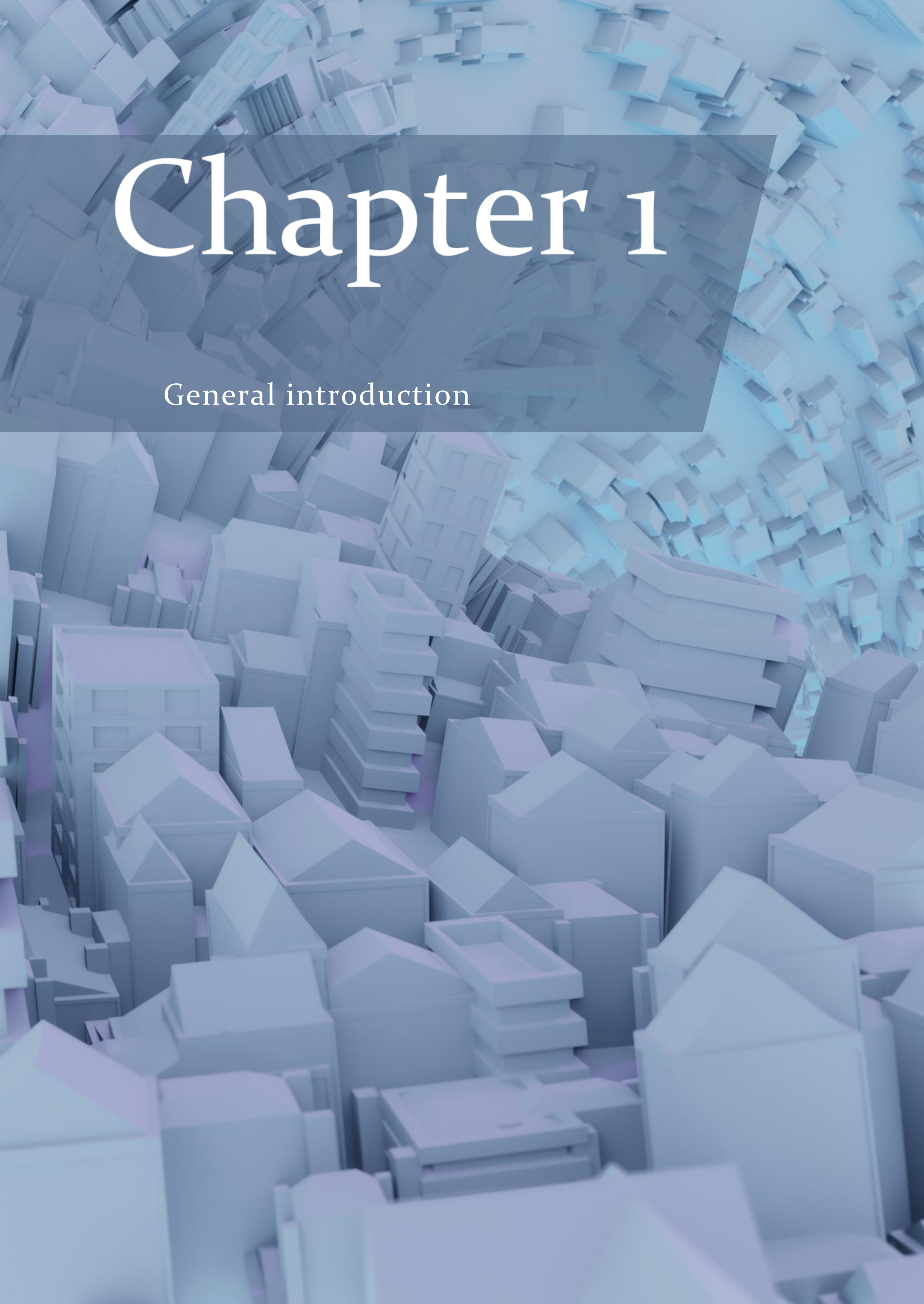
Chapter 1

General introduction



Spatial Navigation

Spatial navigation can be defined as the process by which organisms use multiple cues such as landmarks, path integration and beacons to determine a route to a goal and travel that route (Brodbeck & Tanninen, 2012). The term navigation conjures up images of long journeys to novel and faraway places. While navigation plays an important role in exploration and journeying, the same cognitive processes are involved in more mundane tasks, such as commuting to work or doing groceries. To account for the wide array of spatial challenges humans are confronted with every day, evolution has favoured highly flexible, adaptive and reliable cognitive functions that make up navigation ability (Clint, Sober, Garland Jr, & Rhodes, 2012). However, our navigational abilities are far from perfect. Most people have experienced being lost at some point in their lives. Being unable to determine one's location or having lost one's sense of direction can be a fearful experience (Hill, 1998). Once one has lost one's orientation, anchor points in the environment seem harder to select, distances are more difficult to judge and the environments can look similar. Finding your way back to a known location involves taking risks, such as attempting to backtrack, sampling a route or heading along a direction which should point you on your way home. However, making a wrong decision, might take you further from your intended path. People who get lost experience increasing levels of self-doubt, frustration and anxiety when disoriented (Lawton, 1994; Lynch, 1964; Oliver, Wildschut, Parker, Wood, & Redhead, 2022). This stress response upon disorientation is deeply ingrained in the human psyche. Throughout human evolution, people had to be able to navigate in order to effectively forage for food and return to places of shelter. As such, losing one's orientation can threaten survival.

While most people get lost a few times during their lifetime, for others this is a daily reality. People with brain afflictions such as acquired brain injuries, neurodegenerative diseases and neurological afflictions frequently report difficulties during navigation (Cushman, Stein, & Duffy, 2008; Němá et al., 2021; van der Ham, Kant, Postma, & Visser-Meily, 2013). Such navigation problems are often diverse and complex. Consider the following account by a patient with acquired brain injury after a motorcycle accident.

"I first noticed [that I had navigation impairments] when I still was at the rehabilitation centre. They [therapists] tried to cycle with me through Utrecht. While we were cycling, I told my physiotherapist: "I used to work in Utrecht, in the Nachtegaalstraat. I was store manager of

a computer hardware store". She then replied: "Now that is interesting, we currently are in the Nachtegaalstraat"." I had no idea."

Similar accounts are hardly unique. Over the last decades, there have been numerous neuropsychological case studies in which patients with similar problems are described.

One well-known case is that of a London taxi driver who suffered bilateral hippocampal lesions (Maguire, Nannery, & Spiers, 2006). London taxi drivers are famously required to obtain 'The Knowledge' by following a thorough training program in which the layout of over 25000 streets and thousands of points of interest are studied, before receiving an operating licence. The patient had passed all examinations in the past and had been operating as a taxi driver for 40 years before he suffered a lesion in the hippocampal area. After the injury the patient reported problems when navigating the city he was once very familiar with. Upon investigation, the patient seemed to be able to navigate along the main roads of the city and remembered the landmarks of the city and the spatial relation between them. However, after the lesion, the patient became lost when deviating from the main roads and was required to take the small and irregular side roads he once knew.

Other cases that illustrate the complexity of navigation impairments are those of patients AC and WJ, described by van der Ham et al. (2010). Both patients had suffered damage to the parieto-occipital right hemisphere and reported problems when navigating routes. Further investigation showed that both patients had impaired route-following abilities, but the nature of these problems was vastly different. One patient had problems in remembering the order of important landmarks and scenes along a route, while the other patient had problems remembering what action to take at each decision point along the route. As such, while both patients report similar daily problems, one patient's problem stemmed from temporal route impairments while the other's stemmed from spatial route impairments.

Goals

The goal of this dissertation is to conceive a first, standardized rehabilitation therapy for patients with navigation impairments resulting from acquired brain injuries. The treatment's concept will draw heavily from the existing spatial cognition literature, advances in game technology and best practices in cognitive rehabilitation. As such, a personalized, automated, blended-care treatment will be developed. In this introduction, I will describe the current perspective on the neurocognitive structure of navigation abilities. Furthermore, I will provide a brief overview of earlier attempts to treat navigation problems in patients with acquired brain injuries. Lastly, I will discuss what approach will be taken in the development of the rehabilitation therapy and how recent technological innovations can be utilized to make the treatment accessible to all patients.

Neurocognitive architecture of navigation abilities

Cognitive maps

Over the last century, spatial learning and navigation have been studied intensely in different fields of psychology. Uncovering the mechanisms by which organisms learn about the environment has been of great interest to behaviourist psychologist as it lay at the core of a debate between psychologists adhering to reinforcement and non-reinforcement theories (Jensen, 2006). At the time, researchers such as Hull and Skinner argued that all learning was part of a stimulus-response reinforcement (Delprato & Midgley, 1992), while researchers such as Tolman argued that organisms can learn information without direct reinforcement or motivation, latent learning (Tolman, 1949). To support his theory, Tolman studied navigation and spatial learning in rats. Navigation and spatial learning are ideal functions to study in relation to latent learning as obtaining spatial knowledge itself does not generate immediate rewards, but is necessary to survival. In 1948 Tolman published the iconic article 'Cognitive Maps in Rats and Men' in which he formally introduced the concept of a cognitive map (Tolman, 1948). Tolman proposed that organisms, when given enough exposure to an environment, form a mental representation, analogous to a cartographic map. This cognitive map contains Cartesian elements such as places, distances and angles between locations. As such, the cognitive map contains a representation of the environment, regardless of the current perspective or location of the organism. Given the nature of the ongoing debate between behaviourist psychologists, the cognitive map theory was received with mixed reactions (Skinner, 1950).

Years later, works of O'Keefe and Nadel reinvigorated the cognitive map theory as they provided neurobiological support for the concept of a cognitive map with the discovery of place cells in the rat brain (O'Keefe & Nadel, 1978). Place cells, found in the hippocampus area, correspond to a spatial receptive field and fire whenever a rat is in a specific location in a given environment. Further support for the cognitive map theory was provided with the discovery of additional types of neurons that are involved in spatial mapping such as grid cells and boundary cells (Barry et al., 2006; Hafting, Fyhn, Molden, Moser, & Moser, 2005). The discovery of these neurons in the hippocampus regions provide support for a Cartesian cognitive map and helps us understand how the brain organizes space. Moreover, analogous neuron formations are found in the human brain suggesting that humans form cognitive maps of the environment in a similar fashion (O'Keefe, Burgess, Donnett, Jeffery, & Maguire, 1998).

Landmark, route, survey knowledge

In parallel to the animal studies of O'Keef and Nadel, navigation and spatial learning was studied in the fields of developmental and cognitive psychology. One of the most influential contribution to those fields was the landmark-route-survey model described by Siegel and White (1975). This model placed spatial learning in a clear constructivist framework, proposing that spatial knowledge is obtained in successive stages. First, landmark knowledge is acquired, representing knowledge of the identity of prominent objects or features of the environment that serve as beacons, anchor points and signals at key intersection points. Second, route knowledge arises, as organisms learn fixed paths that connect locations to each other. Finally, survey knowledge is formed. This map-like representation of the environment allows navigators to estimate distances and judge angles between locations and to take short cuts. As such, survey knowledge describes a cognitive map of the environment.

The concepts of landmark, route and survey knowledge are still useful in categorizing the type of spatial information that is obtained. However, the hierarchical nature of the model has been abandoned by most researchers as studies have shown that survey knowledge, can be formed after initial exposure an environment.

Allocentric & egocentric representation in navigation

Organisms rely on spatial reference frames whenever spatial information is encoded, updated or processed (Roberta L Klatzky, 1998). An important functional and neuroanatomical distinction exists between allocentric and egocentric reference frames. The allocentric reference frame, sometimes referred to as the exocentric or geocentric reference frame, is comprised of spatial relations between objects in an environment (**Fig 1.1**). These object-to-object relations are represented independent of the perceiver's position or perspective (Vogeley & Fink, 2003). Conversely, egocentric reference frames constitute spatial relations between the agent and objects in the environment (Fig 1.2). As such, the egocentric reference frame is strongly dependent on a first-person perspective.

All spatial tasks are depended on the allocentric and egocentric reference frames of the agent. For some spatial tasks, the reliance on allocentric and egocentric reference frames are obvious. For example, the allocentric reference frame is used when drawing a map of the environment, when determining one's place in the environment based on distances and angles from prominent objects in the environment or when taking novel shortcuts through an environment. The egocentric reference frame is involved in following a beacon (i.e. 'move towards a visible object in the environment') and when learning a route via stimulus-action associations (e.g. 'go left at the red building'). There are however, more complex instances in which there is an interaction between allocentric and egocentric reference frames. For example, a navigator can encode a route, consisting of a sequence of turns (e.g. left, right, right), into an egocentric reference frame. When the same route is retraced from end to start, the navigator is required to abstract view-dependent (egocentric) information and processes it in an allocentric reference frame (J. Wiener, Kmecova, & de Condappa, 2012).

In most situations, there are multiple ways in which spatial goals can be reached. The approach an agent takes in order to reach a spatial goal when placed in a particular situation can be defined as one's navigation strategy (Hok, Poucet, Duvelle, Save, & Sargolini, 2016). The type of spatial information that is encoded and the manner in which it is processed indicates whether an egocentric or allocentric navigation strategy is employed. In naturalistic environments, it is often hard to measure what strategy is being used. However, Igloi, Zaoui, Berthoz, and Rondi-Reig (2009) have converted animal study paradigms to virtual reality tasks in order to investigate navigation strategy used by humans.

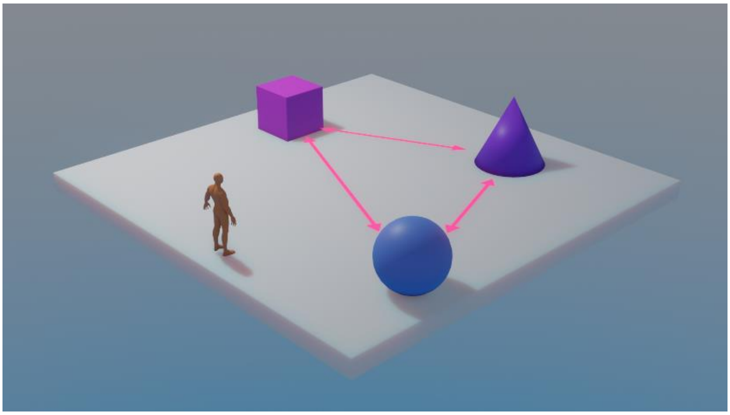


Fig 1.1 Allocentric reference frame

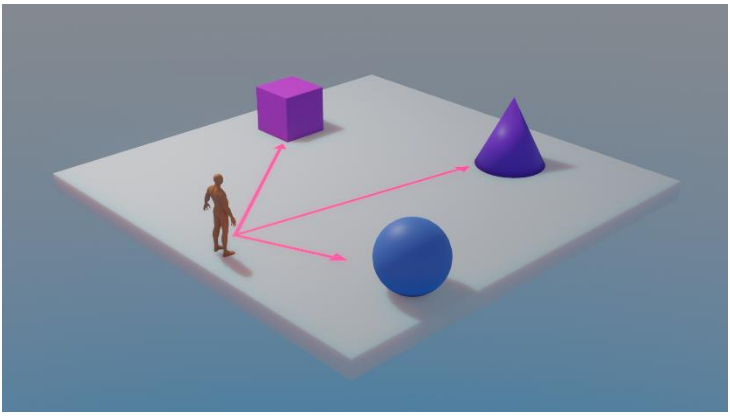


Fig 1.2 Egocentric reference frame

This study shows that humans are able to use egocentric, allocentric or mixed navigation strategies interchangeably. However, most people seem to prefer a strategy. Importantly, both allocentric and egocentric strategies can be observed even after initial exposure to an environment.

The distinction between egocentric and allocentric reference frames is also evident on a neuroanatomical level. Research has shown both overlapping and specific neural correlates involved in egocentric and allocentric encoding and processing. Functional MRI studies have shown overlapping neural correlates for allocentric and egocentric processes in the precuneus, cuneus, superior frontal lobe bilaterally, lingual gyrus, superior posterior parietal lobe and superior occipital gyri (Boccia, Nemmi, & Guariglia, 2014; Zaehle et al., 2007). Both bilateral hippocampal and parahippocampal activation is specifically associated with allocentric memory encoding (Parslow et al., 2004). Another fMRI study in which a non-visual encoding was examined, indicated that allocentric encoding activated the bilateral hippocampal gyri, bilateral inferior temporal gyri, the right inferior and superior frontal gyrus, and of the right inferior and superior parietal lobe whereas egocentric references frames are uniquely encoded in the medial superior parietal cortex (precuneus) (Zaehle et al., 2007).

Taxonomy of navigation impairments

The complex, multifaceted nature of our navigation abilities and the large-scale recruitment of the brain during spatial tasks insinuates its susceptibility to brain injuries. A large variety of navigation problems have been observed in patients with a variety of brain afflictions such as dementia (Cushman et al., 2008; Delpolyi, Rankin, Mucke, Miller, & Gorno-Tempini, 2007), Korsakov (Oudman et al., 2016), multiple sclerosis (Němá et al., 2021) and acquired brain injuries (Livingstone & Skelton, 2007; van Asselen et al., 2006). A taxonomy of navigation problems first appeared in an influential paper by Aguirre and D' Esposito (Aguirre & D'Esposito, 1999). In this paper, navigation problems are referred to as topographic disorientation. Within this taxonomy, four types of impairments were distinguished. Egocentric disorientation, describing the problems patients might have with representing the location of objects with respect to the self. Heading disorientation, which describes the inability to represent the direction of orientation in relation to the environment. Landmark agnosia, describing the inability of patients to represent landmarks, and anterograde agnosia, describing problems patients might have in creating novel representations of the environment. While this taxonomy has been of great use for over two decades, the model lacked a solid neurocognitive bases for its taxonomic division of impairment categories. Recently, the model has been updated by Claessen and van der Ham (2017). This updated model has a more thorough basis with regards to the neuroanatomical substrates associated with navigation impairments and contemporary models in the spatial cognition literature. The model distinguished three domains of navigation impairments: landmark impairments, location-based impairment and path-based impairments.

Patients impaired in the landmark domain have problems recalling or recognising previously known or famous landmarks, or have problems encoding unfamiliar landmarks.

Areas of the brain associated with landmark impairments include lesions in the right temporal and occipital lobes, right hippocampus and right parahippocampal areas.

Patients with location-based impairments have difficulties processing egocentric or allocentric location information. This includes the patients' ability to make spatial judgments (either categorically or co-ordinately), egocentric updating, understanding the interrelation of landmark locations. Areas of the brain associated with location-based impairments include the right temporal lobe, the right parietal lobe, the right retrosplenial lobe and the right occipital lobe.

Finally, patients with path-based impairments report difficulties with regards to the paths that connect locations with each other. Areas of the brain associated with path-based impairments include the right occipital lobe, the right temporal lobe and the right parietal lobe.

Earlier Treatments

Over the past decades, there have been several attempts to treat navigation problems resulting from brain afflictions. Many of these studies concern a single patient with specific navigation problems. Bouwmeester, van de Wege, Haaxma, and Snoek (2015) describe a patient with landmark (unfamiliar landmarks) and location-based navigation impairments who successfully learned to navigate specific routes in his direct environment after repeated exposure to them and training how to utilize a booklet. S. J. C. Davis (1999) describes a treatment for a patient with location-based navigation impairments, who was taught mnemonic techniques to remember specific names and locations of streets in her hometown, allowing her to navigate this part of town. Rivest, Svoboda, McCarthy, and Moscovitch (2018) describe a patient with landmark, location and path navigation impairments who was taught to adopt an errorless learning protocol allowing her to use a smartphone to find routes accurately and reliably. Incoccia, Magnotti, Iaria, Piccardi, and Guariglia (2009) report a patient who never learned to navigate due to complications after congenital hydrocephalus shortly after birth. A training was developed in which the patient was taught to carefully explore the environments and use language-based strategies, resulting in her adopting several cognitive strategies that allowed her to navigate alone.

Kober et al (2013) studied the effects of a navigation training in multiple patients. In this study, patients were trained to learn a route in virtual reality using an errorless learning approach. An increase in general spatial abilities was observed after the training. A more generalizable approach was taken by Claessen, van der Ham, Jagersma, and Visser-Meily (2016). In this study, 6 stroke patients with widely different navigation problems (ranging from landmark-based to path-based impairments) participated. A thorough diagnostic process would take place in which a large number of navigation abilities would be assessed. Depending on the domain of navigation problems, a compensatory navigation strategy would be constructed that focussed on the patient's intact navigation abilities. As such, the compensation component was not determined by the use of tools, mnemonic techniques or specific routes, but rather by the application of a novel navigation strategy. Patients were trained to use this strategy by performing exercises in virtual environments.

While these therapies certainly yielded positive results for the patients, they have not led to a comprehensive treatment that could be employed in clinical settings. There are several reasons for this. The treatments were highly individualized and focussed on specific impairments of the individual in question. As such, these training modules will be of little use to patients with slightly different patterns of impairments. Most studies train patients how to navigate in a specific environment relevant to them. As such, these training modules require substantial adjustments to the training content depending on the locality of a patient. Moreover, it is unclear to what degree training in predetermined environments will allow for transfer of abilities when navigating in different areas. Lastly, most training programmes involved extensive, time consuming face-to-face therapy. While this is admittedly a practical consideration, a blended form of therapy, in which patients receive both face-to-face and online care, might enhance clinical feasibility of a therapy.

Current direction

The previous studies on navigation rehabilitation prove to be an excellent starting point for the development of a novel treatment. In developing the current treatment, we intent to follow a set of core principles.

First, the treatment should be based on the principle of compensation. The complexity and multifaceted nature of navigation, allows for ample opportunity to select strategies that are beneficial to the navigator. In most situations, there are multiple ways to reach a goal location. When patients are aware of their intact navigational abilities and are able to identify which strategy can be applied, patients might be able to navigate in novel environments. This approach is supported by the general rehabilitation literature. Compensatory strategy training has been recommended as standard practice for treatment of memory impairments following brain injury (Cicerone et al., 2019; Cicerone et al., 2011). In addition, two earlier studies have successfully applied a compensation approach in their treatment (Claessen, van der Ham, et al., 2016; Incoccia et al., 2009).

The treatment's underlying concepts should be theory-driven and should be grounded in the neurocognitive literature on spatial navigation. Many earlier treatments have been developed to help a single patient navigate his or her direct environment (Bouwmeester et al., 2015; S. J. C. Davis, 1999). These therapies typically narrow their focus towards an individual and do not take full advantage of the wealth of knowledge available in the field of spatial cognition. Over the past decade, fMRI, lesion and experimental studies have provided a us with a solid understanding regarding the different neuroanatomical and functional dissociations of navigation abilities. These models can be used to systematically diagnose navigation problems and identify intact abilities. Using these models, multiple treatment options can be constructed, allowing for the range of impairments that is to be expected.

The second principle is to develop a treatment with standardization and generalizability in mind. The treatment should be appropriate for patients with a wide variety of navigational problems and varying levels of cognitive functioning. In the context of the content of the training, the compensatory approach should allow us to train beneficial strategies as long as components of navigational abilities are intact. Instead of patient-tailored reconstructed environments, we aim to further increase the generalizability by constructing non-specific, modular environments for the training to take place in. With regard to the interaction with the treatment, we should ensure a high level of usability, suitable for people with severe cognitive impairments. We aim to minimize the complexity of the instructions while the difficulty of the exercises should be adapted to the performance levels of the patient.

As a third principle, we aim to investigate the degree to which innovative technology can be used in rehabilitation therapies. Game technology and virtual reality techniques have seen a rapid development over the past years. Realistic and ecologically valid virtual environments can now be used on most consumer devices (e.g. computers and smartphones). Virtual environments can potentially be of great benefit for diagnostic and treatment purposes for patients with brain injuries (Faria, Andrade, Soares, & i Badia, 2016; Maggio et al., 2019; Spreij, Visser-Meily, Sibbel, Gosselt, & Nijboer, 2020). In the case of navigation strategy training, several aspects of virtual environments seem desirable. Patients require practise to master novel navigation strategies. However, patients with navigation problems often rapport spatial anxiety (van der Ham et al., 2013). As such, practising outside might pose a barrier for these patients. Virtual environments can offer a safe, easily accessible environment to experiment with novel strategies. Furthermore, physical and mental fatigue is a common phenomenon in patients with stroke or traumatic brain injuries and typically hinders recovery and rehabilitation (Belmont, Agar, Hugeron, Gallais, & Azouvi, 2006; De Groot, Phillips, & Eskes, 2003; Schepers, Visser-Meily, Ketelaar, & Lindeman, 2006; Winward, Sackley, Metha, & Rothwell, 2009). Performing exercises in virtual environments might be less exhausting compared to real-life training, which might enhance rehabilitation effectiveness. Over-stimulation is a related phenomenon common in people with brain injuries (Donker-Cools, Schouten, Wind, & Frings-Dresen, 2018; Killington et al., 2015). Many patients experience sensory overload when exposed to crowded environment with loud noises, mixed conversations and flashing lights. As such, training novel strategies in controlled, calm, virtual environments might be more effective compared to real-world environments. Finally, it should be stressed that spatial challenges can often be solved with a variety of approaches in real- world environments. In order to entice patients to adopt a beneficial strategy (and disregard reliance on an old strategy), environments can be constructed in a manner that favours the use of the target strategy.

Lastly, the use of a blended-care paradigm should be a core component of the treatment. The past decade has seen an increase in successfully applied digital health programs. Blended-care programs have several advantages over solely face-to-face therapy. Digital health tools can be designed to closely fit to a patient's needs and preferences. It can increase a patient's access to care, might raise effectiveness of regular interventions and reduce the treatment time of therapists (Kip, Bouman, Kelders, & van Gemert-Pijnen, 2018). In addition, Blended-care interventions can reduce the number of visits to a clinic and might thereby increase treatment adherence. For therapists, such an approach might reduce the working load, increasing the feasibility of the therapy.

Dissertation Outline

The general objective of this dissertation was to introduce a rehabilitation training for patients with navigation impairments as a result of acquired brain injury. This thesis was subdivided into three parts: the problem assessment, the developmental process and the evaluation of the intervention (Fig 1.3).

Part I: Problem assessment

The first aim of the thesis was to identify the prevalence and severity of navigation impairments within the patient population.

Part II: Treatment development

The second goal was to formulate a conceptual framework for the intervention. In this part, we will determine whether the concept of a dissociated spatial representation holds when information is presented from different perspectives. Furthermore, we will determine what the requirements are om terms of usability of a home-based training for the ABI population. Finally, we will assess the views and levels of acceptance of blended-care compensation training interventions from the viewpoint of therapists in the field.

Part III: Treatment evaluation

The third goal of the thesis was to evaluate the effectiveness of the intervention. First, the concept of navigation strategy training will be tested in the healthy population. Second, we will assess the effectiveness of the intervention in the patient population.

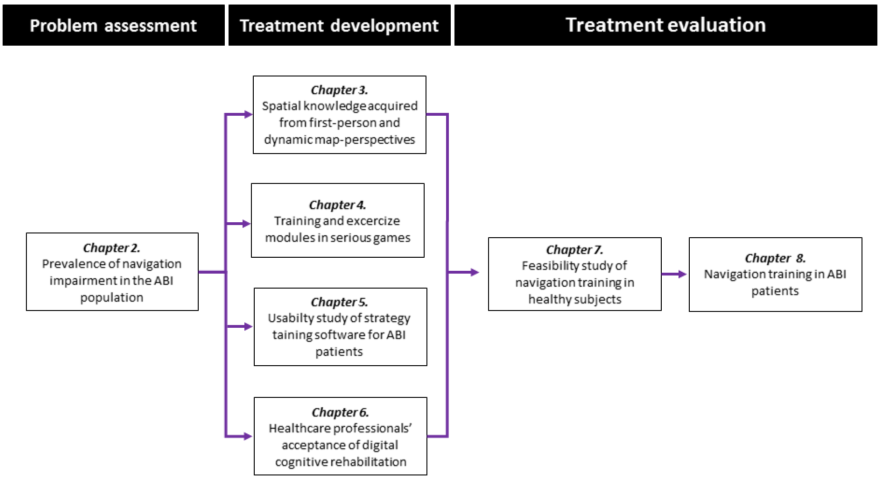


Fig 1.3 Outline of this dissertation.