patients in both familiar and novel environments. Furthermore, many of the selected case reports lacked adequate statistical comparisons of the patient's performances with that of a healthy control group or lacked the use of a healthy control group at all. Given that navigation is an ability with pronounced individual differences, the lack of a healthy control group might bias, for example, the interpretation of a patient's performance on ad-hoc navigation tasks. In addition, statistical programs specially intended for use in case studies are freely available and its use in the field of navigation ability is highly encouraged (McIntosh & Brooks, 2011). Some researchers have even reported scoring procedures to allow comparing a patient's performance to that of a healthy control group on tests for familiar environments, which, of course, highly differ across participants (see for example Herdman et al., 2015). Given all of the above, we strongly advocate the use of a healthy control group, single case statistical procedures, and objective scoring systems in future case studies on navigation impairment. This would, in our view, lead to major improvements in the methodological quality and validity of case studies on navigation impairment. In the current review, we choose not to exclude relevant case studies that lacked the use of a healthy control group, because this would have led to a highly selective and biased set of case studies on navigation impairment.

A further comment concerns the use of map drawing and route description tasks to establish navigation impairment. Many case reports have verified map drawing performance and have mainly used it as an indication of intact or impaired allocentric place representations. It has been stressed, however, that the cognitive mechanisms supporting map drawing and route descriptions are poorly understood (Aguirre &

D'Esposito, 1999; Pick, 1993). In addition, accurate map drawings and route descriptions can be accomplished by different strategies. Defective performance on map drawing and route description tasks might thus be limited in providing reliable information about the origin of navigation impairment. As arises from this review, both patients with location-based and patients with path-based navigation impairment are expected to fail at map drawing. It is thus recommended to administer these tasks in combination with tasks that explicitly address landmark, location, and path knowledge.

4.3 Limitations

The current review made use of a systematic literature search that followed the guidelines of Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA). Such a procedure clearly favors both the quality and replicability of the inventory of the relevant neuropsychological case studies on navigation ability as provided here. Nonetheless, two potential limitations should be considered. First, a relatively high number of potentially relevant case reports were identified, after the systematic literature search had already been completed, by way of manually screening the reference lists of selected studies. This approach led to the identification of an additional set of 38 potentially relevant papers. Closer analysis revealed that, within this set, ten papers used the term “*topographic* disorientation” instead of “*topographical* disorientation”. As the former term was not included in the search terms, these ten papers were not identified in the database search. Analysis of the remaining papers did not indicate that relevant terms were missed. We would like to stress here that the field of navigation ability lacks uniformity in its terminology, which might negatively affect systematic attempts of literature review as well as (theoretical) progress with regard to this topic.

A further limitation of this review might lie in the fact that the PRISMA guidelines could not be applied to guide the data extraction process. Researchers who conducted neuropsychological case studies on navigation ability have made use of a wide variety of small-scale and large-scale spatial tasks. Given this variability in the measures used to establish navigation impairment, an inventory of all spatial tasks was made. The next step was to classify the tasks based on their content. It was then established, for each selected patient, whether his/her performance within each task domain was intact, impaired or untested. The interpretation of these data resulted in the categories of navigation impairments that have been described in this review. Thus, the approach taken here is not supported by statistical analyses and is reliant on our interpretation of the performance patterns.

4.4 Associations with other neuropsychological and neurological conditions

Up to this point, we have mainly discussed our findings in the light of the case study literature on navigation impairment. There are, however, several issues that should be considered in a broader neuropsychological context. Firstly, based on the selected case reports in this review, it appears that visual field defects are relatively common in combination with all three types of navigation impairment as described here (41-54%). It can, of course, be argued that the presence of a visual field defect would prevent or hinder one from perceiving part of his or her surroundings, landmarks for example, but this seems to be only an incomplete explanation for problems with navigation. The association between navigation impairment and visual field defects has never been studied in a systematic manner, however, it most likely results from the fact that the primary visual areas as well as the brain areas mediating navigation ability depend on blood supply through the posterior cerebral arteries (PCA; Busigny et al., 2014). We

also analyzed the prevalence of neglect in the selected case reports. While clinical observations appear to point towards a clear association between neglect and navigation impairment (Guariglia, Piccardi, Iaria, Nico & Pizzamiglio, 2005), our analysis showed that neglect occurred relatively rarely in combination with any of the three types of navigation impairment (8-15%). Guariglia and colleagues (2005) have suggested that it is helpful to differentiate between perceptual neglect (i.e., the inability to perceive left-sided stimuli) and representational neglect (i.e., the inability to describe, depending on the imagined viewpoint, landmarks on the left side of a familiar place from memory). While navigation impairment can occur along with perceptual neglect (e.g., due to a deficit in path integration; see De Nigris et al., 2013), it is more common in patients with representational neglect (Guariglia et al., 2005), which is a disorder of mental imagery. Importantly, the navigation problems of patients with representational neglect do not only concern the processing of mental images of landmarks on the contralesional side, but also more broadly affect the ability to create and use mental representations of the environment (Palermo, Ranieri, Nemmi & Guariglia, 2012). These findings provide a good explanation for the weak association between navigation impairment and neglect in this review, as most cases were only tested for perceptual and not for representational neglect or mental imagery. The co-occurrence of navigation impairment and representational neglect (Guariglia et al., 2005; Palermo et al., 2012, Piccardi, Bianchini, Zompanti & Guariglia, 2008), however, clearly accords with models that have assigned an important role for mental imagery in spatial memory (Byrne et al., 2007) and navigation ability (Brunsdon et al., 2007).

5. Conclusion

Systematic inventory of neuropsychological case studies investigating the nature of navigation impairment has led to the identification of three main types of underlying deficits. Navigation impairment can be classified into defects of landmark, location and path knowledge (see Figure 2). These deficits can affect navigation in familiar and novel environments or in novel environments only. This model has direct implications for the theory of the neurocognitive organization of navigation ability by revealing dissociations between landmark, location, and path knowledge. Also, it provides suggestions for guiding assessment and treatment of navigation-related problems in neurological patients. The assessment procedure should preferably include tests for landmark, location and path knowledge based on familiar and novel environments. Moreover, this paper indicates that the methodological quality of neuropsychological case reports on navigation impairment can be improved by using appropriate large-scale navigation tasks and by comparing the case's performance to that of healthy controls. Specific statistical programs for case studies have been developed to deal with the fact that control groups usually contain only few participants. To conclude, the current review has provided a model that allows navigation impairment to be classified into three main types, which will be of great value to both theoretical and clinical approaches to the study of navigation ability.

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We have no conflicts of interest to declare.

Appendix A: Electronic search strategies

<i>Database</i>	<i>Search strategy</i>
PubMed	((((((((((route learning[Title/Abstract]) OR wayfinding[Title/Abstract]) OR spatial orientation[Title/Abstract]) OR spatial disorientation[Title/Abstract]) OR spatial navigation*[Title/Abstract]) OR navigation impairment[Title/Abstract]) OR topographical disorientation[Title/Abstract]) OR topographical agnosia[Title/Abstract]) OR topographical amnesia[Title/Abstract]) OR spatial disorientation[Title/Abstract]) OR topographical memory[Title/Abstract]) AND (((case*[Title/Abstract]) OR case study[Title/Abstract]) OR patient[Title/Abstract]) OR patients[Title/Abstract]) OR impair*[Title/Abstract]) Filters applied: English, Human No limitation on publication date
Web of Science	(“route learning” OR wayfinding OR “spatial orientation” OR “spatial disorientation” OR “spatial navigation” OR “spatial navigational” OR “navigation impairment” OR “topographical disorientation” OR “topographical agnosia” OR “topographical amnesia” OR “spatial disorientation” OR “topographical memory”) AND (case\$ OR case study OR patient OR patients OR impair*) Filter applied: English No limitation on publication date

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Figure legends

Figure 1

Flow diagram of the systematic literature search

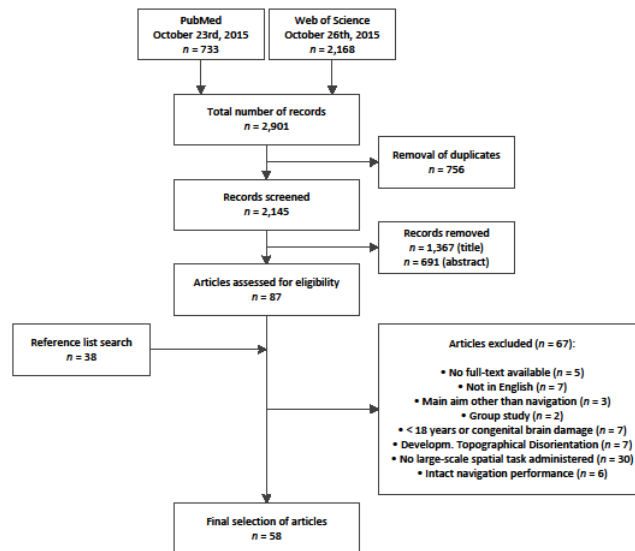


Figure 2

The three main types of navigation impairment as identified in this review

Note. RH = right hemisphere

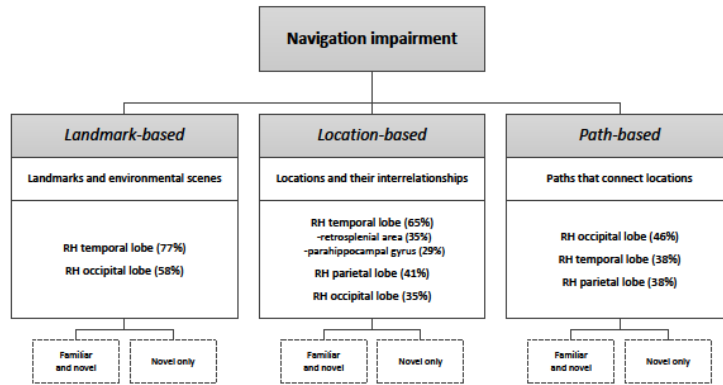


Table 1

Landmark-based navigation impairment: case studies reporting neurological patients with problems related to processing of landmarks and scenes

<i>Report</i>	<i>Case</i>	<i>Subcategory*</i>	<i>Familiar landmarks</i>	<i>Novel landmarks</i>	<i>Lesion type</i>	<i>Lesion site</i>
Incisa della Rochetta, 1996	M.S.	1, primary evidence	–	–	Small vessel ischemic disease	Frontal and parietal lobe bilaterally, left thalamus
Rainville, 2005	F.G.	1, primary evidence	–	–	Progressive atrophy	Right fusiform gyrus and parahippocampal cortex
Takahashi, 2002	2	1, primary evidence	–	–	Ischemic stroke	Right medial temporo-occipital lobe
Takahashi, 2002	3	1, primary evidence	–	–	Ischemic stroke	Right medial temporo-occipital lobe
Takahashi, 2002	4	1, primary evidence	–	–	Ischemic stroke	Right medial temporo-occipital lobe
Landis, 1986	1	1, probable evidence	–	–	Ischemic stroke	Right medial occipital lobe
Paterson, 1945	—	1, probable evidence	–	–	TBI (open head)	Right parietal lobe
Whiteley, 1978	J.C.	1, probable evidence	±	–	TBI (closed head)	NA
Hirayama, 2003	—	2, primary evidence	–	NA	Limbic encephalitis	Bilateral hippocampus, posterior right parahippocampal gyrus, right retrosplenial region, right inferior precuneus
McCarthy, 1996	S.E.	2, primary evidence	–	NA	Viral encephalitis	Right temporal lobe
Rosenbaum, 2000	K.C.	2, primary evidence	–	NA	TBI (closed head)	Widespread damage including the hippocampus bilaterally
Rosenbaum, 2005	S.B.	2, primary evidence	–	NA	Probable AD	Hippocampus, occipito-temporal cortex
Bouwmeester, 2015	R.B.	2, probable evidence	–	NA ¹	Multiple ischemic strokes	Right medial occipito-temporal lobe
Herdman, 2015	D.G.	2, probable evidence	–	NA	Anoxia due to cardiac arrest	NA
Herdman, 2015	D.A.	2, probable evidence	±	NA	Herpes encephalitis	Posterior temporal, occipital, ventral frontal lobes, anterior cingulate, and right posterior thalamus

Hécaen, 1980	A.R.	2, probable evidence	±	NA	Ischemic stroke	Right occipital lobe
Pai, 1997	1	2, probable evidence	–	NA	Hemorrhagic stroke	Right mesial area of the occipito-temporal region (cuneus and lingual gyri) and part of the parietal lobe
Pai, 1997	2	2, probable evidence	–	NA	Ischemic stroke	Right mesial area of the occipito-temporal region (cuneus, lingual and parahippocampal gyri)
Van der Ham, 2010	W.J.	2, probable evidence	NA	–	Debulking of brain tumor	Right occipital, temporal and superior parietal areas along with the fusiform gyrus and the hippocampus
Bird, 2007 / Hartley, 2007	R.H.	3, primary evidence	+	–	Probable ischemic stroke	Right hippocampus
Maguire, 2006	T.T.	3, primary evidence	+	–	Limbic encephalitis	Generalized atrophy primarily implicating the hippocampi
Rusconi, 2008	R.G.	3, primary evidence	+	–	Hemorrhagic stroke	Right temporo-occipital lobe with ventricular flooding
Takahashi, 2002	1	3, primary evidence	+	–	Ischemic stroke	Right medial temporal lobe
Epstein, 2001	G.R.	4; inability to encode new scene-like spatial layouts	+	–	Two ischemic stroke events	Right occipital-temporal lobe
Epstein, 2001	C.O.	4; inability to encode new scene-like spatial layouts	+	–	Ischemic stroke	Right occipital and mesial temporal lobe
Mendez, 2003	G.N.	4; inability to process scenes, but intact landmark processing	+ (LM) – (scenes)	+ (LM) – (scenes)	Ischemic stroke	Right medial occipito-temporal lobe

Note. * 1 = broad impairment in processing of both familiar and novel landmarks, 2 = impaired processing of familiar landmarks, no assessment of novel landmark processing reported, 3 = intact processing of familiar landmarks, impaired for novel landmarks, 4 = isolated deficit in landmark processing. Some cases have been marked as probable evidence of a subcategory, because of absent formal tests for landmark processing or unconvincing statistical findings. ¹ Only tests administered prior to the training are taken into account here. + = intact, ± = borderline, – = impaired, NA = not assessed, LM = landmarks, TBI = traumatic brain injury, AD = Alzheimer's disease.

Table 2

Location-based navigation impairment: case studies reporting neurological patients with defective knowledge of locations or problems in acquiring this knowledge

<i>Report</i>	<i>Case</i>	<i>Type of evidence*</i>	<i>Navigation deficit</i>	<i>Familiar settings</i>	<i>Novel settings</i>	<i>Lesion type</i>	<i>Lesion site</i>
Burgess, 2006	—	Primary evidence	A deficit in allocentric spatial memory possibly underlies problems with familiar route descriptions and acquiring a new virtual environment	—	—	Early dementia of the Alzheimer's type	Brain scan essentially normal
Caglio, 2011	—	Primary evidence	Impaired pointing to landmarks and map drawing	—	NA	Ischemic stroke	Right mesial occipito-temporal region
Descloux, 2015	—	Primary evidence	Impaired performance for indicating distances and directions between familiar landmarks	—	NA	Ischemic stroke	Right-sided lesion in the inferior sulcus, part of the superior parietal sulcus, almost all of the temporal lobe, insular and retrosplenial cortex, inferior frontal sulcus and some occipital areas
Hirayama, 2003	—	Primary evidence	Unable to describe locations of neighboring landmarks and indicating their positions on a map, inaccurate description and drawing of a familiar route, unable to indicate the viewpoint at which photos of landmarks were taken	—	NA	Limbic encephalitis	Hippocampi bilaterally, anterior parahippocampal areas bilaterally, posterior right parahippocampal, right retrosplenial region and the right inferior precuneus
Ino, 2007	—	Primary evidence	Unable to point to familiar locations with respect to his position in the hospital and to describe or draw routes or layouts; impaired egocentric updating	—	—	Hemorrhagic stroke	MRI: lesion in the left retrosplenial region, SPECT: decreased perfusion in the left parietal region
Luzzi, 2000	F.Z.	Primary evidence	Unable to draw a map of his apartment and to indicate positions of the rooms relative to an imagined viewpoint, incorrect descriptions of the apartment and familiar routes	—	—	Two ischemic strokes	Lesion in the right parietal lobe and another involving the right parahippocampal gyrus
Ruggiero, 2014	M.S.	Primary evidence	Impaired map drawing for novel and familiar environments, pointing in a novel setting, route finding in novel and familiar environment,	—	—	Hemorrhagic stroke	Unilateral lesion involving the left parahippocampal gyrus, the

			probably due to deficits in spatial memory and spatial processing				posterior cingulate gyrus and the precuneus
Morganti, 2008 / Rusconi, 2008	R.G.	Primary evidence	Impaired pointing in a newly learned virtual environment	+	–	Two hemorrhagic strokes	Lesion in the right temporo-occipital area including the hippocampus and another in the right medial temporal lobe
Takahashi, 1997	1	Primary evidence	Unable to indicate locations of familiar buildings on a map and to provide accurate descriptions of familiar routes and map drawing for a recently learned environment	–	–	Hemorrhagic stroke	Right retrosplenial region with some extension to the inferior precuneus
Takahashi, 1997	2	Primary evidence	Unable to indicate locations of familiar buildings on a map and to provide accurate descriptions of familiar routes and map drawing for a recently learned environment	–	–	Hemorrhagic stroke	Right retrosplenial region with some extension to the inferior precuneus
Tamura, 2007	T.H.	Primary evidence	Impaired map drawing for familiar and novel environments, pointing and route learning for a novel environment and defective “learned sense of quarters”	–	–	Hemorrhagic stroke	Right-sided lesion of the focal forceps major of the splenium region
Bouwmeester, 2015	R.B.	Probable evidence	Unable to recognize changes in the spatial arrangement of objects in a room in his own home	–	NA ¹	Multiple ischemic strokes	Right medial occipito-temporal lobe
Davis, 1999	K.L.	Probable evidence	Difficulties with indicating the location of landmarks in an environment learned after the stroke event and unable to draw an accurate map for this environment ²	+	–	Severe migraine headache	CT: no abnormalities, MRI was not available
Gardini, 2011	—	Probable evidence	Unable to describe the relative positions of the rooms in his house, incorrect description of a familiar route and incorrect drawing of a familiar path on a city map	–	NA	Posterior cortical atrophy	Pronounced atrophy in the right parieto-occipital lobe
Grossi, 2007	S.G.	Probable evidence	Unable to indicate relative spatial location of landmarks or to describe walking paths	–	NA	Alzheimer’s disease	EEG/MRI: normal; PET: bilateral hypoperfusion in parieto-temporal areas

Habib, 1987	2	Probable evidence	Unable to learn a new route and impaired egocentric updating	NA	–	Ischemic stroke	Lesion in the inner aspect of the temporal lobe, probably involving the (para)hippocampal region
Han, 2011	— ³	Probable evidence	Tactilely recognized landmarks did not provide directional information and difficulties with the arrangement of furniture (landmarks) in his house	–	NA	Multiple ischemic strokes	Bilaterally in the retrosplenial region including the post cingulate and cuneus and lingual gyrus

Note. * Some cases have been marked as probable evidence of this category, because of absent formal tests for locations or unconvincing statistical findings. ¹ Only tests administered prior to the training are taken into account here. ² The navigation tasks in this study are hard to interpret due to a strong reliance on verbal information (i.e., street names). ³ The patient was already blind for 30 years due to glaucoma. + = intact, ± = borderline, – = impaired, NA = not assessed.

Table 3

Path-based navigation impairment: case studies reporting neurological patients with defective knowledge of paths or problems in acquiring this knowledge for new environments and routes

<i>Report</i>	<i>Case</i>	<i>Type of evidence*</i>	<i>Navigation deficit</i>	<i>Familiar settings</i>	<i>Novel settings</i>	<i>Lesion type</i>	<i>Lesion site</i>
Bottini, 1990	V.B.	Primary evidence	Unable to describe (the layout of) his apartment and a familiar place, inaccurate descriptions for familiar routes and defective learning of new routes and map use	–	–	Glioblastoma	Bilateral median and right paramedian hypodense lesion centered on the splenium of the corpus callosum
Hécaen, 1980	A.R.	Primary evidence	Impaired map use with identical landmarks only	+	–	Ischemic stroke	Right occipital lobe
Hublet, 1992	—	Primary evidence	Impaired learning of a recently learned route in the hospital and incorrect description of this path, defective map use with identical landmarks only	NA	–	Ischemic stroke	Lesion in the posterior limb of the right internal capsule
Katayama, 1999	—	Primary evidence	Unable to learn routes in the hospital (only when aided with a list of the order of landmarks), defective map use	±	–	Ischemic stroke	Lesion in the isthmus of the right posterior cingulum and the right lateral thalamus
Maguire, 2006	T.T.	Primary evidence	Strong reliance on main roads when actively navigating in a virtual version of London (suggesting problems with fine-grained structure of paths), unable to learn new routes	±	–	Limbic encephalitis	Generalized atrophy primarily implicating the hippocampi
Rusconi, 2008	R.G.	Primary evidence	Unable to recall information on the order of scenes as encountered in a newly learned route and incorrect reproduction of a route learned from a map	+	–	Hemorrhagic stroke	Right temporo-occipital lobe with ventricular flooding
Suzuki, 1998	T.Y.	Primary evidence	Unable to determine the viewpoints from which familiar buildings were photographed and unable to learn a new route through a map	+ – (VP)	–	Hemorrhagic lesion	Lesion in the right parietal lobe, located mainly in the precuneus and impinging on the cuneus
Turriziani, 2003	—	Primary evidence	Unable to learn new paths (small-scale test) in the absence of landmarks	+	–	Heroin overdose	Marked atrophy of the hippocampi bilaterally, moderate cortical atrophy particularly involving the

					(small-scale)		frontal, parietal, and dorsal aspect of the temporal lobe
Van der Ham, 2010	A.C.	Primary evidence	Unable to recall information on the order of scenes as encountered in a newly learned virtual route	NA	–	Ischemic stroke	Right superior part of the parietal cortex (involving the medial occipital, the angular and a small part of the postcentral gyrus)
Van der Ham, 2010	W.J.	Primary evidence	Unable to couple places and actions for a newly learned virtual route	NA	–	Debulking of a brain tumor	Right occipital, temporal and superior parietal areas along with the fusiform gyrus and the hippocampus
Alemdar, 2008	—	Probable evidence	Learning a new route in the absence of visual cues that could serve as landmarks	+	–	TBI (closed head)	Left parahippocampal and bilateral occipital encephalomalasia (cerebral softening) and left temporal atrophy
Habib, 1987	1	Probable evidence	Impaired map drawing for a recently learned environment (hospital) and routes	NA	–	Ischemic stroke	Lesion in the right PCA territory compromising the most mesial part of the temporo-occipital gyri (parahippocampal/lingual gyri)
Osawa, 2006	—	Probable evidence	Incorrect description of a familiar route, problems with recalling the relationship between the rooms in his house and with learning the layout of the hospital ward	–	–	Subcortical hemorrhagic stroke	Lesion between the left forceps occipitalis and the parietal lobe, involving the left cingulate isthmus

Note. * Some cases have been marked as probable evidence of this category, because of absent formal tests for locations or unconvincing statistical findings. + = intact, ± = borderline, – = impaired, NA = not assessed, PCA = posterior cerebral artery, TBI = traumatic brain injury, VP = viewpoints.

Table 4

Case studies describing patients with navigation impairment as a consequence of another condition

<i>Report</i>	<i>Case</i>	<i>Primary condition*</i>	<i>Navigation deficits</i>	<i>Lesion type</i>	<i>Lesion site</i>
Bisiach, 1993	M.M.	Unilateral neglect	Incorrect route descriptions when left turns are included	Ischemic stroke	Territories of the right middle and posterior cerebral arteries
Bisiach, 1993	A.S.	Unilateral neglect	Incorrect route descriptions when left turns are included	Ischemic stroke	District of the right middle cerebral artery, partial sparing of parietal lobe and basal ganglia
Brain, 1941	5	Unilateral neglect	Incorrect route descriptions when left turns are included	Hemorrhagic stroke	Posterior half of the right cerebral hemisphere
Lin, 2000	—	Associative visual agnosia	Unable to describe a familiar route and became lost in the hospital ward	Ischemic strokes	Left occipital region, left cerebellum and most recently in the right PCA territory
Whitty, 1973	—	Lack of global spatial perception	Defective use of landmarks and impaired map drawing	Brain abscess	Right occipito-parietal areas
Fisher, 1982	1	Disorientation for place	Unable to trace familiar routes on a map and impaired map drawing	Ischemic stroke	Inferior right parieto-occipital region
Hanley, 1995	Mr. Smith	Global spatial disorientation	Impaired map drawing	Not reported	Not reported
Kase, 1977	M.V.V.	Global spatial disorientation	Unable to find back her room when placed in the hospital corridor	Hemorrhagic stroke	Bilateral softening of the parietal lobes, more on the left
Levine, 1985	2	Global spatial disorientation	Incorrect descriptions of familiar and new routes	Two hemorrhagic strokes	Bilateral parieto-occipital regions, more on the left
Stark, 1996	G.W.	Global spatial disorientation	Incorrect descriptions of the lay-out, floor plan and contents of her home	Progressive atrophy	Superior parietal lobules bilaterally
Wilson, 2005	M.U.	Global spatial disorientation	Impaired performance on topographical tasks relying on egocentric perspective	Repeated cardiac arrest and spinal infarcts	Bilateral occipito-parietal areas
Ciaramelli, 2008	L.G.	Working memory deficit	Unable to maintain (the intention to reach) the goal destination active in WM	Subarachnoid hemorrhagic stroke	Bilateral ventromedial prefrontal and rostral anterior cingulate cortices, more on the right

Note. * This column specifies the primary condition that causes the navigation problems of these cases. WM = working memory, PCA = posterior cerebral artery.