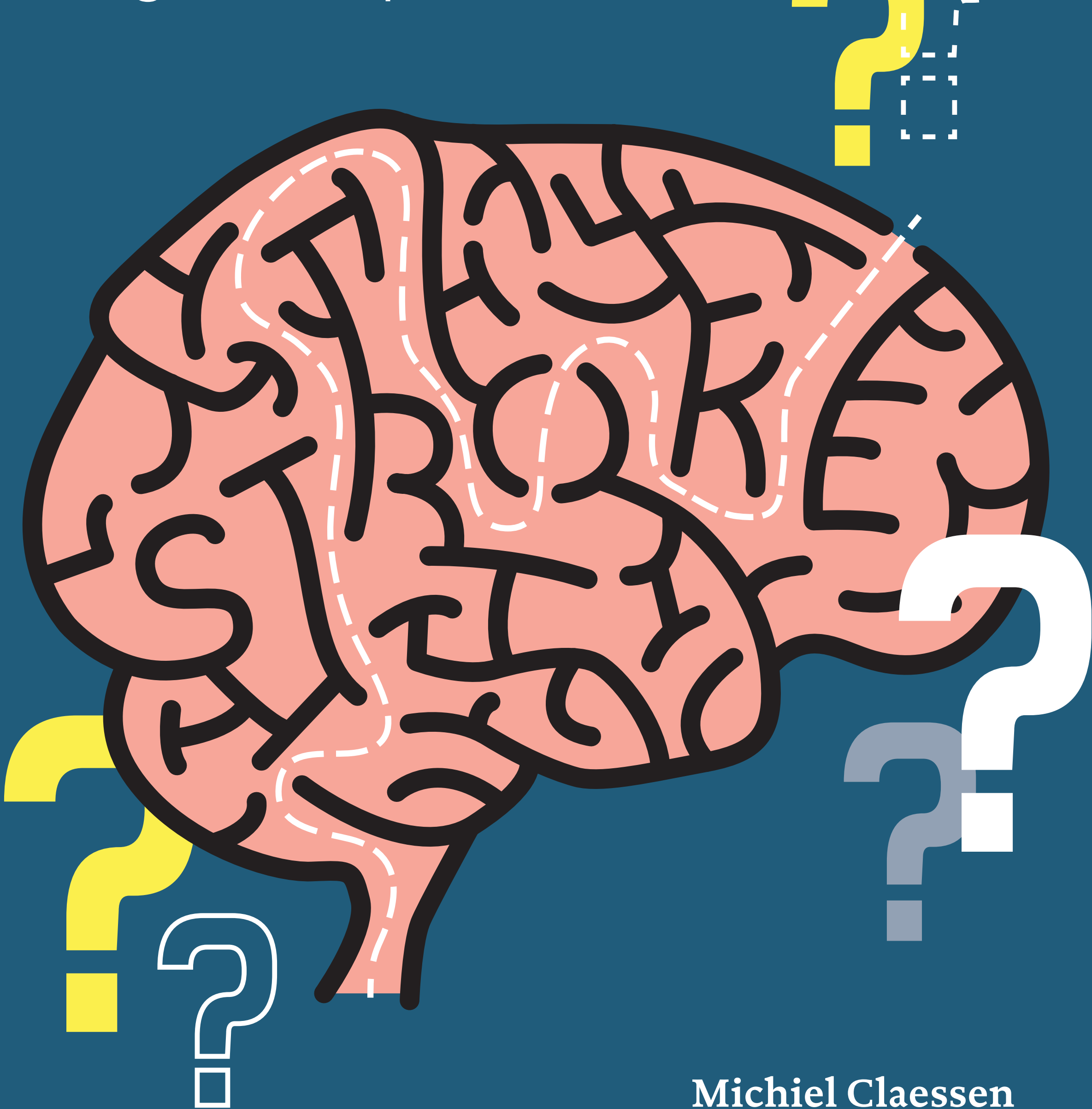
LOST AFTER STROKE:

Theory, assessment, and rehabilitation of navigation impairment



Michiel Claessen

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Lost after stroke:
Theory, assessment, and rehabilitation of navigation impairment

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(met een samenvatting in het Nederlands)

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te Tiel

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CONTENTS

CHAPTER 1

General introduction

GENERAL INTRODUCTION

> "In 1993, at the age of 44, I started having severe epileptic seizures. While I had been the keystone of a family of five children prior to this, the seizures gradually began to seriously hinder my daily life activities. This not only led to a divorce, as my husband found himself unable to cope with this new situation, but I also lost my job after a few years. In the meantime, it had become clear that antiepileptic drugs did not help in controlling the seizures. I was then advised to undergo neurological surgery with the aim to remove the focus of the seizures, which was, according to the doctors, located in the right side of my brain and the hippocampus in particular. In 2004, almost twelve years after the onset of the seizures, the surgery was performed and the seizures almost never reoccurred. While I felt relieved with this result, I was also faced with a new problem. I started to experience severe difficulties with finding my way around, particularly in environments I had never encountered before the surgery."

This quote is from patient Z.R., a now 66-year-old female who was brought to my attention by a colleague from the Neuropsychology department of the University Medical Center Utrecht. In my position as a PhD candidate with expertise in navigation ability, I was asked several times to contribute to the assessments of neurological patients with specific navigation problems. Patient Z.R. is by far the most fascinating case I have encountered. As she explains above, her right anterior-medial temporal lobe and hippocampus were surgically removed twelve years ago in an attempt to stop her intractable epilepsy. The direct effect of this treatment was a nearly absolute inability to learn new routes, while she experienced fewer problems in environments she was already familiar with. This impairment became strikingly apparent when she had to move, six years after the surgery, to a new apartment in a small town she had never lived in before. Over the past years, she has learned only a very limited set of fixed routes and still feels like a stranger in this town. Although she is not anxious to ask other people for directions, she still gets lost in her town and surrounding areas on numerous occasions. When she has to travel to locations not reachable by foot or by bike, a companion must support her. Evidently, this severe impairment in learning new routes has constricted her autonomy and mobility.

In this thesis, I aim to better understand the navigation problems that people with brain damage, such as patient Z.R., are faced with. In this introduction, I will first describe the two most influential models on the neurocognitive structure of navigation ability, which mainly derive from research in healthy individuals. After that, I will review the approach that neuropsychology has taken to the investigation of navigation ability. I will also highlight the ways in which this thesis, as an example of this neuropsychological approach, can contribute to the theory, assessment, and rehabilitation of navigation ability.

Neurocognitive architecture of navigation ability

The ability to find one's way around in both familiar and unfamiliar environments is essential for living an independent life. As we have seen in the report on patient Z.R., problems with navigation can severely affect this autonomy. A widely held view on navigation ability is that it depends on complex interactions between multiple cognitive systems and, thus involves a wide network of brain structures (Brunsdon, Nickels, & Coltheart, 2007; Wiener, Büchner, & Hölscher, 2009; Wolbers & Hegarty, 2010). Navigation involves the perception of spatial information that can be derived from various sensory systems, such as the visual, vestibular, and proprioceptive systems (Berthoz & Viaud-Delmon, 1999). This information allows one to generate and store spatial representations in short-term and long-term memory (Labate, Pazzaglia, & Hegarty, 2014; Ngo, Weisberg, Newcombe, & Olson, 2016; Weisberg & Newcombe, 2016). The resulting representations can subsequently be used for planning routes and guiding navigation behavior (Spiers & Maguire, 2006). Hence, many cognitive functions including visuospatial perception, (working) memory, mental imagery, attention, and executive functions contribute to navigation ability (Chrastil & Warren, 2012; Guariglia & Pizzamiglio, 2007; Wolbers & Hegarty, 2010). As regards the underlying brain areas, navigation researchers have mainly focused on posterior brain regions, such as the parietal lobe, the retrosplenial cortex, medial temporal lobe structures, and striatal systems (Burgess, 2008).

In the past decades, several models have been proposed to describe the underlying neurocognitive architecture of navigation ability. I will describe two prominent models in more detail. The first model concerns the distinction between egocentric and allocentric perspectives for the purpose of navigation (Klatzky, 1998), which has been highly influential in the spatial cognition literature. I will also introduce the landmark-route-survey (LRS) model of navigation, which states that three types of knowledge contribute to navigation (Siegel & White, 1975). These models have influenced theoretical thinking about navigation ability in general as well as guided research into and assessment of navigation ability in brain-damaged patients.

Egocentric and allocentric navigation

Navigation requires people to process the spatial characteristics of an environment and to store this information for later use. The processing of this information can be performed from an egocentric or allocentric perspective (Klatzky, 1998). Egocentric representations contain information about the position of locations with respect to the observer (e.g., "the supermarket is on my left"), while allocentric representations specify how locations are related to each other irrespective of the position of the observer (e.g., "the police station is north of the library"). This distinction was initially thought to be exclusive, but in more recent work researchers have indicated that egocentric and allocentric perspectives interact and play complementary roles

(Byrne, Becker, & Burgess, 2007). Burgess, Spiers, and Paleologou (2004) have also argued that a third process, named "egocentric updating", is of importance in this respect. This mechanism allows for updating of an egocentric viewpoint based on bodily movements.

Neuroscientific results support the distinction between egocentric and allocentric processing. While the former has been linked to parietal lobe activation, allocentric processing relies on activation in the hippocampus (Burgess, 2006, 2008). The link between allocentric representations and the hippocampus dates back to the Nobel prize winning research of John O'Keefe and colleagues in rodents (O'Keefe & Nadel, 1978). It has been shown that, both in rodents and humans, different groups of hippocampal cells are sensitive to coding of places, grids, boundaries, and heading direction. In cooperation, these cells allow for the generation of allocentric representations or "cognitive maps" of the environment (Burgess, Jackson, Hartley, & O'Keefe, 2000; Maguire, Burgess, & O'Keefe, 1999).

Landmark, route, and survey model

The LRS model states that three different types of knowledge contribute to navigation behavior: landmark, route, and survey knowledge (Siegel & White, 1975). This model was initially intended to describe the developmental stages that children go through when learning a new environment, but it has later been extrapolated to spatial learning in adults as well (Chrastil, 2013). In the first stage, people acquire information about landmarks or prominent features in the environment that can be used for orientation. After that, information about particular routes is learned allowing people to navigate along fixed paths. This route knowledge arises from forming associations between turns (actions) and particular landmarks or decision points (places). Navigation based on these place-action associations is, by definition, inflexible. In the last stage, people obtain what is called survey knowledge: configurational information of the environment as well as abstract information of metrical distances and angles. Survey knowledge enables one to navigate in a flexible way, as this type of environmental knowledge makes taking shortcuts and detours between locations possible. The distinct types of environmental knowledge in the LRS model have not encountered much criticism over the years, but its hierarchical organization has been challenged. Multiple lines of evidence indicate that the temporal organization of the LRS model is not as strict as was initially described (e.g., Ishikawa & Montello, 2006). The revised LRS model has therefore refrained from the hierarchical structure of the three representation types (Montello, 1998).

From a neurocognitive perspective, processing of landmark and scene information has been linked to activation of the parahippocampal place area (PPA), a functionally defined region involving the posterior parahippocampal cortex and the anterior lingual gyrus (Epstein, 2014). Route knowledge is supported by activation in the parietal cortex and the caudate nucleus, while survey knowledge is dependent on the hippocampus (Burgess, 2008).

It should be noted that some behavioral and neuroscientific overlap between the egocentric-allocentric navigation model and the LRS model exists. While landmark and route knowledge mainly concern information related to an egocentric or observer-based perspective, survey knowledge is usually associated with a bird's eye viewpoint which is related to an allocentric or environment-based perspective. Neuropsychological researchers have used these models to construct (ad hoc) test procedures with the aim of objectively assessing navigation problems in brain-damaged patients, as I will describe in the next section.

Neuropsychological research into navigation ability

The neuropsychological approach to the investigation of navigation ability can roughly be classified into two types of studies. On the one hand, neuropsychologists have studied individual patients with navigation problems in case reports. In the second type of study, groups of brain-damaged patients were the focal point. Both lines of study have contributed to our knowledge about navigation ability and associated impairments, but in different ways. I will first describe the contribution of case studies to navigation research, followed by a similar discussion of group studies.

The main aim of the case study approach has been to specify the types of impairments in navigation ability that cause these patients to experience difficulties with finding their way around. This is typically done by detailed assessment of cognitive functions and navigation ability in particular, for example, by large-scale navigation tasks based on environments that the patient was already familiar with before the onset of brain damage. In addition, this approach allows individual differences in navigation ability to be taken into consideration. In 1999, Aguirre and D'Esposito reviewed case studies on impairments in navigation ability and identified four types of "topographical disorientation": egocentric disorientation (an inability to represent locations with regard to the body), heading disorientation (an inability to derive directional information from landmarks), landmark agnosia (an inability to identify prominent features in the environment or to use these for orientation), and anterograde disorientation (an inability to learn new routes and environments). While their review has been cited many times, its influence has been mainly restricted to the clinical navigation literature. Also, many new case reports have been added to the navigation literature in the past two decades (e.g., Caglio, Castelli, Cerrato, & Latini-Corazzini, 2011; Ciaramelli, 2008; Mendez & Cherrier, 2003; Rainville et al., 2005; Rusconi, Morganti, & Paladino, 2008; Ruggiero, Frassinetti, Iavarone, & Iachini, 2014; Turriziani, Carlesimo, Perri, Tomaiuolo, & Caltagirone, 2003; van der Ham et al., 2010). Consequently, there seems to be a need for an updated inventory of the types of impairments in navigation ability reported. Ideally, the resulting model should not only be of clinical relevance, but also influence theoretical thinking. A model that connects theoretical and clinical perspectives of navigation ability is currently lacking.

Group studies in neurological patients have focused on exploring the brain-behavior relationships relevant to navigation ability. Patients with amnestic mild cognitive impairment (aMCI) and early stage Alzheimer's disease (AD) have been of particular interest in this respect. In its initial stages, AD is characterized by atrophy in the medial temporal lobe including the hippocampus and the entorhinal cortex (Jack et al., 1997) and later progresses to other brain structures (Braak & Braak, 1991). This leads to the hypothesis that aMCI and early stage AD patients show more difficulties with allocentric navigation, while egocentric navigation remains relatively intact. This assumption has indeed been confirmed and studies have revealed negative correlations between the extent of hippocampal damage and allocentric navigation performance (e.g., Hort et al., 2007; Kalová, Vlček, Jarolimová, & Bureš, 2005; Nedelska et al., 2012; Weniger, Ruhleder, Lange, Wolf, & Irle, 2009). This line of studies provides a clear neuropsychological illustration of establishing relationships between the functioning of the brain and navigation behavior.

Other researchers have been more interested in the clinical aspects, such as the prevalence, severity, and nature of impairments in navigation ability in various brain-damaged patient groups, including mild cognitive impairment (MCI) and Alzheimer's disease (AD; Pai & Jacobs, 2004; Pai & Lee, 2016), temporal lobe epilepsy (Bell, 2012; Pereira et al., 2011), traumatic brain damage (Livingstone & Skelton, 2007), and stroke (Busigny et al., 2014). Attention has mainly been devoted to the patient groups with relatively homogenous brain pathology (e.g., MCI and AD). In contrast, studies in stroke patients, who are by definition heterogeneous in terms of brain pathology, have been relatively scarce thus far. This is striking, as nearly one out of three stroke patients reports problems with navigation after their stroke event (van der Ham, Kant, Postma, & Visser-Meily, 2013). Further research into the occurrence and nature of navigation problems after stroke is thus clearly indicated.

Assessment of navigation ability

Over the years, many different tests have been used to objectively assess navigation ability in healthy and brain-damaged groups. Tests similar to the Route Learning Test (RLT) originally presented by Barrash, Damasio, Adolphs, and Tranel (2000) have been widely applied (e.g., Bell, 2012; Pereira et al., 2011). In this test, the examiner walks a specific route with the participant and upon return at the starting point the participant has to reproduce the studied route in three trials. Other authors have reported test procedures that address multiple aspects of navigation ability rather than using a single outcome measure. For example, van Asselen, Kessels and coworkers (2006) had their participants study a route and afterwards presented them with four navigation tasks: landmark recognition, landmark ordering, route reversal, and route drawing. As I have argued earlier in van der Ham & Claessen (2016; see Part 2), I much prefer the latter approach, as assessment instruments of navigation ability relying on multiple tasks take the cognitive complexity of navigation ability into consideration. Also, assessment of navigation ability should ideally be based on a theoretically guided model of its cognitive organization. This would lead to further integration of the different approaches to the study of navigation ability and facilitate both theoretical and clinical advancements.

In current neuropsychological practice, navigation ability is usually not dealt with in an explicit manner. Clinicians rarely ask for navigation problems in their intakes (van den Berg & Ruis, 2016) and objective assessment of navigation ability is uncommon. This might in part be related to the fact that presently no valid tests for navigation ability are available for use in clinical practice. Many navigation tests are unsuitable in this respect, as they are carried out in the real world and thus reliant on a particular environment or building. I therefore advocate the use of virtual reality techniques in the assessment of navigation ability. Virtual reality allows for strict control over the environment and prevents the influence of potentially disturbing factors (van der Ham, Faber, Venselaar, van Krefeld, & Löffler, 2015).

In addition to a widely applicable objective navigation test, clinical practice will also benefit from a screening instrument that helps in determining whether or not extensive testing of navigation ability is advisable. I think that the previously developed Wayfinding Questionnaire (WQ; van der Ham et al., 2013) is promising as a self-report instrument of navigation-related complaints. Further investigation of its validity and clinical utility is indicated prior to implementation in clinical practice.

Rehabilitation of impaired navigation ability

Research exploring possibilities of rehabilitation or training for impaired navigation ability is currently very limited. Only few reports have described (ad hoc) training procedures for rehabilitation of navigation impairment (Bouwmeester, van de Wege, Haaxma, & Snoek, 2015; Brooks et al., 1999; Davis & Coltheart, 1999; Incoccia, Magnotti, Iaria, Piccardi, & Guariglia, 2009; Kober et al., 2013; Rose, Attree, Brooks, & Andrews, 2001). Most of these reports have two setbacks in common. The procedures described in these studies were only applied in a single patient and therefore lack a systematic approach. Even more importantly, the main goal is usually to teach the patient a limited set of specific routes. A prominent approach in current cognitive rehabilitation is, however, to provide patients with knowledge and skills that allow them to compensate for their cognitive disabilities, for example by teaching them alternative strategies to solve particular types of tasks (Cicerone et al., 2011). In my view, such a compensatory approach can also be applied to the rehabilitation of navigation impairment. By teaching patients to use an alternative navigation strategy, they would be able to approach navigation tasks in a different way. Based on detailed assessment of navigation ability, the pattern of strengths and weaknesses within this ability could give insight into an appropriate alternative navigation strategy for each individual patient. I advocate that the feasibility of using virtual reality in this type of training procedure should be examined, as this technique allows for full control over the environment (Rose, Brooks, & Rizzo, 2005) and does not require physical movement. This latter advantage is of particular relevance to stroke patients as they commonly complain of fatigue (Schepers, Visser-Meily, Ketelaar, & Lindeman, 2006).

Thesis outline

The general objective of this thesis is to gain further insight into navigation ability after brain damage, with a primary focus on stroke patients in the chronic phase. I aim 1) to develop a model that describes the types of impairments in navigation ability that have been observed, 2) to provide instruments that can be used in clinical practice for the assessment of navigation ability, 3) to show that theoretical models on navigation ability can be helpful in guiding assessment, and 4) to introduce a new, compensatory approach to the rehabilitation of impaired navigation ability. The four parts of this thesis correspond to these specific aims.

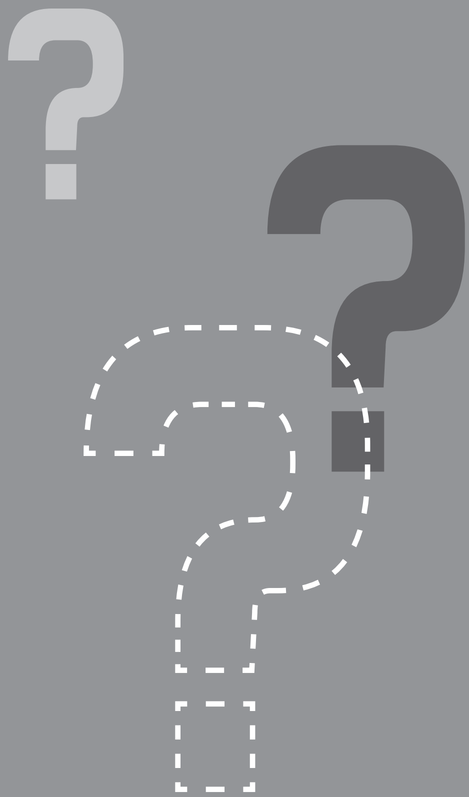
In Part 1, I aim to describe the types of impairments in navigation ability that have been reported in case reports on brain-damaged individuals. A systematic literature search was performed in *Chapter 2* to identify relevant case reports on navigation impairment, and to provide a model describing the types of impairments in navigation ability reported so far.

In the three chapters in Part 2, I focus on the development and validation of subjective and objective instruments that can be used in clinical practice to assess navigation ability. *Chapter 3* provides a first analysis of the Wayfinding Questionnaire (WQ) as a self-report instrument on navigation-related complaints. It can be used to determine whether additional assessment of navigation ability would be required. The focus in this chapter lies on investigation of the internal validity of the WQ in healthy respondents and chronic stroke patients, and on establishing a final version of the WQ. In *Chapter 4*, the discriminative validity and clinical utility of the WQ were studied. *Chapter 5* describes the validation of the Virtual Tübingen test battery, an objective assessment instrument for navigation ability. This was verified by directly comparing navigation performance on the Virtual Tübingen test battery and that on an equivalent real-world navigation test.

Part 3 of this thesis contains three studies in which I aim to unravel the nature of impaired navigation ability by taking a theory-driven approach to its assessment. In *Chapter 6*, navigation performance of chronic stroke patients on the Virtual Tübingen test battery was analyzed. *Chapter 7* describes the assessment of navigation ability in patient Z.R. mentioned earlier. In both chapters, assessment of navigation ability was guided by the model presented in Part 1. *Chapter 8* provides a systematic approach to verify a dissociation between spatial and spatiotemporal aspects of navigational knowledge which has previously been reported in a case study on two patients.

The chapter in Part 4 is devoted to the rehabilitation of impaired navigation ability. *Chapter 9* presents a study in which a novel approach to the rehabilitation of navigation impairment was explored in six chronic stroke patients. The aim was to instruct patients to adopt an alternative navigation strategy instead of having them learn particular routes. The feasibility of virtual reality in this rehabilitation approach was also subject of this study.

Finally, *Chapter 10* summarizes the main findings and conclusions of this thesis. This chapter follows the structure of the four parts described above. In addition, I will discuss possibilities of virtual reality techniques for assessment and rehabilitation of navigation ability. I will conclude by arguing that this thesis as a whole serves as a bridge between theoretical research and clinical practice.



PART 1

Types of navigation impairments

CHAPTER 2

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

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Author contributions:
MC and IH designed the study; MC performed the systematic literature search; MC and IH reviewed and interpreted the selected literature; MC drafted the paper; IH revised the paper for intellectual content.

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.

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 et al., 2007; Wiener et al., 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 et al., 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., 2000; van Asselen, Kessels 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 & Cherrier, 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.

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.

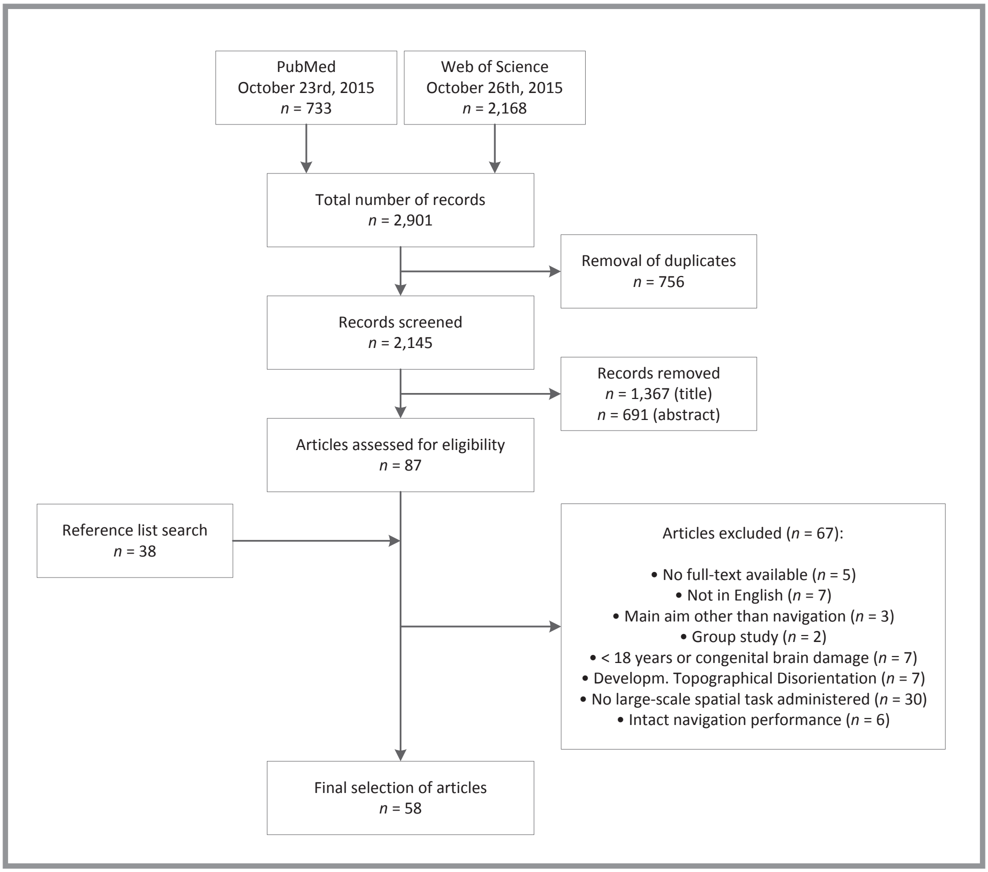


Figure 1. Flow diagram of the systematic literature search.

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.

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.

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.

Table 1. Landmark-based navigation impairment: case studies reporting neurological patients with problems related to processing of landmarks and scenes.

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

Hécaen et al. (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 et al. (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 et al. (2007), Hartley et al. (2007)	R.H.	3, primary evidence	+	–	Probable ischemic stroke	Right hippocampus
Maguire et al. (2006)	T.T.	3, primary evidence	+	–	Limbic encephalitis	Generalized atrophy primarily implicating the hippocampi
Rusconi et al. (2008)	R.G.	3, primary evidence	+	–	Hemorrhagic stroke	Right temporo-occipital lobe with ventricular flooding
Takahashi & Kawamura (2002)	1	3, primary evidence	+	–	Ischemic stroke	Right medial temporal lobe
Epstein et al. (2001)	G.R.	4; inability to encode new scene-like spatial layouts	+	–	Two ischemic stroke events	Right occipital-temporal lobe
Epstein et al. (2001)	C.O.	4; inability to encode new scene-like spatial layouts	+	–	Ischemic stroke	Right occipital and mesial temporal lobe
Mendez & Cherrier (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.

2

A similar pattern of impairments in the processing of famous/familiar and new landmarks was found in the patient reported by Incisa della Rocchetta and colleagues (1996), and cases 2–4 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 Cherrier'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 & Cherrier, 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.

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 (see Table 2).

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 Path-based navigation impairment.

Further primary evidence for location-based navigation impairment is provided by ten case reports (N. 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.

Table 2. Location-based navigation impairment: case studies reporting neurological patients with defective knowledge of locations or problems in acquiring this knowledge.

Report	***Case***	***Type of evidence****	***Navigation deficit***	***Familiar settings***	***Novel settings***	***Lesion type***	***Lesion site***
N. Burgess et al. (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 et al. (2011)	—	Primary evidence	Impaired pointing to landmarks and map drawing	–	NA	Ischemic stroke	Right mesial occipito-temporal region
Descloux et al. (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 et al. (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 et al. (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 et al. (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 et al. (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, probably due to deficits in spatial memory and spatial processing	–	–	Hemorrhagic stroke	Unilateral lesion involving the left parahippocampal gyrus, the posterior cingulate gyrus and the precuneus
Morganti et al. (2008), Rusconi et al. (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 et al. (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 et al. (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 et al. (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 et al. (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 & Coltheart (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 et al. (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 et al. (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 & Sirigu (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 et al. (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.

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. N. 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 (Descloux 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 perceptional 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.

Path-based navigation impairment

The third category of navigation impairment is comprised of thirteen patients (twelve papers; see Table 3) 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

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., 2008), these reports are interpreted as probable evidence for path-based navigation impairment.

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.

Report	***Case***	***Type of evidence****	***Navigation deficit***	***Familiar settings***	***Novel settings***	***Lesion type***	***Lesion site***
Bottini et al. (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 et al. (1980)	A.R.	Primary evidence	Impaired map use with identical landmarks only	+	–	Ischemic stroke	Right occipital lobe
Hublet & Demeurisse (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 et al. (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 et al. (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 et al. (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 et al. (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 et al. (2003)	—	Primary evidence	Unable to learn new paths (small-scale test) in the absence of landmarks	+	– (small-scale)	Heroin overdose	Marked atrophy of the hippocampi bilaterally, moderate cortical atrophy particularly involving the frontal, parietal, and dorsal aspect of the temporal lobe
van der Ham et al. (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 et al. (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 et al. (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 & Sirigu (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 et al. (2008)	—	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.

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.

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 (see Table 4).

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.

Table 4. Case studies describing patients with navigation impairment as a consequence of another condition.

Report	***Case***	***Primary condition****	***Navigation deficits***	***Lesion type***	***Lesion site***
Bisiach et al. (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 et al. (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 & Pai (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 & Newcombe (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 & Davies (1995)	Mr. Smith	Global spatial disorientation	Impaired map drawing	Not reported	Not reported
Kase et al. (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 et al. (1985)	2	Global spatial disorientation	Incorrect descriptions of familiar and new routes	Two hemorrhagic strokes	Bilateral parieto-occipital regions, more on the left
Stark et al. (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 et al. (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.

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).

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.

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.

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., 1977) 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).

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.

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.

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.

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.

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 Turennout, 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 et al., 2006). This functional distinction is further supported by anatomical evidence (Baldassano et al., 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.

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 (N. 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 et al., 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 et al., 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.

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.

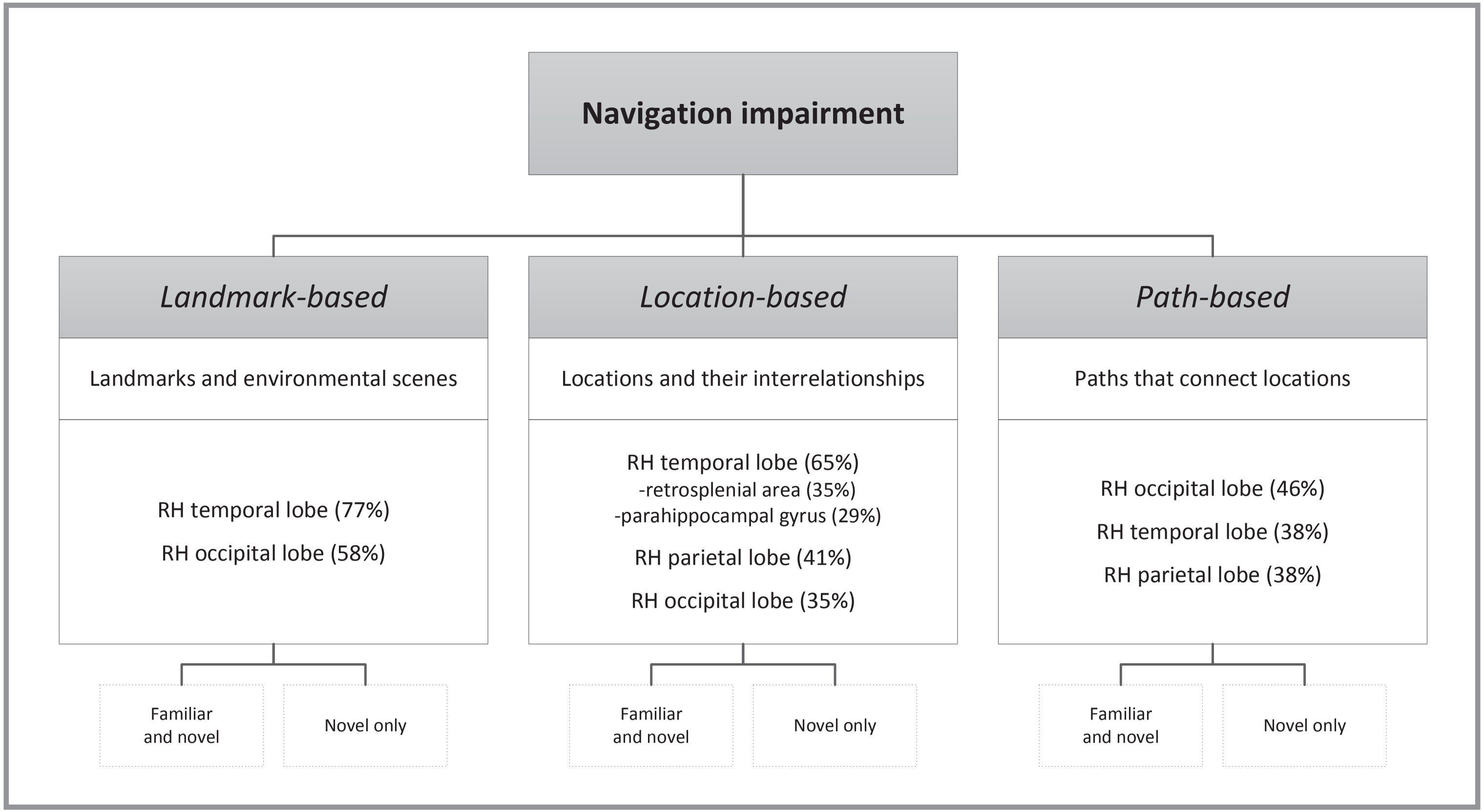


Figure 2. The three main types of navigation impairment as identified in this review.
Note. RH = right hemisphere

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 et al., 2011; Maguire et al., 1997), but more widespread activation in an occipito-temporal network in a landmark ordering task has also been reported (Nemmi, Piras 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 et al., 2008; Iaria et al., 2003; Marchette et al., 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.

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 Rocchetta 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, 2011), and rely on neural circuits that are partly independent (Nemmi, Boccia et al., 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.

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.

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 et al., 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 et al., 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 et al., 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).

CONCLUSION

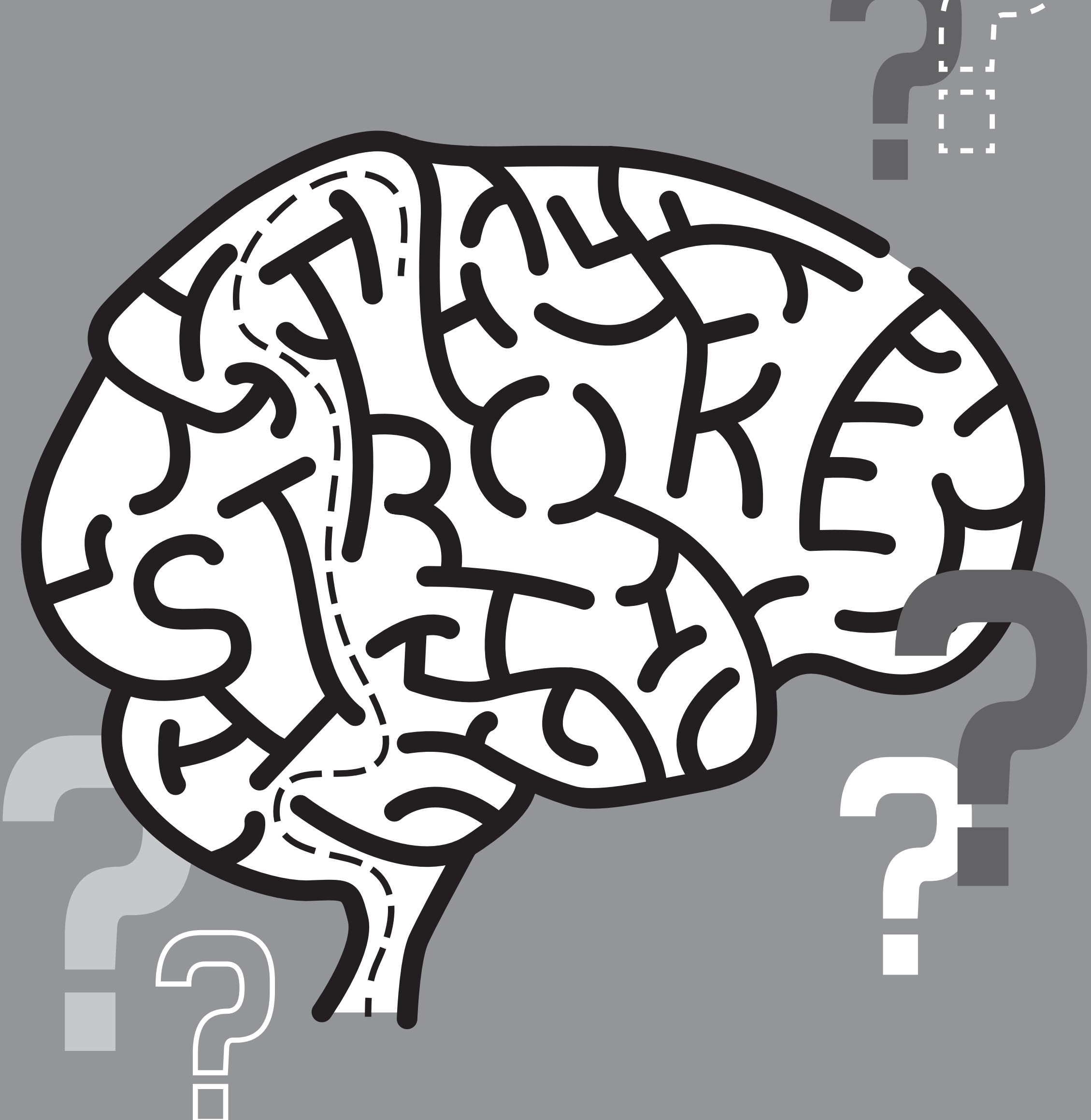
Systematic inventory of neuropsychological case studies investigating the nature of navigation impairment has led to the identification of three main types of underlying deficits. Navigation impairment can be classified into defects of landmark, location and path knowledge (see Figure 2). These deficits 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.

Appendix A: Electronic search strategies

Database	***Search strategy***
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

PART 2

Development and validation of assessment instruments



CHAPTER 3

The Wayfinding Questionnaire as a self-report screening instrument for navigation-related complaints after stroke: Internal validity in healthy respondents and chronic mild stroke patients

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Author contributions:
IH and JV designed the study; MC and IH collected and processed the data; MC analyzed the data; MC, IH, JV, NK, and AP interpreted the data; MC drafted the paper; IH, JV, NK, and AP revised the paper for intellectual content.

ABSTRACT

Objective: In current stroke care, cognitive problems are usually diagnosed in a stepwise manner. More specifically, screening instruments are first applied to support healthcare professionals in deciding whether a second step (an extensive assessment) would be appropriate. None of the existing screening instruments, however, takes navigation ability into account. This is problematic, as navigation impairment after stroke has been shown to be common, more so than previously thought. The Wayfinding Questionnaire (WQ) is therefore presented as a screening instrument for navigation-related complaints after stroke. The internal validity of the WQ was investigated in two samples of participants to establish the final version.

Method and Results: In Study 1, the WQ was administered in a representative sample of 356 healthy participants. Its factor structure was investigated using a principal component analysis. This procedure resulted in deletion of four items and revealed a three-factor structure: "Navigation and Orientation," "Spatial Anxiety," and "Distance Estimation". In Study 2, a confirmatory analysis was performed to directly verify the factor structure as obtained in Study 1 based on data of 158 chronic mild stroke patients. Fit indices of the confirmatory analysis indicated acceptable model fit. The reliability of the three subscales was found to be very good in both healthy participants and patients.

Conclusions: These studies allowed us to determine the final version of the WQ. The results indicated that the WQ is an internally valid and reliable instrument that can be interpreted using a three-factor structure in both healthy respondents and chronic mild stroke patients.

INTRODUCTION

In the past decades, the neuropsychological literature has consistently reported that cognitive impairment is commonly observed after stroke and might affect up to 50% of stroke patients (e.g., Duits, Munnecom, van Heugten, & van Oostenbrugge, 2008). This finding is reason for concern, as the presence of cognitive impairment has been associated with a negative influence on the outcome as well as with significant functional problems in daily life (e.g., Galski, Bruno, Zorowitz, & Walker, 1993; Zinn et al., 2004). It is thus vitally important to adequately assess cognitive problems after stroke, given that the information obtained from the assessment can contribute to the rehabilitation treatment, for instance in establishing the treatment strategy or in providing advice to patients and their caregivers (Duits et al., 2008). It should, however, also be noted that an extensive cognitive assessment is a rather costly and time-consuming procedure that might not be required for all stroke patients.

To achieve efficiency in stroke care, cognitive problems in stroke patients are usually assessed in two stages. Screening instruments are applied in the first stage to obtain an indication of the cognitive complaints that patients have. These instruments are meant to support healthcare professionals in deciding whether or not it would be advisable to refer a patient for a detailed cognitive assessment (i.e., for the second assessment stage). As an example of such a screening instrument, the CLCE-24 has been developed as a checklist for the detection of cognitive and emotional problems after stroke and is suitable to be used by healthcare professionals other than the trained (neuro)psychologist (van Heugten, Rasquin, Winkens, Beusmans, & Verhey, 2007). Obviously, screening instruments are intended to be quick to administer, low in costs and require limited effort of the patient.

Screening instruments, such as the CLCE-24, cover a broad range of cognitive domains to be as sensitive as possible to cognitive complaints that are known to be common after stroke. None of the existing screening instruments, however, takes into account the ability to navigate. This is striking, as adequate navigation ability is crucial for engaging in the instrumental daily life activities that allow for independent functioning in the community (McCusker, Bellavance, Cardin, & Belzile, 1999). For instance, we usually drive from home to the office in the morning. At the end of the day, we have to stop by the supermarket to buy the ingredients for dinner on the way home and we might go out to visit a friend who lives in another part of the city in the evening. People are thus required to find their way around to be able to participate in such activities.

A series of recent group and case studies has convincingly shown that brain damage resulting from stroke may have detrimental effects on the ability to navigate (e.g., Busigny et al., 2014; Claessen, Visser-Meily, de Rooij, Postma, & van der Ham, 2016a; Ino et al., 2007; Mendez & Cherrier, 2003; van Asselen, Kessels et al., 2006; van der

Ham et al., 2010). Using self-report measures, it has even been found that complaints about the ability to navigate are relatively common after mild stroke (± 29%; van der Ham et al., 2013). All of these findings indicate that navigation ability might generally be neglected in stroke care, given the fact that adequate screening instruments for the detection of complaints about navigation impairment are currently lacking. The goal of the current paper is therefore to present a short but comprehensive self-report screening instrument of navigation-related complaints that can be used in clinical practice to decide whether formal testing of navigation ability is appropriate. If so, an objective navigation test could be applied to determine the presence and severity of the navigation impairment (see for various examples: Arnold et al., 2013; Barrash, Damasio, Adolphs, & Tranel, 2000; Claessen, Visser-Meily, de Rooij et al., 2016a; Maguire, Burke, Phillips, & Staunton, 1996).

The Wayfinding Questionnaire (WQ), as presented by van der Ham, Kant, Postma, and Visser-Meily (2013), appears to be the perfect starting point for the development of a screening instrument of navigation-related complaints. Although the WQ has been used as a self-report instrument of navigation ability in mild stroke patients before, it has not yet been investigated in terms of its psychometric properties. The WQ was initially designed to account for the cognitive complexity that characterizes navigation behavior (Brunsdon, Nickels, & Coltheart, 2007; Wiener, Büchner, & Hölscher, 2009; Wolbers & Hegarty, 2010) and therefore includes items concerning navigation (strategy), mental transformation, distance estimation, orientation, and sense of direction (see Table 1). Moreover, the WQ also takes the emotional aspects of navigation behavior, that is, “spatial anxiety”, into account. Spatial anxiety denotes anxious feelings related to performing navigation tasks (Lawton, 1994, 1996) and worrying about getting lost (Schmitz, 1997). Spatial anxiety is a highly relevant concept in the context of navigation, as higher levels have been associated with less adequate and efficient navigation behavior (Walkowiak, Foulsham, & Eardley, 2015).

To summarize, our purpose was to investigate the psychometric properties of the WQ (van der Ham et al., 2013) with the aim to establish it as a short but comprehensive screening instrument for navigation-related complaints after stroke. As such, the WQ could help healthcare professionals in determining whether or not objective testing of navigation ability is warranted. As a first step in the validation process, the WQ was submitted to a careful analysis of its internal validity (i.e., factor structure and reliability) in a series of two studies in the current paper.

STUDY 1: FACTOR STRUCTURE AND RELIABILITY OF THE WQ IN A HEALTHY SAMPLE

METHOD

Participants

In this study, data of 356 healthy participants (185 female, 52%) with a mean age of 48.0 years (*SD* = 11.2; range = 18–87) were used for analysis. The majority of these data were extracted from databases of a number of other experiments (manuscripts in preparation) in which we had asked healthy people to complete the WQ. Furthermore, the remaining participants were recruited specifically for this study by the experimenters in several ways (e.g., via social media, word of mouth, and our acquaintances). Their mean educational level was 5.8 (*SD* = 1.0; range = 2–7) based on the classification system by Verhage (1964; possible range: 1 = 'primary level education' to 7 = 'finished university level education'). The assessment of the WQ was performed manually (paper-and-pencil) or digitally after the participant had signed an informed consent form. The study procedures satisfied the regulations as set by the local ethical review board and the Helsinki Declaration.

The Wayfinding Questionnaire

The WQ contains the 26 items as displayed in Table 1 (van der Ham et al., 2013). The 26 items (in Dutch) were manually selected from a more extensive questionnaire (Bosch & Postma, unpublished thesis) consisting of 106 items. The construction of this extensive questionnaire was based on literature review of all domains relevant to *general* spatial ability. With the literature in mind, six domains were identified as relevant to general spatial ability: mental transformation, mental imagery, angle/distance estimation, orientation ability, navigational strategies, and spatial anxiety. In the next step, items were adapted from existing questionnaires (e.g., Blajenkova, Kozhevnikov, & Motes, 2006; Hegarty, Montello, Richardson, Ishikawa, & Lovelace, 2006; Hegarty, Richardson, Montello, Lovelace, Subbiah, 2002; Lawton, 1994; Lawton & Kallai, 2002; Pazzaglia, Cornoldi, & De Beni, 2000; Schmitz, 1997) or newly developed to cover the six domains that were judged to be relevant to spatial ability. The selection of items for inclusion in the WQ was based on whether the item addressed large-scale spatial ability and not on the theoretical construct it covered. Further expert and non-expert review was conducted to ensure clarity of the items. Based on this approach, no constraints are likely to be imposed on the latent factors of the WQ.

The selected 26 items concerned questions about navigation (e.g., "I can effortlessly walk back a route I have never walked before, the same way I walked up"), orientation (e.g., "I can orient myself well"), mental transformation (e.g., "While reading a map, I constantly turn the map into the direction that I am going"), distance estimation (e.g., "I am good at estimating distances (e.g., from myself to a building I can see)"), and sense of direction (e.g., "I have a good sense of direction"). A number of items on spatial anxiety (e.g., "I am afraid to lose my way somewhere") were also included. Items were formulated as statements and could be answered on a 7-point Likert scale, ranging from 1 ("not applicable to me at all") to 7 ("totally applicable to me"). Items 14, 15, and 16, however, were formulated as questions and scores of 1 to 7 represented "not uncomfortable at all" to "very uncomfortable," respectively. With the exception of Item 5 and the spatial anxiety items, the WQ-items were stated such that a higher score would reflect higher navigation ability.

Statistical analysis

Scores of Item 5 and the spatial anxiety items (Items 10–17) were reversed, such that a high score reflected high ability and low anxiety. Subsequently, descriptive statistics and skewness values were calculated. Skewness was considered to be present if this measure was below –1.0 or above +1.0.

A factor analysis (i.e., principal component analysis; PCA) was then conducted on the questionnaire scores. This is a common approach to reveal the underlying domain structure and verify item redundancy (Pett, Lackey, & Sullivan, 2003). Prior to the actual analysis, data appropriateness for this statistical procedure was established by addressing the correlation matrix using the following criteria. Firstly, mean correlations between items should be >0.30 and <0.80. The Kaiser-Meyer-Olkin (KMO) statistic as a sample adequacy measure for factor analysis should exceed .70 (Hutcheson & Sofroniou, 1999) and individual KMO statistics should also be >0.70. Lastly, Barlett's test of sphericity should be significant ($p < .05$), to indicate that the correlations between the items are sufficiently large for factor analysis.

The actual PCA was then applied to reveal the underlying factor structure of the WQ. The number of factors was determined based on the eigenvalues; factors with an eigenvalue higher than 1.0 were retained. The proposed factor structure was exposed to an oblique (oblimin) rotation to facilitate factor interpretation. An oblique rotation technique was used to allow factors to be correlated, as the WQ-items measured different aspects of the concept of navigation ability but not concepts that are expected to be unrelated. Factor loadings of >0.40 were defined as reflecting a meaningful relationship between the particular item and a given factor.

The reliability of the questionnaire was assessed by calculating the internal consistency (Cronbach's α) of the subscales. Reliability scores between 0.70 and 0.80 are interpreted as good, whereas scores above 0.80 reflect very good reliability (DeVellis, 1991). However, reliability scores exceeding 0.95 might indicate item redundancy (Terwee et al., 2007). Internal consistency was also assessed by correlating the mean scores on the subscales with the other subscales and the mean total score.

Lastly, the relationship between subscale scores and three demographical variables were investigated: gender (independent t-tests), age, and educational level (Pearson correlations). Alpha level was set to 0.05. The statistical procedures were conducted using IBM SPSS Statistics version 22.

RESULTS AND DISCUSSION

Descriptives of the WQ

Descriptive statistics of the WQ are provided in Table 1. None of the items suffered from substantial skewness (only Items 4 and 17 slightly exceeded the value of –1.0).

Factor analysis

Mean inter-item correlations ranged from 0.20 to 0.54, but only the mean inter-item correlation of Item 5 did not reach the criterion of >0.30. The KMO measure of sample adequacy was 0.945; very good and well above the criterion of >0.70. Individual KMO values of sampling adequacy ranged from 0.890 to 0.975. Barlett's test of sphericity was significant, χ^2 (325) = 6912.09, $p < .001$, indicating that the correlations between the items were sufficiently high for PCA. Given the above, Item 5 was removed from further analyses.

The PCA was conducted on the remainder of the WQ-items. Three factors with an eigenvalue higher than 1.0 were retained, commonly explaining 62.5% of the variance. The initial factor structure was subjected to an oblimin rotation to facilitate factor interpretability. Table 2 displays the factor loadings of the WQ-items on the rotated three-factor structure. No items showed substantial cross-loadings (i.e., all items loaded above 0.40 on a single factor), which further supports the validity of the three-factor structure. The first factor ("Navigation and Orientation") consisted of fourteen items addressing several cognitive aspects of navigation ability, such as pointing ability (e.g., Item 2), orientation (e.g., Item 8), and sense of direction (e.g., Item 25). All spatial anxiety items loaded on the second factor ("Spatial Anxiety"). Lastly, three items addressing estimation of distances commonly loaded on the third factor ("Distance Estimation").

Table 1. Descriptive statistics (means, standard deviations (*SDs*), and skewness) for all 26 items of the Wayfinding Questionnaire (WQ) based on the responses of a group of 356 healthy participants.

	Item	***Mean***	***SD***	***Skewness***
1.	I can effortlessly walk back a route I have never walked before, the same way I walked up.	4.68	1.73	–0.57
2.	When I am in a building for the first time, I can easily point to the main entrance of this building.	4.48	1.70	–0.53
3.	If I see a landmark (building, monument, intersection) multiple times, I know exactly from which side I have seen that landmark before.	5.07	1.62	–0.82
4.	In an unknown city I can easily see where I need to go when I read a map on an information board.	5.30	1.67	–1.05
5.	While reading a map, I constantly turn the map into the direction that I am going.	3.49	2.12	0.44
6.	Without a map, I can estimate the distance of a route I have walked well, when I walk it for the first time.	4.32	1.58	–0.43
7.	I can estimate well how long it will take me to walk a route in an unknown city when I see the route on a map (with a legend and scale).	4.47	1.55	–0.66
8.	I can always orient myself quickly and correctly when I am in an unknown environment.	4.54	1.64	–0.53
9.	I always want to know exactly where I am (meaning, I am always trying to orient myself in an unknown environment).	5.04	1.65	–0.84
10.	I am afraid of losing my way somewhere.	5.15	1.72	–0.89
11.	I am afraid of getting lost in an unknown city.	5.17	1.75	–0.81
12.	In an unknown city, I prefer to walk in a group rather than by myself.	4.98	1.85	–0.70
13.	When I get lost, I get nervous.	4.71	1.85	–0.48
	How uncomfortable are you in the following situations (Items 14, 15, and 16):			
14.	Deciding where to go when you are just exiting a train, bus, or subway station.	4.92	1.57	–0.45
15.	Finding your way in an unknown building (e.g., a hospital).	5.11	1.45	–0.59

16.	Finding your way to a meeting in an unknown city or part of a city.	4.42	1.72	–0.20
17.	I find it frightening to go to a destination I have not been before.	5.49	1.72	–1.09
18.	I can usually recall a new route after I have walked it once.	4.50	1.75	–0.41
19.	I am good at estimating distances (e.g., from myself to a building I can see).	4.52	1.59	–0.52
20.	I can orient myself well.	4.89	1.66	–0.76
21.	I am good at understanding and following route descriptions.	5.19	1.47	–0.91
22.	I am good at giving route descriptions (meaning, explaining a known route to someone).	5.02	1.40	–0.75
23.	When I exit a store, I do not need to orient myself again to determine where I have to go.	4.81	1.73	–0.58
24.	I enjoy taking new routes (e.g., shortcuts) to known destinations.	4.88	1.83	–0.67
25.	I have a good sense of direction.	4.78	1.88	–0.71
26.	I can easily find the shortest route to a known destination.	4.85	1.68	–0.67

Note. Scores on the Spatial Anxiety scale were reversed such that high values represent lower spatial anxiety and thus higher navigation ability. *SD* = Standard deviation.

3

Table 2. Factor loadings for the Principal Component Analysis of the Wayfinding Questionnaire (WQ) items (i.e., the pattern matrix) based on the responses of 356 healthy participants.

	Item	***Factor 1***	***Factor 2***	***Factor 3***
1.	I can effortlessly walk back a route I have never walked before, the same way I walked up.	0.856		
2.	When I am in a building for the first time, I can easily point to the main entrance of this building.	0.770		
3.	If I see a landmark (building, monument, intersection) multiple times, I know exactly from which side I have seen that landmark before.	0.750		
4.	In an unknown city I can easily see where I need to go when I read a map on an information board.	0.450		
6.	Without a map, I can estimate the distance of a route I have walked well, when I walk it for the first time.			0.796
7.	I can estimate well how long it will take me to walk a route in an unknown city when I see the route on a map (with a legend and scale).			0.867
8.	I can always orient myself quickly and correctly when I am in an unknown environment.	0.753		
9.	I always want to know exactly where I am (meaning, I am always trying to orient myself in an unknown environment).	0.612		
10.	I am afraid of losing my way somewhere.		0.847	
11.	I am afraid of getting lost in an unknown city.		0.873	
12.	In an unknown city, I prefer to walk in a group rather than by myself.		0.734	
13.	When I get lost, I get nervous.		0.859	
	How uncomfortable are you in the following situations (Items 14, 15, and 16):			
14.	Deciding where to go when you are just exiting a train, bus, or subway station.		0.724	
15.	Finding your way in an unknown building (e.g., a hospital).		0.712	
16.	Finding your way to a meeting in an unknown city or part of a city.		0.701	

17.	I find it frightening to go to a destination I have not been before.		0.810	
18.	I can usually recall a new route after I have walked it once.	0.841		
19.	I am good at estimating distances (e.g., from myself to a building I can see).			0.788
20.	I can orient myself well.	0.798		
21.	I am good at understanding and following route descriptions.	0.631		
22.	I am good at giving route descriptions (meaning, explaining a known route to someone).	0.482		
23.	When I exit a store, I do not need to orient myself again to determine where I have to go.	0.750		
24.	I enjoy taking new routes (e.g., shortcuts) to known destinations.	0.507		
25.	I have a good sense of direction.	0.899		
26.	I can easily find the shortest route to a known destination.	0.771		

Note. Only factor loadings higher than .4 are shown.

3

Reliability analysis (internal consistency)

Cronbach's α was found to be very high (0.922) for the Spatial Anxiety subscale (8 items) as well as for the three items of the Distance Estimation subscale (Cronbach's α = 0.830). Cronbach's α of the Navigation and Orientation subscale was also very high (0.947), but such a high Cronbach's α-value (i.e., around or exceeding 0.95) may indicate item redundancy within the scale. Therefore, Pearson correlations were calculated between Navigation and Orientation items and we screened for correlations higher than 0.80. Correlations between three item-pairs exceeded this criterion: Item 1 and 2 (0.842), Item 8 and 25 (0.803) and Item 20 and 25 (0.834). Consequently, Items 1, 20, and 25 were removed. Item 1 was removed because of its conceptual similarity to Item 18. In respect of the other two pairs, Items 8, 20, and 25 were conceptually very similar (i.e., orientation and sense of direction). Item 8 was retained because it had the lowest skewness value. Cronbach's α had now slightly decreased to 0.921. Internal consistency was still very high, but no longer approaching 0.95. Therefore, 11 items were retained in the Navigation and Orientation subscale.

Further assessment of internal consistency revealed significant weak to moderate correlations between mean subscale scores: Navigation and Orientation and Distance Estimation (r = 0.648, p < .001), Navigation and Orientation and Spatial Anxiety (r = 0.510, p < .001) and Distance Estimation and Spatial Anxiety (r = 0.382, p < .001). Subscale scores were also strongly and significantly correlated with the total score: Navigation and Orientation (r = 0.867, p < .001), Spatial Anxiety (r = 0.774, p < .001) and Distance Estimation (r = 0.824, p < .001).

Relationship with demographical variables

Women scored lower on all three WQ-subscales than men (see Table 3). Because equality of variances could not be guaranteed for the subscales Navigation and Orientation and Distance Estimation (Levene's test: both p's < .001), corrections of degrees of freedom were applied to these tests. Subscale scores were not related to age and educational level, except for two weak positive correlations between Navigation and Orientation and age (r = 0.132, p = .013) and Spatial Anxiety and educational level (r = 0.156, p = .003).

Table 3. Comparison of the mean scores on the three WQ-subscales scores for female and male healthy participants.

Subscale	Females (n = 185)	Males (n = 171)	*t*-value	*p*-value	Effect-size *r*
Navigation and Orientation	4.49 (1.31)	5.35 (1.02)	–6.97	< .001	0.35
Spatial Anxiety	4.58 (1.38)	5.44 (1.23)	–6.18	< .001	0.31
Distance Estimation	3.78 (1.37)	5.15 (0.93)	–11.11	< .001	0.52

Note. Standard deviations are displayed between parentheses. Scores on the Spatial Anxiety scale were reversed such that high values represent lower spatial anxiety and thus higher navigation ability.

3

Interim summary of Study 1

The internal validity of the WQ was verified in a large group of healthy people. The final version comprised 22 of the original 26 items, divided over three subscales: Navigation and Orientation (11 items), Spatial Anxiety (8 items), and Distance Estimation (3 items). All subscales were characterized by very good internal consistency, weakly to moderately correlated to the other subscales, and strongly related to the total WQ-score.

STUDY 2: CONFIRMATORY FACTOR ANALYSIS OF THE WQ IN MILD STROKE PATIENTS

METHOD

Participants, Materials, and Procedure

Participants were chronic mild stroke patients who had visited the rehabilitation clinic of De Hoogstraat Revalidatie or the rehabilitation department of the University Medical Center Utrecht (Utrecht, the Netherlands) between 2007 and 2012. These inclusion criteria were applied: first or recurrent stroke, age 18 years or older, at least six months since first stroke event, and living at home after rehabilitation. Reasons for exclusion from participation in the study were the following: unable to communicate in Dutch, severe global aphasia, and severe mobility problems (i.e., patients had to be able to walk or bike outside without supervision). In total, 158 patients agreed to participate (by signing an informed consent form) and were sent and requested to complete the 26-item-version of the WQ (see Study 1). The patient group (64 female; 40.5%) had a mean age of 60.1 years (SD = 13.1, range = 22–96). Further breakdown of participants into age categories reveals the distribution as presented in Figure 1. Mean educational level in the patient sample was 5.2 (*SD* = 1.4, range = 2–7; Verhage, 1964). Stroke characteristics are presented in Table 4. Time since the most recent stroke event was 40.5 months on average (*SD* = 25.6, range = 5–195). This information was available for 140 patients. The study protocol complied with the Helsinki Declaration and was approved by the medical ethical committee of the University Medical Center Utrecht (no. 12-198).

Table 4. Stroke characteristics (type and location) of the patient group (*n* = 158).

	***n* (%)**
Stroke type	
Ischemic stroke	110 (69.6%)
Hemorrhagic stroke	
- Intracerebral	27 (17.1%)
- Subarachnoid	4 (2.5%)
Missing	17 (10.8%)
Stroke location	
Supratentorial region	
- Left	64 (40.5%)
- Right	53 (33.5%)
- Bilateral	2 (1.3%)
Infratentorial region	
- Left	8 (5.1%)
- Right	3 (1.9%)
- Bilateral	9 (5.7%)
Missing	19 (12.0%)

Note. Patients are classified based on the stroke characteristics of their first stroke event. Twelve patients (7.6%) suffered from two stroke events; three patients (1.9%) suffered from three stroke events.

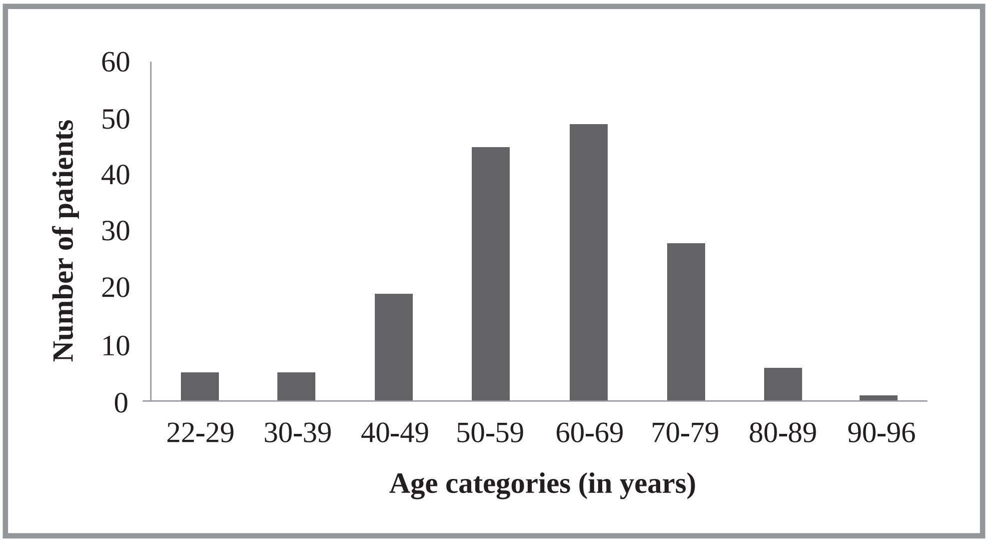


Figure 1. Distribution of mild stroke patients over age categories.

Statistical analysis

Only the 22 items of the validated version of the WQ (see Study 1) were taken into account in this study. The spatial anxiety items (Items 10–17) were reversed, such that a high score reflects high ability and low anxiety. Eight missing scores due to ambiguous responding (0.2% of the total number of data points) were substituted with the patient's median score. The missing scores occurred in six patients (3.8% of the total sample), more specifically, four patients had one and two patients had two missing scores.

A confirmatory factor analysis (CFA – a structural equation modeling approach) was applied to verify the three-factor structure of the WQ as found in healthy participants (see Study 1) in chronic mild stroke patients. This technique enables testing the model fit of a dataset to a specific factor structure of observed (or manifest) and underlying latent variables and to directly compare the model fit with alternative factor structure models.

This statistical procedure was undertaken using the IBM SPSS Amos software (Arbuckle, 2013). This program applies maximum-likelihood techniques to estimate the model parameters based on the covariance matrix of the manifest variables. Three indices of model fit, as recommended by Hu and Bentler (1998), were considered. Firstly, a non-significant χ^2 statistic indicates that the specified model is an adequate fit to the data. However, as χ^2 is highly influenced by sample size, the χ^2 / df statistic has been proposed, with values lower than 2.0 reflecting good model fit. Two further fit statistics were taken into account as well: The Comparative Fit Index (CFI) and the Standardized Root Mean Square Error of Approximation (RMSEA). A CFI value higher than .90 is considered a fair fit, whereas a value exceeding .95 indicates a good fit. An RMSEA value of .08 or lower reflects a fair fit and a value of .05 or below is an indication of good model fit.

Reliability (i.e., internal consistency) of the subscales and their relationships with three demographical variables were investigated in a similar manner as Study 1. An alpha level of .05 was applied. Except for the CFA, the statistical procedures were conducted using IBM SPSS Statistics version 22.

RESULTS AND DISCUSSION

Descriptives of the WQ

Descriptive statistics of the WQ-items are provided in Table 5. None of the items suffered from substantial skewness given values range from –0.6 to +0.2.

Confirmatory factor analysis

The fit of the data with a one-factor model was tested to establish a baseline and because such a model has the highest possible parsimoniousness. This unitary model represented all 22 WQ-items on a single latent variable. All fit statistics demonstrated a very poor fit of the data to the one-factor model: $\chi^2\,(209) = 1278.53$, $p < .001$; $\chi^2/df = 6.12$; CFI = 0.54; RMSEA = 0.18.

Next, the fit of the data with the three-factor structure (Study 1) was tested. The three distinct factors (Navigation and Orientation, Spatial Anxiety and Distance Estimation) were allowed to correlate. The fit statistics provided a better, but still weak fit to the data: $\chi^2\,(206) = 605.29$, $p < .001$; $\chi^2/df = 2.94$; CFI = 0.83; RMSEA = 0.11. Nonetheless, the three-factor model fitted substantially better than the one-factor model: $\Delta\chi^2\,(3) = 673.24$, $p < .001$.

The modifications indices revealed, among others, two plausible correlations between the error terms of item pairs. Consequently, two correlations between error terms were added to the three-factor model, namely between Items 10 and 11, and between Items 21 and 22. Content overlap is very high for both item pairs: Item 11 describes a more specific situation than Item 10, and Items 21 and 22 share overlap in addressing the ability to understand and to provide route descriptions, respectively. The adjusted three-factor model (with the two correlations between error terms included) was a significant improvement over the three-factor model, $\Delta\chi^2\,(2) = 191.57$, $p < .001$, and the fit statistics met or closely approached criteria for acceptable fit: χ^2 (204) = 413.72, $p < .001$; $\chi^2/df = 2.03$; CFI = 0.91; RMSEA = 0.08. The adjusted three-factor model including its factor loadings is depicted in Figure 2.

Reliability analysis (internal consistency)

All three subscales showed very good internal consistency: Navigation and Orientation (0.904), Spatial Anxiety (0.923) and Distance Estimation (0.826). A correlation analysis revealed weak to strong correlations between subscales: Navigation and Orientation and Distance Estimation ($r = 0.756$, $p < .001$), Navigation and Orientation and Spatial Anxiety ($r = 0.353$, $p < .001$) and Distance Estimation and Spatial Anxiety ($r = 0.198$, $p = .013$). Moreover, all mean subscale scores showed strong correlations with the total score: Navigation and Orientation ($r = 0.875$, $p < .001$), Spatial Anxiety ($r = 0.670$, $p < .001$) and Distance Estimation ($r = 0.823$, $p < .001$).

Table 5. Descriptive statistics (means, standard deviations (*SDs*), and skewness) for the final 22 items of the Wayfinding Questionnaire (WQ) items based on the responses of 158 chronic mild stroke patients.

	Item	***Mean***	***SD***	***Skewness***
2.	When I am in a building for the first time, I can easily point to the main entrance of this building.	4.30	1.90	–0.34
3.	If I see a landmark (building, monument, intersection) multiple times, I know exactly from which side I have seen that landmark before.	4.86	1.82	–0.57
4.	In an unknown city I can easily see where I need to go when I read a map on an information board.	4.59	1.98	–0.33
6.	Without a map, I can estimate the distance of a route I have walked well, when I walk it for the first time.	3.92	2.01	–0.07
7.	I can estimate well how long it will take me to walk a route in an unknown city when I see the route on a map (with a legend and scale).	3.83	1.98	–0.01
8.	I can always orient myself quickly and correctly when I am in an unknown environment.	3.93	1.97	–0.02
9.	I always want to know exactly where I am (meaning, I am always trying to orient myself in an unknown environment).	4.76	1.92	–0.49
10.	I am afraid of losing my way somewhere.	4.46	2.07	–0.35
11.	I am afraid of getting lost in an unknown city.	4.48	2.09	–0.28
12.	In an unknown city, I prefer to walk in a group rather than by myself.	4.03	2.37	–0.02
13.	When I get lost, I get nervous.	4.25	2.24	–0.15
	How uncomfortable are you in the following situations (Items 14, 15, and 16):			
14.	Deciding where to go when you are just exiting a train, bus, or subway station.	4.56	1.91	–0.22
15.	Finding your way in an unknown building (e.g., a hospital).	4.62	1.99	–0.37
16.	Finding your way to a meeting in an unknown city or part of a city.	3.90	1.97	+0.19
17.	I find it frightening to go to a destination I have not been before.	4.73	2.02	–0.38

18.	I can usually recall a new route after I have walked it once.	4.32	1.97	–0.24
19.	I am good at estimating distances (e.g., from myself to a building I can see).	4.41	1.88	–0.34
21.	I am good at understanding and following route descriptions.	4.42	2.03	–0.42
22.	I am good at giving route descriptions (meaning, explaining a known route to someone).	4.48	1.93	–0.41
23.	When I exit a store, I do not need to orient myself again to determine where I have to go.	4.82	1.98	–0.60
24.	I enjoy taking new routes (e.g., shortcuts) to known destinations.	3.99	2.21	+0.06
26.	I can easily find the shortest route to a known destination.	4.52	2.05	–0.41

Note. Scores on the Spatial Anxiety scale were reversed such that high values represent lower spatial anxiety and thus higher navigation ability. *SD* = Standard deviation.

3

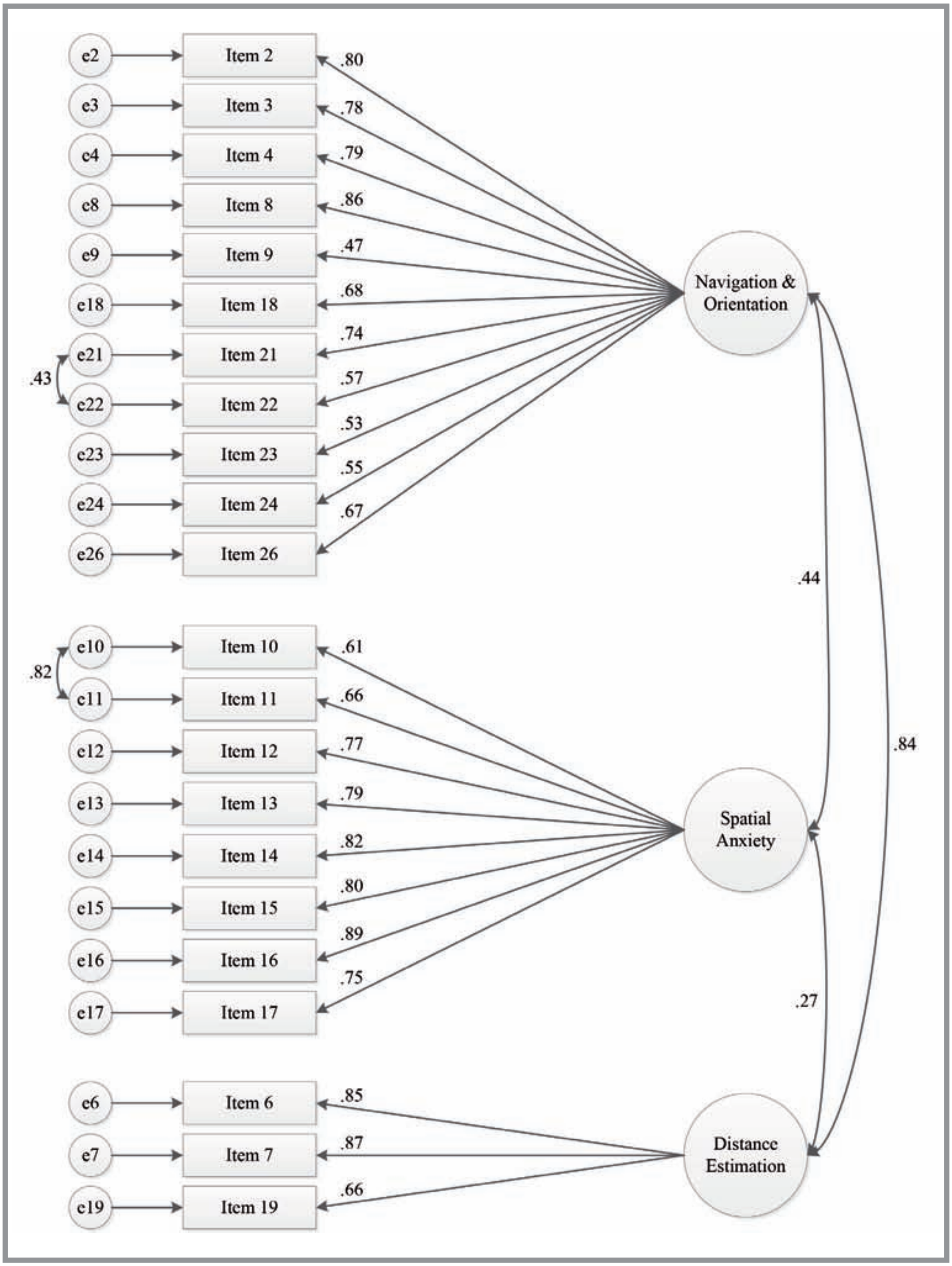


Figure 2. The confirmatory factor analysis (CFA) results (i.e., standardized estimates) are displayed for the adjusted three-factor model. Boxes represent observed variables (WQ items) and variables in ovals represent latent factors. All estimates are significant (*p*'s < .05). The results are based on the responses of a group of 158 chronic mild stroke patients.

Table 6. Comparison of the mean scores on the three WQ-subscales scores for female and male chronic mild stroke patients.

Subscale	Females (n = 64)	Males (n = 94)	t-value	p-value	Effect-size r
Navigation and Orientation	4.00 (1.32)	4.76 (1.40)	–3.44	.001	.27
Spatial Anxiety	3.94 (1.66)	4.68 (1.64)	–2.77	.006	.22
Distance Estimation	3.36 (1.63)	4.53 (1.56)	–4.53	< .001	.34

Note. Standard deviations are displayed between parentheses. Scores on the Spatial Anxiety scale were reversed such that high values represent lower spatial anxiety and thus higher navigation ability.

Relationship with demographic variables

Female patients scored significantly lower than male patients on all three subscales (see Table 6). None of the subscales was significantly correlated with age. Educational level was weakly and significantly related to the Navigation and Orientation subscale ($r = 0.163$, $p = .04$) and the Spatial Anxiety subscale ($r = 0.204$, $p = .01$).

Interim summary of Study 2

The three-factor structure as established in healthy participants (see Study 1) was supported in chronic mild stroke patients in Study 2. The CFA provided evidence for reasonable model fit of the data with the three factors (Navigation and Orientation, Spatial Anxiety, and Distance Estimation). All subscales were characterized by very good internal consistency, weakly to strongly correlated to the other subscales, and strongly related to the total WQ-score.

GENERAL DISCUSSION

In current clinical practice, screening instruments for cognitive complaints are used on a regular basis in stroke patients to decide whether or not extensive cognitive testing is needed. Existing screening instruments have, however, neglected an important cognitive function, that is, navigation ability. Our aim was therefore to develop a short but comprehensive screening instrument for navigation-related complaints after stroke. The WQ, as presented earlier by van der Ham and colleagues (2013), was considered the perfect starting point for developing such an instrument. First, in contrast to existing self-report instruments of navigation ability (e.g., the SBSOD; Hegarty et al., 2002), the WQ takes both the cognitive complexity and the emotional aspects of navigation behavior into account. Moreover, the WQ has already been used as a self-report instrument of navigation ability in mild stroke patients (van der Ham et al., 2013). However, its psychometrical properties had not yet been evaluated. As a first step in the validation process, we examined its internal validity (i.e., factor structure and reliability) in both healthy participants (Study 1) and chronic mild stroke patients (Study 2). The intended result of this approach was to end up with the final version of the WQ, which can be used for further validation studies.

The two studies reported in this paper provide evidence in favor of the internal validity of the WQ as a self-report screening instrument of navigation-related complaints. The results showed that 22 out of the 26 original items were valid and best divided over three subscales: "Navigation and Orientation," "Spatial Anxiety," and "Distance Estimation". This three-factor structure was found to be valid in both healthy participants and mild stroke patients, suggesting that the subscale scores can be interpreted in the same way in these groups. Each of these results will be discussed in more detail below.

In the first study, the WQ was completed by a large, heterogeneous group of healthy participants. The exploratory factor analysis (EFA) led to deletion of four WQ-items. One item was removed because it was related very poorly to the others and three items were deleted due to substantial content overlap. The EFA suggested the existence of three separate latent factors: Navigation and Orientation (11 items), Spatial Anxiety (8 items), and Distance Estimation (3 items). Reliability was found to be very high in this sample: The subscales displayed very high internal consistency, showed weak to moderate correlations with the other subscales and were strongly related to the total WQ-score as well.

The three-factor solution, as proposed in Study 1, was directly verified in a representative group of 158 chronic mild stroke patients. Confirmatory factor analysis (CFA – a structural equation modeling technique) enabled direct assessment of the model fit of the patients' WQ-item scores with the three-factor structure resulting from the EFA in Study 1. Although model fit was not perfect, the fit indices provided support for an acceptable fit. It should be mentioned that perfect model fit would have been rather unexpected, as healthy participants and mild stroke patients are obviously different in their neuropsychological status. Moreover, there were differences in age and educational level between the healthy participants and the patients. More specifically, the patients were somewhat older and slightly lower in educational level than the healthy participants. Nonetheless, the finding of an acceptable model fit indicates that no substantial difference exists in the manner in which the healthy participants and patients perceived and responded to the questionnaire items. In addition, these results allow patients' WQ-subscale scores to be interpreted in the same way as in healthy participants. Reliability was very high in the patient sample as well: Internal consistency of the subscales was very high, correlations between the subscales were weak to strong in degree and the subscale scores were also strongly related to the total WQ-score.

Hence, the statistical analyses provided support, in both healthy participants and patients, for the existence of three latent factors underlying the 22 items of the final WQ (see Appendix A). Firstly, 11 items covered multiple aspects related to the more general concepts of "navigation" and "orientation," which supports the notion of navigation ability as a complex cognitive capacity (Brunsdon et al., 2007; Wiener et al., 2009; Wolbers & Hegarty, 2010). Secondly, eight items concerned the emotional aspects associated with navigation, that is, experiencing anxious feelings when performing navigation tasks (Lawton, 1994, 1996) and feeling worried about getting lost (Schmitz, 1997). We consider the inclusion of the concept of "spatial anxiety" highly important, as it has been shown to affect navigation ability in a negative way (Schmitz, 1997; Walkowiak et al., 2015). In addition, preliminary evidence suggests that spatial anxiety is not a situation-specific derivative of general anxiety. Walkowiak and colleagues (2015) have recently shown that, in contrast to spatial anxiety, general anxiety (based on the well-known State-Trait Anxiety Inventory) was not related to objective measures of navigation ability. These findings suggest that individuals with high general anxiety are not necessarily high in spatial anxiety and vice versa. Lastly, three items addressed the specific ability to estimate distances (Thorndyke, 1981; Montello, 1997, 2009; Proffitt, 2006), either based on direct experience (Item 6 and 19) or a map (Item 7).

Investigation of the relationship between the subscale scores and gender revealed that men scored higher on all three subscales[1] than female participants in both samples. This finding is borne out by a large number of studies that have revealed gender differences in favor of males in navigation ability (e.g., Coluccia & Louse, 2004; Hegarty et al., 2006; Münzer & Hölscher, 2011) and lower levels of spatial anxiety in males (e.g., Lawton 1994, 1996). With regard to future research, these marked gender differences underline the need for development of separate WQ-norms for men and women.

In contrast, the relationships between the WQ-subscale scores and two other demographical variables, that is, age and educational level, were not as clear-cut as in the case of gender. In respect of age, previous research has convincingly shown that actual navigation ability is negatively affected by increasing age (e.g., Cushman, Stein, & Duffy, 2008; Moffat, 2009). However, no such effect (i.e., no significant correlations, except for one weak positive correlation in the healthy sample) was found with regard to the WQ-subscales. Interestingly, Taillade, N'Kaoua and Sauzéon (2016) have provided evidence for this combination of findings in a single study. These authors reported age-differences in objectively measured navigation performance favoring younger adults, whereas such a difference was not identified when comparing self-reported navigation ability between groups of young and older adults.

1 *NB. Scores on the Spatial Anxiety items were reversed such that high values represent lower spatial anxiety and thus higher navigation ability.*

The absence of a significant correlation between self-reported navigation ability on the WQ and age is thus in congruence with this recent paper as well as many earlier studies (see Taillade et al., 2016), and might result from several factors. Older people might have higher levels of experience with navigation than younger adults and, consequently, more successful navigation episodes to base their self-estimates on (Taillade et al., 2016). Another explanation might lie in metacognitive difficulties in older adults, which might hinder them in providing accurate self-estimates. Last, domain-specific age stereotypes might influence self-reported cognitive abilities in the elderly, that is, negatively affecting self-estimates of memory function but not of spatial abilities (see Taillade et al., 2016). Hence, older individuals tend to overestimate their current navigation abilities.

Weak positive relationships were identified between some of the WQ-subscales and educational level. These results indicate that people with a higher level of education tend to report better navigation and orientation ability and lower spatial anxiety as compared with lower-educated people.

Several strengths of this paper deserve to be mentioned. Studies 1 and 2 rely on large samples of healthy participants and chronic mild stroke patients, respectively. The patient group consisted of patients with various stroke types and lesion locations (see Table 4) allowing initial generalization to stroke patients in general. Additional studies based on even larger samples per stroke type and patients with more severe stroke pathology could be helpful in confirming the generalizability of the current findings. A further strength is the confirmatory approach taken in Study 2. The factor structure as established in healthy participants (Study 1) was directly verified in a representative sample of mild stroke patients and was found to be internally valid and reliable in this latter group as well. Given that the WQ is short (22 items), it seems particularly feasible as a screening instrument of navigation-related complaints in stroke patients.

A few limitations of this paper should also be mentioned. First, the two studies specifically focused on establishing the latent factor structure of the WQ and examining its reliability. Further research should therefore scrutinize the validity of the WQ. It should also be mentioned that only chronic stroke patients were included for participation in the study. Further studies could take other relevant acquired brain injury patient groups into account, for instance, patients suffering from traumatic brain injury (e.g., Livingstone & Skelton, 2007) and Alzheimer patients (e.g., Cushman et al., 2008; deIpolyi, Rankin, Mucke, Miller, & Gorno-Tempini, 2007; Pai & Jacobs, 2004) as navigation impairment also occurs regularly in these patient groups.

Another limitation lies in the fact that the WQ-scores rely on accuracy of the patient's insight into actual navigation performance in daily life. The dependence on self-insight is a common issue with the use of self-report measures in brain-damaged patients, as insight in actual cognitive performance can be diminished or even absent after suffering from stroke (Orfei, Caltagirone, & Spalletta, 2009; Starkstein, Jorge, & Robinson, 2010). Future research on the WQ could explore the feasibility of a caregiver version to overcome full reliance on the patient's self-insight. This would help in capturing navigation problems in patients who are unable to provide an accurate indication of their abilities.

Notwithstanding these limitations, the current studies allowed us to draft the final version of the WQ based on the data of healthy respondents. Results showed that the WQ-subscales are reliable in both healthy participants and mild stroke patients. Furthermore, the three-factor structure was found to be a valid interpretation frame in both of these groups. We have shown that the WQ is not only a short but also comprehensive instrument (22 items) as it covers the cognitive complexity of navigation ability and takes spatial anxiety into account as well. As the next step in the validation process of the WQ, we are currently examining further aspects of its validity as well as its clinical utility (De Rooij et al., in preparation). In case this follow-up study results in further substantiation of the validity and usefulness of the WQ, we consider this instrument to be eligible for implementation in clinical practice as an assessment instrument for navigation-related complaints after stroke.

APPENDIX A: WAYFINDING QUESTIONNAIRE (WQ)

The following 22 statements are about navigation ability. For each of these statements, please *circle the number that best describes your ability to navigate.*

The numbers 1 to 7 represent the following:

1	2	3	4	5	6	7
Not at all applicable to me	*Almost never applicable to me*	*Rarely applicable to me*	*Sometimes applicable to me*	*Often applicable to me*	*Almost always applicable to me*	*Fully applicable to me*

1. When I am in a building for the first time, I can easily point to the main entrance of this building.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

2. If I see a landmark (building, monument, intersection) multiple times, I know exactly from which side I have seen that landmark before.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

3. In an unknown city I can easily see where I need to go when I read a map on an information board.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

4. Without a map, I can estimate the distance of a route I have walked well, when I walk it for the first time.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

5. I can estimate well how long it will take me to walk a route in an unknown city when I see the route on a map (with a legend and scale).

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

6. I can always orient myself quickly and correctly when I am in an unknown environment.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

7. I always want to know exactly where I am (meaning, I am always trying to orient myself in an unknown environment).

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

8. I am afraid of losing my way somewhere.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

9. I am afraid of getting lost in an unknown city.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

10. In an unknown city, I prefer to walk in a group rather than by myself.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

11. When I get lost, I get nervous.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

How uncomfortable are you in the following situations (items 12, 13 and 14):

12. Deciding where to go when you are just exiting a train, bus, or subway station.

Not uncomfortable at all	1	2	3	4	5	6	7	*Very uncomfortable*

13. Finding your way in an unknown building (for example a hospital).

Not uncomfortable at all	1	2	3	4	5	6	7	*Very uncomfortable*

14. Finding your way to a meeting in an unknown city or part of a city.

Not uncomfortable at all	1	2	3	4	5	6	7	*Very uncomfortable*

15. I find it frightening to go to a destination I have not been before.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

16. I can usually recall a new route after I have walked it once.

Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

17. I am good at estimating distances (for example, from myself to a building I can see).								
Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

18. I am good at understanding and following route descriptions.								
Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

19. I am good at giving route descriptions (meaning, explaining a known route to someone).								
Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

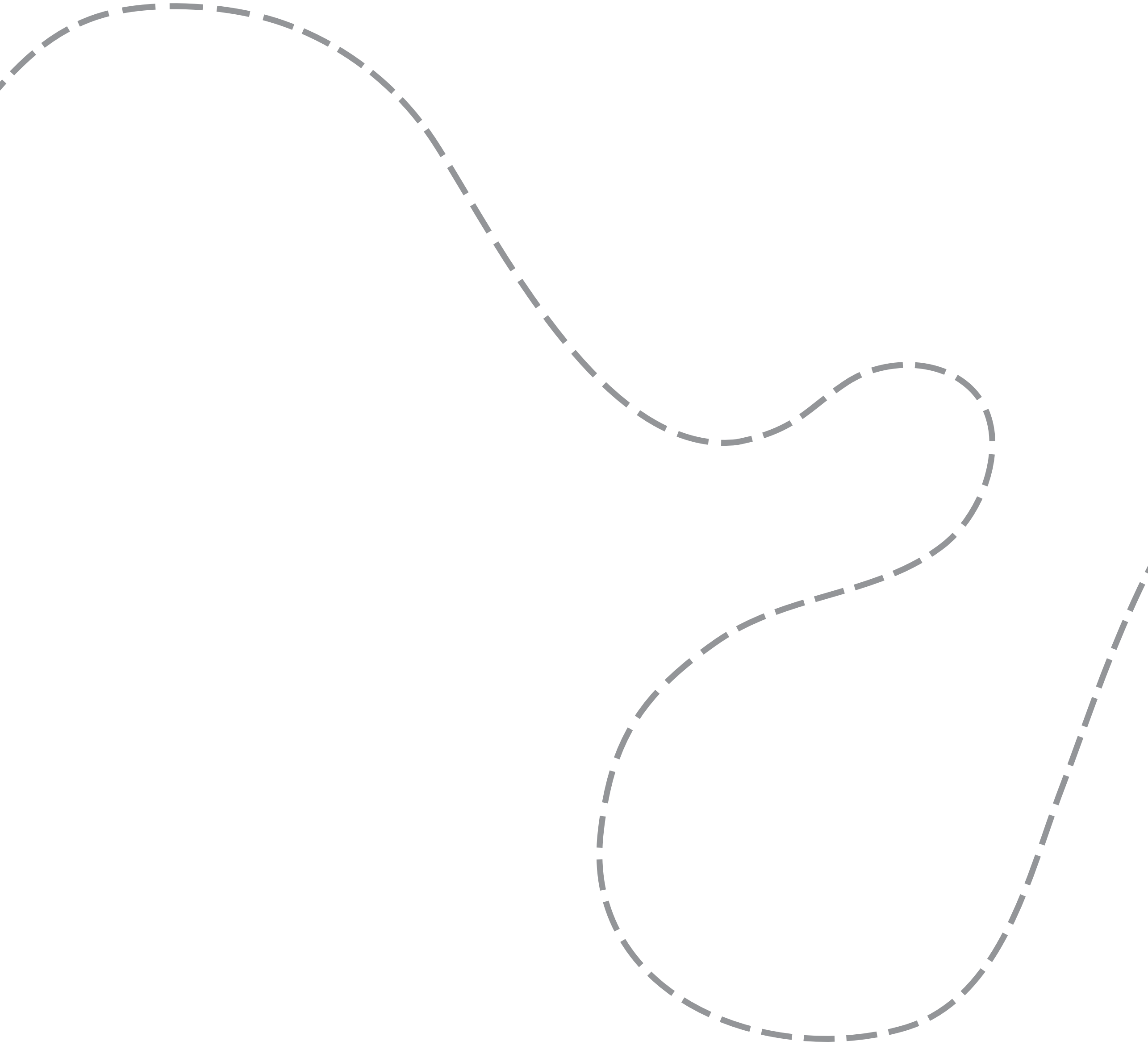
20. When I exit a store, I do not need to orient myself again to determine where I have to go.								
Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

21. I enjoy taking new routes (for example shortcuts) to known destinations.								
Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

22. I can easily find the shortest route to a known destination.								
Not at all applicable to me	1	2	3	4	5	6	7	*Fully applicable to me*

Scoring instructions:
Response possibilities range from 1 ("not at all applicable to me") to 7 ("fully applicable to me") for Navigation and Orientation and Distance Estimation items. On Items 12, 13, and 14, scores of 1 to 7 represented "not uncomfortable at all" to "very uncomfortable" respectively.

Navigation and Orientation subscale: Item 1, 2, 3, 6, 7, 16, 18, 19, 20, 21, and 22
Spatial Anxiety subscale: Item 8, 9, 10, 11, 12, 13, 14, and 15
Distance Estimation subscale: Item 4, 5, and 17



CHAPTER 4

The Wayfinding Questionnaire: A clinically useful self-report instrument to identify navigation complaints in stroke patients

Submitted as:
de Rooij, N. K., Claessen, M. H. G., van der Ham, I. J. M., Post, M. W. M., & Visser-Meily, J. M. A. The Wayfinding Questionnaire: A clinically useful self-report instrument to identify navigation complaints in stroke patients.

Author contributions:
IH and JV designed the study; MC and IH collected the data; NR, MC, and IH processed the data; NR and MC analyzed the data; NR, MC, JV, IH, and MP interpreted the data; NR drafted the paper; MC, JV, IH, and MP revised the paper for intellectual content.

ABSTRACT

Post-stroke navigation complaints are frequent (about 30%) and intervention is possible, but there is no assessment instrument to identify patients with navigation complaints. We therefore studied the clinical validity of the Wayfinding Questionnaire (WQ) in a cross-sectional study with 158 chronic stroke patients and 131 healthy controls. Patients with low (more navigation complaints) versus normal WQ scores were compared for demographics, stroke characteristics, emotional and cognitive complaints, and health-related quality of life (HRQoL). Actual navigation performance of 78 patients was assessed in a virtual reality setting. Effect sizes (d) were calculated. WQ responses (22 items) of stroke patients were compared with those of controls (discriminant validity). Results showed that patients with a low WQ score (n=49, 32%) were more often women ($p = 0.013$) and less educated ($p = 0.004$), reported more cognitive complaints ($d = 0.69$), more emotional problems ($d = 0.38$ and 0.52), and lower HRQoL ($d = 0.40$ and 0.45) and, last but not least, performed worse on the navigation ability tasks ($d = 0.23$–0.80). Patients scored lower than controls on 21/22 WQ items, predominantly with small to medium effect sizes ($d = 0.20$–0.51). We conclude that the WQ is valid as a measure of navigation complaints in stroke patients, and thus strongly advocate its use in stroke care.

INTRODUCTION

Our brain uses a range of cognitive skills when moving around in a particular environment, the so-called spatial navigation ability. This complex cognitive construct is crucial because it enables us to adapt to new environments and allows us to move from one point to another in our daily lives, both indoors, from room to room, and outdoors, from home to the grocery store, to work or to visit family in a different town. Whilst navigation ability varies greatly among healthy people (Hegarty, Montello, Richardson, Ishikawa, & Lovelace, 2006), numerous case reports have described that individuals with brain damage are prone to experiencing navigation complaints (Aguirre & D'Esposito, 1999; Busigny et al., 2014; van der Ham et al., 2010). In a study of mild stroke patients in the chronic phase, 29% reported navigation complaints (van der Ham, Kant, Postma, & Visser-Meily, 2013). Unfortunately, navigation complaints are not routinely assessed in stroke patients nowadays; neither in history-taking nor in standard neuropsychological assessments. Existing questionnaires such as the checklist for cognitive and emotional consequences following stroke, the CLCE-24, do not address navigation complaints (van Heugten, Rasquin, Winkens, Beusmans, & Verhey, 2007). We therefore think that difficulties in navigation ability are currently underdiagnosed.

The Wayfinding Questionnaire (WQ), a self-report questionnaire to assess navigation complaints, was first presented in 2013 (van der Ham et al., 2013). The development of the WQ was based on previous literature and inspired by existing questionnaires that only provided partial coverage of the concept of navigation ability. One of these questionnaires was a "sense-of-direction" 15-item scale (Hegarty, Richardson, Montello, Lovelace, & Subbiah, 2002). This scale, however, does not include any item on spatial anxiety (SA). Inclusion of the concept of SA is essential, because it negatively affects navigation ability, and might not be detected by instruments of general anxiety (Walkowiak, Foulsham, & Eardley, 2015). Questionnaires that do include SA, like the Wayfinding Anxiety Scale and Lawton's Spatial Anxiety Scale, however, do not include other navigation complaints like distance estimation and orientation (Lawton, 1994; Lawton & Kallai, 2002). A 17-item International Wayfinding Strategy Scale focuses on orientation and route strategies, not on the ability to navigate (Lawton & Kallai, 2002). The coverage of the full range of navigation complaints is thus unique to the WQ.

The WQ was recently tested for internal validity in a large group of healthy controls and mild stroke patients. This study resulted in a final version of the WQ containing 22 items and taking less than 10 minutes to complete (Claessen, Visser-Meily, de Rooij, Postma, & van der Ham, 2016b). However, additional evidence to support its clinical usefulness in stroke patients is required for use in clinical practice.

Our aim was therefore to study whether the WQ can be used as an assessment tool to identify complaints concerning navigation ability in stroke patients. To assess whether the WQ is clinically valid, in other words clinically relevant and useful, we considered several aspects of validity that we think are important in clinical practice. We tested association hypotheses to validate the WQ because no gold standard is available. Hence, we analysed differences between stroke patients with a low WQ score and those with a normal WQ score regarding demographics, scores on other self-report instruments, and objective tests of navigation ability. Based on the literature, we hypothesized that women, older patients, and patients with more cognitive, anxious, or depressive complaints would have more navigation complaints (Coluccia & Louse, 2004; Moffat, 2009). Furthermore, we expected patients with more navigation complaints to perform worse on objective tests of navigation ability, and to report lower health-related quality of life (HRQoL), because navigation problems may interfere with independent functioning in daily life. We also used the WQ to explore which navigation complaints were most common in stroke patients, and analysed the differences in WQ responses between stroke patients and healthy controls (discriminant validity).

METHODS

Design and participants

A cross-sectional study was performed including both stroke patients and healthy controls. The study was designed in accordance with the regulations provided by the Declaration of Helsinki. The study procedures were approved by the medical ethical review board of the University Medical Centre Utrecht (protocol number 12-198). The recruitment procedures have been described in detail elsewhere (Claessen, Visser-Meily, de Rooij et al., 2016b). Briefly, 158 stroke patients were included who visited the rehabilitation centre or hospital rehabilitation department in Utrecht, the Netherlands. Inclusion criteria were: (1) first or recurrent stroke; (2) age ≥ 18 years; (3) ≥ 6 months since first stroke event, and (4) living at home after rehabilitation. Exclusion criteria were: (1) unable to communicate in Dutch, (2) severe global aphasia, and (3) severe mobility problems (i.e., patients had to be able to walk outside without supervision). Healthy controls were recruited for several study objectives, including the WQ. For the present study, we used data of 131 controls. Sixty-seven of them completed only the WQ, while 64 completed the WQ as part of the same set of questionnaires as the stroke patients. These control groups were comparable with respect to age and gender.

Data collection

All stroke patients and 64 controls completed a paper/pencil self-report questionnaire. Demographic characteristics collected included age, gender, and level of education (1 "primary education completed" up to 7 "finished university education completed")

(Verhage, 1964). Stroke characteristics were obtained from medical files and included type of stroke, hemisphere involved, and date of stroke.

Navigation complaints

The Wayfinding Questionnaire (WQ) contains 22 items in 3 subscales: navigation and orientation (NO, 11 items), distance estimation (DE, 3 items) and spatial anxiety (SA, 8 items) with scores ranging from 1 to 7, and is displayed in Appendix A (see Chapter 3). A lower score indicates more navigation complaints for all items (all 8 SA item scores were reversed). The subscale scores for NO (range 7 to 77), DE (range 3 to 21) and SA (range 8 to 56) represent different aspects of the "navigation ability" function and are not combined in one total score.

Cognitive complaints

The cognitive domain of "memory and thinking" of the Stroke Impact Scale version 3.0 (c-SIS) was used to assess self-reported cognitive problems (Duncan, Bode, Lai, & Perera, 2003). This domain consists of 7 items and each item is scored from 1 ("not difficult at all") to 5 ("cannot do at all"). The scale score is the average of the item scores and a higher score indicates more problems of memory and thinking. The SIS has been shown to have excellent psychometric properties in terms of concurrent and construct validity, test-retest reliability and responsiveness (Duncan et al., 2003; Carod-Artal, Coral, Trizotto, & Moreira, 2008).

Emotional complaints

The Hospital Anxiety and Depression Scale (HADS) was used to assess emotional functioning in terms of depressive (7 items) and anxiety symptoms (7 items). The total score of all 14 items ranges from 0 to 42. A higher score indicates more emotional problems (Zigmond & Snaith, 1983). The HADS has shown good psychometric properties and is commonly used for stroke patients (Zigmond & Snaith, 1983; Spinhoven et al., 1997).

Health Related Quality of life (HRQoL)

The short-version of the Stroke-Specific Quality of Life Questionnaire (SS-QoL-12) was used to assess HRQoL. This is a validated disease-specific measure that contains 5 items on physical and 7 items on psychosocial HRQoL, each scored on a 5-point scale (Post et al., 2011). Items are averaged to obtain a total score (range 1 to 5), higher scores indicating better HRQoL. In the control group, an adapted version of the SS-QOL-12 was used without the words "due to stroke" in the introduction sentence.

Navigation cognitive ability tasks

A subset of the stroke patients (n = 78) were assessed for navigation ability in a virtual reality setting using the Virtual Tübingen test (van Veen, Distler, Braun, & Bülthoff, 1998; Claessen, Visser-Meily, Jagersma, Braspenning, & van der Ham, 2016; Claessen, Visser-Meily, de Rooij, Postma, & van der Ham, 2016a). Briefly, the patients were shown a video of a virtual route and were requested to remember as many aspects of this route as possible, after which they performed eight subtasks. *Scene Recognition* was tested by presenting 22 images of decision points taken from the route (11 targets and 11 distractors). Patients were requested to indicate if the decision points had been in their route. Scoring was based on the number of correct responses, range 0–22. *Route Continuation* was assessed by presenting 11 decision points taken from the route one-by-one in random order and asking participants to indicate the direction in which the route continued at each decision point. Scoring was based on the number of correct responses, range: 0–11. To test *Route Sequence* patients were requested to indicate the sequence of turns taken during the route, by arranging a set of arrow cards. Scoring was based on the number of correctly indicated turns in the sequence, range 0–7. *Route Order* was tested by instructing the patients to reconstruct the order in which 11 images of decision points occurred during the route. Scores ranged from 0–22. *Route Progression* tested memory for absolute order of scenes. Patients were shown 11 printed images and were provided with a small piece of paper with a printed line representing the length of the route. They were asked to indicate where each image was encountered on the route. Scoring was performed by calculating the relative difference between the correct position and the indicated position. These scores were averaged and varied between 0 and 1 (= perfect performance). For *Route Distance* patients were presented with two scenes and had to indicate the distance between these scenes on a line representing the total distance of the route. Scoring was the average (9 trials) of the percentage of deviation between the indicated and actual position relative to the full length of the line. *Route Drawing* was tested by asking the patients to draw the route they had studied on a map of the test environment, in which only the starting point and starting direction were provided. Scoring ranged from 0 to 11, one point for each correctly indicated direction (left turn, straight ahead or right turn) at relevant decision points. For *Map Recognition* the patients had to select the correct map of the route out of four options. Scoring was dichotomous (correct or incorrect).

Analyses

A cut-off value can help health care professionals to decide which score indicates clinically meaningful problems. Such cut-off values are frequently based on empirical findings, not on theoretical arguments, e.g., the Centre for Epidemiologic Studies Depression Scale (Shinar, Gross, Bolduc, & Robinson, 1986). We chose cut-off values corresponding to the lower (most severe) 5% WQ scores for each subscale in the 131 healthy controls, by *z*-score of < -1.64 (Lezak, Howieson, Bigler, & Tranel, 2012). WQ subscale scores were considered low if: ≤ 32 for NO, ≤ 6 for DE and ≤ 20 for SA.

Patients were classified as having navigation problems (low WQ score) if they had a low score on one or more subscales. Subsequently, we compared the patients with a normal and those with a low score regarding demographics, stroke characteristics, cognitive and emotional complaints, and HRQoL. Effect sizes were defined as by Cohen (small effect $d = 0.2–0.49$, medium effect $d = 0.5–0.79$, and large effect $d \geq 0.8$). Independent t-test or chi-square test was used to identify significant differences. Additionally, Spearman correlation was calculated between the mean scores for each WQ category and the HADS score. A correlation of < 0.3 was considered weak, 0.3 to 0.6 moderate, and > 0.6 good.

Next, we analysed whether the patients with low WQ scores did indeed score lower on the Virtual Tübingen test than patients with WQ scores in the normal range. Effect sizes (*d*) and the significance of differences was calculated with Cohen's *d*, t-test or chi-square test.

Finally, we compared the WQ scores of the 158 stroke patients with those of the 131 healthy controls (discriminant validity). Because navigation ability can be low in healthy people as well, and not all stroke patients will have navigation problems, we analysed the mean differences between patients and controls, and did not attempt to separate sick from healthy. Mean scores were calculated for the 22 individual items and the 3 composite subscales. Effect sizes (*d*) and levels of significance were again calculated with Cohen's *d*, and t-test or chi-square test. To explore the most frequent navigation complaints, we additionally dichotomized all item scores, considering item scores ≤ 3 ("not at all / almost never / rarely applicable to me") as indicating navigation complaints and item scores ≥ 4 ("sometimes / often / almost always / fully applicable to me") as indicating no navigation complaints.

RESULTS

Baseline characteristics of the 158 stroke patients and 131 healthy controls are presented in Table 1. There were some differences in gender, age, and education between the two groups, the control group including more males, while controls were slightly younger and had somewhat higher level of education. There were obvious differences in c-SIS, HADS, and SSQoL-12 scores ($p < 0.001$) between stroke patients and controls. Missing data for 3 stroke patients meant that no reliable assessment was available to determine whether their WQ score was low or normal. We found 49/155 (32%) stroke patients having a low WQ score on one or more subscales (Table 1). Of the patients with a low WQ score, 27/49 (55%) scored low on one subscale (6 NO, 7 DE, 14 SA), while 22/49

(45%) scored low on more than one subscale (9 on NO+DE, 2 on NO+SA, 2 DE+SA and 9 on all three subscales). In the control group we found 14% having a low score on one or more subscales.

Differences between patients with low versus normal WQ score are presented in Table 1. The group with low WQ scores included significantly more women, lower educated patients and patients with more cognitive complaints (higher c-SIS, d = 0.69), more emotional problems (higher HADS, d = 0.38 and 0.52) and lower HR-QoL (lower SS-QoL, d = 0.40 and 0.45). Age, type of stroke, location of stroke, and time after stroke were not significantly different between groups. Spearman correlations between the HADS and WQ subscales were weak to moderate, the highest for SA and HADS-anxiety: HADS and SA −0.41 (anxiety) and −0.33 (depression), HADS and NO −0.30 (anxiety) and −0.33 (depression), and HADS and DE −0.20 (anxiety) and −0.21 (depression). These correlations were significant at the 0.01 level, except that for DE and HADS–anxiety (0.05 level).

Differences in performance on the Virtual Tübingen Test are shown in Table 2. Data was available for 30 (61%) of the patients with a low WQ score and 48 (45%) of the patients with normal WQ score. Performance was significantly poorer in the patients with a low WQ score compared to patients with a normal WQ score for all 8 navigation tasks. Effect sizes were small for 4 tests (d = 0.2–0.5) and medium to large for 3 tests (d = 0.6–0.8). In one test d could not be calculated, but the difference was significant as well (p = 0.017).

Differences in WQ responses between stroke patients and controls are listed in Table 3. Stroke patients scored lower than controls on 21/22 items, and these differences were significant for 14 items. Effect sizes were small to medium (d = 0.2–0.5), with the largest difference for item 21 “I enjoy taking new routes (for example shortcuts) to known destinations” (d = 0.51, p < 0.001). All three subscales showed significant differences between stroke patients and controls with d values of 0.35 for NO, 0.24 for DE and 0.45 for SA. The percentages of stroke patients scoring ≤ 3 on the various items were also higher compared to the controls, except for item 20. The difference was ≥ 10 percent for 14 items (64%), and ≥ 15 percent for 10 items (45%). The largest differences were 20–28% for items 5, 10, 13, 14, and 21. Difference for NO was 8%, for DE 17% and for SA 12% (Table 3).

Table 1. Baseline characteristics of stroke patients and healthy controls, and differences between patients with low versus normal Wayfinding Questionnaire scores.

	Healthy controls	Stroke patients	Significant difference? ‡	Stroke patients with normal WQ §	Stroke patients with low WQ §	Effect size Cohen's *d* and significant difference ‡
Number of patients/controls	***n* = 131**	***n* = 158**		***n* = 106 (68%)**	***n* = 49 (32%)**	
Gender, male	55 (42%)	94 (59%)	0.03	70 (66%)	22 (45%)	*p* = 0.013
Age in years, mean (range)	57.0 (37–87)	60.0 (22–96)	0.03	59.4 ± 13.3 (27–96)	61.0 ± 12.9 (50–83)	0.12 *p* = 0.502
Education[#], mean (range 1–7)	5.7 (*SD* 0.82)	5.2 (*SD* 1.40)	< 0.001	5.4 ± 1.2	4.6 ± 1.6	*p* = 0.004
Stroke type						
- Ischemic stroke	–	113 (71%)	–	75 (71%)	35 (72%)	–
- Haemorrhagic stroke						
- Intracerebral	–	22 (14%)		16 (15%)	6 (12%)	
- Subarachnoid	–	4 (3%)		3 (3%)	1 (2%)	
- Unspecified/unavailable	–	19 (12%)		12 (11%)	7 (14%)	
Stroke location						
- Left	–	72 (46%)	–	48 (45%)	24 (49%)	–
- Right	–	52 (33%)		37 (35%)	13 (27%)	
- Bilateral	–	8 (5%)		4 (4%)	4 (8%)	
- Unspecified/unavailable	–	26 (16%)		17 (16%)	8 (16%)	
Time after stroke in months (mean, *SD*)	–	45 (*SD* 30.4) *Missing: 21*	–	46 (*SD* 30.5) *Missing: 11*	43 (*SD* 31.1) *Missing: 9*	0.10 *p* = 0.696

Cognitive complaints † Stroke Impact Scale, memory and thinking parts (mean and *SD*, range 1–5)	1.54 (*SD* 0.47) *n = 64*	2.21 (*SD* 0.84) *Missing: 1*	< 0.001	2.04 (*SD* 0.69)	2.62 (*SD* 1.00) *Missing: 1*	–0.69	$p < 0.0001$
Anxiety complaints † Hospital Anxiety and Depression Scale, Anxiety parts (mean and *SD*, range 0–21)	2.86 (*SD* 2.46) *n = 64*	5.23 (*SD* 4.23) *Missing: 4*	< 0.001	4.74 (*SD* 4.00) *Missing: 3*	6.35 (*SD* 4.58)	–0.38	$p = 0.029$
Depressive complaints † Hospital Anxiety and Depression Scale, Depression parts (mean and *SD*, range 0–21)	2.00 (*SD* 2.35) *n = 63*	5.22 (*SD* 4.08) *Missing: 6*	< 0.001	4.57 (*SD* 3.51) *Missing: 3*	6.78 (*SD* 4.91) *Missing: 3*	–0.52	$p = 0.008$
Quality of Life, physical † Stroke Specific Quality of Life Scale (mean and *SD*, range 1–5)	4.91 (*SD* 0.21) *n = 64*	4.17 (*SD* 0.82) *Missing: 6*	< 0.001	4.27 (*SD* 0.77) *Missing: 3*	3.94 (*SD* 0.90) *Missing: 3*	0.40	$p = 0.025$
Quality of Life, psychosocial † Stroke Specific Quality of Life Scale (mean and *SD*, range 1–5)	4.75 (*SD* 0.35) *n = 64*	3.60 (*SD* 0.99) *Missing: 5*	< 0.001	3.73 (*SD* 0.96) *Missing: 2*	3.28 (*SD* 1.02) *Missing: 3*	0.45	$p = 0.009$

Education: The education level was based on Verhage (1964); a higher score means higher education level. See text (Methods) for further explanation.

† For cognitive, anxiety, and depressive complaints, a higher score indicates more cognitive problems, more anxious emotions, more depressive emotions. On the Quality of Life Scale (SSQoL), a higher score indicates better quality of life. See text (Methods) for further explanation.

‡ Independent t-test was used or chi-square-test in case of dichotomous outcomes; $p < 0.05$ is a significant difference. Cohen's *d* effect sizes, with 0.2 indicating a small, 0.5 a medium, and 0.8 a large effect. Cohen's *d* was not calculated in case of dichotomous outcomes.

§ Low WQ in stroke patients is defined as a *z*-score < –1.64 on at least one subscale. See text (Methods) for further explanation. Missing data points for 3 stroke patients mean that no reliable assessment was available to determine whether their WQ score was low or normal.

Table 2. Navigation ability performance on the Virtual Tübingen test in stroke patients with normal Wayfinding Questionnaire (WQ) score versus low WQ score. †

Navigation ability tasks †	Stroke patients with normal WQ score	Stroke patients with low WQ score	Effect size Cohen's *d* and significant difference ‡	
Number of patients	48 (45%)	30 (61%)		
Scene Recognition (mean, range 1–22)	16.89 (*SD* 2.28) *Missing: 1*	15.90 (*SD* 2.78)	**0.39**	**$p = 0.091$**
Route Continuation (mean, range 1–11)	7.19 (*SD* 1.95)	6.57 (*SD* 2.14)	**0.30**	**$p = 0.192$**
Route Sequence (mean, range 1–7)	3.71 (*SD* 1.87)	2.53 (*SD* 1.87)	**0.63**	**$p = 0.009$***
Route Order (mean, range 1–22)	8.21 (*SD* 4.96)	6.13 (*SD* 3.55)	**0.49**	**$p = 0.050$***
Route Progression (mean, range 0.0–1.0)	0.794 (*SD* 0.072)	0.734 (*SD* 0.079)	**0.80**	**$p = 0.001$***
Route Distance (mean, range 0.0–1.0)	0.791 (*SD* 0.080)	0.744 (*SD* 0.076)	**0.60**	**$p = 0.013$***
Route Drawing (mean, range 1–11)	4.06 (*SD* 3.11)	3.43 (*SD* 2.29)	**0.23**	**$p = 0.308$**
Map Recognition (mean, score 0 or 1)	0.49 (*SD* 0.51) *Missing: 1*	0.27 (*SD* 0.45)		**$p = 0.017$***

† A subset of the stroke patients had their navigation ability tested in a virtual reality setting. See text for explanation of the navigation subtasks.
‡ Independent t-test was used, * $p < 0.05$ is a significant difference. Cohen's *d* effect sizes with 0.2 indicating a small, 0.5 a medium, and 0.8 a large effect. Cohen's *d* was not calculated in case of dichotomous outcome.

4

Table 3. Wayfinding Questionnaire responses: stroke patients versus healthy controls.

ITEMS *Range 1 to 7, a lower score indicating more navigation complaints.* *A score of ≤ 3 was defined as indicating clinically relevant complaints.§*	**Patients, n = 158 Mean score (SD), % with complaints §**	**Controls, *n* = 131 Mean score (*SD*), % with complaints §**	**Effect size Cohen's *d* and significant difference ‡**
1. When I am in a building for the first time, I can easily point to the main entrance of this building.	4.30 (1.9), 29%	4.44 (1.8), 28%	0.08 (p = 0.527)
2. If I see a landmark (building, monument, intersection) multiple times, I know exactly from which side I have seen that landmark before.	4.86 (1.8), 22%	5.18 (1.6), 15%	0.19 (p = 0.115)
3. In an unknown city I can easily see where I need to go when I read a map on an information board.	4.59 (2.0), 32%	5.28 (1.7), 15%	0.37 (p = 0.001)*
4. Without a map, I can estimate the distance of a route I have walked well, when I walk it for the first time.	3.92 (2.0), 40%	4.25 (1.7), 32%	0.18 (p = 0.123)
5. I can estimate well how long it will take me to walk a route in an unknown city when I see the route on a map (with a legend and scale).	3.82 (2.0), 44%	4.48 (1.5), 22%	0.38 (p = 0.001)*
6. I can always orient myself quickly and correctly when I am in an unknown environment.	3.93 (2.0), 41%	4.51 (1.6), 26%	0.32 (p = 0.006)*
7. I always want to know exactly where I am (meaning, I am always trying to orient myself in an unknown environment).	4.76 (1.9), 29%	5.04 (1.6), 17%	0.16 (p = 0.179)
8. I am afraid of losing my way somewhere. †	4.46 (2.1), 32%	5.23 (1.8), 19%	0.39 (p = 0.001)*
9. I am afraid of getting lost in an unknown city. †	4.48 (2.1), 34%	5.14 (1.8), 24%	0.34 (p = 0.005)*
10. In an unknown city, I prefer to walk in a group rather than by myself. †	4.03 (2.4), 45%	4.89 (2.0), 25%	0.39 (p = 0.001)*
11. When I get lost, I get nervous. †	4.25 (2.2), 40%	4.85 (1.8), 26%	0.30 (p = 0.013)*
How uncomfortable are you in the following situation (12, 13, 14):			
12. Deciding where to go when you are just exiting a train, bus, or subway station. †	4.56 (1.9), 31%	4.95 (1.7), 22%	0.21 (p = 0.070)
13. Finding your way in an unknown building (for example a hospital). †	4.62 (2.0), 31%	5.46 (1.5), 9%	0.48 (p < 0.001)*
14. Finding your way to a meeting in an unknown city or part of a city. †	3.91 (2.0), 46%	4.74 (1.7), 26%	0.45 (p < 0.001)*

15. I find it frightening to go to a destination I have not been before. †	4.73 (2.0), 27%	5.44 (1.8), 18%	0.37 (p = 0.002)*
16. I can usually recall a new route after I have walked it once.	4.32 (2.0), 35%	4.50 (1.8), 27%	0.09 (p = 0.415)
17. I am good at estimating distances (for example, from myself to a building I can see).	4.41 (1.9), 32%	4.52 (1.6), 24%	0.06 (p = 0.582)
18. I am good at understanding and following route descriptions.	4.42 (2.0), 27%	5.18 (1.5), 12%	0.43 (p < 0.001)*
19. I am good at giving route descriptions (meaning, explaining a known route to someone).	4.48 (1.9), 32%	5.04 (1.5), 15%	0.33 (p = 0.006)*
20. When I exit a store, I do not need to orient myself again to determine where I have to go.	4.82 (2.0), 25%	4.69 (1.9), 30%	–0.07 (p = 0.579)
21. I enjoy taking new routes (for example shortcuts) to known destinations.	3.97 (2.2), 45%	4.96 (1.8), 17%	0.51 (p < 0.001)*
22. I can easily find the shortest route to a known destination.	4.52 (2.1), 33%	5.14 (1.6), 16%	0.34 (p = 0.004)*
SUBSCALES			
Navigation and orientation (11 items): *1, 2, 3, 6, 7, 16, 18, 19, 20, 21, 22*	4.45 (1.4), 17% *Missing: 2*	4.90 (1.2), 9% *Missing: 2*	0.35 (p = 0.004)*
Distance estimation (3 items): *4, 5, 17*	4.05 (1.7), 34% *Missing: 2*	4.42 (1.4), 17% *Missing: 1*	0.24 (p = 0.041)*
Spatial anxiety (8 items): *8, 9, 10, 11, 12, 13, 14, 15*	4.37 (1.7), 25% *Missing: 1*	5.07 (1.4), 13% *Missing: 3*	0.45 (p < 0.001)*

§ A score of ≤ 3 was defined as a clinically relevant complaint, see text (Methods) for further explanation. Briefly: a score of 1–3 included the responses "not at all / almost never / rarely applicable", compared to 4 or higher "sometimes/often/almost always/fully applicable".

† The score for these items was reversed, so for all items a lower score indicates more navigation complaints.

‡ Independent t-test was used, *p < 0.05 is a significant difference. Cohen's d effect sizes with 0.2 indicating a small, 0.5 a medium, and 0.8 a large effect.

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Because the baseline characteristics of patients and controls (Table 1) revealed significant differences in gender, age, and education, we additionally compared mean scores on the three WQ subscales for gender, dichotomized age, and dichotomized level of education of patients and controls (Table 4). We found that patients scored lower than controls in all 6 comparisons. Women generally had a lower WQ score than men on all three subscales, but the difference between patients and controls was found for both men and women on all three subscales, most obviously for SA among men. Women with stroke had the lowest scores on DE (mean 3.31). Older participants generally had a higher WQ score, especially among the controls. Differences between patients and controls were largest for older participants, most obviously for NO. Participants with a low education generally had a lower WQ score. Differences between patients and controls were found in both high and low educated persons for all three subscales, most obviously for SA among the highly educated participants.

DISCUSSION

Our study ensues from previous research on the validation of the Wayfinding Questionnaire (WQ) as a clinically useful instrument to identify complaints about navigation ability in stroke patients (Claessen, Visser-Meily, de Rooij et al., 2016b). The hypothesized associations that we regard as being clinically relevant were sufficiently confirmed. As expected, the stroke patients with a low WQ score were more likely to be women, reported more cognitive complaints, more emotional problems, and lower HRQoL, and most importantly, also performed less well on the navigation ability tasks. The proportion of stroke patients with navigation complaints (low WQ scores on one or more subscales; 32%) was similar to the 29% found earlier in another sample of stroke patients (van der Ham et al., 2013), and considerably higher than in the healthy control group (14%). We also confirmed the WQ's discriminant validity: patients generally scored lower than healthy controls on all 3 subscales.

To our knowledge, no assessment instrument other than the WQ is available to cover the complete cognitive complexity that characterizes navigation complaints. Our three-subscale structure, providing separate interpretations for navigation & orientation, distance estimation, and spatial anxiety, is thus unique (Claessen, Visser-Meily, de Rooij et al., 2016b). Our research group is also the first to measure navigation complaints in a large group of stroke patients. More than three-quarters of our patients with low WQ scores were affected in terms of 1 or 2 subscales of this instrument, while only a minority scored low on all three subscales. The different subscales are needed for stroke patients as the different complaints might require different treatment strategies.

Table 4. Comparison of mean scores on the three subscales for different gender, age, and education level (patients versus healthy controls).

Three WQ subscales (mean score, *SD*)			Effect size Cohen's *d* and significant difference ‡				Effect size Cohen's *d* and significant difference ‡	
GENDER	**Men patients *n* = 94**	**Men controls *n* = 55**			**Women patients *n* = 64**	**Women controls *n* = 75**		
navigation & orientation	4.77 (1.40)	5.36 (0.92)	0.51	$p = 0.003$*	4.00 (1.32)	4.56 (1.23)	0.44	$p = 0.011$*
distance estimation	4.54 (1.56)	4.98 (1.09)	0.33	$p = 0.048$*	3.31 (1.60)	4.01 (1.44)	0.46	$p = 0.008$*
spatial anxiety	4.68 (1.64)	5.59 (1.23)	0.63	$p < 0.001$*	3.90 (1.64)	4.68 (1.44)	0.51	$p = 0.004$*
AGE	**Young, age <60y patients *n* = 74**	**Young, age <60y controls *n* = 82**			**Older, age ≥60y patients *n* = 83**	**Older, age ≥60y controls *n* = 49**		
navigation & orientation	4.47 (1.31)	4.70 (1.22)	0.18	$p = 0.259$	4.44 (1.52)	5.25 (1.02)	0.64	$p < 0.001$*
distance estimation	3.98 (1.70)	4.21 (1.49)	0.14	$p = 0.376$	4.11 (1.67)	4.77 (1.13)	0.47	$p = 0.015$*
spatial anxiety	4.46 (1.52)	5.03 (1.45)	0.38	$p = 0.017$*	4.28 (1.81)	5.12 (1.41)	0.52	$p = 0.007$*
EDUCATION	**High education patients *n* = 68**	**High education controls *n* = 83**			**Low education patients *n* = 90**	**Low education controls *n* = 47**		
navigation & orientation	4.66 (1.42)	5.06 (1.11)	0.32	$p = 0.053$	4.30 (1.41)	4.61 (1.24)	0.23	$p = 0.209$
distance estimation	4.23 (1.65)	4.64 (1.30)	0.28	$p = 0.100$	3.91 (1.70)	4.04 (1.48)	0.08	$p = 0.670$
spatial anxiety	4.54 (1.65)	5.30 (1.42)	0.50	$p = 0.003$*	4.23 (1.69)	4.65 (1.36)	0.28	$p = 0.150$

‡ Independent t-test was used. *$p < 0.05$ is a significant difference. Cohen's *d* effect sizes with 0.2 indicating a small, 0.5 a medium, and 0.8 a large effect.

Literature on the subject of spatial navigation that describes findings agree with our results regarding demographic differences. The women in our cohort had a higher level of NO, DE and SA complaints than the men, both among the controls and the stroke patients (Table 4). All three subscales showed more complaints among patients than controls, both for men and women. The greatest difference between patients and controls was that regarding SA for the men (d = 0.63) and that regarding SA for the women (d = 0.51). A large review on gender and navigation has described differences in strategies, with men preferably relying on visuospatial properties of the environment and configurational orientation strategies, while women focus more on landmarks and procedural “route” strategies involving route knowledge (Coluccia & Louse, 2004). The same review discussed differences in the findings of self-evaluation questionnaires on orientation skills, in which men estimate themselves to be better at orientation and show greater confidence in their ability than women. In other words, lower self-confidence (or more honesty to admit failures) might increase the navigation complaints among women. The authors also stated that women report more anxiousness when navigating than men, which agrees with our findings. Our SA subscale might be a good measure of low confidence in one’s navigation ability, due to personality (or changes therein), more fear of getting lost after stroke and/or loss of cognitive navigation skills after stroke. Interestingly, our results reveal that SA is negatively influenced by stroke not only for women, but also (or relatively even more strongly) for men. In our study, the expected correlation between lower WQ score and higher age was not found (Moffat, 2009). This is, however, in line with other studies suggesting that older individuals overestimate their current navigation abilities. It could be that seniors tend to judge their sense of direction and everyday navigation just as favourably or even more so than the younger generations (Taillade, N’Kaoua, & Sauzéon, 2016; Klencklen, Després, & Dufour, 2012).

We found more self-reported navigation problems among patients with more cognitive complaints (Table 1). This was to be expected, as navigation ability is a complex cognitive function, related to a multitude of other cognitive abilities such as episodic memory, mental working speed, and executive functioning (Wolbers & Hegarty, 2010). Navigation complaints and cognitive complaints as assessed by the c-SIS can coincide, but it is important to keep in mind that navigation is a dissociable cognitive function, so navigation complaints can also be present without complaints in other cognitive domains. As regards emotional feelings, more navigation complaints were reported by patients in our study with more anxious and depressive complaints, and moderate correlations between SA score and the HADS–anxiety were found. It is important to mention once again that SA assessment offers additional value to the HADS, because SA is not always found by instruments of general anxiety (Walkowiak et al., 2015). We found that lower WQ scores were associated with lower levels of both psychosocial and physical HRQoL. This could be explained by the fact that navigation complaints interfere with independent functioning and mobility. In conclusion, the fact that our hypothesized associations between navigation and cognitive and emotional complaints and HRQoL were confirmed supports the validity of the WQ.

Last but not least, the validity of the WQ was supported by our positive results using objective measurements of navigation ability: the patient group with a low WQ indeed showed poorer actual navigation performance in a virtual reality setting, with medium to large effect sizes. Although navigation ability in a virtual reality setting is different from that in a patient's personal surroundings, it is known that testing in a virtual reality setting is an ecologically valid way to test real-life navigation ability (Claessen, Visser-Meily, de Rooij et al., 2016a).

Strengths and limitations

A strength of our study is the large group of mild stroke patients in the chronic phase and the comparison with healthy controls. The group consisted of patients with various stroke types and locations, allowing generalization to stroke patients in general. Our patient group was representative of the largest group of stroke patients living at home in the chronic phase. This group includes patients who were discharged directly to their own homes several days after the stroke, but also patients who initially had a severe hemiparesis and/or other neurological deficits in the subacute phase, but who can walk independently notwithstanding these neurological deficits after discharge from a rehabilitation centre. In the chronic phase, this group of patients is confronted with navigation ability on daily basis. We were able to confirm our hypothesized hypotheses of associations between navigation complaints and demographics and other self-report instruments, with relevant effect sizes (small to medium effects). What is also unique to this study is that we performed analyses with both subjective and objective instruments of navigation ability. Objective measurement was based on performance on navigation cognitive ability tasks with the Virtual Tubingen test.

Our study also has some limitations. Our cut-off values should be interpreted with care, because they are based on a group of 131 participants and our control group included more men and younger persons with somewhat higher level of education compared to the stroke patients. However, Table 4 shows that the crude mean WQ scores for dichotomized gender, age, and education each show differences between patients (lower WQ) and controls. Considering the above, we do not think that the differences in gender, age, and education between the groups have greatly biased our main results. Another limitation is that we did not calculate specificity and sensitivity values. This is, however, related to the fact that navigation complaints are also present in healthy people and there is no gold standard. A debatable issue is that a low score on the WQ might result from motor impairment or neglect caused by stroke. Although we cannot fully invalidate this, we consider it unlikely in our study since we included a patient group with a relatively good outcome (walkers, independent in activities of daily living and without language disorder). Finally, a general limitation of every self-reported instrument is that scores rely on accuracy of the patient's insights. Patients with brain injury may have diminished insights into their actual cognitive and navigation performance in daily life, due to their stroke as well as their age (Boosman, van Heugten, Winkens, Heijnen, & Visser-Meily, 2014). The above limitations are processed below in the clinical implications.

Clinical implications

We are convinced that the WQ can already be used in current practice, and future studies will be helpful to improve its interpretation (see next section). We recommend using the WQ in outpatient rehabilitation settings. It can be used in addition to other instruments assessing post-stroke cognitive complaints, such as the CLCE-24 (van Heugten et al., 2007). Our cut-off values (NO sum score ≤ 32, DE sum score ≤ 6, or SA sum score ≥ 20) are helpful to guide the interpretation of WQ scores, but should not to be applied too strictly. We think that individual health professionals can decide whether the WQ responses are abnormal or not, even without (gender-specific and age-specific) cut-off values. Health professionals should take account of three considerations regarding the WQ subscales: men tend to assess themselves as having higher navigation ability than women (as found in the current study), older people might overestimate themselves more than younger people (Taillade et al., 2016; Klencklen et al., 2012) and some patients lack insight into their own cognitive functions and might overestimate themselves (Boosman et al., 2014). It may be valuable to involve the partner or family of the patient in answering the questions if the patient's self-insight is affected, though some items of the WQ will be difficult to answer for proxies. Last but not least, we believe the impact of the navigation complaints should be taken into account to create a suitable interpretation. Hence we recommend that health professionals ask patients (and their proxies) whether their ability to navigate has declined compared to the pre-stroke period and whether this decline is inconvenient to them. These two questions can help to decide whether a particular patient requires further diagnostics and/or treatment for their navigation complaints.

Treatment

Treatment options for navigation problems are currently being developed. An important intervention is that of psycho-education for both patients and their partners/family. Because navigation is such a complex cognitive function in which it is rare for all aspects to be affected, learning alternative navigation strategies can be a successful treatment option. A pilot navigation training programme using a virtual reality setting has shown good results in a small group of stroke patients (Claessen, van der Ham, Jagersma, & Visser-Meily, 2016). Patients can learn compensation strategies, but it depends on a patient's profile which compensation strategies are potentially useful. More research is needed to find out which patients might benefit from a navigation training focused on teaching them to adopt alternative navigation strategies. The WQ, as a short and valid screening instrument, would certainly be valuable for this future research.

Future research

We suggest that confirmation of our cut-off points in another large group of controls and stroke patients will be helpful to improve the interpretation of the WQ by health professionals. It could be useful to define age-specific and gender-specific cut-off points or correction factors, but whether this is necessary is debatable. Next, although the WQ is already a concise questionnaire (less than 10 minutes), future studies could consider further shortening the WQ as regards the number of NO items, if studies should reveal (as the current one did) that item 20 shows no difference between patients and controls. Moreover, as navigation impairment also occurs in other types of acquired brain injury (traumatic brain injury) and degenerative diseases (Alzheimer's disease), future research can examine if the WQ is also clinically useful for these and other neurological patient groups.

CONCLUSION

The Wayfinding Questionnaire (WQ) is a valid and clinically useful self-report instrument for stroke patients to identify post-stroke navigation complaints (present in approximately 30% of stroke patients). The WQ is a fast and easy way to assist health care professionals in deciding whether or not a stroke patient should be referred for detailed objective navigation tests. This is important, as options for treatment of navigation problems are being developed. Although more research on cut-off values would be helpful, we already advocate the use of the WQ, to ensure navigation complaints in stroke patients are no longer ignored.

CHAPTER 5

A direct comparison of real-world and virtual performance in chronic stroke patients

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IH designed the study; MC collected and analyzed the data; MC, IH, JV, NR, and AP interpreted the data; MC drafted the paper; IH, JV, NR, and AP revised the paper for intellectual content.

ABSTRACT

Objective: An increasing number of studies have presented evidence that various patient groups with acquired brain injury suffer from navigation problems in daily life. This skill is, however, scarcely addressed in current clinical neuropsychological practice and suitable diagnostic instruments are lacking. Real-world navigation tests are limited by geographical location and associated with practical constraints. It was therefore investigated whether virtual navigation might serve as a useful alternative.
Method: To investigate the convergent validity of virtual navigation testing, performance on the Virtual Tübingen test was compared to that on an analogous real-world navigation test in 68 chronic stroke patients. The same eight subtasks, addressing route and survey knowledge aspects, were assessed in both tests. In addition, navigation performance of stroke patients was compared to that of 44 healthy controls.
Results: A correlation analysis showed moderate overlap ($r = .535$) between composite scores of overall real-world and virtual navigation performance in stroke patients. Route knowledge composite scores correlated somewhat stronger ($r = .523$) than survey knowledge composite scores ($r = .442$). When comparing group performances, patients obtained lower scores than controls on seven subtasks. Whereas the real-world test was found to be easier than its virtual counterpart, no significant interaction-effects were found between group and environment.
Conclusions: Given moderate overlap of the total scores between the two navigation tests, we conclude that virtual testing of navigation ability is a valid alternative to navigation tests that rely on real-world route exposure.

INTRODUCTION

Spatial navigation is an ability that enables us to find our way from one location to another. Whether we walk, ride a bike or drive a car, we rely on the ability to navigate to arrive at our planned destination. Navigation ability is thus crucial for everyday life, as it allows us to function independently in the community. Notwithstanding the notion of the cognitive complexity of navigation ability (Brunsdon, Nickels, & Coltheart, 2007; Wiener, Büchner, & Hölscher, 2009; Wolbers & Hegarty, 2010), researchers usually distinguish between two fundamentally different memory representations for navigation (Montello, 1998; Siegel & White, 1975). Route knowledge concerns information related to a specific route, such as distinctive features in the environment (landmarks), associations between landmarks and directional information (place-action associations) and the temporal order of landmarks or turns. Survey knowledge, on the other hand, refers to an integrated geometrical representation of the environment which also includes information about distances and angles.

Inherent to the cognitive complexity of navigation ability is its vulnerability to the effects of brain damage. Based on self-report data, nearly a third of stroke patients experience navigation difficulties after their stroke event (van der Ham, Kant, Postma, & Visser-Meily, 2013). Other studies have provided evidence for this notion using objective navigation ability assessments in stroke patients (e.g., van Asselen, Kessels et al., 2006). Special attention to navigation ability should be paid in neglect patients, as deficits in this ability have shown to be associated with the neglect syndrome (De Nigris et al., 2013; Guariglia, Piccardi, Iaria, Nico, & Pizzamiglio, 2005; Nico et al., 2008). Recent studies have indicated that navigation impairment can also be found in other patient groups with acquired brain injury (ABI), including traumatic brain injury (e.g., Livingstone & Skelton, 2007), Korsakoff's syndrome (Oudman et al., 2016) and Alzheimer's disease (e.g., Cushman, Stein, & Duffy, 2008). In general, these and many other studies clearly illustrate the importance of evaluating the status of navigation ability in ABI patients. Strikingly, this skill is scarcely addressed in an explicit manner in current clinical neurological and neuropsychological practice.

The lack of studies with a specific focus on navigation ability in ABI patient groups may partly be due to the fact that no valid objective navigation tests are currently generally available for use in neuropsychological practice. A further obstacle lies in the finding that common spatial neuropsychological tests, such as the Judgment of Line Orientation, the Rey-Osterrieth/Taylor Complex Figure and the Corsi Block-Tapping Task, are hardly able to reliably predict navigation behavior (e.g., Nadolne & Stringer, 2001; van der Ham et al., 2013). It has been argued that this might result from neuropsychological tests falling short in ecological validity (Chaytor & Schmitter-Edgecombe, 2003), with regard to the ability to navigate. Ecological validity refers to the extent to which a neuropsychological test is representative of everyday situations and denotes the degree to which the test results are generalizable to and predictive of everyday life performance (P. W. Burgess et al., 2006).

A cognitive explanation for the inadequate ecological validity of common neuropsychological spatial tests lies in the fact that they are carried out within near or reaching space. Spatial navigation, in contrast, concerns interaction with large or navigational space. Behavioral and neuropsychological studies have drawn attention to this notion by showing that small-scale and large-scale spatial learning abilities can be dissociated (e.g., Piccardi et al., 2010, 2011) and rely on partly independent neural circuits (Nemmi, Boccia, Piccardi, Galati, & Guariglia, 2013). That is, patients suffering from navigation impairment do not necessarily fail on the small-scale spatial tests currently used in neuropsychological practice. These findings thus clearly indicate that assessment of navigation behavior should be based on large-scale tasks that closely resemble everyday navigation situations rather than using existing small-scale spatial neuropsychological tests.

For scientific purposes, researchers have generally adopted two different approaches to measure navigation ability in an objective manner: real-world and virtual reality (VR) navigation tests. In a typical real-world navigation test, the researcher takes the participant along a specific route in a building (for example, a hospital) or on the streets. After this learning phase, participants are asked to retrace the studied route (e.g., Barrash, Damasio, Adolphs, & Tranel, 2000) or tested on their knowledge of it (e.g., van Asselen, Kessels et al., 2006). As the participant has to physically follow the route, real-world navigation tests are likely to be closely related to actual navigation performance. Nonetheless, real-world navigation tests are also characterized by several serious limitations.

Firstly, real-world navigation tests are, by definition, bound to a specific indoor or outdoor environment, for instance a particular hospital building (e.g., Barrash et al., 2000). This is an essential problem, as a navigation test validated in a specific environment is of limited use to clinicians at other locations. A second limitation of real-world navigation testing lies in the fact that identical exposure to the test environment during the learning phase of the route cannot be guaranteed across participants, for example due to differences in exposure time. Moreover, it is hard to control many other potential disturbing factors such as weather conditions, traffic and noise (van der Ham, Faber, Venselaar, van Krefeld, & Löffler, 2015). Another potential confounding factor is the participant's familiarity with the test environment. Some recent studies have shown that the degree of familiarity is an important factor to address, as higher familiarity generally leads to better performance on navigation tests (de Goede & Postma, 2015; Iachini, Ruotolo, & Ruggiero, 2009; Prestopnik & Roskos-Ewoldsen, 2000). More specifically, higher familiarity is associated with higher sense of direction and greater reliance on a survey/allocentric navigation strategy (Iachini et al., 2009). Apart from the above limitations, real-world navigation test procedures also have some practical drawbacks. These tests can be rather time-consuming and require the participant to be physically able to traverse the route. These disadvantages make it nearly impossible to develop a well-validated real-world navigation test that is widely applicable in neuropsychological practice around the world.

Virtual navigation tests have been proposed as a potential alternative to real-world navigation tests, because VR testing is not restricted by the above limitations. VR does not only allow for developing novel environments (to avoid issues with the participant's familiarity with the test environment), but also offers the researcher the ability to generate realistic and highly controllable real-world simulations (Rose, Brooks, & Rizzo, 2005). Most importantly, assessment of a well-validated virtual navigation test is not bound to a specific location.

It should, however, also be mentioned that virtual navigation is associated with an important drawback; the absence of locomotion. When passively studying a virtual route, participants can only rely on visual cues or external landmarks. That is, passive exposure to a virtual route does not provide the participant with vestibular cues or the possibility to internally perceive the body in space. Yet, the sensory input of moving through the environment has been implicated in the creation of an environmental mental map (e.g., Chrastil & Warren, 2013; van der Ham et al., 2015), which contains information about the relative positions of landmarks in an environment. It might thus be possible that the validity of virtual navigation is compromised when it comes to testing the survey knowledge aspects of a route.

The validity of virtual navigation tests has been studied several times in healthy participants. Studies have not only suggested that transfer from real-world to virtual environments is possible (Péruch, Belingard, & Thinus-Blanc, 2000; Wilson, Foreman, & Tlauka, 1997; Witmer, Bailey, Knerr, & Parsons, 1996), but have also shown equivalent navigation performance across real-world and virtual navigation tests (Lloyd, Persaud, & Powell, 2009; Richardson, Montello, & Hegarty, 1999). Three studies have addressed the equivalence of real-world and virtual navigation tests in ABI patient groups. Cushman and colleagues (2008) compared performance on a real-world navigation test to that on a virtual version. They found a strong correlation ($r = .73$) across all participants, including MCI and early Alzheimer's disease patients. Sorita and colleagues (2013) compared a real-world and a virtual navigation test by testing traumatic brain injury patients in a between-participants design. Whereas route retracing performance was comparable in the real-world and virtual conditions, patients in the real-world condition were better in scene ordering and a trend existed for better sketch-mapping performance in this condition. The authors therefore concluded that the spatial representations probably differed between the real-world and virtual conditions. These two studies share the use of identical environments in their real-world and virtual navigation tests. Busigny and colleagues (2014), in contrast, applied different navigation tasks in their real-world and computerized tests.

Nonetheless, they still reported a strong correlation ($r = .80$) between performances on the two test procedures in the patient group. They, however, also argued that their real-world navigation tests were more sensitive in revealing navigation impairment in their patients with posterior cerebral artery infarctions.

In the current study, a group of 68 chronic stroke patients completed both a virtual navigation test, i.e., the Virtual Tübingen test (Claessen, van der Ham, Jagersma, & Visser-Meily, 2016; Claessen, Visser-Meily, Jagersma, Braspenning, & van der Ham, 2016; van der Ham et al., 2010), and a real-world navigation test. This was done to verify the convergent validity of virtual navigation testing. The study focused on this patient group, as they frequently complain about navigation problems after their stroke event (van der Ham et al., 2013). The approach taken here is unique in two respects. Firstly, the study relies on a large and representative sample of chronic stroke patients, which is uncommon in the clinical literature on navigation ability. And, secondly, the within-participants design allows a direct investigation of the relationship between virtual and real-world navigation performance for which significant correlations are expected. Stroke patients' performances on the two navigation tests were compared to that of a group of healthy control participants. It is expected that stroke patients have more difficulties with the navigation tasks than controls and that performance is comparable for the real-world and virtual environments. In contrast to Cushman and colleagues (2008), different rather than identical environments were used in the real-world and virtual tests to prevent unwanted learning effects.

METHODS

Participants

Sixty-eight chronic stroke patients (time post-stroke varied between 14 and 86 months, $M = 38.4$; $SD = 15.3$) were recruited from the rehabilitation clinic of De Hoogstraat Revalidatie and the rehabilitation department of the University Medical Center Utrecht (Utrecht, the Netherlands). Inclusion criteria were the ability to walk independently and the absence of severe aphasia. In addition, 44 healthy participants served as controls. Most of them were directly recruited by the experimenters (relatives or acquaintances) or were partners of patients. None of them reported a history of visual, neurological, psychiatric or mobility problems, or substance abuse. Demographic data (gender, age and educational level) of all participants and stroke characteristics (type and location) of the patients are provided in Table 1.

All participants provided written consent after being informed about the study's purpose. Participants received a small monetary compensation for engaging in the study and their travelling costs were reimbursed. The procedures reported here satisfied the regulations as set by the Declaration of Helsinki and were approved by the medical ethical review board of the University Medical Center Utrecht (protocol no. 12-198). This study's dataset results from a larger project on navigation ability in stroke patients. A small proportion of these data are also presented in Claessen, Visser-Meily, Jagersma, and colleagues (2016).

Materials and Procedure

Each assessment started with participants completing a brief neuropsychological screening comprising four common neuropsychological tests. Next, the virtual and real-world navigation tests were administered in fixed order. The virtual test was always presented first, as we aimed to assess the virtual navigation test in as many stroke patients as possible for the larger project. Participants were required to take a break after the virtual navigation test to prevent fatigue. Additional breaks were given on request in between the neuropsychological tests. It took participants two and a half hours on average to complete the full assessment procedure. Six experimenters were involved in data collection. All experimenters were trained and supervised by the same researcher to minimize differences in the assessment of the tests.

Table 1. Demographic data for patients and controls, and patients' stroke characteristics.

	Patients (n = 68)	Controls (n = 44)	test value	p	effect size
Age in years	59.5 (12.5)	60.3 (10.2)	$t < 1$	.708	-
Male/female (%)	57.4% / 42.6%	45.5% / 54.5%	$\chi^2 = 1.52$	.218	*Phi* = –0.12
Education	5.2 (1.4)	5.7 (0.9)	$U = 1211$	.077	$r = -0.17$
Stroke type					
Ischemic stroke	54 (79.4%)				
Hemorrhagic stroke					
- Intracerebral	10 (14.7%)				
- Subarachnoid	3 (4.4%)				
Unspecified/unavailable	1 (1.5%)				
Stroke location					
Supratentorial region					
- Left	27 (39.7%)				
- Right	29 (42.7%)				
- Bilateral	1 (1.5%)				
Infratentorial region					
- Left	2 (2.9%)				
- Right	2 (2.9%)				
- Bilateral	6 (8.8%)				
Unspecified/unavailable	1 (1.5%)				

Note. The upper part of the table displays demographic data (age, gender, and educational level based on Verhage (1964, possible range: 1–7)) for patients and healthy controls. Differences in demographics were assessed using an independent t-test (age), a chi-square test (gender), and a Mann-Whitney test (educational level). Standard deviations are displayed in parentheses for age and educational level. The bottom part of the table provides descriptive information on the stroke characteristics of the patient group.

Neuropsychological screening

The screening consisted of four neuropsychological tests administered in the order as listed below. These commonly used tests were included to obtain a general indication of the participants' neuropsychological profile. The screening contained only tests assessing the most relevant cognitive functions and was kept brief to ensure feasibility of the entire assessment procedure for the stroke patients.

- The Dutch version of the Adult Reading Test (DART; in Dutch: NLV, 'Nederlandse Leestest voor Volwassenen') was applied as a measure of premorbid intelligence

(Schmand, Lindeboom, & van Harskamp, 1992). Raw scores were converted to an estimated premorbid intelligence quotient adjusted for age, gender and level of education.

- The Corsi Block-Tapping Task was used as a representative of visuospatial attention span (forward condition: Kessels, van Zandvoort, Postma, Kappelle, & de Haan, 2000) and visuospatial working memory capacity (backward condition: Kessels, van den Berg, Ruis, & Brands, 2008). Raw data were converted to percentiles correcting for age.
- Measures of mental processing speed (part A) and divided attention (part B) were obtained by means of the Trail Making Test (TMT; Reitan, 1992). Raw scores were converted to percentiles based on the norms provided by the Neuropsychology section of the Dutch Association of Psychologists (Schmand, Houx, & de Koning, 2012). These norms correct for the effects of age, gender and educational level and provide three scores: part A, part B and part B corrected for performance on part A.
- The Digit Span subtest of the WAIS-III (Wechsler, 1997) was used to measure verbal working memory span. Norms correcting for age from the Dutch manual were used to convert raw scores to a scaled score and an accompanying percentile score.

Navigation test batteries

Participants completed a virtual navigation test (Virtual Tübingen test; see Claessen, van der Ham et al., 2016; Claessen, Visser-Meily, Jagersma et al., 2016; van der Ham et al., 2010) and a real-world navigation test. Knowledge of the studied route was assessed by way of eight subtasks in both navigation tests.

Virtual environment

In the learning phase, participants were shown one of two routes (see Figure 1A) through a photorealistic virtual rendition of the German city Tübingen (van Veen, Distler, Braun, & Bülthoff, 1998), twice in immediate succession. The two movies were nearly comparable in duration (A: 210 seconds and B: 253 seconds), similar in distance (400 m) and in movement speed (somewhat above walking speed). Each route contained eleven decision points. An actual left or right turn was taken at seven of these decision points, whereas the route continued in straight-ahead direction at the other four decision points. Eight subtasks were used to assess the participants' knowledge of the studied route in the testing phase (see below).

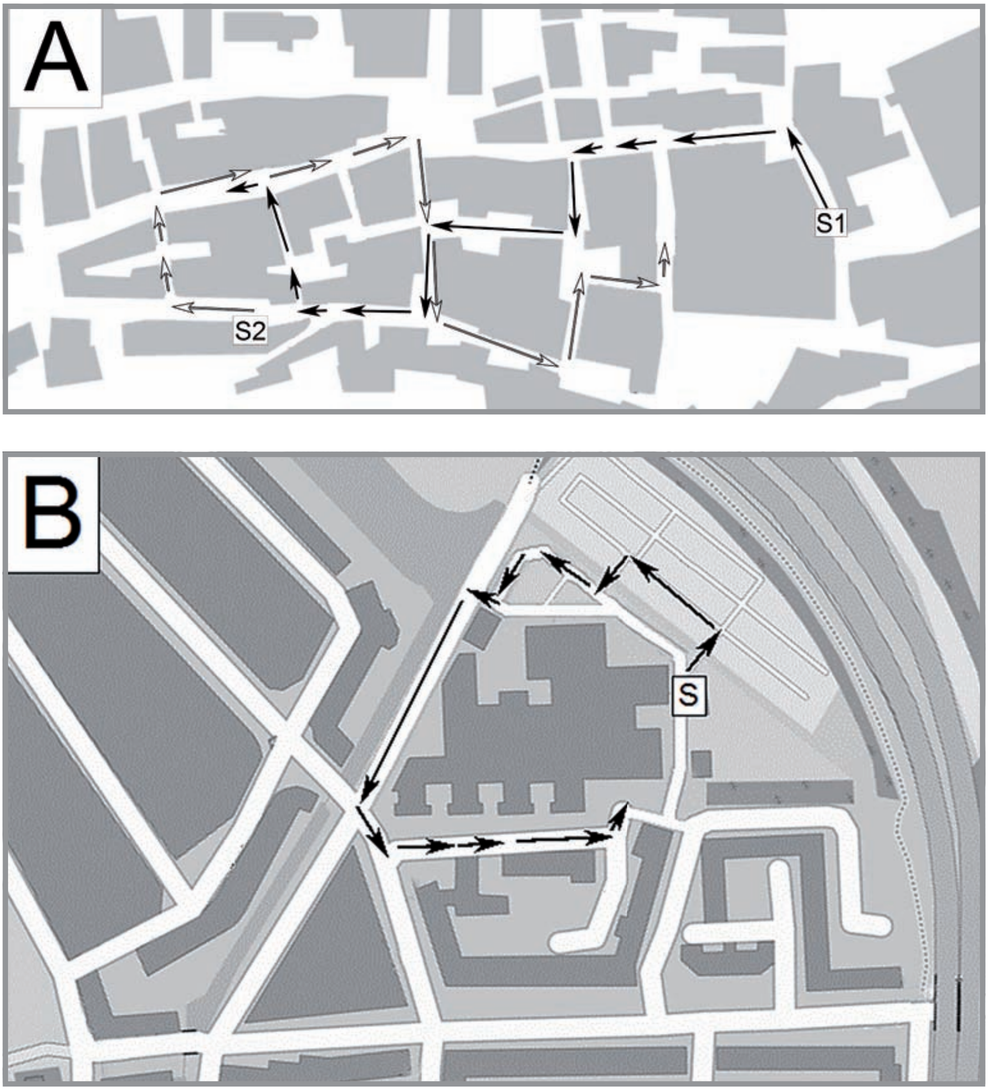


Figure 1. Maps of the two Virtual Tübingen routes and the route applied in the real-world test.

(A) The first map displays the two Virtual Tübingen routes (black and white arrows). Each route segment is represented as an arrow. Starting locations of the routes are marked with an S and the corresponding route number. (B) The second map shows the route as used in the real-world navigation test (direct vicinity of rehabilitation clinic "De Hoogstraat Revalidatie" in Utrecht, the Netherlands). Route segments are displayed as arrows and the starting position of the route is marked with an S.

Real-world environment

A route (426 m) through the immediate vicinity of the rehabilitation clinic of De Hoogstraat Revalidatie was used for the real-world navigation test (see Figure 1B). This environment is located in an urban area (Utrecht, the Netherlands). No exceptionally salient landmarks or route signs were present along the test route. This environment was used for the real-world navigation test for practical reasons. It would have been impossible to take all participants to another test location that would be unfamiliar to all of them.

The participant followed the experimenter throughout the route, which lasted 324.9 seconds (SD = 78.5 sec) on average. Experimenters were instructed to take the walking speed of the participant into account. The configuration of the real-world route was matched as closely as possible to the virtual route: it also contained eleven decision points including seven actual left or right turns. The route continued in straight-ahead direction at the remaining four decision points. The participant was requested to perform the eight subtasks as described below for the real-world route upon return in the test room. Participants were asked to indicate their familiarity with the real-world environment at the end of the test procedure (1 = "not familiar at all" to 7 = "highly familiar"). We asked for this information, as nearly half of the patients had completed their rehabilitation in the rehabilitation clinic of the De Hoogstraat Revalidatie. They might thus have been more familiar with the test environment than the patients recruited through the University Medical Center Utrecht and the healthy control participants.

Navigational subtasks

The navigation tests contained eight subtasks assessed in the order of appearance below. The first four subtasks address route knowledge aspects, while the latter four subtasks rely on integration of the geometrical aspects of the environment, which is considered survey knowledge.

- *Scene Recognition.* Twenty-two images of decision points taken from the studied route were presented to the participant. Eleven of these images[2] were targets (i.e., encountered during the route), whereas the other eleven scenes were distractors. Scoring: Number of correct responses, range: 0–22.
- *Route Continuation.* The eleven decision points taken from the route were presented one-by-one in random order. Participants were asked to indicate the direction in which the route continued at each decision point. Scoring: Number of correct responses, range: 0–11.
- *Route Sequence.* Participants were requested to indicate the sequence of turns as taken during the route. They responded by arranging a set of arrow cards. Only

2 *These eleven decision point images were also used for the route continuation and route order subtasks. Images were taken right in front of the decision point depicting all possible directions.*

actual turns (i.e., left and right turns) were considered. Accuracy: Number of correctly indicated turns in the sequence, range 0–7.

- *Route Order.* Participants were instructed to reconstruct the order in which eleven images of decision points occurred during the route. Scoring: Three points for each image assigned to its correct position in the sequence; two points for images assigned one position too late or too early; one point for images assigned two positions away from correct placement (range: 0–33).
- *Distance Estimation.* Participants were requested to provide a distance estimate of the studied route. Scoring: Absolute deviation from the correct response in meters.
- *Duration Estimation.* Participants were required to provide a duration estimate of the studied route. Scoring: Absolute deviation from the correct response in seconds.
- *Route Drawing.* Participants were asked to draw the studied route on a map of the test environment. Only the starting point and the correct starting direction were already provided. Scoring: One point for each correctly indicated direction (left turn, straight forward or right turn) at relevant decision points, range: 0–11.
- *Map Recognition.* Participants had to select the correct map of the route out of four options. Scoring: Correct or incorrect.

Statistical Analysis

Differences in demographics were assessed using an independent t-test (age), a chi-square test (gender), and a Mann-Whitney test (educational level). Group differences on neuropsychological measures were investigated using independent t-tests. Self-rated familiarity with the real-world environment between the groups was tested using an independent t-test. Relationships between familiarity and real-world subtask performance were investigated by way of a Pearson correlation analysis. A semi-partial correlation analysis was performed to assess relationships between subtask scores on the real-world and virtual navigation tests while controlling for the effect of familiarity on real-world navigation performance. A repeated measures analysis of covariance (ANCOVA) was then performed for each subtask, with environment (real-world vs. virtual) as within-subject factor and group (healthy controls vs. stroke patients) as between-subject factor. ANCOVAs were corrected for educational level and familiarity with the real-world environment, due to the (trend-level) differences between controls and patients on these variables (see Tables 1 and 3). Due to its ordinal scale, educational level was recoded into low and high levels (1–4 vs. 5–7; Verhage, 1964) and included as a between-subject factor rather than as a covariate. Familiarity with the real-world environment was taken into account as a covariate. In case the initial analysis indicated a significant contribution of educational level and/or familiarity ($p < .05$), these variables were maintained in the ANCOVA.

The real-world Scene Recognition score of one patient was missing due to a technical problem. Moreover, one patient did not provide distance and duration estimates for the real-world route. Alpha level was set to .05 for all statistical tests. Analyses were performed using IBM SPSS Statistics version 22.0.

RESULTS

Demographics and neuropsychological screening

Patients and controls were comparable in terms of age and gender (p = .708 and p = .218 respectively, see Table 1). The comparison of educational level between the groups was also non-significant, but a trend (p = .077) existed for patients being slightly lower educated than controls. Patients obtained significantly lower scores on the majority of the neuropsychological screening tasks compared to controls (see Table 2).

Self-rated familiarity with the real-world environment

Patients were significantly more familiar (M = 4.88, SD = 1.88) with the real-world environment than controls (M = 1.66, SD = 1.40), t (107.80) = –10.39, p < .001, r = .71. Hence, a Pearson correlation analysis was conducted to verify the relationship between self-rated familiarity with the environment and performance on the real-world navigation subtasks (see Table 3). Only one significant correlation was found in the control group (Scene Recognition). In the patient group, two correlations were found to be significant (Scene Recognition and Route Order) and two other correlations reached trend level (Route Continuation and Route Sequence).

Table 2. Neuropsychological screening results for patients and controls.

	Patients (*n* = 68)	Controls (*n* = 44)	*t*	*p*	Effect size *r*
Dutch Adult Reading Test (IQ)	97.5 (17.0)	110.9 (12.9)	4.70	< .001*	0.41
Corsi Block-Tapping Task					
- forward (span x score)	37.8 (15.8)	42.6 (12.9)	1.67	.097	0.16
- backward (span x score)	38.8 (20.5)	46.6 (16.3)	2.25	.027*	0.21
Trail Making Test					
- Part A (seconds)	57.3 (39.0)	35.6 (12.3)	–4.26	< .001*	0.42
- Part B (seconds)	124.8 (85.6)	74.0 (24.9)	–4.54	< .001*	0.45
- Part B (B / A)	2.4 (1.0)	2.2 (0.6)	–1.59	.116	0.15
Digit Span (WAIS-III)					
- forward (score)	7.7 (1.8)	8.7 (1.6)	3.00	.003*	0.27
- backward (score)	5.1 (1.9)	6.2 (2.0)	2.91	.004*	0.27

Note. Group differences were tested by way of independent t-tests. Effect size *r* is reported for significant results. Standard deviations are displayed in parentheses. * $p < .05$

Table 3. Correlations between self-rated familiarity with the real-world environment and performance on the real-world navigation subtasks for patients and controls.

	Patients		Controls	
	r	*p*	*r*	*p*
Scene Recognition	.352	.003*	.330	.031*
Route Continuation	.206	.092	.213	.166
Route Sequence	.237	.052	.171	.266
Route Order	.414	< .001*	.211	.114
Distance Estimation	.114	.356	.021	.891
Duration Estimation	–.074	.551	–.163	.291
Route Drawing	.192	.116	–.039	.802
Map Recognition	.130	.292	–.001	.992

Note. Displayed correlations are based on Pearson correlation coefficients, only the correlations of the Map Recognition subtask concern point-biserial correlation coefficients.
* $p < .05$

Relationship between the real-world and Virtual Tübingen navigation tests

Semi-partial correlations reached significance for three subtasks in controls, together with four significant correlations and one trend-level (p = .077) correlation in the patient group (see Table 4). A composite score of overall performance was calculated for the real-world and virtual navigation tests in the patient group (based on the means and standard deviations of controls). The semi-partial correlation between the two composite scores was moderate in degree, $r = .535$, $p < .001$, indicating moderate overall overlap between the two navigation tests in patients. Two further analyses were performed using separate composite scores for the route and survey knowledge subtasks (see Methods section). Moderate overlap was found between the two route knowledge composite scores, $r = .523$, $p < .001$, whereas the correlation between the two survey knowledge composite scores was weak to moderate, $r = .442$, $p < .001$.

Effects of group and environment on navigation performance

Results of the repeated measures ANCOVAs for each of the eight subtasks are presented in Table 5. A significant main-effect of group was found for seven out of the eight subtasks showing that patients had more difficulties with the navigation tasks than controls. The main-effect of environment was significant for six out of the eight subtasks indicating higher performance based on the real-world environment in comparison to the virtual environment. More importantly, the interaction-effect between group and environment was non-significant for all subtasks (except for one trend-level interaction-effect, $p = .053$, on the Route Continuation task), meaning that the differences in performance between patients and controls were similar in the real-world and virtual environment.

Table 4. Performance on the eight subtasks of the virtual and real-world navigation tests and their correlations, displayed for patients and controls separately.

	Virtual environment	Real-world environment	Correlation	
	Mean (*SD*)	*Mean* (*SD*)	VT-Eco, *r*	*p*
Stroke patients				
Scene Recognition	16.8 (2.4)	18.6 (2.2)	.216	.077
Route Continuation	7.0 (2.0)	8.0 (1.6)	.269	.027*
Route Sequence	3.5 (1.9)	4.7 (1.7)	.266	.029*
Route Order	15.0 (6.6)	25.6 (6.8)	.350	.003*
Distance Estimation	1468.7 (1342.3)	535.7 (1320.5)	.306	.012*
Duration Estimation	427.7 (796.0)	319.5 (274.4)	.035	.776
Route Drawing	4.0 (3.0)	8.0 (3.0)	–.028	.823
Map Recognition	44.1% correct	85.3% correct	–.141	.253
Healthy controls				
Scene Recognition	18.0 (2.0)	18.5 (1.8)	.071	.649
Route Continuation	8.1 (1.9)	8.4 (1.3)	.371	.013*
Route Sequence	3.7 (1.9)	5.3 (1.4)	.039	.801
Route Order	18.3 (7.2)	25.2 (7.2)	.306	.043*
Distance Estimation	1294.3 (1209.9)	174.7 (373.9)	.558	< .001*
Duration Estimation	103.2 (471.1)	117.2 (194.9)	.206	.170
Route Drawing	5.3 (3.2)	8.8 (2.3)	.210	.170
Map Recognition	63.6% correct	93.2% correct	.170	.269

Note. Relationships between virtual and real-world navigation performance were investigated by semi-partial correlation coefficients to correct for the effect of self-reported familiarity on real-world navigation performance. The (uncorrected) point-biserial correlation was applied for the Map Recognition subtask. Possible range of scores: Scene Recognition = 0–22, Route Continuation = 0–11, Route Sequence = 0–7, Route Order = 0–33, Distance Estimation = Absolute deviation from correct response in meters, Duration Estimation = Absolute deviation from correct response in seconds, Route Drawing = 0–11, and Map Recognition = correct or incorrect. * $p < .05$

Table 5. Main effects of group and environment on the navigation tests, together with the interaction effect between group and environment.

	Group	Environment	Group x Environment
Scene Recognition	F (1,108) = 8.89, p < .01, ηp^2 = .08*	F < 1	F < 1
Route Continuation	F (1,110) = 8.15, p < .01, ηp^2 = .07*	F (1,110) = 10.32, p < .01, ηp^2 = .09*	F (1,110) = 3.83, p = .053, ηp^2 = .03
Route Sequence	F (1,109) = 6.46, p = .01, ηp^2 = .06*	F (1,109) = 5.46, p = .02, ηp^2 = .05*	F (1,109) = 1.65, p = .20, ηp^2 = .02
Route Order	F (1,109) = 8.55, p < .01, ηp^2 = .07*	F (1,109) = 10.95, p < .01, ηp^2 = .09*	F < 1
Distance Estimation	F (1,109) = 1.33, p = .25	F (1,109) = 51.86, p < .01, ηp^2 = .32*	F < 1
Duration Estimation	F (1,109) = 7.98, p < .01, ηp^2 = .07*	F < 1	F < 1
Route Drawing	F (1,109) = 10.28, p < .01, ηp^2 = .09*	F (1,109) = 23.26, p < .01, ηp^2 = .18*	F < 1
Map Recognition	F (1,110) = 5.98, p = .02, ηp^2 = .05*	F (1,110) = 37.09, p < .01, ηp^2 = .25*	F (1,110) = 1.00, p = .32, ηp^2 = .01

5

Note. ANCOVAs were corrected for educational level and familiarity with the real-world environment, in case a significant contribution of these variables to performance on that subtask existed (p < .05). * p < .05

DISCUSSION

The primary objective of this study was to establish the relationship between performance on a real-world and a virtual navigation test in chronic stroke patients. This was done to investigate whether virtual navigation testing might be a valid alternative to real-world navigation testing, as the latter type of testing is usually associated with many practical limitations.

In line with expectations, there were significant correlations between four subtasks as assessed in both navigation tests in the group of stroke patients. More specifically, real-world and virtual performance on subtasks addressing place-action associations (Route Continuation), order of turns (Route Sequence), order of scenes (Route Order) and Distance Estimation was significantly correlated. These findings seem to suggest that virtual navigation testing is only valid for the administration of route knowledge aspects. That is, three of the four route knowledge subtasks correlated across the environments, whereas this was only the case for one of the four survey knowledge subtasks. Further analyses based on separate composite scores for route and survey knowledge subtasks, however, indicate that this initial conclusion is not correct. Route knowledge composite scores were moderately correlated across the real-world and virtual environments, whereas this correlation was lower but still weak to moderate in degree for the survey knowledge composite scores. Furthermore, the composite scores of overall performance were found to be moderately related indicating moderate overlap between performance on the real-world and virtual navigation tests in patients. These correlation analyses were based on semi-partial correlation coefficients to correct for the effect of self-rated familiarity on real-world performance. With regard to the administration of route knowledge, the current findings thus provide evidence in favor of the convergent validity of virtual navigation testing as an alternative to real-world navigation tests. In addition, when performance on the survey knowledge subtasks is combined into a single composite score, virtual navigation testing might also be suitable for measuring survey knowledge.

A different series of analyses was performed to compare navigation performance of stroke patients to that of healthy controls. The hypothesis that patients would experience more difficulties with the navigation tasks than controls was supported by this analysis. Patients indeed scored significantly lower than controls on seven subtasks with the exception of the Distance Estimation subtask. Furthermore, it was found that the real-world and virtual navigation tests were not equal in their level of difficulty. Regardless of group, performance on the real-world test was significantly better on six out of the eight subtasks as compared to performance on the virtual navigation task. Nevertheless, none of the interaction-effects between group and environment reached significance. This finding indicates that the difference in real-world and virtual navigation performance was thus similar for patients and controls. Importantly, these results were obtained after statistical corrections for the (trend-level) differences between patients and controls on educational level and self-reported familiarity with the real-world environment were applied.

The correlational analysis as described above has indicated moderate overlap between scores on the virtual and real-world navigation tests. Although this result corroborates findings of earlier studies showing overlap between real-world and virtual navigation performance (Busigny et al., 2014; Cushman et al., 2008; Sorita et al. 2013), the correlation between the composite scores was somewhat weaker than reported by two of these studies (Busigny et al., 2014; Cushman et al., 2008). This might in part be a result of methodological differences between these studies and ours. Cushman and colleagues (2008) used exactly the same environment and subtasks in both test procedures, whereas Busigny and colleagues (2014) employed rather different navigation tasks in the real-world and virtual conditions. Both studies relied on a within-subject design. In contrast, we administered the same eight subtasks in the real-world and virtual tests, but used different environments. As a consequence, learning effects with regard to the environment cannot have occurred in our study between the real-world and virtual navigation tests.

When comparing navigation performance based on the two different environments, results showed that the virtual navigation test was consistently more difficult than the real-world navigation test in both groups. Several factors could be responsible for this difference in performance, for example differences in the scenery of the environments or in the configuration of the routes. In our view, however, the higher performance level in the real-world test is the primary result of the fact that the exposure to the real-world environment allowed for a more complete navigation experience. More specifically, previous studies have argued that information from multiple sensory systems contributes to navigation behavior: visual, vestibular and proprioceptive information (Berthoz & Viaud-Delmon, 1999). Whereas exposure to the virtual environment provided participants only with visual information, exploring the real-world environment allowed for integration of visual and physical information (i.e., vestibular and proprioceptive cues). We pose that elevated performance in the real-world test relative to the virtual test follows from the fact that multisensory integration is only possible in the former.

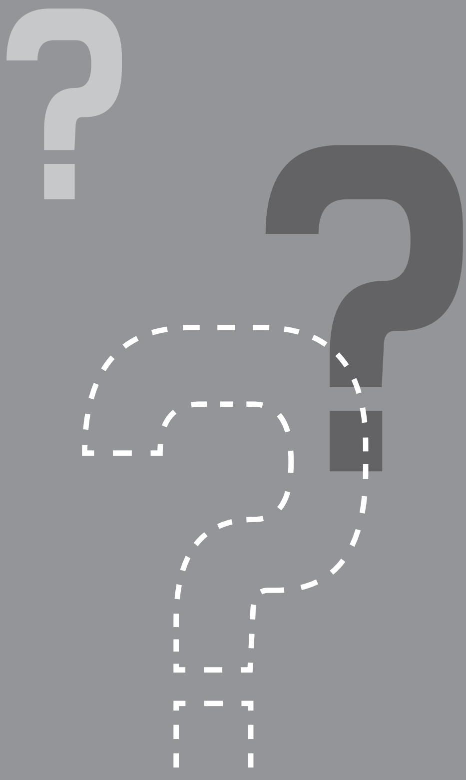
Recent studies have speculated that locomotion contributes to the acquisition of survey knowledge, while visual information alone might be sufficient for acquiring route knowledge (e.g., Chrastil & Warren, 2013; van der Ham et al., 2015). In our study, three of the four subtasks that correlated significantly across the real-world and virtual tests in the patient group concerned route knowledge aspects (i.e., place-action associations, the order of turns and scenes). On the other hand, most of the subtasks relying on survey knowledge aspects showed no significant correlations between real-world and virtual performance. When performance on individual survey knowledge subtasks was, however, combined into a composite score, a weak to moderate correlation was found between the real-world and virtual tests. Although it might thus be necessary to combine performances due to the single-trial nature of three survey knowledge subtasks, these findings suggest that the acquisition of survey knowledge can be measured in a virtual navigation test.

In the current study, self-reported familiarity with the real-world environment was taken into account, as the patient group was more familiar with the real-world environment than controls. This was due to the fact that half of the patients had stayed in the rehabilitation center that is situated in the environment that was used for the real-world navigation test. A correlation analysis showed that familiarity was positively correlated to performance on tasks assessing route knowledge (i.e., recognition of scenes and their order; trends for place-action associations and order of turns) but not to the survey knowledge subtasks in patients. We hypothesize that previous exposure or exposures to the real-world environment might have helped them to infer what landmarks could or could not be present or logically follow each other in the studied route.

The current study has several notable strengths. An important strength is that, in comparison to earlier work, this study incorporates a relatively large sample of chronic stroke patients. The fact that patients with various stroke types and locations are included in our sample allows the current results to be broadly generalized to the stroke patient population. A further strength of our study lies in the fact that the same eight subtasks were assessed for the real-world and virtual navigation tests, while each test was based on a different environment. This enabled us, due to the within-subject design, to directly compare real-world and virtual navigation performance within each participant.

Some limitations should be discussed. Firstly, information with regard to the neuropsychological status of the patients was relatively limited. For example, no information was available on the presence of visuospatial neglect, a syndrome that might affect navigation performance (De Nigris et al., 2013; Guariglia et al., 2005; Nico et al., 2008). Furthermore, for practical considerations, the virtual navigation test was administered first in all participants. Performance in the real-world test might thus be elevated because the participants were already familiar with the content of the eight subtasks. However, it remains unlikely that this fixed order influenced the relationship between real-world and virtual navigation performance itself. Furthermore, the fact that the patient group was more familiar with the environment as used in the real-world navigation test, might be regarded as a limitation of the study. However, statistical corrections for this difference were applied by taking self-rated familiarity with the real-world environment into account. We also state that this group difference in familiarity with the real-world environment clearly illustrates an important practical limitation associated with any real-world navigation test. In contrast, a virtual navigation test can be assessed in a highly standardized manner, guaranteeing equal exposure and familiarity across participants.

In summary, this study compared performance on a real-world and a virtual navigation test in 68 chronic stroke patients. Results demonstrated a moderate correlation between composite scores on the two navigation tests. Additional analyses indicated moderate overlap between real-world and virtual performance on route knowledge subtasks, whereas this relationship was weak to moderate for subtasks addressing survey knowledge aspects. These findings suggest that virtual navigation testing could serve as a valid alternative to real-world navigation tests. As a next step in this line of research, the Virtual Tübingen test should be administered in a large, heterogeneous group of healthy participants. This is necessary to generate normative data which would allow implementation of the test in clinical neuropsychological practice.



PART 3

Theory driven assessment of navigation ability

CHAPTER 6

A systematic investigation of navigation impairment in chronic stroke patients: Evidence for three distinct types

Submitted as:
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Author contributions:
IH and TM designed the study; MC collected and analyzed the data; MC, IH, JV, TM, AP, and NR interpreted the data; MC drafted the paper; IH, JV, TM, AP, and NR revised the paper for intellectual content.

ABSTRACT

Objective: In a recent systematic review, Claessen and van der Ham (2017) have analyzed the types of navigation impairment in the single-case study literature. Three dissociable types related to landmarks, locations, and paths were identified. This recent model as well as previous models of navigation impairment have never been verified in a systematic manner. The aim of the current study was thus to investigate the prevalence of landmark-based, location-based, and path-based navigation impairment in a large sample of stroke patients.

Method: Navigation ability of 77 stroke patients in the chronic phase and 60 healthy participants was comprehensively evaluated using the Virtual Tübingen test, which contains twelve subtasks addressing various aspects of knowledge about landmarks, locations, and paths based on a newly learned virtual route. Participants also filled out the Wayfinding Questionnaire to allow for making a distinction between stroke patients with and without significant subjective navigation-related complaints.

Results: Analysis of responses on the Wayfinding Questionnaire indicated that 33 of the 77 participating stroke patients had significant navigation-related complaints. An examination of their performance on the Virtual Tübingen test established objective evidence for navigation impairment in 27 patients. Both landmark-based and path-based navigation impairment occurred in isolation, while location-based navigation impairment was only found along with the other two types.

Conclusions: The current study provides the first empirical support for the distinction between landmark-based, location-based, and path-based navigation impairment. Future research relying on other assessment instruments of navigation ability might be helpful to further validate this distinction.

INTRODUCTION

Spatial navigation is the complex ability that allows us to familiarize ourselves with new environments and to find our way around in environments that we already know (Wolbers & Hegarty, 2010). This ability is crucial to many tasks we encounter on a daily basis, such as driving from home to work (and back), reaching the kitchen from the living room in our own home or visiting someone in an unfamiliar city.

The importance of navigation ability in daily life activities is clearly illustrated by neurological patients who report difficulties with navigation as a consequence of their brain damage. For instance, nearly a third of chronic stroke patients complain about such difficulties. Their self-reported navigation problems were associated with significant reductions of autonomy and quality of life (van der Ham, Kant, Postma, & Visser-Meily, 2013). Impaired navigation ability has not only been reported in stroke patients (Busigny et al., 2014; van Asselen, Kessels et al., 2006), but also in other clinical groups, such as traumatic brain injury patients (Livingstone & Skelton, 2007), and patients suffering from mild cognitive impairment or Alzheimer's disease (Cushman, Stein, & Duffy, 2008; deIpolyi, Rankin, Mucke, Miller, & Gorno-Tempini, 2007).

Navigation ability has increasingly been recognized as a highly complex cognitive construct and relying upon the integration of many cognitive mechanisms (Brunsdon, Nickels, & Coltheart, 2007; Wiener, Büchner, & Hölscher, 2009; Wolbers & Hegarty, 2010). Clinical researchers have therefore attempted to verify whether distinct types of impairments might underlie navigation problems depending on the cognitive mechanisms affected. These clinical studies can be roughly divided into two approaches: the single-case study approach and the group study approach. Single-case studies are applied on a regular basis in neuropsychology (McIntosh & Brooks, 2011) and have proven to be highly important for the study of navigation impairment. Case studies usually provide a specific pattern of impaired and intact navigation skills in individual neurological patients with navigation-related complaints. In 1999, Aguirre and D'Esposito published a comprehensive review of the single-case literature on navigation impairment. They distinguished between four types of impairments (egocentric disorientation, heading disorientation, landmark agnosia, and anterograde disorientation), and linked each type to a specific lesion location. This review has had a profound influence on the study of navigation impairment in neurological patients through case studies in particular. However, the prevalence of these distinct types of navigation impairment has never been investigated in systematic studies based on groups of neurological patients.

Many new case studies on navigation impairment have been published since 1999 (e.g., Caglio, Castelli, Cerrato, & Latini-Corazzini, 2011; Ciaramelli, 2008; Ruggiero, Frassinetti, Iavarone, & Iachini, 2014; van der Ham et al., 2010) and it thus appeared high time for an updated analysis of the types of navigation impairments as described in this literature. Such an analysis has obvious theoretical implications for the cognitive architecture of navigation ability, but it would also offer guidance to assessment of navigation ability in clinical practice. A recent paper has therefore provided such an update through a systematic literature review (Claessen & van der Ham, 2017). Detailed analysis of all relevant case reports revealed three main types of navigation impairments; deficits in landmark, location, and path knowledge.

Landmark-based navigation impairment entails problems with navigation due to defective processing of landmarks or environmental scenes. Patients with location-based navigation impairment suffer from defective acquisition and/or recall of knowledge about landmark locations and how these places relate to each other. They are likely to fail when asked to indicate the absolute or relative locations of landmarks or to point into their directions when (imagining) standing at a particular location. They also have difficulties with drawing correct maps and with providing accurate route descriptions between locations. Path-based navigation impairment, the most complex category, is associated with difficulties regarding knowledge about the paths that connect locations. Consequently, patients might experience problems in using maps or spatial information alone (e.g., the metrical structure of paths) for the purpose of navigation. Similar to patients with location-based navigation impairment, they might be unable to provide correct maps and route descriptions. While some overlap between location and path knowledge is evident, the case report on patient T.T. (Maguire, Nannery, & Spiers, 2006) shows that they can be dissociated. T.T's navigation problems occur when he has to use the fine-grained structure of paths between London landmarks, but he is accurate when he can rely on main roads only. This performance pattern suggests intact knowledge of locations, while his knowledge of non-main roads is compromised.

Apart from the single-case study approach, navigation impairment has also been investigated more systematically in group studies on neurological patients. The rigorous and large-scale approach of such studies has attracted attention to navigation problems in several neurological disorders. Group studies have also contributed to knowledge on the neurocognitive architecture of navigation ability by correlating navigation performance to lesion characteristics (see e.g., Barrash, Damasio, Adolphs, & Tranel, 2000; Busigny et al., 2014; van Asselen, Kessels et al., 2006). Strikingly, the group study approach has never been applied to systematically and empirically validate the types of navigation impairment as suggested by the single-case study literature. To our knowledge, not a single group study has ever provided a systematic evaluation of Aguirre and D'Esposito's model in a large sample of neurological patients, let alone the model as recently described by Claessen and van der Ham (2017).

Hence, the current study is intended to provide a systematic assessment of the three types of navigation impairment in a large group of stroke patients in the chronic phase. Navigation ability in a virtual reality setting was therefore systematically assessed using the Virtual Tübingen (VT) test (see e.g., Claessen, van der Ham, Jagersma, & Visser-Meily, 2016; Claessen, Visser-Meily, Jagersma, Braspenning, & van der Ham, 2016). This test is a valid measure of real-world navigation ability in stroke patients (Claessen, Visser-Meily, de Rooij, Postma, & van der Ham, 2016a) and is comprised of twelve subtasks that are frequently used in the navigation literature (e.g., Arnold et al., 2013; Busigny et al., 2014; Liu, Levy, Barton, & Iaria, 2011; Maguire, Burke, Phillips, & Staunton, 1996; Sorita et al., 2013; van Asselen, Kessels et al., 2006). Based on the patients' VT subtask performances, the prevalence of each type of navigation impairment will be determined. While the three types of navigation impairment are expected to be dissociable (i.e., can occur in isolation), they are not necessarily exclusive. It is therefore anticipated that some patients will suffer from more than one type of navigation impairment.

METHOD

Participants

Eighty-one stroke patients, living in the community, were recruited from rehabilitation center De Hoogstraat Revalidatie Utrecht and the rehabilitation department of the University Medical Center Utrecht (the Netherlands). Patients were considered eligible to participate when they were able to walk independently and no indications of severe aphasia or neglect were evident. None of the healthy controls suffered from any visual, neurological, psychiatric, or mobility problems and did not report a history of substance abuse. When willing to participate, participants provided written informed consent after the nature of the study was explained. They received monetary compensation for study participation.

Study approval was provided by the medical ethical committee of the University Medical Center Utrecht (the Netherlands; protocol no. 12-198) and the study design complied with the Declaration of Helsinki. The data presented here are part of a larger project into navigation ability in stroke patients. Portions of this data set have been used in earlier studies (Claessen, Visser-Meily, de Rooij et al., 2016a; Claessen, Visser-Meily, Jagersma et al., 2016; de Rooij, Claessen, van der Ham, Post, & Visser-Meily, submitted).

Procedure

Participants were invited to rehabilitation center De Hoogstraat (Utrecht, the Netherlands) for assessment. Participants were asked to complete the Wayfinding Questionnaire (WQ) and were subjected to a cognitive screening based on four common neuropsychological tasks. Participants then performed an extensive navigation test, the Virtual Tübingen (VT) test. When a short break was requested, it was held between the cognitive screening and the VT test. No breaks were allowed during the VT test to prevent differences in the time span between watching the virtual route and the administration of the VT subtasks across participants.

Materials

Wayfinding Questionnaire

The Wayfinding Questionnaire (WQ) is a self-report instrument for navigation-related complaints (Claessen, Visser-Meily, de Rooij, Postma, & van der Ham, 2016b; de Rooij et al., submitted; van der Ham et al., 2013). The WQ contains 22 items divided over three subscales: "Navigation and Orientation" (11 items), "Spatial Anxiety" (8 items), "Distance Estimation" (3 items). Scores range from 1 to 7. Higher numbers indicate high navigation ability and low spatial anxiety.

Cognitive screening

The cognitive screening consisted of four common neuropsychological tasks. These tasks were chosen to gain a general impression of the participants' neuropsychological functioning. Administration was in the following fixed order:

- The Dutch version of the Adult Reading Test was applied to measure premorbid intelligence (Schmand, Lindeboom, & van Harskamp, 1992). An estimated premorbid intelligence quotient was obtained by adjusting the raw score for age, gender, and educational level.
- The Corsi Block-Tapping Task served as a measure of visuospatial attention span (forward condition: Kessels, van Zandvoort, Postma, Kappelle, & de Haan, 2000) and visuospatial working memory span (backward condition: Kessels, van den Berg, Ruis, & Brands, 2008).
- The Trail Making Test (TMT; Reitan, 1992) was administered to obtain measures of mental processing speed (part A) and divided attention (part B).
- Verbal working memory span was measured using the Digit Span subtest of the WAIS-III (Wechsler, 1997).

Virtual Tübingen test

The Virtual Tübingen (VT) test (Claessen, van der Ham et al., 2016; Claessen, Visser-Meily, de Rooij et al., 2016a; Claessen, Visser-Meily, Jagersma et al., 2016; van der Ham et al., 2010) comprised a learning phase and a test phase. In the learning phase, participants watched a movie depicting a route through a realistic virtual reproduction of the German city Tübingen twice (van Veen, Distler, Braun, & Bülthoff, 1998). They were instructed to remember as much as possible from the route.

Two different routes were developed that were counterbalanced across participants (see Figure 1a in Claessen, Visser-Meily, de Rooij et al., 2016a, for a map). The routes were highly comparable in duration (210 and 253 seconds), and equal in distance (analogous to 400 meters), speed (slightly above walking speed), and the number of decision points (seven actual left and right turns and straight ahead on four decision points). A laptop (17.3-inch diagonal HD4 display) was used to present the movie.

After having watched the virtual route two times, the test phase started. The full VT test battery consisted of twelve subtasks, directly related to the studied virtual route. Subtasks were administered in the following fixed order:

1. Scene Recognition. Twenty-two images (1075 x 806, 68 dpi) of decision points taken from VT (see Figure 1 for an example) were presented to the participant one-by-one in random order. Half of these images were encountered during the route, whereas the other half depicted scenes in VT that were not shown in the route. Accuracy: number of correct responses, range: 0–22.

2. Route Continuation. Eleven decision points taken from the route were presented one-by-one in random order to the participant. They were requested to indicate in what direction the route continued at each decision point. Accuracy: number of correct responses, range: 0–11.

3. Route Sequence. Participants had to indicate the sequence of turns as taken during the route. They were instructed to do so by using printed arrows. Only actual turns (i.e., left and right turns) were taken into account. Accuracy: number of correctly indicated turns in the sequence, range 0–7.

4. Route Order. A set of eleven printed images was provided with the instruction to reconstruct the order in which the scenes were encountered in the route. Scoring: Three points were awarded for each scene assigned to its correct position in the sequence; two points for scenes assigned one position too late or too early; a single point for scenes two positions away from correct placement, range 0–33.

5. Route Progression. Participants were shown one-by-one eleven images taken from the route accompanied by a piece of paper with a printed line (17.8 cm) on it. They were asked to mark the location of the presented scene on the line which represented the total distance of the route. Scoring: an averaged deviation score was calculated over eleven trials, range 0–1. A score of 1 represented perfect performance.

6. Route Distance. Participants were shown scenes taken from the route in pairwise fashion. Each trial was accompanied by a printed line along with the instruction to mark the distance between the two scenes relative to the total length of the route. Scoring: an averaged deviation score was calculated over nine trials, range 0–1. A score of 1 represented perfect performance.

7. Pointing to Start. Participants were shown eleven images from the route in one-by-one fashion. They were asked to point to the starting point of the route for each scene using a rotational device. Scoring: average deviation of degrees from the correct response, range: 0–180 degrees.

8. Pointing to End. Similar to subtask 7, but here participants were required to point to the end point of the route using the rotational device. Scoring: average deviation of degrees from the correct response, range: 0–180 degrees.

9. Distance Estimation. Participants were requested to estimate the distance of the route. Scoring: absolute deviation from the correct response (400 m) in meters, regardless of underestimation or overestimation.

10. Duration Estimation. Participants were asked to estimate the duration of the route as shown in the movie. Scoring: absolute deviation in seconds from the correct response (route A: 210 seconds; route B: 253 seconds), regardless of underestimation or overestimation.

11. Route Drawing. Participants were provided with a schematic map of VT and asked to draw the route on it. Only the starting point and the correct direction were shown. Scoring: one point was awarded for each correctly indicated turn (left, straight forward, or right) at relevant decision points, range: 0–11.

12. Map Recognition. Participants were requested to select the correct map of the route out of four options. Scoring: correct or incorrect.

Subtasks 1, 2, 7, and 8 were assessed on a laptop using Presentation software (version 16.3; Neurobehavioral Systems). All other subtasks were paper-and-pencil tasks.

Figure 1. Impression of Virtual Tübingen.

VT subtask classification

Performance on the VT test was interpreted based on the model presented by Claessen and van der Ham (2017). This model has described three main types of navigation impairments related to knowledge about landmarks, locations, and paths. The VT subtasks assess aspects of these types of knowledge and can be linked to the model in the following way: landmark knowledge (Scene Recognition), location knowledge (Pointing to Start, Pointing to End), and path knowledge (Route Continuation, Route Sequence, Route Order, Route Progression, Route Distance, Distance Estimation, Duration Estimation, Route Drawing, Map Recognition). Path knowledge was extensively represented in the VT test, which is directly related to the complexity of the concept of "path".

Statistical analysis

Demographic characteristics of patients and controls were compared: age, educational level (independent t-tests), and gender distribution (chi-square test). Independent t-tests assessed group differences on the neuropsychological tasks. Next, to compare performance of patients and controls on the VT subtasks, univariate analyses of covariance with educational level as a covariate were conducted for each subtask. Due to the nominal scale of the Map Recognition subtask (correct or incorrect), a chi square test was applied to test whether patients and controls differed in their performance. Effect sizes of significant results are reported as Pearson's r (small = 0.10–0.29, medium = 0.30–0.49, large ≥ 0.50) or partial eta squared (η_p^2; small = 0.01–0.05, medium = 0.06–0.12, large ≥ 0.13). The number of participants with an impaired score on each subtask was calculated by converting subtest scores to *z*-scores based on means and standard deviations of the control group. It is a common approach in neuropsychology to mark the lowest 5% of performances as impaired, which corresponds to *z*-scores lower than –1.64 *SD* of the mean of the control group.

All *p*-values of ≤ .05 were considered to be statistically significant. The statistical procedures were performed using SPSS version 23.0.

RESULTS

Demographics and cognitive screening

Data of five participants was excluded from the data set. Three patients and one healthy control reported a lack of motivation during testing and one patient suffered from serious motion sickness during the VT test. The final study sample thus consisted of 77 patients (M = 59.9 years, SD = 12.1, 58% males) and 60 healthy controls (M = 58.5 years, SD = 9.8, 47% males). The groups were comparable in terms of age ($t < 1$) and gender ($\chi^2 = 1.88$, $p = .171$). Patients had an educational level of 5.2 (SD = 1.4) (Verhage 1964; possible range 1–7) and the educational level of controls was 5.6 (SD = 0.9); this difference was not statistically significant but reached trend level ($t = -1.90$, $df = 131.35$, $p = .059$). Educational level was therefore entered as covariant in the group comparisons between patients and controls on VT subtask performances. Information on time between first stroke event and study participation was available for 74 patients and varied between 6 and 98 months ($M = 37.2$; $SD = 16.3$). Stroke characteristics of the patient group are displayed in Table 1.

The scores of patients on all neuropsychological tasks were significantly lower than that of healthy controls (see Table 2). The corresponding effect sizes ranged from small ($r = 0.18$) to medium ($r = 0.46$).

Group performance on the VT test

Group performance on the VT subtasks is displayed in Table 3. Results of univariate analyses of covariance with educational level as a covariate indicate that controls significantly outperformed patients on five out of twelve VT subtasks: Scene Recognition, Route Continuation, Route Order, Route Progression, and Route Drawing. The corresponding effect sizes ranged from small ($\eta_p^2 = .040$) to medium ($\eta_p^2 = .115$). For each subtask, the percentage of patients and controls who obtained an impaired score (< –1.64 *SD* of the controls' mean) was also calculated. The percentage of impaired scores was higher in the patient group on all subtasks with the exception of Pointing to Start (controls: 8.8% impaired; patients: 8.1% impaired).

Table 1. Stroke types and lesion locations in the patient group (*n* = 77).

	n (%)
Stroke type	
Ischemic stroke	60 (77.9%)
Hemorrhagic stroke	
- Intracerebral	13 (16.9%)
- Subarachnoid	3 (3.9%)
Unknown	1 (1.3%)
Stroke location	
Supratentorial region	
- Left	31 (40.3%)
- Right	32 (41.5%)
- Bilateral	2 (2.6%)
Infratentorial region	
- Left	2 (2.6%)
- Right	2 (2.6%)
- Bilateral	7 (9.1%)
Unknown	1 (1.3%)

Note. Classification is based on the characteristics of the first stroke event. Six patients (7.8%) suffered from two stroke events and two patients (2.6%) from three stroke events.

Table 2. Performance on the cognitive screening tests in patients and controls.

	Patients	Controls	*t*	*p*	Effect size *r*
Dutch Adult Reading Test (IQ)	97.7 (17.1)	109.7 (11.5)	–4.85	< .001***	0.39
Corsi Block-Tapping Task					
- forward (span × score)	37.0 (15.1)	42.0 (12.4)	–2.08	.040*	0.18
- backward (span × score)	38.2 (19.9)	48.0 (16.4)	–3.14	.002**	0.26
Trail Making Test					
- Part A (seconds)	58.2 (38.1)	35.1 (11.5)	5.04	< .001***	0.46
- Part B (seconds)	142.4 (109.0)	74.9 (26.1)	5.18	< .001***	0.49
- Part B (B / A)	2.7 (1.6)	2.2 (0.6)	2.24	.027*	0.22
Digit Span (WAIS-III)					
- forward (score)	7.5 (1.9)	9.0 (1.6)	–4.86	< .001***	0.39
- backward (score)	5.0 (2.0)	6.2 (2.0)	–3.37	.001**	0.28

Note. Standard deviations are displayed in parentheses.

* $p < .05$, ** $p < .01$, *** $p < .001$; Pearson's *r* effect size: small = 0.10–0.29, medium = 0.30–0.49, large ≥ 0.50

6

Table 3. Performance on the Virtual Tübingen test battery in patients and controls.

	Controls	Patients			Controls	Patients
VT subtask (*n* controls, *n* patients)	*M* (*SD*)	*M* (*SD*)	*p*	η_p^2	% Impaired	% Impaired
Scene Recognition (60,77)	17.9 (2.2)	16.6 (2.4)	.003**	.066	8.3	20.8
Route Continuation (60,77)	8.2 (1.8)	6.9 (2.0)	.001**	.090	6.7	20.8
Route Sequence (60,77)	3.9 (2.0)	3.4 (2.0)	.152	.015	0.0	5.2
Route Order (60,77)	18.7 (7.2)	14.6 (6.5)	.001**	.081	5.0	14.3
Route Progression (60,77)	0.83 (0.07)	0.77 (0.08)	< .001***	.115	3.3	26.0
Route Distance (59,77)	0.80 (0.08)	0.78 (0.08)	.133	.017	3.4	10.4
Distance Estimation (60,76)	1175.8 (1107.2)	1461.8 (1323.1)	.235	.011	6.7	14.5
Duration Estimation (60,76)	340.9 (728.0)	401.0 (753.5)	.698	.001	6.7	7.9
Pointing to Start (57,74)	51.1 (21.6)	57.4 (20.9)	.168	.015	8.8	8.1
Pointing to End (57,74)	62.5 (22.5)	68.1 (25.8)	.230	.011	6.8	10.8
Route Drawing (60,77)	5.2 (3.1)	3.9 (3.0)	.019*	.040	1.7	13.0
Map Recognition (60,77)	33 correct (55%)	32 correct (42%)	.125	–	–	–

Note. Possible scoring range: Scene Recognition = 0–22, Route Continuation = 0–11, Route Sequence = 0–7, Route Order = 0–33, Route Progression = 0–1, Route Distance = 0–1, Distance Estimation = Absolute deviation from correct response in meters, Duration Estimation = Absolute deviation from correct response in seconds, Pointing to Start and Pointing to End = Deviation from correct response in degrees, Route Drawing = 0–11, and Map Recognition = correct or incorrect.

* $p < .05$, ** $p < .01$, *** $p < .001$; partial eta squared (η_p^2) effect size: small = 0.01–0.05, medium = 0.06–0.12, large ≥ 0.13

Analysis of individual performance patterns on the VT test

Our intention was to analyze only VT performance patterns of patients who actually suffer from navigation problems in daily life to ensure that impaired VT subtask scores reflect clinically meaningful deficits. Therefore, responses on the Wayfinding Questionnaire (subscales: Navigation and Orientation, Spatial Anxiety, and Distance Estimation) were used to make a selection of patients who experience significant navigation problems. Thirty-three out of the 77 patients (43%) obtained at least one impaired WQ-subscale score (< –1.64 *SD* of the controls' mean) and were selected for further analysis of their VT performance pattern. More specifically, eighteen patients obtained a single impaired WQ-subscale score, and two and three impaired WQ-subscale scores were found in eight and seven patients, respectively.

As Figure 2 and Table 4 show, all three types of navigation impairments were identified by the VT test battery and in various combinations in the 33 stroke patients. Both landmark-based (three patients) and path-based navigation impairment (twelve patients) occurred in isolation. Although no patient suffered from location-based navigation impairment alone, this type co-occurred with path-based navigation impairment (three patients). A combination of navigation impairments related to landmarks and paths was also relatively common (six patients). Navigation impairment due to combined deficits in all three domains (i.e., landmarks, locations, and paths) was established in two patients. No objective evidence of navigation impairment was found for the remaining seven patients. Overall, navigation impairments related to paths occurred much more often (23 patients) than landmark-based (eleven patients) and location-based navigation impairment (five patients).

DISCUSSION

The primary objective of this study was to provide a systematic inventory of the prevalence of landmark, location, and path-based navigation impairments, which have recently been identified in a systematic literature review summarizing all relevant single-case reports on this topic (Claessen & van der Ham, 2017). In the current study, it was hypothesized that these impairments can occur in isolation (as they are dissociable by definition), but might co-occur as well. This aim was addressed by analyzing the individual performance patterns of 33 stroke patients with significant navigation-related complaints on a comprehensive virtual navigation test battery. Based on this analysis, objective evidence of navigation impairment was established for 26 patients and all three types of navigation impairments were identified in this group. Both landmark-based and path-based navigation impairment were found to occur in isolation, while location-based navigation impairment was only established in combination with the other two types. Overall, these results provide a first systematic validation of the distinction between landmark, location, and path-based navigation impairment.

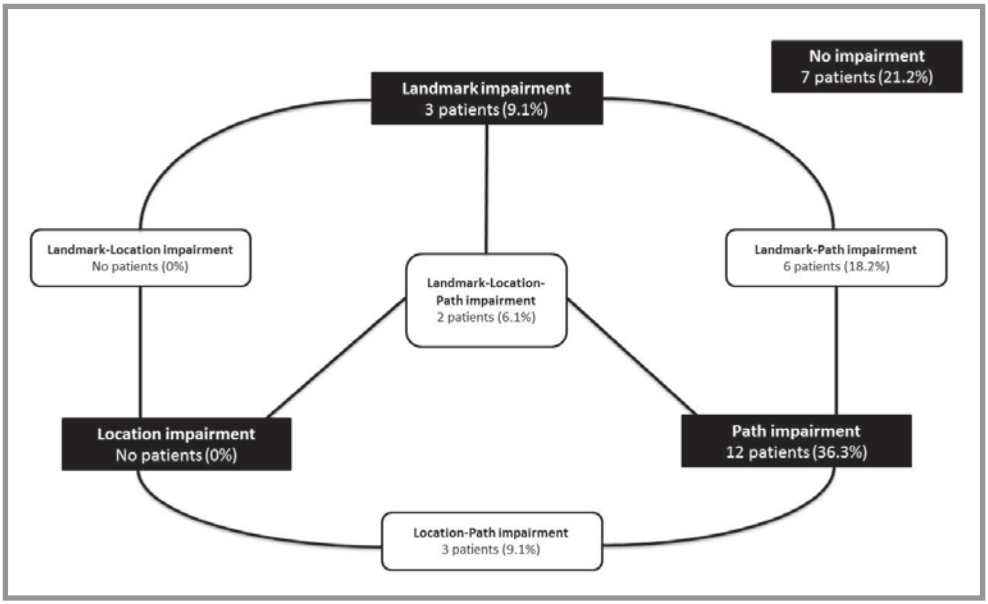


Figure 2. The prevalence of the three types of navigation impairments as measured with the Virtual Tübingen test in 33 stroke patients with complaints of navigation problems.

Path-based navigation impairment was clearly very common, as it occurred in 23 out of the 26 patients with objective evidence of navigation impairment (either in isolation or along with the other types). This finding might result from the fact that nine out of twelve VT subtasks address some form of path knowledge. Indeed, this might have increased the chances of finding an impaired score on a subtask related to path knowledge as compared to subtasks assessing landmark and location knowledge. It should, however, be emphasized that path-based navigation impairment is the most complex type of navigational knowledge (Claessen & van der Ham, 2017). Path knowledge does not solely entail concrete information such as the order of landmarks or turns, but can also be enriched with abstract, metric information about the size of turning angles and segment lengths (Chrastil & Warren, 2014; Mallot & Basten, 2009; Meilinger, 2008).

Some discussion is also needed regarding the finding that no patient in the current study sample suffered from an isolated location-based navigation impairment. However, there appeared to be some overlap between navigation impairments related to locations and paths, as three patients were found to suffer from a combination of these types of navigation impairment. This accords both with the nature of the tasks that were used to measure location knowledge (Pointing to Start and Pointing to End) as well as the partial conceptual overlap between knowledge about locations and paths. In each trial of the pointing tasks, participants were provided with a scene and required to indicate the position of the starting or end point of the route. By showing them scenes in these tasks, path knowledge might have been measured in addition to location knowledge alone, as this task is mostly likely solved by mentally "walking back" or "walking on" to the starting or end point of the route. This strategy directly points out the connection between path and location knowledge. It has been suggested that location knowledge about the interrelationships of multiple locations results from egocentric updating (i.e., integration of paths; Claessen & van der Ham, 2017; Ino et al., 2007), mental imagery as described in the BBB-model (Byrne, Baker, & Burgess, 2007) or mental model construction (Meilinger, 2008). More specifically, Meilinger (2008) has proposed the existence of a hierarchical relationship between path and location knowledge, as location knowledge (needed to solve pointing tasks) is only inferred online in working memory directly from path knowledge. Overall, it appears advisable that future research further explores the relationship between path and location knowledge and, if possible, develops more direct measures of location knowledge to better establish location-based navigation impairment.

Lastly, the finding that the three navigation impairment types can occur independently also has important implications for the cognitive rehabilitation of impairments in this function. It is now common practice in cognitive rehabilitation to teach patients to approach particular tasks in an alternative way; a compensatory strategy, by enabling them to rely on their cognitive strengths (Ponds & Hendriks, 2006; Wilson, 2002). There is recent evidence that the application of compensatory strategies might also be effective in the context of rehabilitating navigation impairment. A group of researchers has taught a patient to apply an external compensation strategy to overcome his navigation problems by using a smartphone with GPS technology (Rivest, Svoboda, McCarthy, & Moscovitch, 2016). Another study has supported the feasibility of internal compensation to rehabilitate navigation impairment by teaching six patients to apply an alternative navigation strategy based on individual cognitive strengths (Claessen, van der Ham et al., 2016). This latter approach in particular, which regards navigation ability as a complex rather than a unitary function, accords with the finding that the three types of navigation ability are dissociable.

The current study is characterized by a number of strengths. To the best of our knowledge, it provides the first systematic inventory of the types of navigation impairment that have been identified in the single-case literature on this topic. The focus was on patients with mild stroke (i.e., stroke patients who have participated in outpatient rehabilitation programs or those who show quick neurological recovery during inpatient rehabilitation). Mild stroke is not only the most common type of stroke; its prevalence is also expected to increase further due to the availability of better treatment options (Rochette, Desrosiers, Bravo, St-Cyr/Tribble, & Bourget, 2007). People with mild stroke usually live at home independently and are therefore reliant on adequate navigation ability. Another strength of this study is that a relatively large group of stroke patients was comprehensively tested on their navigation abilities. In addition, WQ responses were used to select only patients with significant navigation complaints. This procedure ensured that impaired subtask scores on the VT reflect clinically meaningful results.

Several limitations also need to be discussed. Information on the neuropsychological functioning of the patient sample was somewhat limited. To ensure that the duration and mental strain of the test procedure was feasible for them, the cognitive screening was restricted to neuropsychological tasks for premorbid intelligence, visuospatial and verbal attention span and working memory, mental processing, and divided attention. While stroke patients with severe forms of neglect were not included, it should be mentioned that information about representational neglect would have been informative given that navigation impairment has been associated with neglect in mental imagery (Guariglia, Piccardi, Iaria, Nico, & Pizzamiglio, 2005). Also, information on lesion locations was highly limited for many stroke patients (see Claessen, Visser-Meily, Jagersma et al., 2016, for further explanation), therefore it was not possible to link the types of navigation impairments to lesion locations. A final possible critique concerns the fact that this study focused on navigation impairment in novel environments alone, whereas the three types of navigation impairments have been argued to concern navigation in familiar environments as well (Claessen & van der Ham, 2017). However, objective evaluation of navigation ability in environments learned prior to a patient's stroke event would be very difficult to accomplish in a systematic group study. Therefore, methodologically sound reports on individual neurological patients with navigation impairment will remain important in the investigation of this topic.

In conclusion, the current study has provided empirical evidence for the distinction between three types of navigation impairments related to landmarks, locations, and paths. This provides the first validation of the model that has recently been put forward by Claessen and van der Ham (2017) based on a systematic review of single-case studies on navigation impairment. This evidence was established in the current study by systematically assessing navigation ability related to landmarks, locations, and paths in stroke patients using the VT test battery. Both landmark and path-based navigation impairment were found in isolation, whereas navigation impairment related to locations was only objectified in combination with the other types. Future research relying on other assessment instruments of navigation ability than the VT test might help to further validate this model.

CHAPTER 7

Severe navigation impairment after a right anteromedial temporal lobectomy in a patient with intractable epilepsy

In preparation as:
Claessen, M. H. G., van Zandvoort, M. J. E., Leijten, F. S. S., & van der Ham, I. J. M. Severe navigation impairment after a right anteromedial temporal lobectomy in a patient with intractable epilepsy.

Author contributions:
MC, MZ, and IH designed the study; MC, MZ, and FL collected the data; MC analyzed the data; MC, IH, and MZ interpreted the data; MC drafted the paper; IH revised the paper for intellectual content.

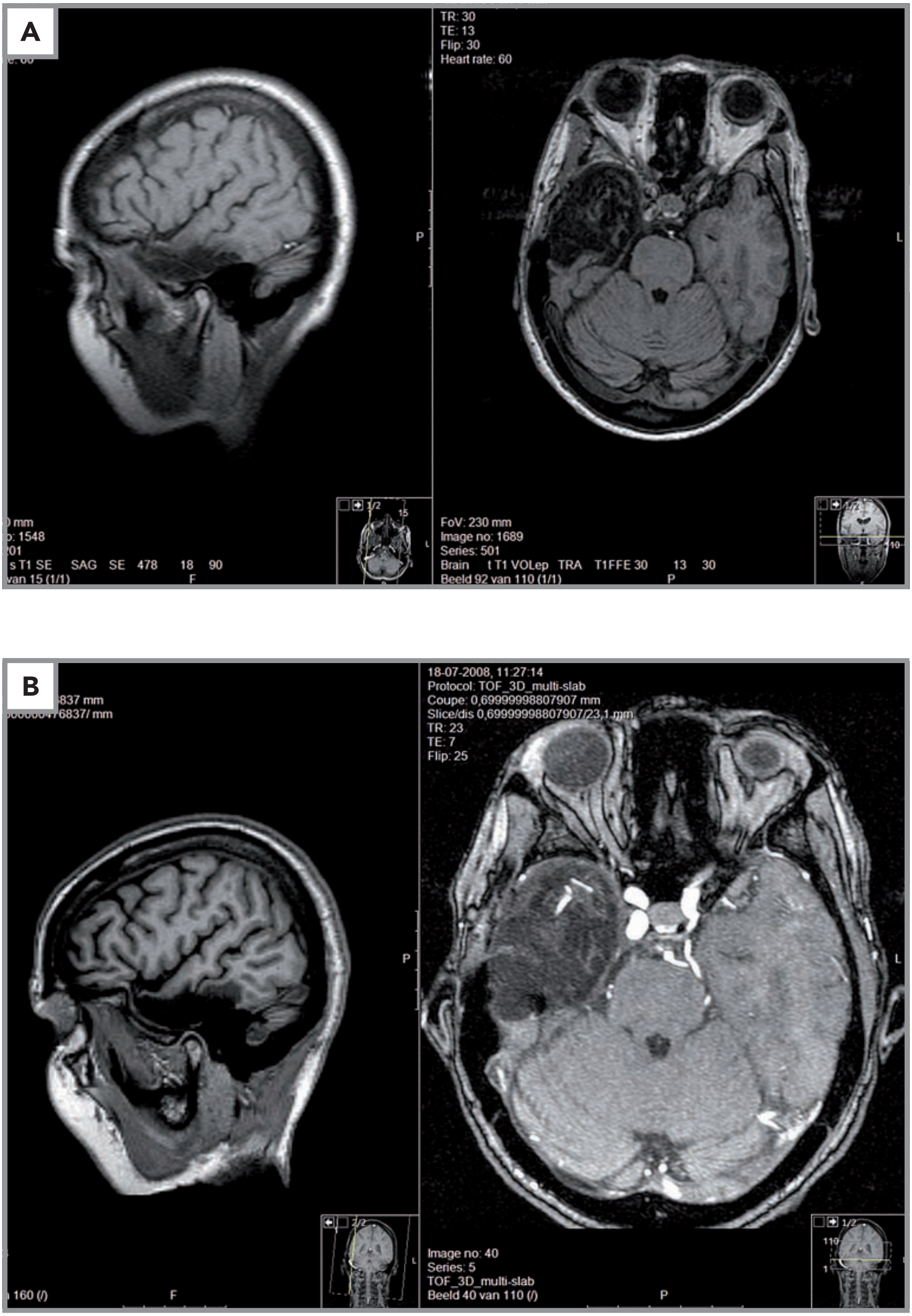
ABSTRACT

This study reports the case of a 66-year-old female patient who came to our attention almost twelve years after she had undergone a right anteromedial temporal lobectomy. She has experienced severe difficulties navigating since the surgery, particularly in areas she has never visited prior to this intervention. The current study aim was to investigate the origin of these problems. Standard neuropsychological testing revealed only a visuospatial working memory deficit. We found objective evidence for her difficulties navigating based on a virtual route learning test. We also tested her knowledge of two familiar real-world environments in two equivalent tests. The first test was based on the area she grew up in (and still visits regularly), while the second test concerned her current place of residence which she has never visited prior to the surgery. Her ability to recognise landmarks in these environments was accurate, but she showed notable difficulties with indicating the locations of these landmarks on a map and with giving accurate route descriptions between them. Severe navigation disability is a rare complication after a right anteromedial temporal lobectomy, as this is the first report on such a case.

INTRODUCTION

In his Nobel Prize winning research on rodents, John O'Keefe has indicated the existence of a relationship between the hippocampus and spatial memory, particularly the ability to create mental maps of the environment (O'Keefe & Nadel, 1978). This is an important element of navigation ability (e.g., Schinazi, Nardi, Newcombe, Shipley, & Epstein, 2013). A relationship between the hippocampus and navigation ability has also been found in human research. Temporal lobectomy patients, who have undergone surgical removal of the hippocampus and adjacent temporal lobe structures for relief of intractable epilepsy, perform worse on navigation tasks than healthy controls (Astur, Taylor, Mamelak, Philpott, & Sutherland, 2002; Maguire, Burke, Phillips, & Staunton, 1996; Spiers et al., 2001; Worsley et al., 2001). Studies have indicated that the right rather than the left hippocampus is crucial to navigation ability (e.g., Spiers et al., 2001; Worsley et al., 2001). Given these results, it is striking that not a single study on an individual temporal lobectomy patient with navigation impairment has been reported. Hence, the current study provides the first case report on a patient who was left with serious difficulties navigating after a right anteromedial temporal lobectomy, suggesting that this is a very rare complication after such a surgical intervention.

Figure 1. MRI scan taken one year before surgery. Note the location of the cavernous haemangioma in the right medial temporal lobe close to the head of the hippocampus and the amygdala. There was no sign of hippocampal sclerosis on T1 images. The right side of the brain corresponds with the left side of the image.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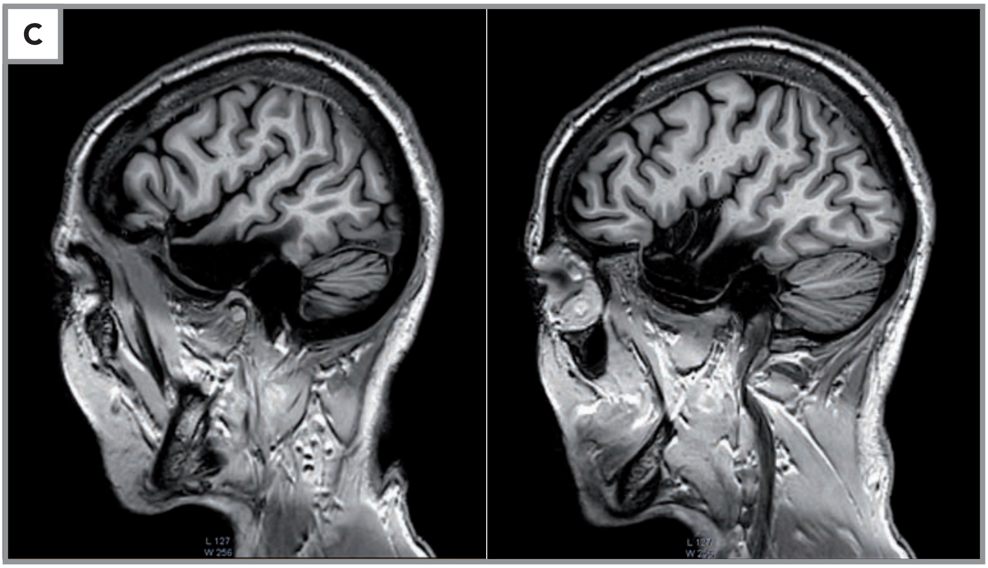


Figure 2. Three MRI scans showing the resection size (i.e., 6 cm from the anterior temporal pole in posterior direction, 5 cm on the left-right axis, and 2 cm on the dorsoventral axis). The scans were taken at different intervals after surgery: (A) 15 months after surgery, (B) almost 4 years after surgery, and (C) 12 years after surgery. These scans show that lesion area has not changed over time; nor are there any indications of atrophy or other brain pathology. The right side of the brain in axial images corresponds with the left side of the image.

CASE STUDY

The patient (Z.R.) is a 66-year-old women who was diagnosed with epilepsy due to a right mesiotemporal cavernous haemangioma at the age of 44 (see Figure 1). Until then, she had functioned well as the cornerstone of a family with five children. Her seizures (partial and generalised seizures, and absences) were associated with postictal complaints of disorientation, sometimes lasting up to three days. The seizures gradually increased in frequency and severity, and medication turned out to be ineffective in controlling the seizures. After a few years, her husband asked for a divorce, as he found himself unable to cope with this situation. Ten years after the onset of the seizures, Z.R. also lost her job as she had to call in sick for a long period of time due to a series of severe seizures. At the age of 54, she underwent epilepsy surgery with a right anteromedial temporal lobectomy and lesionectomy (see Figure 2). Except for around five brief auras a year, she is seizure-free and epileptic medication has been completely tapered off.

Almost twelve years after the surgery, she came to our attention with complaints of severe navigation problems. Although she had consulted others before, no convincing explanation was provided based on these earlier investigations. She reports that her problems with navigation particularly concern environments she has first encountered after the surgery. To cope with these problems, she records elaborate written route descriptions in a notebook as she finds herself unable to learn new routes no matter how many times she has travelled them. She relies rigidly on particular landmarks (e.g., a mailbox) to find her way around, and gets confused when things are only slightly different than expected (e.g., when the design of a shop display has been changed). This condition is the primary reason that she currently lives in an apartment owned by a health facility organisation for people with acquired brain injury such that support is continuously available. She also mentioned some complaints regarding memory (e.g., forgetting that she had put the kettle on the stove to make tea when she leaves the room in the meantime) and severe fatigue.

Z.R. has a medical history of traumatic brain injury following collision with a car at the age of seven; further details concerning this injury are unknown. Her psychiatric history specifies multiple depressive and dysthymic episodes (with at least two periods of hospitalisation) and a diagnosis of personality disorder NOS based on an enduring and stable pattern of difficulties with establishing and maintaining social relationships. Both psychiatric diagnoses were already established before the onset of the epileptic seizures.

Neuropsychological assessments were performed before surgery, briefly after surgery, and one year and three years after surgery. The pre-surgery assessment indicated above average intellectual functioning with a minor discrepancy between verbal (above average) and visual abilities (high average), likely related to the right-sided cavernous haemangioma. Her performance on tests for language, attention and concentration, and mental flexibility was above average. Visuospatial test performance fell in the average range. No memory problems were found. The only remarkable finding regarded minor planning difficulties, as she tended to approach complex tasks using a trial-and-error strategy. The results of all post-surgery assessments revealed identical performance patterns and did not provide a convincing explanation for her profound navigation problems after the surgery.

We started our investigation with a comprehensive neuropsychological assessment to verify the status of her cognitive functioning almost twelve years after the surgery. We found average to above average performance on tests of all cognitive domains, but she performed low on a task addressing visuospatial working memory (see Table 1). This might indicate a disability to manipulate visuospatial information.

Table 1. Z.R.'s performance on the neuropsychological assessment.

Cognitive domain	Test	Raw scores	Interpretation
General cognitive functioning	Cognitive Screening Test	CST-14: 14	Unimpaired
		CST-20: 20	Unimpaired
	National Adult Reading Test	93 (estimated IQ = 123)	Above average
Language	Boston Naming Test	84/87 (171/177)	80th percentile
Working memory	Digit Span (WAIS-IV)	34 (SS = 16)	Above average
	Forward score	12	
	Forward span	8	
	Backward score	12	
	Backward span	6	
	Sorting score	10	
	Sorting span	6	
	Corsi Block-Tapping Task		
	Forward score	6	70th percentile
	Forward span	9	
	Backward score	3	5th–10th percentile
	Backward span	4	
Memory	Rey Auditory Verbal Learning Task		
	Immediate recall	52 (5/9/10/14/14)	84th percentile
	Delayed recall	13/15	95th percentile
	Delayed recognition	29/30 (1 miss)	Unimpaired
	RBMT Story		
	Immediate recall	24.5	88th percentile
	Delayed recall	21.5	86th percentile
	% retained	88%	62th percentile
	Rey Complex Figure		
	Delayed recall (30 minutes)	16/36	> 50th percentile
	Location Learning Test		
	Displacement score	8 (5/3/0/0/×)	60-70th percentile
	Learning index	0.85	70th percentile
	Delayed recall score	0	> 75th percentile
	Benton Visual Retention Test		
	Version C	6/10	Unimpaired

Visuoperception	Cortical Vision Screening Test		
	Symbol acuity	36/36	Unimpaired
	Shape discrimination	8/8	Unimpaired
	Size discrimination	2/2	Unimpaired
	Shape detection	8/8	Unimpaired
	Hue detection	4/4	Unimpaired
	Dot counting	4/4	Unimpaired
	Fragmented numbers	8/8	Unimpaired
	Face perception	8/8	Unimpaired
	Crowding test	4/4	Unimpaired
	Birmingham Object Recognition Battery		
	Size Match task	29/30	Unimpaired
	Length Match task	27/30	Unimpaired
	Judgement of Line Orientation	30/30	> 86th percentile
	Benton Facial Recognition Test	54/54	> 98th percentile
Visuoconstruction	Rey Complex Figure		
	Direct copy	34/36	> 50th percentile
Attention/Speed	Star Cancellation (BIT)	70 sec.; systematic working method, from left to right	Unimpaired
	Colour Word Interference test (D-KEFS)		
	Condition 1 (colour naming)	30 sec. (GS = 11)	Average
	Condition 2 (word reading)	25 sec. (GS = 10)	Average
Executive functioning	Colour Word Interference test (D-KEFS)		
	Condition 3 (inhibition)	44 sec. (GS = 14)	Above average
	Condition 4 (inhibition and switching)	48 sec. (GS = 15)	Above average
Spatial abilities	Road Map test (mental rotation)	90 sec. (1 error)	Unimpaired
	Bergen Left-Right Discrimination Test		
	Condition 1 (back)	31 (2 errors)	Unimpaired
	Condition 2 (front)	33 (1 error)	Unimpaired
	Condition 3 (mixed)	37	Unimpaired

Note. Corrections for sex, age, and education level have been applied to the raw scores if available.

However, as a visuospatial working memory deficit alone appeared an unlikely explanation for the severity of her navigation problems, we also assessed her navigation abilities in detail. The Virtual Tübingen (VT) navigation test battery (see van der Ham & Claessen, 2016) was administered to measure Z.R.'s ability to learn new virtual routes (see Table 2). Her VT performance pattern indicated strong reliance on remembering the order of turns, while lower or impaired scores were found on the majority of the other subtasks. She has difficulties with forming associations between places and actions, and with remembering the order in which places occurred along the route as well as metrical information. She finds it hard to draw accurate route maps and she could not indicate the correct route map out of four options. These results provide objective evidence for her difficulties with acquiring new routes and also show that she attempts to compensate for this inability through reliance on verbal coding of the routes (e.g., left-right-left).

Lastly, we set out to test her knowledge of real-world environments. We first assessed her ability to recognise landmarks by showing her pictures of famous landmarks from Europe, the Netherlands, and the city centre of Leiden. Most of them were accurately named (see Table 3). We then tested whether her difficulties with navigation were more prominent in environments she has never visited prior to the surgery, as she stated. We thus designed two equivalent tests to assess her environmental knowledge of a part of the city she grew up in (and still visits regularly) and the village she has lived in for the last six years (see Table 3 for task descriptions and results). Her landmark recognition performance was sufficient for both environments. In a qualitative sense, we observed that she needed much time to complete the location and route description tests and relied on elaborate verbal reasoning to generate her responses. Although no healthy control data could be obtained for comparison, she had difficulties with accurately indicating locations of landmarks for both environments. However, there seems to be a slight difference on the location tasks favouring the environment in which she grew up. Her ability to describe accurate routes between two landmarks was slightly compromised but comparable for the two environments. In general, we established additional evidence for her difficulties with navigation based on these real-world tests, but a substantial difference between knowledge of environments she has visited prior to and after the surgery was not objectified.

Table 2. Z.R.'s performance on the Virtual Tübingen (VT) navigation test battery.

VT subtask	Route A; 18 January 2016	Route B; 25 April 2016 [1]
	Total: 14/22 (64%)**	Total: 19/22 (86%)
Scene Recognition	Targets: 4/11 (36%)	Targets: 8/11 (73%)
	Distractors: 10/11 (91%)	Distractors (100%)
Route Continuation	5/11 (45%)	5/11 (45%)
Route Sequence	6/7 (86%)	7/7 (100%)
Route Order	8/33 (24%)	5/33 (15%)*
Route Progression	61%**	60%**
Route Distance	Not administered [2]	Not administered
Distance Estimation	400 metres (correct: 400 metres)	500 metres (correct: 400 metres)
Time Estimation	300 seconds (correct: 210 seconds)	300 seconds (correct: 252 seconds)
Pointing to Start	Not administered	Not administered
Pointing to End	Not administered	Not administered
Map Drawing	2/11 (18%)	7/11 (64%)
Map Recognition	Incorrect	Incorrect

Note. Z.R.'s scores were compared to that of a healthy control group comprising 11 women, $M_{\text{age}} = 62.1$ (age of Z.R. = 66), $M_{\text{educational level}} = 5.6$ (educational level of Z.R. = 5, possible range: 1–7). Scores marked with one (*) or two asterisks (**) indicate trend-level impaired performance ($p < .15$, one-sided) and impaired performance ($p < .05$, one-sided), respectively. Statistical comparisons were made using the Bayesian approach for single case studies (Crawford and Garthwaite, 2007).

[1] The VT navigation test battery was administered twice (using parallel versions), as Z.R. misunderstood the test instructions on the first administration (she indicated afterwards she had focused solely on the order of turns instead of memorizing as much as possible information from the route). Her patterns of performance were comparable across the two administrations for most subtasks, except for performance on the scene recognition subtask (impaired at the first assessment; intact at the second assessment).

[2] Z.R. was unable to understand the purpose of the subtask Route Distance.

Table 3. Z.R.'s performance on famous landmark recognition tasks and on two real-world navigation tests based on the city of Leiden and the village of Eemnes.

Leiden landmarks (city centre)	8/10
Dutch landmarks	7/10
European landmarks	8.5/10 *
Leiden South-West landmarks [1]	Total: 15/20 correct Targets: 5/10 correct Distractors: 10/10 correct
Leiden South-West locations [2]	North-South axis: average of 9.1% deviation from the correct location East-West axis: average of 12.0% deviation from the correct location
Leiden South-West route descriptions [3]	3/5
Eemnes landmarks [1]	Total: 17/20 correct Targets: 9/10 correct Distractors: 8/10 correct
Eemnes locations [2]	North-South axis: average of 14.5% deviation from the correct location East-West axis: average of 16.0% deviation from the correct location
Eemnes route descriptions [3]	3/5

Note. Z.R. grew up in the South-West area of the city of Leiden. She still travels on a regular basis to the Leiden South-West area to visit her father who lives there. Z.R. has lived in the village of Eemnes for six years. She did not visit this area prior to the surgery. The stimuli presented in the tests were carefully matched between the two environments in terms of the functions of the landmarks (e.g., church, school, etc.) and distances.

[1] In this task, Z.R. was presented with 20 landmarks one by one (10 targets, 10 matched distractors) and we asked her to indicate whether or not each landmark was located in the target area.

[2] Z.R. was presented with maps of the environment in which only the outer sides were shown, while the centre of the map was covered. Z.R. was asked to indicate the location of the 10 target landmarks. Her performance was scored by calculating the percentage of deviation from the correct location, both on the North-South and East-West axes.

[3] Z.R. was asked to provide five detailed route descriptions between two landmarks in the environment.

* The scoring procedure for the landmark recognition tasks: 1 point was awarded for correct naming of the landmark; 0.5 point was given for a correct non-visual description of the landmark.

DISCUSSION

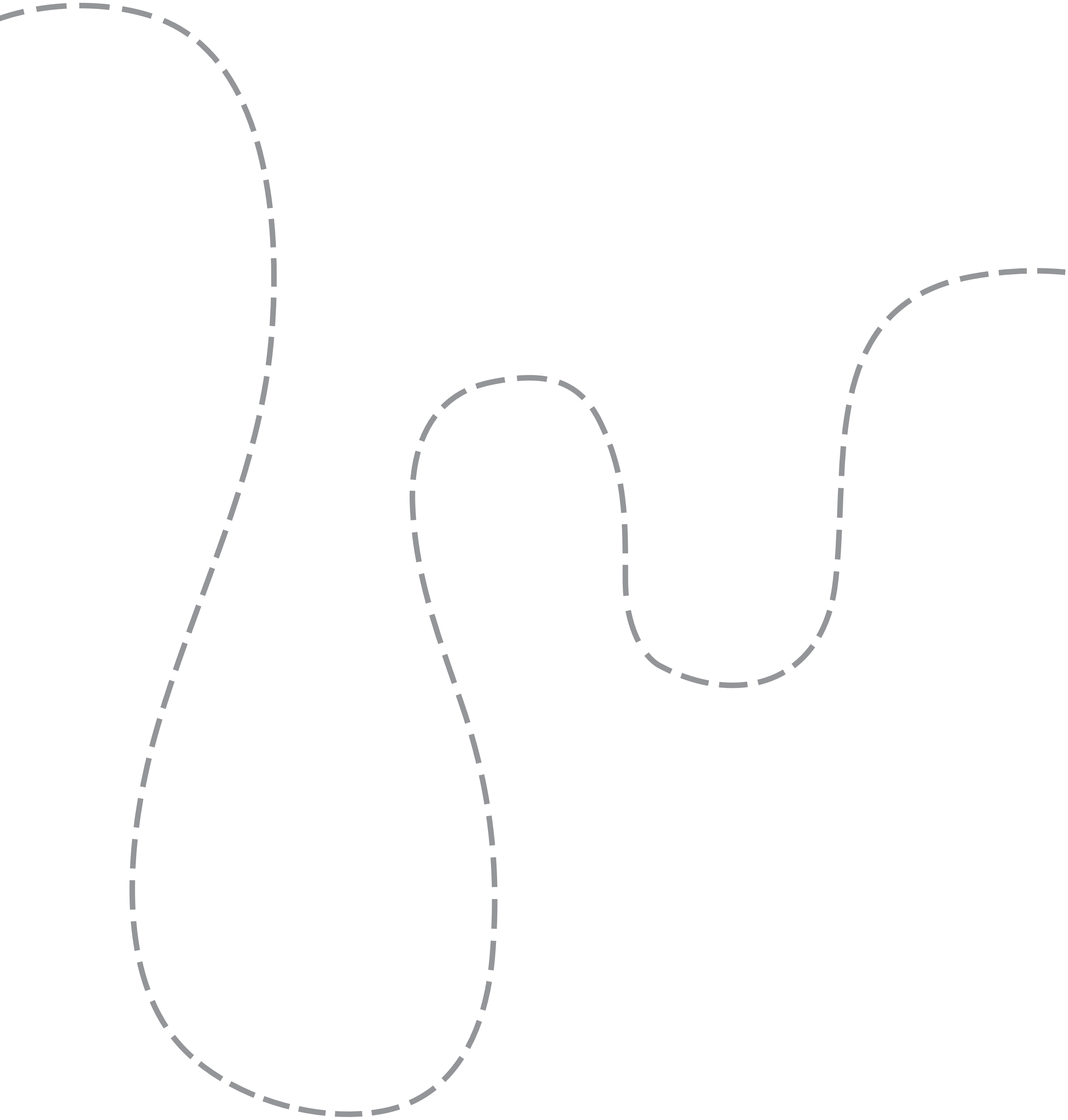
In the current report, we have provided objective evidence for severe difficulties with navigation in a patient who underwent a right anteromedial temporal lobectomy. While her performance on a regular neuropsychological assessment only showed a visuospatial working memory deficit, specific navigation ability tests clearly confirmed her difficulties with learning new (virtual) routes. We also found deficits in her knowledge of landmark locations and the paths connecting these locations for two familiar environments. However, no clear evidence was found for a difference between test performance for an environment visited prior to the surgery and test performance for an environment visited after this intervention.

This latter finding increases our knowledge about the hippocampal contribution to navigation ability. Previous case studies on patients with selective hippocampal damage (no temporal lobectomy patients, however) have reported mixed findings. Two case reports have suggested a time-limited role of the hippocampus in spatial navigation, as their patients had difficulties only in novel and not familiar environments (Rusconi, Morganti, & Paladino, 2008; Teng & Squire, 1999). Other case reports, however, have supported the idea that hippocampal involvement in navigation is permanent by showing navigation problems for both novel and familiar environments in their patients (Maguire, Nannery, & Spiers, 2006; Rosenbaum et al., 2000, Rosenbaum, Gao, Richards, Black, & Moscovitch, 2005). Our case report supports this latter position.

Another issue that needs to be discussed is the marked discrepancy between Z.R.'s intact performance on visuospatial neuropsychological tasks and her impaired performance on the navigation tasks. We think that this discrepancy results from a difference in the spatial scale that these tests address. While the neuropsychological tasks measure small-scale visuospatial skills (i.e., reaching space), our navigation tasks concern large-scale visuospatial skills (i.e., navigational space). Striking dissociations between small and large-scale visuospatial skills have previously been reported in brain-injured patients (Piccardi, Iaria, Bianchini, Zompanti, & Guariglia, 2011) and these types of abilities are supported by partly different brain networks (Nemmi, Boccia, Piccardi, Galati, & Guariglia, 2013).

One alternative explanation that cannot be ruled out at this point is that Z.R.'s difficulties with navigation have a psychological rather than a neurological origin. Z.R. has been diagnosed with a personality disorder NOS due to an enduring and stable pattern of difficulties with establishing and maintaining social relationships. It can be hypothesised that she has once learned that she raises the attention and interest of other people when she has lost her way. For example, a neighbour has intensively helped her with recording written route descriptions, which might have reinforced Z.R. in displaying this behaviour. However, it should also be emphasised that Z.R. is now severely restricted in living an independent life.

Lastly, we would like to emphasise that severe navigation disability after right anteromedial temporal lobectomy is a very rare complication. Nonetheless, the case report of Z.R. demonstrates that such a disability can have far-reaching consequences. By describing the case of Z.R., we intend to increase clinicians' awareness of the possibility of navigation problems as a complication of anteromedial temporal lobectomy, as this would help in gaining a better indication of its frequency of occurrence.



CHAPTER 8

Dissociating spatial and spatiotemporal aspects of navigation ability in chronic stroke patients

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Author contributions:
IH designed the study; MB and MC collected and processed the data; MC analyzed the data; MC, IH, JV, and EJ interpreted the data; MC drafted the paper; IH, JV, EJ, and MB revised the paper for intellectual content.

ABSTRACT

Objective: The notion of distinguishable processing mechanisms for spatial and spatiotemporal information has largely been neglected in the context of navigation. Only a recent neuropsychological case study has provided initial evidence for the idea that these elements can be differentiated at a functional level. The aim of the current study was therefore to critically verify this double dissociation by adopting a systematic, large-scale approach.

Method: 65 chronic stroke patients and 60 matched healthy controls watched a route through a realistic virtual environment. They were assessed on their knowledge of this route in four different tasks after the learning phase. Performance on the *scene recognition* and *route continuation* tasks was taken as an indication of knowledge of the spatial route aspects. By contrast, spatiotemporal knowledge of the route was assessed in the *route order* and *route progression* tasks.

Results: Based on single case statistics, six patients showed an exceptionally large difference in their performance on the spatial and spatiotemporal tasks. Moreover, two patients satisfied formal criteria for a classical dissociation.

Conclusions: Our findings showed that spatial and spatiotemporal performance was closely associated in most patients. Nonetheless, the study also provided partial support for the notion of separate space- and time-based processing mechanisms in the context of navigation. This distinction is of particular relevance to the investigation into the cognitive structure underlying navigation behavior.

INTRODUCTION

In order to remember events, it has been argued that these events themselves must be remembered along with both their spatial ("where") and their temporal ("when") context (Fujii et al., 2004; Johnson, Hashtroudi, & Lindsay, 1993; Shimamura & Wickens, 2009; Tulving, 2002). Spatial and temporal information is, however, not automatically integrated as a unitary mechanism in episodic memory, but should be regarded as independent memory processes (Postma, van Asselen, Keuper, Wester, & Kessels, 2006; van Asselen, van der Lubbe, & Postma, 2006). Moreover, retrieval of spatial and temporal context information of an event activates both a shared pattern of neural activation as well as activation in separate areas of the brain (Fujii et al., 2004). A similar distinction between processing of spatial location and temporal duration has been demonstrated in working memory (Hälbig, Mecklinger, Schriefers, & Friederici, 1998). Overall, these findings are intriguing, as they contradict the evident interpretation of integrated processing of spatial and temporal information given that events are usually highly connected in space and time (van Asselen, van der Lubbe et al., 2006).

In our view, this distinction might also be applicable to navigation, or 'way finding'. Navigation has been shown to be an important, yet complex spatial cognitive ability for adequate daily life functioning (e.g., van der Ham, Kant, Postma, & Visser-Meily, 2013): the ability to find one's way from one location to another. Navigation is a multicomponent behavior that incorporates different cognitive processes, such as perception, attention, memory and executive control functions (Wolbers & Hegarty, 2010). While navigating through an environment, people employ a range of tasks to successfully arrive at their intended destination. For example, people use landmarks to guide their spatial navigation behavior (Blades & Medlicott, 1992; Chan, Baumann, Bellgrove, & Mattingley, 2012; Janzen & van Turennout, 2004) and create mental maps of the environment (Iaria, Chen, Guariglia, Ptito, & Petrides, 2007; Taylor & Tversky, 1992; Thorndyke & Hayes-Roth, 1982; Tolman, 1948). The main aim of the current study was thus to investigate whether a distinction between spatial and temporal processing mechanisms exists for navigation ability as well. This is a unique approach to further unravel the multicomponent cognitive nature of navigation behavior.

Several cognitive abilities underlying navigation behavior primarily rely on spatial features, whereas others engage features that are mainly temporal in nature. A common task in navigation research is to ask participants to indicate whether or not several scenes or landmarks were part of a certain route (*scene* or *landmark recognition* task; e.g., Arnold et al., 2012; Janzen & van Turennout, 2004; Spiers et al., 2001). Although a *scene recognition* task does not necessarily require the participant to make spatial judgments per se, such a task likely activates (visuo)spatial processing (Sewards, 2011). That is to say, scenes inherently contain information about the spatial configuration of several buildings or objects.

Recognition of scenes and landmarks has convincingly been shown to be no simple reflection of overall memory performance. Several studies have described patients who suffer from a specific impairment in using prominent environmental features for navigation and orientation purposes, called 'landmark agnosia' (e.g., Hirayama, Faguchi, Sato, & Tsukamoto, 2003; Mendez & Cherrier, 2003; Rosenbaum, Gao, Richards, Black, & Moscovitch, 2005; Takahashi & Kawamura, 2002). However, scene recognition impairment is not inherently accompanied by impaired performance on other navigation tasks (Aguirre & D'Esposito, 1999; Mendez & Cherrier, 2003; Rosenbaum et al., 2005; van der Ham, van Zandvoort, Meilinger, Bosch, Kant, & Postma, 2010). This finding clearly indicates that navigation ability is not fundamentally dependent on *explicit* scene recognition.

Several authors have explored the different functions of landmarks in guiding people's navigation behavior. For example, it has been shown that people use landmarks to form associations between certain locations and directional information (Chan et al., 2012; Waller & Lippa, 2007). A landmark might thus trigger one to perform a specific navigational action (e.g., "take a left turn at the church"; Chan et al., 2012). These place-action associations are considered an important element of route knowledge (Montello, 1998; Siegel & White, 1975), and can be assessed by a *route continuation* task (van der Ham et al., 2010; but see also Arnold et al., 2013; Liu, Levy, Barton, & Iaria, 2011). In such a task, participants are requested to indicate the direction in which the route continued at a certain scene or landmark. In case of randomized scene presentation, the *route continuation* task likely taps only into place-action associations (spatial in nature) rather than into temporal information.

By contrast, memory for the order in which a series of locations or landmarks appeared along the route clearly engages another type of information. Although memory for landmark order has been described as an element of route knowledge (Montello, 1998; Siegel & White, 1975), order memory is highly understudied in the context of navigation. A recent study has actually shown that this type of order memory plays an important role in navigation behavior (van der Ham et al., 2010), particularly in a neuropsychological context. Nonetheless, the precise cognitive properties of order memory in navigation are still unknown. In fact, most studies investigating the role of order memory in navigation usually refer to order memory as "temporal order" (e.g., Barker, Bird, Alexander, & Warburton, 2007; Ekstrom, Copara, Isham, Wang, & Yonelinas, 2011; van der Ham et al., 2010). However, it should be noted that moving along a route necessarily involves displacements in space. Moreover, if travelling speed remains constant, space and time progress in a parallel manner. The memorization of landmark order might thus be based on the different points in both time and space at which the landmarks are encountered. For this reason, the temporal features of navigation behavior are being referred to as "spatiotemporal" in this study.

An obvious way to assess order memory is to provide the participant with a number of images from a visually shown route and instruct them to arrange these images with regard to the order in which the displayed scenes or landmarks occurred along the route (e.g., Busigny et al., 2014; Maguire, Burke, Phillips, & Staunton, 1996; Sorita et al., 2013; van Asselen, Kessels et al., 2006; van Asselen, Fritschy, & Postma, 2006; van der Ham et al., 2010). Such a task is a measure of relative order, as the position of each scene is determined with respect to the position of other scenes (e.g., scene B occurred earlier than scene C but later than scene A). However, an additional way exists to assess the knowledge of spatiotemporal route features. Instead of asking for relative order, participants can be instructed to indicate the absolute order of a certain scene or landmark in the route. Participants are requested to indicate the image location with regard to the overall route length in such an approach. In the current study, participants will be assessed on their knowledge on the spatiotemporal route properties in both a relative order task (*route order*) and absolute order task (*route progression*).

The distinction between spatial and spatiotemporal processes in navigation ability has currently only been explored in a scarce manner. However, some studies have provided initial evidence for the notion that these processes engage different neurocognitive mechanisms. In a functional MRI (fMRI) study, Ekstrom and colleagues (2011) have investigated brain activation patterns regarding spatial and temporal order retrieval in navigation using a virtual environment. They identified that dissociable networks are engaged for the spatial and temporal components of order information in healthy participants. Although both order tasks activated the hippocampus to the same extent, the spatial task elicited more parahippocampal activation, while greater prefrontal activity was associated with the temporal task. Given these findings, Ekstrom and colleagues (2011) have speculated that spatial and temporal order representations are processed in distinct brain areas, but may merge into a combined representation in the hippocampus.

Further evidence of distinct processing mechanisms of spatial and spatiotemporal information for routes stems from neuropsychological studies. Several of these studies have investigated navigation disabilities in Alzheimer's disease (AD) and amnestic Mild Cognitive Impairment (aMCI) patients. In a study by deIpolyi, Rankin, Mucke, Miller and Gorno-Tempini (2007), both patient groups (AD and aMCI) performed equally compared to controls on a landmark recognition task, whereas the patients were clearly impaired in their ability to recall the order in which these landmarks were encountered during the route. Performance in the order task was correlated to volumes of inferior frontal areas. Moreover, impairment in spatiotemporal order memory for routes tends to occur already in the early stages of AD (Kalová, Vlček, Jarolímova, & Bureš, 2005) and has also been interpreted as reliably discriminating AD and aMCI patients from age-matched healthy controls (Bellassen, Iglói, Cruz de Souza, Dubois, & Rondi-Reig, 2012).

A neuropsychological case study has also contributed to this discussion by reporting on a double dissociation between two neurological patients in spatial and spatiotemporal deficits regarding navigation ability (van der Ham et al., 2010). A.C., the first patient, was a 36-year-old woman suffering from an ischemic infarction, which damaged the right superior parietal cortex including the medial occipital, the angular and a small part of the postcentral gyrus. On the behavioral level, A.C. had a selective impairment in *route order* (a spatiotemporal task). The second patient, W.J., was a 44-year-old woman with lesions in the posterior region of the right hemisphere as a result of multiple surgeries to operate a glioblastoma multiforme brain tumor. More specifically, scans showed damage to the occipital, temporal and superior parietal areas with involvement of the fusiform gyrus and the hippocampus. This patient was, however, impaired in the *scene recognition* and *route continuation* tasks (both spatial tasks), but performed within the normal range on the spatiotemporal task. Note that, despite her notable scene recognition impairment, she performed within the normal range on the *route order* task. Hence, these two neurological patients showed a double dissociation between spatial and spatiotemporal deficits in navigation.

All of the brain areas mentioned above have been identified as being part of an extensive neural network that is associated with performing navigational tasks. The specific patterns of brain activation have, however, been shown to depend on the familiarity with the environment as well as the strategy being used (see for a review: Boccia, Nemmi, & Guariglia, 2014). Several brain structures are particularly relevant for the spatial and spatiotemporal navigation tasks used in this study. The ability to encode scenes to allow for later recognition (*scene recognition* task) has been coupled to the parahippocampal place area, a functionally defined area in the posterior parahippocampal gyrus (e.g., Epstein, 2008; Sewards, 2011). Place-action associations, as assessed in our *route continuation* task, concern information about which action to take at a particular landmark or intersection. Applying such place-action associations for navigational purposes has been named response learning and has been linked to activity in the caudate nucleus (e.g., Iaria, Petrides, Dagher, Pike, & Bohbot, 2003). Furthermore, Aguirre and D'Esposito (1999) have argued that patients with retrosplenial lesions suffer from a condition called 'heading disorientation'. While these patients are able to recognize scenes, they have serious difficulties in deriving directional information from them (Epstein, 2008). With regard to the spatiotemporal aspects, several studies have specifically pointed to areas in the prefrontal cortex as being important for temporal order ability in navigation (deIpolyi et al., 2007; Ekstrom et al. 2011; van Asselen, Kessels et al., 2006). However, at least three studies suggest that additional areas other than the prefrontal cortex are involved in the processing of spatiotemporal aspects of routes (Busigny et al., 2014; Grön, Wunderlich, Spitzer, Tomczak, & Riepe, 2000; van der Ham et al., 2010). The spatiotemporally impaired patient in the study by van der Ham and colleagues (2010) suffered from a right superior parietal cortex lesion incorporating the precuneus. In addition, patients with posterior cerebral artery infarctions (PCAI) have been shown to be less accurate in landmark ordering than controls (Busigny et al., 2014). Several studies have coupled a network comprising of prefrontal as well as parietal areas to temporal order memory in the context of working memory (e.g., Cabeza et al., 1997; Marshuetz & Smith, 2006).

In the current study, we critically verified whether the double dissociation between processing of the spatial and spatiotemporal properties of routes holds (see van der Ham et al., 2010) in systematic approach in a substantial sample of neurological patients and healthy controls. More specifically, navigation ability was assessed in a large group of chronic stroke patients ($n = 65$), as navigation problems tend to be common after stroke. This has been found in a self-report study (prevalence of 29%; van der Ham et al., 2013) but also in an extensive series of case studies (see for a review: Aguirre & D'Esposito, 1999; and for recent examples: Aradillas, Libon, & Schwartzman, 2011; Ciaramelli, 2008; Ino et al., 2007). Chronic stroke patients and controls performed four tasks, which reflect two different aspects of navigation ability. The *scene recognition* and *route continuation* tasks primarily tap into the spatial route properties, while the *route order* and *route progression* tasks mainly activate the spatiotemporal aspects of route knowledge. We hypothesized that 1) stroke patients are less accurate on the navigation tasks than healthy controls. With respect to the association between lesion location and behavioral performance, we assume that 2) stroke patients with right-sided lesions perform poorer on the tasks than stroke patients with left-sided lesions. It should be noted that this hypothesis has been examined in an explorative manner due to limited availability of detailed lesion information for all patients. With regard to the main aim of the study, we assume that performance on the spatial and spatiotemporal tasks are closely related in the majority of patients. However, we also expect 3) to replicate the dissociation between the spatial and spatiotemporal aspects of navigation as previously reported by van der Ham and colleagues (2010).

METHOD

Participants

The 81 chronic stroke patients initially included in this study were either outpatients of the rehabilitation center of De Hoogstraat Rehabilitation Utrecht or the rehabilitation department of University Medical Center Utrecht. Only patients who were able to walk independently and without indications of severe aphasia were selected for study participation. Time between stroke onset and study participation was at least six months for all patients. In addition, 61 healthy participants enrolled in the study to serve as controls. Only controls who reported the absence of visual, neurological, psychiatric, or mobility problems, and substance abuse were included to participate.

Before reaching the final sample, data of several participants had to be removed from further data analyses. Firstly, we excluded data of four patients and one control participant who were unable to complete the whole test procedure due to inability (i.e., severe fatigue or nausea due to motion sickness) or a self-reported lack of motivation. We then removed data of nine patients who suffered from more than one stroke event (i.e., six two-stroke-event patients and three three-stroke-event patients) and of three patients for whom no lesion information was available. Patients with a bilateral lesion, however, were retained in the analyses, because their lesions were the result of a single stroke event. Analyses were conducted on the resulting sample consisting of 65 stroke patients and 60 controls. Demographic information of both groups (gender distribution, age and education) is provided in Table 1, as well as additional information on the patients' stroke characteristics (type and location). Demographics and lesion information of individual patients can be found in Supplementary Table A. Note that lesion information other than the affected hemisphere was not available for all patients. Detailed lesion information was available for patients recruited through the university medical center, because gathering lesion information via MRI or CT is a standard procedure in this institution. The remaining patients were referred to the rehabilitation center after being discharged from a local non-academic hospital. For them, we had to rely on the lesion information that was provided by the hospital doctor who referred the patient for clinical rehabilitation. At the time this study was carried out, they usually only provided lesion information in terms of the artery or hemisphere involved.

All participants gave written informed consent prior to study participation. They received a small monetary reward and reimbursement of their travelling costs. The study was designed following the Declaration of Helsinki and all procedures were approved by the medical ethical committee of the University Medical Center Utrecht (protocol no. 12-198).

Materials and procedure

The experiment consisted of two parts. In the first part, the learning phase, participants passively watched a short movie of a route through a virtual rendition of the German city Tübingen (see e.g., van Veen, Distler, Braun, & Bülthoff, 1998; van der Ham et al., 2010). The second part was the test phase during which participants were assessed on their spatial and spatiotemporal knowledge of the route in four tasks: *scene recognition*, *route continuation*, *route order* and *route progression*.

Learning phase

Participants were shown a movie of a route through a realistic virtual rendition of Tübingen (Germany). As there were two different movies each displaying a different route (see Figure 1), participants were pseudo-randomly assigned to one of the two versions (version A or B). Both movies were nearly comparable in duration (A: 210 seconds and B: 253 seconds), similar in distance (approximately 400 m) and both contained eleven decision points of which seven included a left or right turn. Speed of movement was somewhat above walking speed. The movies were played on a laptop screen (17.3-inch diagonal HD4 display) and participants were seated 60 to 80 cm from the screen. The movie was shown twice in immediate succession with the instruction to pay close attention to the route. No reference was made to the content of the tasks that would follow the learning phase.

Table 1. Demographic data of the patient and the control group as well as stroke characteristics of the patient group.

	Patients	Controls
n	65	60
Age in years	60.2 (11.9)	58.7 (9.6)
Male/female (%)	56.9% / 43.1%	51.7% / 48.3%
Education	5.3 (1.4)	5.6 (0.9)
Stroke type		
Ischemic stroke	51 (78.5%)	
Hemorrhagic stroke		
- Intracerebral	12 (18.5%)	
- Subarachnoid	2 (3.0%)	
Stroke location		
Supratentorial region		
- Left	27 (41.5%)	
- Right	26 (40.0%)	
- Bilateral	1 (1.5%)	
Infratentorial region		
- Left	2 (3.1%)	
- Right	2 (3.1%)	
- Bilateral	7 (10.8%)	

Note. Upper panel: standard deviations are displayed between parentheses. Education level (range: 1–7) is based on the classification system proposed by Verhage (1964).

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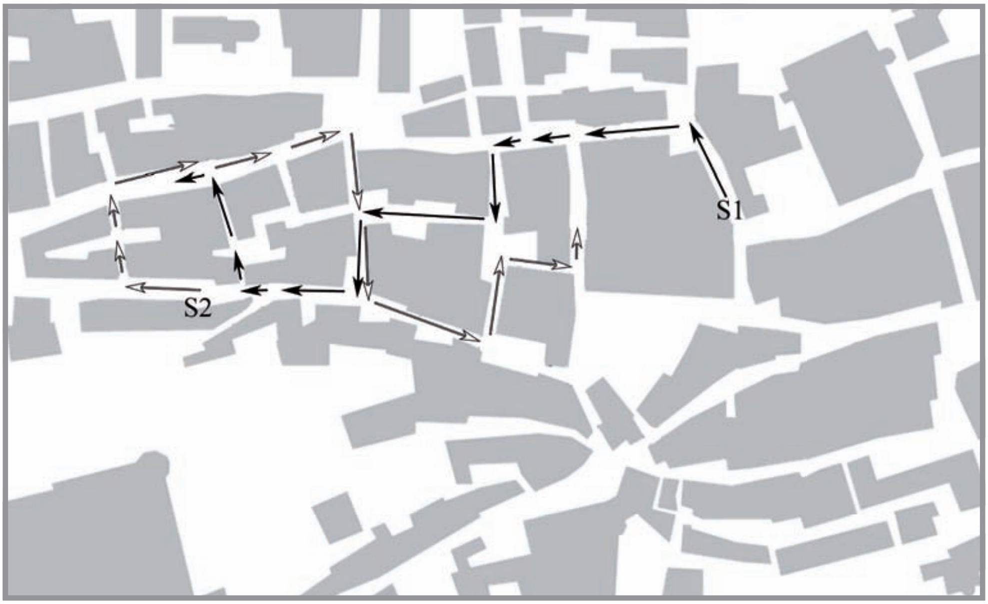


Figure 1. This map shows the two routes (black and white arrows) in the virtual environment of Tübingen used in the experiment. All decision points (intersections) are marked with an arrow. Starting locations of the routes are indicated with an S and the route number.

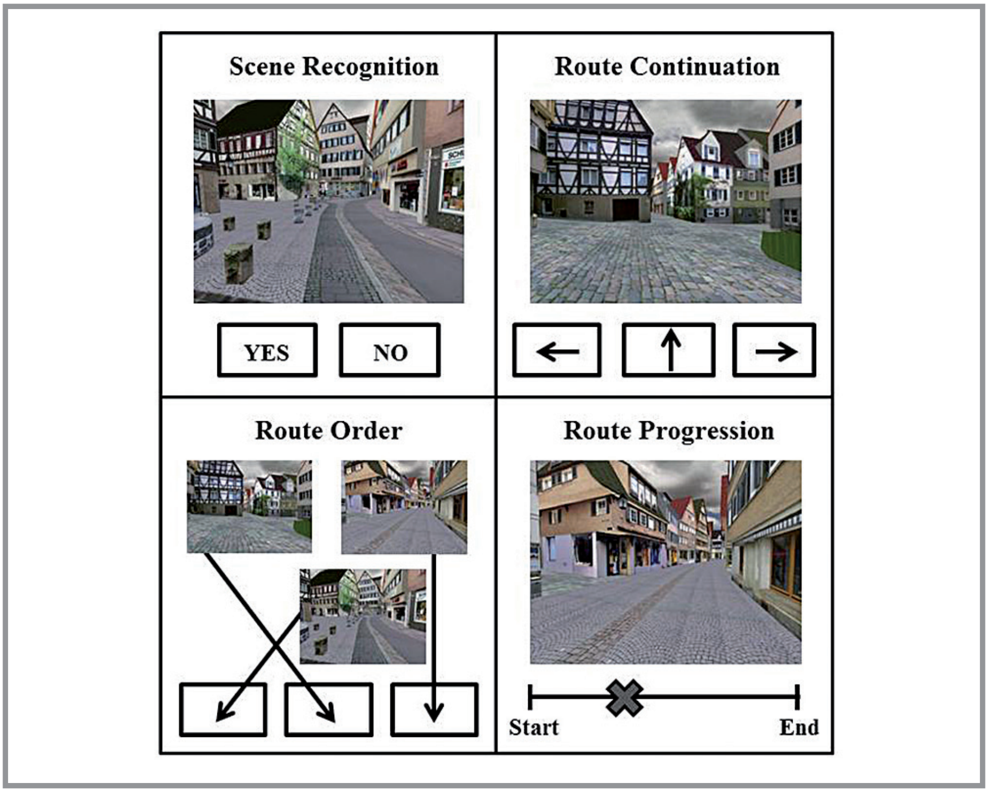


Figure 2. Visual explanation of the four navigation tasks. Spatial tasks: *scene recognition* (indicate whether or not this scene was present in the route) and *route continuation* (indicate the direction in which the route continued at this intersection); spatiotemporal tasks: *route order* (arrange a set of scenes in the correct order) and *route progression* (indicate the position of the scene relative to the total distance of the route).

Test phase

After watching the route movie twice, participants were immediately tested on their knowledge of the route (see Figure 2 for a visual task explanation). No task contained time limits for responding. The first two tasks were used to assess participants' knowledge about the spatial characteristics of the learned route. In the first task, the *scene recognition* task, 22 scene images (1075 x 806, 68 dpi) taken from the virtual environment were presented one by one in random order. Eleven images[3] were indeed shown in the movie (targets), whereas the other half of the images were novel scenes of other sites in Virtual Tübingen that were not encountered in the route movie (distractors). Participants had to indicate whether or not each image was part of the route using two buttons on a regular keyboard. Task accuracy was measured as the percentage of correct answers (hits and correct rejections).

In the *route continuation* task, participants were shown eleven decision points images (one by one in random order, 1075 x 806, 68 dpi) that were present in the route. They were requested to indicate the direction (left, right or straight ahead) in which the route continued at each decision point. Responses were gathered using the arrow keys on a regular keyboard. Performance was measured in terms of the percentage of correct answers. Both the *scene recognition* task and *route continuation* task were assessed on a laptop using Presentation 16.3 (Neurobehavioral Systems).

Memory for the spatiotemporal route aspects was assessed using two different tasks. In the *route order* task, participants had to indicate the relative order of eleven printed scene images (± 8 cm x 14 cm) from the route. All images were presented simultaneously. The participant had to indicate the position of each image. Scoring of the task was performed by means of a three-point-system (range: 0–33 points). Three points were provided for each image assigned to its correct position in the sequence. Two points were given in case the image was assigned one position too late or too early. A single point could be obtained when the indicated position was two positions away from correct placement. A three rather than a two-point-system was used (van der Ham et al., 2010), as this scoring procedure is more sensitive to the relatively long image sequence used here (i.e., eleven instead of seven scenes).

Memory for absolute order was tested in the *route progression* task. Participants were shown eleven printed images (± 8 cm x 14 cm) one by one and asked to indicate where each image was encountered on the route. To this extent, they were provided with a small piece of paper with a printed line (17.8 cm). The left and right ends of the line represented the starting and end points of the route respectively. Participants were instructed to mark the absolute image position on the line. The following procedure was carried out to quantify the difference in the actual and indicated image positions in the route. First, the values of the actual and indicated positions (as measured in

3 *The same eleven images of decision points were used in the other subtasks. All images were taken right in front of the decision point, such that all possible directions were visible.*

centimeters from the left end of the line) were converted to a value between 0 and 1 by dividing it by the total line length (17.8 cm). Next, the relative difference was calculated by subtracting these two values from each other. This value was then subtracted from 1, such that a score of 1 would reflect perfect performance. Lastly, the difference scores were averaged across all eleven items.

Statistical Analysis

First of all, it was checked whether the patient and control group were comparable in their demographics: age and educational level (independent t-tests) and gender distribution (chi square test).

Next, to address the first and second hypothesis, four one-way univariate analyses of variance (ANOVAs) were conducted with Group (controls, patients with left-sided supratentorial damage and patients with right-sided supratentorial damage) as a between factor and performance on each navigation task as dependent variable. The four ANOVAs were preceded by an overall multivariate analysis of variance (MANOVA) to minimize the likelihood of type I error. The effect sizes of significant results are reported in terms of η_p^2 (partial eta squared). Significant results were followed up with Bonferroni-corrected post-hoc tests. Prior to this analysis, stroke locations were subdivided into lesions in structures above (supratentorial) and underneath (infratentorial) the tentorium cerebelli. This approach is common in rehabilitation medicine to differentiate between lesions in the cerebrum (cerebral cortex and subcortical structures) and lesions in the cerebellum and brain stem. Lesions were marked as left-sided, right-sided or bilateral. This classification approach is relatively coarse. However, it allowed inclusion of as many patients as possible, because the required lesion information to make such a distinction was available for all patients. Applying a more specific classification would have led to a less powerful analysis, as more detailed lesion information was not available for all patients.

The third aim of the study was to verify the dissociation between spatial and spatiotemporal aspects of navigation ability (see van der Ham et al., 2010). A multiple single case approach was applied to do so. Firstly, scores of each individual patient were converted to z-scores for the four navigation ability tasks separately. The z-scores were calculated using the means and standard deviations of the control group. Next, two separate composite z-scores were calculated for the spatial tasks (*Scene Recognition* and *Route Continuation*) and the spatiotemporal tasks (*Route Order* and *Route Progression*).

The two composite scores were used to assess whether patients would qualify for a dissociation between spatial and spatiotemporal performance. According to Shallice (1998), a distinction can be made between dissociations of the classical and the strong type. Patients were classified as showing a classical dissociation in case of one impaired and one intact score (i.e., either spatial or spatiotemporal) along with a significant difference between spatial and spatiotemporal performance. Patients with both impaired spatial and spatiotemporal performance as well as a significant difference between the two would, however, qualify for a strong dissociation. These strict criteria were proposed by Crawford and Garthwaite (2007) and allowed us to rigorously assess whether individual patients would classify for a formal dissociation between the spatial and spatiotemporal aspects of navigation.

Crawford & Howell's (1998) test was first used to identify individual patients showing deficits in their spatial and/or spatiotemporal performance. Next, the updated version of the Bayesian Standardized Difference Test (BSDT; with the following settings: Bayesian criteria for dissociations, calibrated prior, one-tailed test) was applied to verify whether the standardized difference between spatial and spatiotemporal performance of each individual patient was statistically larger than in the control group. The BSDT uses the controls' correlation between the two composite z-scores to test whether the standardized difference between spatial and spatiotemporal differs significantly from the standardized differences as observed in the control group. After that, the results of these two tests were combined to establish whether individual patients would meet criteria for a strong or classical dissociation. The statistical procedures described above were performed using the latest version of the computer program "DissocsBayes_ES_CP.exe" (Crawford, Garthwaite, & Ryan, 2011).

The two-step procedure described above was used to identify the patients of interest, i.e., the patients with a spatial and / or spatiotemporal deficit (given Crawford & Howell's test) as well as the patients with a significant standardized difference score between their spatial and spatiotemporal performance (based on the BSDT). We aimed to verify whether the deficits and / or standardized differences in these patients could be the result of more general cognitive impairments. The results of a neuropsychological screening (see Supplementary Table C) were therefore used to individually compare performance of the patients of interest with performance of the remaining patients. This procedure was used rather than a comparison with a norm or healthy control group, as the aim was to verify whether the patients of interest were neuropsychologically different from the other patients. Neuropsychological performance of individual patients of interest was compared with the means and standard deviations of the remaining patients using a Bayesian test for single case studies (Crawford & Garthwaite, 2007).

Alpha level was set to .05 for all statistical tests.

RESULTS

Participants

The final sample consisted of 65 patients and 60 controls (see Table 1). Independent t-tests showed that age was comparable for the two groups, $t < 1$, as well as educational level, t (110.5) = 1.65, p = .102. Since equality of variances could not be guaranteed for the comparisons of age and educational level according to Levene's test (p = .028 and p = .003 respectively), corrections of degrees of freedom were applied to these independent t-tests. Furthermore, a chi square test showed that the gender distributions of the patient and control groups were comparable, $\chi^2 < 1$.

Group performance (controls vs. left patients vs. right patients)

The overall MANOVA results, using Pillai's trace, showed that Group had a significant effect on navigation performance, $V = 0.22$, F (8,216) = 3.25, $p = .002$, $\eta_p^2 = .107$. Next, four separate ANOVAs were conducted, to reveal the effect of Group on performance on each navigation task (see Table 2). *Scene Recognition* performance was significantly affected by Group, F (2,110) = 5.78, $p = .004$, $\eta_p^2 = .095$. Post-hoc tests showed that controls performed better than left ($p = .048$) and right-sided supratentorial patients ($p = .01$), whereas the two patient groups had comparable *Scene Recognition* performance ($t < 1$). The effect of Group was also significant for the *Route Continuation* task, F (2,110) = 6.26, $p = .003$, $\eta_p^2 = .102$. Post-hoc comparisons revealed better performance of controls relative to left (trend level: $p = .052$) and right-sided supratentorial patients ($p = .005$). No significant difference was found in *Route Continuation* performance between the two patient groups ($t < 1$). A significant effect of Group was found on the *Route Order* task as well, F (2,110) = 7.53, $p = .001$, $\eta_p^2 = .120$. Controls performed better than left ($p = .002$) and right patient groups ($p = .029$), whereas the two patient groups performed comparably on the *Route Order* task ($t < 1$). Lastly, Group also significantly affected Route Progression performance, F (2,110) = 8.58, $p < .001$, $\eta_p^2 = .135$. Post-hoc analysis showed better performance in controls relative to both left ($p = .011$) and right patients ($p = .001$). Once again, the difference in performance on the *Route Progression* task between the two patient groups was non-significant ($t < 1$).

Table 2. Performance on the navigation tasks in the patient groups and the control group.

Navigation tasks	Healthy control participants (n = 60)	Left supratentorial lesion (n = 27)	Right supratentorial lesion (n = 26)
Scene Recognition (SR)	81.44 (10.12)	75.25 (12.18)	73.78 (11.23)
Route Continuation (RC)	74.39 (16.78)	64.31 (17.99)	60.84 (20.69)
Route Order (RO)	18.70 (7.17)	13.26 (4.92)	14.58 (7.00)
Route Progression (RP)	0.83 (0.07)	0.78 (0.06)	0.77 (0.10)

Note. Scores: SR = percentage of correct responses, RC = percentage of correct responses, RO = 0–33, higher values indicate better performance, RP = 0–1, higher values indicate less deviation from correct responses. Standard deviations are displayed between parentheses.

Individual case analyses

Firstly, patients with deficits on the spatial z-score, the spatiotemporal z-score or on both z-scores were identified. All performances of –1.69 *SD* of the mean or below were classified as a deficit by the Crawford & Howell's test (1998). In total, 16 out of 65 patients satisfied criteria for at least one impaired z-score. More specifically, four patients (no. 20, 25, 55, and 57) had a spatial deficit, five patients (no. 1, 5, 18, 27, and 65) showed a spatiotemporal deficit and for seven patients (no. 12, 13, 33, 38, 41, 51, and 61) both the spatial and the spatiotemporal z-score met the criteria for a deficit. Next, the Bayesian Standardized Difference Test (BSDT) was used to analyze the standardized difference between the spatial and spatiotemporal performance of each individual patient. Six patients showed a significantly larger standardized difference between spatial and spatiotemporal performance than in the control group. Four of them (no. 5, 18, 37, and 44) showed relatively better spatial performance, whereas the other two (no. 29 and 53) demonstrated relatively better spatiotemporal performance. When combining the results of Crawford & Howell's test and the BSDT, two individuals (no. 5 and 18) met the strict criteria for a classical dissociation. Case 5 (suffering from a right supratentorial lesion in the parietal cortex) obtained a spatial z-score of 0.19 (no deficit: $t < 1$) and a spatiotemporal z-score of –2.32 (deficit: t (59) = –2.301, p (one-tailed) = .012, Z_{CC} = –2.32). The standardized difference between these scores was significant, p (one-tailed) = .006, Z_{DCC} = 2.62, and more extreme discrepancy was estimated to occur in only 0.64% of the controls (95% *CI* = 0.07 to 2.18%). Case 18 (suffering from a bilateral infratentorial lesion in the brain stem) had a spatial z-score of 0.24 (no deficit: $t < 1$) and a spatiotemporal z-score of –1.71 (deficit: t (59) = –1.696, p (one-tailed) = .048, Z_{CC} = –1.71). The standardized difference between these scores was significant, p (one-tailed) = .025, Z_{DCC} = 2.04, and a more extreme discrepancy was expected in 2.50% of controls (95% *CI* = 0.62 to 6.09%). The details of the patients referenced above are presented in Table 3. See Supplementary Table B for the individual results of all 65 patients.

Table 3. Statistical results of Crawford & Howell's test (1998) and the BSDT for the patients referenced in "Results: Individual case analyses".

	Spatial tasks			*Spatiotemporal tasks*			*BSDT*		*Dissociation*	
Patient	*z-score*	*p-value*	*deficit*	*z-score*	*p-value*	*deficit*	*p-value*	*difference*	*type*	*nature*
1	–0.84	.204	-	–1.83	.037	yes	.159	-	-	-
5	0.19	.426	-	–2.32	.012	yes	.006	yes	classical	spatiotemp.
12	–2.55	.007	yes	–2.83	.003	yes	.392	-	-	-
13	–1.70	.049	yes	–1.90	.032	yes	.420	-	-	-
18	0.24	.406	-	–1.71	.048	yes	.025	yes	classical	spatiotemp.
20	–1.70	.049	yes	–0.48	.318	-	.109	-	-	-
25	–2.11	.020	yes	–1.07	.146	-	.148	-	-	-
27	–1.38	.088	-	–1.80	.040	yes	.336	-	-	-
29	–0.43	.336	-	1.39	.087	-	.033	yes	-	-
33	–2.01	.025	yes	–2.54	.007	yes	.300	-	-	-
37	0.78	.221	-	–1.43	.081	-	.013	yes	-	-
38	–2.19	.017	yes	–2.35	.012	yes	.437	-	-	-
41	–2.19	.017	yes	–2.12	.020	yes	.472	-	-	-
44	1.41	.084	-	–1.02	.158	-	.008	yes	-	-
51	–2.01	.025	yes	–1.88	.034	yes	.448	-	-	-
53	–1.65	.054	-	0.26	.399	-	.027	yes	-	-
55	–2.06	.023	yes	–0.66	.258	-	.080	-	-	-
57	–1.97	.028	yes	–1.29	.103	-	.247	-	-	-
61	–2.37	.011	yes	–2.08	.022	yes	.387	-	-	-
65	–1.15	.129	-	–2.21	.016	yes	.144	-	-	-

Note. BSDT = Bayesian Standardized Difference Test (Crawford et al., 2011)

Table 4. Neuropsychological screening results for individual patients of interest and the remaining patients.

	DART	*Corsi Block TT*		*TMT*	*Digit Span (WAIS-III)*			*Line Bisection*
	Est. IQ	Forward	Backward	B given A	Forw. span	Back. Span	Cor. Items	Deviation %
M (SD)	100.0 (14.5)	41.1 (16.5)	44.7 (19.2)	2.3 (0.8)	5.5 (1.0)	3.9 (1.3)	13.1 (3.5)	–1.0% (4.6)
Patient 1	110	30	30	4.2*	5	5	13	—
Patient 5	113	35	12	2.1	8	5	19	—
Patient 12	102	20	25	1.9	6	3	12	—
Patient 13	59*	20	4*	3.2	5	3	10	—
Patient 18	90	20	12	2.5	4	4	10	—
Patient 20	74	16	9	1.9	3*	3	7	—
Patient 25	109	20	20	4.2*	4	4	10	—
Patient 27	110	12	12	5.5*	5	4	14	—
Patient 29	135	48	70	1.6	6	5	17	—
Patient 33	68*	12	25	1.7	4	3	8	—
Patient 37	92	35	30	2.4	5	5	13	—
Patient 38	109	48	24	3.3	6	3	11	—
Patient 41	90	40	77	2.5	4	0*	6*	—
Patient 44	121	45	50	1.4	7	6	21	2.3%

Patient 51	98	35	30	4.8*	3*	5	10	0.9%
Patient 53	74	20	4*	1.8	4	3	8	–5.9%
Patient 55	88	40	24	6.0*	5	4	11	0.8%
Patient 57	80	40	35	2.7	5	4	12	5.9%
Patient 61	105	20	12	7.4*	4	3	8	9.7%*
Patient 65	88	24	30	—	5	4	12	–6.9%

Note. DART = Dutch Adult Reading Test (Schmand, Lindeboom, & van Harskamp, 1992); Corsi Block TT = Corsi Block-Tapping Task (Kessels, van den Berg, Ruis, & Brands, 2008; Kessels, van Zandvoort, Postma, Kappelle, & de Haan, 2000); TMT = Trail Making Test (Reitan, 1992); WAIS-III = Wechsler Adult Intelligence Scale-third edition (Wechsler, 1997). Line Bisection (Hausmann, Ergun, Yazgan, & Güntürkün, 2002). Individual test scores that significantly differ from the mean and standard deviation of the remaining patient group (see first line), given results of Crawford & Garthwaite's test (2007), are marked with an asterisk (*). An overview of the neuropsychological tasks and their scoring procedures can be found in Supplementary Table C. The Line Bisection was added later to the screening and thus not assessed in all patients.

Neuropsychological screening for the patients of interest

In this section, the aim was to verify whether the patients of interest differed in their neuropsychological functioning from the other patients. Bayesian tests for single case studies (Crawford & Garthwaite, 2007) were applied to compare the neuropsychological performance of individual patients of interest with the mean performance of the remaining patients (see Table 4). Nine out of the twenty patients of interest were comparable in their performance on the neuropsychological screening to the remaining patients. Recall that six patients of interest showed a significant standardized difference between their spatial and spatiotemporal navigation performance on the BSDT. Importantly, five of them (including patient 5 and 18 who met formal criteria for a dissociation) were similar in their performance on the neuropsychological screening to the remaining patients. These findings indicate that differences in neuropsychological functioning are no likely explanation for the large differences in their spatial and spatiotemporal performance.

DISCUSSION

In this study, a large group of chronic stroke patients and healthy controls were systematically assessed on their knowledge of the spatial and spatiotemporal features of a newly learned virtual route. This study was undertaken to test the notion of dissociated space- and time-based processing mechanisms in navigation (Ekstrom et al., 2011). Specifically, the aim was to critically verify a double dissociation between these features in navigation as presented earlier in a case study of two neurological patients (van der Ham et al., 2010). Here, the double dissociation was evaluated using a systematic, large-scale approach in 65 chronic stroke patients and 60 controls.

Based on earlier group studies into navigation ability in stroke patients (Barrash et al., 2000; Busigny et al., 2014; van Asselen, Kessels et al., 2006) it was anticipated that the stroke patients, as a group, would have more difficulties with the navigation tasks than controls. In addition, performance on the navigation tasks was compared between patients with left- and right-sided lesions in the supratentorial region. Such a comparison was performed to test the second hypothesis stating that navigation performance is lowest in the patients with right-sided supratentorial lesions. Given the limited availability of detailed lesion information for all patients, we approached the second hypothesis in an explorative fashion.

Both hypotheses were tested in a single analysis by comparing performance of healthy controls, patients with left supratentorial damage and patients with right supratentorial damage on the four navigation tasks. Firstly, controls were found to perform best on all navigation tasks relative to both patients groups. This indicates that the brain damage caused by the stroke, regardless of the location of the lesion, has a clear negative effect on the navigation abilities of this patient group. This finding accords with a previous study that investigated navigation ability in patients with posterior cerebral artery infarctions (PCAI) by way of a real-world navigation task (Busigny et al., 2014). On group level, PCAI patients performed worse than controls on four navigation tasks, including two tasks that were comparable to the ones applied in the current study (scene recognition and ordering). Jointly, the study by Busigny and colleagues (2014) and ours underline that a substantial number of stroke patients might suffer from navigation impairments. While it is clear that navigation impairment affects daily life functioning and mobility in a negative way (van der Ham et al., 2013), navigation ability is still not addressed in neuropsychological practice in an explicit manner.

Former research has attributed an important functional role to the right hemisphere in spatial processing and spatial navigation (see for an overview: Jacobs et al., 2010). Therefore, we expected lower navigation performance in patients with lesions in the right supratentorial regions as compared to their counterparts with left-sided lesions. This second hypothesis was, however, not confirmed, in direct comparisons of performance between the patients with left and right supratentorial damage. Although unexpected, at least two earlier studies were also unable to find overall lateralization effects while comparing stroke patients with left-sided and right-sided lesions (Busigny et al., 2014; van Asselen, Kessels et al., 2006). For example, van Asselen, Kessels and colleagues (2006) reported no group differences in landmark recognition and landmark ordering between stroke patients with left-sided and right-sided lesions. Busigny and colleagues (2014) could only find lateralization effects by closely analyzing individual performance profiles, while their group analyses did not show any performance differences between left and right PCAI patients. These results do not detract from the role of the right hemisphere in spatial processing, but rather suggest that the left hemisphere might be of importance as well. Findings of several recent studies implicitly suggest that the involvement of the left hemisphere in spatial processing should not be neglected (e.g., Ruggiero, Frassinetti, Iavarone, & Iachini, 2014; van der Ham & van den Hoven, 2014).

A different line of explanation for the absence of performance differences between patients with left and right hemispheric lesions might lie in methodological aspects of the study. A rough lesion classification system was applied in the current study, which discriminated between supratentorial lesions in the cerebrum (cerebral cortex and subcortical structures) and infratentorial lesions in the cerebellum and brain stem. Lesions were marked as left-sided, right-sided or bilateral. Such a coarse system was used, as detailed lesion information was not available for all patients, especially not for the patients recruited through the rehabilitation center. Furthermore, given that detailed brain scans are not available, we were unable to determine the precise influence of secondary cerebral pathology (i.e., outside the location of the major stroke event) and the extent to which lesions were truly focal and lateralized.

Regarding the third hypothesis, the results of this study were partly in congruence with the distinction between spatial and spatiotemporal aspects of navigation as presented earlier in the case study by van der Ham and colleagues (2010). Two patients satisfied the strict criteria for a classical dissociation (Crawford & Garthwaite, 2007; Shallice, 1998). They were both selectively impaired on the spatiotemporal measure, whereas their spatial performance was well within the normal range, along with a significantly large standardized difference between spatial and spatiotemporal performance. The latter finding indicated that the standardized difference between the spatial and spatiotemporal measures was significantly different from the standardized differences as observed in the control group. Furthermore, differences in neuropsychological functioning as compared with the other patients were no likely explanation for this finding.

One of the patients (case 5) suffered from a lesion in the right parietal cortex. Interestingly, both the localization of the lesion as well as behavioral performance on the navigation tasks closely resembles the spatiotemporally impaired patient in the study by van der Ham and colleagues (2010). This finding further substantiates the role of the parietal cortex in the processing of temporal order information, especially in the context of navigation ability. Marshuetz and Smith (2006) have, for example, speculated that the parietal cortex is involved in coding the temporal distance between items. When integrating results of several studies (e.g., Cabeza et al., 1997; deIpolyi et al., 2007; Grön et al., 2000; Marshuetz & Smith, 2006; van Asselen, Kessels et al., 2006), it appears that a prefrontal-parietal network is primarily responsible for processing temporal order information. The other patient (case 18) who also showed a selective deficit in spatiotemporal performance, had bilateral damage in the brain stem. There is no information available to further investigate the relationship between this lesion and the behavioral performance. It might, however, be the case that secondary cerebral pathology could be a factor of explanation for the selective spatiotemporal deficit of this patient.

Apart from these two patients displaying a formal classical dissociation, four other patients showed exceptionally large standardized differences between spatial and spatiotemporal performance. Two of them demonstrated relatively better spatial performance, whereas two others showed the reverse pattern with relatively better spatiotemporal performance. The number of six patients showing such exceptionally large performance differences (either in favor of spatial or spatiotemporal performance) is relatively low as compared to the total number of 65 patients. This indicates that spatial performance and spatiotemporal performance are not necessarily dissociated but might be rather strongly associated. Still, as shown in this study, a small number of stroke patients showed unusually large differences in these two aspects of navigation. Our findings thus provide evidence that dissociations in spatial and spatiotemporal abilities in navigation can occur (Ekstrom et al., 2011; van der Ham et al., 2010; van der Ham & van den Hoven, 2014).

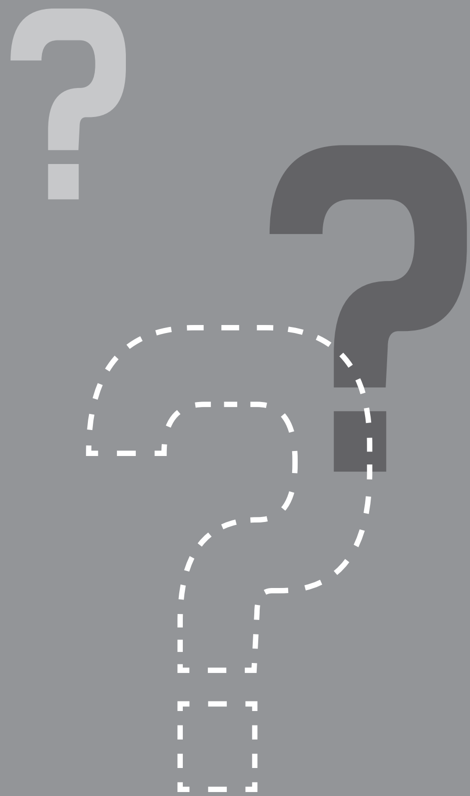
As mentioned above, a total of six patients showed an exceptionally large standardized difference either in favor of spatial or spatiotemporal performance. This implies that there are not only patients showing normal scene recognition performance along with impaired spatiotemporal order memory, but that the opposite pattern is also possible. The latter combination of impaired scene recognition and normal spatiotemporal order memory seems counterintuitive in particular. This is specifically true when one assumes that intact recognition memory is a requirement for adequate spatiotemporal order memory performance. Our results, however, support the view that scene recognition and memory for the spatiotemporal order of routes are not hierarchically related processes. In contrast, they might rely on qualitatively different mechanisms that function independently. By all means, our findings show that explicit scene recognition is no absolute prerequisite for adequate performance on the other navigation tasks. This is in line with earlier studies showing that an inability to explicitly recognize scenes or landmarks is not inherently accompanied by impairments on other navigation tasks (e.g., Mendez & Cherrier, 2003; Rosenbaum et al., 2005; van der Ham et al., 2010).

The navigation tasks that we administered are highly common in the field and are applied on a regular basis to measure egocentric navigation. In the current study, we separated the tasks according to the involvement of spatial and spatiotemporal aspects of route knowledge. We defined the *scene recognition* and *route continuation* tasks as primarily tapping spatial knowledge of the route and, on the other hand, the *route order* and *route progression* tasks as indicators of spatiotemporal performance. Clearly, the *scene recognition* task is likely to activate primarily visuospatial processes. Although the *scene recognition* task might not necessarily require the participant to make spatial judgments, such a task does activate visuospatial processing (Sewards, 2011), given that scenes incorporate information about the spatial configuration of buildings or objects. The *route continuation* task assesses the associations between a certain place (an intersection) and certain direction (a turn or going straight ahead). Due to the randomized presentation order of the intersections in this task, the influence of spatiotemporal processes was reduced to an absolute minimum.

Some elaboration is also needed on the operationalization of order memory for routes in our study. Order memory for routes was defined as the memorization of the order in which a series of landmarks were encountered along the route (van der Ham et al., 2010; deIpolyi et al., 2007). This definition is related, but not identical, to the concept of sequence memory for navigational purposes. An important line of studies has looked into the strategy of using a sequence of body movements for navigational purposes (see for a review: Fouquet et al., 2010). The results of the current study clearly show that the memorization of landmark order also constitutes an important source of information for navigational purposes. Furthermore, order memory impairment has convincingly been shown to interfere with successful navigation behavior in daily life (van der Ham et al., 2010). A further remark concerns our interpretation of order memory for routes as being of spatiotemporal rather than temporal order memory alone. Encountering landmark order in a route is certainly not only associated with different points in time but also in space. As all route elements were encountered at constant speed, it remains difficult to separate the two types of encoding.

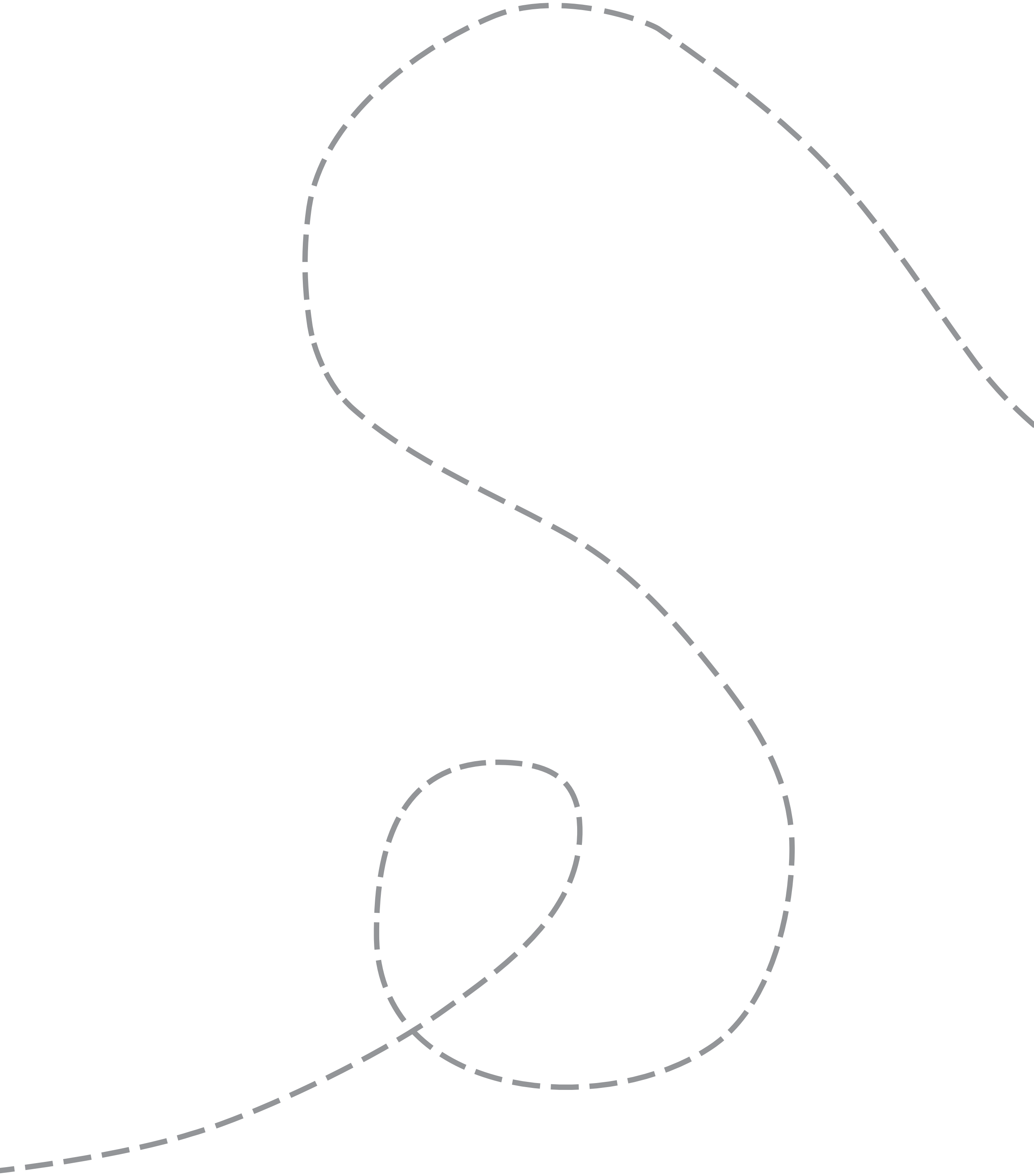
Lastly, the potential functionality of the dissociation between the spatial and spatiotemporal aspects of navigation might be of importance. We speculate that the spatial and spatiotemporal components do not only reflect (partly) independent subsystems, but could serve different purposes in the context of navigation as well. More specifically, we suggest that spatial information of routes is mainly important in coding of route geometry as well as the generation of cognitive maps. In contrast, temporal route information could be particularly helpful in keeping track of one's position within a route.

To summarize, we provide support for a dissociation between spatial and spatiotemporal features in navigation ability. We found that, for most patients, spatial and spatiotemporal performance was closely related. Nonetheless, we also identified six patients showing unusually large differences between their spatial and spatiotemporal performance. Two of them satisfied strict criteria for a dissociation, both suffering from a selective spatiotemporal deficit. Thus, whereas spatial and spatiotemporal aspects of navigation might be closely associated, this does not exclude the possibility that selective impairments in either of these aspects can occur. These findings complement the results of a recent case study (van der Ham et al., 2010). The distinction between space- and time-based processing mechanisms is a novel finding in the context of navigation. These findings are of considerable importance in defining the cognitive structure underlying navigation ability.



PART 4

Rehabilitation possibilities for patients with impaired navigation ability



CHAPTER 9

Navigation strategy training using virtual reality in six chronic stroke patients: A novel and explorative approach to the rehabilitation of navigation impairment

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Author contributions:

MC, JV, and IH designed the study; MC collected the data; MC, JV, IH, and EJ interpreted the data; MC drafted the paper; JV, IH, and EJ revised the paper for intellectual content.

ABSTRACT

Recent studies have shown that navigation impairment is a common complaint after brain injury. Effective training programmes aiming to improve navigation ability in neurological patients are, however, scarce. The few reported programmes are merely focused on recalling specific routes rather than encouraging brain-damaged patients to use an alternative navigation strategy, applicable to any route. Our aim was therefore to investigate the feasibility of a (virtual reality) navigation training as a tool to instruct chronic stroke patients to adopt an alternative navigation strategy. Navigation ability was systematically assessed before the training. The training approach was then determined based on the individual pattern of navigation deficits of each patient. The use of virtual reality in navigation strategy training in six middle-aged stroke patients was found to be highly feasible. Furthermore, five patients learned to (partially) apply an alternative navigation strategy in the virtual environment, suggesting that navigation strategies are mouldable rather than static. In the evaluation of their training experiences, the patients judged the training as valuable and proposed some suggestions for further improvement. The notion that the navigation strategy people use can be influenced after a short training procedure is a novel finding and initiates a direction for future studies.

INTRODUCTION

The ability to find one's way around has been shown to be crucial for adequate and autonomous daily life functioning. When we navigate from one location to another, we rely on multiple cognitive functions and, thus, on the cooperation of different brain structures (Brunsdon, Nickels, & Coltheart, 2007; Wolbers & Hegarty, 2010). The cognitive complexity of navigation behaviour makes this function highly vulnerable to brain damage, as shown in a large number of case studies (e.g., Aradillas, Libon, & Schwartzman, 2011; Ciaramelli, 2008; Ruggiero, Frassinetti, Iavarone, & Iachini, 2014; van der Ham et al., 2010). The navigation problems of these cases clearly interfere with their adequate and independent daily life functioning. Further evidence for a close relationship between navigation ability and daily life functioning comes from a systematic study in mild stroke patients (van der Ham, Kant, Postma, & Visser-Meily, 2013). Overall, these studies show a clear need for interventions that aim to improve navigation skills in brain-damaged patients suffering from navigation impairment.

The foremost challenge to overcome in developing an effective navigation training programme is to understand and take into account the substantial cognitive complexity that characterises navigation. Numerous cognitive processes are involved in solving any type of navigational task (Brunsdon, Nickels, & Coltheart, 2007; Wiener, Büchner, & Hölscher, 2009; Wolbers & Hegarty, 2010). Information originating from multiple sensory systems is relevant to navigation behaviour, such as from vision, the vestibular system and proprioception (Berthoz & Viaud-Delmon, 1999). Moreover, several cognitive functions, including, but not limited to, spatial processing, (working) memory, mental imagery, attention, and executive functions (e.g., decision-making and planning) interdependently contribute to guide navigation behaviour (e.g., Brunsdon et al., 2007; Guariglia & Pizzamiglio, 2007; Labate, Pazzaglia, & Hegarty, 2014; Wolbers & Hegarty, 2010). A further complexity is that individuals differ considerably in their general spatial abilities as well as in their specific navigation skills (e.g., Hegarty, Montello, Richardson, Ishikawa, & Lovelace, 2006; Ishikawa & Montello, 2006). It has even been suggested that such individual differences might not only be related to variables such as gender and age but also partly to personality traits such as neuroticism (Burles et al., 2014).

An extensive range of studies investigated healthy populations in order to unravel the types of environmental representations that humans use and the strategies they employ to approach navigation challenges. Most of these studies support a fundamental distinction of two different mental representations: route and survey knowledge (e.g., Foo, Warren, Duchon, & Tarr, 2005; Latini-Corazzini et al., 2010; Newman et al., 2007; Thorndyke & Hayes-Roth, 1982; Wolbers & Büchel, 2005; Wolbers, Weiller, & Büchel, 2004). Route knowledge contains information about distinctive features in the environment (landmarks), associations between landmarks and directional information (e.g., left turn at the post office), and sequences of landmarks or turns. This type of knowledge is obtained by adopting the perspective of a ground-level observer. Survey knowledge, in contrast, refers to the general layout of the environment from an aerial or map-like perspective. It results in a mental representation of the area, including information about metric distances and angles. This knowledge is typically developed as a result of extensive exploration of an environment or by map learning. The fundamental distinction between route and survey knowledge is helpful in guiding treatment of navigation impairment in brain-injured patients. In our view, however, it is essential also to get hold of the cognitive complexity of navigation as well and to look beyond this heuristic distinction of the two types of representations and strategies.

Although the number of studies on navigation (as a cognitive ability) has increased over the past decade, a comprehensive theoretical model is still lacking. Nonetheless, this has not prevented us from exploring in this study how currently available knowledge about navigation can benefit the development of a navigation strategy training. Currently, only a limited number of studies has evaluated the effectiveness of navigation rehabilitation programmes (Bouwmeester, van de Wege, Haaxma, & Snoek, 2014; Brooks et al., 1999; Davis & Coltheart, 1999; Incoccia, Magnotti, Iaria, Piccardi, & Guariglia, 2009; Kober et al., 2013; Rose, Attree, Brooks, & Andrews, 2001). Typically, most of these attempts are characterised by two limitations. First of all, four of these studies are single case reports. More importantly, another shared characteristic of the majority of these navigation training studies is that they focus on learning and recalling a limited set of specific routes. Such an approach has two setbacks: firstly, the tools provided are only applicable for specific navigational tasks (e.g., navigating from home to the supermarket), and secondly, it does not take into account the complex cognitive nature of navigation behaviour. As such, it is unclear whether learning a restricted set of (virtual) routes helps patients to cope with their daily life navigation challenges.

With respect to the tools used in the navigation training, virtual reality (VR) clearly has a number of important advantages in performing exercises in a real environment. VR provides highly realistic and controllable simulations of real-life situations (Rose, Brooks, & Rizzo, 2005) and allows dynamic interplay with the virtual environment. Specifically regarding navigation training for stroke patients, VR provides patients a safe practice environment (without the need to go through busy traffic, etc.) and enables them to practise without delivering any notable physical effort. As fatigue is a common complaint after stroke (Schepers, Visser-Meily, Ketelaar, & Lindeman, 2006), VR facilitates patients to train at a higher intensity than would be possible on the streets. The advantages of VR have already been appreciated by navigation researchers. Its contribution therefore rapidly increased in navigation research (e.g., Ekstrom, Copara, Isham, Wang, & Yonelinas, 2011; Janzen & van Turennout, 2004;

Spiers et al., 2001). Moreover, an increasing number of attempts have also been made to implement this technology in neuro-rehabilitation training programmes (e.g., Rose et al., 2005; Yip & Man, 2013).

Given the above considerations, we developed a virtual reality (VR) navigation training, which aimed to instruct patients to adopt an alternative navigation *strategy*. The content of the training is based on the pattern of navigation deficits of each individual patient. Our expectation is that training patients to use alternative navigation strategies will help to compensate for the navigation difficulties they encounter in daily life. Our approach is unique, as compared to other navigation training studies, in assessing navigation abilities in a very broad sense (including landmark knowledge, sequence of turns, memory for scene order, pointing, etc.). As such, our approach acknowledges the cognitive complexity of navigation behaviour. Furthermore, our focus to instruct patients to use a navigational compensation strategy is novel as well.

The aim of the current exploratory study is threefold. First of all, we will examine the feasibility of the virtual environment as used in this navigation training. Secondly, we will evaluate whether or not it is possible for patients to adopt a different navigation strategy in the virtual environment after the training. Lastly, the experiences of the patients with the navigation training programme will be discussed.

METHODS

Participants

Six chronic stroke patients (4 female, 2 male), who participated in a larger study on navigation impairment in stroke patients, were recruited from an existing sample of 77 chronic stroke patients (Claessen, Visser-Meily, Jagersma, Braspenning, & van der Ham, 2016). They lived in the community and were able to move independently. All patients were assessed in their navigation ability by means of a navigation questionnaire and an extensive virtual navigation test battery. Based on the following selection criteria, we contacted eight patients to participate voluntarily in the training: (1) navigation complaints measured as at least one impaired subscale on the self-report Wayfinding Questionnaire (van der Ham et al., 2013), and (2) at least one impaired navigation subtask score in the Virtual Tübingen test battery. Two of the contacted patients refused, because they were not able to travel multiple times to the rehabilitation centre. The six participating patients confirmed their navigation complaints when they were invited to participate in the training programme. The cut-offs (i.e., below –1.65 *SD* of the mean) for the first and second criteria were determined based on the performance of 60 healthy controls. The controls were highly similar in age ($M = 58.7$, $SD = 9.6$) to the six patients ($M = 57.0$, $SD = 8.9$), as well as in educational level based on Verhage (1964, range: 1–7): patients, *M* = 5.7, *SD* = 1.4, and controls, *M* = 5.6, *SD* = 0.9. The control group comprised 31 females (51.7%) and 29 males (48.3%). A description of the demographic characteristics of the participating patients is provided in Table 1. All training procedures in this study were performed in agreement with the regulations set by the local ethical review and the Declaration of Helsinki.

Measures

The scores on the Wayfinding Questionnaire, the neuropsychological screening, and the Virtual Tübingen test battery were used to determine the specific training approach for each individual patient. The ability to adopt the learned alternative navigation strategy after completion of the training was investigated by reassessing a parallel version of the Virtual Tübingen test. The patients were asked to fill out an evaluation form after the training in order to make an inventory of their training experiences. Where available, we report on the daily life effects of the training.

Wayfinding Questionnaire (WQ)

The Wayfinding Questionnaire (van der Ham et al., 2013) is a Dutch self-report measure of cognitive ability and anxiety regarding navigation in daily life. There were five subscales (response scale: 1–7): navigation (2 items), mental transformation (3 items), distance estimation (4 items), spatial anxiety (8 items), and sense of direction (9 items) (see Appendix A).

Neuropsychological screening

To assess relevant neuropsychological impairments, patients were subjected to a short neuropsychological screening pre-training. First, patients performed the Dutch version of the Adult Reading Test (DART, in Dutch: NLV, "Nederlandse Leestest voor Volwassenen") to estimate their premorbid intelligence (Schmand, Lindeboom, & van Harskamp, 1992). The forward and backward versions of the Corsi Block-Tapping Task (Kessels, van den Berg, Ruis, & Brands, 2008; Kessels, van Zandvoort, Postma, Kappelle, & de Haan, 2000) were used to measure visuospatial attention and working memory, respectively. Next, the Trail Making Test (Reitan, 1956) was applied to assess psychomotor speed (part A) and divided attention (part B). Lastly, the Digit Span subtest of the Wechsler Adult Intelligence Scale–III (WAIS–III; Wechsler, 1997) served as a measure of verbal attention (forward span) and verbal working memory (backward span). All scores were converted to percentiles based on the accompanying norm groups and scores at or below the 5^{th} percentile were interpreted as "impaired".

Table 1. Demographic characteristics of the patients and their scores on the Wayfinding Questionnaire.

	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**	**Case 6**
Age (at pre-test)	43	63	53	58	56	69
Gender	Female	Male	Female	Male	Female	Female
Education (1–7)	7	7	6	4	4	6
Diagnosis	Ischaemic stroke	Haemorrhagic stroke	Ischaemic stroke	Ischaemic stroke	Ischaemic stroke	Ischaemic stroke
Affected hemisphere	Right supratentorial	Right supratentorial	Left supratentorial	Bilateral supratentorial	Left supratentorial	Left supratentorial
Date of stroke event	21 October 2009	27 July 2008	8 August 2011	28 March 2009	27 December 2010	28 October 2010
Start of training	24 June 2013	25 October 2013	21 October 2013	5 November 2013	11 November 2013	5 December 2013
Number of sessions	4	3	5	4	4	4
Ratio PE/VR/RL	40/40/20%	50/25/25%	50/50/0%	50/50/0%	50/50/0%	40/40/20%
	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**	**Case 6**
WQ:						
Navigation	1.5*	3.5	4.0	2.0	3.0	1.5*
Mental transformation	2.0*	3.0	2.3*	3.7	4.0	3.7
Distance estimation	2.8	4.3	2.3	3.0	5.0	2.0*
Spatial anxiety	1.9*	2.0*	2.1*	2.6*	1.5*	2.6*
Sense of direction	2.2	2.6*	2.7*	4.4	5.3	3.0

Note. Higher scores indicate better self-reported navigation ability on the WQ (range: 1–7). The WQ-subscale "Spatial Anxiety" was reversed, so that a higher score would indicate less spatial anxiety and thus better navigation ability. Impaired scores on the WQ (below –1.65 *SD* of the control group mean) are marked with an asterisk (*). Abbreviations: PE = psycho-education, VR = virtual reality exercises, and RL = real-life exercises.

9

Virtual Tübingen test (VT test)

Navigation ability was assessed using the Virtual Tübingen test (Claessen, Visser-Meily, Jagersma et al., 2016; van Veen, Distler, Braun, & Bülthoff, 1998; van der Ham et al., 2010), which comprises two phases. In the first learning phase, patients watched a film of a short route through a virtual representation of the German city Tübingen twice and were instructed to pay careful attention to the route. Next, the test phase consisted of 10 tasks (see Appendix B for task descriptions and scoring methods) to assess both route and survey knowledge of the watched route. The first four of these tasks are assumed primarily to tap into aspects of route knowledge, whereas the latter six are regarded as mainly measuring survey knowledge features. As there were two highly comparable routes, patients performed a parallel version in the evaluation session after the training. Both films depicted a route with 11 intersections. At seven of these intersections a left or right turn was taken. At the other four intersections the route continued in a straight-ahead direction. The order of the two films differed between the patients. These two films were only used in the VT test, but not for exercises during the training sessions.

Feasibility and patients' training experiences

Feasibility of the training programme was assessed based on the trainer's observations, for example, with regard to the length of individual training sessions and the user-friendliness of the virtual environment in this patient group. The training experiences of the patients were assessed by way of an evaluation form after completion of the training programme.

Procedure

Pre-training

The VT test was used to assess patients on a range of navigation abilities that are known to underlie successful navigation. The performance pattern on the 10 tasks of the VT test was interpreted by authors MC and IH to establish a profile of strengths and weaknesses within navigation ability for each individual patient. Furthermore, the results on the Wayfinding Questionnaire and the neuropsychological screening were also taken into account as well to determine the specific training approach for each individual patient.

Training procedure

The default number of training sessions was set to four one-hour sessions. All training sessions were provided by a certified neuropsychologist (author MC). In the first session, psycho-education on navigational strengths and weaknesses was provided to the patient. The trainer and patient tried to relate these findings to the patient's navigation difficulties as experienced in daily life. The trainer also explained the specific, individual approach of the training programme. In the next sessions, patients performed exercises to improve specific navigation skills or learned to change their navigation strategy in general (e.g., from route-based to survey-based). Most exercises were executed using a dynamic version of Virtual Tübingen that could be controlled by means of a joystick. This version not only allows free exploration but also following specific routes. The rehabilitation centre building (De Hoogstraat Rehabilitation, Utrecht, The Netherlands) and its immediate vicinity were also used for some real-life exercises in three patients (no. 1, 2, and 6). These patients were able to independently walk distances of ± 1000 metres without getting extremely tired. In between sessions, patients were encouraged to practise the instructed navigational strategy in daily life as well and describe these experiences in a navigation diary. This "homework" was then discussed and evaluated with the trainer in the next session. Information on the relative contribution of the three elements (psycho-education – including discussion of homework, virtual reality exercises, and real-life exercises) is provided in Table 1 for each patient separately.

For example, for patients with impaired route knowledge (e.g., cases 4 and 5), the training procedure was focused on encouraging them to use a survey-based strategy. Exercises, for instance, addressed the adequate coupling of the ground-perspective with the map view. To do so, patients were provided with a route specified on a map and were then asked to follow this route through the virtual environment. On-screen feedback ("turn around") was provided in case a wrong turn was taken. In another type of exercise, participants had to plan and draw a route on a map and then follow the planned route through Virtual Tübingen. Such an exercise encouraged the patient to prepare a route carefully and adopt a survey-based strategy as well. Most of the sessions included discussing the homework and the completion of two of such exercises in the virtual environment. Further information on the specific exercises used can be found in the case descriptions in the Results section.

Post-training

To evaluate the patients' ability to adopt the instructed navigation strategy in the virtual environment, the VT test was reassessed using a parallel version post-training. They were also asked to fill out a form to evaluate their experiences with the virtual navigation training.

RESULTS

In this section, we first discuss the feasibility of the virtual environment in the navigation training. After that, we briefly describe the pre- and post-training results (see Tables 1–3) as well as the specific approach that was taken during the navigation training for each patient. Lastly, we evaluate the experiences of the patients with the navigation training.

Table 2. Patients' scores on the screening of standard neuropsychological tests pre-training.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
DART / NLV						
Est. premorbid IQ	113	128	110	80	91	107
Corsi Task						
Forward product	35 (15th)	35 (15th)	12 (5th)*	40 (30th)	30 (15th)	40 (30th)
Backward product	12 (2nd)*	60 (93rd)	12 (2nd)*	35 (30th)	25 (13th)	24 (18th)
Trail Making Test						
Part A	52 sec. (1st)*	32 sec. (42nd)	44 sec. (5th)*	78 sec. (1st)*	47 sec. (14th)	52 sec. (14th)
Part B	111 sec. (1st)*	102 sec. (12th)	244 sec. (1st)*	211 sec. (1st)*	86 sec. (34th)	105 sec. (21th)
B corrected for A	(8th)	(10th)	(1st)*	(5th)*	(58th)	(38th)
Digit Span (WAIS-III)						
Forward span	8	6	5	5	5	5
Backward span	5	6	4	4	2	3
Correct items	13 (84th)	19 (95th)	14 (40th)	12 (25th)	8 (2nd)*	11 (16th)

Note. Percentiles are displayed between parentheses. All impaired scores (≤ 5^{th} percentile) as compared to accompanying norm groups are marked with an asterisk (*).

Table 3. Patients' scores on the Virtual Tübingen navigation task pre- and post-training.

	Case 1		**Case 2**		**Case 3**		**Case 4**		**Case 5**		**Case 6**	
	Pre-test	*Post-test*	*Pre-test*	*Post-test*	*Pre-test*	*Post-test*	*Pre-test*	*Post-test*	*Pre-test*	*Post-test*	*Pre-test*	*Post-test*
Scene Recognition	86%	68%	64%*	91%	55%*	59%*	59%*	73%	82%	64%*	77%	77%
Route Continuation	73%	45%*	100%	55%	73%	45%*	45%*	45%*	45%*	55%	73%	91%
Route Sequence	100%	57%	100%	57%	43%	29%*	0%*	0%*	14%*	86%	14%*	57%
Route Order	5%*	45%	73%	32%	18%	36%	18%	18%	23%	5%*	23%	32%
Route P rogression	67%*	80%	88%	83%	68%*	86%	75%	85%	82%	75%	75%	80%
Route Distance	72%	72%	91%	84%	75%	83%	67%*	85%	74%	66%*	71%	79%
Pointing to Start*	63˚	54˚	28˚	53˚	45˚	55˚	68˚	88˚*	48˚	84˚	100˚*	43˚
Pointing to End*	44˚	63˚	26˚	69˚	116˚*	112˚*	81˚	107˚*	62˚	87˚	62˚	47˚
Map Drawing	0%*	9%	100%	27%	36%	36%	18%	18%	55%	9%	36%	91%
Map Recognition	Correct	Incorrect	Correct	Incorrect	Incorrect	Incorrect	Incorrect	Incorrect	Correct	Correct	Incorrect	Correct

Note. Impaired scores on the Virtual Tübingen test (below –1.65 *SD* of the control group mean) are marked with an asterisk (*).
** Scoring: average deviation in degrees; more deviation means less ability.

Feasibility

The feasibility of the virtual environment (Virtual Tübingen) was found to be high in our training programme. All of the six patients learned to control the virtual environment within a single training session, although only patient 2 stated he had some prior experience with virtual reality. Moreover, Virtual Tübingen was considered fairly realistic by all of the patients. All sessions lasted 60–70 minutes, which was an appropriate duration for five of the six patients. For patient 3, who suffered from fast emergent mental tiredness, pauses had to be built in on a regular basis.

Patients' training results

Case 1

This 43-year-old female reported navigation problems on four WQ subscales (Table 1). The neuropsychological screening showed indications of impaired visuospatial working memory, mental processing speed and divided attention (Table 2), which led the trainer to repeat important information throughout the training and encourage her to focus on only one type of information or task at once. She performed within the normal range on most of the VT tasks except for measures of absolute (*Route Progression*) and relative order (*Route Order*) (Table 3). The training was focused on instructing her to apply a survey-based strategy (i.e., cognitive mapping) and to plan routes ahead using maps. The latter goal was chosen, because she usually felt very uncomfortable while navigating in an unknown environment. During the training, several virtual reality exercises were used to practise pointing ability and facilitate coupling of the ground-perspective with the map view. In the last session, a real-life exercise was performed in which she was asked to plan a route ahead using a map and then follow the chosen route in the real-life environment. Initially, the patient rigidly used only street names to keep track of her current position on the map. However, after a while, she also started to use other types of information for orientation purposes (e.g., the shape of buildings and intersections). In order to practise pointing ability in the real world as well, she was asked to point to the starting point on a regular basis while following the route. In the post-VT test, she had clearly improved on tasks assessing order memory, but this change in focus had a negative effect on performance of five other tasks (Table 3). With regard to daily life effects, the patient noted that she used maps to plan routes ahead on a regular basis and got better at using maps for navigation purposes. Although she felt that her confidence in navigation challenges had increased, she still found it hard to cope with the negative emotions (mostly anxiety) that she experienced when she had problems navigating.

Case 2

The second participant was a 63-year-old male complaining of spatial anxiety and reduced sense of direction (WQ; Table 1). After his stroke, he quit sailing, as he was no longer able to navigate properly on the water in the absence of landmarks any more. On the streets, he managed to reach his intended destinations, but he regularly noted that he had not taken the shortest route possible. His pre-training VR test performance was fairly accurate; he was only impaired in scene recognition (Table 3). The training aimed to improve his sense of direction by practising pointing tasks in VR and real-life environments (also described as path integration; e.g., Liu, Levy, Barton, & Iaria, 2011; Wolbers, Wiener, Mallot, & Büchel, 2007). In one of the VR exercises, he was given a map of Virtual Tübingen with a specific route indicated. His task was to follow the route in the virtual environment while regularly being asked to point to the starting point of the route. A comparable task was practised in a real-life exercise as well, in which he was required to follow a route he planned himself. As he was very fast in performing the exercises and mastering the alternative navigation strategy, his training procedure was limited to three sessions. Strikingly, in the post-training assessment, he performed worse on almost all subtasks of the VT test after the training, except for the *Scene Recognition* task (Table 3). This finding suggests that, due to his focus on remembering scenes and landmarks while watching the route, he might have missed other types of information (e.g., survey knowledge). Although he found the training valuable to gain insight in his navigation abilities, he had expected that his navigation abilities in daily life would have been improved to a larger extent.

Case 3

This 53-year-old female showed impaired scores on three WQ-subscales including spatial anxiety (Table 1). The screening suggested impaired visuospatial attention and working memory, reduced mental processing speed and notable difficulties with dividing attention (Table 2). The VT test pre-training revealed evident difficulties in the route knowledge domain (Scene Recognition and Route Progression) as well as in the survey knowledge domain (Pointing to Start) (Table 3). It was decided to focus on the survey strategy, because the ability to recognise landmarks is essential for the route strategy to be effective. It seems difficult to navigate based on remembering landmark-action associations (e.g., “left at the church”) or remembering the order of landmarks in case of impaired scene recognition ability. Hence, instructing her to apply a survey-based strategy would reduce the need to rely on scene recognition processes. Due to her attention dividing problems, the purpose of most VR exercises was to teach her to prepare routes using maps beforehand. For example, she had to prepare a route on the map of Virtual Tübingen and was asked to focus on the shape of the route. After that, she used this information in order to follow the planned route in the virtual environment. Given that she suffered from fast emergent mental tiredness, pauses had to be built in. To compensate for these pauses, an additional training session was added to her training programme. Post-training results suggested a clear change in focus on the VR test battery (Table 3). Her performance on two survey knowledge-based tasks was ameliorated (*Route Progression* and *Route Distance*), but this had a negative effect on some tasks that primarily rely on route knowledge (*Route Continuation* and *Route Sequence*).

Case 4

This 58-year-old male suffering from hemianopia in the right visual field reported spatial anxiety on the WQ (Table 1). The screening revealed reduced mental processing speed as well as difficulties with dividing attention (Table 2). VT test performance particularly indicated route knowledge impairment (Table 3). The approach of the training was comparable to that of the third patient: preparing routes using maps and promoting the survey-based strategy. To do so, he was given multiple exercises to practise pointing ability and coupling of the ground-perspective with the map view. Reassessment of the VR test showed improvement on two survey knowledge-based tasks (*Route Progression* and *Route Distance*) as well as better *Scene Recognition* performance (Table 3). However, there were negative effects on the pointing tasks as well. These results show that he was partly successful in adopting a survey-based strategy.

Case 5

The fifth participant was a 56-year-old female with an impaired spatial anxiety WQ-score (Table 1). There were indications of impaired verbal attention and working memory on the neuropsychological screening (Table 2). Pre-training performance on the VR test demonstrated difficulties in the route knowledge domain (Table 3). For this reason, the training was focussed at promoting a survey-based strategy. Different types of VR exercises were applied for this purpose: a route preparation exercise, a pointing exercise, and an exercise to practise coupling the ground-perspective with the map view. Although her post-training VR test results seem to point to a general decline in navigation ability, her improvement on the *Route Sequence* task is remarkable and suggests the opposite (Table 3). The patient was highly accurate in reproducing the overall shape of the route using the printed arrows in this task, suggesting that she constructed a correct mental representation of the route from a survey perspective. In this sense, she was at least partially successful in adopting the survey-based strategy that was being promoted throughout the training. She indicated she was highly content with the training. She found it valuable to have learned to become more aware of the survey aspects of the route as well as knowing how to use maps for navigation purposes. During the training, she applied the newly learned strategy while visiting a city she had not previously been to and reported that it helped her to find her way around there.

Case 6

This 69-year-old female reported navigation difficulties on three WQ-subscales including spatial anxiety (Table 1). The screening showed no indications of neuropsychological impairments (Table 2). However, she stated she had difficulties with dividing her attention between driving and route following in unfamiliar environments. She never drove an unknown route by car, unless someone showed her the route before. She was impaired on two VT subtasks pre-training: *Route Sequence* and *Pointing to Start* (Table 3). Her performance pattern suggested a preference for a route-based strategy guided by landmarks, but sticking to this approach would rather reinforce her to drive only routes that were known to her. To give her confidence in driving in unknown environments, the training focused on instructing her to plan carefully (new) routes ahead by using maps and coupling the ground-level perspective with the map-view. Two types of VR exercises were performed for this purpose. In the first type of exercise, the patient was asked to reconstruct a watched route onto the map of Virtual Tübingen. The second type of exercise required her to follow a route in the virtual environment as specified on a map. A real-life exercise was carried out in the fairly complex building of the rehabilitation centre to promote route preparation and coupling the two different perspectives as well. To this end, she was given a map of the building in which the starting and end points were marked. She had to determine an appropriate route herself and was asked to focus on the route characteristics (e.g., landmarks she would pass along the way). Results of her post-training VR test suggested considerable improvement on all but one subtask of the VT test (Table 3). With regard to navigation on foot, she reported that using maps would now be sufficient to find her way around.

General results

Review of the pre- and post-training results of the participating patients indicates that one of them (case 6) had clearly improved in navigation ability in general. At least four other cases (i.e., patients 1, 3, 4, and 5) were (in part) successful in adopting an alternative navigation strategy and improved on most of the trained abilities. However, for five of the patients (i.e., patients 1 to 5), there were negative effects on performance of the navigation abilities that were not targeted during the training.

Patients' training experiences and their evaluations

The majority of the patients clearly stated that the training was very valuable and provided more insight into the origin of their difficulties in navigation and/or in learning to adopt an alternative navigation strategy. However, several recommendations were made for improvement of the training. Most of the patients had expected a more extended programme, including a larger number of sessions. It was also suggested that exercises could have been more in-depth. Furthermore, one patient noted that the training was focused too narrowly on navigation on foot. Her suggestion was to broaden the focus to navigation by car as well. It was also noted that Virtual Tübingen displays a city without people or vehicles and did not provide an opportunity to exercise while having to cope with interfering cars and distracting noises.

DISCUSSION

In the current study, we conducted a virtual reality navigation strategy training in six chronic stroke patients with navigation difficulties. The focus of the training was to instruct patients to adopt an alternative navigation strategy as a way to compensate for their navigation impairments. Virtual reality was used as an important tool to practise the newly learned navigation strategy in a safe environment (on average 42.5% of the training), in addition to psycho-education and real-life exercises. We will discuss our findings in the light of the three main aims of the study.

Firstly, virtual reality proved to be an appropriate tool for allowing patients to practise the application of a compensatory navigation strategy. Our finding that the use of virtual reality is suitable for rehabilitation purposes accords with earlier navigation training studies (Brooks et al., 1999; Kober et al., 2013; Rose et al., 2001) as well as with rehabilitation studies focussing on other cognitive functions (Rose et al., 2005; Yip & Man, 2013). In addition, sessions lasted approximately 60 minutes, which was found to be appropriate for five of the six patients.

Next, we made comparisons of the pre- and post-training VT test battery results for each patient individually to evaluate our training. This approach was taken as patients showed highly different performance patterns pre-training. For this reason, we did not conduct analyses on group level performance. We found that one of the cases firmly improved on nine out of the 10 virtual navigation subtasks. Four other cases were also (at least in part) successful in adopting an alternative navigation strategy given their improved performance on most of the trained abilities. However, in five cases, we found that changing their navigation strategy or focus had unexpected negative effects for non-trained abilities or strategies. We assume that patients are limited, most likely due to their brain damage they are suffering from, in their ability to focus broadly on all information from the virtual route. That is, instructing them to focus on a particular type of survey information might result in reduced ability to focus on other types of survey information at the same time. This makes the trainer responsible for finding out what focus will lead to the most beneficial results for each individual patient. These results seem to suggest that the strategy people use to approach navigational challenges can be influenced by a relatively simple and short training procedure.

The above notion that navigation strategies might be mouldable rather than static is important as it encourages further research into navigation *strategy* training programmes. Prior navigation training studies, however, described programmes that focused on patients memorising a limited set of particular routes (Bouwmeester et al., 2014; Brooks et al., 1999; Rose et al., 2001) or street names and their locations (Davis & Coltheart, 1999). As such, these studies trained patients to perform specific navigational tasks (e.g., navigating from home to the railway station) rather than providing them compensatory strategies applicable to any route. As a consequence of this difference in approach, it might well be that our approach places higher demands on the cognitive abilities of the participant. In other areas of neuropsychological rehabilitation compensatory or strategy training is rather common practice (Cicerone et al., 2011). However, in the context of rehabilitation of navigation impairment, the *strategy* training that we introduced here is a novel approach.

Furthermore, in correspondence with the finding that navigation is a substantial complex cognitive construct (Brunsdon et al., 2007; Wolbers & Hegarty, 2010), we found that all six patients showed different and specific patterns of navigation impairment pre-training. This clearly highlights the importance of individualised interventions to match the specific navigation problems of each individual patient. Our approach of determining the content of the training programme on the pattern of strengths and weaknesses of each individual patient is thus sensible.

It should, however, be noted that the current study design does not yet allow us to draw firm conclusions about the effectiveness of our training procedure. An important limitation of this study is the lack of data on performance on the Virtual Tübingen tests in a control group of non-trained patients. As a consequence, it was not clear whether performance on two successive administrations of the VT test would be stable over time in such a group. Including a control group of non-trained patients would allow one to calculate what a reliable change in performance (i.e., the reliable change index; Jacobson & Truax, 1991) is on the different subtasks of the VT test. We therefore recommend that future research evaluating this training approach should incorporate a non-trained control group and apply the reliable change index as well. Moreover, the current study design does not allow us to establish the relative contribution of the three training components separately (i.e., psycho-education, virtual reality exercises, and real-life exercises).

Lastly, we aimed to evaluate the experiences of the patients with the virtual reality navigation training. Two important recommendations were proposed by the patients for improvement of the training: firstly, a more extensive programme, including a larger number of sessions and exercises and, secondly, a broader focus to take into account navigation by car as well.

Firstly, in contrast to the patients' recommendation, the objective results of the current study seem to suggest that three to five one-hour training sessions might be rather sufficient for influencing one's navigation strategy. Extension of the number of training sessions in the presence of the trainer thus does not seem advisable, as it would also lead to an increase of the training costs. Apart from the above conclusion, possibilities for extension of the training could lie in developing additional daily life homework exercises and by adapting the virtual environment such that it would enable practising at home. The current version of VT requires a fairly powerful computer and lacks a convenient and user-friendly interface. Currently, however, the initial results suggest that the present training duration is sufficient. However, whether or not the patients continue to apply the alternative navigation strategy over time as well is not known.

The second recommendation addresses the fact that the training was primarily focussed on navigation on foot. There are two reasons for emphasising this type of navigation in our training. Firstly, navigation on foot is an important mode of transportation in the Netherlands due to the relatively short distances. Secondly, navigation by car (or bike) mainly differs from navigation on foot in higher speed of motion and in requiring someone to divide attention between driving and route following. However, this comment also relates to the nature of the used virtual environment in the training as well. The current version of VT does not display people or vehicles. It might therefore be argued that this limits its generalisability to real-life situations, as there is neither interfering traffic nor distracting noises. Ideally, the virtual environment should include both options, for example, so that distractions can be added as the training progresses.

We would like to mention two further recommendations for future studies based on our observations. Firstly, our findings encourage future research to investigate how to gain more control over changing a participant's preferred navigation strategy without affecting the navigation abilities that were intact pre-training. It is also unknown whether these negative effects, when they occur, have an influence on daily life navigation as well. Further research into navigation strategies and how to change them is therefore also desirable in non-clinical groups. In a more general sense, there is a great need for a comprehensive and empirically tested model of navigation as a cognitive function. Such a theoretical model would be helpful in guiding the development of effective and evidence-based training programmes aiming to improve navigation abilities of brain-damaged patients suffering from such difficulties in daily life. On the other hand, waiting for a finalised theoretical model of navigation as a cognitive structure to become available before further investigation of its trainability would be an ineffective approach. We therefore recommend that the two lines of study should run in parallel and, through an interactive approach, their results should affect the direction taken in both.

A useful addition, in order to better evaluate the effects of the navigation training in daily life, would have been the use of goal attainment scaling (GAS; e.g., Bouwens, van Heugten, & Verhey, 2009). GAS provides a standardised way to evaluate a training programme, such as the navigation training presented here, while taking the goals and needs of the individual patient into account as well. A limitation of our study is that the daily life effects of the training were addressed in a non-systematic manner.

Lastly, we found that all six patients were impaired on the “Spatial Anxiety” subscale of the Wayfinding Questionnaire. The participating patients thus tended to experience higher levels of anxiety in the context of navigational tasks as compared to a group of matched healthy controls (see also Lawton, 1994; van der Ham et al., 2013). The topic of spatial anxiety is relatively unexplored, but the few studies reported have revealed a negative relationship between spatial anxiety and a preference for a survey-based navigation strategy (Lawton, 1994, 1996). More specifically, people who experience lower levels of spatial anxiety tend to rely more strongly on survey knowledge for navigation purposes than people with rather elevated levels of spatial anxiety. As such, it could be argued that the concept of spatial anxiety is highly important to our study, as we encouraged patients to adopt an alternative navigation strategy. We strongly advocate further exploration of the concept of spatial anxiety and its effect on actual navigation performance in both healthy and brain-injured participants.

To conclude, the use of a virtual environment in the context of a navigation training was highly feasible in a group of middle-aged stroke patients. In addition, we found initial support for the idea that navigation strategies are mouldable rather than static, even after a relatively short training programme of three to five one-hour sessions. We recommend that the content of interventions aiming to improve people’s navigation abilities should fit the specific needs and specific impaired navigation pattern of the individual participant. The current results suggest that teaching brain-damaged patients, who suffer from navigation impairment, to adopt an alternative navigation *strategy* is a sensible approach. Given the limitations of the current study design as discussed above, however, additional investigation of the effectiveness of this approach in a more systematic and controlled study design is certainly necessary.

APPENDIX A: WAYFINDING QUESTIONNAIRE (26-ITEM VERSION; TRANSLATED FROM DUTCH)

Navigation

1. I can effortlessly walk back a route I have never walked before, the same way I walked up.
2. When I am in a building for the first time, I can easily point to the main entrance of this building.

Mental Transformation

3. If I see a landmark (building, monument, intersection) multiple times, I know exactly from which side I have seen that landmark before.
4. In an unknown city I can easily see where I need to go when I read a map on an information board.
5. While reading a map, I constantly turn the map into the direction that I am going.

Distance Estimation

6. Without a map, I can estimate the distance of a route I have walked well, when I walk it for the first time.
7. I can estimate well how long it will take me to walk a route in an unknown city when I see the route on a map (with a legend and scale).
8. I can always orient myself quickly and correctly when I am in an unknown environment.
9. I always want to know exactly where I am (meaning, I am always trying to orient myself in an unknown environment).

Spatial Anxiety

10. I am afraid of losing my way somewhere.
11. I am afraid of getting lost in an unknown city.
12. In an unknown city, I prefer to walk in a group rather than by myself.
13. When I get lost, I get nervous.
14. How uncomfortable are you in the following situations:
    a. Deciding where to go when you are just exiting a train, bus, or subway station.
    b. Finding your way in an unknown building (for example, a hospital).
    c. Finding your way to a meeting in an unknown city or part of a city.
15. I find it frightening to go to a destination I have not been before.

Sense of Direction

16. I can usually recall a new route after I have walked it once.
17. I am good at estimating distances (for example, from myself to a building I can see).
18. I can orient myself well.
19. I am good at understanding and following route descriptions.
20. I am good at giving route descriptions (meaning, explaining a known route to someone).
21. When I exit a store, I do not need to orient myself again to determine where I have to go.
22. I enjoy taking new routes (for example, short cuts) to known destinations.
23. I have a good sense of direction.
24. I can easily find the shortest route to a known destination.

Possible responses ranged from 1 (not at all applicable to me) to 7 (fully applicable to me). Scoring of item 5 and all items of the *Spatial Anxiety*-subscale were reversed such that a high score would indicate high self-reported navigation ability. The version that the patients filled out did not include the subheadings.

APPENDIX B: THE TEN SUBTASKS OF THE VIRTUAL TÜBINGEN TEST BATTERY AND THEIR SCORING

1. *Scene Recognition*: Participants had to indicate whether or not 22 individual scenes (11 targets and 11 distractors) were encountered during the route. Scoring: Percentage of correct responses on 22 trials.
2. *Route Continuation*: Participants were presented with 11 images of decision points and had to indicate in what direction the route continued from each of these decision points. Scoring: Percentage of correct responses on 11 trials.
3. *Route Sequence*: Participants were asked to replicate the order of the seven turns that were taken during the route by using a set of printed arrows. Scoring: Percentage of correctly indicated left and right turns.
4. *Route Order*: Participants were required to arrange a set of 11 printed scenes according to the order in which they were encountered during the route. Scoring: Two points were awarded when a scene was assigned to its correct position and one point if it was assigned one position too early or too late. The percentage of obtained points (maximum of 22) was calculated.
5. *Route Progression*: Participants were shown 11 scenes from the route and asked to indicate the location of each individual scene in the route on a line representing the total distance of the route. Scoring: Percentage of deviation between the indicated and actual position relatively to the full length of the line. These scores where averaged over 11 trials.
6. *Route Distance*: Participants were shown two scenes in each trial (total of nine trials) from the route and had to indicate the distance between these scenes on a line representing the total distance of the route. Scoring: Percentage of deviation between the indicated and actual position relatively to the full length of the line. These scores where averaged over nine trials.
7. *Pointing to Start*: Participants were shown 11 scenes from the route and were asked to point, for each scene, to the start point of the route using a rotational device. Scoring: Deviation in degrees between indicated and correct response averaged over 11 trials.
8. *Pointing to End*: Participants were shown 11 scenes from the route and were asked to point, for each scene, to the end point of the route using a rotational device. Scoring: Deviation in degrees between indicated and correct response averaged over 11 trials.
9. *Map Drawing*: Participants were asked to draw the route on a map of Virtual Tübingen. Scoring: Percentage of correctly drawn decision points (11 in total).
10. *Map Recognition*: Participants were shown four routes on different maps of Virtual Tübingen and were required to indicate which of these depicted the route as seen during the film. Scoring: Correct or incorrect response.

CHAPTER 10

Summary and conclusions

SUMMARY AND CONCLUSIONS

The general objective of this thesis was to better understand the navigation problems that nearly a third of stroke patients are faced with. Insight into these types of problems is currently very limited in this patient group. I adopted four different approaches to address this main objective, corresponding to the four parts of this thesis. In the first part, I performed a systematic inventory and interpretation of neuropsychological case studies on patients with navigation problems. This review provides insight into the types of navigation impairments that can occur and also gives an overview of the neuropsychological study approach to navigation ability. The aim of the second part was to develop and validate both a subjective and an objective assessment instrument of navigation ability, eligible for implementation in clinical practice. As regards the aim of the third part, I illustrated how to design navigation assessment in a theory-driven manner. This approach connects the theoretical and clinical views on the study of navigation ability and demonstrates the importance of making such a connection. In the fourth part, I explored rehabilitation possibilities for patients with impaired navigation ability. The main findings and conclusions of these four parts will be discussed in detail here. Furthermore, I will highlight the potential of virtual reality (VR) techniques for assessment and rehabilitation of navigation ability. I will conclude this chapter by arguing that this thesis serves as a bridge between scientific research and clinical practice, and, as such, should be interpreted as an attempt to bring these two fields closer together.

Part 1: Types of navigation impairments

A common way of studying the origin and nature of navigation impairment in brain-damaged patients is by performing neuropsychological single-case studies. This approach allows the researcher to perform an in-depth assessment of the cognitive functions directly and indirectly associated with navigation ability. This is typically done by administering a combination of standardized neuropsychological tasks and tasks specifically designed to assess navigation ability. An important advantage of this single-case approach is that individual differences can be taken into account, which is of particular relevance to the study of navigation ability, as even healthy people differ considerably in this ability (Hegarty, Montello, Richardson, Ishikawa, & Lovelace, 2006). In contrast, the fact that researchers have not been very consistent in assessing problems in navigation ability makes it hard to integrate and summarize the findings of these numerous case reports. It therefore appears that there is a need for a systematic inventory and interpretation of these studies. The most recent review aiming to provide such an overview was conducted in 1999 by Aguirre and D'Esposito. Given that many new neuropsychological case studies on navigation impairment have been added to the literature in the meantime, it was high time for an updated review on this topic.

In Chapter 2, I presented a systematic review of neuropsychological case studies on navigation impairment. This review led to the identification of three main types of navigation impairments (see Figure 2 in Chapter 2). One type of navigation impairment is related to defective knowledge of landmarks or environmental scenes. These patients experience navigation problems as they are unable to recognize or use landmarks for navigational purposes. I also identified location-based navigation impairment as a distinct category. These patients have difficulties with knowledge about locations and their interrelationships and fail on tasks that require them to describe absolute or relative spatial locations of landmarks or to point into their directions. Lastly, defective path knowledge can lead to navigation problems. All three types of navigation impairment can either affect navigation in a broad sense (in both familiar and novel environments) or can be confined to novel environments.

Besides this functional analysis of distinct types of navigation impairment, I also made an inventory of the associated lesion locations. This inventory has indicated that landmark-based navigation impairment is mostly related to right temporal and occipital lesions. Right occipital damage was relatively more common in patients with a broad landmark processing deficit than in patients with landmark-based navigation impairment for novel environments only. Location-based and path-based navigation impairment, however, were much more diffusely associated with right temporal, parietal or occipital damage. The fact that lesions in all of these brain areas could be linked to deficits in location and path knowledge might indicate that they are commonly part of a network involved in these types of knowledge. It has already been stressed in neuropsychology that focusing on disruption of networks rather than that of specific lesion locations can lead to a better understanding of the cognitive deficits associated with brain damage (e.g., Pascual-Leone, 2016). Indeed, a recent neural framework for visuospatial processing has stated that a parieto-medial temporal network relying on occipital input plays a crucial role in navigation ability (Kravitz, Saleem, Baker, & Mishkin, 2011).

This model of the main types of navigation impairments has both theoretical and clinical implications. From a theoretical viewpoint, the model states that three distinct types of knowledge contribute to navigation behavior, that is knowledge about what (landmarks), where (locations), and how to get there (paths). As such, this model makes predictions about the (neuro)cognitive architecture of navigation ability, which can be further explored in future research. From a clinical viewpoint, the model implicates that assessment of navigation ability should at least entail tests for landmark, location, and path knowledge. Ideally, tests should be based on environments that were already known to the patient prior to the onset of brain damage and on novel environments. The model states that navigation in these environments can be dissociated. Part 3 of this thesis illustrates the application of the model to navigation ability assessment in both a group and a single-case study.

The systematic review has not only identified the existence of the three distinct main types of navigation impairments, but also provides an overview of the neuropsychological case study approach to navigation ability. I identified several factors that hindered the process of reviewing these studies. First, researchers have been very inconsistent in their use of terminology regarding navigation ability and associated impairments. Terms have been continually changing over the past decades. Furthermore, the ways in which navigation ability was assessed in these studies is highly variable, which makes integration of these findings hard. Also, the use of healthy control groups to verify performance of the patients under study is frequently lacking. Chapter 2 should therefore also be read as a plea for a more uniform approach to the study of navigation impairment to enable further progress to be made in this field.

Part 2: Development and validation of assessment instruments

In current neuropsychological practice as well as neurological and neurorehabilitation care, clinicians hardly ever devote any attention to problems with navigation in their anamnesis with brain-damaged patients. Moreover, they rarely use tests to assess this ability in an objective manner. In part, this is caused by the lack of assessment instruments for navigation ability that are available for use in clinical practice. In Chapters 3 and 4, my aim was therefore to develop and validate a self-report questionnaire for navigation-related complaints that would help the clinician in determining whether additional and objective assessment of navigation ability would be advisable. The previously developed Wayfinding Questionnaire (WQ; van der Ham, Kant, Postma, & Visser-Meily, 2013) was deemed suitable to serve as the starting point for this purpose. We also considered the well-known Santa Barbara Sense of Direction Scale (SBSOD; Hegarty, Richardson, Montello, Lovelace, & Subbiah, 2002), but this questionnaire only covers one aspect of navigation ability (sense of direction). As the psychometric qualities of the WQ were not yet investigated, the specific aim of Chapter 3 was to examine the internal structure of the WQ in healthy respondents and stroke patients. This procedure helped in determining whether this (factor) structure can be used to guide interpretation of the WQ-scores in both of these groups, and in establishing a final version of the WQ. The studies in Chapter 3 revealed a three-factor structure, which was valid in both healthy respondents and stroke patients. The factors concerned “Navigation and Orientation”, “Spatial Anxiety”, and “Distance Estimation”, each with high internal consistency and good reliability with regard to the total WQ-score. The final version of the WQ consists of 22 items.

While I focused on the internal validity of the WQ in Chapter 3, the objective of Chapter 4 was to substantiate its clinical validity (i.e., clinical relevancy and usefulness). I found that stroke patients, as a group, scored lower on the WQ than healthy respondents. More specifically, it was identified that 32% of the stroke patients had substantial navigation-related complaints as evidenced by low WQ-scores on at least one subscale. A comparison between stroke patients with low and normal WQ-scores revealed that low WQ-scores were more commonly found in women and patients with lower levels of education. Also, patients with low WQ-scores reported more cognitive complaints in other domains, emotional problems, and a lower quality of life. No differences between patients with low and normal WQ-scores were found in terms of age, lesion location, stroke type, and time after stroke. Another important finding was that, on group level, patients with substantial complaints about navigation obtained lower scores on an actual navigation test battery, which substantiates the discriminative validity of the WQ. This study corroborates earlier findings reported by van der Ham and colleagues (2013) on the WQ indicating that navigation problems occur more frequently in stroke patients than previously thought. This shows that this topic is currently highly overlooked in clinical practice.

The research as presented in Chapters 3 and 4 has indicated that the WQ is a useful and valid screening instrument for helping the clinician determine whether a patient's complaints about navigation ability are of substantial nature. Further research into the WQ is needed to develop clear normative data, which should also account for response differences between males and females. Also, the generalizability of the WQ could be further increased by conducting validation studies in groups of brain-damaged individuals other than stroke patients.

The next step in the assessment process would preferably entail the administration of an actual navigation test to objectively measure navigation ability. Current neuropsychological tests for spatial learning have shown to be unsuitable for this purpose, as nearly all of these instruments (paper-and-pencil administration) only address small-scale spatial abilities (see for an overview: van den Berg & Ruis, 2016). Importantly, small-scale and large-scale spatial abilities can be dissociated both in behavioral and neuropsychological terms (e.g., Piccardi et al., 2010; Nemmi, Boccia, Piccardi, Galati, & Guariglia, 2013; Piccardi, Iaria, Bianchini, Zompanti, & Guariglia, 2011) and small-scale spatial tasks are unable to predict navigation performance in large-scale environments (Nadolne & Stringer, 2001). These findings might relate to the fact that small-scale spatial tasks lack in ecological validity with regard to navigation ability, given that they do not sufficiently represent the abilities needed for navigation in daily life. A clear need thus exists for a valid and clinically useful objective assessment instrument of navigation ability.

In Chapter 5, I examined whether the Virtual Tübingen navigation test battery might serve this purpose. In this test, participants were asked to study a route through a virtual rendition of the German city Tübingen (van Veen, Distler, Braun, & Bülthoff, 1998). After this learning phase, the testing phase started in which knowledge about multiple aspects of the studied route was assessed. The full test battery contained twelve subtasks addressing multiple aspects of navigational knowledge. The specific aim of Chapter 5 was to verify whether the Virtual Tübingen test can indeed serve as a valid alternative to navigation tests conducted in the real-world. Real-world navigation tests are associated with various practical limitations, given that they are bound to a particular environment and that exposure cannot be controlled very strictly. Furthermore, the level of familiarity with the test environment can influence performance (de Goede & Postma, 2015; Iachini, Ruotolo, & Ruggiero, 2009; Prestopnik & Roskos-Ewoldsen, 2000). Our results confirmed that the Virtual Tübingen test is a valid alternative to real-world navigation tests. Virtual and real-world navigation performance were significantly correlated. A moderate correlation was found for subtests assessing route knowledge and the correlation for survey knowledge subtests was weak to moderate in degree. While both patients and controls performed better on the real-world test, no significant interaction effects were found between group and environment. These findings lead to the conclusion that the virtual and real-world navigation tests were equally sensitive to navigation problems.

Part 2 of this thesis provides the clinician with two tools that can be used in clinical practice to assess navigation ability in stroke patients and, most likely, also in other patient groups with acquired brain damage. If self-reported navigation disability on the WQ turns out to be very high, the Virtual Tübingen navigation test battery should be applied to establish whether or not a patient's navigation ability is indeed impaired. Importantly, this instrument gives insight into a patient's relative strengths and weaknesses within navigation ability and provides an indication of the origin of the navigation problems. The profile resulting from the Virtual Tübingen test is thus highly informative, for example, for cognitive rehabilitation of navigation impairment (see Part 4). Given that problems with navigation are quite prevalent after stroke, I expect that many patients will benefit from these new tools.

Part 3: Theory driven assessment of navigation ability

As described in Part 1, my model of navigation impairment distinguishes between three dissociable types, related to loss of knowledge of landmarks, locations, and paths. The main aim of Chapter 6 was to empirically verify this distinction in a large group of stroke patients based on the Virtual Tübingen test. An analysis of the VT performance patterns of stroke patients with navigation complaints provided the first empirical evidence for this distinction. I found that landmark-based and path-based navigation impairments occurred in isolation, while the location-based type was only established along with path-based navigation impairment. This latter finding might relate to partial overlap between the concepts of location and path, as knowledge about locations might result from integration of paths (Ino et al., 2007). However, the network of reference frame theory even predicts a hierarchical relationship between knowledge about paths and locations, as this theory states that location knowledge has to be computed online in working memory based on path information (Meilinger, 2008). It might therefore be helpful to further clarify the concepts of location and paths and investigate whether a more direct measure of location knowledge can be developed. An alternative location task was described in Table 3, Chapter 7.

Chapter 6 also indicated that the VT test served as an adequate assessment instrument of navigation ability to systematically test the landmark-location-path model. The VT test incorporates subtasks related to all three types of knowledge. It might, however, be argued that path knowledge is overrepresented in the VT test (i.e., nine of twelve subtasks), but this clearly accords with the conceptual complexity of path knowledge. In my view, path knowledge encompasses not only concrete information (such as the order of turns or associations between places and actions), but also more abstract and metrical information. This makes path knowledge notably different from the concept of route knowledge in the so-called landmark-route-survey model (Siegel & White, 1975; Montello, 1998), as this model states that abstract and metrical features should be considered survey and not route knowledge.

Chapter 7 illustrated that the landmark-location-path model is also useful in guiding comprehensive assessment of navigation ability on the level of the individual patient. This chapter concerns a patient who underwent right anteromedial temporal lobectomy to manage her intractable epilepsy. Post-surgery, she complained of severe navigation impairment in particular for novel routes and environments. Standard neuropsychological assessment could not provide a solid explanation for her navigation difficulties. A comprehensive assessment of navigation ability was therefore designed. Her VT test performance indicated severe problems with many aspects of learning a new virtual route. Only her performance on Scene Recognition and Route Sequence was adequate. We then decided to systematically test her landmark, location, and path knowledge based on two familiar environments (one learned prior to and one learned after the surgery). Her performance on these tasks was interpreted with caution, as no healthy control data could be obtained for comparison. Results were indicative of largely intact landmark knowledge, but her knowledge about locations and paths for both environments was reduced at least to some extent. Qualitatively, it was evident that she needed much time to complete all tests and that she relied heavily on verbal reasoning. A clear difference between performance on the two environments could, however, not be objectified, as her subjective complaints would have suggested.

The study described in Chapter 8 has illustrated the idea of theory driven assessment of navigation ability in a somewhat different way than the previous two chapters. More specifically, it provides a systematic verification of a dissociation between performance on spatial and spatiotemporal tasks in the context of navigation. This distinction mirrors a theoretical idea about the cognitive mechanisms underlying episodic memory, which states that episodic memories (e.g., events) are stored along with the spatial ("where") and temporal ("when") context in which they occurred (e.g., Tulving, 2002). Previous research has confirmed that the processing of spatial and temporal information in episodic memory can become selectively impaired (Postma, van Asselen, Keuper, Wester, & Kessels, 2006; van Asselen, van der Lubbe, & Postma, 2006). It has now been shown that the idea of distinct processing mechanisms for spatial and spatiotemporal information might also be relevant to navigation (van der Ham et al., 2010). Van der Ham and colleagues (2010) described two neurological patients showing a double dissociation between these processing mechanisms. The study in Chapter 8 aimed to provide a systematic and large-scale verification of this double dissociation. Results indicated that six out of sixty-five stroke patients showed exceptionally large performance differences either favoring spatial or spatiotemporal performance; however, only performance patterns of two patients satisfied criteria for a classical dissociation (Crawford & Garthwaite, 2007; Shallice, 1988). Both of them were selectively impaired in their performance on the spatiotemporal navigation tasks. Overall, this study has suggested that performance on spatial and spatiotemporal navigation tasks is usually closely related, but selective impairments can occur. As such, this study has contributed to broaden knowledge about the cognitive structure of navigation ability.

In general, the chapters presented in Part 3 of this thesis have allowed a solid empirical validation of theoretical ideas about navigation ability and increased knowledge about its underlying cognitive architecture (the landmark-location-path model). This theoretical model has also proven to be helpful in systematically and comprehensively assessing navigation ability at the level of the individual patient.

Part 4: Rehabilitation possibilities for patients with impaired navigation ability

Rivest, Svoboda, McCarthy, and Moscovitch (2016) have recently argued that any intervention in the context of cognitive rehabilitation must be adapted to individual patients based on five considerations: 1) their neuropsychological functioning is well known, 2) realistically attainable goals and desires are set in discussion with them, 3) the provided tools enable them to maximize the utility of their cognitive strengths and to overcome their weaknesses, 4) the intervention gives them a sense of mastery of the desired skills, and 5) the skills and outcomes are relevant to real-life and ecologically valid. Rivest and colleagues (2016) have themselves applied these considerations to the development of an intervention for a patient with navigation problems. I will return to their study in more detail later on.

Once again, I would like to emphasize that only very few attempts have yet been undertaken to rehabilitate brain-damaged patients with impaired navigation ability. This might primarily relate to the highly variable nature of navigation problems across patients (Incoccia, Magnotti, Iaria, Piccardi, & Guariglia, 2009). Thus, Rivest and colleagues' statement (2016) that an effective intervention should be based on the pattern of cognitive abilities and disabilities of each individual patient appears particularly important in the light of rehabilitation for navigation problems.

A common approach in current cognitive rehabilitation is to teach patients alternative ways to cope with particular tasks, which is called compensation (Ponds & Hendriks, 2006; Wilson, 2002). This approach requires in-depth knowledge about a patient's cognitive strengths and weaknesses, as it provides important hints about the compensation strategies that might be helpful to this particular patient. Researchers usually distinguish between compensation strategies that rely on internal or external aids. An example of an external compensation strategy, in case of memory problems, would be the use of a calendar to keep up with appointments. Internal compensation strategies for memory problems, for example, would be the use of visual imagery or intensive rehearsal of information.

It is rather striking that the compensatory approach is highly unexplored in the context of navigation problems. Of the few available reports, the majority has focused on teaching their patient(s) to recall a particular set of routes (Bouwmeester, van de Wege, Haaxma, & Snoek, 2015; Brooks et al., 1999; Davis & Coltheart, 1999; Rose, Attree, Brooks, & Andrews, 2001). An important setback of this approach is that the tools provided in these interventions can only be applied to highly specific and location-bound navigational tasks, for which generalization is not possible. There is a clear need for the development of compensation strategies that can be applied to all kinds of navigational tasks.

To date, only a single study has investigated the effectiveness of an external compensation strategy applicable to all navigational tasks (Rivest et al., 2016). These authors taught their patient to use a smartphone with GPS technology to find his way around. Results indeed showed that his navigation ability improved and he also gained in confidence. While the use of assistive technology affects his navigation ability in a positive way, he is now dependent on it. Since technology changes rapidly, his smartphone skills might become outdated or interfere with the skills he has learned during the intervention.

Two studies have described verbal strategies to cope with navigation problems (Davis & Coltheart, 1999; Incoccia et al., 2009). Davis and Coltheart (1999), for example, taught their patient a mnemonic technique to associate street names to their positions on a map. Although the patient successfully applied the technique to a limited range of streets in a familiar town, she proved to be unable to generalize this technique to streets in another town. We propose that teaching patients with navigation problems to apply an alternative navigation strategy, which makes use of their cognitive strengths, would overcome most of the above concerns. Our idea is based on the view of navigation ability as a complex cognitive function. Also, we have found that at least some aspects of navigation ability are preserved in nearly every patient (see Part 3).

In Chapter 9, we verified whether it is a sensible approach to teach patients with navigation problems to adopt an alternative navigation strategy. I will discuss our findings guided by the five considerations of Rivest and colleagues (2016). First, we used several standard neuropsychological tests to gain an indication of each patient's cognitive profile. In addition, we administered the Virtual Tübingen navigation test to establish strengths and weaknesses with regard to navigation ability. In accordance with Rivest's first consideration, we had detailed information about each patient's neuropsychological functioning. We distinguished between patients with difficulties related to route knowledge on the one hand and survey knowledge on the other hand. In our training, patients with impaired route knowledge were taught to adopt a survey knowledge strategy and vice versa. With this compensatory approach, we taught our patients to use their navigational strengths in an optimal way, while overcoming their navigational weaknesses (Rivest's third consideration). The majority of them stated afterwards that the navigation training was a valuable experience to them. It helped them to gain insight into the origin of their navigation problems and enabled them to adopt an alternative way of navigating. These qualitative findings suggest that our patients felt that they had mastered the trained skills, which is in line with Rivest's fourth consideration. Lastly, Rivest argued that the taught skills and outcomes of the training should be ecologically valid and relevant to real-life. We attempted to facilitate generalization of the instructed navigation strategy to real-life situations by providing patients with exercises in both virtual and real-world environments.

Our navigation training is the first to rehabilitate patients with navigation problems by teaching them to adopt an alternative navigation strategy. Our findings have indicated that this is a sensible approach, as five out of six patients were at least partially successful in applying the taught navigation strategy in a parallel version of the Virtual Tübingen test. The navigation strategy one uses can thus be influenced. Some improvements are, however, needed. As Rivest has indicated in her second consideration, a successful intervention should set realistically attainable goals in collaboration with the patient or a caregiver. We therefore propose the use of goal attainment scaling (GAS; Bouwens, van Heugten, & Verhey, 2009) along with our navigation training. GAS not only allows for a standardized evaluation of the intervention, but also takes the goals and needs of the individual participant into account. Furthermore, effects of the training on navigation in daily life situations could be qualitatively measured to allow a more objective inventory of these effects. Still, we have shown that a compensatory approach in the context of rehabilitation of navigation problems is fruitful and might serve as the basis for future studies.

Use of virtual reality techniques

As is evident by now, I have intensively applied virtual reality (VR) techniques for the purpose of assessment and rehabilitation of navigation ability. The use of VR in the field of navigation ability has rapidly expanded and parallels a similar, more general development in neuropsychological assessment. The increasing contribution of VR to the assessment of cognitive abilities in brain-damaged patients has been related to the changing role of neuropsychology (Parsons, 2011). While the initial purpose of neuropsychological assessment was to contribute to the diagnosis of patients with brain damage or disease, nowadays neuropsychologists are more often requested to make statements about a patient's functioning in daily life. This calls for assessment instruments that are predictive of abilities in everyday life, which is limited for many traditional neuropsychological paper-and-pencil tasks (Chaytor & Schmitter-Edgecombe, 2003). VR-based tests are now increasingly regarded as a serious alternative to paper-and-pencil tests, as VR allows for simulations that closely resemble real-world situations (Parsons, 2011).

Whereas neuropsychologists remain cautious about the actual implementation of VR in clinical practice, navigation ability researchers have already widely applied these techniques for the investigation of this ability in healthy individuals (see e.g., van der Ham, Faber, Venselaar, van Krefeld, & Löffler, 2015) and, to a somewhat lesser degree, in brain-damaged patients (see for a review: Cogné et al., 2016). This arises from a strong need for navigation tests that are reliant on large-scale environments, as traditional neuropsychological measures of spatial cognitive abilities only tap into small-scale space and are hardly predictive of navigation ability. It would be, however, nearly impossible to actually implement real-world navigation tests for use in neuropsychological practice, given practical limitations associated with this type of testing (see also Part 2) as well as logistical and financial concerns. VR-based navigation testing offers solutions to the majority of these practical problems, as the content of the VR environment can be modelled to the real world with great detail. Also, exposure to the environment can be controlled very strictly in VR.

Despite the many advantages of virtual over real-world navigation tests, a number of researchers have expressed their concerns about navigation tests relying on desktop VR environments (e.g., Ruddle & Lessels, 2006). They have argued that the absence of locomotion during route learning in a desktop VR environment, as opposed to a real environment, would lead to distorted or reduced acquisition of survey knowledge. This statement arises from the assumption that survey knowledge requires integration of visual and body-based input, while for the acquisition of landmark and route knowledge visual information alone may suffice (Montello, Hegarty, Richardson, & Waller, 2004). Experimental studies investigating the contribution of body-based information to survey knowledge have been inconsistent in their findings (Chrastil & Warren, 2013; Montello et al., 2004). Some studies have shown reduced levels of survey knowledge in route learning under the absence of body-based input (Chrastil & Warren, 2013; Ruddle & Lessels, 2006; van der Ham et al., 2015; Waller, Loomis, & Haun, 2004), while a number of other studies have indicated that this type of input adds little to survey knowledge beyond visual information alone (Mellet et al., 2010; Richardson, Montello, & Hegarty, 1999; Waller, Loomis, & Steck, 2003).

In Chapter 5 of this thesis, I have indirectly touched upon the role of locomotion in the generation of survey knowledge by comparing virtual and real-world navigation performance in stroke patients. One of the main findings was that performance based on the real-world environment was consistently higher than that based on an equivalent virtual navigation test. This finding suggests that the integration of visual and body-based information leads to higher levels of both route and survey knowledge. However, I also found significant correlations (weak to moderate in degree) between virtual and real-world navigation scores. This latter finding adds to the convergent validity of virtual navigation testing as an alternative to real-world navigation tests. Overall, the results suggest that the acquisition of navigational knowledge might not be optimal in a desktop virtual environment, but it still provides a relatively accurate indication of a patient's ability to acquire route and survey knowledge.

The potential of VR has not been restricted to neuropsychological assessment alone, but it is also suitable for use in cognitive rehabilitation (Rose, Brooks, & Rizzo, 2005). Rose and colleagues (2005) have described four advantages of VR in this context. VR allows for simulation of many real-world or imaginary situations in a dynamic way and with high ecological validity. Given that consistency in VR can be absolute, it is possible to perform infinite repetitions to practice a particular task, for example. Also, flexibility is high, such that task complexity, response requirements, and the nature and pattern of feedback can be adjusted to the user's needs. Lastly, VR provides the opportunity of precise performance measurement. The former two of these advantages apply particularly to our navigation training (see Chapter 9). In the training, I intensively used the Virtual Tübingen environment to teach six patients to adopt an alternative navigation strategy. In this way, patients were able to practice the taught navigation strategy in a fairly realistic environment. The use of VR also gave the trainer the opportunity to briefly interrupt a trial to provide feedback and then resume the trial or to present an identical repetition of it. In our training approach, VR imposed much lower requirements on the physical fitness of the patient than real-world navigation exercises would do. This made it possible for the patients to practice with high intensity. As a result, three to five one-hour sessions were sufficient to influence the navigation strategy of the patients.

Navigation training could, however, make even better use of VR by the incorporation of serious game elements in its procedure. The ideal training approach would, of course, also start with detailed assessment of navigational strengths and weaknesses and provide the patient with psycho-education about navigation ability and his or her own pattern of navigation performance. Then, the trainer teaches the patient to use the serious game without supervision and, more importantly, to link the trained skills to real-world situations. In the next weeks, the patient plays the navigation game at home, which comprises several mini games that help to master and consolidate the alternative navigation strategy. As the game keeps close track of the patient's progression, the complexity of the presented tasks matches with the patient's level of performance. In combination with consistent reinforcement of accurate performances, these elements make sure that the patient remains motivated to play the game (and thus to participate in the training) over a longer period of time. Also, relevant data are registered to allow the researcher or training to analyze a patient's progression and navigation behavior both in the game and the real world. This updated approach to the navigation training is currently under investigation in a new research project in our lab, Navigation Lab Leiden (see https://navigationlableidendotcom.wordpress.com/).

A bridge between scientific research and clinical practice

Cognitive rehabilitation is a field which holds a holistic, biopsychosocial rather than a strictly medical view on persons with brain damage (Rose et al., 2005). In accordance with this view, cognitive rehabilitation makes use of the World Health Organization's International Classification of Functioning (ICF model; WHO, 2000). This system distinguishes four levels to describe any person with an illness (Wade, 2005). I will illustrate these levels in the light of this thesis. The first level describes the disease, diagnosis or pathology of a patient, in this case a stroke event in a particular area of the brain. The second level concerns impairments; losses or abnormalities of bodily skills or functions. Here, this might be an impairment in remembering the order of landmarks, in keeping track of one's position in a route or in generating a cognitive map of the environment. The problems that arise in the interaction between a person and the environment are described at the third level. These are called disabilities and are formulated in terms of limitations on activities performed. For example, this might concern an inability to find the route from home to work or to the supermarket. Lastly, the fourth level describes limitations in societal participation, such as not being able to work or do the groceries. As arises from the above illustration, the integration of biological, psychological, and social factors related to disease is necessary to better understand a patient's functioning.

As will be evident by now, the integration of knowledge from multiple scientific disciplines, such as (cognitive) neuroscience, neuropsychology, and cognitive rehabilitation is strongly needed to provide brain-damaged patients with better treatments for their cognitive impairments (Clarke, Bindschaedler, & Crottaz-Herbette, 2015). This requires close collaboration between these fields. In the current situation, however, the fundamental knowledge arising from (cognitive) neuroscience is not always translated into everyday clinical practice. As a consequence, individual patients sometimes do not directly benefit from new insights. This might be related to the fact that 'translational research' is a costly and time-consuming process. Over the past years, attempts to connect basic and clinical research fields have clearly increased. But still, these field have their own targets and use different terminologies, which may hinder the process of optimal communication.

With this thesis, it was my intention to show that translational research in the context of navigation ability might not be easy, but is certainly possible. The basic knowledge on the (neuro)cognitive architecture arising from this thesis (see Chapter 2 and Part 3, for example) was successfully translated into clinical applications for assessment (see Part 2) and rehabilitation of navigation ability in brain-damaged patients (see Part 4). I am glad that I had the opportunity to contribute to bringing scientific research and clinical practice in the context of navigation ability closer together in this thesis.

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NEDERLANDSE SAMENVATTING

Aanleiding

Recent onderzoek heeft uitgewezen dat problemen met navigeren (d.w.z. moeite met het vinden van de weg, moeite met oriënteren en angst om te verdwalen) na een beroerte vaak voorkomen. Ongeveer 30% van de patiënten met een beroerte geeft aan meer moeite te hebben met navigeren dan voor de beroerte. Vaak zijn zij minder goed in staat om nieuwe routes en omgevingen te leren, maar ook problemen met navigeren in bekende omgevingen komen in deze patiëntengroep voor. Juist voor de mensen die een relatief milde beroerte hebben doorgemaakt – en nog kunnen lopen en maatschappelijk actief willen en kunnen zijn – vormen navigatieproblemen een forse beperking van hun mobiliteit en zelfstandigheid. Door zorgverleners en onderzoekers wordt echter weinig aandacht aan dit probleem geschonken.

Opbouw proefschrift

Met dit proefschrift beoog ik daarom meer bekendheid te geven aan navigatieproblemen na een beroerte. Dat is duidelijk nodig, omdat naar navigatieproblemen in de huidige klinisch neuropsychologische praktijk zelden wordt gevraagd in het consult. Ook zijn er geen meetinstrumenten beschikbaar die de neuropsycholoog kunnen helpen om eventuele klachten over navigatieproblemen verder te onderzoeken.

Dit proefschrift is opgebouwd uit vier delen om dit doel te bereiken. Het eerste deel heeft betrekking op het inzichtelijk maken van de aard van de cognitieve stoornissen die onderliggend kunnen zijn aan navigatieproblemen. Op basis van een systematische literatuurstudie presenteer ik in dit deel een model waarin verschillende typen navigatieproblemen beschreven worden. In het tweede deel ga ik in op het ontwikkelen van klinisch bruikbare meetinstrumenten om navigatieklachten te kunnen objectiveren en de aard van de navigatieproblemen vast te kunnen stellen. Het tweede deel start met twee studies waarin de validiteit en klinische relevantie van de “Wayfinding Questionnaire” zijn onderzocht. Deze vragenlijst kan als screeningsinstrument worden gebruikt om te bepalen of verder onderzoek naar de aard van de navigatieproblemen raadzaam is. Deel twee sluit af met een studie naar de validatie van de Virtual Tübingen test. Deze virtuele navigatietest dient als instrument om op objectieve wijze de aard van de navigatieproblemen vast te kunnen stellen. In het derde deel vindt vervolgens de integratie van het model (zoals beschreven in deel 1) en de ontwikkelde meetinstrumenten plaats (zoals beschreven in deel 2). Ik laat zien dat het opgestelde model een systematisch en theorie-gestuurd onderzoek met behulp van de ontwikkelde meetinstrumenten naar de aard van navigatieproblemen mogelijk maakt. Uit de drie hoofdstukken in deel 3 blijkt het model van waarde te zijn voor onderzoek naar navigatieproblemen zowel in groepen hersenletselpatiënten als in individuele patiënten. In deel 4 rond ik af met een studie waarin de revalidatiemogelijkheden voor patiënten met navigatieproblemen worden geëxploreerd. Daarbij wordt ingegaan op compensatiestrategieën en op de mogelijke rol van virtuele technieken.

Deel 1: Verschillende typen navigatieproblemen

Het belangrijkste kenmerk van het navigatievermogen is dat het vanuit cognitief oogpunt een zeer complexe functie betreft. Het doet een beroep op een complex samenspel tussen meerdere cognitieve functies zoals de ruimtelijke waarneming, het geheugen en de executieve functies. Daarnaast zijn er ook specifieke processen betrokken waaronder het herkennen van “landmarks” (herkenningspunten in de omgeving), het onthouden van afslagen (“links bij de kerk” of “links-rechts-links”) en het gebruiken van een mentale plattegrond van de omgeving. Juist door de complexiteit van het navigatievermogen is deze functie erg kwetsbaar voor de gevolgen van een hersenbeschadiging. Dit komt duidelijk naar voren in de beschrijvingen van vele tientallen patiënten met hersenletsel in de neuropsychologische literatuur over dit onderwerp.

In hoofdstuk 2 beschrijf ik een systematisch literatuuronderzoek waarin ik een inventarisatie heb gemaakt van alle relevante neuropsychologische casusstudies. In deze studies worden patiënten beschreven die als gevolg van hersenletsel problemen kregen met navigeren. Een systematische analyse van deze studies toont dat er tot op heden in de literatuur drie duidelijk te onderscheiden typen van navigatieproblemen zijn beschreven. Het eerste type van navigatieproblemen is gerelateerd aan een onvermogen om herkenningspunten in de omgeving te herkennen en te gebruiken om te navigeren. Veel patiënten met dit type navigatieproblemen hebben een beschadiging in de rechter occipitaal- of temporaalkwab. Patiënten met het tweede type navigatieproblemen hebben een gebrek aan kennis over de locaties van herkenningspunten en waar deze locaties zich ten opzichte van elkaar bevinden. Ten slotte is er een groep patiënten die navigatieproblemen ervaart door een gebrek aan kennis over de paden die herkenningspunten en hun locaties met elkaar verbinden. De laesielocaties van deze laatste twee groepen patiënten bevinden zich doorgaans in de rechter occipitaal-, pariëtaal- of temporaalkwab. Bij alle typen kunnen de navigatieproblemen zich voordoen in zowel nieuwe als bekende omgevingen of zich beperken tot alleen nieuwe omgevingen. Het resulterende model is in theoretisch opzicht van belang omdat het uitspraken doet over de neurocognitieve structuur van het navigatievermogen. Het heeft echter ook klinische relevantie. Zoals in deel 3 van dit proefschrift is gebleken vormt het model namelijk een handleiding voor hoe klinisch onderzoek naar de aard van navigatieproblemen idealiter vormgegeven zou moeten worden.

Deel 2: Het ontwikkelen en valideren van meetinstrumenten

In het tweede deel van het proefschrift beschrijf ik de ontwikkeling en validatie van klinisch bruikbare meetinstrumenten om de aard van navigatieproblemen in kaart te brengen. In de klinische praktijk wordt doorgaans gewerkt met vragenlijsten of gestructureerde interviews waarmee de klachten van patiënten systematisch worden uitgevraagd. In geen van de beschikbare screeningsinstrumenten wordt aandacht besteed aan problemen met navigeren of het vinden van de weg. In hoofdstuk 3 heb ik me daarom gericht op het ontwikkelen en valideren van een vragenlijst om navigatieklachten vast te stellen. Het uitgangspunt hiervoor werd gevormd door de reeds ontwikkelde "Wayfinding Questionnaire" (WQ), waarvan nog geen psychometrische gegevens bekend waren. In hoofdstuk 3 heb ik daarom de interne structuur van de WQ onderzocht door deze vragenlijst in grote groepen gezonde mensen en patiënten met een beroerte af te nemen. Analyse van de interne structuur resulteerde in een drie-factorstructuur ("navigatie en oriëntatie", "navigatie-gerelateerde angst" en "afstandsschatting") die in beide groepen, gezonde proefpersonen en patiënten met een beroerte, valide blijkt. Deze factoren vertonen een hoge interne consistentie en zijn sterk gecorreleerd met de totale WQ-score. Op basis van dit onderzoek werd de definitieve versie van de WQ samengesteld, die bestaat uit 22 vragen met een 7-punts antwoordschaal.

In hoofdstuk 4 is de klinische validiteit van de WQ onderzocht door te kijken naar de klinische relevantie en bruikbaarheid. Bij vergelijking van WQ-scores tussen gezonde proefpersonen en patiënten met een beroerte werd gevonden dat patiënten als groep lager scoren dan gezonde proefpersonen. 32% van de mensen in de patiëntengroep behaalde een zeer lage WQ-score op ten minste een van de subschalen. Deze gegevens bieden een duidelijke ondersteuning voor de klinische relevantie van de WQ. Verder werd gevonden dat lage WQ-scores vaker voorkomen onder vrouwen en mensen met een laag opleidingsniveau. Ook bleken lage WQ-scores geassocieerd met meer cognitieve en emotionele problemen evenals met een lagere kwaliteit van leven. Voorts bleek het onderscheidend vermogen van de WQ in orde, omdat patiënten met lage WQ-scores ook lage scores op een daadwerkelijke navigatietest behaalden.

Tezamen laten de onderzoeksgegevens uit hoofdstuk 3 en 4 zien dat de WQ een valide en klinisch bruikbaar instrument is om navigatieklachten in kaart te brengen. Het kan gebruikt worden als screeningsinstrument om te bepalen of verder onderzoek naar navigatieproblemen geïndiceerd is. Vervolgonderzoek gericht op het ontwikkelen van duidelijke normgegevens (waarin rekening wordt gehouden met verschillen tussen mannen en vrouwen) en in andere patiëntengroepen is wenselijk.

Indien op basis van de WQ aanwijzingen voor significante navigatieklachten worden gevonden, zou men dit in het diagnostisch proces idealiter willen opvolgen met het afnemen van een daadwerkelijke navigatietest om de precieze aard van de navigatieproblemen te achterhalen. Navigatietests die gebaseerd zijn op de "echte wereld" kennen echter veel beperkingen; ze zijn sterk locatie-gebonden en het is vrijwel onmogelijk om vergelijkbare blootstelling tussen participanten te bewerkstelligen. Bovendien kan bekendheid met de testomgeving in kwestie de resultaten beïnvloeden. Om die reden heb ik in hoofdstuk 5 onderzocht of een navigatietest gebaseerd op een virtuele omgeving een bruikbaar alternatief is. Daartoe is de Virtual Tübingen (VT) test bij een grote groep gezonde proefpersonen en patiënten met een beroerte afgenomen. Bij de VT-test krijgt de participant twee keer een identieke route door een virtuele weergave van de Duitse stad Tübingen te zien. Hierna wordt middels twaalf subtesten de opgedane kennis van de participant over de bekeken route getest. Met deze subtesten wordt zowel gekeken naar concrete kennis over de route (ook wel routekennis genoemd, zoals herkenning van scènes, de volgorde waarin scènes in de route voorkwamen, de volgorde van afslagen etc.) als meer abstracte kennis (ook: surveykennis) zoals afstanden en de onderlinge relaties van locaties in de route. In dit onderzoek werden middelmatige correlaties gevonden tussen routekennis-scores op de VT-test en een vergelijkbare navigatietest in de “echte wereld”. Voor surveykennis-scores werden zwakke tot middelmatige correlaties gevonden. Daarnaast werd gevonden dat patiënten over het geheel genomen meer moeite hadden met de navigatietesten dan gezonde proefpersonen, echter er was geen sprake van een interactie met het type omgeving. Dit geeft aan dat de virtuele en “echte” navigatietest even gevoelig waren in het vaststellen van navigatieproblemen. Over het geheel genomen laten deze resultaten zien dat de VT-test een valide instrument is om de aard van navigatieproblemen objectief vast te stellen. Hiermee heeft het tweede deel van dit proefschrift geleid tot de ontwikkeling en validatie van twee klinisch bruikbare meetinstrumenten die de clinicus zullen helpen in diagnostisch onderzoek naar navigatieproblemen. Indien op de WQ significante navigatieklachten worden vastgesteld, kan dit worden opgevolgd door de VT-test af te nemen. Door de uitgebreide opzet van de VT-test stelt deze de onderzoeker tevens in de gelegenheid een patroon van sterke en zwakke navigatievaardigheden in kaart te brengen. Dit patroon van sterktes en zwaktes kan belangrijke input geven voor de invulling van het revalidatieproces, zoals in deel 4 van dit proefschrift aan bod zal komen.

Deel 3: Theorie-gestuurd klinisch onderzoek van navigatieproblemen

In het derde deel van het proefschrift laat ik zien dat het in hoofdstuk 2 ontwikkelde model een belangrijk uitgangspunt is voor de invulling van een diagnostisch onderzoek naar de aard van navigatieproblemen. In hoofdstuk 6 wordt de uitgebreide dataset gepresenteerd van een studie waarin de VT-test in een grote groep patiënten met een beroerte is afgenomen. Door middel van de twaalf subtaken in deze test kan op uitgebreide wijze kennis over herkenningspunten, locaties en paden worden getoetst. Analyse van de individuele prestatiepatronen op de twaalf subtaken liet zien dat navigatieproblemen gerelateerd aan gebrekkige herkenning of gebruik van herkenningspunten en gebrekkige kennis over paden geïsoleerd voorkwamen in deze patiëntengroep. Navigatieproblemen door gebrekkige locatiekennis werden alleen in combinatie met pad-gerelateerde navigatieproblemen gevonden. Deze bevindingen vormen een eerste empirische ondersteuning van het in hoofdstuk 2 opgestelde model. Dat locatie-gerelateerde navigatieproblemen niet in isolatie werden gevonden kan te maken hebben met de conceptuele overlap van "locatie" en "pad". Daarom wordt verder onderzoek naar deze concepten en naar een meer directe maat van locatiekennis geadviseerd.

In hoofdstuk 7 laat ik zien dat het model ook van waarde is voor de invulling van de diagnostiek van navigatieproblemen op het niveau van de individuele patiënt. In dit hoofdstuk beschrijf ik het diagnostisch proces bij een patiënte die na operatieve verwijdering van haar rechter anteromediale temporaalkwab vanwege onbehandelbare epilepsie met ernstige navigatieproblemen in nieuwe omgevingen te maken kreeg. Omdat standaard neuropsychologisch onderzoek geen verklaring bood voor deze problemen, werd een uitgebreid onderzoek naar haar navigatievaardigheden uitgevoerd. Om het vermogen een nieuwe route te leren in kaart te brengen werd de volledige VT-test afgenomen. De patiënte scoorde laag tot zeer laag op bijna alle subtaken met uitzondering van het herkennen van scènes en het onthouden van de volgorde van afslagen. Vervolgens werd haar navigatievermogen in twee bekende omgevingen getest. Een van deze omgevingen kende zij al van voor de operatie, terwijl zij de andere omgeving pas daarna leerde kennen. Haar vermogen om herkenningspunten en scènes te herkennen en te gebruiken om te navigeren bleek voor beide omgevingen intact. Haar kennis over locaties en paden was echter zeer beperkt voor beide omgevingen. Hoewel er geen duidelijk verschil tussen de twee omgevingen werd gevonden, wat op basis van haar subjectief gerapporteerde navigatieklachten wel verwacht werd, kon de aard van de navigatieproblemen die patiënte ondervindt wel duidelijk geobjectiveerd worden.

In hoofdstuk 8 wordt het thema "theorie-gestuurde diagnostiek" van navigatieproblemen vanuit een andere hoek belicht dan in de voorgaande twee hoofstukken. In dit hoofdstuk ga ik in op de dissociatie tussen prestaties op ruimtelijke en temporele navigatietaken. Dit onderscheid bouwt voort op het idee dat gebeurtenissen in het episodisch geheugen worden opgeslagen samen met de ruimtelijke ("waar") en temporele ("wanneer") context waarin zij plaatsvonden. Eerdere studies lieten zien dat deze aspecten selectief gestoord kunnen raken als gevolg van een hersenbeschadiging. Op basis van een eerdere casusstudie werd bewijs gevonden voor een dubbele dissociatie tussen de ruimtelijke en temporele aspecten van het navigatievermogen in twee patiënten met hersenletsel. In hoofdstuk 8 werd deze dubbele dissociatie op systematische wijze onderzocht in een grote groep patiënten met een beroerte. De resultaten lieten zien dat zes van de 65 patiënten een ongebruikelijk groot verschil vertoonden tussen hun prestaties op de ruimtelijke en temporele navigatietaken. Twee van deze patiënten voldeden ook aan de criteria voor een klassieke dissociatie, beiden met selectief gestoorde prestaties op de temporele navigatietaken. In de eerste plaats toont deze studie dat prestaties op ruimtelijke en temporele navigatietaken sterk geassocieerd zijn, maar selectieve stoornissen kunnen voorkomen. Tezamen illustreren de drie hoofdstukken in dit deel van het proefschrift het principe van theorie-gestuurde diagnostiek van navigatieproblemen zowel in groepen als individuele patiënten met een hersenbeschadiging.

Deel 4: Revalidatiemogelijkheden voor patiënten met navigatieproblemen

In hoofdstuk 9 verken ik de mogelijkheden tot het revalideren van navigatieproblemen bij patiënten met hersenletsel. De opzet van de navigatietraining zoals beschreven in dit hoofdstuk is gebaseerd op het principe van het inzetten van compensatiestrategieën om zo min mogelijk last te hebben van cognitieve stoornissen. Dit is doorgaans de eerste keuze in de klinische praktijk van de cognitieve revalidatie. Hiervoor is nauwgezet onderzoek naar de cognitieve sterktes en zwaktes van de individuele patiënt van essentieel belang. De patiënt wordt vervolgens bewust gemaakt van deze sterke vaardigheden en krijgt begeleiding bij het zo optimaal mogelijk inzetten hiervan met het doel zwakke punten te compenseren.

Tot op heden zijn er nog maar weinig pogingen ondernomen om revalidatieprogramma's of -trainingen te ontwikkelen die specifiek gericht zijn op het navigatievermogen. De weinige beschikbare studies hebben zich doorgaans gericht op het herhaaldelijk oefenen ("inslijpen") van een beperkt aantal routes. Het nadeel van deze aanpak is dat generalisatie naar andere routes niet mogelijk is. De door mij ontwikkelde navigatietraining zoals beschreven in hoofdstuk 9 maakt daarentegen gebruik van het compensatieprincipe. Allereerst werden de relatieve sterktes en zwaktes van het navigatievermogen van zes patiënten met een beroerte nauwgezet in kaart gebracht door middel van de VT-test. Op basis van elk van hun prestatiepatronen op de subtaken van de VT-test werd voor ieder van hen een persoonlijk trainingsprogramma opgesteld. Kort gezegd werd patiënten met relatief intacte routekennis in de navigatietraining geleerd te navigeren aan de hand van een routestrategie, terwijl patiënten met relatief intacte surveykennis een vergelijkbare training kregen aangeboden maar zich richtten op het toepassen van een surveystrategie. Na afloop waren bijna alle deelnemende patiënten tevreden met de training en gaven aan deze als behulpzaam te hebben ervaren. Op basis van een parallelversie van de VT-test vond ik voor vijf van de zes patiënten een veranderd prestatiepatroon op de verschillende subtaken, wat indicatief is voor het hanteren van een andere strategie dan bij de pre-training test. Deze resultaten suggereren dat het compensatieprincipe ook van waarde is binnen een specifieke navigatietraining. Vervolgonderzoek is echter nodig om deze resultaten te bevestigen met meer systematische en groter opgezette studies. Daarnaast is het van belang om te onderzoeken of het patiënten daadwerkelijk lukt de aangeleerde strategie in het dagelijks leven toe te passen en of dit een positief effect heeft op hun kwaliteit van leven. De eerste stappen voor vervolgonderzoek zijn reeds gezet binnen een nieuw promotietraject in de onderzoeksgroep waarvan ik deel uitmaak.

In hoofdstuk 10 worden de resultaten uit de eerdere studies bediscussieerd en geïntegreerd. Daarnaast ga ik in dit hoofdstuk dieper in op de mogelijke rol van virtuele omgevingen bij de diagnostiek en behandeling van navigatieproblemen bij patiënten met hersenletsel. Op dit moment wordt in onze onderzoeksgroep gekeken naar de haalbaarheid en effectiviteit van een virtuele navigatietraining met gebruik van spel-principes ("serious gaming"). Het uitgangspunt van deze training is, zoals in dit proefschrift beschreven, om intacte onderdelen van het navigatievermogen verder te versterken en optimaal te benutten. Ik sluit het hoofdstuk af door te stellen dat dit proefschrift als een vorm van "translationeel" onderzoek beschouwd dient te worden. De opgedane kennis over de neurocognitieve structuur van het navigatievermogen (zie hoofdstuk 2 en deel 3) werd op succesvolle wijze vertaald naar klinische toepassingen op het gebied van de diagnostiek (zie deel 2) en behandeling (zie deel 4) van navigatieproblemen bij patiënten met hersenletsel in het algemeen en patiënten met een beroerte in het bijzonder. Daarmee sluiten het hoofddoel van dit proefschrift en de daaruit voortvloeiende bevindingen perfect aan bij mijn persoonlijke ambitie om de wetenschappelijke en klinische neuropsychologie dichter bij elkaar te brengen.

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In de tijd dat ik aan dit proefschrift werkte heb ik verschillende werkplekken gehad. Ik begon in het Kenniscentrum in revalidatiecentrum De Hoogstraat en zat later vooral bij de afdeling Psychologische Functieleer van de Universiteit Utrecht en soms in het UMC. Al mijn oud-collega's wil ik hartelijk bedanken voor de prettige werksfeer, hun collegialiteit en de goede feedback die ik kreeg bij de research meetings.

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CURRICULUM VITAE

Michiel Claessen (31 July 1987, Tiel, the Netherlands) started his academic career in 2005 at Utrecht University studying German Language and Culture. At the time, it was his ambition to become a German teacher. In the second year of his bachelor's degree, he followed a course on psycholinguistics, a field of study at the interface of linguistics and psychology. This course introduced him to neuropsychology and he became interested in the relation between human cognition and the functioning of the brain. A new ambition was born. In 2008 he graduated with honors and started pursuing a bachelor's degree in Psychology (specialization Neuropsychology, Utrecht University). He also took part in the honors minor of this program; the Von Humboldt College. In 2011, he received his bachelor's degree in Psychology with honors and continued his education with a master's degree in Neuropsychology, also at Utrecht University. He completed his clinical internship at the Neuropsychology and Rehabilitation Medicine departments at the University Medical Center Utrecht. A year after obtaining his master's degree with honors, he was asked by Ineke van der Ham to continue a research project into navigation problems in stroke patients. Michiel wrote his thesis based on the findings of this project. Following his PhD thesis, Michiel has dedicated himself to combining research and clinical neuropsychology in his work. To this end, he works in scientific education as a lecturer in Clinical Neuropsychology at Leiden University, and also as a psychologist in direct patient care. In the second half of 2016, he was temporarily employed as a psychologist at the Laurens care facility, Antonius Binnenweg location, and in December 2016 started his position as psychologist at Beweging 3.0 in the Amersfoort region. Both care facilities predominantly focus on providing elderly care.

Michiel Claessen (31 juli 1987, Tiel) begon in 2005, na het behalen van zijn vwo-diploma, met de bachelor Duitse taal en cultuur aan de Universiteit Utrecht. Op dat moment had hij de ambitie om docent Duits te worden. Voor deze opleiding volgde hij in het tweede jaar een cursus over psycholinguïstiek, een vakgebied op het snijvlak van de taalwetenschap en psychologie. Hij raakte door deze cursus geïnteresseerd in de relatie tussen het menselijk denkvermogen en de werking van de hersenen en ontdekte het bestaan van de neuropsychologie. Een nieuwe ambitie was geboren. In 2008 rondde hij zijn bachelor Duitse taal en cultuur cum laude af en startte met de bachelor Psychologie (studiepad Neuropsychologie, Universiteit Utrecht). Hij nam tevens deel aan de honours-minor van deze opleiding; het Von Humboldt College. In 2011 behaalde hij zijn bachelordiploma Psychologie (cum laude) en vervolgde zijn opleidingstraject met de master Neuropsychologie, eveneens aan de Universiteit Utrecht. Zijn klinische stage volgde hij bij de afdelingen Neuropsychologie en Revalidatiegeneeskunde van het Universitair Medisch Centrum Utrecht. Een jaar na het behalen van zijn cum laude masterdiploma werd hij door Ineke van der Ham gevraagd om een onderzoeksproject naar navigatieproblemen bij CVA-patiënten voort te zetten. Op basis van de bevindingen van dit project heeft Michiel zijn proefschrift geschreven. Na zijn promotieonderzoek heeft Michiel zich gericht op het combineren van de wetenschappelijke en de klinische neuropsychologie in zijn werk. Hiertoe werkt hij enerzijds als docent aan de Universiteit Leiden waar hij wetenschappelijk onderwijs over neuropsychologie verzorgt. Anderzijds werkt hij als psycholoog in directe patiëntenzorg. In de tweede helft van 2016 heeft hij een tijdelijke positie als psycholoog bij Laurens Antonius Binnenweg gehad en sinds december 2016 is hij werkzaam als psycholoog bij Beweging 3.0 in Amersfoort en omstreken. Beide zorginstellingen zijn voornamelijk actief op het gebied van de ouderenzorg.

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