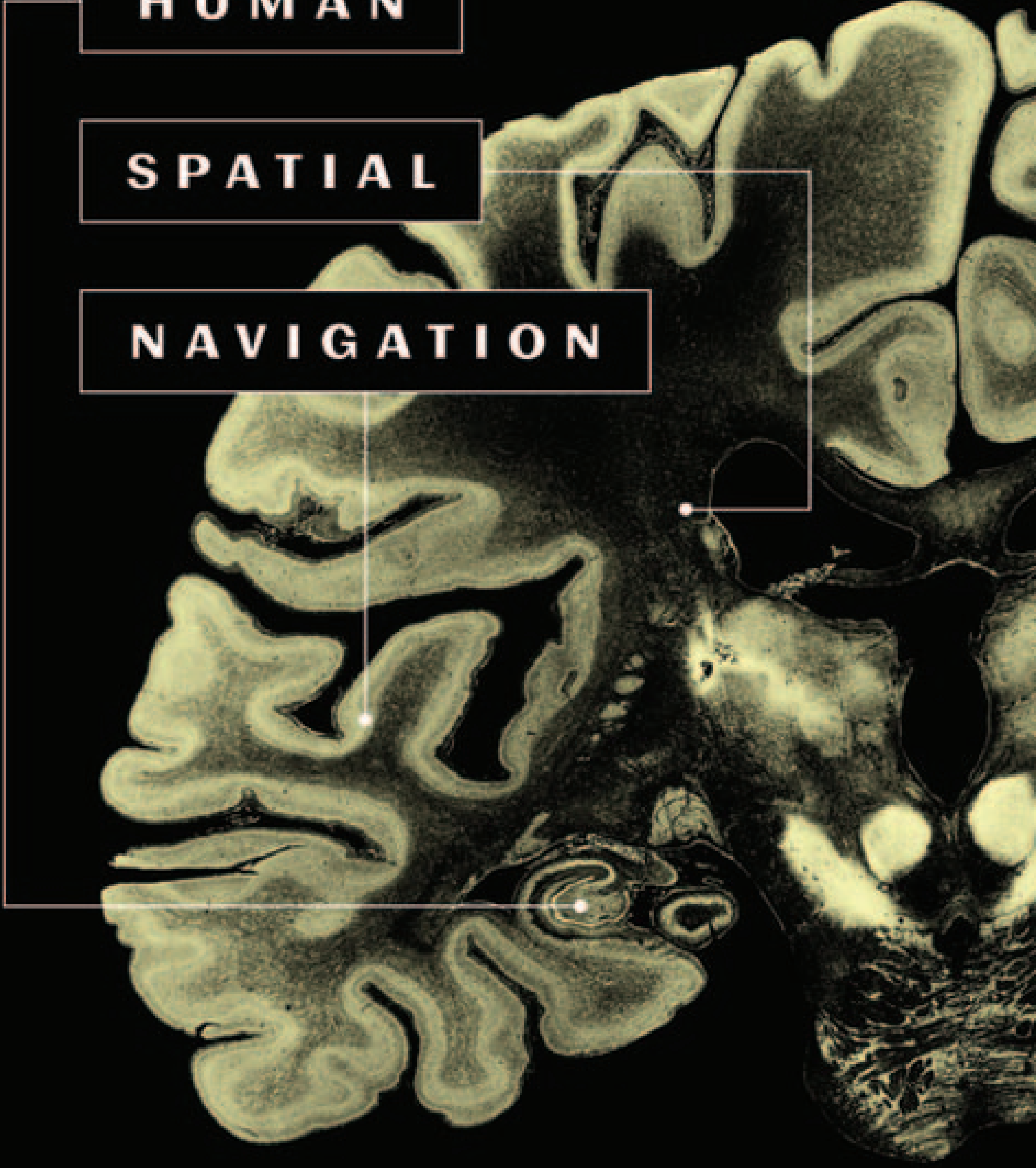
# HUMAN SPATIAL NAVIGATION



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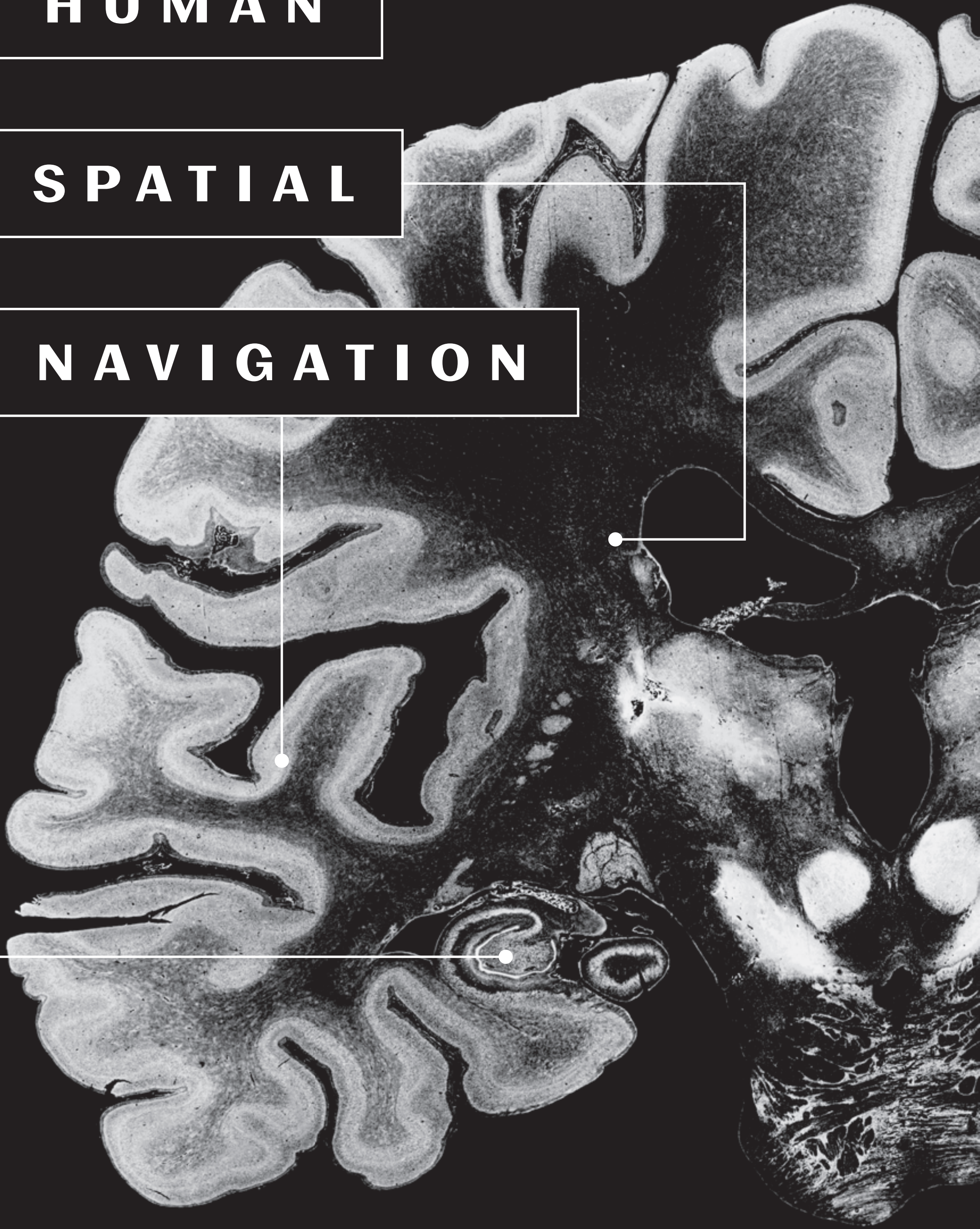

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We would like to thank our families for their patience and understanding as we took time off to work on this book. We dedicate this book to Dr. Howard Eichenbaum, a leader in the field of memory and navigation who tragically passed away in 2017. Howard was an inspiration and a leader to many of us, and his work is discussed extensively and cited throughout this book.

# CONTENTS

# PREFACE

Consistent with the importance of understanding how we spatially navigate and remember where we are in space, the Nobel Prize committee recently recognized the contributions of researchers studying the rodent navigation system. One intriguing implication of this work is that many species, including humans, may possess an internal global positioning system (GPS), as indicated by the neural activity patterns of *place cells*. This research has enormous implications—it can help explain everyday navigation errors such as getting lost, even in our hometown. Furthermore, by providing a more mechanistic basis for understanding spatial navigation and cognition more generally, this research can also help explain why characteristic symptoms of neural diseases like Alzheimer's disease and stroke include disorientation and difficulty navigating.

Yet an important question, and the focus of the book, regards the neural basis of *human* spatial navigation. In fact, early research in humans fundamentally challenged the idea that our spatial representations are GPS-like, or as "smart" as our smartphones. Specifically, this research showed that numerous factors bias our judgments about all scales of navigational spaces. These include simple mistakes such as grouping cities together based on whether they are part of a geographical boundary (a state or a country) rather than estimating their actual distance. They also include biases such as using familiar viewpoints to substitute for actual GPS-like knowledge of an environment. Other studies suggest that how we navigate is fundamentally more visually oriented compared to other species. Thus, a main purpose of this book is to fill in some of the pieces of an important void in our current knowledge: What are the neural mechanisms underlying human spatial navigation?

Indeed, since 1978, when O'Keefe and Nadel published *The Hippocampus as a Cognitive Map* (primarily based on findings from the rodent), the field has seen a veritable explosion in knowledge about human spatial navigation and its neural basis. The advent of desktop virtual reality (VR), functional magnetic resonance imaging (fMRI), and more widespread involvement of clinical populations to study navigation impairments has provided a wealth of knowledge regarding human spatial navigation. In addition, behavioral studies of human spatial navigation have yielded important insights arguing against the idea that our navigational system is anything comparable to the GPS on our smartphone. Yet despite these numerous advances, there is no comprehensive source for those interested in gaining an understanding of this diverse and complex literature.

This book provides an in-depth account of our current state of knowledge of human spatial navigation and the way forward toward a more complete integration between the neural basis of navigation in rats and humans. Whereas past books have explored the issue of human spatial memory in the context of geographical science alongside other chapters devoted to rodent memory, these publications were primarily targeted to scholars. Given the striking advances in human cognitive neuroscience and accumulated knowledge regarding human spatial navigation, it is surprising that no book has tackled our navigational system in a comprehensive and accessible fashion. To accomplish the dual goals of comprehensiveness and accessibility, each of the four authors of this book has contributed substantial yet complementary expertise from their combined decades of work on human spatial navigation. We bring together an international team whose members have worked with both virtual and real-world environments, have experience with numerous recording methodologies, and have substantial neuropsychological expertise. The team has collectively published over 200 papers, including work in the very top journals in neuroscience and psychology.

Each team member contributed critical pieces to this introduction to the human spatial navigation system. Dr. Ekstrom contributed his knowledge of direct, invasive recording in humans navigating virtual environments and his work on both behavioral and neural assays of wayfinding and map learning. Dr. Spiers focused on his extensive work and expertise using functional imaging in both real and virtual environments as well as his work with lesion patients and rodent single-unit recordings. Dr. Bohbot provided a substantial wealth of knowledge based on her decades of cutting-edge work on how hippocampal and extrahippocampal lesions affect spatial navigation. She used functional and structural imaging to study navigation in healthy participants, as well as how navigation training may serve as an intervention for cognitive decline accompanying neural and psychiatric disease. Dr. Rosenbaum contributed her vast experience working with healthy older adults and with patients with navigation and memory deficits as well as her extensive work investigating how we represent real-world spatial environments using fMRI.

# HUMAN SPATIAL NAVIGATION

## CHAPTER 1

# INTRODUCTION

As researchers in human spatial navigation, we are frequently told: “I’m such a bad navigator, you should study me.” Indeed, almost half of the college students in one study rated their navigational abilities as below average (Hegarty et al. 2006). One particular complaint is trouble when navigating in new places. These types of complaints fall into a category of navigational errors that we will discuss in some detail in this book: our tendency to favor habitual, well-learned routes, affecting the ability to reason about new spatial layouts. These complaints showcase how navigation is often error prone and, for many people, a source of significant frustration. They also highlight how all forms of navigation are not the same and can differ simply based on our familiarity with a route.

Difficulties navigating can lead to serious consequences for individuals with neurological conditions affecting brain function. One particularly devastating example of this is Alzheimer’s disease and dementia, where patients often report difficulty navigating and a tendency to get lost, even in familiar neighborhoods (Cushman, Stein, and Duffy 2008; Kunz et al. 2015). As the disease worsens, some patients become lost even in highly familiar neighborhoods, wandering along the paths of telephone lines into the wilderness (Johnson 2010). Even normal aging involves a decline in spatial navigation, with changes in the ability to navigate using landmarks and a tendency to favor using familiar paths. Thus, errors in everyday navigation are not only a part of life but also a hallmark of neurobiological diseases and even healthy aging (Moffat 2009).

Is it possible that we as a species are just poor navigators? Evidence from studies of navigation in other species might readily seem to support this argument. Sea turtles can navigate thousands of kilometers in the ocean to search for food using combinations of ocean currents and sensitivity to the magnetic pole, and they can still manage to find their way back to the same nesting grounds (Lohmann and Lohmann 1996). Desert ants search for food at distances of up to hundreds of meters from their nest, covering a radius that would be equivalent, in human terms, to about 38 kilometers. Yet these ants, once they find food, can plot a direct course back to their nest and find it within 1 square centimeter of error (Wehner and Srinivasan 1981; Gallistel 1990). While the mechanisms underlying these nonhuman feats of navigation differ, there is little doubt that other species are capable of incredible feats of navigation, which nonetheless would appear central to their daily survival.

Still, if we consider human history, there are many examples of navigational feats that are so remarkable they might seem to better represent those of a sea turtle or a desert ant. Perhaps some of the most striking examples, which we will discuss in detail, involve humans navigating—in some cases, thousands of kilometers across the open ocean—with few or no mechanical aids. These feats will also introduce us to important and useful concepts we will use throughout this book. Our first example involves Puluwat sailors, a seafaring people in the Polynesian Islands, which in turn will help us understand the important concepts of *externally* versus *internally* guided navigation and the idea of *path integration*. Lest we think that Puluwat navigation represents a feat that only a highly adept, practiced, and skilled subset of our population is capable of, we will also consider the journey of the *James Caird*, in which stranded sailors navigated nearly 1000 kilometers to safety in a completely unfamiliar part of the Antarctic Ocean. The journey of the *James Caird*, in turn, will help us understand the idea of the *cognitive map*. Last, we discuss how exceptional navigational skills in Inuit living above the tree line, close to the North Pole, are fundamental to their survival in some of the harshest living conditions of the world.

## Navigation of the Puluwat: Path Integration in Action

Puluwat is a small island in the southern Pacific Ocean that is part of a larger chain of islands known today as the Carolines. The Puluwat are renowned within the Carolines for their wayfinding abilities, which include navigating between islands separated by distances of up to 800 kilometers. Much of their navigation occurs across the open ocean with no visible islands or landmarks. In fact, recent attempts to circumnavigate the globe using *no mechanical aids* (spearheaded by Nainoa Thompson) involved training with such Polynesian sailors in order to perfect their techniques (Parker 2015). So what do the Puluwat know that the rest of us do not?

For centuries, the Puluwat have relied on multiple nonmechanical *internal* and *external* cues to navigate. The internal cues, which we will discuss in detail throughout this book, include using mental estimates of direction and distances over the course of their journey; we term this approach to navigation *path integration*. The external cues involve using the stars as a compass and other landmarks, like reefs and islands, as reference points. These achievements are quite amazing when one considers the specifics involved. The Puluwat outrigger sailing canoes are approximately six to nine meters in length and about two meters across and must accommodate groups of five to six people, including a navigator. Yet the Puluwat can navigate these boats between islands even over great distances, successfully arriving at their destination and returning home with little problem (Gladwin 1970). How is this possible? What navigational strategies do these sailors employ?

To learn to navigate, the Puluwat spend their first decades of life in an apprenticeship that focuses on one of two different schools of navigational training: *Warieng* and *Fanur* (figure 1.1A). One aspect of training focuses on learning relevant external cues: the locations of the constellations within the sky and how these change over the course of the night from sundown to sunrise. The stars serve as a basic compass system, providing Puluwat sailors with a bearing to maintain their course. For example, if a sailor wishes to plot a course to an island such as Satawal, he would use the star Beta Aquilae, which provides an approximate heading direction for arriving at this island (figure 1.1B; in our terminology, this would be

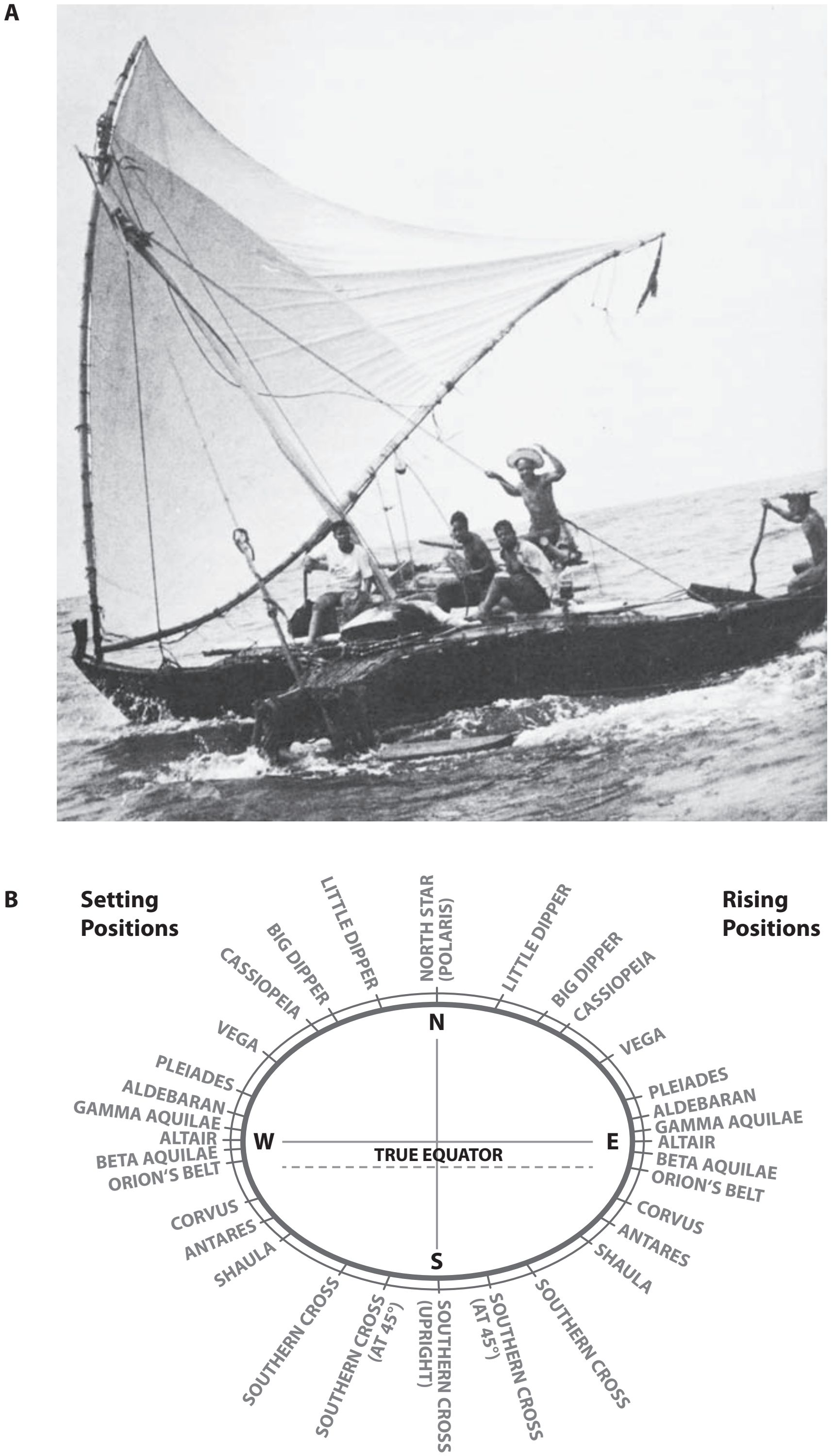


**FIGURE 1.1.** Feats of human spatial navigation: navigation in the Puluwat. A. Puluwat sailing boat. B. The star compass employed by the Puluwat to navigate (see Goodenough and Ward 1953).

approximately northwest). However, the star course they are taught also takes into consideration the ocean currents surrounding these islands. Thus, using Beta Aquilae as a navigation compass takes into account the slight push northward that will occur owing to typical currents and is thus slightly southward of the true goal. In this way, the Puluwat use the stars as external cues much like we use a compass.

Another critical aspect of the Puluwat training involves learning to use internal cues, like one's sense of direction, to navigate. This is because stars alone are not sufficient to navigate between islands. For example, the vast majority of Puluwat trips begin in the daylight (around noon), and thus the initial direction cannot depend on using the stars to determine bearing. Instead, this is where the use of internal cues becomes important. The Puluwat use another island that they have mentally located (but that they cannot see) to determine the direction in which to head out from their home island. This method is referred to in Puluwat as *etak*—roughly the equivalent of a term that we will use throughout this book: a *cognitive map*. Put simply, a cognitive map is a mental representation of the position and spatial relations among multiple landmarks in the external world (Tolman 1948; O'Keefe and Nadel 1978; Sholl 1987).

After having determined their initial bearing based on their knowledge of the relative positions of islands from their cognitive map, navigators must then be sure to plot as straight a course as possible. As the navigator departs with his crew, he looks *behind* him at prominent landmarks on the island—in this case, using external cues to validate his sense of internal heading. Plotting a course to one island will involve sighting the position of himself relative to several different landmarks on the island, which must line up precisely based on the navigator's viewpoint as the boat heads out to sea (figure 1.2). Using a landmark to guide our navigation, either toward or away from that specified landmark, is termed *piloting*. In this case, piloting involves using the position of multiple landmarks relative to the sailor to plot his exact angle of departure, which we term *egocentric navigation* because he bases

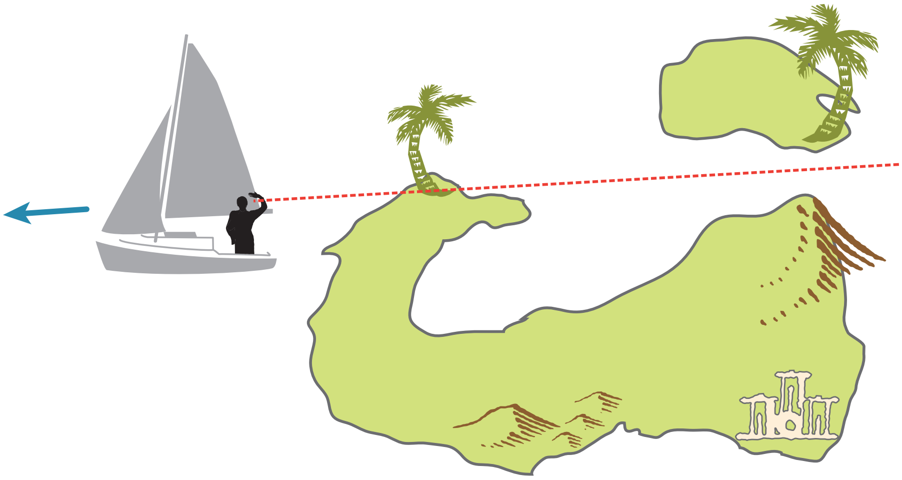


**FIGURE 1.2.** Backsighting employed by the Puluwat to estimate their initial heading when beginning a journey out into the sea.

his estimate of direction and distance relative to himself and landmarks. In this way, the sailor can estimate fairly precisely his angle of departure based on his memory for the view angles corresponding to relative bearings.

Once the island is out of sight, the Puluwat navigator must be sure to maintain his course and not to veer too far from his initial bearing. Here is where his ability to *path integrate*, or keep track of both direction and distance traveled, becomes most important (figure 1.3). From his position on the boat, the Puluwat navigator tries to maintain a specific bearing based on his internal sense of how much the boat has turned. The Puluwat have detailed knowledge of different types of waves that present within the Caroline Islands, some of which originate from the north and others from the east. When one of these waves hits the boat, by determining the angle at which the main boat and outrigger hit the wave, the navigator can estimate direction and update his sense of direction. In this way, the Puluwat sailor uses a keenly developed internal representation of bearing and then updates his course based on information he obtains from knowledge of waves that hit the boat at different angles.

In addition to bearing, the navigator also computes distance traveled based on his estimate of the speed of the boat and the time of day. Again, he uses external cues to update and correct this estimate. Based on the time it takes for the crests of two different waves to pass, the sailor can estimate the relative speed of the boat. The Puluwat sailor thus uses these various external cues to update and estimate his internal estimate for direction and distance. By having an internal representation for both direction and distance, which the sailor continuously updates based on

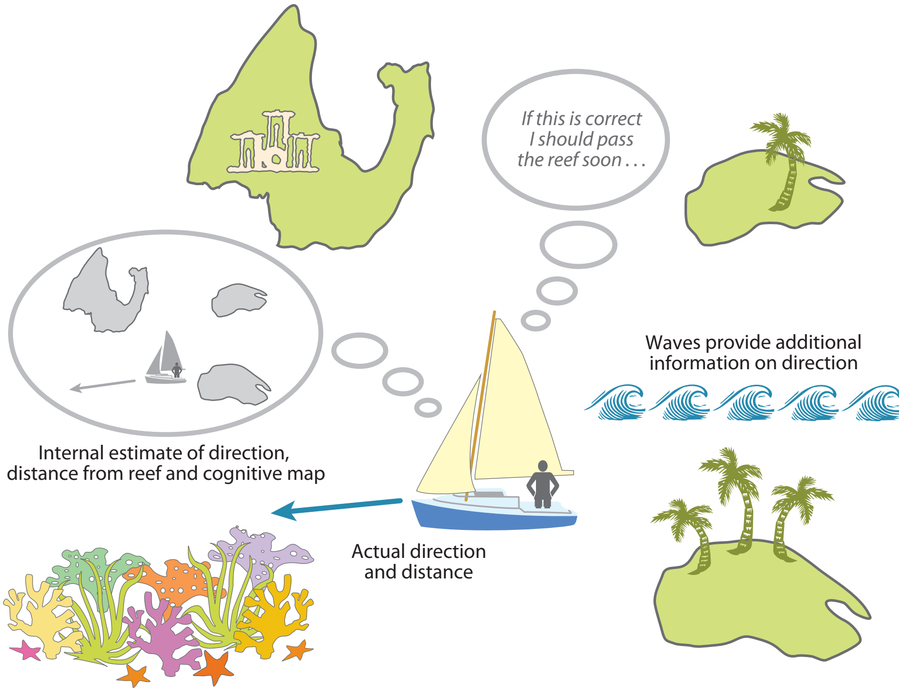


**FIGURE 1.3.** Path integration in the Puluwat.

external cues, he is able to maintain a fairly good idea of how far he has traveled and in what direction.

Path integration, though, would not be particularly helpful to the sailor unless he had some idea of where islands were located as he traveled. Recall that the Puluwat, upon beginning the journey, have a precise idea of their initial bearing based on their representation of their home island relative to other islands in the Carolines—what we have termed the cognitive map. This knowledge of the relative positions of other islands and landmarks is what we term an *allocentric* form of navigation and reasoning because it is based on the relative position of multiple external landmarks to each other independent of the navigator. Thus, as a sailor navigates to a distant island, he uses a reef or another island that is not visible but can be pictured in his mind's eye based on his estimate of progress from his path integration representation.

Confirmatory evidence of the position of an island or a reef can be obtained by seeing it (from about 16 kilometers away) or, in the case of an island, by sighting seabirds, which can range up to 64 kilometers from a given island. In this way, the cognitive map serves the important function of combining path integration information with the expectation of different landmarks the sailor will encounter (see figure 1.3). Encountering these landmarks, which can occur in a manner either consistent or inconsistent with path integration representations, provides an indication either of success or of the need to make a slight adjustment to course. The final landmark the sailor looks for is the destination island—his goal—at which time the sailor relies on piloting by simply using the island as a visual aid and correcting course accordingly until the island is finally reached.

## What We Can Learn from the Puluwat

For anyone not accustomed to sailing and traveling by sea, even getting a boat out of a harbor might appear challenging and certainly requires a fair amount of skill; the idea of navigating hundreds of kilometers in the open ocean with no obvious visual cues seems, at first, impossible. As we discussed earlier, however, the Puluwat make use of a wealth of cues, both external and internal, that most of us are probably unaware are even useful for navigation. As we will see in chapter 2, we use similar estimates of direction and distance during walking in new and familiar environments, and, just like the Puluwat, we correct our internal estimates based on evidence from visual features. In this way, we can think of navigation as an inherently *multisensory integration* process that combines multiple cues to accurately find our way to our goal (Berthoz and Viaud-Delmon 1999; Angelaki and Cullen 2008).

But what is perhaps most striking is the Puluwat's highly cultivated and sophisticated use of an internal tracking of direction and distance: their path integration system. It may seem difficult to believe that our brain has a built-in system for estimating the direction we are traveling and how far we have traveled. But this is precisely what path integration, at its core, involves. Right now, you are probably sitting in a chair or lying on a couch reading this book. Try standing up for a moment. Now, close your eyes and try walking to a location that you can picture in your head, like another chair in your living room. Stop when you think you have reached your destination. As you walk, you will probably have a fairly good sense of how far you need to travel and whether you need to take any turns to get there. Hopefully, you have experienced the sense that our brain can, in fact, keep track of both direction and distance, even in the absence of any visual cues to confirm that our internal system was correct.

## Computing Head Direction

We may often forget about what some call our “sixth sense,” our *vestibular system*, because its specific contributions to everyday life may not be obvious (Wolfe 2006). Our vestibular system, an intricate series of fluid-filled canals in our inner ear, is critical for functions like balance and updating our eye position with head movements. Perhaps most important for our current considerations, our vestibular system is also critical to tracking our bearing by updating our brain about changes in our head position. As an example of its importance, lesions to our vestibular system produce profound deficits in navigation (Russell et al. 2003; Brandt et al. 2005).

Our vestibular system works much like a level, a tool frequently used by carpenters to estimate the angle of a board or other object (figure 1.4A). A level is usually a long, straight bar containing one or more tubes filled with water and an air bubble, with marks indicating the center position. If a carpenter wishes to determine whether an object is level or at an angle, she can position a level relative to the object. If the bubble deviates to the side, she knows that the object is not level. If the bubble is even relative to the center marks, she knows that the object is level.

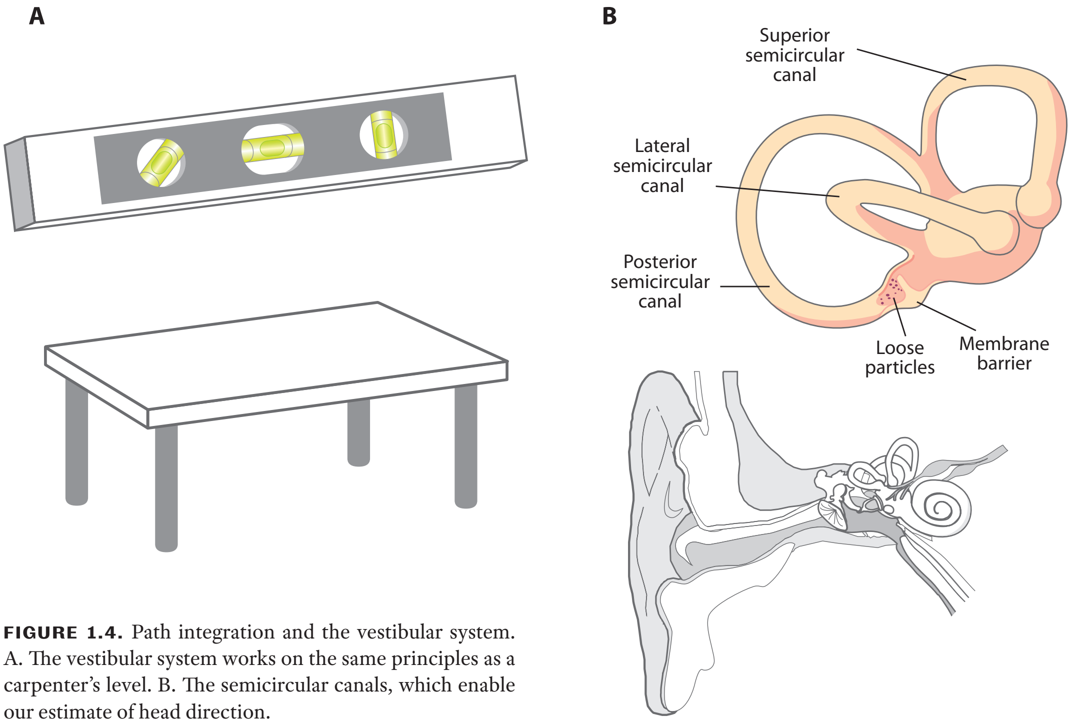


**FIGURE 1.4.** Path integration and the vestibular system. A. The vestibular system works on the same principles as a carpenter’s level. B. The semicircular canals, which enable our estimate of head direction.

The vestibular system works in much the same way, except it contains vessels for each of three different perpendicular directions. These curved canals contain a watery fluid that moves, or is displaced, every time we move our head. The three canals that detect these rotations are termed *semicircular canals* (figure 1.4B). Because each semicircular canal is perpendicular to the other two, the three curved canals cover all three possible primary orientations in three-dimensional space. Thus, movement of your head in any direction in three-dimensional space will activate at least one of your semicircular canals, allowing you to detect displacement in almost any angular direction.

Within each semicircular canal, tiny hairs called *cilia* detect the movement of this fluid. The hairs act much like seaweed does when a wave passes over it in the ocean. Just as the seaweed bends to follow the direction of the current's movement, the hair cells in our semicircular canal are pushed by the movement of the water in our inner ear. For example, when you shake your head from left to right and back, fluid in your semicircular canals moves hair cells in your inner ears in opposite directions. Based on the rate at which the fluid deflects the hair cells, we now have a way of computing the angular acceleration of our head movement. When we turn our head, either with our body or independent of our body, our semicircular canals, via our hair cells, provide information about how quickly we moved our head and when we stopped. Neurons in our vestibular nerve code this displacement by a change in the activity of neural signals called *action potentials*, which we will discuss in greater depth later. These, in turn, provide a signal for the acceleration of your head in one direction versus another.

Based on the degree of angular acceleration and the time between accelerating and stopping, we can then get a fairly good estimate of how far our head has turned. Thus, our semicircular canals provide relevant information—particularly when combined with input from our proprioceptive system and our other vestibular organs, the otoliths—for estimating the angle at which we have turned our head (another example of *multisensory integration*; see also Angelaki and Cullen 2008). This information is then read out, in some detail, by a network of brain areas called the *head direction* system, which provides an estimate of the position of our head relative to where we are in the environment (Valerio and Taube 2012), a topic that we will discuss in depth in chapter 3. In this way, our vestibular system, in conjunction with our head direction system, provides a fairly precise readout of our angular rotation.

## Path Integration: Direction and Distance

While our semicircular canals, in conjunction with our head direction system, provide a fairly precise means of estimating angular head direction, our *otoliths* provide information on linear acceleration. Our otoliths are another component of our vestibular system and provide information about changes in our movement as we initiate a step and when we counteract gravitational forces to balance. Using this information, the otoliths can decode linear accelerations and decelerations (Angelaki and Cullen 2008). From this, we can obtain a rough initial estimate of our velocity, and, in principle, a good guess at our distance.

In practice, though, our ability to estimate durations of time, a critical piece of estimating our velocity, is not particularly good (Friedman 1993; Grondin 2010). A much better way of estimating our distance, as it turns out, is keeping track of approximately how many steps we have taken. When we walk, our legs swing back and forth at different angles, and thus a part of our sensory system, called our *proprioceptive system*, can provide a fairly good estimate for how fast our feet and legs are moving. If we add in our sense of touch when our feet hit the ground and how frequently this occurs in time, we now have a way of estimating the distance we have traveled.

But even without any movement of our legs and updating of our vestibular system, we can use other cues to estimate how fast we are traveling. An important such cue is called *optic flow*, which refers to the rate at which objects pass us by visually when we navigate (Warren 2001). Humans can use optic flow to estimate distance of travel (Redlick and Harris 2001). Another source of useful information comes from something called *motor efference copy*. Here, we can compare our expected movement, based on muscle output, with our actual movement, based on sensory feedback. For example, if we begin to take a big step, we have a sense of going a larger distance than a small step, which we can confirm based on subsequent sensory and proprioceptive feedback as we complete the step (Gallistel 1980). Together, all of these multisensory cues (yet another example of *multisensory integration* in navigation) allow us to path integrate as we walk.

## The Cognitive Map: Is It the Map in Your Head?

Navigation on the ocean, of course, involves no walking. Instead, distance must be computed based on a combination of estimates of movement speed from the otoliths, windspeed, and ocean currents. Thus, in addition to using their path integration system, the Puluwat also use landmarks such as other islands or reefs to correct any mistakes in their estimate of their direction and distance. In the case of the Puluwat training, an apprentice may spend years learning the relative positions of different islands and reefs in the Caroline Islands chain. A core element of this training is extensive study and testing of the ability to accurately draw the relative direction and positions of islands in the sand. In this way, the sailor's *memory* for the relative positions of reefs and islands forms the basis of an internal representation that we often refer to as a *cognitive map*.

As tempting as it might be to think of a cognitive map as an actual map, it is important to note that it is not the same as the type of map we buy at a gas station or consult at a shopping mall (termed a *cartographic map*). We discuss the reasons for this throughout this book, but the primary reason is that our cognitive map must serve first and foremost as a good-enough approximation for what we need when navigating and does not necessarily include all the details we might expect from an actual cartographic map. In this way, we can think of a cognitive map as *topological*, or maintaining the relationships between objects, rather than necessarily providing the exact metric distances. A second reason is that a cognitive map must allow interpretation of information primarily from a first-person perspective rather than from looking down on an environment from above, as is the usual setup of a cartographic map. If a Puluwat sailor fails to see a reef after traveling for several hours northeast, he must adjust his position with the expectation that he needs to travel slightly south. In this way, the cognitive map does share some of the qualities of a cartographic map in that it must represent relative directions and distances of important landmarks, but it must be applied based on current bearing (Sholl 1987).

Whether the Puluwat actually *need* a cognitive map to navigate, though, is less certain. The Puluwat apprenticeship involves receiving feedback from more experienced navigators while sailing. The extensive training and apprenticeship the Puluwat experience, particularly while sailing, leaves open the possibility that they are not actually using the map they have learned but, instead, have fine-tuned their path integration system based on feedback from their instructor. For example, while sailing, if the apprentice's internal estimate is slightly too far off to the north, the instructor might point this out based on seeing a reef or an island. The navigator will learn to correct his estimates, and the more he navigates the route, the better he will get. For highly familiar routes, though, as we will discuss in chapter 6, no map is even necessary (Packard and McGaugh 1996; Iaria et al. 2003). To demonstrate the importance and utility of a cognitive map in a completely unfamiliar situation, perhaps one of the best examples involves an incredible feat of navigation: the voyage of Ernest Shackleton's crew following marooning of their ship in the Antarctic.

## Journey of the *James Caird*: The Cognitive Map in Action

Ernest Shackleton intended to be the first European to discover Antarctica, but in 1911 was beaten by Norwegian Roald Amundsen. Not to be deterred, Shackleton returned to Antarctica, where he intended to be the first to complete a transantarctic expedition involving crossing the entire continent by sea and land. Unfortunately, disaster struck, and his ship, the *Endurance*, along with Shackleton and all of his crew, were marooned within the shifting ice of Antarctica. Needing a means of escape, his crew used three smaller boats to successfully navigate to the nearby Elephant Island (figure 1.5). Elephant Island, however, was uninhabited and proved difficult to live on owing to the strong winds and few sheltered locations to avoid the driving snow. Therefore, Shackleton's crew plotted a course to distant Georgia Island, which offered a whaling camp and thus the possibility of rescue.

Shackleton assembled a small crew, including the skilled navigator Captain Frank Worsley. Worsley packed a compass, a chronometer, and a sextant, which would normally provide sufficient information for estimating both latitude and longitude. He also packed sea charts and maps, which he could then use to compare his progress based on published positions for latitude and longitude. As it turned out, these devices were of only limited help during their voyage, which involved traveling approximately 700 nautical miles (1300 kilometers) northeast to Georgia Island across the Weddell Sea (see figure 1.5). Extremely difficult weather conditions made using all of these devices next to impossible.

Upon embarking in the relatively small (6.5 meters long) vessel named the *James Caird*, the crew encountered large waves and vicious gale storms, with wave crests reported to be as high as 15 meters and wind gusts over 250 kilometers per

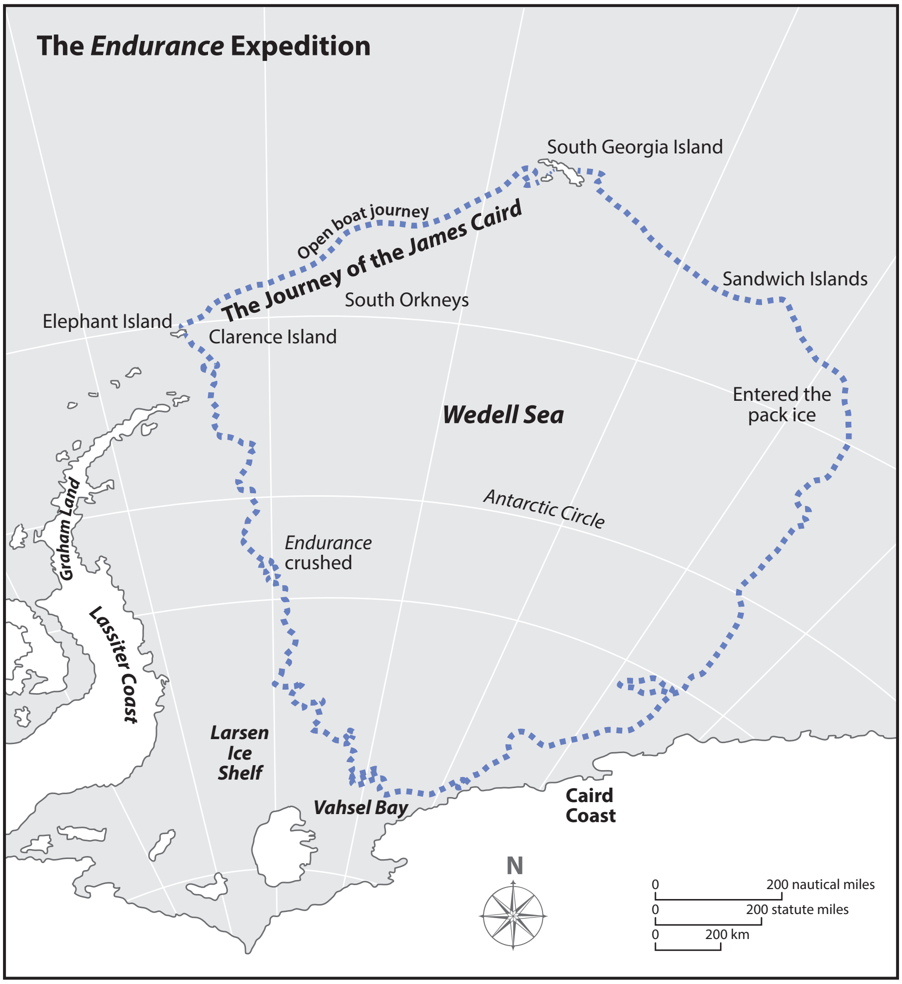


**FIGURE 1.5.** The journey of the *James Caird* through the Antarctic Ocean.

hour. All the contents of the *James Caird* were completely soaked and then frozen over, with all of Worsley's maps rendered essentially useless. Using a cartographic map—normally indispensable in naval navigation—was not an option. Even more problematic, estimation of latitude and longitude with a sextant became extremely difficult owing to the rocking movement of the boat. Thus, navigation depended almost completely on Worsley's internal sense of direction and distance as well as his detailed memory for the positions of islands within the Weddell Sea.

Worsley was limited primarily to compass readings. We can think of a compass much like the Puluwat sense of direction. It can tell us if our heading is correct, just as one's passage relative to celestial bodies does, but it provides no readout of distance or where landmarks are. Because the storms produced extremely strong crosswinds, Worsley relied primarily on his ability to estimate distance based on sea currents, wind strength, and a compass reading to path integrate. It is worth emphasizing what was at stake. Based on the wind and sea currents, missing Georgia

Island would mean sailing into completely open ocean in the Atlantic, with the next land being South Africa.

Amazingly, Worsley navigated to Georgia Island with little overall error and only intermittent positional readings when these were possible. Because his charts were unavailable, he relied on his internal cognitive map for the positions of Elephant Island relative to Georgia Island and his ability to update his representation of his position based on the knowledge of their relative positions. While his path integration and bearing helped him estimate his relative position, successful navigation required intimate knowledge of both the distance and directions of these islands relative to each other. While it is valid then to think of his cognitive map as a memory for the cartographic maps and charts with which he was so intimately familiar, it is important to note that *Worsley had never navigated this precise route before*. Thus, unlike the Puluwat sailors, he had no teacher or master to train him in estimating the relative positions of islands in the Antarctic. The essence of what Worsley was doing was remembering the relative position of landmarks in his head and using these to update his path integration system. Without his cognitive map, his path integration system would have been useless because he had never before navigated between these different islands.

## What Did We Learn from the Voyage of the *James Caird*?

Perhaps what we can best understand from the voyage of the *James Caird* is that a mental representation that resembles, in some form or another, an actual cartographic map is extremely useful for navigation. In Worsley's case, because he had never navigated the route that he took from Elephant Island to Georgia Island, he relied on his memory for the positions of these islands in the Weddell Sea as well as estimates of how far he had traveled (based on the wind speed and ocean currents) and the relative bearing of the boat (based on his compass). We can compare Worsley's navigational feat, although on a much smaller scale and with far less at stake, to how we might navigate in a new city. If someone tells us that a restaurant we are searching for is about a ten-minute walk, two streets up and to the left, we may form some kind of rough image in our head of the different blocks we are going to pass and that we will need to walk about a quarter of a mile. It may even be useful to remember other landmarks we have seen on a map that we may pass, such as a different restaurant. While there would certainly be other ways to navigate to the restaurant (for example, simply remembering that we walk straight past two streets and turn left), it is also fairly clear that many of us use a strategy of imagining positions and directions of objects to help us navigate. What is perhaps most amazing about the journey of *James Caird* is that Worsley and his crew were able to navigate this way under some of the most inhospitable and difficult conditions imaginable.

We have discussed so far the idea that in many situations it is highly advantageous to have a mental image of the positions and directions of locations we might pass when we have a navigational goal in mind. We may form these representations either by repeatedly navigating (like the Puluwat) or by having seen these locations on a cartographic map (like Worsley). While a cognitive map may not always be necessary for navigating—for example, when we are walking to our next-door neighbor's house—using one to navigate is extremely advantageous. In the case of the voyage of the *James Caird*, it is clear that a cognitive map, an internal representation of the direction and position of the islands in the Weddell Sea, played a central role in this accomplishment.

## Navigation of the Inuit in the Arctic

The Inuit in Northern Canada live in extraordinarily harsh conditions. Most reside permanently above the tree line—that is, the earth's parallel above which no plants have sufficient warmth to grow during their short summer, or for their roots and seeds to survive the harsh arctic winter. For millennia, the Inuit's only food source came from hunting and fishing. Yet they live so close to the North Pole that they have complete darkness three months out of the year. The other nine months, visibility during navigation is often obstructed by blizzards in the winter or fog during the summer. So how can they navigate to survive?

For centuries, they have found their way through seemingly homogeneous landscapes without using maps or navigation devices, and thus their exceptional navigational skills are one of the primary reasons for their survival (Aporta 2009). Like the Puluwat, the Inuit employ a variety of environmental features to navigate, including the direction of prevailing winds that they identify by name. They then use the shapes of snowdrifts created by these wind currents to orient themselves in space. Just like the Puluwat, they also make use of the stars by memorizing their positions at the different times of the year (MacDonald 1998). When traveling by boat, they use the direction that seaweed points toward when a stone is attached to the tips to determine water currents and thus their relative direction.

The Inuit language itself includes these spatial relations—for instance, different words are used for inbound and outbound travel. The Inuit refer to eight different cardinal directions, instead of the four cardinal directions used in southern Canada. In addition to their environmental cues, the Inuit use an *inuksuk* (a cairn to identify a location) when an important landmark needs to be identified, such as a food source buried under the snow, a dangerous cliff, or a nearby village. The fact that they use these ever-changing features implies that they are constantly forming complex spatial relationships between their current location, these environmental features, and their destination. Lessons from the Inuit remind us of one basic fundamental fact: before our current technological age, navigational skills were essential to our survival.

## Studying Neural Signals in Humans

While it is always helpful to use anecdotes and examples to try to explain a scientific concept, this approach does not necessarily *prove* that this is how our brain works. To demonstrate that our brain uses a code like a cognitive map, we will need to show through quantifiable behavior and neural measurements that this is actually a means we employ to navigate, with the additional hope that we can demonstrate a link between behavioral and neural signals. We will discuss behavioral approaches to understanding human spatial navigation in detail in chapter 2, and much of the rest of this book will be concerned with neural recordings (both in rats and in humans), brain imaging, and patient studies that help us understand how we navigate. Here, we will briefly review some of the neural approaches, particularly the use of a cognitive map.

Studying navigation in humans, particularly its neural basis, is challenging. One of the major obstacles we face, in contrast to work in nonhuman animal models, is that direct *intracranial* recordings (that is, performed within the skull) are rare and are possible only in clinical situations in which patients already have electrodes implanted for surgical planning (for example, treating epilepsy or removing a tumor). Much of what we know about navigation more generally, however, was discovered from freely navigating rodents with implanted intracranial electrodes. In fact, this was how neurons called *place cells*, which are an important component of the cognitive map, were first discovered in 1971 by John O'Keefe and Jonathan Dostrovsky (O'Keefe and Dostrovsky 1971). We will discuss this topic in detail in chapter 3. The goal of our book, however, is not to understand rat navigation but instead to understand the fundamentals of how the human brain enables navigation. Although place cells have been identified in humans through invasive recordings in patients with implanted electrodes (Ekstrom et al. 2003), much of our focus will be on noninvasive methods, which have also provided important insight into the neural basis of human navigation. These include functional magnetic resonance imaging (fMRI) and the study of lesions caused by brain injury and disease.

Another important question regards exactly how we might study navigation in the lab in the first place, particularly given our examples in which navigation occurs over large scales of space and even time. Simply put, it would not be practical or even possible to perform brain recordings, which involve expensive equipment that is usually stationary and delicate, under most ecological navigation conditions. While it is possible, of course, to study people's *memory* of navigational experiences, such as navigating in a city like Toronto or Santa Barbara, and many researchers have (Rosenbaum et al. 2004; Uttal et al. 2010), studying in situ navigation provides the most direct insight into what behavioral processes and neural signals underlie navigation.

One of the most widely used approaches for studying human spatial navigation is virtual reality (VR), which allows us to construct complex, large-scale environments on desktop and laptop computers, and even some that can be navigated actively by walking (Grant and Magee 1998). Virtual reality had its origins in the 1980s at institutions like NASA, the Air Force, and Bell Labs that were eager to use increasingly complex computer graphics to create flight simulators and military applications (Biocca and Levy 2013). As VR caught on in these specialized research applications, researchers began to ask to what extent it captured the same "essence" that navigation in physical space did. In one such study, researchers compared individuals who navigated a virtual version of a building with participants who navigated a real-world building and studied a map. When participants imagined the building following navigation, both route distance and straight-line estimates of distances (estimating the most direct route between two landmarks) were correlated with the real-world distance and angles. These findings suggested that VR does mimic at least some aspects of the real world (Richardson, Montello, and Hegarty 1999).

Given our discussion of the importance of path integration to navigation, which involves using our vestibular, sensory, proprioceptive, and motor systems to estimate direction and distance, it might be surprising that VR could mimic real-world navigation at all (Taube, Valerio, and Yoder 2013). At the same time, we are primarily visual creatures (see chapter 4), particularly compared to rodents, and *optic flow*, the relative movement of visual objects as we navigate, is a core part of how we path integrate (Warren et al. 2001; Ekstrom 2015). Importantly, in this regard, several studies suggest that our path integration system may be at least partially active when we navigate virtual environments. This is based on the fact that we can extract relevant navigational information in terms of estimating turns and distance traveled primarily, or even exclusively, from optic flow (Wolbers et al. 2008). How good an approximation of reality is virtual reality? Our current understanding is that it is overall a reasonable approximation, although detailed studies comparing navigation in VR during visual-only tests versus vestibular input in large-scale space remain to be performed to fully address this issue.

The value of VR is most obvious, though, when we consider neural recordings. As mentioned earlier, performing brain recording during real-world navigation in humans, at least with intracranial recordings, is extremely difficult and potentially hazardous, as patients with implanted electrodes are at a greatly increased risk of falling and therefore suffering head injuries. fMRI is possible only in an environment involving strong magnetic fields when participants are lying supine. Thus VR provides the unprecedented opportunity to study navigation using a laptop or a computer display, allowing us to examine the neural correlates of navigation. An additional advantage of VR in this case is that we have tighter control over exactly what participants encounter and when. While recollections of real-world experiences are valuable, it is difficult, if not impossible, to control for the degree of familiarity across subjects for different geographical locations. Thus VR also offers the unique advantage of presenting novel spatial environments to participants, allowing us to better control for the tricky issue of *preexposure* (exposure to environments before testing).

## Direct Intracranial Recordings from the Human Brain

The discovery of the neuron by Ramon y Cajal in the 1880s (Ramon y Cajal [1892] 1995) and subsequent demonstration that cells carry electrical signals called *action potentials* (Curtis and Cole 1942; Hodgkin and Huxley 1952) led to a focus in contemporary neuroscience on recordings of single neurons. This is not without good reason: many of the seminal discoveries relating to how we understand the relationship between brain and behavior have come from such recordings, three of which were the subject of the Nobel Prize. These studies involve the placement of wires that can conduct weak electrical signals to a system that can amplify and record them. We term these types of recordings *extracellular recordings* because they involve recording from neurons that are located near where we have placed our electrode (figure 1.6A).

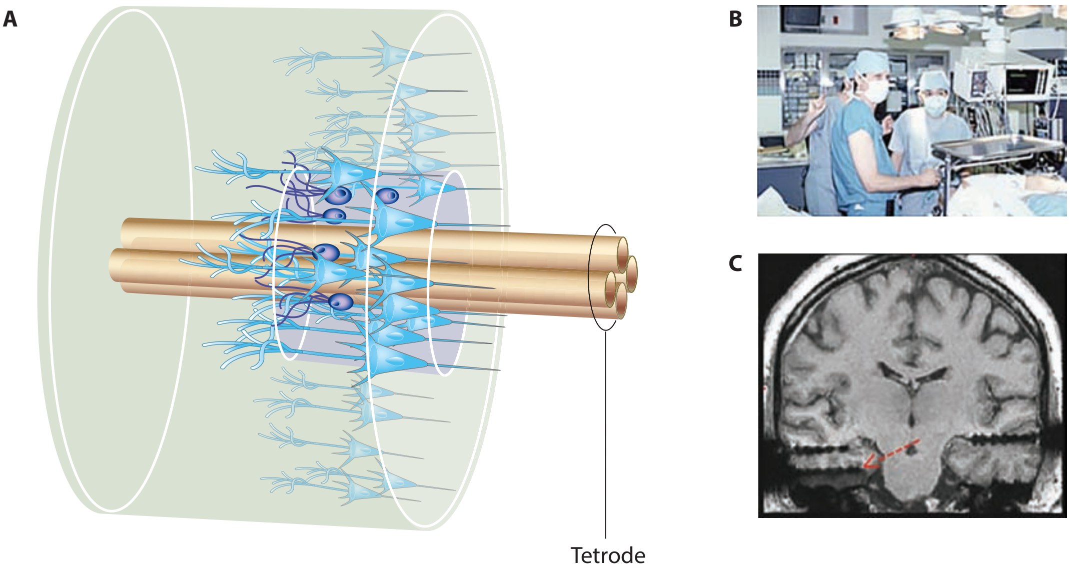


**FIGURE 1.6.** Extracellular recordings in humans. A. An example of how both action potentials and local field potentials can be isolated with electrode recordings (Buzsaki 2004). B. Neurosurgeon Itzhak Fried (center), an early pioneer in invasive recordings in humans. C. Placement of electrodes in the human parahippocampal cortex, an area in humans important to navigation (red arrow). Also shown is the human hippocampus, which is located just superior (above) the parahippocampal cortex. Reproduced from Ekstrom et al. 2003.

There are many examples of important brain functions that we have learned about from extracellular recordings. These include the idea that the visual cortex has neurons that respond to the orientation of lines, which forms the basis of how we understand the neural underpinnings of visual perception (Hubel and Wiesel 1962). Another example is place cells, which we discussed previously and which are neurons that increase their activity during navigation at specific spatial locations (O'Keefe and Dostrovsky 1971). Both these examples involve recordings that were performed in monkeys and rats, respectively. However, given the enormous impact of being able to relate changes in the activity of neurons to behavior, it seems that similar recordings would be invaluable in humans for (1) determining if we even have such neural codes for behavior, and (2) determining if we might differ in any way from what is observed in other species.

As it turns out, such recordings are indeed possible in humans in clinical situations, as mentioned earlier (Fried et al. 1999; Engel et al. 2005; Mukamel and Fried 2012). These recordings are most commonly taken from patients with epilepsy that is resistant to treatment from drugs, termed *pharmacologically intractable epilepsy*. To treat seizures in these cases, one approach is to remove the brain tissue thought to produce the seizure activity (figure 1.6B). To do so, however, surgeons must attempt to localize the region of the brain from which the epilepsy originates. Therefore, prior to performing the surgical removal, certain cases require that neurosurgeons lower electrodes into the brain and perform recordings in these patients, either acutely in the operating room or over the span of several weeks while the patient is

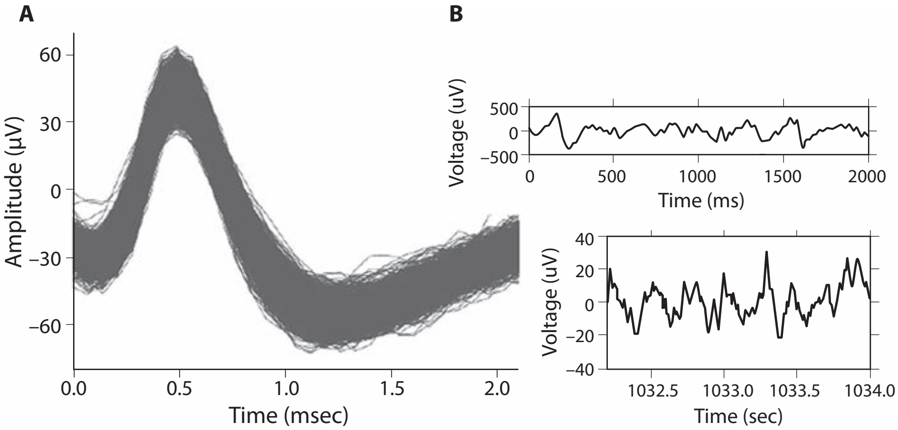


**FIGURE 1.7.** Action potential and local field potential recordings from humans. A. An example of an action potential recorded from the human hippocampus. B. An example of oscillations recorded from the human hippocampus.

monitored in an epilepsy unit. In both situations, it is possible to have patients perform behavioral experiments while recording from these extracellular electrodes. For example, while being monitored on the epilepsy ward patients can navigate virtual environments on a laptop computer, thus providing insight into how neurons respond during navigation (Ekstrom et al. 2003). In this way, the frequency of action potentials, which are the fundamental electrical signaling mechanism of the single neuron, can be compared with different epochs during navigation (figure 1.7A).

In addition to providing insight into the frequency of action potentials of individual neurons, extracellular recordings in surgical patients also provide insight into a signal called the *local field potential*. The local field potential is thought to arise from the summation of activity of thousands of neurons around the tip of the electrode (Buzsaki, Anastassiou, and Koch 2012), primarily from a smaller but slightly more sustained signal deriving from electrical signals at the synapse called *postsynaptic potentials*. Early work in rodents noted several important features of the local field potential—perhaps, most notably, that rhythmic signals often manifest during behavior (figure 1.7B). One of the most obvious of these oscillations, termed the *theta oscillations*, manifests in a range of about 3 to 12 cycles per second in rats and about 3 to 8 cycles per second in humans (Green and Arduini 1954; Vanderwolf 1969; Ekstrom and Watrous 2014). These oscillations often increase during movement and other navigationally relevant behaviors, thus explaining their historic link to navigation (Buzsaki 2005). We will discuss these oscillations in some detail in chapter 3, as they form a core component of regulating the timing of neural signals important to navigation, and even provide a basic code for movement speed.

## A Noninvasive Window into the Neural Basis of Navigation

Functional magnetic resonance imaging (fMRI) is a noninvasive brain imaging technique with a high spatial resolution (~1–3 mm) that provides images of changes in blood flow related to a task (figure 1.8A). fMRI has a temporal resolution of

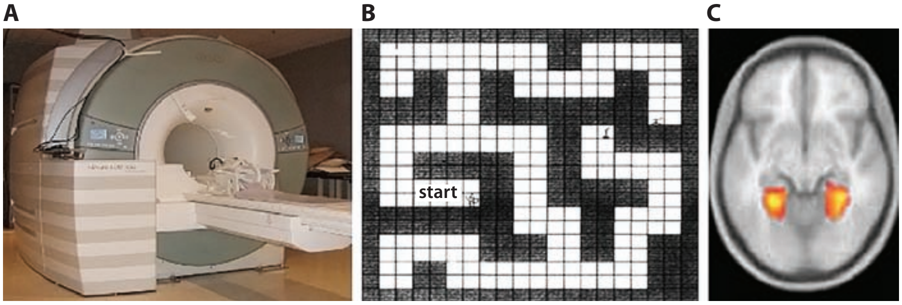


**FIGURE 1.8.** fMRI: A noninvasive measure of neural activity in humans. A. An MRI scanner. Note that participants are lying down when in the scanner. B. An overhead view of the virtual maze used in the Aguirre et al. (2006) study. C. An example of parahippocampal cortex activation.

approximately 6 to 10 seconds, which is around the time interval in which many interesting behaviors are likely to occur during navigation, such as looking at a landmark or retrieving details about a spatial layout. fMRI measures changes in blood flow and blood oxygenation, which are in many cases correlated with changes in neural activity (Ogawa and Lee 1990; Logothetis 2003). Thus, fMRI provides a useful way of looking at changes in neural activity during behaviors like navigation and lets us try to pinpoint neural differences underlying specific components of such behaviors.

fMRI is based on a signal called the *blood oxygen level–dependent (BOLD) signal*, which derives from combinations of the preceding parameters. The BOLD signal itself does not have units, and in this way is considered a *relative* measure (unlike other brain measurements we have discussed, such as extracellular recordings, which have units of current and voltage, and are often referred to as *absolute* measures). Thus, a "baseline" or control condition in which zero or low activation is expected is also needed for all contrasts (Friston et al. 1995; Stark and Squire 2001). In most experiments, then, we include a baseline condition as well as two additional contrasts. In this way, we can isolate neural activation patterns for specific conditions of interest.

Let's consider one potential contrast. Say we have participants navigate a complex maze in which they must learn specific routes and employ shortcuts. As a comparison, we can employ a second maze in which they take a restricted route, by following either arrows or a simple track. We can then compare this with a condition in which we expect little activation in brain areas important for navigation, such as indicating odd numbers as they appear on a screen. The experiment earlier actually describes a classic experiment by Geoff Aguirre (figure 1.8B,C), one of the first to demonstrate that a portion of a brain region called the parahippocampal cortex is important for spatial navigation in humans (Aguirre et al. 1996).

fMRI is an enormously valuable tool because it allows us to understand the neural basis of spatial navigation in healthy, awake humans. This stands in contrast to extracellular recordings, which are limited to patients with implanted electrodes. At the same time, there are several limitations with fMRI to consider, some generally related to the method and others related specifically to spatial navigation. One issue, particularly in comparison to extracellular recordings, is that the neural basis of the BOLD signal remains debated. There are certainly conditions under which cellular activity, both at the level of single cells and the local field potential, correlate with the BOLD signal (Logothetis 2003), but there are also other situations when this correlation appears to break down (Ekstrom 2010). Currently our understanding of exactly when neural activity and the BOLD signal relate or dissociate is unclear, with the emerging consensus being that different brain regions appear to show different relationships with underlying neural activity (Ekstrom 2010; Ojemann, Ojemann, and Ramsey 2013). This means that we must be cautious in interpreting BOLD differences between different brain areas, although we can feel fairly confident that BOLD relates, in some form, to neural processing during navigation.

Another issue for fMRI with regard to spatial navigation specifically is that participants must lay supine in the scanner (for example, see figure 1.8A). For participants to navigate, they must view an environment by looking up (either through MRI-compatible goggles or through a mirror system) and navigate with a joystick. This produces a mismatch between how we would normally experience navigation and how we experience it in the scanner, as lying down is an awkward and unnatural way to navigate. Furthermore, it produces a mismatch between vestibular and visual cues (Taube, Valerio, and Yoder 2013). Our vestibular cues tell us we are lying down, while our visual cues tell us we are moving forward! While this is a potential issue with studying navigation in the scanner, as discussed earlier our path integration system can often rely largely on visual input (via optic flow) and ignore vestibular input, as unnatural as this might seem (Ekstrom 2015).

Another way to deal with this issue, as alluded to earlier, is to have participants retrieve memories of spatial environments rather than navigate them directly. It might seem surprising that having people merely think about a navigational experience would recruit similar networks to actually navigating; however, if we consider our everyday lives, visual imagination is a powerful way of re-creating past experiences and even envisioning new experiences (Addis et al. 2004). Just the act of remembering details from a recent event is powerful enough to recruit many of the same brain areas involved in encoding the event in the first place (Watrous and Ekstrom 2014). This approximation of navigation seems to work well overall, as several studies suggest partially overlapping brain networks when imaging navigational experiences versus actually navigating (Mellet et al. 2000).

There is one last issue to mention with both extracellular and fMRI approaches to studying navigation. Both approaches are what we term *correlational*. They indicate that a neural signal or brain region is involved, in some form, in computations important to navigation, but they do not show that these signals are *necessary* (Rosenbaum, Gilboa, and Moscovitch 2014). Given how striking neural responses to location often are in the rodent brain, it seems surprising not to think of these changes in neural activity as necessary for successful navigation. While it is the case that lesions to some of the same brain regions where we see location-specific coding often impair spatial navigation (Morris et al. 1982), this is not always the case (Ekstrom, Arnold, and Iaria 2014). We might think of a brain signal as contributing in some form to navigation but that navigation could occur without it.

How could this be? Think for example of the battery of a car. A car can still start without a battery (if it is jump-started), and the car will run just fine in this case. Similarly, a car can still go from one location to another without a muffler, although it will be noisy. So neither of these important components of a car are *necessary* for it to run. However, damage or loss of either component will result in changes in how the car runs, even though it may not be clear that either component is damaged if we happen to pass the car on a highway. Thus, we can think of brain regions that show changes in activation or changes in neural firing rate as likely contributing something important to navigation, but their necessity to navigation cannot be proven.

## Brain Lesions and Navigation

Brain damage can occur in a variety of different ways, including from stroke, from brain damage owing to a traumatic episode, from surgery to treat epilepsy or tumors, and from viral infections (Gazzaniga, Ivry, and Mangun 2014). We discuss many of these types of damage in detail in chapter 7. These patients, particularly those who suffer damage that is selective (also termed *focal*), provide a rare opportunity for better understanding deficits that might occur in navigation following certain types of brain damage. The relative absence of a brain region also allows us to make a critical inference about the potential necessity of a brain region to navigation because we are now positioned to see how the brain functions differently in the absence of that critical brain region (Sarter, Berntson, and Cacioppo 1996). It is essential, however, that we select our *control* participants in a way that accounts for other differences that might occur following brain damage, including lowered intellectual functioning. Assuming we can accomplish this, however, patients with selective brain damage offer a powerful way of examining which brain regions are most fundamental to navigation.

One of the most famous examples of how selective brain damage can inform us about behavior is the case of H.M., a patient who had parts of his hippocampi and surrounding cortex removed bilaterally to treat epilepsy (see also chapters 6 and 9). The surgery that successfully reduced the number of seizures experienced by H.M. had the unfortunate consequence of leaving him densely amnesic, unable to recover memories of events from before the surgery and severely impaired at encoding new memories (Scoville and Milner 1957). Memories from before his surgery—for example, members of the hospital staff, or evenwhere he was—were completely abolished. In addition, for decades following his surgery H.M. showed profound impairments in learning new information, such as what he had had for dinner and different people he had met over various periods of time. Thus, damage to H.M.'s hippocampi resulted in profound amnesia (Corkin 2002).

Subsequent work, however, demonstrated that patients with amnesia, like H.M., do have some intact forms of memory, including the ability to learn new motor skills as well as new facts about the world (Tulving, Hayman, and Macdonald 1991; Gabrieli et al. 1993). In contrast, patients with damage outside their hippocampus show impairments in acquiring both new motor skills and semantic memories, suggesting that other brain regions mediate these important functions (Martin and Chao 2001; Yin and Knowlton 2006). Patterns of impaired episodic memory for events but not skill learning in patients with hippocampal damage, and impaired skill learning but not episodic memory in patients with an intact hippocampus but with damage elsewhere in the brain represent a *double dissociation* (Baddeley 2003; Rosenbaum, Gilboa, and Moscovitch 2014). In other words, damage to different brain regions results in different patterns of effects on memory, suggesting that different brain circuits handle, at least in part, these various components of behavior. Together, these findings argued for the so-called multiple memory systems perspective—that different brain regions were responsible for different aspects of memory (Milner, Squire, and Kandel 1998).

The history with regard to studying the effects of brain damage on navigation is a little more complicated, at least with regard to the hippocampus. H.M., although densely amnesic, showed some intact navigational abilities (Bohbot and Corkin 2007). Other patients with similar patterns of damage to the hippocampus and related regions within the medial temporal lobes who are also densely amnesic also show intact navigation—for example, in neighborhoods that were familiar to them for many years (Teng and Squire 1999; Rosenbaum et al. 2000). We will discuss this issue in chapter 9 in some detail and thus will leave more in-depth consideration of this issue until later. Again, though, situations in which brain lesions severely impair some processes, like episodic memory, but leave at least some aspects of spatial navigation intact also provide important insight into how the two behaviors might depend, to some extent, on different brain circuits. Thus, throughout this book we will turn to the study of brain lesions as a valuable technique for understanding the necessity of a brain region to a cognitive process, particularly when we compare and dissociate different cognitive processes and patterns of brain damage from each other.

Like many topics of study in science, however, the effects of brain lesions are not typically as straightforward as "one brain region, one necessary cognitive function" (Rosenbaum, Gilboa, and Moscovitch 2014). This is particularly true with the complex set of intertwined processes that make up spatial navigation, an issue we will discuss in depth in chapters 4 and 8. For example, neurologists and physicians have appreciated for some time that lesions often give rise to widespread neural changes well outside of the area of damage—a process called *diaschisis*, which was first identified in 1902 by Constantin von Monakow (for a review, see Finger et al. 2004). Indeed, new techniques for studying the brain as an interconnected network—rather than a set of modules operating in relative isolation—have significantly changed how we view both localized brain function and the specificity of lesions to cognitive function, an issue we will consider in detail in chapters 8 and 9. These include the idea of looking at connectivity and functional interactions across the brain, rather than activity isolated within brain regions (Sporns 2011; Carrera and Tononi 2014).

That said, the idea of neural specialization—that certain brain regions perform specific cognitive functions and not others—forms a core of much of the research in cognitive neuroscience since the first work by Scoville and Milner on H.M. Indeed, there is plenty of evidence to support the idea of neural specialization with regard to navigation, much of which we will review in detail throughout this book, starting in chapter 3. We believe that the correct answer is probably somewhere between: that there is certainly neural specialization in different brain regions that predisposes them to certain cognitive functions, but that at the same time the human brain is a fundamentally flexible, adaptive organ, and different brain regions can alter their function, dependent on the demands of the task. Throughout this book, we have tried to strike a balance, as much as possible, between a historic focus in spatial navigation on specialized function with an emerging new consensus that the brain acts in many ways more as an interconnected yet specialized network than as a set of disconnected modules operating in relative isolation.

## Summary

Although we often view ourselves as poor navigators, there are numerous counterexamples among our species, three of which we discuss in detail. As our examples demonstrated, the Puluwat sailors, Worsley, and the Inuit used mechanisms to navigate that are present within all typical humans: the path integration system and the cognitive map. Although these three examples are helpful in terms of understanding the basis of how we might navigate, the study of human spatial navigation is a scientific discipline rooted in methods that span numerous different areas, including psychology, cognitive neuroscience, geographical science, and environmental psychology. We focus on methods for studying human spatial navigation, particularly its neural basis, that include invasive electrophysiological recordings, functional and structural magnetic resonance imaging, studies of patients with focal lesions that affect their ability to navigate, and techniques that allow us to consider the brain as an interconnected, dynamic network. As we begin our voyage into the study of human spatial navigation, we invite you to keep an open mind regarding our navigational abilities and the notion that brain systems present in all of us allow these unique skills to emerge.

## CHAPTER 2

# BEHAVIORAL STUDIES OF HUMAN SPATIAL NAVIGATION

Two core components that comprise how we navigate space, as discussed in the previous chapter, are our path integration system and our memory for the locations of spatial landmarks, termed the *cognitive map*. We illustrated this idea in the last chapter by discussing the Puluwat sailors and the journey of the *James Caird* led by the skilled navigator Frank Worsley, both of whom used a combination of path integration and detailed knowledge about the position of islands and other landmarks to estimate their progress toward their goal. Our job in this chapter is to try to understand these core components through the scientific study of navigation. We will turn primarily to tools in the field of cognitive psychology to accomplish this, but also include discussion of knowledge we have gained from the fields of environmental psychology and geographical science.

Before we begin our discussion of some of the classic studies that have helped us understand how we navigate, it is critical to explain some concepts that are fundamental to experimental testing in behavioral psychology. The first regards how we go about measuring and understanding spatial navigation in the first place. To understand any psychological process, we require tools that allow us to observe and measure underlying mental processes. How can we understand the mental processes important to spatial navigation? Just like any other area of psychology, we require measures that specifically tap into processes related to our area of interest with hopefully minimal contamination from processes not directly involved.

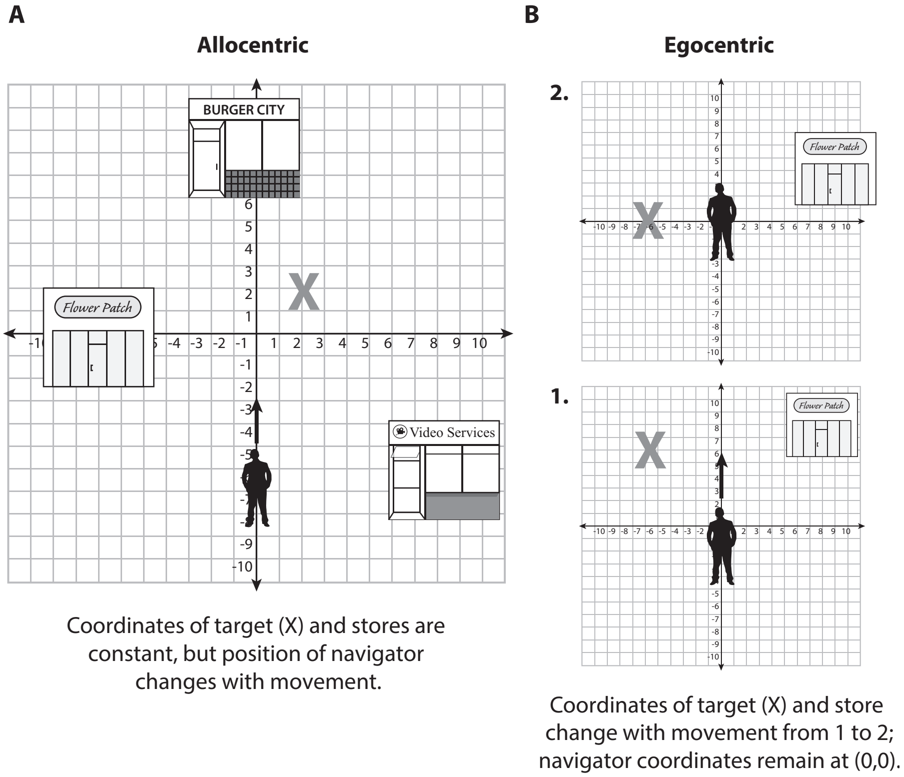
In the case of navigation, however, we can hypothesize that many different cognitive processes might be important. In this sense, navigation is not *process pure* but involves a range of different cognitive processes that are likely to be dynamic and multisensory, depending on what is happening while we are navigating. We can think of the idea of *navigation* as involving a variety of different forms of information during self-movement that may lead to different cognitive strategies useful for ultimately finding our way to a given destination. This information is not only visual but also vestibular, proprioceptive, somatosensory, and auditory, and thus navigation is an inherently multisensory process. Although humans have a bias toward using visual information, information from our other senses is often processed as well, and they may all contribute (either in a combined fashion or independently) to extracting information about the environment (for example, its shape and scale), the location of items, and our own position.

While navigating, we become familiar with an environment and acquire knowledge about it, thereby extracting information from it and storing this information in our memory so that we can recall it later for a variety of purposes. In this way, navigation is a *dynamic* process. The process, which involves attention and memory among other cognitive capacities, can be quite rapid, particularly if we can view useful features, like landmarks, by scanning the environment (Ishikawa and Montello 2006; Wolbers and Wiener 2014); it can also take time, depending on the size of the environment (Siegel and White 1975). We will focus in particular on two fundamental forms of representation that will likely be important as we navigate. The first is our representation of where we currently are relative to our self in our environment, termed our *egocentric representation*, which, in turn, is heavily influenced by our path integration system. Egocentric navigation is dependent on the position of the observer—for example, when I leave my house, I turn right, walk two blocks, and turn left to reach to my goal. One issue with an egocentric representation, however, is that it is dependent on the navigator's current position, which will change during movement and may be difficult to track. In this way, *allocentric representation*, referenced to objects "other than the navigator" (*allo* means "other," so "centered on other coordinates"), provides a stable reference frame. Allocentric navigation, much like a cognitive map, involves using information about the positions of multiple landmarks relative to each other to reach a goal. An example would be that our goal is located one-third of the way between two buildings and approximately 30 meters south of a third building (Klatzky 1998). We detail the nature of an egocentric and an allocentric representation in figure 2.1. The dynamic nature of navigation is helpful to keep in mind when we consider how exactly we can determine experimentally what factors are important to how we navigate.

## Tools of the Psychologist and Geographer: Measuring Direction and Distance

How do we measure spatial knowledge acquired during navigation in the first place? Perhaps one of the most intuitive measures is what we term our *sense of direction*: Can we accurately point to an unseen object from where we are? This task, which we term the *scene- and orientation-dependent pointing* (SOP) task, involves several basic cognitive processes central to navigation: knowledge about our current orientation and our memory for the location of another object relative to our current position. For example, to point to the location of your kitchen, you need to know how you are oriented (either relative to your kitchen or some other object) and where exactly your kitchen is relative to you (or other objects in the room). The SOP task primarily measures our knowledge of our *egocentric* position within an environment (figure 2.2), although it can also involve some relative knowledge about other objects that can help us orient and remember where our kitchen is (Ekstrom, Arnold, and Iaria 2014).

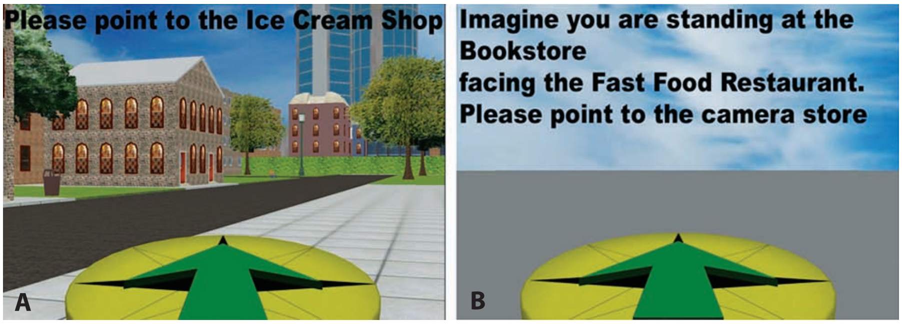
*Directional knowledge*, or being able to indicate where something is located by pointing to it, is important and fundamental to navigating correctly. If we want to walk a mile to the nearest supermarket and we start in the wrong direction (for example, heading north rather than south), we will double the distance we need to



Coordinates of target (X) and stores are constant, but position of navigator changes with movement.

Coordinates of target (X) and store change with movement from 1 to 2; navigator coordinates remain at (0,0).

**FIGURE 2.1.** Allocentric versus egocentric coordinates. A. An allocentric coordinate system. We represent the target relative to multiple landmarks whose position is stable during navigation. In contrast, the position of the navigator changes continuously with movement. B. An egocentric coordinate system. In contrast to the allocentric coordinate system, the positions of all landmarks and targets change continuously but the position of the navigator is “locked” to the origin and thus remains constant with movement. Reproduced from Ekstrom and Isham 2017.



Please point to the Ice Cream Shop

Imagine you are standing at the Bookstore facing the Fast Food Restaurant. Please point to the camera store

**FIGURE 2.2.** Ways to assay spatial directional knowledge. A. The scene- and orientation-dependent pointing (SOP) task. Participants point to a location while oriented from their current location. B. The judgments of relative direction (JRD) task. Participants imagine themselves at one position, facing a second location, and point to a third location. Reproduced from Ekstrom et al. 2014.

walk to our location. In fact, *disorientation*, which is a lack of knowledge of our position relative to other objects in our surroundings, can lead to significant confusion and in some extreme cases, death. For example, imagine we are in the wilderness and are unable to find our way back to our car; not only that, but we continue to walk in circles and cannot find a food source. In fact, disorientation is often a hallmark of certain forms of stroke, an issue we will consider in depth in chapter 7, when we consider clinical disorders that affect navigation. Overall, it is easy to see that our sense of direction is fundamental to how we orient ourselves in space and navigate.

A slightly more complicated way of assessing our sense of direction involves our memory for the relative directions of objects to each other, termed *judgments of relative direction* (JRD) (Rieser 1989; see figure 2.2). Instead of asking us to point to objects while we are in that environment, which is strongly influenced by our current sense of orientation, we can ask people to imagine themselves in specific positions within the environment and then determine how accurately they point to objects. Importantly, this can involve either locations that have previously been experienced (for example, imagine you are sitting in your bedroom, facing your bathroom; now, point to your closet) or entirely new ones (imagine you are standing in the middle of a highway close to your house facing north; now, point to your house). In this case, we tap into a more *allocentrically* based type of knowledge in that we need to know the positions of objects relative to each other to correctly perform this task.

While direction knowledge is important, particularly of our egocentric position, distance knowledge is also important. If our car breaks down on the highway, it is critically important to have some idea of how far it will be to walk to the nearest service station. Distance knowledge also forms a critical part of our mental estimate of allocentric positions of objects in an environment. In the case of the Puluwat sailors, errors in their knowledge of the relative distance between an island they have just passed and an upcoming one can lead to errors in predicting the next turn they might need to make based on future landmarks.

How can we measure direction and distance knowledge? In psychological experiments, there are many ways to estimate distance, but one approach is to ask people to compare distances. Which is farther: the distance between our house and our office or the distance between our house and the closest supermarket? In this instance, we don't necessarily need to know anything about relative direction; we can simply imagine a route to either of the two destinations, and based on our past experience, derive which one is closer. We can term these types of tasks *judgments of relative distance* or *distance estimations*.

Of course, it is often useful to combine both directional and distance knowledge, and perhaps the easiest way to do this involves sketching a map (Lynch 1960), perhaps the purest measure of an *allocentric* representation (Ekstrom, Arnold, and Iaria 2014). While maps can involve a range of different details and spatial scales (both of which we will discuss in some depth shortly), a map, at a simple level, is a rendering of positions of objects within an environment. The ideal map will involve an accurate depiction, albeit on a smaller scale, of where in space different pieces of furniture are located in our living room, for example. A less accurate map may fail to correctly depict the absolute positions of each piece of furniture in our house but may still capture the relative positions—for example, that a couch is closer to a coffee table than a TV but not the exact distance. In this way, simply having people draw maps can be enormously useful in understanding their knowledge of both direction and distance.

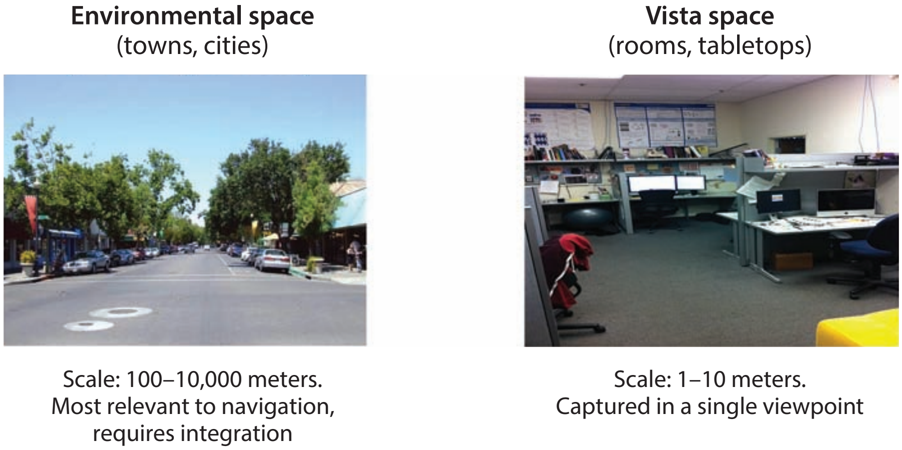
We can consider many different ways in which to analyze a map. One of these would be to compare the positions of each of the different objects that have been drawn on the map, such as critical landmarks, and see how far off they are from the "true" position. This method, termed *bidimensional regression* (Tobler 1994; Friedman and Kohler 2003), takes into consideration how far off the reported points are from the "true" positions, similar to how one might perform a regression on a single dimension. Another way to consider maps is to instead examine the amount of detail that they contain. For example, amnesic patients who have damage to their medial temporal lobe, like the patient H.M., who was discussed in chapter 1, can draw maps that capture some of the spatial relationships in their environment (Rosenbaum 2000). However, many "details" are often missing, and thus methods that take into consideration missing elements in maps are also very useful (Herdman et al. 2015), an issue we will consider in detail in chapter 9.

Of course, all of the methods we have outlined so far focus on tests either interspersed with or following episodes of navigation. Ideally, we would also like to get an idea of the accuracy of one's knowledge during the process of navigation. There are a number of methods by which to analyze the accuracy of one's routes. Perhaps the most straightforward is a method called *excess path*, which considers the deviation in the distances traveled from the optimal, most direct route possible. To compute excess path, one calculates the straightest path between two locations and then calculates how far off the subject was from the ideal (Newman et al. 2007). Other methods involve measuring how much time was spent closest to the correct location when that target is no longer present (Morris et al. 1982) or having subjects point out the most direct path (not including moving around obstacles) to a target while standing nearby (Thorndyke and Hayes-Roth 1982). For a more detailed discussion of methods for analyzing distance, see Montello (1991).

## Scales of Space: Zooming In and Out

Before we begin our discussion of some of the most illustrative studies on human spatial navigation, it is useful to consider an issue we often overlook when studying spatial navigation: *spatial scale*. Close your eyes and imagine rising above yourself; you may picture the objects that surround you immediately, such as a chair next to the couch that you are sitting on and, as we zoom out farther, your kitchen. As you zoom out farther, you may picture locations outside your house, such as your garden and the street in front of your house. Zooming out farther still, you may picture your favorite neighborhood coffee shop and eventually, nearby towns, and, eventually even nearby states or countries. This mental example also illustrates an important point about *spatial scale*: how we picture what is around us differs fairly dramatically according to how far away things are from us (Montello 1993; Wolbers and Wiener 2014).

When discussing the Puluwat, we focused largely on what researchers frequently term *environmental space*, space that requires navigating over several kilometers to ascertain its nature (such as the distance between islands; see figure 1.3).



**Environmental space**
(towns, cities)

**Vista space**
(rooms, tabletops)

Scale: 100–10,000 meters.
Most relevant to navigation,
requires integration

Scale: 1–10 meters.
Captured in a single viewpoint

**FIGURE 2.3.** Some examples of different spatial scales we encounter when navigating.

Environmental space is simply too big to view from a single viewpoint. This is different from the kind of space we typically experience in rooms and in fact in most cognitive psychology experiments: one in which the layout of the environment can be viewed from a single vantage point. We term this type of space, from which we can perceive important features like the geometry and landmarks from a small number of viewpoints, *vista space* (figure 2.3). This type of space is quite different from environmental spaces for two critical reasons.

First, environmental space requires remembering and integrating information over multiple viewpoints as we are moving. For example, when we arrive at a college campus for the first time, we may turn our head and observe buildings, trees, and other stable landmarks as we walk from one place to another. As we pass each one, we need to try to remember them ("I passed a distinctive tree five minutes ago") and integrate that with what we are currently seeing. Second, environmental space also requires extrapolating multiple paths over time. When we return to the campus, it is helpful to remember what we encountered last time because it can provide insight into more general properties of the environment. For example, knowing a shortcut between buildings is not only useful but also revealing about how these buildings are arranged relative to each other. These properties of environmental space are different from a vista space, which we can learn quite a lot about simply by remaining stationary and looking around for even brief periods of time.

## Experimental Design and Control of Unwanted Variables When Studying Navigation

As we begin our consideration of studies of human spatial navigation, an important issue to address is how we might isolate what we are interested in studying. Recall that navigation itself is dynamic, involving different cognitive processes at different times. How can we possibly isolate just a single process during navigation? Considering a different discipline, the study of human memory (another complicated topic), can be helpful in understanding how we might approach navigation (see chapter 9). For example, if we want to understand how we organize lists of words in memory, ideally we want to minimize the fact that some words are easier to remember than others, some orders of words may be easier to remember than others, and some people can remember more words than others. We can do this by employing some useful tools in cognitive psychology called *normalization*, *counterbalancing*, and *randomization*.

*Normalization* refers to the idea that if we show words to a group of subjects, we want to be sure that we are showing them words that are generally not overly difficult to read and pronounce. One way of doing this is by giving a separate group of participants words to rate in terms of how similar they are to each other and how frequently they are used in the English language. This will allow us to determine what types of words we might want to choose. For example, we might want to avoid very frequent "easy" words like *go* and *to* or infrequent words like *rutabaga*. Instead, we might favor words that are neither too common nor too rare, like *princess*. One example of a selection of normalized words is the Toronto noun pool, which allows cognitive psychologists to design experiments using words that have a balanced usage within the English language (Friendly et al. 1982).

In the case of spatial navigation, ideally we want to choose spatial environments that are neither too difficult nor too easy to remember and that participants don't have differing degrees of knowledge about or facility with before starting the experiment. For example, if we were to study a college campus with a peculiar design, we might conclude that subjects are bad at map drawing when in fact it was the environment itself that was simply challenging to remember. In practice, though, normalization, which we could accomplish by having participants navigate hundreds of environments and determining how they learn about them, is impractical, to say the least. Thus, we aim to choose environments that appear neither too complex nor too simple to learn.

Let's say we are conducting an experiment and are concerned that the environment we have chosen is somewhat complicated—for example, the city of Boston (notorious for its meandering streets that seem to defy the rules of Euclidean geometry). We might find another city—for example, Los Angeles—that has a more grid-like arrangement. The problem here is that this might seem too easy to learn. Here, we could use the important tool called *counterbalancing*: we could have one-half of the participants navigate both cities and assess their spatial knowledge but then have the second group learn the cities in the opposite order (that is, Los Angeles and then Boston). This counterbalancing helps us better control for the fact that the order or difficulty of some stimuli we encounter might affect how we learn them.

How do we deal with the problem that some people will simply be better at navigating than others? Just as some people learn lists of words faster than others, there is a rich literature suggesting that some people learn spatial environments more quickly and efficiently than others (Ishikawa and Montello 2006); these are termed *individual differences*. We may be interested in this topic in its own right (an issue we will discuss in more detail in chapter 6); however, we may also want to determine how the *typical* person navigates rather than focusing on individual differences. Here, we turn to another crucial tool in cognitive psychology (and science more generally) called *randomization*. If we want to understand the properties of how humans navigate, we ideally want to sample the navigational skills of as many people as possible. While in practice we can't test every human being, by *randomly* selecting the individuals we test we can better approximate how people more generally might navigate. If we were to sample only from Puluwat, we would have an inflated sense of our navigational abilities! Thus, we sample a range of different navigational abilities from our subjects.

A final important issue in experimental design is the idea of experimental and control conditions. This is a particularly critical tool for isolating specific cognitive processes during navigation. For example, an experiment in which we repeat each word in a list three times versus only once will allow us to assess the effects of repetition on memory, providing us with the finding that repeating words generally improves memory. In the case of navigation, we might want to study the effects of exposure to a spatial environment, so ideally we would want to compare people who had spent different amounts of time exploring an environment. Control comparisons are also very important: Is there a condition in which there is zero exposure that is still meaningful? In practice, with navigation in particular, control comparisons can be difficult because there are so many variables we might want to account for. An example of a simple control to compare the effects of walking on spatial knowledge might be to have a group that does not walk in the environment at all but simply views it passively while being moved around.

## Early and Influential Studies on Human Spatial Navigation

Armed with some important tools for understanding human behavior, we are now ready to consider some experiments on human spatial navigation. It is worth noting that not all of these studies, for reasons that will become obvious, have been able to deal with all of the experimental design issues that we mentioned. Thus, as we consider such studies it will be useful to keep in mind some of these limitations and how we might deal with them in future studies. What we will focus on as much as possible is general principles that we can learn from these studies, with some of the limitations in what we can learn inherent in the design.

One early and particularly influential study looked at spatial knowledge acquired from a city in Venezuela for which few (if any) maps existed (because the city had just been built), providing an opportunity to study navigation "in the wild." In particular, this provided a rare opportunity to study how people learn about an environmental space by navigating (riding in a bus or driving a car), without any strong bias from having seen the city's layout via a map. The city, Ciudad Guyana, was not arranged in a clear geometric pattern, being centered around a curving river with several roads branching off in different directions. This allowed for a situation in which the city would not be too easy to learn but was also of a small enough scale (about 20 kilometers from one end to the other) that it could still be learned with sufficient experience. In this way, the study's author attempted to deal with the issue of normalization (Appleyard 1970).

In the study, Appleyard tested people on how long they had lived in Ciudad Guyana to attempt to understand the impact of exposure to the environment on spatial learning. In this way, Ciudad Guyana also offered a rare opportunity to determine what type of spatial knowledge could be acquired depending on how long people were in the environment. This provided one of Appleyard's primary comparisons of interest: How does exposure to the environment modulate spatial knowledge? In this case, Appleyard compared people who had been in Ciudad Guyana for less than a year with those who had lived there for over five years. He also compared people whose primary means of transport was taking a bus versus driving.

Finally, Appleyard's measure of spatial memory involved map drawing accuracy (what psychologists term the *dependent measure*). To obtain these data, Appleyard recruited 75 men and women to draw maps of Ciudad Guyana. He also asked them how long they had lived there and what their primary means of transportation was so that he could compare these independent variables. Appleyard assessed not only the accuracy of each person's map but also whether characteristics such as distances and directions were accurate in an absolute sense or simply relatively correct (termed *metrically* versus *topologically correct*). He also looked at factors like whether the map was accurate locally (for example, details within a kilometer radius) versus whether the map was accurate globally (were streets and landmarks that were far away from each other correctly placed?).

Although Appleyard's study, now over 50 years old, was largely qualitative (meaning it categorized most map drawing errors and tendencies rather than quantified them), his seminal study provided critical information about how subjects learned to navigate their city. While there was a range of different errors in maps that people drew, everyone in the study possessed a basic knowledge of how to position roads, rivers, train tracks, stores, schools, and other landmarks relative to each other—in many cases, with a high degree of accuracy. While people often made errors, their maps clearly displayed a detailed topological knowledge of objects and, in some cases, accurate knowledge of the actual metric distances between locations.

Another important finding from Appleyard's study was that *how* people experienced the environment, either via riding a bus or driving, influenced how they structured their maps. In particular, those who drove generally showed more detailed maps and greater knowledge about the relative locations of roads and landmarks in the city compared to those who rode the bus. This suggests that actively navigating an environment, which would likely involve reasoning and making errors while experiencing the environment, is critical for learning. In contrast, riding a bus, which would provide only limited information about the distance between locations (based on how long it might take to travel between them), generally provided impoverished spatial knowledge.

## Navigation in the Lab: Controlling Variables

While we can learn a lot from studies of how individuals navigate cities like Ciudad Guyana, there are also clear limitations with these types of studies. For one, Appleyard had no control over the amount of exposure any individual had to the city, an important issue we consider in more depth in chapter 9. Simply based on how much time these individuals spent in one part of a city, one could expect very different levels of knowledge. Additionally, Appleyard had no control over the paths or roads that participants took while going about navigating Ciudad Guyana on a daily basis. Thus, in practice, some participants could have traversed the city hundreds of times on different routes, while others would simply walk or drive the same path within their neighborhood repeatedly. Finally, Appleyard had little control over the strategies that an individual might use to navigate the city. One might rely completely on another person to drive her across the city, another might use signs or ask someone for directions, a third might navigate with a compass, and a fifth might rely merely on his "sense of direction." All of these issues thus emphasize the importance of more controlled studies performed in the laboratory, where we can better equate exposure and other variables across participants.

Perhaps one of the best examples of such a study, which involves path integration, comes from something called the *triangle completion task,* pioneered by Jack Loomis and his colleagues in the 1990s (Loomis et al. 1993; Klatzky et al. 1998). In this task, participants are blindfolded and guided along two legs of a triangle; they must then estimate the angle and distance they need to travel to complete the triangle (figure 2.4). Importantly, because participants were doing this with no visual information, they had to base their estimate of how far they had traveled and what angle they had turned solely on their internal estimates. Remarkably, participants' trajectories correlated strongly with the ideal path (directly back to the origin), both in terms of linear and angular distance. The study did note, however, that participants tended to underestimate both the angle they needed to turn and the distance they needed to walk (figure 2.5). So for example, instead of turning 30 degrees back to the origin, a participant might instead turn only 20 degrees. Instead of walking 6 meters back, a participant might walk only 5 meters, on average.

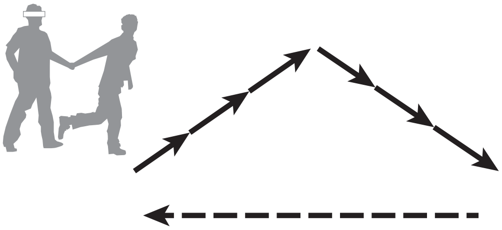


**FIGURE 2.4.** The classic triangle completion task first employed by Jack Loomis and colleagues (1993).

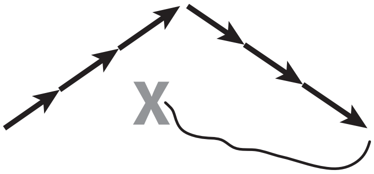


**FIGURE 2.5.** Errors in the triangle completion task. A schematic rendering of one participant's path in the triangle completion task, reproduced from Loomis et al. (1993). Note that participants tend to undershoot both the direction and distance they must turn in the triangle completion task.

You might think that even blindfolded, it could still be possible that participants were using visual cues in some form. We have all played with blindfolds before, and whenever we can see any shades of light, we are always happy to use this to our advantage. However, Loomis et al. also tested a separate group of participants who in this case were *congenitally blind*. Given how much most of us rely on our vision to navigate, we might wonder how individuals who have never used their visual system might be able to navigate at all. Yet the striking finding of the Loomis et al. study was that blind individuals performed the triangle completion task almost as well, if not better in some cases, than blindfolded sighted individuals. The Loomis et al. experiment thus illustrates two important components of path integration: it is a system present in all of us that allows us to track both position and direction with little training, and it can work in the complete absence of any visual cues.

## How Good Is Our Path Integration System in Practice?

As we discussed in chapter 1, the Puluwat sailors are quite good at estimating both their bearing and speed. However, they use many other sources of information, including visual landmarks (for example, seeing other islands, either directly or via seabirds) and the celestial compass. While their path integration system is certainly part of estimating this information, we might expect our ability to keep track of turns and distance traveled to be somewhat error-prone. If our path integration system were so good, why would we even need to use landmarks at all to navigate?

As it turns out, studies that have investigated our path integration system in natural environments suggest that, indeed, it is prone to error. One study by Souman et al. (2009) transported willing but untrained subjects to the Sahara Desert. Amazingly, participants agreed to wear blindfolds and walk distances up to one kilometer. Most participants, at about 100 meters or so, began to double back and walk in circles. Just as in the Loomis et al. study we discussed earlier, in which participants tended to underestimate the degree and distance they needed to turn to complete a triangle, participants tended to underestimate the amount they needed to adjust to continue on a straight path and tended to slowly turn. Thus, over time, participants made small errors in their angular heading that eventually resulted in them turning in circles.

How do we correct these errors in our path integration system? As primates, we possess a visual system with unparalleled high-resolution visual capacity compared to most other species, which we discuss in detail in chapter 4. Because the average person can see objects at a distance of approximately 4.7 kilometers when level with the horizon (Young and Kattawar 1998), our visual system provides a powerful way of updating our path integration system. In the same study by Souman et al. (2009) involving navigating in the desert, participants also navigated in a condition in which they were not blindfolded and thus were free to use mountains and other natural features of the Saharan landscape to navigate. In this case, they no longer walked in circles and could navigate quite directly using visual cues such as landmarks. Together, these findings show that we use external cues, as detected by our visual system, to correct for errors in our internal path integration system, similar to how the Puluwat estimate distances internally and externally.

On the other hand, the example of the naive desert navigators in the Souman et al. study did not require a cognitive or cartographic map at all. These individuals either attempted to maintain a straight route when blindfolded (and failed miserably!) or, when without a blindfold, used the mountain backdrop to navigate. This latter form of navigation (using visual cues to navigate), which we discussed earlier with the example of the Puluwat using backsighting to begin an ocean journey, is what we call *piloting*. When piloting, we simply need to move toward or away from a landmark, like a mountain. As the mountain gets bigger in our visual field, we know that we are closer to the landmark. Piloting (also referred to as a *stimulus-response strategy* or *response-strategy*) does not require a map specifically or any coordinate system like an egocentric or allocentric reference frame, just a prominent visual feature that serves as a stimulus to move toward (Wolbers and Wiener 2014; Mou and Wang 2015).

## Orientation Matters: Knowing That North Is Up

As our previous discussion helps make clear, walking a straight path is advantageous for our survival because this allows us a way of estimating our path back. But as we might imagine, the paths that we take when we navigate also play a role in influencing how we structure space in the first place. Now, imagine that we always walk the same route to work every morning. It will be very easy for us to imagine the position of buildings relative to how we have walked. Imagining walking a new path—for example, one that is at a different angle than one we typically take to get to a destination. This will be more difficult. In this way, we often have a preferred orientation in which we appear to store and remember spaces that we navigate (Shelton and McNamara 2001).

Studies by Tim McNamara and others have demonstrated, again and again, that both the original viewpoint from which we experience a spatial layout and the geometry of the environment strongly influence how we retrieve spatial information about that environment. In one example widely replicated across different experiments, Diwadkar and McNamara (1997) had participants study an array of objects on a tabletop from a single viewpoint. They then viewed pictures of the objects from the same viewpoint versus different viewpoints. The participants' task was to indicate whether the picture they saw indicated the "true" layout or a different arrangement of objects. Diwadkar and McNamara found that the time it took participants to respond increased linearly as a function of distance from the original studied viewpoint (Diwadkar and McNamara 1997). These findings suggest that the original viewpoint at which we experience an array strongly biases the ease with which we can access a representation (see also Shelton and McNamara 2001 for similar findings in room-size environments).

In a similar vein, the surrounding environment also biases how we access spatial representations. In one study, for example, Mou and McNamara (2002) found that when participants performed the judgments of relative direction task (as earlier, "imagine you are sitting in your bedroom, facing your bathroom; now, point to your closet"), they were significantly faster and more accurate when aligned with

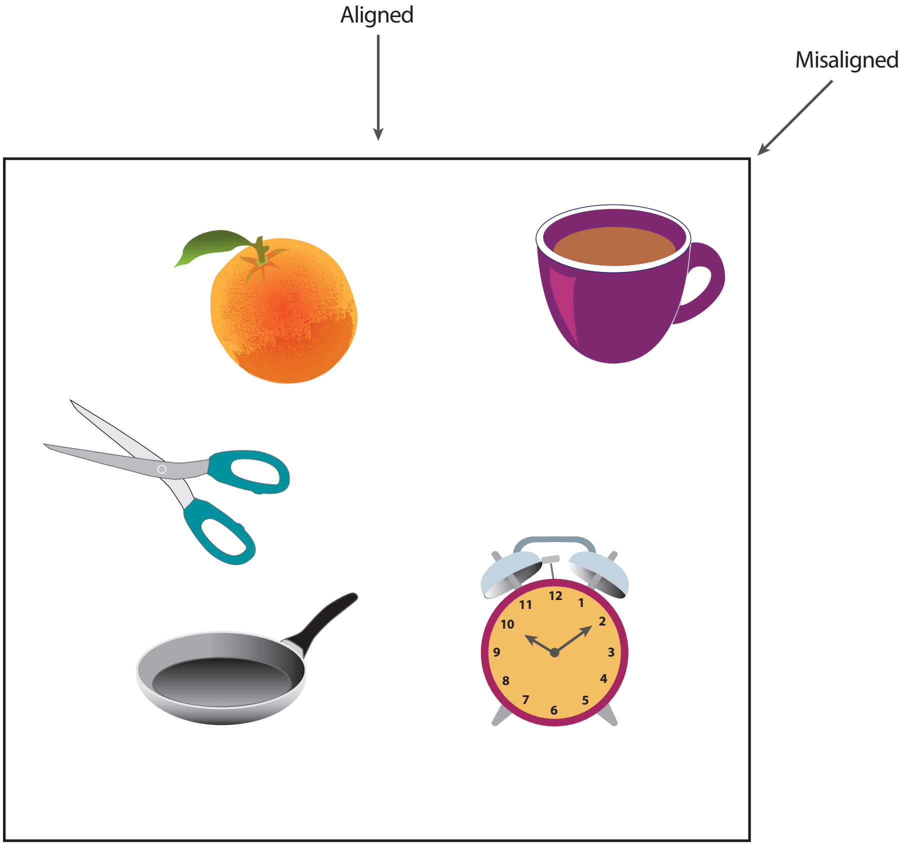


**FIGURE 2.6.** Alignment effects in experiments in room-size environments containing objects.

the axes defined by objects than when misaligned (figure 2.6). Specifically, there was a strong advantage for retrieving objects arranged on a table when participants were asked to retrieve these objects in a manner that aligned with the axes defined by the room, the table, or the objects themselves compared to a manner that was misaligned, although these studies often typically also note advantages for the learned view. This in turn led to what is often referred to as *sawtooth* functions in the literature: accessing spatial layouts aligned with the dominant axes defined by the room or objects was faster (that is, 0, 90, 180) than accessing misaligned layouts (45, 135, and so on; figure 2.7).

A reasonable question, though, given our earlier discussion about scales of space, is whether these alignment effects are a peculiar result of small-scale environments. One might easily imagine that for a room or a table-size environment, the surrounding structure and even the arrangement of the objects themselves might heavily influence how we encode and retrieve this information in the first place. This could arise simply owing to the fact that we learn about squares and rectangles from an early age and using this information makes it much easier to remember things. Could it be that viewpoint and alignment effects are simply an artifact of the size of the environment we test in?

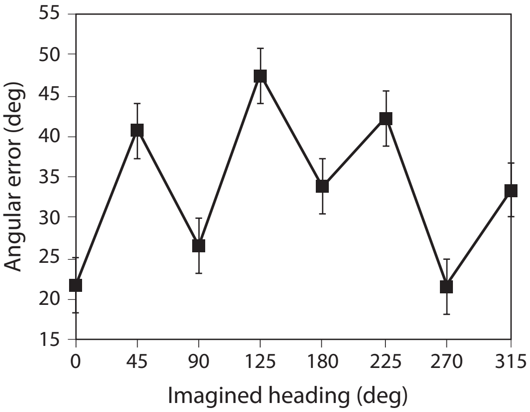


**FIGURE 2.7.** Alignment effects and the "sawtooth" function. Reproduction from Mou et al. (2002) of typical sawtooth alignment effects produced when pointing either aligned (0, 90, 180) or misaligned (45, 135, and so on) from an imagined heading.

Testing similar issues in large-scale environments suggests that the answer is no, although there are some qualifications to this issue. In one study, McNamara et al. had participants navigate a park in downtown Nashville (McNamara, Rump, and Werner 2003). The park was centered around a prominent landmark known as the Parthenon building, with some surrounding roads that helped to define the park's generally rectangular shape (figure 2.8). The park also contained a lake and parking area that were not clearly aligned with these axes. Participants walked paths that were both aligned and misaligned with these rectangular axes; subsequently, during testing with the JRD task, participants who had walked the misaligned path showed higher error than those who had walked the aligned path. In addition, both groups of participants had greater success when pointing in a manner aligned with rectangular axes as opposed to misaligned. The only somewhat surprising finding was that participants pointed more accurately when aligned with the lake (at about 135 degrees). Together, these findings suggest that while alignment effects are also prevalent in large-scale spaces, other landmarks may override these in some cases.

Orientation and alignment effects are so strong that even viewing a map that indicates which direction is north may bias one toward remembering some directions better than others. In an experiment by Frankenstein et al. (2012), residents of Tubingen viewed scenes from their home city on a computer. Once participants indicated that they knew the scene and were oriented, a text prompt indicated a location within the city that they should point to. Consistently, participants pointed most accurately when oriented northward, with pointing accuracy significantly lower for all other cardinal directions (east, south, and west). Thus, simply having viewed a map or encoded a city based on north-south-east-west cardinal directions may heavily bias and distort how we encode and retrieve actual spatial locations. In fact, some have suggested that "north is up" is such a powerful organizing principle that we use landmarks like mountains to determine "north" (Brunye et al. 2012). It is likely, however, that the "north is up" effect is more of a bias to use cardinal directions than to prefer a southern route (Brunye et al. 2015).

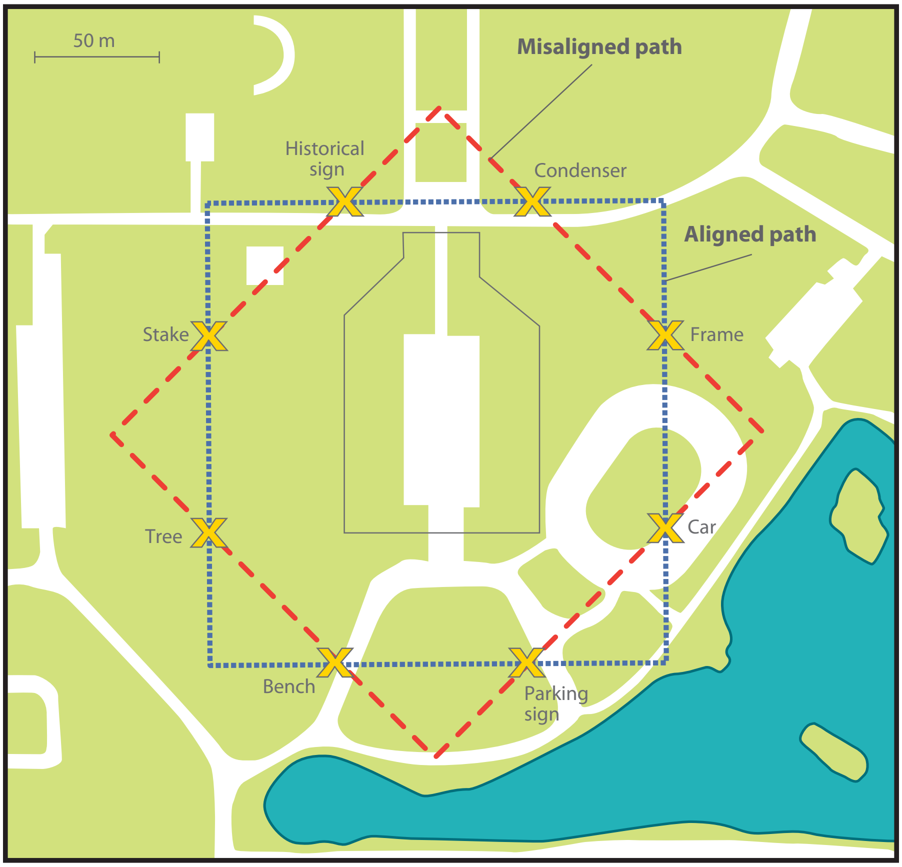


**FIGURE 2.8.** Alignment effects in real-world navigation. Example of the park used in McNamara et al. (2003). Note that alignment effects were also present in the large-size park tested here.

One potential criticism that we could level at orientation and viewpoint effects, as acknowledged at some points in the literature (Diwadkar and McNamara 1997), is that these effects are likely to be highly experience dependent. Recall the example mentioned earlier regarding walking the same route to work every day. It is not surprising that we will be better at remembering locations consistent with how we typically walk because we will have the most opportunity to encode this information in memory in the first place. On the other hand, when we try to imagine viewpoints we don't typically experience—for example, walking off the path—we will have little experience with this perspective and thus might expect to do significantly worse. Researchers of memory term these effects *encoding specificity effects* to indicate the typical advantage for remembering information that contains more cues about the original encoding events versus fewer (Tulving and Thomson 1973). While encoding specificity may be one way of explaining viewpoint and orientation specificity, it cannot more generally explain the pointing advantage of alignment to the surrounding geometry, which we will consider in more detail next.

## How We Represent Space: Egocentric versus Allocentric Representations

As we have discussed so far, orientation plays a powerful role in how we remember locations. Just having viewed a scene from a specific angle makes it easy to subsequently remember that view compared to others. We refer to these effects as *egocentric* because these cues are referenced to a viewpoint we have experienced previously. In contrast, environmental cues, such as the surrounding geometry defined by roads or a lake at a park, although not dependent on a specific viewpoint, are also powerful organizational features. We refer to these as landmarks and other cues that can help us form an *allocentric* representation. While it is clear that both of these ways of representing our environment play a role in our spatial memory, a logical question might be to what extent one versus the other is important in how we remember spatial information.

In some situations—for example, when remembering configurations of objects within a room—egocentric representations may be particularly important (Wang and Spelke 2000; Wang and Spelke 2002). In one such study demonstrating the dominance of egocentric viewpoints, the authors had participants learn the locations of objects in a room. Participants were then blindfolded and rotated either slowly or quickly enough to induce disorientation. While knowledge of the positions of objects in the room remained high when participants remained oriented, disorientation resulted in almost complete loss of knowledge of locations of objects in the room. Even following disorientation, however, participants could accurately point to corners of the room (particularly in terms of their relative locations). These findings argue that self-orientation cues may be particularly powerful when we remember a new set of locations within a relatively small-scale environment.

Whether participants appear to rely on egocentric versus allocentric representation may emerge, in part, from how we ask participants to retrieve information in the first place. A subsequent study by Waller and Hodgson (2006), which used a similar paradigm to Wang and Spelke, showed that during the JRD task, which involved reference to external landmarks (see figure 2.2), pointing accuracy actually improved following disorientation, while SOP accuracy dropped (Waller and Hodgson 2006). Recall that in the JRD pointing task, participants made reference to least two other objects when pointing to a third (for example, imagine you are standing at the flower pot, facing the jar; now point to the coffee mug; see figure 2.2). Thus, when asking participants to respond using the relative positions of multiple objects within the environment, their pointing accuracy actually improved. This *dissociation* suggested that part of what may happen to disoriented participants is that when asked to rely on a task involving their current orientation (like the SOP task), they are unable to access any allocentric knowledge. In contrast, when solving a task like the JRD task, which explicitly asks participants to think in terms of spatial relationships of recently learned objects, they employ a more allocentric-based strategy (Burgess 2006). Thus, these data argue that participants can utilize an allocentric reference frame when reasoning about the spatial positions of objects, but when and how they do so depends to some extent on how they are queried.

Another important issue with the Wang and Spelke (2000) study regards the issue of scale of space. As we have alluded to earlier, many studies of human spatial memory involve learning arrays of objects in relatively small, regularly shaped rooms over a single trial of learning. As pointed out earlier, though, if we consider environmental space rather than vista space, utilization of an allocentric representation might be more obvious, since viewpoints cannot be used readily to solve the task. In these situations, however, given the complexity of the environment to be learned, it may take several trials for different forms of spatial knowledge to manifest. We will return to this issue when we consider testing in virtual reality.

To summarize, experiments such as those of Wang and Spelke and Diwadkar and McNamara suggest that we typically employ egocentric representations as a relatively accurate and quick way of remembering spatial information. When this information is not available, however, we may instead employ allocentric representations. These representations are often coarser and therefore less accurate, even if they give us access to knowledge outside our immediate viewpoint. Thus, findings from past studies suggest that both egocentric and allocentric representation are important to how we represent our surrounding environment, but that we may favor more precise but transient egocentric representations when faced with an option between the two (Waller and Hodgson 2006).

## Theoretical Models of Human Spatial Navigation

When trying to assemble various ideas to both explain and generate new testable hypotheses, it is useful to try to put them together into a coherent theoretical model. Like many domains of cognitive psychology, there are several theoretical models that attempt to explain how we use spatial representations when we navigate. While our focus in this particular book is on the neural basis of human spatial navigation, a brief discussion of some of the influential cognitive models in human navigation is helpful for framing some of our later discussions about its neural basis (starting in chapter 3). Theoretical models of human spatial navigation can be broadly classified into two types: those that assume a hierarchy of different stages of representation and those that assume much of the relevant information for representing space during navigation occurs in parallel.

One of the more intuitive models of how we learn when we navigate assumes that formation of a cognitive map depends first on assembling all of the relevant subcomponents. Specifically, Siegel and White (1975) hypothesized that spatial representations occur in three distinct, hierarchical steps: *landmark learning*, *route knowledge*, and then finally *survey representation*. We can consider the survey representation largely akin to a cognitive map in that Siegel and White theorized that this step contained the metric relationships, like a cartographic map, necessary for navigation. The model states that egocentric route knowledge cannot occur without first learning landmarks, and a survey representation depends first on formation of egocentric route knowledge, thus assuming that spatial learning occurs in distinct stages. The model had strong roots in ideas about how children acquired spatial knowledge, which argued that one developmental phase could not happen without another happening first—for example, without orientation, allocentric knowledge could not occur (Piaget and Inhelder 1967). The model also provided a nice description of why people more familiar with an environment, like those in the Appleyard study, drew more accurate maps, which was based on the idea that they were further along in the stages of spatial knowledge acquisition.

In contrast, contemporary models of spatial navigation generally reject many of these assumptions (Poucet 1993; Montello 1998; Chrastil 2012; Ekstrom, Arnold, and Iaria 2014). Based on our previous discussions regarding egocentric and allocentric representations, it is clear that one form of spatial knowledge does not always have to precede another (Montello 1998; Ishikawa and Montello 2006; Zhang, Zherdeva, and Ekstrom 2014). One influential model by Montello (1998) argues exactly this point, suggesting that, in fact, most of these steps occur in a parallel yet noisy (error-prone) fashion. Thus, as we first learn an environment we may acquire knowledge of the names and locations of landmarks, the routes that contain some of these landmarks, and even their approximate topological (two-dimensional, sequential, allocentric) relationship. As we learn more about the environment, we gradually fine-tune all this information and develop more precise allocentric knowledge. In addition, Montello argued that participants may learn little metric knowledge unless required by the task and in comparison with other environments. For example, knowing that two landmarks are 5 meters or 5.5 meters away is probably not needed to navigate the environment, and this precision will likely develop, Montello argued, only if specifically required. While we will return to a more detailed discussion of the cognitive map in chapters 3 and 4, including its strengths, particularly from a neural perspective, and its weaknesses, it is useful to remember that one form of spatial knowledge does not have to depend on another. Instead, much of what we learn when we navigate can happen in parallel and is likely to depend heavily on what is required by the specific situation (for example, Ekstrom and Ranganath 2017).

## The New Frontier of Virtual Reality

The studies and theoretical models we have discussed so far have focused on testing participants' memory for real, large-scale cities or the arrangement of objects on a table. One limitation with testing in the real world, even from a behavioral standpoint, is that it is difficult to configure and control details of the environment, particularly for large-scale environments. When testing real-world, large-scale environments, another significant limitation is controlling exposure to the environment. For example, let's say we want to test college freshman on their knowledge of campus, as was done in one real-world navigation study (Uttal et al. 2010). It is difficult, if not impossible, to control the extent to which a participant has navigated one part of campus versus another and the extent to which one participant may have looked at a campus map versus another who uses a smartphone to navigate. Particularly given that theoretical models of navigation place a great emphasis on explaining environment familiarity, these are significant limitations with testing in the real world, which makes environments that we can configure in virtual reality very attractive.

Currently, there are several approaches to testing navigation in virtual reality that warrant our attention. Perhaps the simplest involves having participants navigate on a large-scale desktop virtual environment using a joystick (for example, Richardson, Montello, and Hegarty 1999; Newman et al. 2007; Zhang, Zherdeva, and Ekstrom 2014). These studies, like comparable real-world studies, demonstrate that participants acquire both egocentric and allocentric forms of knowledge (Zhang, Zherdeva, and Ekstrom 2014), consistent with Montello's 1998 model. In one such study, participants learned a large virtual spatial layout (~300 square meters) either by directly navigating it on a desktop computer in VR or by learning it from a map. Testing a total of five blocks of navigation and map learning interspersed with either the SOP or JRD task, the study found differential improvements in SOP and JRD pointing accuracy depending on whether participants had learned the environment from a route or a cartographic map. Specifically, map learning resulted in the fastest improvements in JRD pointing accuracy, while route learning resulted in the fastest gains in SOP pointing accuracy. Importantly, map learning resulted in fast, nonlinear improvements in JRD pointing accuracy compared to route learning (Zhang, Zherdeva, and Ekstrom 2014). Together, these data suggest that while both learning modalities affect putative egocentric (measured via the SOP task) and allocentric (measured via the JRD task) knowledge, route learning provides preferential access to egocentric knowledge and map learning provides preferential access to allocentric knowledge. The study also suggests, however, that both egocentric and allocentric forms of representations are typically involved in spatial learning, consistent with previous behavioral studies in humans (Mou et al. 2004; Waller and Hodgson 2006).

An important issue, though, when considering using virtual reality, particularly desktop VR, to study human spatial navigation, is the extent to which it can approximate similar real-world navigational experiences. This relates most directly to the issue of *transfer*, the extent to which we can naturally take information we learned in virtual reality and apply it to the same environments in the real world. In one study by Richardson et al., participants navigated a virtual version of a building and pointed to locations based on imaging them in the JRD task. Both route distance and straight line estimates of distances (estimating the most direct route between two landmarks) were correlated with both their real-world distance and angles. These findings suggested that virtual reality does mimic at least some aspects of the real world (Richardson, Montello, and Hegarty 1999).

Richardson et al., though, also found some evidence that virtual reality does not provide a perfect imitation of reality. In the same study, Richardson et al. also examined the effect of first navigating a virtual version of an environment on a desktop computer, followed by navigating a real-world version of the same environment. They compared this with a separate group who navigated a real-world version of the building first or studied a map. They found that using VR resulted in overall the worst pointing accuracy to landmarks and estimation of distance in the real version of the environment, particularly between different floors of the building. Pointing accuracy and distance estimation, however, were still well above what we would expect from chance, suggesting that participants did indeed acquire information that transferred to the real world following VR navigation.

**FIGURE 2.9.** Using VR to study human navigation. A head-mounted display provides peripheral visual input and stereoscopic vision.

One important feature missing from desktop virtual reality, as we mentioned earlier in chapter 1, is the presence of body-based cues—the combination of vestibular, proprioceptive, and somatosensory cues that we typically use to path integrate. One way to add these features to virtual reality is to have participants wear a head-mounted display (HMD) that renders a virtual environment (figure 2.9). The HMD naturally models the offset in how objects in VR hit your retina (termed *stereoscopic depth cues*) and also provides input to your peripheral visual system. Together, these provide a rich, immersive experience with depth cues that can be updated based on either joystick maniuplation or actual movement in the environment. For example, HMDs can be updated based on participant movement, either on a treadmill (figure 2.10) or in the real world. In this way, participants can experience continual visual input while they freely ambulate, providing a close approximation of real-world experiences.

One study by Waller et al. compared continuous exposure to an environment on desktop VR to navigating the same environment with an HMD with full head control and a joystick and navigating the same real-world environment. HMD exploration with full-head turning led to greater transfer than desktop VR, although real-world navigation led to the highest transfer (Waller, Hunt, and Knapp 1998), suggesting the importance of body-based cues to navigation. One possibility though is that because this study did not involve walking, the limited proprioceptive cues led to overall poor encoding of head direction information owing to a mismatch

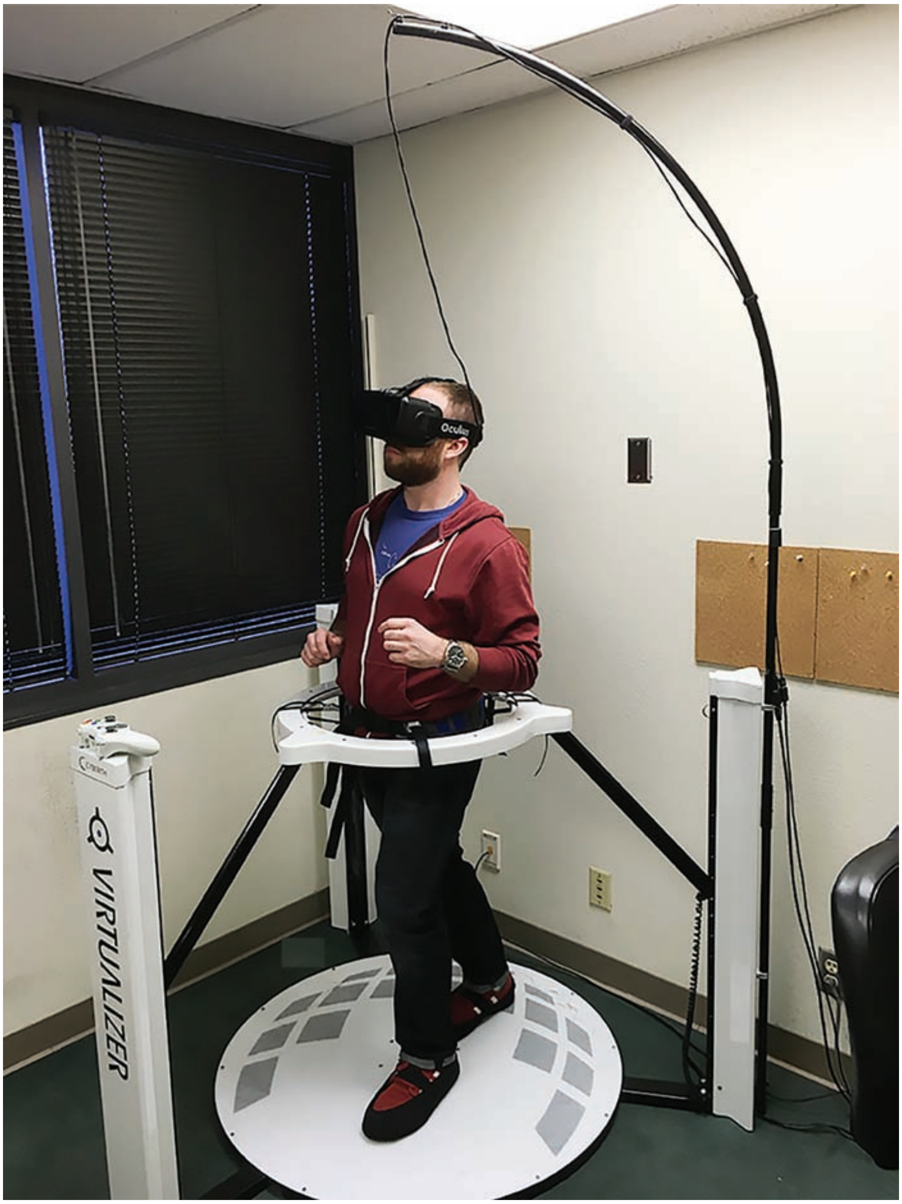


**FIGURE 2.10.** New tools to study human navigation. Example of an omnidirectional treadmill to test navigation in environmental space.

with the joystick movements. Thus, we might expect that the presence of more enriched body-based cues could lead to better transfer to the real world.

In support of the importance of richer body-based cues to large-scale navigation, Grant and Magee (1998) compared navigation with an HMD, head turns, and walking in place by shuffling the feet to navigation via joystick movements. While the HMD/walking condition did result in improvements in taking shortcuts compared to desktop VR, both conditions resulted in worse direction estimates compared to real-world navigation. One limitation of this study, however, is that shuffling steps likely produced vestibular/proprioceptive mismatches because no forward body translations actually occurred. Thus, while studies of transfer from VR to real-world environments suggest advantages to some vestibular input rendered by an HMD, the absence and mismatch, in some cases, with other body-based cues (that is, walking-based input from sensory and muscle receptors) may be a possible reason for incomplete transfer (Ruddle and Lessels 2006; see also Klatzky et al. 1998).

## Summary

Navigation involves several different cognitive processes, all of which are likely to be dynamic. This creates serious obstacles for cognitive psychologists and geographers who want to try to isolate specific cognitive processes during navigation, like path integration or how we represent landmarks relative to each other. Fortunately, cognitive psychology has innovated a number of important tools for understanding the mental processes important to cognition more generally, a number of which we typically use when studying navigation. Studying navigation also involves employing dependent measures, which refer to how we measure spatial knowledge acquired during navigation. We reviewed the pioneering work of Appleyard, who studied the quality and accuracy of maps drawn by individuals in the recently built town of Ciudad Guyana in Venezuela. We then discussed some of the limitations of this early real-world study and turned to focus on more controlled laboratory studies that have taught us about egocentric representation and path integration. We explored the idea of allocentric representation, involving reference of multiple landmarks to each other, and how we might study this using the JRD task, and then described some of the influential models of human spatial navigation, which help make the important point that both egocentric knowledge and allocentric knowledge can occur in parallel and are often topological (rather than metric). We then discussed the importance of virtual reality in expanding the scale of space that we can study because it allows us to readily construct environments up to several kilometers in size, as well as the limitations of desktop virtual reality and the new frontier ahead of us involving rendering virtual reality environments on head-mounted displays with free ambulation. Now that we have obtained a sufficient understanding of how we might measure behavioral and cognitive components of navigation, we will begin to focus our attention on the neural basis of spatial navigation.

# CHAPTER 3

# THE NEURAL BASIS OF SPATIAL NAVIGATION

Imagine you are lost and you are speaking to a friend on the phone to determine where you are and how to find her. What are the three things that would be most helpful to you in determining your location and how to get to your destination? First, and perhaps most important, is your immediate heading. How are you oriented relative to the environment? Are you facing north or south? Second, where are you located? Are you downtown? Or are you in a less populated area on the outskirts of the city? Finally, approximately how far off from your intended destination are you? Kilometers? Tens of kilometers?

These three components—location, heading, and the metric properties of the environment—may relate to several fundamental types of cellular coding mechanisms described in the rat brain and, to a lesser extent, the human brain. These mechanisms are the *place cell*, the *grid cell*, and the *head direction cell* (figure 3.1), each of which contains a critical piece of the previously described cognitive components widely assumed to be important to navigation. These cellular responses also have both historical and conceptual significance to the field of navigation because they have been tied, perhaps more so than other cellular response types in navigation, to the idea of the cognitive map, which we have discussed in some detail already in chapters 1 and 2. Later in this chapter we will also describe the *speed cell*, the *border cell*, and *conjunctive cells*.

Such cellular responses in rodents during navigation form the foundation on which we have built much of our understanding of navigation-related coding systems in humans. Thus, we will first lay out the neural coding systems as described in rats, and then focus on evidence for aspects of this neural code that also appear to be present in humans. In chapter 8, we focus on some of these representations again, but in the specific context of human spatial navigation and lesions that disrupt this process. The vast majority of what we know from rodents comes from extracellular recordings, which involve placing electrodes within the brain of the rat, just outside neurons, and recording while the rat freely navigates. As we mentioned in chapter 1, however, such recordings in humans are possible only in clinical situations and involve significant limitations for studying navigation. For example, it is extremely difficult to study freely ambulating patients with electrode recordings because of the dangers of trip hazards, augmented by the risk of epileptic seizures, as well as potential damage that could occur to the skull with implanted electrodes (although see Bohbot et al. 2017 for an extremely rare instance in which this was

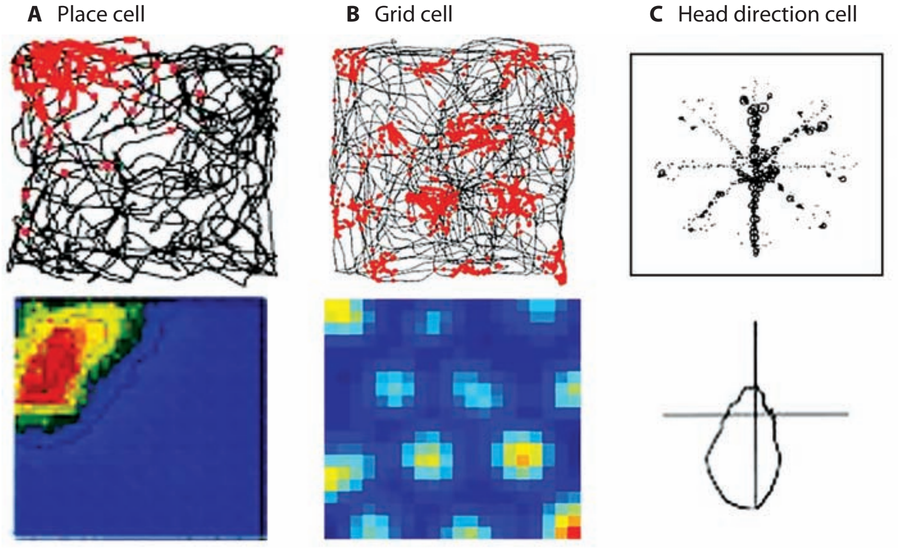


**FIGURE 3.1.** Place cells, grid cells, and head direction cells. A. Place cell. The trajectory of the animal, with the occurrence of action potentials while navigating the environment, is shown on top. The bottom panel shows the firing rate per area occupied during navigation. B. Grid cell. The trajectory of the animal, with the occurrence of action potentials when navigating the environment, is shown on top. The bottom panel shows the firing rate per area occupied. C. Head direction cell. The cell fires only when the animal walks in a southward direction in the maze, as shown in the top panel. The bottom panel shows the firing rate plotted as a function of looking direction.

possible, which we will discuss in more detail shortly). For this and other reasons, the vast majority of work on the neural basis of spatial navigation in humans has involved using virtual reality (VR) to simulate navigation for either extracellular recordings in patients or neuroimaging of healthy participants. In both cases, there are important limitations in exactly what we can conclude about our navigational code compared to the rodent, some of which we will cover here but we will also discuss in greater detail in chapters 4 and 8.

## Place Coding System in the Rat Hippocampus

The first breakthrough in understanding how cells in the brain underlie navigation came from the discovery of place cells. O'Keefe and Dostrovsky (1971) first discovered these cells by video recording the location of a rat while it foraged for food in a box and simultaneously acquiring extracellular recordings from the rat's hippocampus. They found that neurons in the main output region of the hippocampus (the pyramidal cell layer) had very low firing rates but that each neuron would discharge at a high rate whenever the rat moved into a specific part of the box. Each neuron appeared to prefer a different part of the box: for example, one would fire in the southwest region of the box and another near the middle of the north wall (see figure 3.1A). The researchers termed these cells *place cells* because they effectively provided code for which place in the box the rat was in.

By eavesdropping on enough place cells via the electrodes, it is possible to determine exactly where the rat is as it runs around the box. For example, watching a rat run from southeast to northwest, you would know which cells were active. This is also true the other way around, observing the sequence of active place cells, you could guess the recent path of the rat. In this way, the collection of place cells active in an environment provide a fairly good estimate of the rat's actual location. These cells have been identified in countless subsequent studies and form the basis, in many neural models of spatial navigation, for one's memory for location (for a review, see Moser, Kropff, and Moser 2008).

Follow-up studies by O'Keefe and other early pioneers of spatial memory research showed that the place cell firing was controlled by multisensory information. Changes in the positions of landmarks, termed *distal cues*, or specific odors could alter where a place cell fired (Muller and Kubie 1987; O'Keefe and Speakman 1987). So, for example, if experimenters rotated the positions of landmarks in an environment, the locations at which the place cells fired would also rotate along with the landmarks. These findings are important because they suggest that the location at which a place cell fired is critically dependent on the sensory input provided by landmarks. This is similar to what we might expect to happen if we closed our eyes and all of a sudden the paintings on the wall had each moved one wall over! Specifically, our idea of our location would change to reflect the new rotations of the visual landmarks.

Place cells also maintained their activity in the dark, indicating that path integration cues provided sufficient information for them to remain active (Quirk et al. 1990). This second critical finding demonstrated that visual cues themselves are not the only important cue to determining where in space a place cell might fire. Importantly, an animal's sense of direction, which is also provided by path integration via the vestibular, proprioceptive, and sensorimotor system (see chapter 1), also provided sufficient information for an animal to update its location. In support of this idea, lesions to the vestibular system severely disrupt place cell firing patterns (Russell et al. 2003). Thus, place cells fire because of an important combination of two different navigation systems we have discussed in chapters 1 and 2: the locations of landmarks via visual input and the direction and distance traveled via the path integration system.

Finally, and perhaps most intriguing, there is the phenomenon of remapping. *Remapping* refers to the idea that where a place cell fires can depend not only on its current location but also on what environment the rat perceives itself to be in. For example, let's say we move an animal from one environment to another. In the first environment, we may have noticed place cells A and B firing in certain locations in a square-shaped box. As we move the animal to a new square-shaped box, we now observe place cells A and B firing in different locations. In this case, we have given the animal two different cues that it is now in a different place: the visual features may be quite different (for example, checkered instead of plain walls) and the path integration information may also indicate that the animal has been relocated (Muller and Kubie 1987; Skaggs and McNaughton 1998). In this way, place cells represent a fairly precise "map" of the surrounding spatial environment; these cells are updated with movement and can represent multiple environments based on differences in which places cells are active and where. It is also worth noting that in this respect place cells are *not* very much like a smartphone's global positioning system (GPS) , which would represent global coordinates and not those specific to a building or a room. We will return to this issue later, because this suggests that while place cells provide an important basis for navigation, they are unlikely to serve a navigation function exclusively.

A logical question to ask, then, is how place cells are organized in the hippocampus, as one might expect that place cells for neighboring locations might be situated next to each other. Indeed, cortical maps in the brain, such as in the primary visual cortex, represent the position of information in the world such that cells next to each other tend to code similar locations (Hubel and Wiesel 1962). This does not appear to be the case for place cells, however. As suggested in both computational models and meta-analyses (studies that analyze numerous studies), place cells located near each other in the hippocampus have no relation to the location they will represent in a given environment (Samsonovich and McNaughton 1997; Redish et al. 2001). Thus, for the hippocampus, it is the unique combination of active place cells that provides a signal for current location in the environment.

An exciting discovery about place cells was that while they represented the current location of the rat when it was running, in other states, such as when pausing to obtain rewards, making decisions, and sleeping, groups of place cells “replayed” past or upcoming trajectories (Foster 2017). These replay events occurred at many times the normal running speed of the rat (Johnson and Redish 2007). This finding is important because it has given neuroscientists a mechanism for how memories might be strengthened (internal repetition) and be used to guide behavior (for example, where do these two different paths lead?). Together, these core findings on place cells—that they fire at specific locations and not others, that they change their firing depending on the spatial environment, that they do not have a location-wise *anatomical* mapping in the hippocampus, and that they fire during “offline periods” as an animal plans its trajectory—all suggest a fundamental role in coding for location during navigation but also additional roles in memory.

## Grid Cells

As we have discussed, place cells provide a fairly good representation of an animal’s location as it navigates. An important question, though, is how the place-specific activity is generated by place cells. Also, how is distance information coded by the brain? In 2005, Edvard Moser, May-Britt Moser, and their colleagues found neurons in the rat medial entorhinal cortex showing a remarkable pattern of activity—firing in a precisely spaced fashion to cover the entire environment a rat explored. Specifically, Hafting et al. (2005) observed that with sufficient exploration of an environment, medial entorhinal cortical cells fired in an intriguing pattern across more or less the entire space, tessellating the environment with firing patterns arranged in a grid composed of equilateral triangles (see figure 3.1B). Such a firing pattern is consistent with a “metric for space” that could allow the calculation of the distance traveled in an environment (Hafting et al. 2005). Although their exact computational relationship to place cells remains debated (Kanter et al. 2017), these cellular responses form an important neural foundation for computing spatial location (Barry et al. 2006; Sargolini et al. 2006).

## Head Direction Cells

As proposed in their book, *The Hippocampus as a Cognitive Map*, O'Keefe and Nadel (1978) speculated that the hippocampus would need information regarding facing direction in relation to the environment in order to compute location. For example, without knowing whether one is facing a certain direction in a room, it is difficult to determine exactly where in space one will end up when moving. The current thinking in the field is that different types of cells in regions such as the entorhinal cortex, subiculum and pre- and parasubiculum, retrosplenial cortex, and a number of subcortical regions provide directional information to the hippocampus. As one example of a cell that codes facing direction, Dr. J. D. Ranck, performing extracellular recordings in the dorsal presubiculum, reported the discovery of *head direction cells* (Ranck 1984). These cells increase their firing rate when the rat faces in a particular direction in the environment but are virtually silent when the rat faces other directions (see figure 3.1C). These cells have now been found in many limbic regions of the brain, including the anterior thalamus, lateral mammillary nuclei, and dorsal tegmentum (Taube et al. 2007). Each head direction cell has its own preferred direction, such that the population signals the rat's current facing direction relative to the distal stable cues in the environment. Like place cells, head direction cells continue to fire in the absence of visual inputs and are the first spatial cells to emerge in the developing rat brain (Wills et al. 2010).

## Neural Basis of Human Spatial Navigation

In the previous section, we described one of the most striking neural codes for a higher cognitive function in all of biology: the rodent hippocampal place cell. We discussed several core properties of this coding system, including the fact that changes in visual landmarks alter place responses. We also explored the idea that path integration is important to the place coding system, in part via input received from the head direction system. All of this information, however, would be merely an intellectual curiosity if it did not have the potential to help us understand the organization of the human neural code for place.

To study place coding in humans, we must use different approaches than those employed in the rat studies. Instead, we must turn to rare situations in which we can perform extracellular recordings in humans, which involve patients with electrodes implanted in their brains for clinical monitoring of epilepsy. As we discussed in chapter 2, as part of epilepsy surgeries neurosurgeons often place electrodes in both suspected seizure-generating tissue and healthy tissue to test rival hypotheses about where the seizures are coming from. This allows researchers with special permission to work with these populations to record directly from relatively healthy parts of the brain as patients navigate virtual reality. (Alternatively, we can study these phenomena in healthy individuals indirectly and noninvasively by using functional magnetic resonance imaging [fMRI]).

## Place Cells and View Cells in Primates

Prior to the advent of single neuron recordings from the human hippocampus during navigation, studies in monkeys provided evidence for two different, possibly conflicting, types of neural responses: place cells and view cells. In one study, Matsumura et al. (1999) trained monkeys to drive themselves to different locations while restrained inside a cab mounted on a train track. In this way, monkeys received extensive experience navigating a small-scale environment while at the same time their heads remained immobile, which allowed the authors to eliminate head movement and any accompanying artifact this might add to their recordings. The restraint also prevented the monkeys from removing their electrodes. The authors found clear evidence of neurons that fired at specific spatial locations that could not be accounted for by eye movements. Reports on freely navigating squirrel monkeys have also suggested place-specific responses, although under less controlled conditions (Ludvig et al. 2003; Ludvig et al. 2004).

Other studies reported little place responsiveness in monkeys walking in an open room with a restraint system that provided for head-fixed movement. Instead, these studies reported neurons that increased their firing upon viewing specific parts of the room (Rolls and O'Mara 1995). These neurons, often called *view cells*, were present in the parahippocampal cortex, and, to some extent, the hippocampus. The authors argued that these cells represented a truer picture of the monkey representation for space during navigation because view forms such a fundamental part of primate (monkey and human) neural representations more generally (an issue we explore in more depth in chapter 4). An important question that follows is whether primates respond to place, view, or some combination of the two.

An early observation using noninvasive fMRI suggested that an area in the posterior parahippocampal cortex responded strongly when participants viewed spatial landmarks during navigation (Aguirre et al. 1996; Janzen and van Turennout 2004). Specifically, when participants searched for specific locations within a maze compared to simply navigating in circles through an environment, the authors found significant levels of activation in the parahippocampal cortex. The parahippocampal cortex was similarly activated in participants as they navigated a virtual environment and viewed objects that were relevant for deciding whether to turn right or left—what we might consider to be "landmarks"—compared to when they viewed the same types of objects in a context that provided no information relevant to navigation. These data suggest that even in humans, view-related processing might be more important to navigation than what had been observed in rodents previously.

Tying together view and place coding, in a study in 2003 Ekstrom et al. found evidence for both location- and landmark-responsive cells in the human medial temporal lobes. In this study, the authors investigated patients undergoing extracellular recordings during seizure monitoring as they freely navigated virtual environments on a laptop computer. They analyzed both the trajectories that patients took when exploring the maze and what they viewed during navigation. The authors found neurons in the hippocampus that fired at specific spatial locations, independent of the angle at which the patients entered the place field or what they

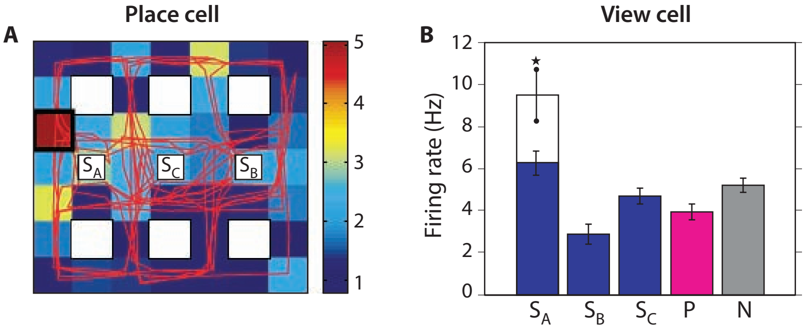


**FIGURE 3.2.** Place cell and view cells in humans. A. Place cell. The firing pattern of a cell from a patient with implanted hippocampal electrodes. Red shows the trajectory of the patient in virtual reality over a 30-minute exploration period. The overlaid colors show the firing rate as a function of occupancy in different sectors of the environment. The black box shows an identified area of high firing, called a *place field*. B. View cell. The firing pattern of a cell from a different patient when looking at one of five different objects: one of three different stores (A–C), the background (N), or a passenger (P). The cell fired at its highest rate when store A was a goal. Reproduced from Ekstrom et al. 2003.

viewed on the screen (Ekstrom et al. 2003). They also found cells in the parahippocampal cortex that responded when patients viewed landmarks, regardless of the angle at which they viewed them (Ekstrom et al. 2003). These studies suggested the presence of both location and view coding responses during navigation in humans (figure 3.2). The findings thus helped resolve an important debate by suggesting that both view and place coding are important to how we code space during navigation.

## fMRI Evidence for Place Coding in the Human Hippocampus

As mentioned previously, early work using fMRI suggested the importance of the parahippocampal cortex to coding view-related information during navigation, particularly when coding landmarks important to finding the correct way to go in a maze. Other fMRI evidence, though, suggested the importance of location coding mechanisms in humans, consistent with Ekstrom et al. (2003). These results are significant because they are based on the performance of healthy volunteers, indicating that the findings extend to a healthy population. They also provide additional convergent evidence that both view and location are important to how we navigate.

One issue with using fMRI to understand place coding, however, is that place cells, as mentioned earlier, are uniformly distributed across the hippocampus and do not show a clear anatomical clustering—that is, a cell that fires in the northwest corner of a box will not necessarily be anatomically next to other cells that fired in the northwest corner of the box (Redish et al. 2001). This is consistent with the idea that place cells may code specific locations in one environment, but unlike our sensory systems, they may also "remap" or alter where they fire in a different environment. If neighboring place cells fired at the same location in one environment, this high degree of connectivity would create a problem for mapping location in a new environment. The lack of anatomical mapping for place cells also creates a problem for identifying location-specific responses using fMRI because a given *voxel*, the basic "unit" of fMRI, will contain around 1000 place cells (Ekstrom 2010). Thus, both the scale of fMRI and the organization of place cells in the hippocampus make classic activation-based approaches to fMRI inappropriate for identifying location-specific responses.

To understand the fMRI evidence regarding coding of location, we need to consider a new approach to fMRI, termed *representational similarity analysis* (RSA) or, alternatively, *multivoxel pattern similarity* (MPS) (Kriegeskorte and Bandettini 2007). This technique harnesses the diversity of changes in groups of voxels to a condition rather than how one specific voxel changes in relation to a task. Why might this approach be advantageous here? Because when we collect patterns of voxels from an entire brain region, we can look for distributed changes in voxels across that region rather than how a small subset of voxels changes in response to an experimental variable. This is valuable because it provides insight into how distributed patterns in the hippocampus relate to a change in location, even if we are unable to pick out a single neuron with a 1.5-millimeter voxel.

In one of the first such papers to use MPS to identify whether there might be location-specific responses in the human hippocampus, Hassabis et al. (2009) had a small number of participants explore several different virtual environments. Hassabis et al. divided the environment into distinct sectors and then tried to determine whether there was sufficient information in the pattern of fMRI signals in the hippocampus to predict the participant's position. Recall, however, that what a participant views can provide a strong driving force for the blood oxygen level–dependent (BOLD) signal in the parahippocampal cortex, which, in turn, provides strong input to the hippocampus via the entorhinal cortex (Amaral and Insausti 1990). Thus, what a participant sees, which will differ by spatial location, could potentially influence the BOLD signal.

To deal with this issue, Hassabis et al. had the virtual view experienced by the participant "pan down" for several seconds at points where the participant paused. In this way, the influence of viewing specific scenes on the BOLD signal, which is based on blood flow to different brain regions, had sufficient time to wear off. Hassabis et al. could then look at whether the patterns of voxels in a specific location, in the absence of specific views, provided sufficient information to decode spatial location. The answer was "yes," suggesting that the hippocampus contains codes for spatial location, supporting results from place cell recordings in humans. Using a different approach in which the experimenters induced an illusion that participants were at different spatial locations within the fMRI scanner, Guterstam et al. (2015) also found evidence that the patterns of voxels within the hippocampus contained information about specific spatial locations. Together, these data confirm the idea that the hippocampus contains unique codes for spatial location.

These fMRI studies, however, do not address the issue of whether the hippocampus contains codes that are specific to different spatial environments. Recall in our discussion of rat place recordings that a place cell that is active in one environment may not be active in a different environment, or may be active at a different place. The tendency for place cells to shift where they fire, which forms the core

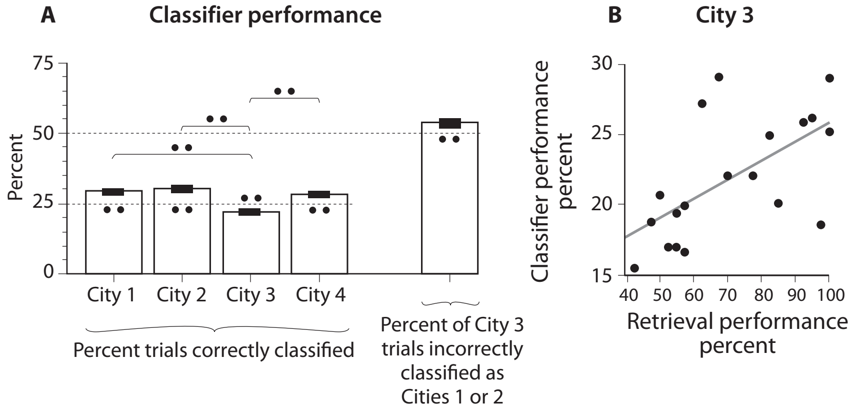


**FIGURE 3.3.** Remapping in humans. A. Unique voxel patterns permitted decoding of environment-specific codes when participants recalled spatial environments in the scanner. A computational technique called classification revealed such voxel-specific codes for nonoverlapping cities (cities 1, 2, and 4). B. The performance of the classifier correlated with participant recall rates, suggesting that the city-specific codes sharpened with better learning. Reproduced from Kyle et al. 2015.

of the idea of hippocampal selectivity for specific spatial environments (termed *remapping*), is central to the idea that the hippocampus codes location. In both the Hassabis et al. (2009) and Guterstam et al. (2015) studies, no demonstration was made specifically of remapping within the hippocampus, although one would predict the hippocampal code for location to change in different spatial environments.

One major issue in tackling spatial remapping is that when navigating different environments, it is difficult, if not impossible, to eliminate confounds from what is being viewed in one environment versus what is being viewed in another, since these necessarily must differ in order for the environment to differ. To deal with this issue, Kyle et al. (2015) designed an experiment in which participants navigated spatial environments and then retrieved information about the distance between different landmarks in those environments. Because what differed between the environments was their configuration, the authors could test how recalling these different configurations affected hippocampal voxel patterns (figure 3.3). Kyle et al. found that when participants correctly retrieved specific spatial environments, they could decode that environment from hippocampal voxel patterns at levels well above chance (Kyle et al. 2015). In contrast, when retrieval failed, they were unable to decode what environment participants were imagining. These data supported the idea that the hippocampus not only contains codes about location but also contains codes about specific spatial environments.

## Comparing Human and Rat Place Codes

Our previous discussion demonstrates not only that humans do have location-specific responses in their hippocampus but also that these types of responses can be identified via two different methodological approaches: single-neuron recordings and fMRI. Given that it is rare to conduct fMRI studies with rats, it is useful to consider similarities in single-neuron responses to locations in rats and in humans. One concern that could point to differences between rats and humans/nonhuman primates is that the observed human place responses differ in their selectivity. Location-specific firing rates in the epilepsy patients typically increased 2 to 5 times above baseline, ranging from about 1 to 15 Hz within a place field, with similarly modest changes in nonhuman primate place cells (Matsumura et al. 1999). This is less selective than place cells in the hippocampus of rodents, where firing rates often increase 100 times or more above baseline within a place field. Nonetheless, the responses in humans were well above chance (Ekstrom et al. 2003) and similar to single-neuron responses revealed in subsequent studies investigating the presence of human place cells (for example, Miller et al. 2013). Furthermore, a neural coding scheme does not require much more than a statistically significant change in firing rate to convey relevant information (Rieke et al. 1999), and thus a statistically meaningful change is still certainly relevant to the brain. We return to this issue in more detail in chapter 4, but perhaps the most important point here is that place cells in both rats and humans provide spatial codes for location.

Could selectivity differences relate in some form to differences in how we code space? Of course, other factors could be relevant as to why human place cells fire at a lower peak rate than those of rats, including the fact that human recordings do not involve movable electrodes. It is intriguing, though, to consider this issue from an environmental standpoint: humans experience a multitude of different cognitive demands both related and unrelated to spatial navigation that are likely to enrich hippocampal function, whereas rats undergoing place cell recordings are reared for this sole purpose. Consistent with this argument, in addition to responding to locations, neurons in the human hippocampus respond to other stimuli, such as famous faces (Quiroga et al. 2005) and conjunctions of locations, views, and goals (Ekstrom et al. 2003), likely supporting episodic memory (Miller et al. 2013). Similarly, when trained and tested on tasks requiring coding of odors and their position, rat hippocampal neurons respond to these task demands as well as conjunctions of locations and odors (Wood, Dudchenko, and Eichenbaum 1999). Thus, one possibility for why our place cells appear to fire at lower peak rates could relate to differences in how humans and rats are “raised.” Specifically, in the vast majority of cases we raise rats in impoverished environments consisting of mazes and cages, while humans experience a much richer array of visual and other multisensory input (Winocur et al. 2005; see also the discussion in chapter 9). While the exact reasons for why place cell firing rates differ between rats and humans remain to be elucidated, some possible explanations point to differences between rats and humans, which we will discuss in more detail in chapter 4. We will also consider more fundamental anatomical differences between species as a possible explanation in chapters 4 and 8.

## Grid Responses in Humans

Grid cells—cells in medial entorhinal cortex that fire in a regular pattern as a rat moves—provide a potential basis for determining metric properties of a room. For example, evenly spaced grid firing covers the entire geometry of a room-size environment in a rat, thus suggesting a code for spatial distance. Furthermore, grid cells

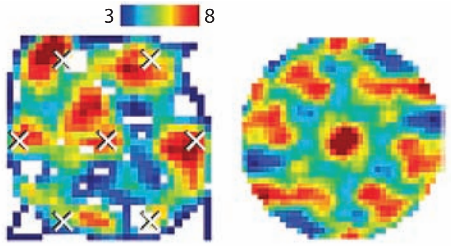


**FIGURE 3.4.** Human grid cells. The firing patterns of cells recorded during free exploration of a virtual environment in a human patient. Cells were recorded from the entorhinal cortex. Notice the grid-like pattern of these cells. Reproduced from Jacobs et al. 2013.

also have a preferred angle, suggesting that these cells also code information about orientation and direction during navigation. Thus, grid cells, simply in terms of their neural responses, appear to possess many important components fundamental to path integration, and, more broadly, to finding one's way about a room.

An important issue, though, regards the extent to which humans use similar mechanisms, either neurally or behaviorally. In chapter 2, we discussed in some depth the idea that humans can code both direction and distance information. Thus, two important questions for consideration are: (1) Do humans have grid cells? (2) Do we (and rats) utilize these grid cells to code direction and distance information? As we will discuss shortly, the answer to the first issue (whether we have grid cells and grid-like coding mechanisms) is "yes." The second issue (how grid cells relate to behavior) remains somewhat of an open question and one we will also explore here.

The first demonstration of human grid cells involved direct intracranial recordings in patients undergoing seizure monitoring. In this study, Jacobs et al. (2013), using tests in a large, open virtual environment, compared single-neuron responses in the entorhinal cortex with activity in other brain areas such as the hippocampus and cingulate cortex. The authors compared the firing rate as a function of position, finding that cells in the entorhinal cortex showed a tendency to fire in multiple locations rather than at one or two locations like place cells. Additional analyses—specifically, correlating the patterns of firing in two different dimensions— revealed that these areas of increased firing (figure 3.4) tended to be evenly spaced, demonstrating a grid-like pattern.

An additional property that the authors explored was the degree of rotational symmetry of the firing of these cells. This could address exactly how the grids were arranged within the virtual environment—for example, in a triangular shape, a square shape, or some other shape. The authors found that the grids tended to be arranged as 60-degree equilateral triangles stacked on top of each other (like a hexagon), similar to previous findings in the rat (Hafting et al. 2005). These data suggested that humans possess a neural code that codes the distance and direction of the navigator relative to external features in the environment (the room) and that these responses have a remarkable similarity to those shown previously in the rodent.

## Grid Cells and Spatial Memory: Do We Need Them to Navigate?

In a second study to demonstrate grid-like coding in humans, Doeller et al. used fMRI to try to detect such responses in the human brain. Doeller et al. reasoned that if the firing rate of large groups of neurons correlates with the BOLD signal and that firing rate is higher when a participant is aligned versus misaligned with a grid, they should be able to detect a response using fMRI (Doeller, Barry, and Burgess 2010). Doeller et al. also capitalized on the fact that grid cell firing increases with increasing movement speed, at least in rodents in real-world environments (Sargolini et al. 2006). Thus, participants in the Doeller et al. study navigated large virtual environments while undergoing fMRI imaging, which also allowed the researchers to relate BOLD responses during free exploration to metric properties of the environment (Doeller et al. 2010).

Doeller et al. divided their fMRI data into two different segments. In the first segment, they attempted to determine the angular alignment of the grid response based on changes in the BOLD signal for movement in some directions versus others. They then looked at the second half of their data, a common practice in fMRI approaches to decoding (Hassabis et al. 2009), to determine whether these grid-like BOLD responses persisted. The authors found that, indeed, there were statistically higher BOLD levels in the entorhinal cortex when participants were aligned versus misaligned with the grid, with the BOLD signal further increasing with increases in movement speed. In addition, BOLD signal changes showed repeated patterns of activation based on directionality, also reminiscent of grid cells. While these findings cannot eliminate the possibility that these responses were related to head direction or velocity, similar findings have been found in the rodent entorhinal cortex (Sargolini et al. 2006), which does provide support for the idea that the entorhinal cortex in humans contains neural codes similar to what has been shown in rodents during navigation.

Perhaps most significant, however, Doeller et al. also demonstrated a correlation between the magnitude of BOLD periodicity for different movement directions and spatial memory. Specifically, the authors found a statistical relationship between the degree of coherence between BOLD periodicity during movement in different directions and the ability of participants to accurately place landmarks on a map. Although the correlation was modest, the findings provide a potential link between spatial memory and the presence of periodic coding cells in the entorhinal cortex. As indicated earlier, we can't be sure of the exact nature of the cellular responses in the Doeller et al. study, but evidence of such hexadirectional coding has been observed in three subsequent studies, suggesting that the response is reliable and that it can even be observed when people merely imagine traveling to their goal (Horner et al. 2016).

## Head Direction Coding in Humans

Although no experiments in human patients, to date, have investigated head direction cellular responses, there is copious evidence from fMRI for these types of responses. We will discuss many of these studies in more detail in chapter 5, which relates direction to how we find a goal. For sake of completeness, though, we mention here one study by Shine et al. (2016). In this study, participants experienced different viewpoints of a virtual environment while wearing a head-mounted display. They then recalled these viewpoints while undergoing fMRI. The authors found that the BOLD signal in the retrosplenial cortex and thalamus remained high for repeated viewpoints but changed for new ones, comparable to what has been observed for rodent head direction cells (Taube et al. 2007). This lack of BOLD *adaptation* has often been taken in other studies to support the idea that neural codes are specific to a certain type of stimulus class (Grill-Spector et al. 2006). Because these BOLD responses were also in similar regions to those that showed head direction responses in rodents, the Shine et al. study supports the idea that we and rodents may possess some similar mechanisms for coding facing direction.

## Border Cells, Speed Cells, Conjunctive Cells, and Low-frequency Oscillations

Place, grid, and head direction cells form the cellular basis for a navigational code that includes location, direction, and distance. There are other important cellular responses that are also important to navigation. These include the border cell, the speed cell, and the conjunctive cell. *Border cells* are cells that fire at or near the boundary of an environment, like a wall. They alter where they fire if the experimenter moves the border, and are likely critical to marking the outer extremities of an environment—important, in turn, for computing location (Solstad et al. 2008). The *speed cell*, present in both the hippocampus and the entorhinal cortex, as its name implies, codes the speed at which an animal travels, firing at a higher rate when the animal runs faster (McNaughton et al. 1983; Kropf et al. 2015). Speed cells are likely an important component to position and distance, because they provide a basis for judging how these change during movement. Finally, *conjunctive cells*, also described in humans (Ekstrom et al. 2003), fire for conjunctions of these and other variables (Sargolini et al. 2006) and are likely an important component for how all of these different aspects of navigation are integrated and combined to represent space.

As we discussed in chapter 1, however, a disadvantage with single-neuron recordings is that they provide only a microperspective on what the brain is doing at any given time. While fMRI can provide us with a better “macro”-level picture of brain functioning, fMRI offers only an indirect measure of neural activity because it is based on vascular signals rather than directly on spike rate. While fMRI studies have been helpful in confirming and, in some cases, extending findings from rodents to humans, it would be helpful to have a measure that might bridge between the macro scale of fMRI and the micro scale of single-neuron recordings. As it turns out, this signal exists, and it is called the *local field potential* (LFP).

Cornelius Vanderwolf, performing electrical recordings from the rodent hippocampus in the late 1960s (before place cells were discovered!) described a low-frequency signal that appeared to increase as the rat began to move or performed other volitional movements. This signal was different from the spiking activity of single neurons in that it was present only when Vanderwolf filtered for frequencies from about 3 to 12 Hz (Vanderwolf 1969). As demonstrated in subsequent work, this signal did not derive from spiking activity of single neurons but instead arose from the combined activity of many thousands of neurons in synchrony (Ekstrom 2010). Thus, Vanderwolf identified a signal that resulted from the combined activity of thousands of neurons yet appeared to change depending on the state of the

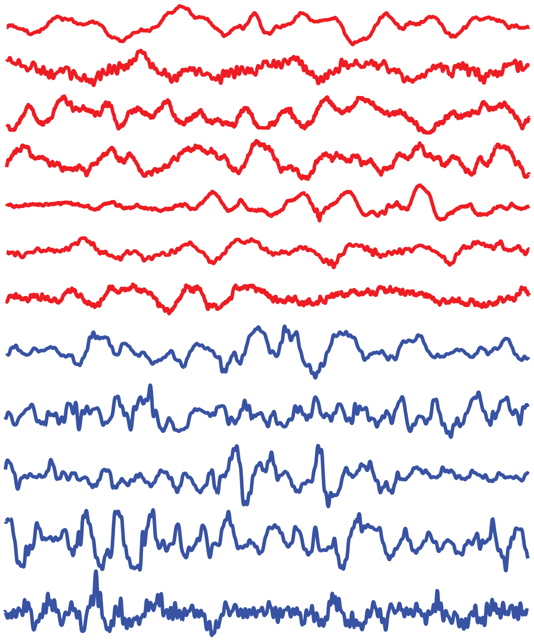


**FIGURE 3.5.** Theta oscillations. Low-frequency oscillations recorded during virtual navigation in humans (red) and rats (blue). The scale is approximately 250–500 microvolts for the peak of an oscillation. Reproduced from Watrous et al. 2013.

animal. Vanderwolf termed this oscillation the *hippocampal theta oscillation*, examples of which, from both rats and humans, are shown in figure 3.5.

As with many great discoveries, it took several decades to realize the implications of this important oscillation to rodent navigational behavior. Subsequent work demonstrated that one of the primary drivers of the theta oscillation was an area called the *septal nucleus*, part of the basal forebrain important for the control of acetylcholine release (Givens and Olton 1990). In particular, deactivating this area with pharmacological manipulations significantly reduced hippocampal theta oscillations. Importantly, deactivating the septal nucleus also increased the likelihood of a rat making a memory error, which, in this case, involved going to the wrong arm in a maze task (in the task, the rat's job was to choose the opposite arm from where it had previously been rewarded, so going to the same arm meant an error). These findings thus suggested the importance of theta oscillations to spatial memory and spatial navigation more generally.

## Low-frequency Oscillations in Humans

Studies have also demonstrated low-frequency oscillations in patients with electrodes implanted in the hippocampus (Ekstrom et al. 2005; Watrous, Fried, and Ekstrom 2011). As in the rodent, these oscillations increase in amplitude and overall prevalence as patients begin to move in virtual environments. Interestingly, at least in virtual reality, these oscillations tend to manifest at a lower frequency and are less continuous overall than those recorded in the rodent (Watrous et al. 2013; Jacobs 2014). As mentioned, a limitation with virtual reality is that it does not involve vestibular input; thus, it is possible that the lower frequency of theta in humans

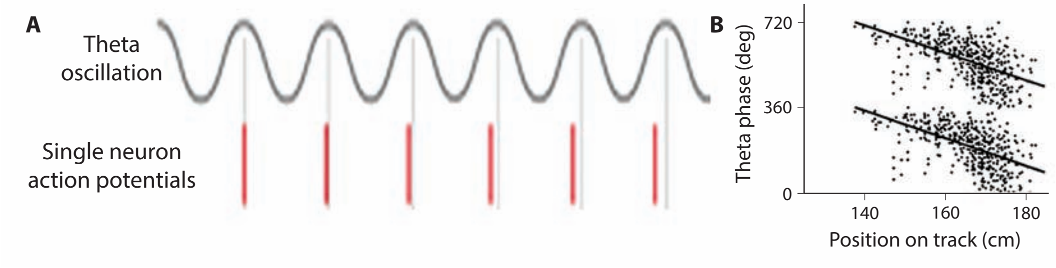


**FIGURE 3.6.** Phase precession. A. The firing rate of a single neuron in the hippocampus as it occurs relative to the ongoing low-frequency theta oscillations. Note that spikes tend to occur earlier and earlier relative to the phase of the oscillation. B. Phase plotted as a function of position for a single place cell in the rodent hippocampus. Note that action potentials occur earlier and earlier on the theta phase as the rat moves through its place cell.

could come about because testing occurs in virtual reality. Bohbot et al. (2017) tested patients with electrodes implanted in the hippocampus while they were freely ambulating in a small room. The patients demonstrated 1 to 12 Hz oscillations elicited by movement, which appeared to peak at a slightly higher frequency than those recorded during virtual reality exploration on a desktop computer. Thus, while it is fair to say that there are important differences between rodent and human low-frequency oscillations, particularly in terms of continuity and frequency, at least some of these differences may emerge owing to testing conditions—that is, testing in VR versus reality.

## How Do Low-frequency Oscillations Relate to Place Cells?

How does the activity of low-frequency oscillations relate to cellular responses? One prevalent idea is that hippocampal theta oscillations provide a gating mechanism for the excitability of place cells, thus regulating when exactly such firing will occur. This mechanism, termed *phase precession* (O'Keefe and Recce 1993), involves gradual changes in terms of when a place cell fires relative to the theta oscillation. Specifically, as a rat enters a place field, spikes occur on late phases of theta cycle (that is, 180). Then, as a rat moves through the place field, spikes occur on earlier and earlier phases of the theta oscillation (that is, 90, 0 degrees; figure 3.6). Although the exact importance of phase precession to navigation has yet to be demonstrated, the regular phase coding it provides improves the ability to reconstruct location from place cell firing (Jensen and Lisman 2000) and may also be important to coding the order in which place cells fire during navigation (Dragoi and Buzsaki 2006).

In humans, whether phase precession occurs remains unknown, in part because these studies are difficult to perform with human patients. Part of the reason for this is that we typically need many place fields to compare with the theta oscillations, and currently the yield of place cells appears to be lower in humans than rats owing to the immobility of recording electrodes (Ekstrom 2015). We do know, however, as pointed out earlier, that humans have both place cells and low-frequency oscillations. Given these commonalities, it would be surprising if humans did not show phase precession. At the same time, theta oscillations do manifest differently in humans, and thus it is possible that the relationship between theta and place cell firing is different from what has been described in the rodent. Future studies will hopefully help to elucidate this issue.

## Hippocampus and the Cognitive Map: The Beautiful Model

Some books can be considered truly ahead of their time, and *The Hippocampus as a Cognitive Map*, written by John O'Keefe and Lynn Nadel in 1978, is an excellent example of this type of literary prescience. Their book accounted for a range of data collected by O'Keefe, in particular the place cell, which was first described by O'Keefe and Dostrovsky in 1971. But perhaps most impressive—and the reason why this book continues to be one of the most influential in neuroscience, with over 8000 citations—is that it also accounted for many phenomena that were not described until decades later.

Few cognitive neuroscience theories proposed in the 1970s continue to be nearly as influential as the idea that the hippocampus houses the necessary neural architecture for the cognitive map, the central tenet of *The Hippocampus as a Cognitive Map*. In essence, what O'Keefe and Nadel argued was that because the hippocampus contained place cells, it possessed the foundational neural machinery for representing space in an allocentric reference frame. Fundamentally, this meant that in order to remember a location based on its position relative to multiple landmarks, place cells, in some form, were needed. In contrast, egocentric forms of navigation, which would depend on simply remembering a direction relative to yourself and past trajectories, were less flexible in nature and could occur without a hippocampus. *The Hippocampus as a Cognitive Map* thus elegantly tied together the idea of a cognitive map, a rough sketch of position in abstract Euclidean coordinates first articulated by Tolman (1948), to a specific structure within the brain, the hippocampus, based on the presence of the machinery necessary for this process, the place cell.

What was particularly prescient about *The Hippocampus as a Cognitive Map* was the ability to account for subsequent findings, including the finding that hippocampal cells are selective for a specific spatial environment and "remap" when moved to a new environment (Muller and Kubie 1987), that place cell firing rotates with rotations of visual landmarks (Knierim, Kudrimoti, and McNaughton 1995), that place cells depend on a combination of path integration and landmark-based information (McNaughton et al. 1996), and that place cell firing can be organized via low-frequency theta oscillations (O'Keefe and Recce 1993). In this way, cognitive map theory accounted for a range of electrophysiological phenomena before they were even discovered!

Perhaps even more presciently, the cognitive map theory predicted that damage to the hippocampus should severely impair the ability of a rat to use an *allocentric* reference frame (that is, a place strategy) to navigate. As we discussed before, this form of navigation would involve using external (also called *distal*) landmarks to recall an unseen location, such as remembering that our car is parked between three different poles, approximately two-thirds of the way to one of them and one-third of the way to other two. As predicted, Richard Morris demonstrated that rats with hippocampal lesions fail to learn to find a hidden location while swimming in a pool of water based on landmarks arranged outside the pool (Morris et al. 1982).

However, the cognitive map theory also predicted that the hippocampus is not involved in stimulus-response (taxon) memory. This was also later confirmed: if a local cue (a brightly colored card or flag) is placed above the platform, it will act as a stimulus that will elicit a response of navigating toward it. As per O'Keefe and Nadel's predictions, rats can still find the hidden platform when it is associated with a cue. Decades later, research from the laboratory of Norman White demonstrated that this kind of navigation was primarily dependent on another region of the brain called the *striatum* (Packard, Hirsh, and White 1989), which is further discussed in chapter 6. Thus, *The Hippocampus as a Cognitive Map* beautifully predicted many core electrophysiological and behavioral results—perhaps most presciently, the idea that the hippocampus is necessary for allocentric navigation, which was distinguished from other types of memory, such as stimulus-response and egocentric forms of memory.

Head direction and grid cells, both discovered after publication of *The Hippocampus as a Cognitive Map*, also fit in nicely with the idea of a specialized structure for processing space allocentrically. Head direction cells provide critical information about direction, which is central to path integration, while grid cells provide both direction and distance representation, also critical to path integration (McNaughton et al. 1996; Hafting et al. 2005). In this way, modern theories of the cognitive map have argued that grid cells and head direction cells provide the basis for a path integration system, while the hippocampus combines this information with landmark-related representation to produce the cognitive map. Grid cells and head direction cells can be easily accommodated to strengthen the idea of the hippocampus as a cognitive map.

## Issues with the Cognitive Map Theory in Rodents

Despite the widespread impact and influence of the cognitive map theory, there are several discoveries that it did not fully predict (for example, the existence of grid cells) and some topics that have received criticism. These challenges to the theory include the question of how place cells come about in the first place, the necessity of the hippocampus to spatial learning, what "allocentric" means more generally, and, perhaps most importantly for this book, the connection to human spatial navigation. We briefly review the first three issues and then delve into a more in-depth consideration of the hippocampus as a cognitive map in humans.

Based on the organization of the hippocampus, grid cells (located in the medial entorhinal cortex) provide strong input to an area of the hippocampus to CA3, and secondarily, CA1, via the perforant path (fibers entering the hippocampus), in which place cells are ubiquitous. One might easily predict, then, as many computational models did, that more distributed grid cells form the basis of place cell coding in the hippocampus. Thus, it was quite surprising when several studies showed that lesions and optogenetic silencing (a technique to selectively dampen the neural firing of specific cells) of the medial entorhinal cortex failed to abolish place cell firing, although it did make it less precise (Brun et al. 2008; Hales et al. 2014; Kanter et al. 2017). Furthermore, very young rats (termed *preweanling*) do show place cells but do not show grid cells, suggesting that place cells may emerge independently from grid cells (Langston et al. 2010). These data challenge the idea that place cells emerge in an obvious way from grid cells and that path integration (assuming this is computed in the entorhinal cortex) forms the basis for place cell coding (Bush, Barry, and Burgess 2014). While cognitive map theory did not predict grid cells, and it is possible place cells could emerge from border cells, the lack of a clear connection between place and grid cells complicates what could have been an elegant theoretical unification of these two electrophysiological discoveries.

Another issue regards whether the hippocampus or entorhinal cortex is necessary for allocentric navigation. This can best be approached by lesioning a structure: if we take out a structure necessary for a cognitive process, it should no longer work (see also chapter 7). While the original studies of Richard Morris using the Morris water maze demonstrated profound impairments in finding a hidden platform following hippocampal lesions (Morris et al. 1982), subsequent work demonstrated that rats with hippocampal lesions could learn the Morris water maze with sufficient pretraining, sufficient exposure, and training on alternative strategies (Day et al. 1999; for a review, see Ekstrom, Arnold, and Iaria 2014). These findings suggest that the hippocampus is not necessary for allocentric navigation but rather that the hippocampus is needed for normal acquisition of the Morris water maze. We explore this idea in significantly greater detail in chapter 8, where we argue for the idea that the hippocampus is simply one of many brain regions that are part of a larger network important for navigation (for example, Ekstrom, Arnold, and Iaria 2014; Eichenbaum 2017).

## Issues with Cognitive Map Theory in Humans

What is perhaps the largest obstacle for cognitive map theory, however, has been its translation into a meaningful and testable theory in humans. Specifically, how cognitive map theory in rats connects to verbal memory in humans remains unclear. Human episodic memory, which involves retrieving details from past events, also depends critically on the hippocampus (see chapter 9). Patients with damage to this area of the brain are severely impaired at recalling recent events, although they are able to learn new information, like motor skills (Scoville and Milner 1957; Corkin 2002). This has created an issue, because while cognitive map theory argued that in humans time and space were represented in the hippocampus, it was not clearly defined exactly how the idea of metric map-like knowledge can be applied to the diversity of the episodic memory domain, in which information is often abstract rather than allocentric and metric (Eichenbaum and Cohen 2014).

The lack of a clear connection between human verbal memory skills, amnesia, and the cognitive map led to alternative ideas and theories, such as relational memory theory and multiple trace theory (Eichenbaum, Otto, and Cohen 1992; Nadel et al. 2000; Eichenbaum and Cohen 2014). We discuss multiple trace theory, and how it relates episodic memory and navigation, in detail in chapter 9. Relational memory theory postulated that the primary role of the hippocampus was not spatial memory but rather in coding the complex interrelations of stimuli during navigation and in other domains involving memory. Relational memory theory thus explained allocentric navigation as another example of remembering relationships between multiple stimuli—for example, that the hidden platform in the Morris water maze was between multiple landmarks. Based on learning abstract relationships between stimuli, relational memory theory also provided an elegant account of how we might learn a new list of words or recall our last visit to a diner, which would typically involve complex interrelationships of different kinds of stimuli.

Relational memory theory also provides a clearer account than cognitive map theory for why the hippocampus is often involved in prospective, or future, thinking, even that which involves no spatial details (Addis and Schacter 2008). While we will return to the idea of episodic memory and spatial navigation and discuss multiple trace theory in more detail in chapter 9 as it applies to navigation, one issue with relational memory theory in our particular context is that it doesn't provide new predictions about how human spatial navigation might work under varying conditions. The development of relational memory theory and other theories specifically devoted to explaining episodic memory and the hippocampus like multiple trace theory makes clear that perhaps one of the largest gaps in cognitive map theory is that it does not account for a range of behaviors dependent on the hippocampus—in particular, verbal memory performance in humans.

Even if we focus more specifically on spatial learning in humans, however, the idea that the hippocampus houses the unique neural machinery necessary for allocentric navigation runs into problems. As we have already discussed in chapter 2, unlike a cognitive map, much of our spatial knowledge, including the knowledge applied when we draw maps, does not appear to be metrically accurate and is better described as topologically accurate (Montello 1998). Indeed, as we consider in detail in chapter 9, patients with damage to the hippocampus can draw accurate maps and even navigate allocentrically, although they do show deficits in the numbers of details they can reproduce when they draw such maps (Rosenbaum et al. 2000). Even a taxi driver with damage to his hippocampus could navigate mostly normally, likely using allocentric navigation to arrive at his various goals (Maguire, Nannery, and Spiers 2006). This leaves several nonexclusive possibilities—for example, that the hippocampus alone does not store the cognitive map, that spatial knowledge need not always be metric, or that spatial knowledge obtained in the distant past is different from more recently acquired knowledge.

Indeed, there is a good evidence to suggest that there is more to the cognitive map than the hippocampus and that remote and recent memories are not the same with regard to navigation and the brain. Several studies have in fact demonstrated that patients with damage to the hippocampus, even fairly extensive damage that occurs following surgical resections, can still navigate using landmarks allocentrically with little impairment in new environments (Bohbot et al. 1998; Kolarik et al. 2016). While one could possibly come up with alternative accounts based on response or egocentric navigation strategies for their allocentric navigation, some of which we consider in chapter 6, these explanations appear unlikely. Importantly, they cannot naturally explain the high degree of complexity in these individuals' navigational skills and their ability to draw maps, such as the taxi driver with damage to his hippocampus who can still navigate London with little obvious impairment (Maguire, Nannery, and Spiers 2006) and amnesic patients who can otherwise draw overall accurate maps (Herdman et al. 2015). Interestingly, while patients with selective damage to the hippocampus in the Bohbot et al. (1998) study were not impaired at learning a target location in an environment, these same patients were impaired when required to create a mental map of the environment by learning the locations of objects from a first-person view and translating that into a bird's-eye view. Thus, while patients with damage to the hippocampus are not consistently impaired at spatial navigation, they may be impaired in situations when a detailed map of the environment needs to be constructed from memory, as we will discuss in chapter 9. Further research will be needed to understand the exact contribution of the hippocampus to allocentric navigation and the conversion of information obtained by navigating into a map.

Another issue with cognitive map theory, as it relates to human spatial navigation, is how well it can describe the underlying nature of representations we use when we navigate. In other words, how faithfully do we represent physical space when we experience it? Specifically, one of the core postulates of cognitive map theory is that we employ metric, map-like representations of space when we navigate allocentrically. Numerous behavioral studies, as reviewed in chapter 2, have shown that humans tend to have preferred orientations by which they code spatial layouts. In addition, how we represent space involves systematic distortions of direction and distance based on our surrounding spatial boundaries. In fact, our spatial knowledge most often does *not* appear to be Euclidean (that is, metric like a cartographic map) but often shows systematic errors at larger scales and distances (Moar and Bower 1983; Philbeck and Loomis 1997; Ekstrom, Arnold, and Iaria 2014; Brunec et al. 2017; Jafarpour and Spiers 2017). It is overall more accurate, as Montello (1998) argues, to describe our spatial knowledge as topologically rather than metrically accurate. Thus, the idea that our knowledge is map-like in the first place, and that our hippocampus is necessary for this, appears questionable, at least under some testing conditions.

We might ask then: Why has the cognitive map theory been so influential if, in general, it is not very good at describing the species we are perhaps most interested in studying—humans? Perhaps it is worth reiterating that, despite some limitations, the cognitive map theory has been enormously influential in spawning new studies and providing a framework for thinking about spatial navigation more generally. Place cells remain one of the most influential concepts connecting electrophysiology and cognition and have taught us an enormous amount about the organization of the hippocampus.

## Summary

We have discussed three fundamental cellular mechanisms that would appear central to the types of codes we need to navigate: place cells, grid cells, and head direction cells. Together, these cellular responses are thought to contribute to and underlie the cognitive map. Extracellular recordings in humans have confirmed at least some of these responses during navigation. Although enormously important in terms of understanding how the brain might code navigation, the insight provided by the cognitive map metaphor into the neural basis of human spatial navigation is somewhat limited, as it is primarily focused on rats and the hippocampus specifically. While fMRI is one potential tool to provide us with a more “macro” perspective on the link between neural responses and behavior in humans, and therefore how other brain regions outside of the hippocampus might contribute to spatial navigation, it lacks the spatial resolution of cellular recordings and is indirect. Thus, a challenge in human spatial navigation is to connect the findings in rats with those in humans. One major issue, which we consider in the next chapter, is that rats and humans are fundamentally different species, and how we navigate differs in many ways. After addressing these differences, we will start to delineate some of the similarities in subsequent chapters.

## CHAPTER 4

# LANDMARKS AND VISUALLY GUIDED NAVIGATION

When considering navigation as a matter crucial to survival across all mobile species, it is easy to consider humans as no different from others: we navigate to survive. In fact, this is typically how past books on spatial navigation have treated humans: as one of many different examples of species that can navigate employing similar fundamental mechanisms like the cognitive map (O'Keefe and Nadel 1978; Gallistel 1990). Indeed, navigation in humans serves the same basic functions of survival on a daily basis as many other species: finding food and mates, and avoiding things that could hurt us.

In this basic way, we are no different from the desert ant, which, upon finding a dead scorpion during random foraging, must return to the nest carrying the corpse to consume for food. Similarly, when we find a food source (a supermarket), we must be able to find our way quickly back with our groceries to feed ourselves and/or our offspring. We can think of navigation across long distances in a similar way: just as the sea turtle crosses thousands of miles of open ocean to return to its nesting ground, humans, in some cases, have migrated extremely long distances to colonize new ecosystems (think, for example, of migration across the Bering Strait). In this way, we might think of human spatial navigation as comparable to navigation in a variety of different species.

Just as our navigational needs have many parallels with those of other species, the same fundamental navigational mechanisms that are present across a range of animal species are also present in us: path integration and landmark-based navigation. After randomly foraging for hundreds of meters to find food, a desert ant uses path integration to choose the most direct route back to the nest. However, just like experienced navigators, if it makes slight errors in its path, it can use the sight of the ant hill to correct deviations in its course (Gallistel 1990). Similarly, as we discussed in chapter 1, Puluwat sailors, who navigate using no maps or other mechanical aids, employ path integration to navigate across the open ocean, where islands or other visual aids are not present. Upon sighting an island—either the island itself or other indicators that they might be near the island (such as a reef or seabirds)—the sailors can correct for any accumulated errors. In these ways, the mechanisms we use to navigate appear no different, in any fundamental way, from those of a desert ant.

Two other examples of navigation feats from nonhuman animals, though, provide some perspective on how navigation in other species can differ profoundly from that in humans. One particularly striking example of a navigational skill we humans do not possess is the ability to use geomagnetic maps, which is one of the primary mechanisms for how sea turtles navigate (Lohmann et al. 2004). Sea turtles must travel long distances through open oceans from their nesting ground to areas where they mate, journeys that can involve, in some cases, migrations of thousands of miles. In an elegant series of experiments, Lohmann et al. demonstrated that a strong magnetic field, oriented either north or south, results in a sea turtle changing course and navigating toward the magnetic field (figure 4.1). In contrast, there is no evidence that humans naturally use magnetic fields to navigate; however, for a historic review of attempts to find magnetoreception in humans, we refer the interested reader to Hand (2016). If humans did possess the ability to use magnetoreception to navigate, one might expect that the journey to the South Pole would have happened much earlier in human existence than Roald Amundsen's expedition!

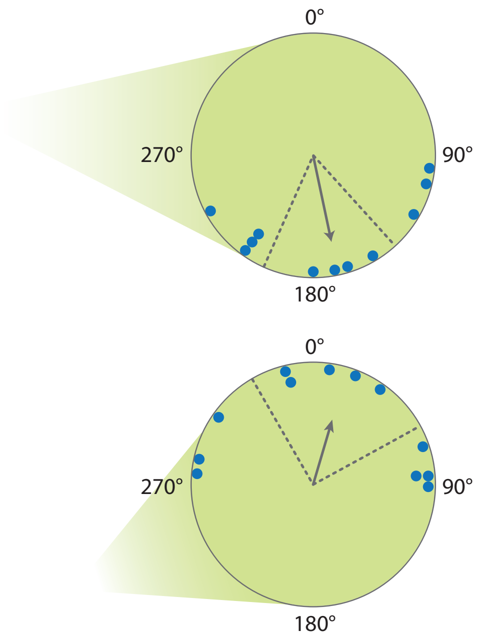


**FIGURE 4.1.** Navigation in sea turtles. Unlike humans, sea turtles use the magnetic fields produced by the earth to navigate. In one experiment, Lohman et al. manipulated magnetic fields to determine how that affected sea turtle navigation. In the top panel, a magnetic field was oriented southward, and the turtles navigated in that direction. In the bottom panel, a magnetic field was oriented northward, and the sea turtles navigated northward. Figure from Lohman et al. (2004).

Another striking example of navigational skills that humans do not possess is the ability to navigate based on the azimuthal position of the sun. *Azimuthal* refers to the angle between a line drawn northward and the projection of a star onto the horizon, which can be considered a "constant" heading in that it does not change based on the time of day. While we can certainly navigate toward the sun by walking in its direction, using the varying position of the sun to navigate would lead us to walk in circles because its position relative to the cardinal directions changes continuously (and nonlinearly, depending on the season) throughout the day. Amazingly, though, bees and ants are able to navigate using the azimuthal position of the sun, which they do by averaging the change in its position over a 20-minute period and then updating their representation (Gould 1980; Gallistel 1990). Such a navigational mechanism appears completely absent in humans under normal conditions; otherwise, we might expect to be significantly less likely to walk in circles over longer distances (Souman et al. 2009). While it is possible for us to train ourselves to update the position of the sun as a navigational tool, a technique employed in some instances in orienteering (Burns and Burns 2015) and in some cultures like the Inuit (MacDonald 1998; see also chapter 1), this is clearly neither an inborn nor a naturally developed mechanism that we possess.

Before we become envious of the navigational abilities of sea turtles and bees, however, we should remind ourselves that there are many forms of navigation we utilize everyday that one would be hard-pressed to find in any other species. Perhaps most unique to humans is our ability to rapidly reconfigure our knowledge about the scale of space using visually complex abstract representations. Take for example our ability to use a cartographic map. Whether we view a cartographic map of a small town, a drawing that we create of our house, or a map of our progress toward our destination on an airplane, humans can readily take renditions of properties of large-scale space rendered in small-scale space and convert this information to something we can use in large-scale space. This is a remarkable feat if one considers it in detail and especially given that it is not present in any other form in any other species. Simply by looking at (or imagining) a series of interconnected lines and, perhaps, some words (*north*, *south*, *east*, *west*), we can learn extremely valuable information about the distance and direction of objects in an environment we may never have experienced! These environments can range in scale from as big as our entire planet, or even our solar system, down to a floor plan of our house (figure 4.2).

Another striking example of an ability to navigate that does not appear to be present at nearly the same level of sophistication in any other species is our ability to use visually and acoustically communicated abstract linguistic codes and integrate them with our existing spatial knowledge. For example, we can verbally describe a series of directions to someone based on either allocentric or egocentric codes, and the listener can translate either into spatial codes just as readily as a visual map (Taylor and Tversky 1992). We could explain that to find a park, one walks about 50 feet, then turns right about 45 degrees, cuts through an alleyway for 20 feet, and then walks along a path in the forest until one reaches the park. Or we could explain that the park lies about two-thirds of the way between our house and our office, about 20 degrees offset from the north. Although we have described directions in completely different coordinate systems (egocentric versus allocentric), our listener can readily translate this into knowledge that gets them to their destination.

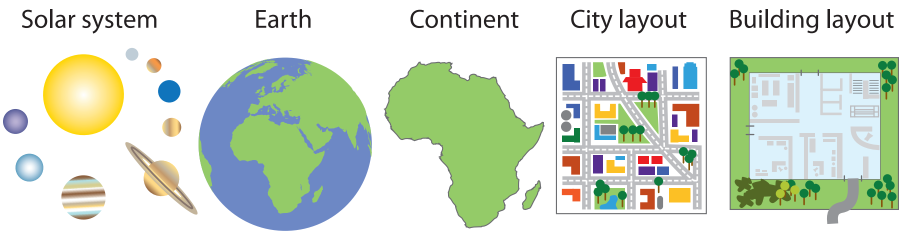


**FIGURE 4.2.** The human visual system and scales of space. Unlike other species, our high-resolution visual system endows us with the ability to imagine visual landmarks on multiple scales. This allows us to imagine and reason about spatial environments we will never directly traverse (like the solar system) but can readily make spatial inferences about (which is closer to the sun—Jupiter or Saturn?).

The preceding considerations have hopefully made it clear that different species possess, in some cases, fundamentally different mechanisms for navigation. Additionally, and perhaps most importantly, we as humans possess several mechanisms that appear to have no homologue in other species. Most germane to our current considerations, however, it is also important to consider navigation from the bottom up. In other words, what important differences between our brains and those of other species might allow us to navigate using cartographic maps and language? As we will argue shortly, differences in the predominance and sophistication of the visual input received by structures like the hippocampus and neocortical structures like prefrontal and parahippocampal cortices, as well as brain structures devoted to language, episodic memory, and planning and decision making, underlie these unique abilities.

## Humans versus Other Mammals: Are We Really That Different?

Because our previous comparisons between human navigation and other species were with insects and reptiles, one could argue that navigational mechanisms in mammals might nonetheless be largely similar to ours. Indeed, there are many similarities in basic brain structure across mammals as well as many behavioral similarities (Simpson 1945; Finlay and Darlington 1995). Perhaps the most commonly researched mammal in navigation is the rat (likely because of its amenity to invasive recordings), which many argue is fundamentally homologous to humans in terms of the brain structures underlying cognitive functions (Squire 1992; Cenci, Whishaw, and Schallert 2002). In terms of navigation, the rat, just like us, uses a combination of its path integration and visual-based landmark systems to navigate. Similarly, the brain structures involved in spatial navigation, particularly the hippocampus, appear homologous between rats and humans, at least at a first pass. Last, rats in particular have excellent navigational skills, and, much like humans, can learn complex spatial environments, even when provided with little reward (Tolman 1948).

There is an important reason why we might hope for there to be greater similarities overall between rats and humans in terms of navigational abilities. Specifically, rats provide a model system in which experiments can readily be performed that would be impossible in humans. In particular, extracellular recordings from freely moving and navigating rats, notably from the hippocampus and including both single-neuron and local field potential recordings, are relatively easy to acquire, provided one has the technology. In this way, we have learned a tremendous amount, on a basic level, of how neurons in the hippocampus and nearby cortical structures—the entorhinal and postrhinal cortices of the medial temporal lobe (MTL) and the retrosplenial cortex behind the splenium of the corpus callosum—respond as a rat freely navigates. These include the discovery of the place, grid, and head direction cells, all of which have been foundational in understanding the neural basis of spatial navigation (see chapter 3).

There are also reasons to think that what we learn from rats about the brain and navigation readily translates to humans. As we discussed in chapter 3, recordings from humans in virtual reality (VR) have revealed place cells and grid cells, with fMRI providing additional evidence for head direction coding systems in humans (see chapters 3 and 5). There are also many similarities between how rats and humans navigate—for example, both species are capable of allocentric and egocentric navigation. Both rats and humans employ piloting to navigate. As we will discuss in chapter 6, there are also important similarities in how both species utilize place versus response strategies, and in terms of the brain regions involved. Many of the brain structures critical to navigation are also present in the rat, particularly the hippocampus. Rats can also navigate in VR, a process that would appear difficult if view-related information were not important to how they navigate (Harvey et al. 2009). Last, phylogenetically it seems reasonable to think that evolution would not have changed us that dramatically from the common ancestor that we share with the rodent, which most likely was a four-legged, land-dwelling animal hundreds of millions of years ago. Thus, it would seem that both behaviorally and neurally there would be few major differences between humans and rats in terms of how we navigate.

As we will describe here, though, there are numerous reasons to doubt an exact translation of navigational mechanisms from rodents to humans. Findings related to detailed *phylogenetic* (comparing genetic differences between species) and *neurophylogenic* (comparing the evolution of different brain structures) analyses suggest important differences between rats and humans on a number of levels, as we will discuss. Neuroanatomically, there are also differences between our navigational brain structures and those of the rodent, particularly in those structures related to the relative weighting of visual input. There are also key physiological differences in the properties of how neurons in our brain respond during navigation, including the presence of landmark-responsive neurons that are not readily apparent in rodents. Finally, and perhaps most importantly, there are many behavioral differences between how humans and rats navigate, particularly in relation to our ability to use abstract maps and linguistic codes to aid in navigation. As we will argue, humans are best thought of as being in their own class of navigation, or perhaps alongside nonhuman primates.

## Phylogenetic and Neuroanatomical Differences in Mammals

The classic view of mammalian evolution, based on differences in body shape and embryonic commonalities, is that mammals split off from a common reptilian ancestor and then radiated into the diverse set of species that they currently represent (Simpson 1945; Finlay and Darlington 1995). According to this perspective, we might expect rats and humans not to differ substantially, and how they evolved would be a simple question of differences in environmental demands (Simpson 1945). For example, differences in capacities like intelligence and executive function might simply be a product of the need to hunt for food, which requires greater abstract planning (Jerison 2012). This perspective tends to emphasize the overwhelming commonalities between mammals, which are, in part, supported by commonalities in neuroanatomy—a topic we will discuss shortly.

This perspective of brain evolution thus suggested a similar conclusion to that of the classic view of evolution more generally: as mammals evolved and diversified, they grew larger in size, and in brain size in particular. Along with a larger brain came more complex machinery, including an increase in neocortical neurons and dendritic branching. According to this account, brain regions themselves ought not to differ fundamentally across mammalian species and should generally be highly conserved (Finlay and Darlington 1995). What should differ is the number of available neurons and their interconnectivity, which should in turn lead to more sophisticated, but not substantially different, computations from rats to humans (Jerison 2012).

Recent work tracking changes in differences across mammalian gene sequences, however, challenges the classic perspective that rats and humans simply gradually diverged. Another way to look at how evolutionary changes accumulated between different species is to simulate random mutations in their genes "backward" and see when these become similar. This is akin to traveling back in time and seeing what changes might have occurred genetically and thus when different mammalian species might have diverged. These detailed simulations and statistical analyses suggest that rodents are better considered a distinct branch, separate from humans, nonhuman primates, and other carnivores like dogs (Cannarozzi, Schneider, and Gonnet 2007). In fact, according to these simulations, dogs and humans, as carnivores, have much more in common with each other than they do with rats and other species of prey.

Similarly, recent analyses suggest that brain evolution did not follow a one-dimensional course in terms of increasing the number of neurons with greater body size. Rather, detailed analyses of volumes and connectivity patterns of different mammalian brain regions suggest significant variations in how they changed relative to each other across species. Specifically, such analyses reveal that mammals separate into three distinct groups based on individual brain volume and connectivity patterns (rather than genetics as considered earlier): rats (insectivores), bats, and primates (de Winter and Oxnard 2001). The rodent cluster diverges from humans and bats based on differences in volume of the hippocampus, septum (one of the major inputs into the hippocampus involved in the generation of low-frequency oscillations referred to in chapter 3), and striatum. In contrast, the human cluster differs from bats and rodents primarily based on neocortical and cerebellar variations. This perspective is consistent with the idea that a major evolutionary pressure on rodents, in particular, involved navigation and escape from prey (hippocampus), while the human cluster involved areas important to motor and cognitive coordination (cerebellum and neocortex).

## How Do Brain Structures Important for Navigation Differ between Humans and Rats?

In addition to comparing genetic and neuroanatomical variations between mammals from an evolutionary perspective, we can also consider simple differences in neuroanatomy of some of these key brain structures. Comparative neuroanatomy, the field concerned with comparing brain anatomy between species, involves extracting brains postmortem, staining them, and looking at them under a microscope to determine how cell types and connections differ. With regard to the

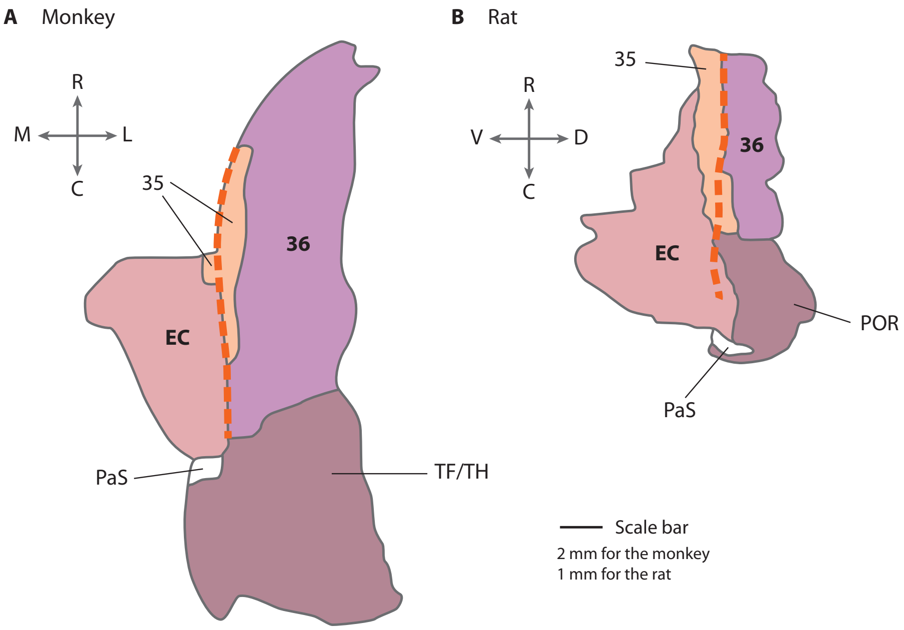


**FIGURE 4.3.** Postrhinal versus parahippocampal cortex in rats and primates. One of the major inputs into the hippocampus is the postrhinal cortex (POR) in rats and parahippocampal cortex (PHC: areas TF, TH in figure) in humans/monkeys. These are anatomically and functionally different structures, however, with POR receiving a mixture of input from multisensory areas and PHC receiving primarily visual input. Figure adapted from Burwell et al. (1995).

neocortex, the evidence clearly suggests that humans have a vastly more developed and different structural arrangement from what is typically observed in rodents. Specifically, some of the major inputs into the hippocampus, a structure we have discussed extensively in chapter 3, differ significantly between rats and humans.

Although the postrhinal cortex (POR) in rats and parahippocampal cortex (PHC) in primates, thought to be homologous structures, feed into the hippocampus via the entorhinal cortex, the two structures differ fairly dramatically between the two species (figure 4.3). Specifically, the primate parahippocampal cortex (and more anterior perirhinal cortex) both receive heavy degrees of visual input from the occipital, parietal, and temporal cortices, representing about 48 percent of its total input. In contrast, the postrhinal cortex in the rat receives input more evenly distributed across sensory modalities, with only about 17 percent of its input coming from visual processing areas, while the majority of inputs to the postrhinal cortex instead comes from somatosensory and olfactory areas (such as areas involved in feeling touch to its whiskers). Thus, there are major differences between primates and rodents in at least two structures important to navigation, the prefrontal cortex and hippocampus.

The differences in visual input via POR and PHC relate to significant differences between how rats and primates use vision to navigate, perhaps most important to our current consideration. Even if the neuroanatomy were identical between rats and primates (which it is not), the massive differences in visual input would dictate different functional properties—that is, that the input will alter how these cells respond, via synaptic plasticity, and thus their “mechanistic” properties. One example of this that we have already discussed is view cells, which numerous studies have reported in monkeys and humans but which have yet to be observed in any similar form in rats. As we will discuss shortly, this is one of the major differences we observe in terms of how we process space compared to rats and other mammals (Ekstrom 2015): our predominant dependence on vision to navigate.

## Rats as a Creature of Prey and Humans as Predators

Perhaps one of the most obvious differences between rats and humans is that humans sit at the relative top of the carnivore food chain while rats are mostly prey animals. As such, the behavioral demands for predators versus prey differ substantially. The primary goal of predators is to stalk potential prey as a food source, and thus high-acuity sensory systems, coupled with sensory-motor systems capable of attacking prey unsuspected, typically accompany predatorial species. In contrast, a primary goal of most prey species is to detect threats, in some form, before they are too close, and either escape or camouflage into the surroundings (explaining, perhaps, why we cluster more genetically with dogs than rats in the phylogenomic analyses described earlier). Thus, there are significant differences between humans and rodents simply by virtue of the former being carnivores versus the latter being primarily prey animals (Lima 2002).

These differences in predator versus prey behavioral adaptations manifest perhaps most dramatically in terms of differences in our visual system. Owing to their eye position on the sides (rather than the front) of their heads, mammalian prey species, like rabbits and rats, can see almost 360 degrees in front and behind them, with only about 20 percent (75 degrees) seen by both eyes (figure 4.4A). This adaptation dramatically improves the ability to detect predators, which will often attempt to sneak up on prey. In contrast, our eyes sit in the front of our head, allowing us to see about 60 percent of world in front of us with both eyes, at the compromise that we can only see at maximum about 190 degrees around us (Block 1969; Wolfe 2006). A significant advantage of binocular vision, in addition to increasing visual acuity, is that it greatly enhances depth perception via binocular disparity (the difference in how images hit our retina allows us to better perceive their location in space). Our high-acuity binocular zone thus dramatically increases our likelihood of visually detecting prey at a distance (figure 4.4B). Thus, simply how our eyes are oriented versus rats dramatically alters our visual system and reflects different behavioral demands as predators versus prey.

In addition to binocular vision, our retinas, the basis for vision, differ in other important ways. The rat retina is primarily made up of rods (not high-acuity cones) and lacks a fovea (Euler and Wassle 1995). In contrast, primates have densely packed, high-acuity, color sensing cones within the fovea at densities far exceeding anything present in the rat. As a result, the visual acuity of humans versus rats differs dramatically.

How might this cause differences in terms of what rats versus humans perceive visually? One way of estimating visual acuity is called cycles per degree (CPD),

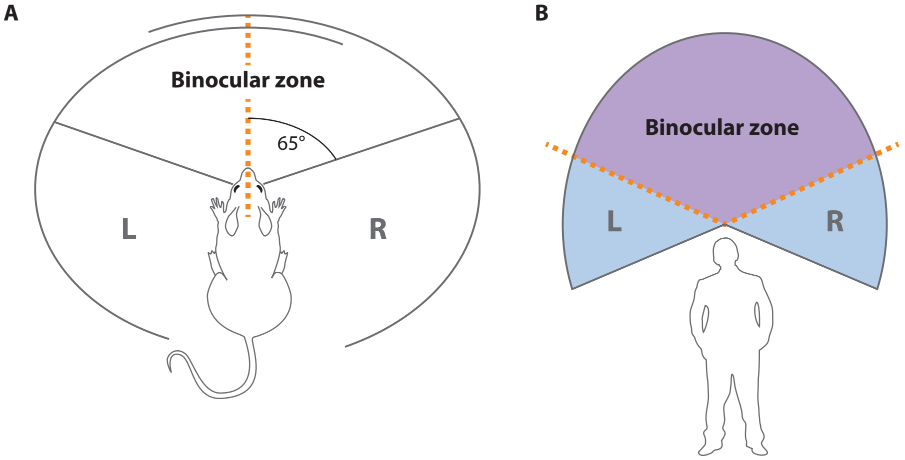


**FIGURE 4.4.** Rat versus human vision. Due the positions of their eyes, rats have a significantly larger peripheral zone in which they can detect predators compared to humans. In contrast, humans have a much higher acuity visual system, in part due to the convergence of the eyes' movements and greater density of cones within their binocular zone.

which reflects how many lines a species can perceive within a visual angle. Current estimates for rat visual acuity are from 0.5 to 1.5 CPD, while that of humans is around 30 CPD, about 30 times better (Prusky et al. 2002). Or put another way, compared to a healthy human, a rat has about 20/1200 vision. This means that a typical rat sees a letter at 20 feet as a human would see the same letter at 1200 feet. Thus, simply at the level of our visual acuity, we see a far clearer world (in a much higher variation of colors) than a rat. These differences alone suggest that our vision confers significant advantages for navigation over that of the rat.

Analysis of eye fixations in freely moving rats further demonstrates that our visual system may be "oriented" differently from rodents during navigation. Eye tracking in rats during navigation demonstrates that, rather than converging on a single location in front of them (like humans), rat eyes often move out of synch. Instead of fixating on a location in front of them, rodent eye movements often converge at locations *above* them (Wallace et al. 2013), a possible adaptation to predators such as hawks and owls. In contrast, our eye movements appear particularly optimized to fixate in front of us, with binocular alignments outside 1 to 2 degrees resulting in double vision and failure to fuse images. These differences in visual processing support the idea that vision is a more important factor in how we navigate than rats.

These dissimilarities in rat and human visual systems also relate to differences in navigation using vision. Rats who undergo retinal enucleation (blind rats) show surprisingly little impairment at navigating to hidden targets (Lindner et al. 1997). In contrast, blind humans, particularly congenitally blind individuals, suffer profound navigational impairments (Thinus-Blanc and Gaunet 1997). In fact, a major endeavor in the field of blind navigation is to develop global positioning system (GPS) devices that can help substitute for visual deficits during navigation (Loomis, Klatzky, and Golledge 2001; Schinazi, Thrash, and Chebat 2016). In the case of rats, their path integration system may provide sufficient input, along with information provided by whisking (moving their whiskers to detect objects), to update their position when lacking vision (Etienne and Jeffery 2004). While blind individuals can certainly employ path integration mechanisms to navigate, in many cases, better than sighted individuals (Loomis, Klatzky, and Golledge 2001), there is little debate that vision forms a central part of everyday navigation in humans. This may be particularly evident in sighted humans when path integration, which accumulates errors as a function of distance, breaks down in the absence of visual cues (Foo et al. 2005).

Perhaps one of the most striking examples of how we employ our high-acuity visual system differently from rats to navigate manifests in our ability to use cartographic maps. Using a map held in front of us to navigate space "out there" is a striking example of being able to perceive subtle differences in shape and form in small-scale space and transform this abstract visual knowledge into large-scale space. Simply from a visual perspective, it is highly unlikely that a rat could see the variations in lines on a map and make use of any of that information. Even if a rat could somehow perceive the lines and shapes on a map, it also remains dubious that a rat could transform this abstract knowledge into something that could be used to navigate. While rats do demonstrate some examples of simple abstract rule learning—for example, if rewarded for A-B and B-C, they expect A-C to be rewarded (Roberts and Phelps 1994)—this pales in comparison to the routine transformation our visual and linguistic brain systems perform using letters and symbols to extrapolate to properties of the world.

## Linguistics and Navigation: North, South, East, and West

Although there are important differences in the human versus rat visual system, arguably the most significant difference between humans and rats (and all other mammals) is our ability to use complex language to communicate. While rats do employ a form of social communication, which involves the exchange of odors and ultrasonic calls to warn of predators and other threats, this system does not involve abstract grammar and mapping of complex symbols in nearly the same way that human language does. In support of language as a fundamentally human property, we possess specialized brain structures in our inferior frontal gyrus (often termed *Broca's area*) and superior temporal gyrus (*Wernicke's area*) that are central to the complex grammatical communication that humans are capable of producing (Gazzaniga, Ivry, and Mangun 2014). No such systems in any comparable form have been described in rodents, or even nonhuman primates, suggesting that the interface between our linguistic abilities and navigation is likely unparalleled in any other species. In particular, it may be that extensive connectivity patterns between language and navigation areas, possibly in part mediated by left and right hippocampus (Spiers et al. 2001), underlie some of our ability to readily use linguistic codes to navigate.

Indeed, linguistic codes form a fundamental part of how we navigate on a daily basis, and using linguistic information to navigate appears largely comparable to how we use cartographic maps. In one study, Taylor and Tversky (1992) had participants read text descriptions of routes and learn maps of these same routes. For text, participants might read: “To reach Etna, drive east along the River Highway to where the highway crosses the White River. Continuing on the River Highway for another half mile past the river, you come to, on your left, Mountain Road.” Another group of subjects learned maps of the same routes. Then, both groups drew maps and made inferences about novel routes within the directions provided. One might expect that because participants had viewed maps they would later draw, they would perform significantly better than the verbal description group. This was not the case though: both map learning and verbal description groups performed comparably. These findings suggest that we can readily convert linguistic information to abstract visual representations used to draw maps (Taylor and Tversky 1992).

One potential limitation of our close linkage of linguistics, symbolic codes, and maps when we navigate is a strong bias to represent spatial environments using cardinal directions. Numerous studies have found that participants typically point to locations most accurately when oriented in a north-south direction compared to any other direction (Frankenstein et al. 2012). In fact, this effect may be so pronounced that we may be biased to use mountains as a simple heuristic to discover which direction is north because mountains (in the northern hemisphere), more often than not, tend to be associated with northward directions (Brunye et al. 2012; Brunye et al. 2015). Thus, cardinal directions exert a powerful bias on how we structure our knowledge of environments, and their use as a verbal cue is a powerful way to encode and retrieve new spatial layout.

Based on differences in how we occupy our surrounding environment, with rats as creatures of prey and humans as predators, we find significant differences between humans and rats. This is perhaps most striking in terms of the differences in the setup and acuity of our visual system, which in turn predicts substantial differences in how our brain processes and uses visual information in the first place. In addition, there are substantial differences in how we can employ this visual information to extrapolate from the information in front of us (maps, letters, and symbols) to the world around us, which also suggests substantial differences in how our brains are set up. Thus, it is important to also consider the functional properties of neural systems important for navigation between humans and rats—in other words, how and what these neurons respond to during navigation.

## Differences in Functional Neural Systems Studied (So Far) between Rats and Humans

As we discussed in chapter 3, an important difference between rats and primates, at least in terms of what has been observed with electrophysiological recordings, regards the presence of cells that respond to visual landmarks during navigation. In particular, neurons responding to viewing locations (Rolls and O’Mara 1995) and landmarks (Ekstrom et al. 2003) are a hallmark of recordings in the primate medial temporal lobes. These findings are consistent with the high degree of visual input from occipital and parietal visual areas that feed into the primate temporal lobe via the parahippocampal cortex (for example, figure 4.5). In contrast, while place cells in rodents respond to changes in distal visual cues, no cells specifically

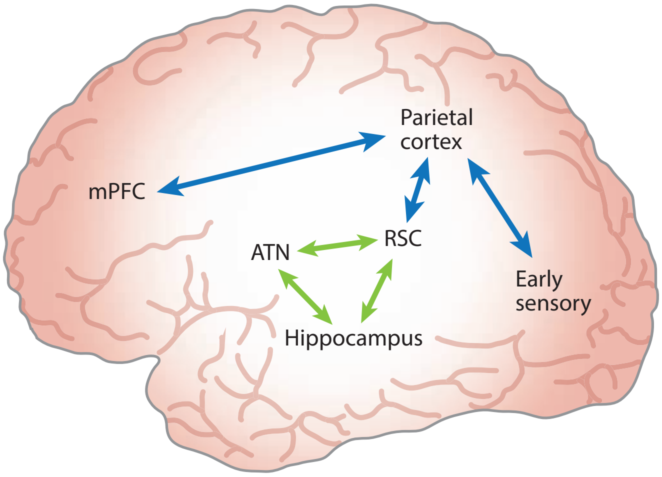


**FIGURE 4.5.** Visual input is critical to human spatial navigation. Visual information flows into the human hippocampus from the primary visual cortex ("early sensory"). RSC stands for retrosplenial cortex; mPFC stands for (medial) prefrontal cortex; and ATN stands for anterior thalamic nucleus. Figure adapted from Miller et al. (2014).

responding to viewing landmarks have been reported to date. While these may be present in some form in the rodent, it seems likely that these representations are significantly lower in resolution than in the primate, and, perhaps, are combined with place responses rather than existing as their own type of cellular response.

In addition to the presence of cellular responses in the primate but not rodent parahippocampal cortex, another important difference between rats and humans regards the development of the neocortex—particularly, the prefrontal cortex. We will discuss this structure in more detail in chapter 5 in relation to goal-oriented navigation. It is not clear if rats have a prefrontal cortex in any way comparable to the six-layered laminar prefrontal cortex in humans. Indeed, the rodent homologue appears more comparable to that of the anterior cingulate cortex in primates, an emotion-motor integration center (Preuss 1995). An important question then is why the prefrontal cortex might be important in the first place, for cognition and navigation more specifically.

The prefrontal cortex in humans and nonhuman primates appears to form the apex, or hub, for an important cognitive function termed *cognitive control*. In particular, the prefrontal cortex integrates visual information from two different fundamental streams that divide into dorsal (superior) and ventral (inferior) processing streams within primates. The dorsal visual stream is important for locating areas in space relative to our body position and is considered a top-down attentional system important for orienting attention to locations that we might consider relevant in the environment (Mishkin, Ungerleider, and Macko 1983). In contrast, the ventral visual stream involves neural systems that code for objects independent of their position in space (Kravitz et al. 2013). As such, the ventral visual stream may be more important for bottom-up orienting of attention based on features of objects. In many situations, however, we require integration of location (where) and object (what) features: indeed, integration and modulating different components of these two systems may be a primary function of the prefrontal cortex. This role is further consistent with the connectivity patterns of the prefrontal cortex, which have massive projections to and from these important visual processing streams.

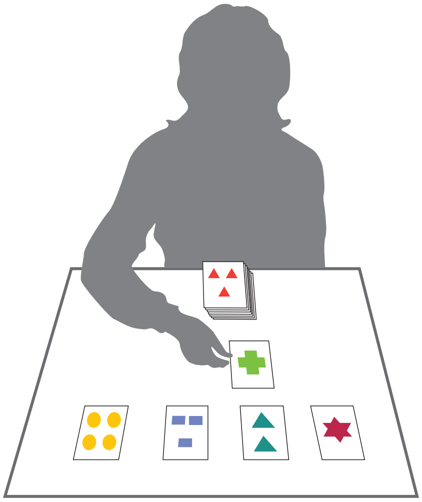


**FIGURE 4.6.** The Wisconsin card sort task. This widely used neuropsychological assessment is critically dependent on human prefrontal cortex.

Consistent with its role as a regulator of these two streams, damage to the prefrontal cortex in humans produces substantial deficits in cognitive control, the ability to regulate responses based on current task demands and inputs. One example of cognitive control involves a task termed the *Wisconsin card sorting task*. The participant must guess the rule that an experimenter is using (figure 4.6) in order to match cards. The images on the cards vary in shape, color, and number (for example, two green stars). If the participant draws a card with two red crosses, should she match the new card in terms of number (for example, two objects), color (for example, green), or shape (for example, cross)? At some point after the participant has guessed the rule (typically after 10 trials) the experimenter will change it, and the participant must then determine the new rule. While most people can readily perform this task, damage to the prefrontal cortex results in significant deficits in the ability to switch to new rules. In other words, a patient with prefrontal cortex damage tends to incorrectly stick to an old rule and is not able to update to a new rule based on conflicting information provided by the experimenter.

Navigation, similarly, involves high demands in the ability to flexibly utilize rules and modulate different types of information. Let's say we are driving along a familiar route (for instance, from work to home), and we find that one of the roads is closed owing to an accident. We have a couple of options: we could wait for the road to open, or we could try to come up with a route that will allow us to navigate around the roadblock in order to get home. This task involves suppressing the current route we have activated and instead activating a new set of routes. We may have to imagine several different routes and decide which is most likely to get us home efficiently or effectively. For example, if we turn around and take a left, this may simply take us back the way we came. Driving 30 miles out of the way is not likely to be efficient, and there are likely better routes. Thus, coming up with new routes puts heavy demands on cognitive control and our prefrontal cortex in particular, an issue we will return to in chapter 5 (Spiers and Gilbert 2015).

While rats can certainly employ shortcuts if a route is blocked (Tolman 1948), it is unlikely that they possess the same sophistication in terms of visual imagination. Additionally, without a developed prefrontal cortex, rats almost certainly cannot actively compare multiple complex routes, suppressing some and activating others. It seems likely that the high degree of connectivity patterns between prefrontal cortex and many different brain areas, including the dorsal and ventral visual streams, underlies at least some of our abilities to perform complex and abstract tasks during navigation, including using maps and employing shortcuts.

Given our discussion of the importance of cartographic maps to navigation in humans, it is worth considering what other differences we might expect in terms of functional differences in our brain responses between rats and humans. While it remains unclear whether cartographic maps are useful in any form to a rat, we can readily use map information to find more efficient paths to navigate in a way that appears to involve novel mechanisms beyond simply thinking about locations. In support of this, the brain systems involved in using a cartographic map also do not appear to be the same ones involved in place coding (Zhang, Copara, and Ekstrom 2012). In fact, one interesting possibility is that our ability to use cartographic maps may derive, in part, from our high-resolution ventral (object) stream (Shelton and Gabrieli 2002). In this way, the brain systems involved in learning from and using a map are different from those involved in navigation.

## Is the Hippocampal Code for Space Different in Humans Compared to Rats?

So far, we have focused primarily on neocortical brain structures, parahippocampal and prefrontal cortex, which one might expect to be different between rats and humans because of the substantial difference in cortical neuron number and development between the species (Jerison 2012). In addition, as we have discussed, these structures differ substantially neuroanatomically between rats and humans and thus it is not surprising that they might endow the two species with different navigational behaviors. Yet there are also differences in hippocampal anatomy between species and the strong degree of visual input into the hippocampus via the parahippocampal cortex does differ substantially. Given that both primates and rats have place cells, is there any evidence to suggest that hippocampal functional properties might differ in any meaningful way during navigation?

As we saw in chapter 1, the vast majority of recording studies of humans happen in virtual reality, for a number of different reasons. In contrast, the vast majority of rodent navigation studies involve freely moving rats that explore an environment with few restrictions except the electrodes implanted into their brain. Because most human studies involve virtual reality and most rat studies involve full body movements, this sets up a possible difference in how the hippocampus might receive its primary input. In the case of humans, this input will be almost exclusively visual because desktop VR involves only limited movement of the keyboard. In contrast, freely moving rats employ their vestibular and other proprioceptive and sensory systems like their whiskers. In fact, it is somewhat striking that both rats and humans show place cells under fairly different conditions.

One way to more directly compare the properties of the hippocampus during navigation is to have rats navigate in virtual reality. At first glance, particularly given our discussion about the low visual acuity of the rodent visual system, this might

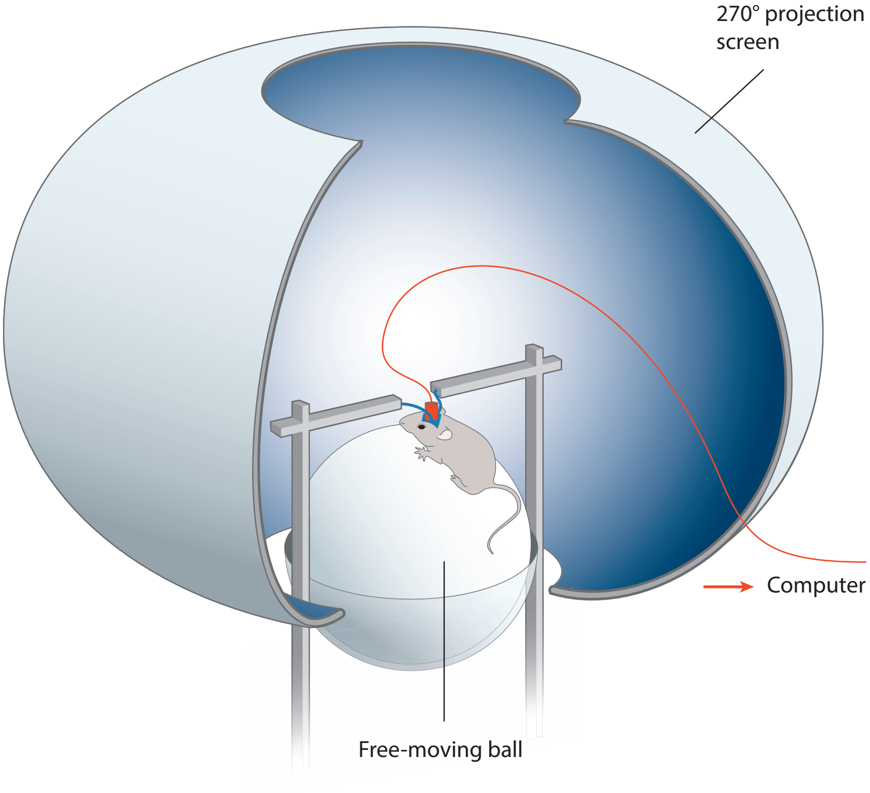


**FIGURE 4.7.** A rat navigating virtual reality by running on a ball.

seem laughable. How would a rodent navigate in virtual reality? As surprising as it might sound, though, several research teams have successfully developed systems that allow rodents to freely navigate VR. This typically works by having a rat freely walking on a ball in front of a large computer monitor that renders the VR environment, which drives the rate of movement on the screen (termed *optic flow*; figure 4.7). Rats, and even mice, when receiving extensive training on these tasks, can navigate virtual reality in much the same way that humans do (Harvey et al. 2009).

When rats freely navigate in VR by walking on a ball, at least in some reports, both place cells and low-frequency oscillations appear present in a similar way to what is observed during real-world navigation (Chen et al. 2013). A difference between humans and rodents, however, is that humans typically experience little body movement in VR, whereas most rodent VR setups require the rats to move about to drive what they experience. Under these conditions, there is an attenuation in hippocampal low-frequency oscillations as well as a decrease in place cell selectivity. Remarkably, though, both of these important hippocampal signals are still present and, other than a reduction in their prevalence, are still largely comparable to real-world navigation. Subsequent reports of VR navigating rats confirmed the reduction in place selectivity, further suggesting a reduction in the frequency of the theta rhythm by about 1 Hz (Aghajan et al. 2015), which may be comparable to the reductions in low-frequency oscillations humans experience between real-world and VR navigation (Bohbot et al. 2017). However, when rats experience only optic flow, with no body movement, theta is reduced further still, suggesting the possibility that the rat visual system does not compensate for the lack of body-based input in the same way as humans (Chen et al. 2013).

## Visually Rich Episodic Memory as Different in Humans versus Rats

Yet another ability that sets us apart from rats is our capacity to displace ourselves in time to reexperience past events in what is known as our *episodic memory*, discussed in chapter 1. Episodic memory is intimately connected with spatial memory in a number of ways. In particular, the spatial layout of environments in which we navigate provides the backdrop for the many events that we personally experience on a day-to-day basis. Each event is defined by the time at which it occurs, the people involved, and the particular interactions or activities that take place. However, it is the space occupied by the event that seems to hold a special status (Robin and Moscovitch 2014), suggesting that space serves as a scaffold for encoding these episodic memories (see also chapter 9).

When reexperiencing an event in episodic memory, we presumably conjure up the rich contextual and sensory details experienced at the time that the event was first encoded. Like human spatial memory, these details seem to be disproportionately visual (Greenberg et al. 2005). Indeed, many of the same regions important for spatial navigation appear to be important for episodic memory. At least some of these features may hint that the rat, or even the more visual avian or nonhuman primate, is unlikely to have episodic memory and related *episodic prospection* to imagine spatially bound events that might be personally experienced at a future time. However, there is growing evidence that "episodic-like" prospection may be possible in at least some species, although almost certainly in a diminished form (Wittig and Richmond 2014).

## Spatial Memory as a Defining Feature of Episodic Memory

*Episodic memory* refers to specific, contextual details of personally experienced events that occurred at a particular point in time and at a particular place, from words presented on a list in a laboratory to details of autobiographical events experienced in everyday life (Tulving 2002). The events are unique in that they are not recurrent (for example, annual Thanksgiving dinner at Aunt Alice's) and are unlikely to be experienced in the same way by any two people. It is unclear which details we need to re-create to have an episodic memory, but space, time, and sense of self are widely viewed as key elements (Tulving 2002; Kraus et al. 2013; Robin and Moscovitch 2014). Details may be reshuffled and even replaced or distorted (Schacter 2012), but as long as one has a temporal and spatial context on which to hang those details, along with having experienced the original episode firsthand in the past, an episodic memory should persist. Another feature that defines episodic memory is the type of consciousness that is associated with it: *autonoetic* (self-knowing). Tulving, who coined the term, proposed that autonoetic consciousness allows for the subjective reexperiencing of an episode in relation to time, providing the phenomenological quality of transporting oneself across time to mentally relive an event (Tulving 2002). This is why when we remember an event, we are aware that we experienced it personally in the past.

This subjective awareness is not restricted to remembering the past; it also applies to imagining future personal experiences and thus has been described as enabling "mental time travel." Semantic memory, in contrast, is characterized by its own type of consciousness: *noetic* (knowing). Noetic consciousness allows organisms to act on their knowledge of the world in a flexible manner, and to be aware of and perform cognitive processes on objects and events, and the relations among them, in their absence. The two types of consciousness, autonoetic and noetic, were contrasted with a third form of consciousness tied to procedural memory: *anoetic* (nonknowing). Anoetic consciousness was believed to be temporally and spatially restricted to the current situation. Organisms that possess anoetic consciousness can perceive, internally represent, and respond behaviorally to their current internal and external environment but lack the conscious ability to process and integrate this information.

Studies of neurological patients and neuroimaging have provided strong support for dissociations between episodic memory and semantic memory, and between autonoetic and noetic consciousness. These studies assign the hippocampus and adjacent medial temporal lobe (MTL) structures (entorhinal, perirhinal, and parahippocampal cortices) a prominent role in episodic memory, but differ in terms of the time course, nature, and specificity of that role, a topic that we will return to in chapter 9 (Squire 1992; Moscovitch et al. 2005). While some view the role of the hippocampus as essential for episodic memory, others view its role in episodic memory as reflecting the connections between details that are framed in spatial-relational form of the memory, as argued by cognitive map theory (O'Keefe and Nadel 1978). One possible resolution to this debate, which we will advance here, is that humans possess a particularly rich visual-episodic memory system, compared to rats, which can also work in the service of navigation.

The intimate relationship between episodic memory and spatial context has long been recognized through the ancient mnemonic practice of method of loci, which involves mentally assigning to-be-remembered items to salient locations along a familiar route, a method often used by those with superior memories (Maguire et al. 2003). The prominence of spatial context in episodic memory is also illustrated by a recent finding that familiar spatial contexts (previously visited Toronto landmarks) facilitate the recall of detailed autobiographical episodic memories, spatial scenes, and novel imagined events, over less familiar contexts (Robin and Moscovitch 2014). For example, Robin, Wynn, and Moscovitch (2016) found that familiar landmarks can also serve as more useful cues than unfamiliar places and familiar people when participants are trying to retrieve details of newly learned event scenarios. Indeed, participants took it upon themselves to conjure up a spatial context when one was not provided, and scenarios with a spatial context led to retrieval of more details as well as vivid reexperiencing of those details (Robin, Wynn, and Moscovitch 2016). The nature of perceptual details recalled by participants was not specified, but it seems plausible that interactions between episodic memory and familiar settings are mediated by the rich visual imagery induced by well-known environments.

## Visual Details in Episodic and Human Spatial Memory

A challenge to classic views on spatial memory and episodic memory and, perhaps more critically, traditional boundaries between memory and perception, is the suggestion that regions within the medial temporal lobes (MTLs), including the hippocampus itself, support perceptually rich representations, both visual and in visual imagery (Erez, Lee, and Barense 2013). Patients with MTL lesions that encompass perirhinal cortex have difficulty visually discriminating among objects and among faces presented from different viewpoints within an array to detect the one that is slightly different from the rest; patients with lesions limited to the hippocampus show visual discrimination impairment, but for scenes (Warren et al. 2012). This major shift in understanding the separable roles of individual MTL structures was in fact based on animal research showing that MTL regions surrounding the hippocampus make unique contributions to visual perception (Barense et al. 2012). These findings, which link episodic memory and perceptual details, will be discussed in greater detail in chapter 9. It is possible that impoverished detailed representations of environments do not just parallel episodic memory impairment found in hippocampal amnesia, but interact with or contribute to it. As discussed earlier, a paucity of perceptual details may contribute to impoverished episodic memory, as context-specific perceptual details are required to form a rich episode and engage in vivid reexperiencing (Robin and Moscovitch, 2014).

St-Laurent et al. (2014) had individuals with unilateral MTL epilepsy and healthy controls describe the perceptual features and story lines for film clips, written narratives, and personal autobiographical memories. They found that patients showed a deficit in perceptual details, particularly in the autobiographical memory and film clip conditions, suggesting that an inability to generate sufficient perceptual episodic memory details may impair reexperiencing of the past (St-Laurent et al. 2014). These findings are consistent with neuroimaging work that shows that the hippocampus is often involved in the vividness of episodic memories (Gilboa et al. 2004). Imagining the future, particularly when it involves visually rich episodic memories, also involves the hippocampus (Addis and Schacter 2008). Together, these findings suggest that the hippocampus plays an important role in binding details from multiple modalities, particularly vision, into vivid recollections, as predicted by the transformation hypothesis presented in chapter 9 (Winocur and Moscovitch 2011).

As our discussion so far has demonstrated, episodic memory and navigation involve many similar core features. Perhaps most central to the intersection is the fact that navigation involves remembering past experience to facilitate how we navigate future routes. In particular, our ability to mentally time travel and imagine routes we have taken in the past is a core part of our ability to form rich, visually based maps. These maps in turn are a critical part of our ability to navigate efficiently using information we have formed from past experiences.

As we have argued up to now, what makes episodic memory and thinking about routes we have traveled in the past uniquely human, in our view, is the high degree to which vision in particular underlies this process. While episodic-like processing certainly exists in other species, like rodents and birds (Clayton and Dickinson 1998; Eichenbaum, Yonelinas, and Ranganath 2007), it is doubtful that these contain any of the visual complexity of humans. In fact, one of the hallmarks of functions of the hippocampus, a brain structure important to both navigation and episodic memory, involves the rich visual input that it receives from the perirhinal and parahippocampal cortex compared to other creatures like rats. Thus, the presence of a structure deeply involved in memory, and also navigation, which operates in a primarily visual manner, argues for visual input as a critical substrate for how we process information compared to other species.

## Summary

A core assumption of much of modern research on spatial navigation has involved the fundamental similarities between humans and rats. In many ways, given where we were 40 years ago, when *The Hippocampus as a Cognitive Map* was first published, this assumption made a lot of sense. At that time, extracellular recordings in freely moving rodents were in their infancy, fMRI/MRI did not exist, and extracellular recordings in humans were rarely employed in research contexts. Thus, because research always must involve some assumptions, it made sense to focus initially on the rat hippocampus as a way of understanding navigation more generally. However, there are clear, obvious differences between humans and rats readily visible on the surface: We use language; rats do not. We use cartographic maps; rats do not. We rely heavily on vision to navigate; rats do not. Navigation, for most individuals, involves visually rich replaying of memory-related events and imagination; rats do not have the same visually rich episodic memory system. As we then look “under the hood,” we observe many basic differences between rats and humans in terms of the visually based inputs that our brain receives compared to a rat. Indeed, the argument made many times in the literature, that our medial temporal lobes are an evolutionary conserved structure from the rat, has flaws, and there are clear differences between rats and humans both anatomically and in terms of functional neural responses during navigation. Overall, behavioral, neuroanatomical, and genetic/evolutionary lines of evidence argue against the idea that what we learn from rats will automatically “port” to humans in terms of navigation structures, an issue we will frequently revisit in the upcoming chapters.

## CHAPTER 5

# KEEPING THE GOAL IN MIND: NAVIGATIONAL GUIDANCE SYSTEMS

There are many reasons why we might travel to a place: we might do so to explore a new part of town, to find somewhere to eat or a particular shop, or simply to get to work. We can describe traveling to a destination as goal-directed navigation, and this constitutes much of the literature on spatial navigation. This is partly because spatial navigation tests in animals have been used as a proxy for memory processing—that is, an animal must remember a goal when navigating.

Goal-oriented navigation is also fundamental to our daily lives and survival: without a goal in mind, we wander aimlessly with little need for learning about an environment. Sometimes, we might have a specific goal—for example, to get home—at other times, our goal might be to seek out food, or to forage for things we need. In this chapter, we review how the brain supports goal-directed navigation, in which a participant seeks a specific goal and the brain performs specific computations related to the spatial distance of the goal. Our focus will be on how goals might be represented and the neural systems that might provide the guidance information to determine how to travel to the current goal—how the brain keeps the goal in mind.

### Three Factors That Strongly Affect Goal Coding: Environment, Knowledge, and Strategy

The engagement of different neural systems to support goal-directed navigation depends on three important components: (1) the environment, (2) knowledge and experience of the environment, and (3) navigation strategies used (Spiers and Barry 2015). When it comes to environments, finding an oasis in the Sahara Desert is a very different challenge from navigating the road network of Manhattan. In the Sahara, you must be sure that you are traveling in a straight line using distant global landmarks, such as mountains. By contrast, in New York keeping straight is rarely a problem, but seeing distant global landmarks is difficult, and knowing which turns to take becomes crucial. These differences between learning turns and judging movement relative to distant mountains draw on different neural circuits. Thus, traveling different types of environments will engage different brain systems.

Knowledge and experience with an environment also makes a substantial difference in terms of what neural circuits are engaged. Take for example the licensed

London taxi driver. Such taxi drivers typically train for up to four years to learn the 25,000 streets of London and have to pass a grueling exam on what is known as “The Knowledge of London.” In contrast, imagine a newcomer to the city who has gained enough information to discover shortcuts, but has far from the complete knowledge a taxi driver has. Both can undertake impressive navigation in the same environment, but it is likely that different neural circuits will be engaged. For example, the hippocampus would likely be engaged in a recently learned environment, but less so in an environment learned many years ago (see chapter 9 for a discussion about how familiarity affects the brain regions needed for spatial memory). Thus, levels of knowledge also interact in important ways with goal-directed navigation.

## Knowing a Route versus Having a Map

It is not just the nature of our experience, the complexity of the environment, the task (that is, finding a specific goal or randomly searching for something), or prior exposure to it that matters. There are different ways in which the brain can use information to guide navigation. These different systems can be thought of as “controllers.” It is important to draw the distinction between knowledge of the environment and knowledge of the particular route to the goal. Exposure to the environment might be similar in two cases, but while one person might focus on learning the turns involved in getting from one place to the next, another might focus on the landmarks and how they are interrelated. Such differences mean that the neural systems engaged to navigate to the goal are quite different despite what appears to be a similar exposure to the environment.

For example, as we discussed in chapter 2, knowing the surrounding environment and how landmarks relate to each other is an example of allocentric knowledge, while knowing individual routes is an example of egocentric knowledge. Thus, egocentric and allocentric knowledge interact in distinct ways with finding one’s goal. For example, extensive learning of a route can lead to a separate engagement of brain circuits involved in highly habitual behavior. Evidence indicates that the lateral striatum is likely important for guiding navigation along familiar, overlearned routes (van der Meer, Kurth-Nelson, and Redish 2012). One of its roles is to store overlearned habitual behavior, likely to include habitual routes, which we discuss in more detail in chapter 6. Having a system that allows us to simply repeat a complex set of visually guided movements to reach a goal is highly useful in freeing up neural resources for other functions, such as working out what we will do when we reach our goal.

Distinct from the lateral striatum’s role in representing overlearned habits, the medial striatum appears to be important for learning the habitual route information. This learning process is considered in detail in the field reinforcement learning (RL) theory (Sutton and Barto 1998). In this theory, the actions that need to be learned can be achieved via a number of different control systems. For example, learning to approach a particular reward requires a simple Pavlovian conditioned learning circuit. When the rewarded location is not visible, actions or sequences of actions need to be learned in order to reach the goal location—for example, it feels correct to turn left at the clock tower. The learning of the appropriate actions to take is a gradual process, and appears to rely on the striatum (Packard and McGaugh 1996; van der Meer, Kurth-Nelson, and Redish 2012). Such a control system is known as a *model-free* controller, since there is no explicit knowledge structure of how different sequences of actions are related to reaching the goal or the need to remember any specific coordinate system (that is, egocentric or allocentric). In this sense, the system is akin to an automatic pilot, but one that doesn't know anything about the destination—it just provides information about what actions to take at each given step along the journey.

A route-based, model-free system contrasts with a model-based, map-like control system that learns about the structure of the action-state transitions and how they are related in order to reach the current goal. As we discussed in chapter 3, O'Keefe and Nadel (1978) made this distinction in *The Hippocampus as a Cognitive Map*, in which they argued for a separate route-based taxon system (also referred to as *stimulus-response*) and a map-like *locale system* they termed the *cognitive map*. For example, when attempting to navigate a set of city streets, one might recall the layout of the streets and consider which streets are connected and the best route through the streets. Such a process would involve retrieval of map-based information, also referred to as *model-based control* of the action sequences required to reach the goal. However, such model-based processing need not be a fully conscious deliberation of all the information. We outline some of the different ways that goal information might be coded as we navigate in figure 5.1.

An experiment by Hartley et al. (2003) helps nicely illustrate the two systems. Participants initially learned two virtual reality towns, A and B, each containing approximately 15 streets (Hartley et al. 2003). In town A, participants learned to

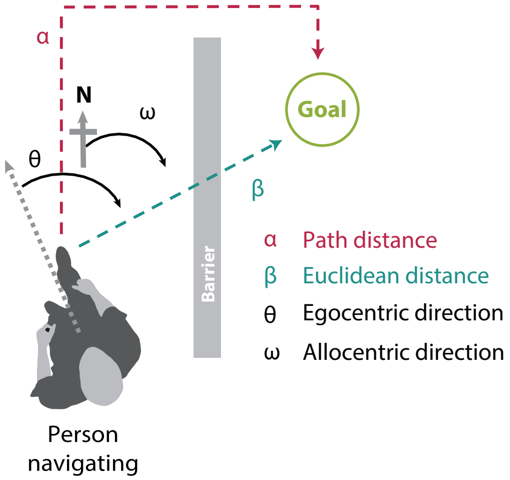


**FIGURE 5.1.** Different forms of goal-oriented navigation. Four different spatial relationships are depicted between a person navigating and the person's goal. Path distance refers to the distance along the path to the goal (also referred to as the "city-block distance" or "geodesic distance"). Euclidean distance is the distance along the shortest straight line connecting current position and the goal. Egocentric direction is the angle between the person's current facing direction and the direction along the Euclidean. Allocentric direction is the angle between a fixed reference direction in the environment (for example, north) and the Euclidean. Adapted from Spiers and Barry (2015).

find their way between a set of landmarks by taking all the paths between them (*wayfinding*), learning an internal map of their relations. In town B, they were required to simply follow the same route between the set of landmarks over and over again (*route following*). Exposure to the landmarks was identical in the two towns (which were counterbalanced across subjects for the learning tasks); the difference was in what the participants knew about their spatial relationships. Using functional magnetic resonance imaging (fMRI), the researchers revealed that the hippocampus was more active in the wayfinding task, while the caudate nucleus (which is part of the striatum) was more active in the route following task. This supports the view that the caudate nucleus is involved in guiding navigation using a system akin to an internal *autopilot* and that the hippocampus is involved in navigation requiring retrieval and selection of the paths with the environment—the cognitive map (see chapter 6 for a detailed discussion about these two navigation systems).

## Vectors, Charts, and the Autopilot

In the domain of navigation, another controller also appears to guide navigation: the path integration system (see chapters 2 and 3). This is typically considered as a system used to guide navigation to a recently visited location, where the brain integrates information about the set of steps and turns from a starting point to calculate a vector back to the initial location. A similar system may allow a navigator to retrieve a vector to a remembered goal and then use information about body turns and translation to return to that goal location. Such a vector system might exist in the hippocampus, although it remains unclear whether place cells underlie this process and where exactly in the hippocampus this occurs. Regardless of its exact anatomical location, which is still debated, path integration plays an important role in guiding to goals using a vector-based approach.

The vector, the cognitive map, and the autopilot each have something to offer the navigator. Otherwise, we might argue, evolution would likely have stripped them from the brain. The autopilot frees up precious resources from the brain's memory system for considering the past or the future, making it easier to keep an eye out for danger or to chat to a friend while navigating. Being able to think about what we might do when we reach our goal is a useful thing, as is reflecting on what happened the last time we were there. However, the autopilot is limited. If we are off the beaten track, it will not guide us, as we don't have sufficient knowledge of the environment or enough learning about the route. The model-based map (locale) system thus allows us to make journeys that are not yet so well learned that we have an autopilot to tell us where to go, but, critically, it also allows us to plan optimal paths that are essential for everyday life. The model-based map is a more sophisticated system compared with the autopilot and allows us to make novel connections between locations that we might not otherwise have visited.

However, the map system has the limitation of being composed purely of the connections within the environment—the *topology*—and thus unable to extrapolate or estimate the direction to the goal. The vector system achieves this by indicating the direction and distance to the goal. This means that when two new options for travel open up, the navigator can tell which one will lie in the direction of the goal and may be more useful. The vector system, though, is limited. If the path leading directly in the direction of the goal is a dead end, then the vector system needs to be suppressed to reach the goal; otherwise, navigators will find themselves banging repeatedly into a wall that obstructs their path!

Thus, a combination of a vector system, a path-based system, and an autopilot are helpful adaptations evolution has sculpted in our nervous system to allow us to navigate. Evidence for these different navigation systems has come either from studying rodents with experimental lesions/electrophysiological recordings or from human neuropsychological studies/functional neuroimaging. In the following sections, we will focus on the role of the hippocampus and the prefrontal cortex in representing information needed for navigational guidance that requires flexible representations and adapting to changes in the environment because of forced detours.

## Rodent Studies of Navigational Guidance Systems

A large body of research using experimental lesions suggests the importance of the hippocampus in allocentric map-based navigation and the dorsal striatum in response-based navigation (see chapter 6). Such research highlights that these areas are necessary to map- and response-based learning, but in vivo single-unit methods provide additional critical information about the *mechanisms* underlying this process. Much of this research has focused on place cells (see chapter 3). This research has either involved rats exploring mazes with connected compartments or tracks where the rat must learn to make choices at junctions or in open arenas where typically a hidden goal must be navigated to and from a range of locations.

When rats have to learn which pot contains food in which room, changes in the activity of the cells mirrors the changes in learning which is the correct pot (Komorowski, Manns, and Eichenbaum 2009). When running along tracks to reach a goal, a set of place cells will differentiate which route the rat is taking to get to the goal (Wood et al. 2000; Ainge et al. 2007; Grieves, Wood, and Dudchenko 2016). For example, while some place cells will fire in their field whenever the rat passes through that region of space, other place cells will fire only when the rat makes a turn in a certain direction at the end of the track. Such route selective activity is consistent with the hippocampus learning a set of connections between locations in the environment.

When rats navigate open-field environments, several studies have provided evidence showing increased activity at goal locations. In a study by Dupret et al. (2010), rats had to discover each day where food was hidden in a large open arena composed of lots of holes where food could be placed (Dupret et al. 2010). While rats foraged across the surface of the arena, CA1 (a subarea of the hippocampus) place cells showed activity randomly distributed across the surface. After the rats had begun to repeatedly run to the three different reward locations, the activity of the place cells shifted to overrepresent the areas near the rewarded locations. This did not occur in area CA3 (another subarea of the hippocampus), suggesting that such goal coding may be specific to CA1. As an important control, the shifting of place cell activity did not occur when the goals were marked with a visual cue. Similarly, in a study by Hok et al. (2007), place cells formed extra firing patterns at unmarked goal locations in an open arena. Thus, overrepresentation of goal locations by place cells is one potential mechanism by which goal- and map-based navigation might be combined.

While studies exploring place cell clustering at goals help in understanding how goals might be represented, they do not explain how the cell activity dynamics during navigation relate to planning a route to the goal or considering the route. One influential study was conducted by Pfeiffer and Foster, who had rats explore for rewards in a 1.5 m × 1.5 m arena (Pfeiffer and Foster 2013). This arena contained a grid of 8 × 8 ports that released a liquid reward when the rat was at the correct port. On each day, one of the ports was designated as the "home" location. The rat had to explore the arena to find a port (randomly allocated) that provided the reward. After this, the rat had to return to the home location to get another reward before being able to seek out a new rewarded goal and so on until the rat has navigated all the space in the arena. Remarkably, during the pause before running, when a neural signal called the sharp-wave-ripples occurred in the hippocampus, place cells that represent the space in the maze in the upcoming journey to the new goal were rapidly activated. The order of place cell activation occurred roughly in the direction of the goal, as if the rats' place cell map was "examined" to read out the parts of the path ahead of the rat. This finding is important because it shows how activity patterns might relate to future navigation during periods before the rat has even begun to travel toward its goal.

Other research has shown that during the rat's initiation of running to the goal, the place cells that code locations along the future part of the track will become activated, with cells farther along the track ahead of the animal firing at greater rates for goals farther away than goals closer to the animal (Wikenheiser and Redish 2015). Thus, it appears the hippocampus sets up a readout of upcoming locations with knowledge of the route ahead. While the entorhinal grid cells might support vector coding of the distance to future goals (Erdem and Hasselmo 2012; Kubie and Fenton 2012; Bush et al. 2015), there is currently no empirical evidence to support this idea. This is owing to the challenge of developing experiments in which rats run to goals that allow the distance and the direction to the goal to be sampled across a full range of distances and directions. For example, in a Morris water maze (discussed in chapter 3), the initiation of the navigation phase starts at the edge of the maze and ends near the middle each time. After learning, the rat more or less swims directly to the goal, without exploring other areas of the maze. This makes it difficult to determine how distance and direction are represented by cells in the brain during navigation.

## Bat Goal Vector Cells

While it is hard to get rats to take novel routes running around a goal, this is not a problem for bats, which can fly directly to their goal. Sarel and colleagues recorded from the hippocampus of Egyptian fruit bats as they flew around a platform baited with food in a large room (Sarel et al. 2017). The bats learned to keep circling the platform to receive additional food rewards. The swooping bats thus provided numerous time periods when different angles and directions from the goal were

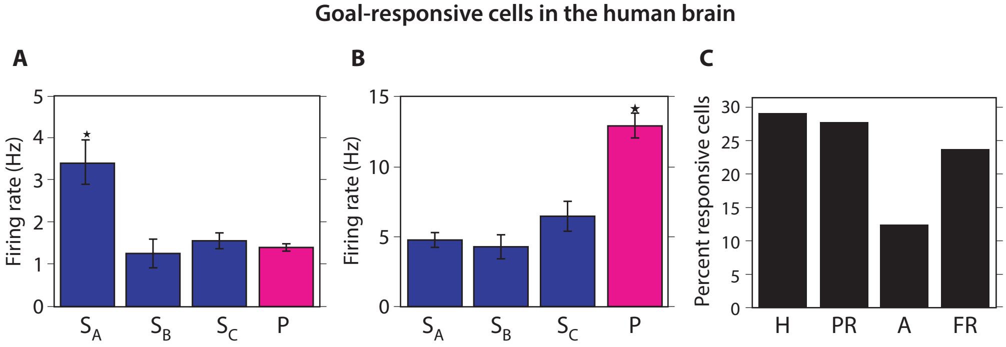


**FIGURE 5.2.** Extracellular recordings from the human brain during goal-based navigation reveal goal responses distributed across a variety of different brain regions. SA refers to store A, SB refers to store B, SC refers to store C, and P refers to passengers—all of which were goals.

sampled in the recordings, helping provide information on how the bat hippocampus might represent the distance and direction to goal. Sarel et al. (2017) found that a subpopulation of cells in the hippocampus increased activity with proximity to the goal, and some were tuned to specific egocentric directions (for example, to the bat's left) to the goal with several cells that combined distance and direction information. See figure 5.1 for an explanation of different types of distance and direction considered in the Sarel et al. (2017) experiment. The team described these as *goal vector* cells in the bat hippocampus. When two goals were present and only one active during a session, the goal vector cells were tuned to the currently active goal and suppressed for the other goal.

Whether these cells are shared with rodents and humans is unknown. When it comes to humans, three methods have been used: functional magnetic resonance imaging (fMRI), extracellular electrophysiology, and patient lesion studies. Both fMRI and electrophysiology methods required participants to remain immobile for recording, thus employing virtual reality (VR), while the human patient lesion study involved freely walking patients.

## Human Electrophysiological Studies

Rodent extracellular electrophysiology studies provide strong evidence for the modulation of neural activity by the intended goal. Similar findings have been demonstrated in humans freely navigating in virtual reality using extracellular recordings in patients. In the Ekstrom et al. (2003) study reviewed in previous chapters, the authors recorded from place cells neurons that fired at specific spatial locations as the patient was navigating in virtual reality. As other studies have also shown in rats (Ainge et al. 2007), a subset of these neurons changed the location of firing depending on the intended goal. For example, if that patient was trying to find Mike's Restaurant, a place cell would fire in one place, yet this place cell would no longer be present (or would occur somewhere else) when the patient was trying to find Burger City (figure 5.2). These findings suggest that goals can modulate codes for spatial position in the hippocampus.

We might wonder why such types of goal-modulating place responses might occur, given that the environment was not changing when the patient was navigating it. One possibility is that paths to find a goal might vary somewhat. Having a place cell that can indicate a specific set of routes to find a goal might be helpful in finding one goal over another. Another possibility, which we discuss in some detail in chapter 9, is that such types of responses might be indicative of memory-related coding. For example, in order to remember information about your experience navigating, it is helpful to remember not only the environment but also the specific routes you used to get there. Regardless of whether the place cells modulated by goals were a function of navigation or memory, they indicate an important component of the basis for how we code goals.

Another type of goal response observed in the Ekstrom et al. (2003) study is also worth mentioning: cells that responded to specific goals regardless of spatial position. These types of "goal-related" cells fired continuously regardless of position but only for one goal and not another. For example, if the patient was trying to remember that the goal was to find Mike's Restaurant, cells recorded in a variety of brain areas, including the frontal lobes, showed increases in firing when searching for that specific store. Importantly, when searching for another store, like Burger City, the cell did not show selective firing (see figure 5.2). These findings suggest that neurons in the frontal lobe (and elsewhere) coded specific goals.

We can imagine that this type of goal response might be highly useful to navigating, as it provides a means of coding a location of a goal regardless of our position. Note that this type of response is different from some of the working memory-related responses we might expect when people are holding things in their short-term memory—for example, reminding themselves that they are trying to find Burger City (Leung, Gore, and Goldman-Rakic 2002). We would expect this type of response to show continuous activity regardless of the goal. In this way, the goal coding cells observed in Ekstrom et al. (2003) coded a specific goal, providing information about its location within the environment.

Thus, the Ekstrom et al. (2003) study observed two different types of single-neuron goal-related responses. One type of cell was the typical place cell that changes its location depending on the goal. The other was a new type of cell, not reported in past rat work, that fired for a specific goal whenever the patient was searching for it. This research thus demonstrates important properties of goal coding: on the one hand, that neurons can code route-related information to specific goals, and on the other, that neurons code-specific goals whenever we are searching for them.

## Human fMRI Studies

As we discussed in chapters 2 and 3, for our purposes in this book, it is critical to connect findings from rodent navigation to humans. As discussed earlier, neurons show goal-related responses in patients freely navigating in virtual reality. However, these studies are rare and limited to human patients. Another way to learn about goal-related responses is with noninvasive fMRI. Such studies are extremely valuable in extending and expanding what we learn about basic mechanisms of navigation in other species to humans. Indeed, many studies have investigated goal-related responses using fMRI, providing an important additional link to the distance of the goal.

Several fMRI studies have explored how the brain activity is correlated with the distance between landmarks or to goals during navigation. Two studies have reported increased activity in the anterior–middle hippocampus at the initial moment when a route needs to be planned (Spiers and Maguire 2006; Xu et al. 2010). Such responses may relate to the demand to retrieve the representations of environment needed to plan the route. However, it was not clear whether this activity was related to the distance to the goal. Thus, these initial studies, while valuable in showing that route planning related to a goal occurs in the hippocampus (and other structures), could not relate the activation to metric information about the distance of the goal. While they allow us to conclude that goals are coded in the brain, as also suggested by the human electrophysiological studies discussed earlier, they don't tell us much about how goal distance is coded.

The first fMRI study to explore how the human brain might track the distance to the goal examined London-licensed taxi drivers navigating a detailed virtual simulation of London (Spiers and Maguire 2007). While navigating to locations in virtual London, activity in the entorhinal cortex was positively correlated with the Euclidean distance to the goal (see figure 5.1 for Euclidean distance). In other words, when the taxi drivers were far from their goal, the activity in the entorhinal cortex was greater. Thus, the Spiers and Maguire findings were consistent with the idea that navigating to a goal involves computations of vectors conveying information about distance.

Since this initial study, several studies have explored how the brain represents distance and direction to the goal. These studies differ in the environments used (city versus abstract terrain devoid of landmarks), the amount of learning (10 seconds versus 4 years), and the task demands (visible versus hidden goals). Despite such differences, these studies provide general evidence that the hippocampus also represents information about the distance to the goal.

However, in many studies, it has not been clear whether the distance represented by the hippocampus was the Euclidean distance or the path distance (see figure 5.1 for the distinction between these two distances). For example, it could be that the hippocampus codes the distance of a path to a goal, regardless of whether it is the shortest way to get there. Alternatively, such a distance vector in the hippocampus could instead code the shortest possible distance to a goal, what we often refer to as "how the crow flies" or "beeline distance." This is important to determine because a path-based code is consistent with the hippocampus representing the environment's structure and layout, whereas the Euclidean distance code is consistent with a vector-based approach.

To explore vector and path coding in the brain, Howard et al. (2014) had subjects learn, via a walking tour and a map, a previously unfamiliar real-world environment (the Soho region of London). On the following day, participants navigated to goal locations in a film simulation of streets during fMRI scanning. Routes were fixed, but at each junction participants had to indicate which direction they would choose to travel to the goal and were paid money depending on the accuracy of their answers. Routes were also chosen that separated Euclidean and path distance to the goal. For example, sometimes the goal would be very close in Euclidean distance but the streets required for travel to it would require going far around the block to reach the goal. In contrast, in other cases, the goal would be close in both Euclidean and path distance. At various stages of the journey to the goal (travel, decision points, forced detours), activity in the posterior right hippocampus was significantly correlated with the path distance to the goal and not Euclidean distance.

One interesting question emerges regarding the direction of this correlation. Some studies, for example, have shown a positive correlation between hippocampal activity and the distance, suggesting that the closer to the goal, the less the activity in the hippocampus (Howard et al. 2014; Chrastil et al. 2015). In contrast, others have shown the opposite pattern, with hippocampal activity higher when closer to the goal (Viard et al. 2011; Sherrill et al. 2013; Balaguer et al. 2016). In the case of Howard et al. (2014), at decision points, activity was a combination of the path distance and the egocentric direction to the goal in a pattern predicted by the goal vector cells in bats. One possible interpretation of these conflicting findings may relate to different processing demands within the different tasks, which would occur when trying to update position during travel versus demands of considering the streets ahead at decision points (Spiers and Gilbert 2015). However, more research will be required to discover what causes a positive or negative correlation between hippocampal activity and distance. It is intriguing, though, to consider that both types of codes are possible depending on whether knowledge about proximity to the goal or the start point are part of the task.

In the preceding studies, activity in the posterior hippocampus was selectively correlated with the path distance. In contrast, Howard et al. (2014) found the entorhinal region selectively correlated with the change in the Euclidean distance to the goal when a new goal location was specified. This is consistent with the data from London taxi drivers and computational models in which the entorhinal cortex, but not the hippocampus, computes a vector to the goal. A correlation with the Euclidean distance is consistent with a vector, but it does not by itself link entorhinal activity to the direction to the goal. Models of navigation have argued that the direction that *should* be coded in the entorhinal cortex is the allocentric direction to the goal (for example, to north; see figure 5.1). Consistent with this prediction, current fMRI evidence indicates that the entorhinal region specifically codes the allocentric direction to the goal location during route planning (Chadwick et al. 2015). By contrast, the posterior parietal cortex appears to code the direction to the goal in an egocentric reference frame (Spiers and Maguire 2007; Howard et al. 2014; Chadwick et al. 2015). It is not yet established whether grid cells in fact represent the distance and direction to the goal, but recent work has shown that grid-like representations can occur in the human entorhinal cortex when participants imagine traveling to goal locations (Horner et al. 2016; Bellmund et al. 2016). Thus, fMRI evidence suggests that the hippocampus may code distance to the goal, while the entorhinal cortex may code direction.

## Prefrontal Contributions to Goal-based Navigation

Numerous fMRI studies have reported increased activity in regions of the prefrontal cortex during navigation (Spiers 2008). Areas in the anterior and lateral prefrontal cortex appear to respond to the need to take detours, detecting a change in the environment (Spiers and Gilbert 2015). Activity in prefrontal regions tracks the distance to the goal in certain contexts (Spiers and Maguire 2007; Viard et al. 2011; Howard et al. 2014; Balaguer et al. 2016), though this may relate to processing reward proximity or probability of success (Spiers and Gilbert 2015). More direct evidence of the prefrontal role in spatial planning comes from analysis of responses when participants in the study by Howard et al. (2014) were given a detour to take that required a new route to be planned. The greater the number of options in the paths beyond the next junction, the more activity was elicited in the bilateral lateral prefrontal cortex (Javadi et al. 2017).

## Patient Studies

As we mentioned in chapter 1, patient studies are extremely helpful for understanding the necessity of a brain region to cognition. And, as we mentioned in chapter 4, it is clear that lesions to the prefrontal cortex significantly impair goal-oriented behavior more generally, although the exact link to navigation remains to be explored. Insight into how the prefrontal cortex is necessary for this form of navigation comes from a study of a neuropsychological patient by Ciaramelli (2008). Patient L.G. was a resident of Cesena, Italy, who suffered a subarachnoid hemorrhage damaging his ventromedial prefrontal cortex (Ciaramelli 2008). Before the injury, L.G. had no problems finding his way around Cesena. After the injury, L.G. reported having great difficulties navigating the town. When tested on his wayfinding in the town, he would make errors.

Interestingly, the errors were not random. Rather than arriving at the intended destination, he would end up at other locations in the town that were personally well known to him, but not the correct location he should have gone to. For example, he would arrive at his workplace when he should have gone to a shop. It seemed that he was unable to inhibit his habits to follow usual routes to places that were highly familiar to him. When the task was conducted with an occasional reminder of what his current goal was (for example, “go to the shop”), his performance showed a dramatic improvement. Thus, while he appeared not to have a problem using the regions of his brain required to navigate a complex city, his problems stemmed from an inability to keep his current goal in mind and avoid distractors. Thus, it is clear that the prefrontal cortex plays a necessary role in goal-oriented behavior more generally, and a critical role in selecting the correct goal during navigation.

It is also clear, however, that the medial temporal lobes are also necessary, in some form, for accurate representation of the goal. In one study investigating human patients with medial temporal lobe lesions (which therefore included the hippocampus), Yamamoto et al. (2014) found deficits in goal-oriented navigation. Specifically, Yamamoto et al. had patients perform the triangle completion task described in chapter 2, which involves path integration. These patients tended to overshoot the goal (walk too far) when blindfolded compared to healthy controls. These findings suggested that their path integration system inaccurately represented the location of the goal that they needed to remember. While the exact role of the hippocampus and medial temporal lobes more generally in path integration in humans remains debated, they may, for example, instead play more of a memory-centered role in this context (see Shrager et al. 2008 and chapter 9). The fact that patients with damage to the medial temporal lobe show impairments, in some instances, in finding the goal suggests an important link between the medial temporal lobe and goal-oriented navigation. Consistent with the hippocampus interacting with the prefrontal cortex to support navigation, Dahmani and Bohbot (2015) found that activity in the ventromedial portion of the prefrontal cortex was correlated with hippocampal activity during spatial navigation (Dahmani and Bohbot 2015; see also Jones and Wilson 2005).

## Summary

Several different navigational guidance systems appear to operate in the brain. At the most simple level, a system for following repeated habits operates in a non-goal-directed fashion that appears to involve the striatum. A goal-directed system for navigating based on a representation of the environment's layout and vectors to locations within it appears to rely on the hippocampal-entorhinal network. In addition, for keeping goals in mind and planning routes, regions in the prefrontal cortex appear to play an important role.

## CHAPTER 6

# RESPONSE-BASED NAVIGATION AND THE COGNITIVE MAP

Have you ever had the experience of intending to drive to one place and making a wrong turn, thus falling back on a route that you habitually visit? For example, say you are intending to visit a friend you haven't seen in a while. You jump in the car, back out of your driveway, and five minutes later find yourself on the road you would normally take to work. What happened? You fell back on taking a well-worn, habitual route instead of going to your intended location—that is, your friend's place. As we discussed in chapters 3 to 5, novel, flexible routes involve, in part, the hippocampus, while habitual, well-worn routes involve, in part, the caudate nucleus, a part of the striatum within the basal ganglia. Here, we will explore these distinctions and brain systems in more depth.

The types of errors in navigation described earlier—that is, falling back on a habitual route—are common and represent an important interplay, and even competition, between brain systems involved in different forms of navigation. Indeed, with practice, a habit can become unconscious in the sense that it frees up cognitive demands so that we can undertake new challenges. If we continue with the example, when we go to work out of habit, we often can't think of what we saw on our way. This is because the habit works unconsciously, and we operate on a kind of autopilot. Furthermore, this kind of habitual route is often inflexible in the sense that it relies on a specific series of left and right turns, and if our road is blocked, we get lost unless we had previously acquired a mental map of the relationships between landmarks in the environment—that is, spatial memory—which allows us to derive a novel route to go around the blocked road.

Indeed, decades of work support the idea that different brain systems underlie flexible versus inflexible, more habitual forms of route following. While we have touched briefly on these two systems in chapter 5, we will now explore in significantly more depth the idea that two competing brain systems, one centered on the hippocampus and the other on the striatum, form the basis of flexible (*place-based*) versus inflexible habit (*response-based*) learning. We will return to the discussion of familiar versus novel routes in the context of memory and navigation in chapter 9.

The existence of different brain regions that might support different forms of cognition—particularly, memory—was first suggested by Brenda Milner through her work with patient H.M., an amnesic patient we introduced in chapter 1 (Milner 2005). These different brain regions are sometimes referred to as memory systems and have been studied extensively in both humans and nonhuman animals. Thus, these data support the idea that brain areas like the hippocampus support a form of memory called *episodic memory*, memory for events, which includes aspects of spatial memory. In contrast, other brain regions, such as the caudate nucleus, putamen, and cerebellum, can support the ability to encode and retrieve skills and motor sequences.

There are several theories concerning the function of the hippocampus; however, numerous lines of evidence implicate its importance in spatial memory and navigation (see chapter 3). As discussed, part of spatial processing involves learning associations between multiple landmarks in an environment in order to form a cognitive "map," a function often ascribed to the hippocampus (see chapter 3). The hippocampus has also been implicated in a number of other functions in memory, and in particular learning relationships between encoded stimuli, which we discussed in chapter 3 with regard to relational memory theory (Cohen and Eichenbaum 1991; Eichenbaum 2001). We discuss this interface in detail in chapter 9. Importantly for our considerations here, the integrity of the hippocampus is not necessary for all forms of memory and associations. These findings reinforce the idea that brain structures outside the hippocampus likely play important roles during navigation.

Stimulus-response learning (Packard, Hirsh, and White 1989; Packard and Knowlton 2002; White and McDonald 2002) and habit formation (Knowlton, Mangels, and Squire 1996) are forms of long-term memory that rely on structures outside the hippocampus, such as the striatum in animals, which is equivalent to the caudate nucleus and putamen in humans. In particular, these forms of memory are intact in patients with hippocampal lesions (Squire 1992; Chun and Phelps 1999; Milner 2005). How these different brain systems interact in healthy participants then is an important consideration to understanding navigation more generally (Packard, Hirsh, and White 1989; McDonald and White 1994; Packard and McGaugh 1996). Indeed, many studies have examined the interaction between the hippocampus and striatum and how the disruption of one system can affect the learning rate of the other (Packard, Hirsh, and White 1989; Packard and McGaugh 1996), which in turn provides insight into the functions of these different brain areas, particularly over learning. Here, we first consider the classic studies that suggest a dichotomy between place and response learning and the dynamics of interactions between these two systems.

## Place and Response Navigation Strategies in Rodents

Two memory systems subserve two different strategies one might use to navigate, involving the hippocampus and caudate nucleus of the striatum (Packard, Hirsh, and White 1989; Packard and McGaugh 1996; Hartley et al. 2003; Iaria et al. 2003; Voermans et al. 2004). The first strategy is often termed a *place strategy* or a *spatial memory strategy*. This involves navigating within an environment using the relationships between different landmarks and orientating oneself in relation to those landmarks, much like allocentric navigation as described in chapters 1 to 3. In addition, as first discussed by O'Keefe and Nadel in *The Hippocampus as a Cognitive*

*Map*, knowledge about the relative positions of landmarks can be employed flexibly (O'Keefe and Nadel 1978) in the sense that a target can be reached in a direct path from any starting position in our mental map based on storing this information in an allocentric reference frame.

In contrast, another way to navigate an environment involves a *stimulus-response strategy*, or *response strategy* for short. A response strategy involves learning a series of behavioral actions from specific points in the environment that act as stimuli. For example, one can learn to navigate from home to work in an automatic fashion with a series of stimulus-response associations such as "turn right at the white building, turn left when I see the statue," where the white building and the statue act as stimuli and the response involves a right or left turn. The striatum, a brain structure that includes the caudate nucleus in humans, is critical for response learning (Packard, Hirsh, and White 1989; Packard and Knowlton 2002; White and McDonald 2002). A response strategy is inflexible in the sense that it does not allow deriving a novel path to a target location. Furthermore, this strategy is often egocentric, particularly if the series of stimulus-response associations are based on the starting position of the navigator.

However, this does not always have to be the case. If a series of stimulus-response associations involve a specific landmark that is reached from many different starting positions, this would not be considered an egocentric form of representation. A typical example is a *beacon* strategy (also termed *piloting*; see chapters 2 and 5), where the beacon—for example, a tall building or tower—acts as the stimulus and the traveler navigates toward it. Importantly, a beacon strategy is also a type of response strategy, and it requires no memory for spatial coordinates. Thus, while a place strategy is conceptually similar to allocentric navigation, a response-strategy can involve both egocentric and beacon-based forms of navigation (see chapter 1 for more discussion of these forms of navigation).

McDonald and White (1994) studied the roles of the hippocampus and striatum in a navigation task using the Morris water maze (Morris 1981). In order to study the role of these brain structures in rats, they lesioned the striatum in one group and the fornix in another. Lesioning the fornix, which provides major outputs from the hippocampus, is one way to impair hippocampal processing. Unlike the standard version of the water maze, here rats were either required to swim to a visible platform, which could be used as a stimulus that would elicit a response, or they were trained on the standard spatial memory version of the water maze with the platform submerged.

After the rats were trained for several days, McDonald and White administered a *probe trial*, in which the visible platform was moved to a new location. The goal of this probe trial was to investigate the strategies used by rodents when they previously learned the task. Rats that had learned to find the platform because they could see it above the water level were identified as *response learners*. Rats that learned the platform location in space, but ignored the visible platform, were identified as *place learners*. Interestingly, when the visible platform was moved to a new location, only 50 percent of the rats swam directly to it, indicating that they used a response strategy. The other 50 percent swam to the old invisible target location, indicating that they used a place strategy. Damage to the striatum (and an intact hippocampus) increased the probability of rats to behave as place learners, whereas damage to the fornix/hippocampus (and an intact striatum) increased the probability of rats tending to behave as response learners.

The results from McDonald and White (1994) additionally showed that during the training phase, rats with a disconnected hippocampus were impaired at finding the hidden platform on the invisible trials—that is, they were impaired at using place learning but would swim to the visible platform instead, using stimulus-response learning. These results also showed that rats with a disconnection of the hippocampus did not use the distal cues to find the hidden platform and therefore had spatial memory impairments.

In contrast, rats with damage to the striatum were able to find the visible platform as well as the hidden platform when the location remained the same. However, when the visible platform was moved to a new location on the probe trial, rats with damage to the striatum swam to the old location rather than to the new visible platform. These rats therefore remembered the location of the platform using distal cues and thus had intact spatial memory. These findings further bolster the idea that the hippocampus and striatum processed fundamentally different strategies during this navigation experiment.

Since both the place and response strategy involve the use of landmarks, it is important to further distinguish the basis of their navigational strategies. According to O'Keefe and Nadel (1978), cognitive maps are not sensitive to deletions of any single landmark. In other words, allocentric navigation based on a cognitive map will be resilient, even if an important landmark, such as one of the World Trade Center Towers in New York City, is gone, because the map is rich in contextual details that involve many landmarks. On the other hand, navigation based on a single landmark (stimulus-response), such as a beacon strategy or piloting, is inflexible such that it will fail when this landmark is gone. As we will see in the rest of this chapter, navigation based on response strategies does not depend on the hippocampus, but when navigation requires memory for the allocentric positions of multiple landmarks, this process necessitates contributions from the hippocampus.

Another study provides valuable information about the distinct roles of the hippocampus and striatum in processing information about space. McDonald and White (1995) trained rats to learn which of two arms in a radial maze contained food. When the two arms were adjacent to each other, they found that the contribution of the hippocampus was critically required. Interestingly, the rats with lesions to the hippocampus (via a disconnection of the output pathways through the fornix) were not impaired when the choice arms were far apart. How could that be if the hippocampus is needed for place learning? Further investigation showed that the striatum was sufficient to learn the task when the arms were separated by 135 or 180 degrees. When both the striatum and hippocampus were lesioned, rats could no longer find the food when the choice arms were far apart. This study shows that either the hippocampus or the striatum can process information that will help the rat find the food. However, the hippocampus is most critical for remembering the details of the maze—for example, when the two arms are closest together.

As an additional demonstration of the different characteristics of place versus response learning, Packard et al. (1996) tested rats on a plus maze task to show that the two navigation strategies can partially function separately and have different temporal dynamics. In this study, the hippocampus was needed early in learning, as opposed to the striatum, which was needed later in learning, the same way that habits develop with practice over time. Rats were trained for seven days, during which they had to find food in the west arm of the maze, always starting from the same position—that is, the south arm. On day 8, a probe trial was administered in which rats started the task from the north arm. Packard et al. hypothesized that if the rat had learned the goal location with a response strategy during the first seven days of training, the rat should make a left turn (response) at the intersection of the maze (stimulus), when going from the south arm to the west arm. Conversely, if a rat had learned the location of the target arm based on room cues using a place strategy, it would end up in the west arm on the probe trial because it used environmental landmarks rather than a turn at the intersection to navigate. This eight-day procedure was repeated, and rats received another probe trial on day 16.

Packard et al. found that control rats used a place strategy early in learning, which was evidenced by the fact that they went to the west arm to find the bait on the first probe day—that is, the rats learned the location of the target arm based on room landmarks. As predicted, disrupting the function of the hippocampus impaired performance on day 8, confirming that learning a location with respect to room landmarks relies on the hippocampus. Disrupting the striatum had no effect. However, over time, control rats switched to using a response strategy (which was applied on the second probe day) and went to the east arm to find the bait—that is, they followed a stimulus-response association and turned left at the intersection. Disrupting the function of the hippocampus had no effect, and rats maintained the use of a response strategy, as controls did. On the other hand, disrupting the function of the striatum led to an impairment in the use of the response strategy on the second probe day.

Interestingly, disruption of the striatum had a significant impact on behavior. Rats with a disrupted striatum on day 16 used a place strategy. This is an important finding because it suggests that it was necessary to block the stimulus-response strategy in order to allow for the place strategy to guide behavior. This experiment illustrates the fact that stimulus-response strategies (or habits) can be strong and override behavior, thus leading us to a wrong location, even in the presence of a healthy hippocampus. Also, the Packard et al. (1996) study demonstrates a temporal dynamic between the two systems and also provides evidence that the two systems can function independently in some instances. Results from this study showed that the hippocampus is critical early in learning, while the striatum, in contrast, contributes over time through repetition of the same behavior while navigating in a familiar environment.

This experiment helps understand the everyday life example provided at the start of this chapter. If we take the same route to work from home every day, at some point it can become such a strong habit that we take this route on autopilot, even on days when we are not going to work. This is a situation in which a habit can be so strong that it becomes detrimental to our daily lives. However, one system is not necessary for the other to function normally, at least in the study discussed earlier. Hippocampal-lesioned animals could use a response strategy and striatum-lesioned animals could use a place strategy to navigate. While the two systems involve different temporal dynamics, the functional interactions between place and response strategies (competitive, cooperative, or independent) are still under debate and appear to shift depending on the task demands.

## Place and Response Navigation Strategies in Humans

An important question we have asked throughout this book is whether what we have learned from rats applies to human spatial navigation. The four-on-eight virtual maze (4/8VM) was developed as means of addressing whether the place versus response dichotomy also applies to humans (Iaria et al. 2003; see figure 6.1). In the first part of the 4/8VM, participants had to retrieve four objects at the end of four available paths out of eight that extended from a central platform. In a second part, participants had to remember which of the paths they had already visited and avoid these in order to find the remaining four objects. Similar to the procedure used in rodents, a probe trial in which all landmarks were removed was given after a few learning trials in order to distinguish place learners from response learners. Participants who used environmental landmarks to remember the positions of objects would be affected during the probe trial. However, those who used a series of left and right turns from a given position would be able to locate all objects irrespective of the absence of landmarks during the probe trial. In addition to the probe trial, participants were asked to verbally describe how they solved the task.

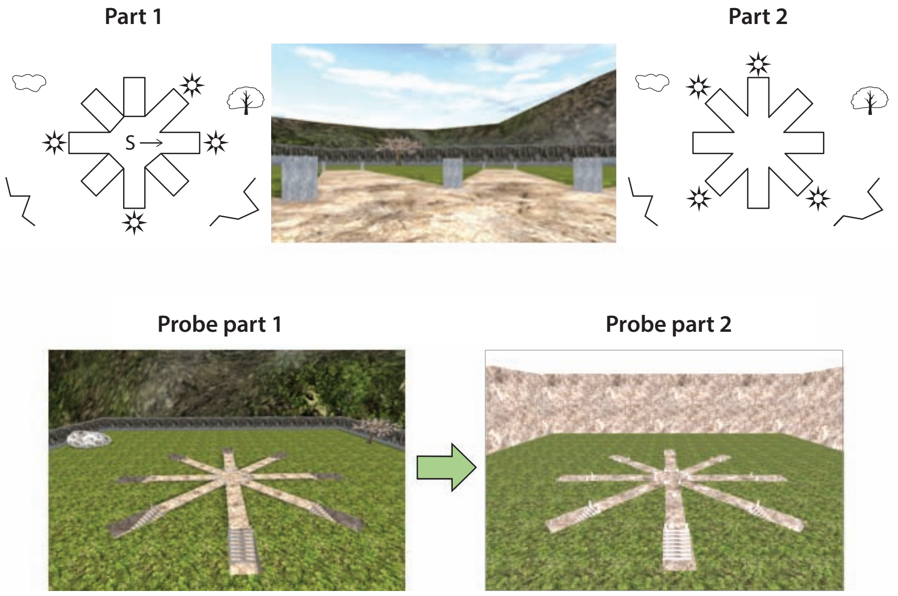


**FIGURE 6.1.** Illustration of the four-on-eight virtual maze (4/8 VM) used to assess navigational strategies. In part 1, participants have to retrieve four objects from four unblocked arms. The four rewarded arms are indicated with crossed circles. In part 2, all arms are unblocked, and participants have to retrieve objects in the same arms as those visited in part 1. In the probe trial, part 1 is the same as during regular trials, but in part 2, a wall is erected around the radial maze, blocking the participants' view of landmarks in the environment. This trial assesses to what extent participants relied on landmarks to learn the location of the objects.

Iaria et al. (2003) found that participants who reported using landmarks made significantly more errors on the probe trial than those who reported using a series of turns in a sequence. In addition, similar to what has been demonstrated in some animal models, 50 percent of the people tested on the 4/8VM used a response strategy, in equal proportions of men and women. Those participants who employed a response strategy performed significantly faster and made significantly fewer errors throughout training than people who used a place strategy. Similar results were obtained in rodents, in a study by Colombo et al. (Colombo, Brightwell, and Countryman 2003), where rats using the response strategy also made fewer errors and were significantly faster. Interestingly, in the Iaria et al. study, 40 percent of the people who used place strategies shifted to the more efficient response strategy with further training, a finding similar to the one observed by Packard and McGaugh (1996) in rats described earlier. The shift of strategy over time—in this case, from a place strategy to a response strategy—implies that humans likely have the potential to shift from one strategy to another depending on the demands of the task, similar to what has been observed behaviorally in rodents.

An important question then regards the neural basis of place versus response strategies in humans. One way of testing the predictions from rats regarding the neural basis of place versus response strategies is to test participants using functional magnetic resonance imaging (fMRI), although as we discussed earlier, this indicates the involvement of a structure and not its necessity. Contrasting experimental 4/8VM trials with a visuo-motor control in the same virtual environment while participants underwent fMRI, Iaria et al. found that participants who used place strategies had significant fMRI activity in the right hippocampus early in learning (trials 1 and 2; see figure 6.2, "fMRI"). Participants who used a response strategy from the start, however, did not show significant levels of hippocampal activity; instead, they showed fMRI activity in the caudate nucleus (included in the striatum), which appeared later in training (trial 4) until the end of the fMRI training session (see figure 6.2). The Iaria et al. study thus fits with the earlier findings from Packard and McGaugh and supports the idea that the engagement of the hippocampus and caudate in place and response strategies also involves different temporal dynamics. Specifically, during navigation on the 4/8VM, the hippocampus contributes as an early learning system, while the caudate nucleus of the striatum contributes as a later learning system.

While fMRI is useful for studying what brain regions might be involved in healthy participants, as discussed in chapter 1, we must turn to patients with selective brain lesions to address the necessity of different structures to place versus response learning. Bohbot et al. (2004) tested this issue with patients with a unilateral surgical resection of the medial temporal lobe (MTL), which was performed to alleviate intractable epilepsy. According to the place versus response dichotomy discussed so far, we might anticipate that medial temporal lobe resection, which includes the hippocampus, would impair all patients' usage of a place strategy such that all would instead employ a response strategy in the 4/8VM. Inconsistent with this prediction, the brain-lesioned patients used place and response strategies in proportions equal to those of healthy young volunteers. About 60 percent of the patients attempted to perform the task using the allocentric relationships between landmarks available in the environment (place strategy), and 40 percent of patients

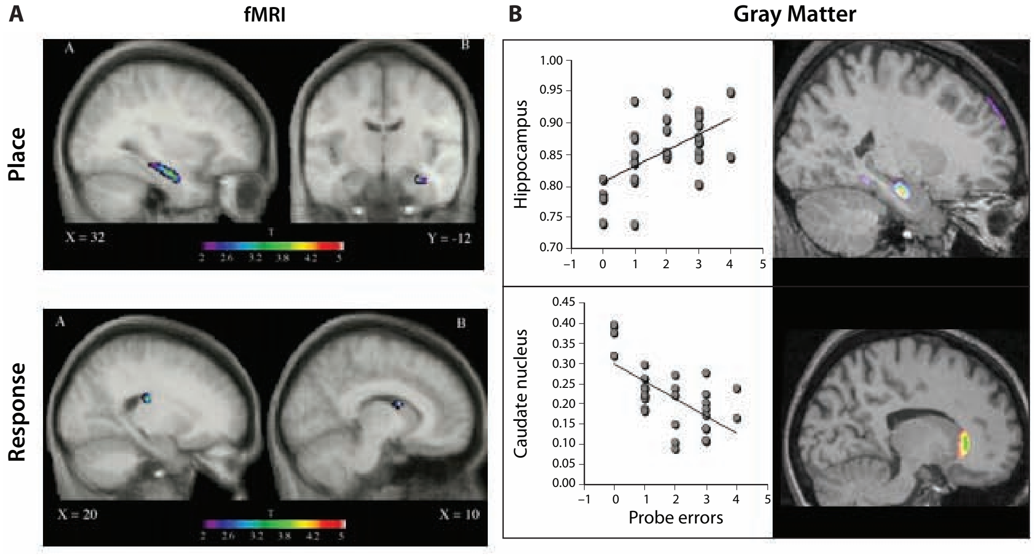


**FIGURE 6.2.** A. Activity in the hippocampus (top) and caudate nucleus (bottom) found in the place and response strategy groups, respectively. B. Gray matter differences found in hippocampus (top) and caudate nucleus (bottom) of the place and response strategy groups. The scatter plots indicate regression analyses between the gray matter in the hippocampus or caudate nucleus and the errors made by the group of young adult human participants while performing the probe trial. These results indicate that individuals who rely more on landmarks have the greatest amount of gray matter in the hippocampus and least in the caudate nucleus

performed it by using a series of turns from a given starting position (response strategy). Those using a place strategy with damage to the hippocampus, though, were significantly impaired on the 4/8VM relative to response learners with similar damage to the hippocampus (Bohbot, Iaria, and Petrides 2004).

The preceding patient study allows us to draw some important conclusions. First, the hippocampus is necessary, in some form, for normal execution of a place strategy, consistent with other work we discussed in chapter 3 (and will again in chapter 7) relating the hippocampus to allocentric forms of navigation. Second, these findings suggest that patients with damage to the hippocampus may also resort to a response strategy, also consistent with the ideas put forward in rodents discussed earlier. These findings also suggest, though, some possible interspecies differences in the flexibility of the use of these strategies based on what brain regions are damaged (as discussed broadly in chapter 4). This is because a proportion of patients with damage to the hippocampus attempted to use landmarks (place strategies) although that strategy was often inefficient, since patients were impaired overall relative to healthy controls.

## Neurobiological Differences between Place and Response Learners

Another way of potentially determining differences in how participants navigate, instead of looking at patients with brain lesions, is to look for relative differences in *gray matter* (the part of the brain that contains neurons, including cell bodies and dendrites). In this way, we could determine if increases in the sizes of brain structures important to place versus response strategies, like the hippocampus and striatum, show differences in participants who are more likely to use one strategy over another. In conjunction with structural MRI, *voxel-based morphometry* (VBM) is one method that allows us to look for differences in brain tissue, voxel by voxel, throughout the entire brain (Ashburner and Friston 2000). Specifically, this technique allows one to determine how tissue, automatically classified as gray matter, differs as a function of learning or groups.

Bohbot et al. (2007) scanned a large group of participants using structural MRI and then used their navigational pattern in the 4/8VM to divide them into groups of place versus response learners. Analysis of their structural brain images using VBM showed morphological differences in the right hippocampus between place and response strategy users (see figure 6.2, "Gray Matter"). Specifically, place strategies were associated with increased gray matter in the hippocampus, while response strategies were associated with increased gray matter in the caudate nucleus (Bohbot et al. 2007; see figure 6.2). Together, these findings suggest that those who use place strategies might have more developed and enlarged hippocampi, while those who employ response strategies might have more developed and enlarged caudate nuclei, consistent with the idea that individuals use either the place strategy or the response strategy, but not both at the same time, a finding that was also reported in rodents (figure 6.3).

Consistent with this idea, in one classic study, Maguire et al. (2000) studied London taxi drivers to examine the relationship between spatial memory and gray matter in the hippocampus. As mentioned previously in chapter 5, London taxi drivers train for several years in order to qualify for an exam called "The Knowledge of London." In this way, taxi drivers can be thought of as individuals with extensive expertise in navigation, specifically with knowledge of the spatial relationships between the streets of London (see also chapters 5 and 7). Consistent with the findings of Bohbot et al. (2007) in the 4/8VM, Maguire et al. (2000) found that gray matter in the hippocampus of taxi drivers positively correlated with years of driving experience.

Taxi drivers were then compared to London bus drivers, who have equal driving experience; however, they have not undergone the study of the spatial relationships between the different streets of London. Unlike taxi drivers who generate novel trajectories to their clients' destinations (place strategy), bus drivers have experience following a route (response strategy). When London taxi drivers were compared to non-taxi controls and bus drivers, they had significantly more gray matter in the hippocampus, demonstrating that the previously demonstrated differences in gray matter in the hippocampus were unrelated to general driving experience (Maguire, Woollett, and Spiers 2006). If we make the additional assumption that taxi drivers are likely to depend heavily on allocentric place strategies to navigate, these findings reinforce the idea that the hippocampus plays an important role in such navigational strategies, and may even "expand" in response to such demands. Alternatively, it may also be the case that taxi drivers are those predisposed to using place strategies in the first place, and thus may have more developed brain structures to support such forms of navigation. While these experiments

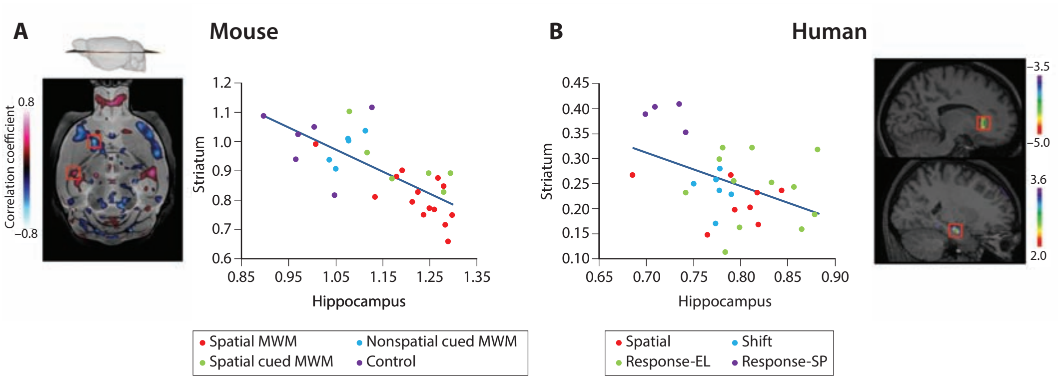


**FIGURE 6.3.** Inverse relationship between gray matter in the hippocampus and caudate nucleus gray matter in mice (A) and humans (B).

suggest correlation, a more direct influence was suggested in another study where Maguire et al. (2003) scanned taxi drivers before and after the study of their exam. Indeed, those who successfully finished the course showed increased gray matter in the posterior hippocampus. The connection between hippocampal integrity and navigational ability is intriguing and potentially of great relevance to understanding neurobiological diseases, like stroke and Alzheimer disease, that frequently affect the hippocampus (which we will discuss in more detail in chapter 7).

## Habit, Repetition, and Routine

Habit formation occurs with the repetition of a behavior. As we have discussed so far, a frequent observation in navigation experiments is that repetition promotes a shift from place to response learning (Packard and McGaugh 1996; Iaria et al. 2003). In rats, inactivation of the hippocampus disrupted memory for the location of a food reward early in learning, but the same manipulation had little effect after twice as much training, showing that the memory was no longer as strongly dependent on the hippocampus. Instead, the ability to find the food was disrupted by inactivation of the striatum (caudate nucleus). As described earlier, with practice, control rats reduced their use of a place strategy in favor of a response strategy based on repetition. The results from the Iaria et al. (2003) fMRI and Bohbot et al. (2007) patient study support similar findings for humans: an early involvement of the hippocampus, when a place strategy is more prevalent, and a late involvement of the caudate nucleus, when a response strategy is more prevalent.

Across multiple studies, this shift from hippocampus to caudate nucleus involvement manifests across different times scales: within individuals across a session (Iaria et al. 2003), across multiple sessions (Gold 2004), and across the lifespan (Bohbot et al. 2012). Indeed, Bohbot et al. (2012) showed that 85 percent of children used place strategies on the virtual radial maze task; this proportion decreased to 39 percent in healthy older adults. With aging, humans and rats alike show a significantly increased proportion of spontaneous use of response learning on the mazes (Barnes et al. 1980; Moffat 2009). Consistent with previous studies, Konishi et al. (2013) showed that place strategies are associated with increased fMRI activity and gray matter in the hippocampus compared to response strategies. Since low gray matter in the hippocampus can be a predictor of future diagnosis of Alzheimer's disease (Apostolova et al. 2006) as well as other neuropsychiatric disorders (Gilbertson et al. 2002), the use of flexible place strategies may be beneficial for healthy cognition. Consistent with these results, patients with Alzheimer's disease have a larger caudate nucleus than undiagnosed controls (Persson et al. 2017). We return to these issues in chapter 7 when we discuss aging and Alzheimer's disease. Taken together, though, these findings suggest that individual differences in the functions of the place and response learning and memory systems interact with aging processes. While the exact mechanisms for the reduction in activity in the hippocampus in favor of the caudate nucleus is still unclear, there are lines of studies suggesting that this may occur during sleep (Orban et al. 2006) and may generalize to other types of learning, such as procedural learning of a spatial sequence (Albouy et al. 2013).

## Stress

Have you ever been rushed to get to a job interview and found it difficult to "think straight" and plan your route? There is a rich literature in spatial navigation suggesting that stress may adversely affect how we navigate, potentially leading to a greater dependence on response than place strategies. For example, Packard and coworkers (2001) showed that stress increased the use of a response strategy when rats were tested on a water maze task. In that task, rats learned to swim to the location of an invisible (submerged) platform on alternating days. On the other days, the platform was in the same location but was identified with a visible flag. On a test trial, the invisible platform remained in the same location, but a second platform identified with the flag was placed in a new location. Under normal conditions, rats swam to the invisible platform in the old location, based on place learning. However, when Packard et al. (2001) introduced a stressor (a tail-pinch while restrained) before testing, a significant number of these rats swam to the platform with the flag in the new location, thus demonstrating a dependence on the response strategy.

Humans may have a similar tendency to rely on response strategies when stressed. For example, Schwabe et al. (2008) found an increased use of response strategies in people with high chronic stress compared with individuals with low chronic stress on a two-dimensional spatial task. In another study, Schwabe et al. (2007) produced an artificial stressor by having young adults give a public speech—a highly stressful experience for many individuals. These same "stressed" individuals were more likely to learn a target location with respect to local cues (response strategy) as opposed to using distal spatial cues (place strategy). One interesting possibility is that the link between stress and navigational strategy may manifest as early as in utero. A prenatal stress study showed a significant impact of a major life stressor during pregnancy (for example, divorce, death in the family, and so on) on navigational strategy in the virtual maze described earlier. Specifically, the group of young adults who had experienced prenatal stress used a response strategy to a greater extent than controls when tested in the virtual radial maze (Schwabe, Bohbot, and Wolf 2012). These findings suggest that stress can play a fundamental role in shifting strategies, from place-based to response-based navigation strategies.

### Video Games

Certain types of video games, like action video games, involve quite a bit of navigation. One might wonder the extent to which these might involve different forms of navigation, which could in turn provide insight into how they relate to everyday behavior. Particularly given the addictive potential of video games, is it possible that those who habitually play them show different preferences for one navigational strategy over another? Consistent with this idea, West and colleagues (2015) showed that those who play action video games (first-person shooting games) were more likely to employ response strategies in the 4/8VM than those who played nonaction games (West et al. 2015). Moreover, the action video game players had significantly less gray matter in the hippocampus than the nonaction game players. Indeed, when tested in the lab, 90 hours of in-lab video game playing further decreased the use of place strategies, and was linked to further reductions in hippocampal gray matter (West et al. 2017). However, this occurred primarily in response strategy users (as assessed prior to the in-lab video games). These findings thus suggest that video gaming itself may be linked with a reduction in hippocampus-dependent place strategies and an overdependence on response strategies.

One hypothesis then to explain the difference in the involvement of the hippocampus as a result of video games relates to the timing of the reward. Many studies have linked striatal activity to reward (for example, see Schultz 1998). Action video games might be thought of as producing quite a bit of immediate gratification and reward, which might lead to a tendency for greater use of response strategies and fewer place strategies. In support of this hypothesis, increasing the delay of feedback timing in a learning and memory task was sufficient to shift striatal-based learning to hippocampus-based learning (Shohamy et al. 2004). In further support of this, those who employ response strategies more often may also show a tendency to using illicit substances in significantly greater proportions (Bohbot et al. 2013). While promising, the exact links between reward, drug use, and place versus response strategies remain to be fully elucidated.

### Individual Differences and GPS Use during Navigation

Different people we meet in life appear to have different levels of facility with navigation. As we discussed in chapter 1, there are individuals like the Puluwat and Inuit who have incredible navigational abilities. On the other end of the spectrum, we have likely all met individuals who appear to get lost in their hometown. Indeed, as we will discuss in chapters 7 and 8, there are individuals with a rare disorder called developmental topographical disorientation (DTD) who suffer from severe disorientation and difficulty navigating, even in their hometown. Yet, even without a clinical condition, there is clear variability in people's abilities to navigate, as illustrated by our discussion at the beginning of this book. Specifically, the average person rates his navigational ability at about 3.6/7, suggesting that slightly fewer than half of college-age adults consider themselves poor navigators (Hegarty et al. 2006).

The place versus response classification we have discussed so far provides a useful means of understanding these individual differences. In one study, Marchette et al. (2011) had participants learn the location of objects in a large virtual maze. Participants then underwent fMRI while attempting to find where these objects were located. During navigation, participants could either take a shortcut, which was classified as a place strategy, or employ a familiar route, which was classified as a response strategy, to get the location of the object. Marchette et al. found a large variability across participants in the tendency to use a place or response strategy, suggesting a fairly broad spread in individual preferences for place-based versus response-based strategies. Interestingly, the tendency to use a place strategy correlated strongly with their ability to take novel perspectives of a drawing, suggesting it tapped into some form of spatial flexibility. Most importantly for our current considerations, the authors additionally found that those more likely to employ a place strategy were more likely to show significant levels of activation in the hippocampus. In contrast, those more likely to use a response strategy were more likely to show activation in their striatum. Thus, this study helped relate individual differences in use of a place versus response strategy, like the Iaria et al. (2003) study, to recruitment of brain structures, including the hippocampus versus striatum.

Why might individual differences in the use of a place versus response strategy be relevant? The studies discussed so far have shown that when people decrease their use of place learning strategies, they favor navigation strategies involving response learning. The response strategy, which involves the caudate nucleus, implies reacting to a stimulus in the environment—for instance, “turn right at the corner after the park.” We could therefore move about with a series of stimulus-response actions, in principle, with little engagement of the hippocampus and other brain structures important to flexible wayfinding. With practice, this process could become automatic, like an autopilot mode.

A good example, described earlier, would be when we use the same route to go to work every day, and we go about our route in such an automatic fashion that we sometimes end up on our way to work on the weekend, even if that wasn’t our intention. We are also on autopilot mode when we enter a room in the house to go and get something, and then, upon entering the room, we forget why we are there. This, in turn, leads to an important potential question: if we’re using a global positioning system (GPS), which strategy are we using? If we are using the GPS by following a set of directions in an autopilot mode with a response strategy, this might suggest that we are not using our spatial memory to the optimal extent, which could become problematic.

The answer, as suggested in one study, is that GPS decrements our spatial knowledge compared to all other ways of learning a spatial environment. In a study by Ishikawa et al. (2008), participants navigated a part of a city (Tokyo) either by studying a map first, being guided by an experimenter, and then navigating the route or by navigating it with GPS (Ishikawa et al. 2008). GPS users tended to make more errors when having to later navigate without the device compared to those who studied the environment using a map or being guided by the experimenter. Specifically, these participants made more errors in judgments of direction and in map drawing compared to those with direct navigation experience (see chapter 2 for a discussion of these methods). While participants did acquire some spatial knowledge using GPS, it was significantly lower than using a map or simply being guided by an experimenter, suggesting that GPS generally decrements and impairs our normal acquisition of spatial knowledge.

The potential for an overreliance on following familiar routes with a response strategy or GPS has potentially significant ramifications for society. Many of us have heard of cases of people getting lost, led astray owing to their GPS or running out of batteries on their wayfinding device. Knowing where we are in space has clear advantages, particularly when navigating under hazardous conditions, and it is likely that numerous lives would have been spared if people had taken the time to look at a map before heading off on a road trip to avoid heading in the wrong direction. Unfortunately, other types of tragedies have occurred as a result of the people going on "autopilot" and driving to work out of habit.

Indeed, in some cases, the likely use of a response strategy resulted in the loss of lives. In 2003, a Montreal father changed his morning routine. On his way to work, he used to drop off his one-year-old daughter at daycare and then he would drop off his wife at the subway. It was a warm summer day. That day, his wife was late, so he dropped her off at the subway first, thinking he would bring his daughter to the daycare afterward. Tragically, his autopilot took over. After the subway, he went straight to work as he did every day. He forgot his daughter, who was sleeping peacefully in the back seat of the car. In the evening, when he found his daughter, it was too late. A similar fatal case occurred in 2016, in Saint-Jérôme, Quebec, when a father forgot his child in the back seat of the car on a hot summer day. Thus, while the response strategy could sustain our sense of autopilot, occasionally it can also do more harm than good. It allows us to automatize numerous behaviors, making our lives easier. However, these examples do illustrate that it should be kept in check.

## Place versus Response Learning: A Macro-scale Lens into Interspecies Similarities

As outlined in chapter 4, there are differences between humans and rats in terms of how we navigate, particularly in terms of how we use vision to navigate. The place versus response classification of navigation is a useful and informative method of providing a "macro"-level way of dichotomizing behavior. While there are other useful ways of dichotomizing behavior across species and individuals—for example, whether individuals rely more on landmarks or the surrounding spatial geometry (see Cheng and Newcombe 2005)—the place versus response classification has been particularly useful in helping us to understand fundamentally different forms of navigation that rely on partially independent memory systems.

McDonald and White (1994) demonstrated that similar to humans (Iaria et al. 2003), 50 percent of adult rodents use the place strategies and 50 percent use the response strategies. Packard and McGaugh (1996) demonstrated that place learning, as partially reliant on the hippocampus, tends to be a fast learning system, while response learning, which depends primarily on the caudate nucleus, tends to be a slow learning system that requires repetition, as also demonstrated in humans by Iaria et al. (2003). McDonald and White (1995) showed that the critical difference between place and response navigation involved details perceived from the center of the radial maze, as did Etchamendy et al. (2012) in humans. There are biological differences in both rodents and humans that predict whether an individual is more likely to use a place or response strategy (see Gold et al. 2004; Bohbot et al. 2007). Colombo et al. (2003) showed that the response strategy is more efficient than the place strategy in some situations, as reported in humans by Iaria et al. (2003). Barnes, Nadel, and Honig (1980) showed an increase in response strategies with aging, as reported by Bohbot et al. (2012). Lerch et al. (2011) showed that gray matter in the striatum and hippocampus is negatively correlated (see figure 6.3), as did Bohbot et al. (2007) in humans. Last, factors that promote one strategy over the other, such as stress, are found in both rodents (for example, Kim et al. 2001) and humans (Schwabe et al. 2007). Together, these findings suggest that the place versus response dichotomy captures some important behavioral similarities across different species and also involves contributions from similar brain regions, the hippocampus and striatum.

At the same time, simply because there are similarities across some studies in tendencies to use one strategy to navigate versus another does not mean that the underlying mechanisms are identical. For one, studies in rodents that assay place versus response strategies involve them freely navigating in a real-world maze. In contrast, those in humans typically involve desktop virtual reality (VR), which, as discussed in chapters 1 and 3, lacks body-based input and therefore likely results in some differences in neural codes. Additionally, as we discussed in detail in chapter 4, humans have a much more highly developed visual system than rodents, and our navigation, and corresponding brain areas, depend on visual input to a greater extent. This suggests that while some aspects of place versus response strategy may be mechanistically similar—for example, the place strategy likely involves place cells in all species—it is not necessarily true that a place strategy involves identical neural mechanisms. Thus, while the place versus response classification is highly useful for understanding behavior, and appears to show striking interspecies similarities at a macro level, it is likely that the underlying micro-mechanisms have significant differences, which are ultimately important to understanding what is unique about human spatial navigation.

Another constructive criticism that we can offer about the place versus response dichotomy is that it is likely to capture only one dimension of a highly rich and complex set of behaviors involved in human spatial navigation. As discussed in several studies, the use of a place versus response strategy itself is likely dynamic, and although some individuals might favor one over the other, individuals possess the ability to switch between these strategies when searching for an optimal solution to a task. Similarly, while we have learned much from this approach about what brain regions are typically involved in navigation, the hippocampus and striatum are likely only two of many important players in a network of different brain regions devoted to human spatial navigation and memory. In this way, the involvement of either the hippocampus or the striatum in a task is unlikely to be binary (all or none) and instead will exist on a continuum dependent on the task demands, with other brain regions like the parahippocampal retrosplenial, prefrontal, and parietal cortex also performing critical contributions. We discuss these ideas in significantly more detail in chapters 7 to 9.

## Summary

The place versus response classification of human navigation provides a highly useful way for understanding not only the brain regions important to navigation and memory but also individual differences in navigation, the ways stress affects how we navigate, and the aging process, which we discuss in more detail in chapter 7. One intriguing implication of this work, additionally, is that the volume and engagement of a structure like the hippocampus may even predispose us to certain navigational strategies, like use of a place over a response strategy. In contrast, addiction and chronic video gaming may tend to involve those with less gray matter in the hippocampus who frequently favor response strategies. Additionally, the place versus response strategy dichotomy provides a useful means of understanding the advent of GPS in society, which has important ramifications for our navigational ability and brain health more generally. Finally, the place versus response dichotomy also provides a highly useful macro-level interspecies lens, although how it translates at the micro-mechanistic level discussed in chapters 3 and 4 remains unclear. It also bears repeating that the hippocampus and striatum are only two of many structures important to navigation, an idea we will expand on greatly in chapters 7 to 9.

## CHAPTER 7

# HOW HEALTHY AGING AND CLINICAL DISORDERS AFFECT NAVIGATION

Imagine you have lived in the same neighborhood for most of your adult life. You have frequently walked to the supermarket within your neighborhood, walked to a nearby bus stop to catch a ride downtown, and met friends at a coffee shop not far from your house. You have extensive experience navigating to all of these locations, often via the same route from your house, but in other cases via different routes. If someone asks you for directions to any of these locations, you can easily imagine and provide a verbal description of how to get to these places. You can also readily draw maps of your neighborhood and show others how to get around on a map. In short, much like the London taxi drivers we have talked about in past chapters, who have highly detailed knowledge of London neighborhoods, you are an expert at getting around your neighborhood.

Now imagine that you wake up one day unable to navigate your neighborhood. You walk outside your house and are no longer oriented. Trying to find your way to the supermarket, which you have been to countless numbers of times in the past, is pointless, as you simply don't know where you are. You try to ask someone for directions but using the information they have given you ("go up two blocks on Center Street and take a left past the laundromat on North Street") is incomprehensible. For starters, your basic sense of orientation is off and you don't know where you are relative to other landmarks or streets in the neighborhood. To put it mildly, you are disoriented and even highly familiar routes through your neighborhood seem foreign.

What we have just described is essentially what patients who experience certain forms of stroke, suffer some forms of encephalitis, or suffer from Alzheimer's disease experience, although particularly with Alzheimer's disease, the experience is more gradual than what we have described and seeps into multiple domains beyond memory. Strokes, though, such as those that affect the retrosplenial cortex, can occur in the space of hours, and individuals who experience them sometimes are completely disoriented in the aftermath. In fact, some of these patients may not even know that they had a stroke, and the only way they have of knowing something went wrong is the experience of disorientation, above and beyond anything they would normally experience. We describe one such example later with regard to a taxi driver.

In this chapter, we will discuss neurological conditions like stroke, encephalitis, and Alzheimer's disease, all of which can profoundly influence one's ability to navigate. People with these conditions are not the only ones who experience disorientation, though, and sometimes suddenly with little warning. Even simply as a function of aging, many individuals experience greater difficulty learning to navigate in newly encountered places. There is even a class of individuals, described as having developmental topographic disorientation (DTD), which we mentioned briefly in chapter 6 when we discussed individual differences in navigation, who have a selective deficit in their ability to navigate. We will discuss these disorders of navigation here from the angle of how clinical conditions might impact navigation. We will return to this topic in chapter 8 to discuss how focal brain damage, particularly accompanying stroke, can impact navigation.

## What Is a Stroke?

*Stroke* is defined as the blockage of the blood supply to the brain (termed an *infarction* or *ischemic stroke*) or rupture of a blood vessel (called a *hemorrhagic stroke*) leading to the death of neurons supplied by those vessels. Stroke can occur for a variety of reasons, with high blood pressure (hypertension) as the leading cause. Lacunar stroke or infarct, the most common type of stroke, involves the blockage of vessels deep within the brain, such as parts of the posterior cerebral artery (figure 7.1). These often occur as a result of plaque buildup within the arteries and thinning of the vessels. Just like the plumbing in your house, small vessels can become blocked, leading to lack of blood flow to the areas of the brain supplied by those vessels (Fisher 1982). Because blood carries oxygen and nutrients to neurons so that they can function, even a small cerebral infarct can cause neurons to lose function and even die. Although the brain appears to recruit numerous compensatory mechanisms in a desperate attempt to restore oxygen concentrations and save

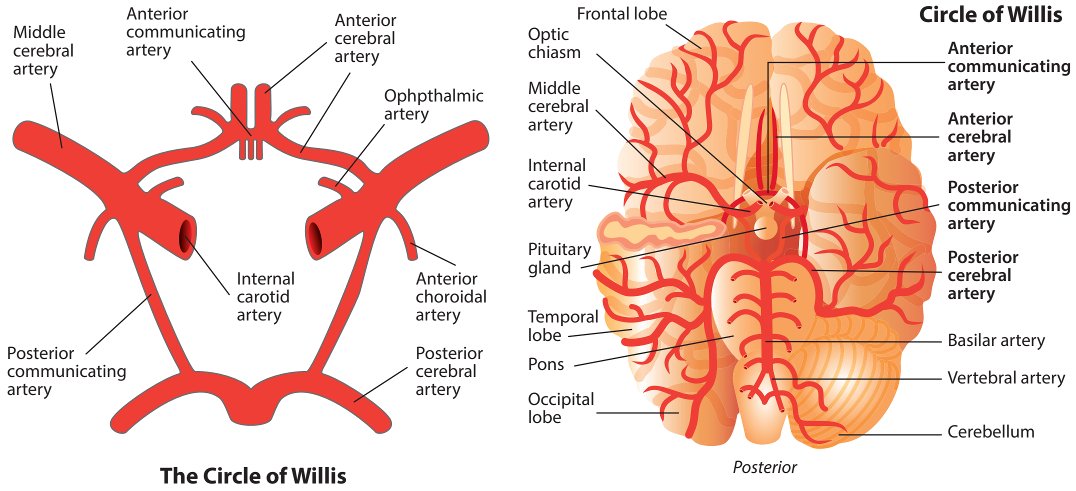


**FIGURE 7.1.** The major blood supply to the brain, which includes the posterior cerebral artery (PCA) and branches off the circle of Willis.

neurons within the ischemic region, the attempt is often futile (Powers, Grubb, and Raichle 1984), and loss of function within the population of affected neurons, although often temporary, is inevitable.

As one can imagine, the effects of a hemorrhage or an ischemic event, even if it results in only a temporary loss of blood flow and oxygen to the brain, can nevertheless be devastating and somewhat unpredictable. Metabolic impairments can be variable, with the nature and severity of the effects depending on the stage of vessel branching at which they occur, and the extent of occlusion within a blood vessel (see figure 7.1). The most frequent (and often the most obvious) symptoms of stroke include weakness and loss of motor movements, typically on the side of the body opposite to the side of the brain in which the stroke occurred, blurred vision, and often complex effects on cognition. Using magnetic resonance imaging (MRI), which we discussed in some detail in chapter 1, physicians can determine the extent to which neurons in the brain may have been damaged based on evidence of gray matter abnormalities (Moseley et al. 1990; Schellinger et al. 1999).

While occlusions can occur within a variety of arteries within the brain, some parts of the brain appear particularly susceptible to the effects of oxygen loss, termed *hypoxia*, which can also be a consequence of cardiac arrest, premature birth, and other medical conditions. These include areas we have discussed previously, such as the retrosplenial cortex, the posterior parietal cortex, parts of the lateral temporal cortex, and the hippocampus, all of which receive blood supply from the posterior cerebral artery (PCA; see figure 7.1). Not surprisingly, oxygen loss to these brain structures often affects navigation and memory (Anderson and Arciniegas 2010). In fact, symptoms of spatial disorientation and memory impairment are one of the hallmarks of blockage of the posterior cerebral artery (Cals et al. 2002).

## Posterior Cerebral Artery Infarctions and Impairments of Navigation

While we must always be careful when relying on single case reports to make strong conclusions in science, anecdotes often provide an important basis for considering future studies (Rosenbaum, Gilboa, and Moscovitch 2014). Anecdotes may then be validated in follow-up studies of additional single cases and larger patient groups that confirm initial, cursory observations. One striking example of this involves the effects of some strokes to the posterior cerebral artery (PCA) on navigation, particularly those that primarily affect retrosplenial cortex. Here, we will review a particularly compelling case, as it illustrates how devastating the impact can be on spatial orientation. We will return to a more thorough and scientific consideration of these case reports in chapter 8, when we consider a detailed influential taxonomy of how damage to specific brain regions can affect different aspects of spatial cognition.

In particular, case reports of taxi drivers who suddenly lose the ability to navigate following PCA strokes provide compelling examples of the effects of such infarctions (blood blockage) on navigation. We would tend to think of taxi drivers as particularly skilled navigators (especially before the advent of GPS), because these individuals must navigate around complex cities every day for a living. Indeed, their very livelihood depends on the ability to take their passengers to the right locations as quickly as possible. As we mentioned earlier, London taxi drivers, one of whom we will describe in detail shortly, undergo an extensive exam testing their spatial knowledge, including knowing the names, contours, and intersections of approximately 25,000 streets, simply to get their taxi license (Maguire, Nannery, and Spiers 2006)!

Our first example of a taxi driver who experienced disorientation as a result of a stroke involves a study conducted in Kawasaki, Japan. A group of neurologists and neurosurgeons there (Takahashi et al. 1997) described one patient in particular who stands out in terms of the changes to his exceptional navigational abilities that occurred following a stroke. Patient #2 in their paper was a 55-year-old former taxi driver. The following description provides a moving picture of the changes he underwent as a result of the brain damage:

> On January 12, 1993, as [the patient] was driving his taxi in the same city [Kawasaki], he suddenly lost his understanding of the route to his destination. As he could quickly recognize the buildings and landscape around him, he was able to determine his current location. However, he could not determine in which direction he should proceed. He stopped taking passengers and tried to return to the main office, but didn't know the appropriate direction in which to drive. Using the surrounding buildings, scenery, and road signs he eventually arrived back at the office, although he made several mistakes along the way. He remembered, during this time, passing the same places over and over again. The next day when he left his house to receive a medical examination at a neighborhood hospital, he could not determine whether he should go left or right, so he was obliged to take a taxicab (Takahashi et al. 1997, 465).

As subsequent testing with the patient revealed, although he could easily recall the names of prominent landmarks, such as the post office and bank in his neighborhood, he could not accurately place these buildings relative to each other on a map. Nor was he able to recall the route he would take to get from one of the buildings to another. As he stated: "I don't even know which way I should go first, left or right." It is important to note that despite these problems, this patient, and the other patients in the study, did not show basic problems with attending to stimuli (hemispatial neglect), nor did they show any difficulty with the idea that there were objects located to the left and right sides of their bodies. The presenting deficits could best be described as a problem with deriving heading direction from an external reference position.

Difficulties with heading direction, in which patients are unable to orient themselves with respect to their immediate surroundings, is one of the hallmarks of damage to a part of the brain known as the *retrosplenial cortex* (named for its location "behind" the splenium of the corpus callosum, which is the band of white matter connecting the two hemispheres so that they can communicate with one another). Interestingly, this region is one of the first to be affected in Alzheimer's disease, along with regions of the medial temporal lobe (hippocampus and parahippocampal cortex) to which it is strongly interconnected. We have discussed the retrosplenial cortex previously in the context of head direction cells in rodents (see chapter 3), which corresponds with behavioral findings in humans. We will engage in a more detailed discussion of the role of the retrosplenial cortex and how it fits within a larger network of brain structures involved in topographical orientation in chapter 8. Indeed, as we will discuss in that chapter, additional case studies support the fundamental importance of the retrosplenial cortex and other brain areas, supplied by branches of the PCA, to spatial orientation and navigation more generally (Barrash et al. 2000).

## Limbic Encephalitis

Encephalitis typically arises owing to infections, either viral or bacterial, which result in an immune system response. It can also arise from an autoimmune response, which is essentially the immune system attacking itself for unknown reasons. Antibodies, produced by the immune system to combat the infection, or produced as an aberrant autoimmune response, treat cells in the body as foreign invaders. In the case of limbic encephalitis, antibodies target neurons in the medial temporal lobe (MTL)—in particular, the voltage-gated potassium channel (Vincent et al. 2004). This results in an alteration in the normal functioning of neurons, resulting in seizure activity and cell death.

Patients with limbic encephalitis often show profound amnesia and memory loss, a common symptom of medial temporal lobe damage. Because spatial memory may be considered a specific type of declarative memory (see chapter 9), and the hippocampus and parahippocampal gyrus within the affected medial temporal lobe contain place and view cells (see chapter 3), topographical disorientation in recently encountered environments is not entirely surprising. What is more surprising is that patients appear to be relatively unimpaired when navigating within their home environments, although it is possible they are using some compensatory strategies (see chapter 6), and more subtle deficits in spatial representations can be apparent (Maguire, Nannery, and Spiers 2006).

In one particularly striking example of intact navigation following damage to the hippocampus, an experienced London taxi driver, T.T., became amnesic after limbic encephalitis. As mentioned previously, London taxi drivers must pass a rigorous exam that requires years of study and practice. Thus, studying such a taxi driver who experiences limbic encephalitis provides one way determine to the effects of the disease on navigation, and by proxy, the effects of medial temporal lobe damage on navigation, which we consider in more depth in chapters 8 and 9. Maguire et al. administered a series of tests to T.T. and compared his performance to that of age- and education-matched control participants who were also London taxi drivers. T.T., while densely amnesic, was able to recognize landmarks shown to him around London. He was also able to accurately estimate distances between these landmarks. His deficits became apparent only after more dynamic tests of wayfinding through the streets of London that he had regularly navigated as a taxi driver, prior to his diagnosis of encephalitis.

To study this issue in depth, Maguire et al. adapted a virtual taxi driver game in which the streets, cabs, and other details of London were rendered as accurately as possible. The authors then asked all the taxi drivers to navigate approximately fifteen different routes through London that they would routinely take while performing their jobs. In many ways, T.T.'s navigation abilities were normal. He was able to get from one place to another through London, and overall, compared to controls, showed little deficit (Maguire, Nannery, and Spiers 2006).

His deficits became more obvious only when Maguire et al. performed a detailed analysis of the routes he took compared to the control participants. In particular, T.T. showed a tendency to take what in London are referred to as the "A" roads. "A" roads in London would be considered akin to the main arteries or roads in any city. For example, in Los Angeles, this would involve the highways (I-10 and I-405) that cut through the metropolis. In Manhattan, this would involve streets like 34th Street and Park Avenue, which define east-west and north-south directions. T.T.'s deficit, specifically, involved a tendency to favor major roads over minor roads when navigating (figure 7.2). This led, overall, to instances in which his navigation was

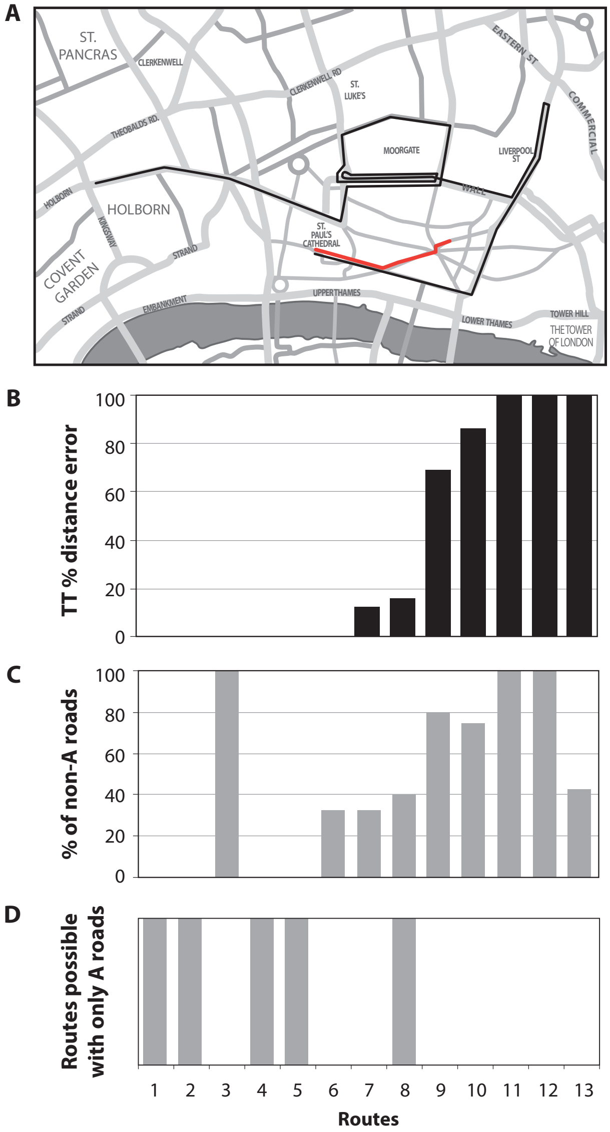


**FIGURE 7.2.** A. Example of patient T.T.'s dependence on major "A" roads in London, shown in black. B–D. Although he made no significant distance errors compared to controls overall (B), he relied on major roads to a significantly greater extent (C and D). Reproduced from Maguire et al. 2006.

inefficient because of his overreliance on such streets. Note that the patient may have employed compensatory strategies, although it is difficult to prove this because in many ways his allocentric navigation, other than relying on major roads, was normal.

T.T.'s deficits mirror those shown in other cases of medial temporal lobe damage. For example, Rosenbaum et al. (2005) studied a former Toronto taxi driver who developed Alzheimer's disease, which, as described next, affects the medial temporal lobe in early stages. Rosenbaum et al. (2000) showed that the patient made accurate judgments of distance and direction between landmarks located in Toronto and could draw sketch maps of his home and neighborhood that were accurate in terms of overall layout. Like patient T.T.'s navigational patterns, though, the patient described by Rosenbaum et al. drew maps that lacked detail compared to other healthy retired taxi drivers (Rosenbaum et al. 2000). Similarly, Kolarik et al. (2016) showed that a patient with medial temporal lobe damage could navigate normally in a novel virtual navigation task but showed impairments in the precision of her search for hidden targets. Overall, these findings suggest that one result of damage to the medial temporal lobe is impairment in the precision of navigation searches. We consider this issue in more detail in chapters 8 and 9.

## Alzheimer's Disease and Navigation

Alzheimer's disease is an age-related degenerative neurological condition that involves gradual collapse of neural circuits owing to neurofibrillary plaques and tangles. Years prior to clinical diagnosis of Alzheimer's disease, patients manifest a condition called amnesic mild cognitive impairment (aMCI). Fifty percent of older adult patients with mild cognitive impairment (MCI), typically over 65 years of age, will eventually convert to Alzheimer's disease (Gauthier et al. 2006). This particular condition is defined by loss of memory over and above what is expected in healthy aging (Knopman et al. 2003) in relation to functional changes in the medial temporal lobe and regions connected to it. As with other pathologies of the medial temporal lobe, resulting memory impairment often includes aspects of spatial memory and navigation.

As discussed in our earlier example, individuals with mild cognitive impairment, and eventually Alzheimer's disease, often show devastating symptoms of spatial disorientation, particularly in new environments (Hort et al. 2007). In fact, one of the early symptoms frequently noted by spouses of those in the early stages of mild cognitive impairment is spatial disorientation. Compendia of neurologist visits suggest that the first reports of these diseases, particularly full-blown Alzheimer's disease, often involve difficulty navigating and a tendency to get lost, even in familiar neighborhoods (Cushman, Stein, and Duffy 2008; Kunz et al. 2015). One of the reasons for this is that the entorhinal cortex, an area we discussed previously in connection with grid cells, often shows early degradation in Alzheimer's disease–related MCI, even before the disease manifests (Burggren et al. 2008; Braak et al. 2011). Other areas, like the hippocampus and parts of the brainstem important for modulating the cortex, also show early degradation (Braak et al. 2011). Thus, these findings link the earliest stages of degradation in the entorhinal cortex, the hippocampus, and the subcortical areas within the brainstem important to modulation of these areas to deficits in navigation.

Recall that in chapter 3, we discussed the idea of the grid cell, neurons in the entorhinal cortex of the rat and the human that fire in grid-like fashion during navigation. Although the exact role of the grid cell in navigation remains unclear, one of the intriguing suggestions, described in chapter 3, is that it may underlie our ability to represent spatial distances and directions as we navigate. Intriguingly, one study by Fu et al. (2017) took the human gene responsible for producing tau-proteins, which underlie the formation of neurofibrillary plaques that are a hallmark of Alzheimer's disease, and inserted these into a mouse, producing a mouse model of Alzheimer's disease. These mice had an abnormal accumulation of neurofibrillary tangles, abnormal grid cells, and impaired navigation. These deficits, though, did not develop until the mouse was older (30 months), suggesting an important link between the entorhinal cortex, grid cells, Alzheimer's disease, and age.

How exactly might these findings apply to humans? As also discussed in chapter 3, Doeller et al. and Jacobs et al. (Doeller, Barry, and Burgess 2010; Jacobs et al. 2013) found evidence for grid-like coding in the human entorhinal cortex. In particular, Jacobs et al. found, using extracellular recordings in the human entorhinal cortex, that neurons fired in regularly spaced intervals as patients navigated virtual environments. Doeller et al., using noninvasive fMRI, found that activation changes scaled with movement speed in a grid-like fashion. As a follow-up to these studies, Kunz et al. (2015) studied patients genetically at risk for developing Alzheimer's disease and MCI. Even before these individuals developed the disease, Kunz et al. found that the grid-like coding of their entorhinal cortex during navigation was impaired compared to healthy participants. This study thus provided a possible link between early degradation in navigation-related circuits in these patients and the development of Alzheimer's disease.

As might be expected, the most devastating consequences to navigation are seen in individuals with a diagnosis of possible or probable Alzheimer's disease, as these eventually affect widespread areas with the cerebral cortex (Braak et al. 2011). In particular, a common symptom of full-blown Alzheimer's disease is wandering, even in highly familiar neighborhoods (Klein et al. 1999), consistent with a fairly broad loss of function within multiple neural circuits. In fact, some patients become so disoriented that they follow telephone lines or other prominent structures, a response strategy, into the wilderness (Johnson 2010). Patients are sometimes found miles from their homes, without food or water, disoriented and wandering aimlessly, unable to identify a goal and without any idea of where they are.

Why would patients with full-blown Alzheimer's disease follow telephone wires and telephone poles? Recall our discussion of piloting or "beacon" strategies, which we often consider to be one of the simplest, most basic forms of navigation because it involves simply moving to a visual, stationary target (see chapters 2 and 5). If all other forms of egocentric and allocentric navigation are lost, owing to widespread cortical damage, a patient may fall back on this form of navigation (discussed in chapter 6). In this way, the tendency for patients to follow telephone lines, which are typically visually prominent, represents usage of the simplest form of navigational strategy, beaconing, likely because all other forms are compromised.

Other studies have specifically linked the development of Alzheimer's disease and another structure related to navigation that we have discussed extensively—the hippocampus. Apostolova et al. followed patients with MCI for five years in order to investigate MCI risk factors in those who would later develop Alzheimer's disease. Their studies show that approximately 50 percent of patients with MCI later develop Alzheimer's disease (Apostolova et al. 2006). They also found that the individuals diagnosed with MCI who later developed Alzheimer's disease had atrophy of the hippocampus at baseline, when they were still relatively healthy, even when their subjective memory complaints were not substantiated by standard neuropsychological testing. These studies thus provide an intriguing prediction: that atrophy of the hippocampus (and the entorhinal cortex; see earlier work mentioned previously) to begin with may put patients at risk for the development of Alzheimer's disease.

Consistent with this idea, one interesting argument about the development of Alzheimer's disease and navigation deficits involves the "use it or lose it" principle. For example, those who use rich, map-based strategies to navigate on a daily basis will likely have well-developed neural circuits for navigation. Based on what we have discussed so far, including in chapter 6, this would predict that those who navigate using a place strategy would have greater connectivity and increased gray matter within important navigation circuits like the medial temporal lobes than those who do not navigate using such strategies. This in turn leads to the interesting prediction that practicing such navigation would potentially protect one against the development of Alzheimer's disease (Konishi and Bohbot 2013). In support of this, a retrospective study showed that patients with dementia had deficits in spatial cognition that preceded conversion to dementia by three years, in contrast to verbal memory and working memory deficits that occurred only one year before patients were diagnosed with dementia (Johnson et al. 2009). Furthermore, a recent study showed that the volume of the caudate nucleus was larger in patients with Alzheimer's disease relative to controls and relative to patients with Parkinson's disease (Persson et al. 2017; see chapter 6), suggesting that this structure could be favored compared to the hippocampus even in Alzheimer's disease. While it remains to be determined whether the biological symptoms of Alzheimer's disease, which can manifest early during aging (Braak et al. 2011), navigation deficits that precede the development of Alzheimer's disease, or lack of engagement of these circuits for some other reason puts one at risk, it is clear that the two show an intimate link.

## Healthy Aging and Navigation

A decline in spatial navigation ability is a frequent complaint of healthy aging. Older adults often report becoming lost more frequently when they drive and less able to stay oriented on a daily basis, particularly in new environments (Burns 1999). One of the consequences of this is that older individuals tend to navigate less and therefore "get out less." This may contribute to increased social isolation, a diet that is nutritionally deficient, and less cognitive stimulation. This, in turn, may increase the risk for developing a wide range of diseases, including diabetes, hypertension, heart disease, liver disease, arthritis, emphysema, tuberculosis, kidney disease, cancer, asthma, and stroke (Tomaka, Thompson, and Palacios 2006). Therefore, disorientation and spatial navigation problems have far-reaching consequences and represent a critical issue for older adult populations.

Several studies have shown impairments in first-person navigation, which we term the *route system*, in elderly adults compared to younger normal (YN) individuals, during both real-world (Wilkniss et al. 1997) and virtual navigation (Moffat and Resnick 2002). Specifically, compared to young adults, elderly individuals make more errors when navigating, often retracing the same route they took earlier and failing to remember a previously encoded route to a goal. Overall, these deficits manifest in particular as an allocentric and "place" form of navigational impairment (see chapters 2 and 6), compared to a response-based or egocentric form of navigation.

What deficits in underlying neural circuits may contribute to age-related navigational deficits? While many cortical circuits may undergo changes and atrophy during aging (Sowell et al. 2004), one frequently implicated brain area is the hippocampus. Moffat et al. (2006) investigated functional activity patterns of young and older adults during navigation in a virtual spatial memory task (Moffat, Elkins, and Resnick 2006). Results showed that younger adults had significantly more fMRI activity in the hippocampus compared to older adults. Antonova et al. (2009) found similar results when testing young and older participants on their "Arena" spatial memory task, a virtual adaptation of the rodent Morris water maze for humans (Morris 1981). During the encoding phase, young participants showed significant fMRI activity in the hippocampus bilaterally. Decreased fMRI activity in the hippocampus in older adults was accompanied with poor performance on the task. Older adults also made significantly more errors than young adults on this task. These studies suggest that with aging there is decreased fMRI activity in the hippocampus, implying an important link between activation of the hippocampus, aging, and navigation (Antonova et al. 2009).

Structurally, there is also an accelerated decrease in hippocampal volume with aging, particularly when hypertension is involved (Raz et al. 2004). Regional volumetric studies in older adults have reported correlations between hippocampal volume and spatial memory as assessed with wayfinding (Driscoll et al. 2003; Chen et al. 2010; Head and Isom 2010). These studies showed that better spatial memory correlated with increased hippocampal volume. In contrast, Moffat et al. (2007) tested younger and older adults on a virtual Morris water maze and found that spatial memory correlated with hippocampal volume only in younger adults but not in older adults. Although the exact link between hippocampal integrity and cognitive function remains debated (Van Petten et al. 2004), two studies suggested a possible solution to these discrepancies involving measuring place versus response strategies (see chapter 6). Specifically, Bohbot et al. (2007) and Konishi and Bohbot (2013) found that utilization of a place strategy correlates, in part, to gray matter in the hippocampus of both young and older adults. Overall, these findings support the idea that impairments in hippocampal function may underlie some of the deficits in first-person navigation.

As noted earlier, however, there is more to aging than the hippocampus, including degradation of areas of frontal and parietal cortex (Sowell et al. 2003). We have already discussed the importance of parts of the prefrontal cortex to navigation, particularly goal-oriented navigation, in chapters 4 and 5. In chapter 8, we will discuss parietal cortex in more detail—in particular, its possible relationship to egocentric navigation. As we will also discuss in chapter 8, it is also correct to consider navigation as a network phenomenon rather than based on single brain regions working in relative isolation. From this standpoint, the gray matter degradation that occurs in multiple lobes within the aging brain is also highly relevant to navigation. We will consider the contributions of specific brain regions versus a network-based perspective in more detail in chapter 8.

## Cellular Mechanisms Underlying Age-related Navigational Impairments

Perhaps one of the most important connections between a biological mechanism and behavior is that of synapses, a primary means by which neurons communicate with each other. When cells are active together, this causes an influx of $Ca^{2+}$ through n-Methyl D-aspartate (NMDA) receptors in the postsynaptic terminal, which then leads to a cascade of events that eventually result in long-term potentiation (LTP). LTP in turn causes synaptic changes that are believed to support memory formation (McNaughton and Morris 1987). Numerous studies link changes in synaptic excitability with learning and memory, with impairments in LTP and NMDA function directly linked to navigational deficits (Morris et al. 1986).

Relevant to our current consideration, changes in synaptic plasticity occur with aging and may underlie some of the navigation deficits we described previously. In aged rats, there is an LTP-induction deficit in the hippocampus (Barnes, Rao, and Houston 2000). Specifically, the threshold required for LTP induction is higher in aged rats—that is, a larger current amplitude is required in order to elicit LTP. Thus, the fact that plasticity thresholds are higher in the aged hippocampus suggests an important link between spatial learning, the hippocampus, and impaired cellular mechanisms (Shen et al. 1997).

There is also an issue with LTP maintenance in aged rats, whereby over several days, LTP decays faster in aged rats compared to young rats (Barnes 1979). This decay correlates with performance on spatial memory tasks, suggesting that memory deficits in aged rats may be related to deficits in LTP induction and maintenance. In contrast to LTP, long-term depression (LTD) decreases the strength of synaptic connections. LTD is induced by low-frequency currents and low levels of $Ca^{2+}$ influx. In contrast to young rats, aged rats are more susceptible to LTD and depression of synaptic strength happens with lower frequency stimuli (Norris, Korol, and Foster 1996). Taken together, changes in synaptic plasticity may cause slower learning and faster forgetting in aging.

The stability of place cells, particularly their ability to change where they fire in a new environment (termed *remapping*; see chapter 3) also decreases with aging. Aged rats are more likely to show remapping when reentering an environment that was previously visited (Barnes, McNaughton, and O'Keefe 1983; Barnes et al. 1997). Specifically, when moved from one environment to another, aged rats show a greater likelihood of using the same place representations, even though they are in a new environment, than younger rats. This appears to correlate with impairments in the ability of older rats to find hidden locations in the Morris water maze. Thus, impairments in plasticity, place cell remapping, and navigation deficits all appear correlate in older rats.

These properties may also have homologues in humans. Older adults tend to employ a greater proportion of response strategies compared to young adults tested on various virtual navigation tasks (Etchamendy et al. 2012; Rodgers, Sindone, and Moffat 2012). Similarly, in a sample of 599 participants from ages 8 to 80, Bohbot et al. (2012) showed that there was a decrease in the proportion of place to response learners with age from childhood to senescence. These studies indicate a tendency to use response strategies with greater probability with aging, proving a potential link between hippocampal degradation and age-related navigational impairments (see also chapter 6). While the exact cellular mechanisms underlying these deficits remains to be linked between rats and humans (see chapters 4 and 6), it is clear that hippocampal function, as well as that in other structures, declines with age, as does the ability to navigate using more flexible place strategies.

## Use It or Lose It: Navigation Interventions to Protect against Age-related Cognitive Decline

One intriguing implication of the higher reliance on response and egocentric strategies during aging, just like with MCI, is the possibility of training older adults to use more navigationally rich, map-based strategies. Indeed, research groups have designed spatial training programs with the intention of improving memory and increasing hippocampal volume. In one study, older adults underwent a 16-hour spatial memory training program that required participants to learn the location of objects and places in fifty virtual environments. Following this training program, participants made significantly fewer errors on radial arm maze and wayfinding tests than controls, and had significant increases in gray matter in the right and left hippocampi that were not observed in placebo controls (Bohbot et al. 2016).

A second experiment by Lövdén et al. (2012) encouraged spatial training in young and older adult participants by asking them to engage in a spatial navigation task for 50 minutes, every other day, for four months. The experiment showed that this training program significantly improved spatial navigation compared to controls in young and older adults; following training, older adults performed as well as the young adult controls (Lövdén et al. 2012). Though this training did not increase gray matter in the hippocampus, it prevented the age-related decrease in hippocampal volume in young and old adults, an effect that was maintained four months following the end of the program (Lövdén et al. 2012). A third study showed that a six-session navigation training program, comprising viewpoint shift and path integration tasks, improved spatial memory significantly more than a perceptual training program did (Hötting et al. 2013). Following training, participants in the navigation training group had a significant reduction in brain activity in the medial temporal lobe, including the hippocampus and parahippocampal cortex, which the authors suggest reflects more efficient neural processing (Hotting et al. 2013). Together, these studies reflect the fact that the hippocampus as well as other brain regions related to navigation are highly plastic structures that may be modulated in size and function as a result of cognitive activities such as spatial memory training.

## Developmental Topographical Disorientation

Imagine that, instead of linking spatial disorientation symptoms and neurological/age-related conditions, as we have done so far, we instead try to categorize navigational impairments as their own disorder. A subset of individuals who are otherwise healthy complain of severe problems staying oriented and navigating on an everyday basis. Note that this is different from anything we have discussed so far: these individuals do not have a neurological condition and do not begin to experience symptoms with advanced age. The following is a description of a representative case described in the literature (Iaria et al. 2009; Iaria and Barton 2010):

> When she was 29, Sharon Roseman's brother called her, sick, to ask for a ride to the hospital. On her way over, she got lost two blocks away from his apartment and eventually had to call him from a payphone for directions. Though he was able to direct her from his house to the hospital, her secret was out. After he had recovered, he pressed her to tell him and their other sister more about the condition she had kept hidden.
>
> Indeed, every morning when she wakes up, Ms. Roseman (now age 68) has to re-learn her way to her kitchen. When she can, she gets friends to drive her places; the rest of the time, she limits herself to destinations that require few turns, which sometimes means taking 30 minutes on a journey that would have otherwise taken 10. Dating was a nightmare, she said, because she could never tell potential boyfriends how to bring her home. And even though she had a successful career as an executive assistant before retiring in 2011, she could only take jobs that allowed her to commute entirely along straight roads (even curvature threw her off), and after-work happy hours at new bars were out of the question (Foley 2015).

Ms. Roseman is not the only person who suffers from developmental topographical disorientation (DTD). As described by Iaria and his colleagues, numerous people across the world suffer from this condition. They have otherwise normal memory and neuropsychological profiles—their only major cognitive deficit is a complete inability to navigate. The self-reported struggles with navigation described earlier have received more objective verification from detailed observation of how they navigate within their neighborhoods and virtual reality (VR) tests (Iaria et al. 2009; Iaria and Barton 2010). Systematic testing has revealed that their impairments relate to an inability to use cognitive maps, or place-based navigation strategies, to find their way around familiar and novel environments.

Interestingly, DTD does not seem to show an obvious pattern of brain impairments, such as we might expect from our discussion so far. Studies to date have been unable to detect degradation in gray matter, including areas we might expect to be important, like the hippocampus, retrosplenial cortex, and other navigation-related areas discussed in chapters 3 to 5 (Iaria et al. 2014). Instead, the only obvious brain abnormality is decreased functional connectivity between the hippocampus and the prefrontal cortex, two areas important for navigation and decision making whose interaction is critical for normal functioning during navigation (Jones and Wilson 2005).

The authors revealed this surprising finding using a technique called diffusion tensor imaging (DTI) and resting state functional connectivity, methods that allow tracking of connectivity patterns between brain regions rather than local damage to the gray matter that defines individual brain regions. DTI tracks the ordered flow of water molecules through white matter (so called because these tracts appear as white on postmortem microscopy of brains). White matter typically contains axons, suggesting it contains important fibers of passage through the brain. Changes in DTI thus indicate that fibers of passage between areas, which we can think of as highways of communication, show impairments in processing. Resting state functional connectivity, in contrast, tracks connectivity patterns while the brain is resting, giving us information about the baseline interactions between brain regions in the absence of a task. While resting state functional connectivity often correlates with white matter tracts, it can show additional pathways DTI cannot reveal (Honey et al. 2009). Thus, both of these methods suggest impairments in how the prefrontal cortex and hippocampus communicate with each other in DTD patients, rather than their structural integrity in the first place.

Why might communication be important to structures involved in navigation? We consider this issue in detail in chapter 8, when we discuss network-based models of navigation. Briefly, though, it is similar to the way we might imagine a map containing cities that are connected by numerous highways. If we lose a city like Los Angeles, we can imagine that many of the things that come from Asian countries like China and Japan will thus fail to arrive in the country, as well as all the other things supplied by Los Angeles, like movies and entertainment. Now imagine we damage one of the major highways between Los Angeles and the rest of the country, like I-10. In a similar way, we might imagine that much of the important information both received and supplied by Los Angeles will be impaired. Of course, with regard to ground transportation, there are other ways to get things to cities in the country (for example, I-5), but impairing I-10 will severely impair the normal transit of information throughout the country.

In a similar way, if white matter tracts connecting the hippocampus with prefrontal cortex are compromised, information processed by one structure will have difficulty reaching the other structure, with the expectation that navigational information supplied by the hippocampus will now fail to transmit in the normal fashion to prefrontal cortex. Perhaps more problematic, though, is that the normal bidirectional interactions between these two structures will be impaired. An increasingly supported perspective in neuroscience in that communication between structures forms the basis of much of cognition (Bassett and Gazzaniga 2011). While we consider these issues in more detail in chapter 8, it is easy to imagine that impairing interactions between brain regions important to navigation would likely have devastating consequences for how it normally manifests.

## Summary

There are many clinical disorders that affect navigation, only a few of which we have discussed here. Others include temporal lobe epilepsy, brain tumors, schizophrenia, depression, attention deficit hyperactivity disorder (ADHD), and traumatic brain injury. However, the disorders we have covered so far—stroke to the posterior cerebral artery, limbic encephalitis, and early Alzheimer's disease and Alzheimer's-related MCI—are the most thoroughly studied owing to the significant effects on navigation that often result. In the case of stroke and limbic encephalitis, the effects are often owing to more focal or selective damage that affects a specific brain region or set of regions. We will return to a discussion of focal brain damage in chapters 8 and 9 and the implications of such damage for different aspects of navigation. We will also return to our discussion of DTD when discussing how spatial cognition and navigation is the product of a collective network of brain regions.

## CHAPTER 8

# THE NAVIGATION NETWORK

The focus of our book so far has been on understanding the cognitive and neural processes that underlie human spatial navigation. Cognitive psychology and neuroscience, two of the core approaches that we employ when trying to understand the neural basis of human spatial navigation, involve attempting to isolate functions within the brain unique to a specific cognitive process. As we discussed in chapter 2, if we are interested in understanding a cognitive process like the effects of repeating a word when learning a list, this approach is fairly straightforward: we have participants study lists under two different conditions that are otherwise identical (that is, matched for numbers of words and retention interval), with one condition including a subset of the words that are repeated and another in which none of the words are repeated. We typically apply the same logic when attempting to isolate which part of the brain is important for a cognitive function by employing this design but recording from the participants' brains while they do the same task, in the hope that we will be able to compare the two conditions. We have reviewed much of the evidence to date that supports this "localization" perspective on cognitive function and navigation more generally, and this assumption forms the core of much of how we have considered navigation in this book so far.

At the same time, we can also consider cognitive processes, and the brain more generally, from a more integrated perspective. In chapter 2, we mentioned the idea of egocentric and allocentric navigation, and in chapter 6, we discussed the idea of place-based and response-based navigational strategies. As we acknowledged briefly in these chapters, these dichotomies are not as clean-cut as one might hope. For example, let's say we are trying to remember where we parked our car. We might try to remember the position of our car based on how close it was to the shopping mall and the street. Even if we do this successfully (attempts to develop computerized parking lots suggest that we often do not; see, for example, Hall 2002), it is unclear the extent to which we can completely separate egocentric and allocentric or place versus response navigation in this context.

Specifically, following our example, while the shopping mall and street are useful allocentric landmarks, we still need to know the position of the car relative to ourselves. Even when using a map of the parking lot to remember where we parked our car, we still need to know the position of objects on the map relative to our current position facing the map. Similarly, with a place and response strategy, we may fall back on our memory for where our car was parked last time we were at the mall (a response strategy) but quickly suppress this in favor of a reminder from landmarks in the parking lot that allow us to use a place strategy. In short, it is likely that our use of different behavioral forms of navigation involve more of a continuum than a simple cutoff between two clear strategies or representations. In support of this, most metrics of egocentric and allocentric representations, like the scene- and orientation-dependent pointing (SOP) and judgments of relative direction (JRD) tasks discussed in chapter 2, likely involve some of both forms of representation (figure 8.1).

This leads to an interesting conundrum when considering the neural basis of navigation. If there are no "process-pure" forms of spatial navigation, then it will be difficult to identify a single brain region fundamental to a single form of spatial navigation. Even if we were able to isolate a "pure" allocentric representation, for example, we may still find that multiple brain regions are important to this—for example, some brain regions may be important for representing landmarks, while others are important for spatial distances. We may find that there are not single, isolatable brain regions underlying each aspect of cognition and instead that these are *distributed* across brain regions. Indeed, the idea of distributed processing was an early proposal from computational biology and computer science that suggested that large groups of neurons with similar functions could accomplish significantly more in terms of explaining properties of cognition, like learning, than highly specialized "nodes" (for example, Rumelhart and McClelland 1987; Hopfield 1995). The idea of distributed processing argues that instead of highly specialized, independent modules in the brain, much can be accomplished by highly similar, redundant coding spread across thousands of similar neural "units."

Work in cognitive neuroscience sits at an important crossroads between approaches that assume "one brain region, one function" and those that assume a more distributed, network-based interpretation. So far in this book, we have largely adopted a localization approach, consistent with decades of work on place cells and the hippocampus. In the first part of this chapter, we will therefore focus on one of the most influential "localization" models to human spatial navigation, the Aguirre and D'Esposito model, which ascribes specific aspects of navigation to specific brain regions. In the second part of this chapter, in deference to the idea of distributed functions in navigation, we will focus on network models of human spatial navigation. Given the early stage of knowledge in human spatial navigation, we do

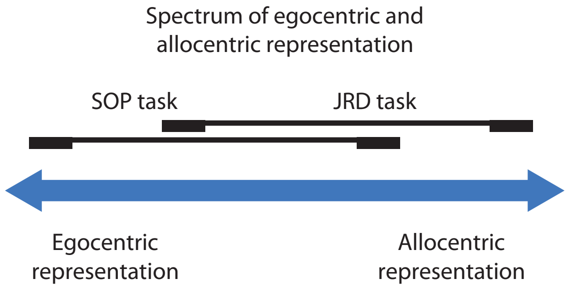


**FIGURE 8.1.** Overlapping allocentric and egocentric computations during commonly used assessments of direction.

not advocate either one strongly, and attempt to argue for the validity and strengths of both. We note, however, that the idea of localized function in navigation remains strong and compelling and while intriguing and promising, network and distributed conceptualizations remain under active development.

## The Aguirre and D'Esposito Taxonomy of Human Spatial Navigation

Nearly two decades ago, Aguirre and D'Esposito (1999) developed a taxonomy of topographical orientation, grounded in developmental and environmental cognitive theory, to characterize the collaborative effort of varied, segregated neural processes that support the many ways in which mental navigation and landmark identity may be represented (figure 8.2). Though largely guided by anecdotal observations of relatively small patient samples, and published at a time when neuroimaging studies on memory for large-scale (virtual) space were just beginning to emerge, this framework has proven effective in predicting focal deficits in diverse cases with restricted and larger lesions to neocortex. More sophisticated neuroimaging studies in recent years appear to support aspects of the taxonomy, with efforts to elaborate on its core divisions. The core ideas of this taxonomy suggested that egocentric position, heading direction, landmark identity, and the ability to encode new spatial layouts formed cognitive components supported by independent yet interacting modules within the brain.

These four major components in the network, largely concentrated in the right hemisphere, were initially envisioned by Aguirre and D'Esposito to involve the following brain regions: (1) posterior parietal cortex, involved in egocentric processing of locations; (2) retrosplenial cortex of the posterior cingulate to process allocentric heading; (3) inferior temporal cortical regions, such as the lingual gyrus, specialized for the perceptual identification of landmarks; and (4) medial temporal lobe (MTL) to code new spatial locations and form allocentric spatial configurations (*cognitive maps*) based on those locations. The taxonomy was heavily influenced by the then highly publicized view that two visual streams exist, a dorsal "where" stream to code spatial

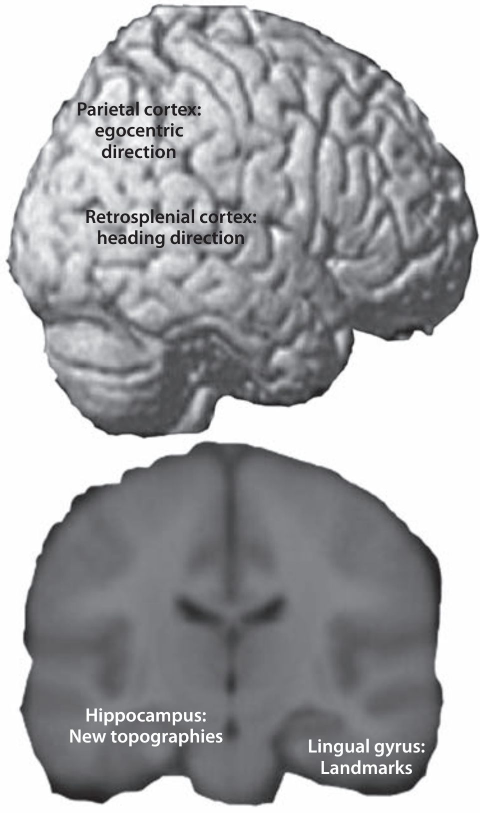


**FIGURE 8.2.** The Aguirre and D'Esposito model. Top panel shows a sagittal slice; bottom panel shows a coronal slice.

locations of visual stimuli in service of action, captured by (1) to (3), and a ventral "what" stream to code the visual identity of those stimuli in service of perception, captured by (4) (Ungerleider and Mishkin 1982).

## Posterior Parietal Cortex and Egocentric Position

The first component of their taxonomy, the self-localization, or egocentric, component, involves posterior parietal cortex. This is part of the dorsal visual stream (Ungerleider and Mishkin 1982), a network of interconnected brain areas starting at the primary visual cortex and extending into the parietal cortex that plays a critical role in determining the position of objects relative to the body in order to act on them (Goodale and Milner 1992) or to use them to guide navigation. Posterior parietal cortex, a multimodal brain area integrating visual, motor, and somatosensory information, was viewed as central to coding environments within an egocentric coordinate system that allows for accurate reaching toward objects and movement with respect to landmarks in the environment and imagination of scenes. In support of this idea, patients with lesions to posterior parietal cortex typically suffer from what is known as *hemispatial neglect*, or inattention to one side of space, because the side of the visual field opposite, or *contralateral*, to the lesioned hemisphere is completely ignored or neglected. The neglect usually occurs on the left side owing to a right-sided lesion, meaning the patient attends selectively to the right side of visual space (left-sided lesioned patients may also suffer right-sided neglect, but such cases are difficult to assess owing to the concurrent severe language comprehension deficits these patients suffer from).

This deficit is present, interestingly, despite the fact that patients can still perceive and see objects normally within both visual fields. A patient with right hemisphere damage may shave the right half of his face, eat food off the right side of his plate, and draw only the right side of an object or scene when asked to copy it, thereby neglecting the left half of space. Note, however, that not all cases of neglect are egocentric. If a patient suffering from hemispatial neglect looks at a book standing straight in front of her, she will pay attention to the right side and neglect the left side of the book. However, if the patient tilts her head 90 degrees to the right toward her shoulder, she will neglect the left side of her visual field, which is now the top of the book, but she will also neglect the left side of the book itself, which falls in the bottom right part of her visual field. In this way, neglect can affect both a specific visual field (usually the left) but also be object centered (to parts of the book in this example). Thus, it is most accurate to think of neglect as a multifaceted condition acting on the underlying representation of visual and object space rather than simply what is perceived (Vallar et al. 2001).

A striking example of the effects of hemispatial neglect on spatial navigation comes from a classic study on the Piazza del Duomo in Milan, Italy, involving patients with damage to the right posterior parietal cortex (Bisiach and Luzzatti 1978). For Italians, particularly those living in Milan, the Piazza del Duomo is one of the prides and joys of their city. Almost all Milanese can thus readily describe the layout of this famous piazza and describe the individual locations that comprise it. However, two patients who had a high degree of familiarity with this piazza who also suffered strokes to their right posterior parietal cortex showed a particularly dramatic deficit when describing it.

The patients were first asked to imagine the cathedral in the center of the Piazza del Duomo from the opposite side of the square (this is like the judgments of relative direction task we described in chapter 2). While the patients had no problem describing objects on the right side of the Duomo, like the Royal Palace and the Arengario, the patients omitted many of the landmarks on the left side of the square, like Via Dante. In this way, the patients were blind to one side of the piazza, even though their vision was otherwise normal. But could it be that they simply forgot these locations, despite the importance of this Piazza to any Milanese?

In a brilliant control comparison, the authors then had the patients reverse their perspective, imagining themselves with their back to the cathedral looking out through the doors. Now, the opposite pattern of deficits occurred: the patients could name objects on their right side, like Via Dante, that were previously invisible to them. However, they were completely impaired at naming objects on the left that they previously had no trouble naming, like the Royal Palace. Thus, the one element that remained constant was their ability to imagine objects on their left side, which, in turn, depended on their facing angle. What this study tells us is that hemispatial neglect operates not only on the patient's *perception* of the visual world but also on the patient's *internal representation* of the visual world.

Subsequent studies have helped us to better understand this important connection between hemispatial neglect during mental imagery, damage to the posterior parietal cortex, and impairments in egocentric navigation. In addition to hemispatial neglect, damage to this area often leads to disorientation in both novel and familiar environments, poor spatial imagery, and poor drawings of maps. This deficit appears to come about because the individual has lost the ability to appreciate the spatial relation between objects or landmarks and the self. Interestingly, though, the patients can still perceive and name landmarks when they see them and their vision is otherwise normal (Stark, Coslett, and Saffran 1996). Thus, damage to this area leads to an inability to map positions of objects relative to one's body position.

One could easily argue, however, that hemispatial neglect would have profound consequences to attending and integrating objects in front of oneself independent of any deficits in navigation. In an experiment directly addressing this issue, Ciaramelli and colleagues (2010) had patients imagine navigating from one landmark within Toronto to another. In their task, they had to imagine a new route by assuming the typical way was blocked, which would require knowing the position and direction of objects relative to themselves as they moved. As control comparisons, the authors also tested the ability of the patients to accurately place objects on a map, taking into account whether or not they showed spatial neglect. None of the patients showed obvious symptoms of spatial neglect (they could all attend equally well to objects on their right and left sides), and all patients could draw accurate maps of Toronto. All patients, however, showed deficits in their ability to describe navigating from one landmark to another. In particular, patients made more errors when having to judge how to get from one landmark to another than control participants. This difficulty was accompanied by an inability to conjure up a rich representation of the visual features passed along the imagined route and a general feeling of disembodiment and lack of immersion in the environment, as though someone else was navigating for them. Thus, while the patients could name the landmarks, place them on a map, and judge the distance between them, their ability to picture themselves navigating relative to these landmarks was greatly impaired.

In addition to the evidence from lesion studies, there is also copious evidence from fMRI, nonhuman primate, and rodent navigation studies that the posterior parietal cortex plays a critical role in egocentric forms of navigation (Kesner, Farnsworth, and DiMattia 1989; Snyder et al. 1998; Wolbers et al. 2008; Iaria et al. 2009). As we suggested earlier, this is most likely because of the specific role that this area plays in visuo-spatial sensorimotor integration, placing it in ideal position to integrate information from the senses with body position. These types of deficits can then manifest in a variety of forms—for example, the inability to imagine one side of space relative to your current position, as shown in the Duomo study, or an inability to imagine routes as one navigates, as shown in the Ciaramelli et al. study. It is also fair to say that the idea that parietal cortex is important for egocentric navigation is probably one of the least controversial areas in human spatial navigation! Whether all aspects of navigation can be distilled to an egocentric versus an allocentric form of judgment is less clear, but navigational tasks involving a prominent need for egocentric forms of representations clearly require parietal cortex (see figure 8.2).

However, it is also important to consider that the posterior parietal cortex is implicated in a host of other perceptual and cognitive activities (Aguirre and D'Esposito 1999; Simons and Mayes 2008; Kesner and Bucci 2009). The seemingly disparate roles of posterior parietal cortex in attentional capture and control, holding information online in working memory, retrieval of events that are unique to time and place in episodic memory, and perspective taking may reflect separable processes governed by distinct regions of posterior parietal cortex or a common mechanism that underlies at least some of these processes (Cabeza et al. 2008; Olson and Berryhill 2009). All may contribute to spatial representations of both new and old environments (Ciaramelli et al. 2010).

## Retrosplenial Cortex and Heading Direction

The second major component of the Aguirre and D'Esposito model is the retrosplenial cortex, which is located within the posterior cingulate cortex. Consistent with lesion and fMRI studies, Aguirre and D'Esposito hypothesized that this region plays a critical role in coding heading direction, which, in turn, relates strongly to the idea of head direction cells discussed in chapter 3. Imagine you have just exited the building that you work in and need to decide how to get to where you parked your car. Perhaps most important to knowing which way to walk is knowing how you are oriented relative to the parking lot. If we walk north instead of south and the parking lot is located to the south, knowledge of distance or location is simply irrelevant without accurate knowledge about our facing angle. Thus, knowing our heading direction is arguably one of the most fundamental components of determining whether we get to our destination or not.

Given our earlier discussion of the importance of the parietal cortex to coding egocentric direction, it is worth considering what might be different about the type of heading direction coded by the retrosplenial cortex. As it turns out, neither egocentric nor allocentric coding are accurate terms for the type of coding performed by the retrosplenial cortex in regards to facing direction (Muller et al. 1994). The retrosplenial cortex is a particularly interesting area of cortex in that it represents somewhat of a transition zone between the six-layered neocortex in the parietal cortex and the older, three-layered cortex in the medial temporal lobe (Maguire 2001). In this way, we can think of the retrosplenial cortex as a means of translating heading from primarily egocentric coordinates in the parietal cortex to a more world-centered form of reference coded in the medial temporal lobes.

For the retrosplenial cortex, then, facing direction relates to one's facing angle relative to an external reference or landmark. So, for example, if we are facing forward, that is an egocentric form of facing angle. In contrast, if we are facing north, or facing the city center, we are referenced to an external set of landmarks, and thus we refer to an allocentric reference frame. Critically, though, the key part is how these external references translate into our facing angle—that is, facing either toward or away from a landmark. In this way, the type of facing angle coded by the retrosplenial cortex is best thought of as a form of egocentric to allocentric translation (Byrne, Becker, and Burgess 2007).

A series of studies involving patients with damage to the retrosplenial cortex nicely illustrates exactly how deficits in facing direction can emerge and how they differ from egocentric deficits described in patients with damage to the parietal cortex. A groundbreaking paper from a group of neurologists and neurosurgeons in Japan (Takahashi et al. 1997) described three patients with such deficits, which we have already discussed in chapter 7, when we considered strokes to the posterior cerebral artery. All of these patients suffered problems with knowing their relative heading direction, even though they were highly familiar with the town they were navigating. The patients' deficits could best be described as a problem with knowing their heading direction relative to some external reference position.

As we discussed in chapter 2 and at the beginning of this chapter, however, single case anecdotes are strengthened when followed up with systematic testing in other single cases and groups of patients (Rosenbaum, Gilboa, and Moscovitch 2014). While the patients described by Takahashi et al. are intriguing (see also Ino et al. 2007 for another description of a taxi driver with retrosplenial cortex damage), it is important that we can also demonstrate specific deficits in knowledge of heading direction with carefully designed *cognitive paradigms*. In particular, it is important that we have quantifiable data that can rule out other explanations and specifically point to a deficit in heading direction. Otherwise, we run the danger of overattributing an idiosyncratic observation without knowing its underlying cognitive cause or whether other patients with similar lesion profiles will exhibit similar symptoms (Tversky and Kahneman 1973).

Hashimoto et al. developed such a paradigm, termed the card placing task (CPT; Hashimoto, Tanaka, and Nakano 2010). In part A of the task, they asked three patients with retrosplenial cortex damage to recall the locations of three unique cards that had been placed in front of them. The patients did this by placing each of the cards exactly as it had originally been oriented relative to themselves. In this way, part A of their task tested for both the patients' memory and their ability to orient objects egocentrically. All patients' performance on this task was comparable to that of healthy controls, indicating that their memory was overall intact and that their ability to reproduce the egocentric positioning of objects was also intact.

Their impairments in using their facing direction were not revealed until part B of the task. Just as in part A, the patients had to remember the locations of cards positioned in front of them. The key difference, though, was that Hashimoto et al. then had patients rotate either 90 or 180 degrees from their original position. After the patients were rotated, they were asked to place the cards in the exact same position in which they were first encoded. In this case, patient performance dropped to near-chance levels, with patients getting less than half of the card placements correct. Thus, the simple change of facing direction devastated their ability to correctly remember the location of the cards.

What are the critical differences between parts A and B? The only important difference was the patients' facing direction when attempting to retrieve the original card positions from memory. Why would this be important? This is because patients had to take the angle at which they had encoded the objects relative to themselves and then rotate this to a new orientation relative to their new facing angle. Most of us would solve this by simply remembering how the objects and our body position are oriented relative to the room surrounding us. However, retrosplenial cortex damage caused a specific deficit in the patients' ability to use their facing angle relative to the objects and the room—what we term here *egocentric-to-allocentric translation*—leading to severe impairment on part B of the task.

The idea that retrosplenial cortex damage impairs the ability to perform translation of egocentric headings into allocentric ones (and possibly vice versa) has received strong support from both fMRI and computational models of navigation. For example, one computational model of memory, termed the *BBB model* (for Byrne, Becker, and Burgess 2007), suggests that to translate egocentric information in a way that can be used to derive things like location (discussed in chapter 3), we must call on a system that can translate allocentric coordinates from egocentric ones. Consistent with this idea, an fMRI study conducted by Zhang et al. (Zhang, Copara, and Ekstrom 2012) showed retrosplenial cortex activation specifically when healthy participants translated information they learned from first-person navigation of a virtual environment into the JRD task (discussed in chapter 2), one that we would expect to place high demand on allocentric processing. These examples indicate converging evidence for a selective role of retrosplenial cortex in our ability to represent our facing angle with respect to extrinsic, or world-centered, coordinates. These findings are in line with the second part of the Aguirre and D'Esposito description of specific components of navigation and how they relate to the brain (see also our discussion of head direction cells in chapter 3).

## Landmarks and the Lingual Gyrus

When navigating, the importance of landmarks is fairly obvious. As we walk in a familiar neighborhood, we often look for things we recognize to figure out where we are. For example, seeing a statue we recognize in a town square, a familiar gas station, or the intersection of a highway evokes a strong sense of familiarity and orientation, and even comfort if we are lost. In this sense, these objects have importance beyond simply being items that we know and with which we have experience: they have the potential to provide us with information about our location, even if we have never visited them before. For example, if we see the Taj Mahal in front of us, we know we must be in Agra, India. In this way, landmarks form a critical component of our ability to know where we are in space (see figure 8.2).

The third core component of the Aguirre and D'Esposito taxonomy involves brain areas devoted to representing spatial landmarks. It is important to note that this type of representation is different from representations for other types of objects, like animals or tools. Indeed, decades of research in cognitive psychology have revealed the privileged status of a number of different stimuli in terms of their underlying brain representations, which we will discuss shortly. What is important about the landmark "module" in the brain is that it provides a means for detecting navigationally relevant stimuli from which to derive location as opposed to simply classifying a building as a grocery store versus a gas station.

Pioneering studies prior to the Aguirre and D'Esposito taxonomy helped establish that objects like faces and tools have a privileged representation in the brain, paving the way for landmarks to potentially have their own area of representation (Desimone et al. 1984). Subsequent fMRI work helped establish that there are a number of different cortical areas sensitive to different types of objects. For example, a part of the fusiform gyrus, termed the *fusiform face area*, shows particularly robust responses to faces compared to other objects and scrambled faces (Kanwisher, McDermott, and Chun 1997). Indeed, faces seemed to be defined by the spatial configuration of the features that make up a face—the nose, the eyes, and mouth—as scrambled faces do not activate this area. While some have argued that faces are a more general example of object expertise (Tarr and Gauthier 2000), since we likely have more experience with faces than any other objects, the fact that a specific brain area is highly selective for faces also likely reflects the potential evolutionary value of this type of representation. Overall, such findings suggest that different cortical areas are more heavily dedicated to processing some types of stimuli than others, arguing for the idea that something as basic as object identity receives a high degree of emphasis in terms of cortical representations.

Like faces, recognizing landmarks also confers a potential evolutionary advantage, thus granting a privileged status to landmarks in terms of their representation in the brain. In one experiment that helped establish the privileged status of landmarks in the brain, Aguirre et al. showed images like buildings, faces, cars, and other objects to participants while they underwent fMRI. Aguirre et al. identified an area in the right lingual gyrus (part of the inferior temporal lobe bordering the parahippocampal cortex) that responded selectively to buildings as opposed to other stimuli like faces and objects (Aguirre, Zarahn, and D'Esposito 1998). A similar discovery was made by Epstein and colleagues, who assigned the region the colloquial term *parahippocampal place area*, or PPA (Epstein et al. 1998). In their experiment, Epstein and colleagues showed that the parahippocampal cortex responds to buildings, landmarks, scenes, and even empty rooms. These findings mirrored what had been shown in other parts of the cortex like the fusiform gyrus for faces. Together, these studies established the idea that buildings have a specialized form of representation within the lingual gyrus part of the "what" pathway.

As we discussed in chapter 2, however, fMRI cannot establish whether a brain area is necessary for a function such as identifying landmarks. In this way, studying patients with selective lesions to the lingual gyrus is extremely helpful. A study by Landis et al. investigated patients who showed a peculiar pattern of *landmark agnosia*, which means loss of knowledge about landmarks when presented visually (Landis et al. 1986). The patients generally had intact memory and other cognitive functions, like the ability to recognize other objects, and they could describe the location of the landmark when provided with the landmark's name. Some of the sixteen patients did have trouble recognizing faces, although this finding is consistent with the idea that many lesions that affect the lingual gyrus are large enough to affect neighboring fusiform gyrus. The following is a description of the specific deficit in recognizing landmarks experienced by one patient in the Landis et al. study:

> On several occasions, his sister found him walking up and down the street looking for their apartment. He stated that he could "logically" figure out the correct building but could not recognize it. What he did recognize were the small, distinctive features such as the garage, mailbox, and doorway. On more distant trips, he often ended up on the wrong side of town and had to call his sister to fetch him (Landis et al. 1986, 133).

There are several important pieces to note in this patient description. In particular, the patient was able to figure out where a building might be "logically," which indicates he could infer its position based on its distance and direction from other locations he was able to surmise. He could even recognize a landmark based on the pieces or components that made it up, such as the doorway. However, when looking at a landmark on its own, he was unable to recognize it as a whole in terms of its value in placing his location. Thus, these findings suggest that this specific module within the inferior temporal cortex is also necessary for the ability to recognize landmarks as topologically relevant to navigation. (For another detailed description of a patient with landmark agnosia, see Incisa della Rocchetta, Cipolotti, and Warrington 1996.)

## Medial Temporal Lobe and Spatial Position

The final part of the Aguirre and D'Esposito taxonomy involves the medial temporal lobe and new topographic information (see figure 8.2). As we have also pointed out in chapter 3, numerous rodent studies suggest that the hippocampus is the principal locus of the cognitive map. As we discussed in detail in chapters 3 and 4, extracellular recording studies in humans, rats, and monkeys all suggest that the hippocampus contains cells that provide a code for spatial position, albeit with some important differences related to visual input. Following damage to the medial temporal lobes, despite the evidence that place cells are active in both familiar and novel environments, navigational deficit often appears selective to novel environments (Teng and Squire 1999; Rosenbaum et al. 2000). Consistent with this idea, Aguirre and D'Esposito focused on the role of the hippocampus and surrounding parahippocampal cortex in coding new topographic information, which they termed *anterograde disorientation*.

One particularly vivid description of a route from patient E.P., who had extensive damage bilaterally to his medial temporal lobes, as well as dense amnesia, is useful for illustrating selective impairments in novel environments, an issue we will return to in more detail in chapter 9. Note that his descriptions of Hayward, California, come from where he was born, and thus are highly familiar, while those from San Diego come from where he currently resides, and thus are relatively "novel":

> Experimenter: How about your house on Castro Valley Boulevard to the Hayward Theater. [Can you] remember where the Hayward Theater is?
> E.P.: Yes. I leave the house, turn to the right to A Street. Down A Street to Castro Boulevard, then turn to the left and it's in the middle of the block. Hayward . . .
> Experimenter: And if you didn't go down A Street. If you instead took another street, what would you do?
> E.P.: Redwood Road, Redwood Road would run right into it.
> Experimenter: The last thing I want to talk to you about is the neighborhood that we're in now.
> E.P.: Here.
> Experimenter: How about any of the streets around here? Can you tell me any of the street names in the neighborhood here?
> E.P.: No, I cannot. I cannot.

It is fairly clear from these descriptions that patient E.P. had no problem remembering buildings, routes, and positions from his childhood in Hayward, California. However, he had complete amnesia for his current neighborhood in San Diego. Consistent with this idea, Aguirre and D'Esposito proposed that damage to the medial temporal lobes specifically affects the ability to form *new* topographical representations. Thus, it may be that other brain regions can maintain codes for spatial position but the medial temporal lobe specifically is needed for formation of new topographic position codes.

## Evaluation and Critique of the Aguirre and D'Esposito Taxonomy

More recent models of human spatial navigation and other theoretical considerations have challenged some aspects of the Aguirre and D'Esposito model. One issue that was given limited consideration in the original taxonomy regards the degree of familiarity and exposure to an environment. While Aguirre and D'Esposito acknowledged the importance of novelty to the medial temporal lobes, they did not deal with this issue in much detail and did not specify the "age" of a navigational experience required to depend on the medial temporal lobes (Moscovitch et al. 2005). Even for highly familiar environments, it is unclear whether any aspect of retrieval of spatial memories learned in the remote past must rely on egocentric reference frames at all, as this might imply a re-creation of the same body-centered coordinates in which landmarks were initially encoded (Burgess et al. 2001). Thus, the novel/familiarity dichotomy challenges aspects of the Aguirre and D'Esposito taxonomy by pointing out that not all memories are treated identically in the brain as a whole, an issue we consider in more depth in chapter 9.

Another perspective on the function of these brain regions, which partially overlaps with the Aguirre and D'Esposito taxonomy, is that they support the processing of spatial and visual-perceptual properties of environments within an allocentric (map-like) coordinate system, the integration of allocentric and egocentric reference frames, and the translation of one to the other (Byrne, Becker, and Burgess 2007). The BBB model, which we have discussed in chapter 2, argues that parietal cortex handles egocentric representation, retrosplenial cortex egocentric-to-allocentric translation, and hippocampus allocentric representation. In particular, this perspective offers a more computationally based way of approaching these functions by offering a quantitative framework for each of these coordinate representations. The BBB model, though, suffers from some of the same limitations with familiarity/novelty.

Another angle that we might consider as a limitation with the Aguirre and D'Esposito model is the assignment of one cognitive function to one brain region, as we discussed at the beginning of this chapter. Let's consider our earlier points of how we might isolate the unique cognitive processes involved in navigation. Let's say we compare freely navigating a large maze in virtual reality with being guided through the environment, as was done in one of the first fMRI experiments on spatial navigation (Aguirre et al. 1996). As it turns out, there are in fact other important differences between these tasks that we may not have realized, which are unrelated to simply freely finding one's way.

For example, wayfinding is more difficult than following arrows. Could activation relate simply to the difficulty of the task? Free navigation is likely to involve a greater variety of visual input since we can explore more areas than we would by simply following arrows. Could this be a difference? Even seeing arrows versus not could influence activation patterns. Thus, isolating unique brain structures, or even cognitive processes, may not be as straightforward as it might seem. Another view expressed earlier is that while there are multiple areas of the brain involved in spatial navigation, with each brain structure performing its own unique contribution that results from computations performed in that brain structure, they nonetheless all act in concert with one another to generate resulting behavior. Thus, the extent to which unique brain areas contribute to navigation versus a broad network of interacting brain areas is debatable.

When considering interactions between brain structures, one can also argue that it is improbable that a brain region, in the context of the neural network in which it operates, is devoted to a single cognitive domain (for example, Eichenbaum and Cohen 2014) . For example, simply because we see the hippocampus or parahippocampal cortex active during spatial navigation does not mean that it is involved only in spatial navigation. Other parts of our bodies, such as our arms or legs, are so useful for a variety of behaviors that it would be strange for them to be involved in only one type of behavior. While our legs may indeed be most helpful when we are walking, there are many other tasks that we use them for, including jumping, standing, and balancing when sitting. In a similar way, simply because a brain region is involved in one set of functions in no way precludes it from also being important for other functions.

## The Brain as an Interconnected Network

We have discussed so far the idea that different brain regions serve different cognitive functions, like representing a landmark, and that the hippocampus may be uniquely positioned to integrate this information. Is it possible, though, that no one single brain region serves as the primary neural underpinning for what manifests in behavior as allocentric or egocentric navigation or even memory more generally, and instead, that these functions are distributed throughout multiple brain regions? This argument essentially involves the idea that (some) higher cognitive functions cannot readily be decomposed into the contributions of a single brain region and rather that their function is distributed across multiple brain areas in a way that does not map "cleanly" onto behavior. This perspective also aligns with the ideas from computational biology we discussed earlier suggesting the importance of distributed coding to behavior.

Thus, it might be that employing an allocentric or egocentric strategy to solve a task recruits a network of different brain regions, with no single process or brain region contributing a unique, separable process (figure 8.3). This account would still allow for the idea that lesions to brain "hubs"—highly connected, interacting brain structures—would disrupt allocentric or egocentric navigation. In this particular network, we refer to the hippocampus, retrosplenial cortex, posterior

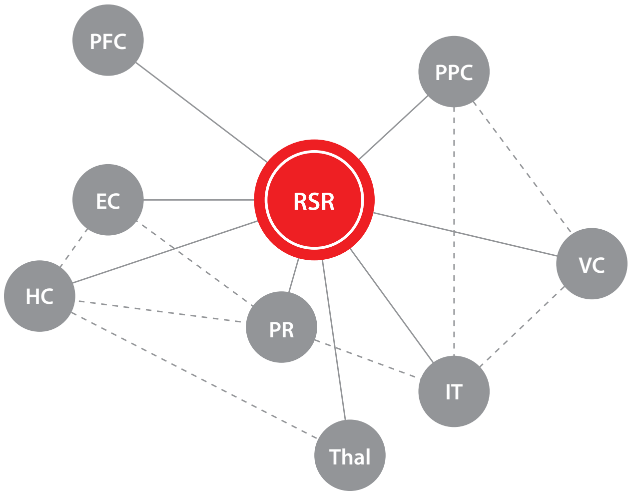


**FIGURE 8.3.** A network-based model for human spatial navigation. The model emphasizes interactions between brain regions rather than purely local computations. PFC = prefrontal cortex, RSR = retrosplenial region, EC = entorhinal cortex, PR = parahippocampal region, IT = inferotemporal cortex, Thal = thalamus, VC = visual cortex, HC = hippocampus. Allocentric and egocentric representations involve information processing centered on different hubs yet still involve largely overlapping brain regions. Reproduced from Ekstrom et al. 2017.

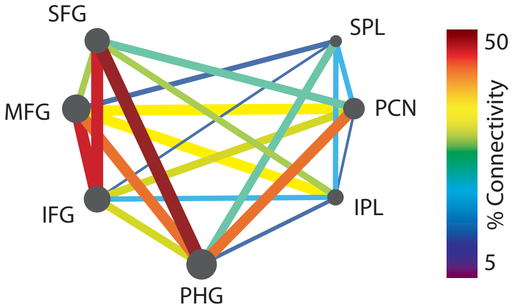
parietal cortex, prefrontal cortex, and parahippocampus cortex as such "hubs," although these will differ depending on the type of navigation (for example, egocentric, in which we might expect that the posterior parietal cortex would serve as more of a hub and the hippocampus as less of one). This account would not require, though, that a single brain region is exclusively necessary for all forms of tasks involving allocentric or egocentric navigation. In this way, we can account for the fact that damage to multiple brain regions could impair our ability to remember topographic details, particularly spatial position, and no one brain region is the only one required for these critical aspects of navigation (Ekstrom, Arnold, and Iaria 2014; see also Chrastil 2012).

For example, it is possible to consider the functions of a system along a spectrum, with one end representing *aggregate* (that is, unique additive) functions and the other representing *emergent* (that is, nondecomposable) functions. Along with other attempts to explain cognitive processes in terms of complex systems theory (Bassett and Gazzaniga 2011), an allocentric or egocentric representation might best be thought of as sitting in the middle of this spectrum and is an example of a complex neurocognitive process that is decomposable into dynamical network properties but also nonadditive in nature. As argued by Bassett and Gazzaniga (2011), attributing single cognitive functions to separate brain regions and aggregating them together may underestimate the dynamical processes at play in the brain. A nonadditive model would involve integration of processes across spatially and temporally distributed brain networks, which could better capture precisely how the emergence of an allocentric or egocentric representation during behavior is coupled to neural processes. According to the nonadditive account, then, no single brain region contributes to either egocentric or allocentric representation independently, and thus an allocentric representation is a nonadditive, dynamic property generated through interactions between multiple brain regions.

The basic idea of the model, as shown in figure 8.3, is that the areas we have already discussed—retrosplenial cortex, posterior parietal cortex, hippocampus, posterior parahippocampal gyrus, and dorsal prefrontal cortex—function as a coherent network during navigation (Ekstrom, Arnold, and Iaria 2014; Ekstrom, Huffman, and Starrett 2017). The computations underlying navigation, such as allocentric versus egocentric representation, involve small switches in the interactions of groups of neurons within each of these different brain regions. Consistent with the idea of distributed coding discussed earlier, groups of neurons fire at different time points while a subject navigates, in a way that is spread somewhat evenly across different brain regions in terms of the computations performed. While the hippocampus may be more active for coding location, and retrosplenial cortex more active when coding facing direction, in line with the Aguirre and D'Esposito model, these computations are also partially redundant across different brain regions. Importantly, the allocentric or egocentric representations emerge from the shared computations and interactions across these different brain regions.

Studies by Watrous et al. (2013) and Schedlbauer et al. (2013) provide some support for the idea of nonadditive computations being important to remembering spatial position. These studies used a method termed *functional connectivity*, measured with oscillatory coherence, fMRI, and graph theory, to characterize network

**FIGURE 8.4.** Evidence for network-based computations. SFG, MFG, and IFG are parts of prefrontal cortex; SPL and IPL are parts of parietal cortex; PCN is the precuneus, which includes retrosplenial cortex; and PHG refers to an electrode in parahippocampal gyrus capturing medial temporal lobe signals. Reproduced from Watrous et al. 2015.



dynamics during retrieval of spatial information about the relative distance between environmental landmarks. Watrous et al. (2013) found that frequency-specific (1–4 Hz) increases in pairwise phase consistency correlated with retrieval accuracy within a network distributed across the PFC, MTL, and parietal cortex (figure 8.4). In a separate study using fMRI, Schedlbauer et al. (2014) showed that greater connectivity to multiple brain "hubs" including the hippocampus correlated with overall better participant spatiotemporal memory. Together, these findings suggested that the integrative dynamics of the spatially distributed network, rather than the activity of a single region alone, was critical for accurate recall.

In another study, the capacity of a similarly distributed network to integrate information was compared against accuracy in using allocentric information to orient within a virtual city (Arnold et al. 2014). The authors found that the global efficiency (that is, a graph theoretical index of integrative capacity; see Bullmore and Sporns 2009) was highly predictive of accurate orientation and that some regions previously associated with allocentric orientation (for example, hippocampus) were more central within the networks of accurate participants. This suggests that the topological composition of functional networks may constrain the degree to which separate brain regions exhibit coherence and integrate information during memory tasks. Considered together, these findings support the perspective that the degree to which a spatially distributed memory network is able to rapidly exchange information is critical for the effectiveness of its functional output. Importantly, each of these studies identified regions, such as the MTL, that showed increased centrality within the memory network correlating with accurate recall. Thus, owing to its centrality within the network of brain areas important to spatial navigation, the MTL specifically may often be identified in fMRI studies attempting to localize brain activity during navigation tasks.

The idea that multiple regions of the brain may interact during spatial representation, with no one area contributing exclusively to allocentric representation, offers a partial reconciliation for contradictory findings attempting to localize egocentric and allocentric representations to a specific brain region. In the case of egocentric and allocentric representations, a navigational system in the brain that can dually process both types of representations could theoretically adjust its topological configuration to emphasize processing occurring in preserved cortical regions through increasing their centrality within the functional network active during navigation. This, in turn, might explain why many navigational situations typically involve a dynamic interplay between egocentric and allocentric representations (Byrne, Becker, and Burgess 2007; Zhang, Zherdeva, and Ekstrom 2014; Wang 2017) rather than the exclusive presence of one or the other. Note that while the hippocampus is an important "hub" or area of significant interactions, other areas outside the hippocampus, like the parahippocampal, retrosplenial, posterior parietal, and prefrontal cortex, also contribute significantly.

Another attractive aspect of this explanation is that it helps account for some of the varied findings regarding navigational impairments and brain lesions. In one large study of patients with lesions in multiple brain areas (127 patients total), the authors investigated memory for routes in a large hospital (Barrash et al. 2000). Each patient was led along a 1/3-mile path within a hospital and then led by a different route back to the start location. The patient's job was to retrace the route they just took. Since patients had a variety of different lesions, the authors could compare them not just on their route-following ability but also on a number of different neuropsychological tests. What the authors found was that patients who showed navigational impairments, which was the tendency to make mistakes when retracing the route, had lesions in the medial occipital lobe, parietal lobe (superior parietal lobule and intraparietal sulcus), medial temporal lobes, and/or inferior temporal gyrus (lingual gyrus). The fact that a network of different brain areas impaired something as basic as route learning suggests these multiple areas likely work in concert during navigation rather than as single, modular areas with discrete functions.

Another line of evidence that supports the idea that interacting networks of brain areas may be a better way to understand the neural basis of navigation comes from an interesting example of individuals with developmental topographical disorientation (DTD), discussed in chapter 7. These are individuals, described in detail by Giuseppe Iaria, who have had a lifetime of difficulty navigating and finding their way about but otherwise are cognitively healthy (Iaria and Barton 2010; Iaria et al. 2014). These individuals allow us to ask the question in a slightly different way: If we take otherwise healthy people who report being extremely poor navigators, what types of brain abnormalities, if any, do they have? It turns out that the only consistent pattern of damage in these patients is white matter tracts connecting the medial temporal lobe to the prefrontal cortex. Intriguingly, they had no damage to actual brain structures like the hippocampus. These findings support the idea that connectivity patterns and interactions between structures, rather than activity in specific brain areas alone, are critical components to successful navigation.

One additional possibility is that specific parts of the hippocampus play roles in the fidelity of the spatial representation (Xu et al. 2010; Poppenk and Moscovitch 2011). The anterior hippocampus could contain coarser, more general codes for space (like "I am in room A"), while the posterior hippocampus may contain more precise, metric codes for space ("I am three meters northwest of the bottom corner of the room"). According to this framework, then, interactions with posterior hippocampus might be particularly important for encoding and retrieving high-resolution spatial information, while those with anterior hippocampus might be more involved in coarse spatial information. Importantly, the posterior hippocampus shows overall greater connectivity with areas like the parahippocampal cortex, retrosplenial cortex, and parietal cortex, while the anterior hippocampus shows higher degrees of connectivity with the perirhinal cortex and prefrontal cortex. These connectivity patterns are thus also consistent with the idea that the posterior hippocampus is a highly connected hub when it comes to processing detailed, high-resolution spatial information, as compared to the anterior hippocampus. While critical components of this idea remain to be tested in the context of navigation, the idea that the anterior and posterior hippocampus, in conjunction with other cortical areas, code specific aspects of navigation is gaining increasing acceptance in the field.

## Networks versus Modules: Two Extremes of an Argument?

We have discussed essentially two different models at the extreme ends of a spectrum (figure 8.5). One, the Aguirre and D'Esposito model, assumes that specific brain regions are dedicated, largely independently, to different aspects of navigation. This idea can be termed loosely *specificity coding*. For example, the parietal cortex serves egocentric navigation, and the medial temporal lobe underlies novel topographic representation. This model depends on two critical assumptions: that we can isolate different aspects of navigation in our behavioral paradigms and that specific brain regions serve clear, isolatable functions. A strength of the model is that it helps integrate decades of work in both humans and rats by suggesting that the parietal cortex serves egocentric representation, the medial temporal lobe new topographic information, the retrosplenial cortex heading information, and the lingual gyrus landmark representation. This model also nicely ties together much of what we have discussed in chapters 3 to 6 regarding the hippocampus.

On the other end of the spectrum, we have discussed the idea of distributed processing of navigation within a network of brain regions, the exact function of which varies. The strength of this model is that it helps explain data suggesting that the allocentric and egocentric representation do not map onto a single brain region and that lesions to the hippocampus do not impair all forms of allocentric navigation (discussed in chapters 3 and 6). It also incorporates findings from developmental topographical disorientation (DTD) patients and other work that focuses on interactions between brain regions rather than isolated processing within distinct brain areas. Last, it helps explain why we typically don't observe process-pure computations during navigation and that navigation, in itself, is a flexible and dynamic process.

While we do not claim to have all the answers in this book, the truth regarding the neural basis of human spatial navigation likely lies in between. As discussed in chapter 1, we have known for almost a century that brain lesions rarely impact a single brain region or cognitive function, and in this way, the brain appears to function in a nonadditive fashion (Finger et al. 2004). At the same time, we also have

**FIGURE 8.5.** A spectrum of models for navigation.

copious evidence, largely from the double dissociation technique, that specific brain lesions can result in damage to specific cognitive functions, topics we have discussed throughout this book. In this way, the brain clearly functions in an additive fashion. Thus, it seems that the most accurate model will have a little bit of both elements to it. In other words, there exists some degree of unique functions in a brain region and some functions that are shared and distributed across brain regions. The frontiers for understanding the neural basis of human spatial navigation thus remain to be explored and elucidated.

## Summary

The neural underpinning of human spatial navigation remains an active area of investigation. The Aguirre and D'Esposito taxonomy for spatial navigation, probably one of the more widely accepted in the field, focuses on the idea that specific brain regions contribute to specific aspects of navigation. Yet this model also has significant limitations, including how it handles the degree of familiarity a person has with an environment and that distilling navigation to four fundamental components may miss many of the nuances and integrative tendencies of navigation-related behavior in the first place. Network conceptualizations, where no one brain region contributes uniquely to navigation (the sum is greater than the parts), offer an important alternative and are gaining increasing support in the navigation literature. We suspect that overall the truth is somewhere between, with our ability to understand the neural basis of human spatial navigation increasing as we conduct more sophisticated experiments controlling for specific variables during navigation, such as memory, and our experimental and computational tools improve.

## CHAPTER 9

# NAVIGATION AND MEMORY

Throughout life, our brain changes as we encounter new places, learn from the world, and age. One of the many things that changes over time is the memory demands on different brain circuits to support navigation. The hippocampus is widely regarded as playing an important role in spatial memory, as has been emphasized up to now. However, the hippocampus is perhaps even better known for its role in learning and memory, as first discussed in chapter 1 and returned to throughout this book. Clearly, navigation and memory have an intricate relationship and interplay, and thus considering navigation from a memory perspective is also extremely important in understanding its neural underpinnings.

As we discussed in chapter 3, there is little debate that the rodent hippocampus is necessary for new allocentric spatial navigation (Olton, Becker, and Handelmann 1979; Morris et al. 1982). As we also discussed, in chapters 3, 4, and 8, the role of the human hippocampus in spatial navigation is more variable and less agreed upon (Bohbot et al. 1998; Rosenbaum et al. 2000; Spiers et al. 2001; Kolarik et al. 2016). One possibility that we discussed in detail in chapters 3 and 4 is that rats and humans are simply different in many ways with regard to navigation. Alternatively, as we introduced in chapter 8, and likely not exclusively, it could also be that the human hippocampus plays a temporary role in memory for novel, coarse-grained information and a more permanent, long-term role in memory for contextual details. Thus, this second account, which we elaborate on in this chapter, reconceptualizes our understanding of navigation, and the hippocampus more specifically, from the perspective of human memory rather than navigation alone.

### Navigation: The Memory Perspective

The emerging picture from decades of work in human memory suggests the possibility that the role of the hippocampus in acquiring new spatial memories is simply an instance of its more general role in acquiring all sorts of memories that are explicit or "declarative" in nature (Eichenbaum and Cohen 2014). In other words, the role of the hippocampus is not general to memory but specific to events or objects that we encountered in the *recent* past that we can consciously recognize or recall in memory. We highlight *recent* because other types of declarative memories—at least those that are semantic (relating to facts)—seem to become independent of the hippocampus with the passage of time, when they are considered *remote* (very old) memories.

As we have argued throughout this book, particularly in chapters 3 and 4, the exact role of the human hippocampus in navigation remains unclear. While the hippocampus itself is not the focus of our book, if it is true that the hippocampus is not specialized for allocentric navigation, but rather for detailed memories, then we would also expect to find a time-limited role for the hippocampus in representing remote memories for navigating environments that were encountered in the distant past, which, over time, lack comparative detail. However, the majority of our focus in human spatial navigation, and our discussion so far in this book, has been on how we navigate relatively newly acquired spatial environments. Recent research involving techniques specific to understanding remote spatial knowledge, such as places we navigated when we were children, is beginning to shed new light on an important difference in spatial memories based on the age at which they were acquired.

It may come as a surprise that remote spatial memory is understudied when one considers that navigation most often takes place in well-known environments experienced over many years. Indeed, most of our waking life is spent traveling from home to school or to work and back again, with social events taking place along the way at local parks, friends' houses, or coffee shops. When venturing to a new location by car, it is often necessary to first travel through familiar territory, which could anchor learning of the novel environment. Similarly, we navigate the hallways of familiar houses and buildings on a daily basis, quickly adapting to a new painting, a rug, and even a major renovation. Thus, familiarity would appear to form a core component of almost any daily navigational experience.

One reason that this area of research had received less attention is that it is difficult to investigate memories that were formed long ago—in some cases, decades ago. Studies of new spatial learning can be assessed with artificial mazes in real-world and virtual reality (VR) environments or with tabletop tests—literally small-size tasks that can fit atop a table, such as memorizing the positions of an array of objects and then later recalling them after the objects have been removed (see chapter 2). By contrast, studies of remote spatial memory require long-term exposure to spatial stimuli, ideally based on naturalistic, large-scale environments that were navigated extensively over decades. Because of the necessary passage of time, remote memories of large-scale environments are therefore difficult to access and verify. Even if verifiable, the stimuli with which to test participants are not always available in their original form if the environment had changed drastically over the years. The environment itself may be idiosyncratic to the participant being tested, which is problematic given that rural and urban neighborhoods and downtown designs vary considerably from one city to another. Take, for instance, the relatively organized, grid-like structure of much of New York City versus the intricate twists and turns of Venice, Italy, a kind of archipelago divided by canals and joined by bridges that could lead even a return visitor astray. Differences in environments are compounded by difficulties recruiting adequate control participants who have similar experiences with the same environment.

Despite differences in navigational experiences and the environments in which they occur, research has revealed a common set of properties of urban environments that may be extracted to examine both recent and remote spatial memory representations, and a common set of brain regions that support these representations. We will first discuss the interdependence of spatial memory and other forms of remote memory, touching on some theoretical and methodological approaches discussed in chapter 2 that have been adapted from the fields of geography and environmental cognition to assess their integrity. We will then turn to a discussion of which aspects of remote spatial memory are supported by the hippocampus versus other regions of the *spatial memory network* discussed in chapter 8. We will end by discussing whether the role played by the hippocampus in remote spatial memory resembles its role in supporting other memory and nonmemory functions.

## Navigation in the Context of Multiple Memory Systems

It is difficult to take memory out of any form of navigation. When you navigate, it is important to be able to conjure up some kind of representation of where you think you are and where you are going. We often refer to your memory for your surroundings as your current *context* and memory for where you are heading as your *goal* (see chapter 5). Without any contextual and goal memory, you would be completely disoriented in any environment. At the same time, as discussed in chapter 1, memory is not the only thing we need when we navigate. We need information about how far away we are from a landmark, which we can estimate simply by looking at the landmark if it is visible. Similarly, to navigate our surrounding environment, we need some information about the direction and distance of obstacles and landmarks in front of us, which in many ways is a perceptual problem. Thus, while memory is clearly critical to successful navigation, it is not the only component either, and as discussed throughout this book, navigation is a multisensory process involving multiple cognitive components.

When considering the role of memory in navigation, it is particularly important to consider the level of familiarity with a spatial environment, a topic we tend to overlook when we consider navigation. For example, we discussed cognitive map theory extensively, as well as other theories specific to human spatial navigation, in chapters 3 and 8. Yet, as we will explore in more detail, these theories do not consider the age of a memory specifically. This is something that several, more geographically inspired models do consider, as we will discuss shortly, and numerous studies in human memory suggest the fundamental importance of the age of a memory when determining what brain structure might be involved.

In particular, one influential view, known as the *multiple memory systems perspective*, an idea we touched on in chapters 2 to 6, takes the age of a memory into detailed consideration. Specifically, the memory systems view postulates that there are many different forms of memory that can exist in parallel in the brain. As just one example, consider how different it is to ride a bike compared to remembering what you had for dinner last night. With sufficient practice, it is quite easy to ride a bike, and it is not something you really ever forget once you've learned how to do it. Describing verbally how you might do so, though, is quite different! In contrast, remembering what you had for dinner last night is something we typically describe verbally, and not something we would "show by doing," but it is also a memory that is likely to fade after a short time. These examples illustrate two very different forms of memory, *procedural memory* and *declarative memory*, with very different properties (Tulving 1987; Squire, Stark, and Clark 2004).

Work with patients with focal lesions to their brain supports a similar perspective. We discussed the patient H.M. in detail in chapter 1 and again in chapter 6 as an example of a patient with extensive amnesia owing to damage to his medial temporal lobes, with subsequent work revealing that many forms of memory nonetheless remained intact in H.M., including his procedural memory and learning. Studies of H.M. have been followed by countless studies of other patients with damage to their medial temporal lobes, like K.C. and E.P. (described shortly), all of which support the idea that this structure stores or processes important aspects of declarative memories. As discussed in chapter 4, another important distinction is between episodic and semantic forms of memory (Tulving 2002). Briefly, *episodic memory* involves specific details related to a personal event, including its spatial and temporal context, and a subjective element of reexperiencing it in memory. In contrast, *semantic memory* involves facts about the world, familiar memories with little need to remember the specifics of where, how, and when we learned this information. Patient studies also support this distinction, which we will discuss in more detail shortly.

Navigation often involves a high degree of familiarity, particularly everyday navigation. As Tulving argued originally, however, these forms of memory may often be semantic in that we don't need to remember a specific instance of an event, but instead we need to know general properties of an environment to navigate within it. For example, when navigating we may often need to know that two streets connect up at a later point if we walk north. However, we don't need to remember the last time we walked that route to remember where the two roads intersect; instead, we may just "know" or consider it a "fact" that the two roads intersect two-thirds of the way to our destination. In this way, many aspects of navigation involve use of semantic, rather than episodic, forms of memory.

One issue raised by semantic versus episodic memories in the context of navigation is the role of fact-based knowledge versus detailed memory for routes we have taken before. Recall in chapter 3 that we discussed the *cognitive map theory*, which is based on the discovery of place cells and has as a core postulate the idea that the hippocampus is needed for all forms of allocentric spatial memory. An issue here is that if the hippocampus is not needed for all forms of memory, particularly semantic memories, then the exact nature of hippocampal engagement when we navigate must be reconsidered.

In a similar vein, we often use semantic memories when we recall information from our distant past, termed *remote memories*. Episodic memories, while certainly possible from our distant past, tend to be blurred, possibly owing to repetition, reencoding, and interference from other memories. Assuming that we often use semantic memory for remembering remote spatial environments, this raises another important issue with regard to cognitive map theory, navigation, and memory: the age of the memory matters. In fact, remote memories, familiarity, and the degree to which a memory may be semantic or not have long been considered, often implicitly, in geographically inspired models of spatial navigation. We consider these models and the issue of familiarity in detail before delving into a more detailed discussion of the importance of memory "age" to navigation.

## Cognitive Maps: An Environmental Cognition and Geographical Perspective

To better understand the importance of familiarity to navigation, it is useful to reconsider some of the cognitive and geographic models of navigation we discussed in chapter 2. In one of the first examples of a *stage model*, Lynch (1960) argued that urban elements were organized into five categories: paths, nodes, landmarks, districts, and edges. According to the Lynch model, for example, the first stage involves memory of isolated points of reference in environmental space, analogous to a type of memory for visual scenes (Lynch 1960). The second stage is identified by the rudimentary organization of routes around the single points of reference. In the third stage, a number of distinct spatial clusters become cognitively integrated. Orientation ability appears in the fourth stage, signaling the development of a more objective reference system. Last, additional routes within the environmental space are coordinated in relation to the system of reference formed in the former stages. The Lynch model thus nicely illustrates the importance of the ordered development of spatial knowledge over time and experience. While different models assume different numbers of stages and components and have been challenged in past work (see chapter 2 for a detailed discussion of this topic, including the Siegel and White 1975 model), importantly, all of these models of human spatial navigation assume that familiarity develops in a stepwise fashion based on experience with the environment in question.

Indeed, several studies have noted the existence of links between the degree of familiarity individuals have with their own urban environments and the characteristics of their cognitive maps. For example, familiarity is thought to be the best predictor of the transformation of landmarks into reference points (Sadalla, Burroughs, and Staplin 1980). As might also be expected, when participants are asked to draw a "sketch map" of an environment, detail and accuracy of the map tend to increase as a function of an increase in the length of residence in the urban vicinity (Moore 1973). For example, a study of sketch maps of a university campus drawn six months apart by new students showed significant increases not only in the amount of information but also in the integration of that information (Schouela et al. 1980).

Think about a recent trip that you took to a country that you had never visited before. You may have experienced what many other people experience: the trip from home to the unfamiliar location feels much farther than the return trip home. It turns out that people are actually more accurate in estimating time of arrival to unfamiliar destinations, but they underestimate the time of arrival to familiar ones (Jafarpour and Spiers 2017). Interestingly, familiarity seems to have the opposite effect on representations of distance: there is a tendency to overestimate the size of familiar areas (Milgram and Jodelet 1976; Jafarpour and Spiers 2017).

How might we go about assessing the level and accuracy of familiarity with an environment with a metric that can capture all of the important stages of spatial knowledge acquisition? The most widely used procedure for the empirical study of spatial cognition, popularized by Lynch (1960), involves reproducing the configuration of spatial elements of a specific environmental setting in a sketch map (see chapter 2). This method is advantageous in that it assesses the most *advanced* stage of allocentric processing, but it is also possible to achieve accurate task performance by taking a route-based perspective, what can be considered *earlier stages* of learning. Note again that a common thread in all of these experiments is the progression of different types of knowledge of an environment based on familiarity with its features, with sketch maps being a means of integrating all of these different levels into a common metric.

## Role of the Hippocampus in Remote Memory

While geographic and environmental psychology models of navigation have long since recognized the possibility of stages of processing and familiarity in spatial knowledge, how this scheme maps onto the hippocampus is less clear. Before turning to results involving the brain regions supporting spatial memories formed long ago and whether they correspond to those supporting spatial memories learned recently, it is important to consider cognitive map theory in the context of recent versus remote spatial memory. We have considered cognitive map theory in detail throughout this book but have yet to consider it in the context of environmental familiarity.

As the reader may recall, to account for findings of place cells in the hippocampus of rats freely navigating a newly learned maze, O'Keefe and Nadel (1978) postulated that the hippocampus supports the formation of a *cognitive map*, which contains allocentric spatial representations (flexible, viewer-independent knowledge of spatial relations among landmarks) of an environment (O'Keefe and Nadel 1978). In extending the cognitive map theory to humans, they offered that allocentric spatial representations may provide the context in which episodic memories unfold. However, the original version of the theory did not distinguish between recently and remotely formed cognitive maps and, by extension in humans, episodic memories. The assumed prediction is that both forms of memory should always depend on hippocampal function and that hippocampal damage would lead to impaired spatial and episodic memory, regardless of when the memory was first formed.

Another influential theory of hippocampal function, which derives primarily from consideration of human memory, is known as *standard consolidation theory* (Squire 1984; Alvarez and Squire 1994). In contrast to cognitive map theory, standard consolidation theory explicitly considers the age of a memory and makes different predictions about the role of the hippocampus in spatial memory and declarative memory in general. The standard consolidation theory posits that any type of declarative memory, whether it is episodic, semantic, or spatial in nature, initially relies on the hippocampus for its storage and retrieval. However, with the passage of time, presumably as the memory gradually becomes established within the neocortex, the hippocampus is no longer required for representing declarative memory. We find support for the consolidation view in observations of individuals with hippocampal damage. These individuals are unable to form new declarative memories for information to which they were exposed *after* the time of their lesion, called *anterograde amnesia*. These individuals also seem to have lost declarative memories that were formed *before* the time of their lesion, called *retrograde amnesia*.

Crucial to standard consolidation theory, not all prelesion memories are lost: those that were formed within the few years prior to the lesion—in the recent past—seem to be compromised, but those that were formed many years prior to the lesion—in the remote past—remain relatively intact. If you've ever encountered individuals with Alzheimer's disease, you may have witnessed them failing to recognize their own grandchildren despite their seeming ability to reminisce about a trip that they took as a teenager. This pattern of impaired recent memory but preserved remote memory represents a *temporal gradient* in retrograde amnesia and has been taken as evidence that remote memories are more likely than recent memories to have had sufficient time to become firmly integrated, or *consolidated*, within neocortex. According to this account, and in contrast to cognitive map theory, remote memories should no longer require the hippocampus for their storage or retrieval (Scoville and Milner 1957; Squire 1992). To summarize, cognitive map theory would predict that the hippocampus would have equal involvement in supporting recent and remote memories, whereas standard consolidation theory would predict that remote memories do not depend on the hippocampus.

## Differences in How Remote and Detailed Spatial Memories Involve the Hippocampus

Do remote spatial memories continue to rely on the hippocampus for the life of the memories as cognitive map theory predicts? Or do the memories gradually become independent of the hippocampus as predicted by standard consolidation theory? Casual observation of people with hippocampal damage navigating in environments that were familiar to them, since long before the time of their lesion, suggests that they have little, if any, difficulty finding their way in old, familiar environments (Milner, Corkin, and Teuber 1968; Corkin 2002). Indeed, more systematic investigation of individuals with compromised hippocampal function, as discussed in chapters 3, 7, and 8, indicate that these individuals can make accurate decisions about spatial relations, particularly within remotely learned environments, such as the locations and identity of landmarks, and the distances and routes between them (Teng and Squire 1999; Rosenbaum et al. 2000).

However, at least some of these individuals appear to have difficulty representing details contained within old environments, such as landmarks and minor roads (Maguire, Nannery, and Spiers 2006), consistent with impairments in their episodic memory. Patients with MTL damage, in some circumstances, can also learn new spatial layouts, although with some evidence of impairments in their spatial precision (Kolarik et al. 2016). These findings, though, pose challenges to both cognitive map theory and standard consolidation theory. Neither would predict intact allocentric spatial knowledge in familiar environments learned long ago yet with some loss of details for both new and familiar environments.

To address this issue in depth, Rosenbaum and colleagues (2000) tested recent and remote spatial memory in an extensively studied amnesic person, K.C., who had major brain damage from a severe closed head injury that nearly obliterated his hippocampi in addition to other brain structures within and beyond his medial temporal lobes. Despite the widespread nature of his brain damage, K.C.'s memory impairment seemed relatively limited, mostly affecting episodic memory; remarkably, other aspects of his memory, including his remote semantic memory, seemed to be largely spared, as were other cognitive capacities (Rosenbaum et al. 2005). As expected based on cognitive map theory, K.C.'s ability to acquire new spatial memories by learning to navigate in new environments was severely impaired, similar to his anterograde amnesia in other domains. To test his remote spatial memory, he was asked to imagine a highly familiar neighborhood where he had lived for many years before his accident, and continued to live afterward. He then answered questions that assessed his representations of distances, directions, and routes between landmarks contained within the neighborhood as well as the identity of those landmarks.

K.C. performed normally on all tests of spatial memory, whether more allocentric or egocentric in nature, including landmark sequencing (the order in which landmarks are encountered on a route). He even found alternative routes between two points when the typical route was blocked, and used "vector mapping" (representing the distance and direction between two points as the crow flies). K.C. also was also able to recognize and identify photographs of major landmarks that are likely used as choice points when navigating. Cognitive map theory, however, would postulate a central role for the hippocampus in all of this processing, particularly his ability to retrieve "maps" of past environments or formulate new shortcuts within existing maps. In this way, the case of K.C. suggested that the age of the spatial memory was fundamentally important to the hippocampus, an issue overlooked by cognitive map theory.

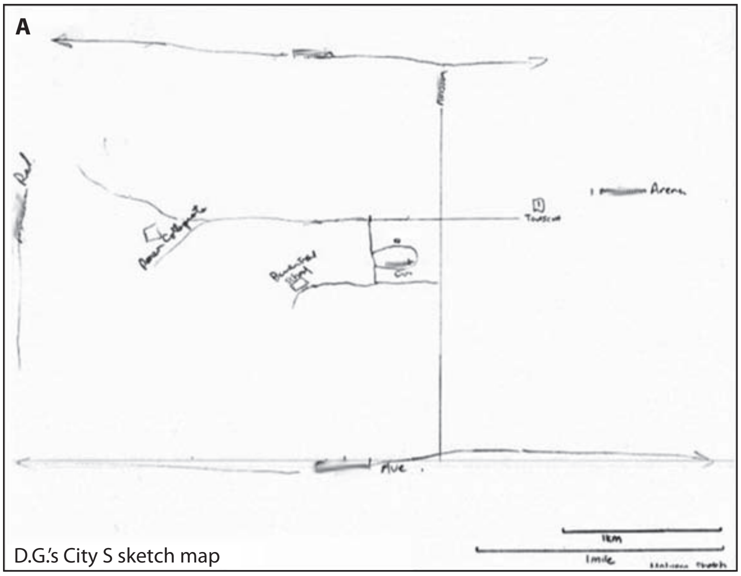
Another amnesic case, E.P., who developed severe amnesia owing to viral encephalitis and was discussed in chapter 7, had been the subject of numerous studies on contributions of the hippocampus and surrounding MTL structures to the consolidation of declarative memories (primarily episodic versus semantic memory). Intact performance on tests of remote spatial memory, some of which resembled the tests used by Rosenbaum et al. (2000), was confirmed in E.P. (Teng and Squire 1999). Similarly, patient S.B., a former taxi driver who was tested after receiving a diagnosis of probable Alzheimer's disease (Rosenbaum et al. 2005), showed similar preservation of remote spatial memory. Unlike K.C., however, S.B. was unable to recognize major landmarks, but this was likely owing to additional damage to higher-order visual cortex specialized for the perception and recognition of spatial layouts (discussed in chapter 8). Overall, these findings suggest that remote spatial memories have different properties than recently learned ones. While these findings present problems for cognitive map theory, they also present issues for the standard model of consolidation. Specifically, the standard consolidation theory does not emphasize distinctions within memory or navigation. Thus, it does not distinguish between episodic and semantic memory, and, as discussed next, not all aspects of spatial memory are, in fact, preserved in the patients discussed earlier.

K.C., S.B., and others showed significant deficits in the details of their spatial memories. For instance, although patient K.C. retained the ability to negotiate his way in his well-learned home neighborhood and drew a sketch map of this neighborhood with the general schematic layout intact, his sketch map contained noticeably fewer landmarks and streets compared to the controls' sketch maps. In addition, K.C. performed poorly compared to controls on a landmark recognition task as a result of his inability to recognize individual houses and landmarks that were salient but unlikely to be critical for navigation (Rosenbaum et al. 2000). Additional findings of impoverished detailed representations are suggested in Maguire and colleagues' (2006) report of the case T.T., the former London taxi driver with bilateral hippocampal damage owing to viral encephalitis described in chapter 7. These studies converge on the idea that hippocampal damage impairs the details of spatial memory but leaves many aspects of these intact in the first place.

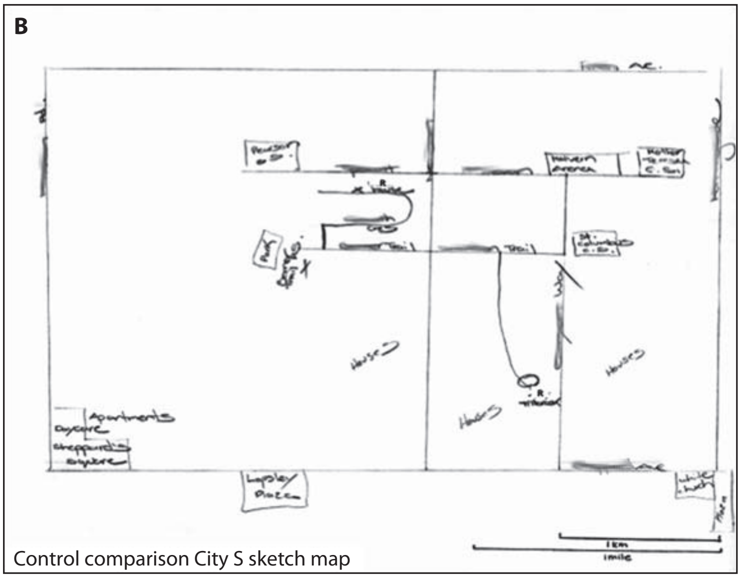
These impoverished representations of large-scale environments resemble the patients' episodic memory impairment, where narratives of personal events lack contextual details that would otherwise enable them to vividly reexperience their past (Rosenbaum et al. 2000; Rosenbaum et al. 2008). Recent research has examined whether finer dissociations might be revealed between impaired and preserved aspects of spatial memory in a way that more closely parallels known dissociations between impaired reexperiencing of events in episodic memory but intact semantic memory for facts. One way to examine this is to assess the degree of visual richness of route descriptions. In a study by Hirshhorn, Newman, and Moscovitch (2011), healthy older adults described routes with and without the requirement to provide vivid descriptions of details along the way. Results suggested that the hippocampus is required for vivid reexperiencing of a route, but not for map-like knowledge of it (for related findings, see Ciaramelli et al. 2010 and Rosenbaum et al. 2012).

To further elucidate the role of the hippocampus in retrieving schematic and detailed representations of familiar environments in a more direct way, Herdman et al. (2015) extended Hirshhorn and colleagues' (2011) route description task to test K.C. and two additional amnesic patients with hippocampal/medial temporal lobe damage and episodic memory impairment (Hirshhorn, Newman, and Moscovitch 2011; Herdman et al. 2015). Performance on the route description task was contrasted with the ability to judge spatial relations and recognize landmarks based on remotely learned environments that had been navigated extensively by amnesic and control participants. The authors found that, like K.C., the two additional hippocampal amnesic patients produced fewer details in sketch maps of well-known neighborhoods, although the general configuration of the sketch maps was found to be intact (see figure 9.1). Moreover, all three amnesic participants generated fewer details (such as landmarks and sensory descriptions of perceptual features along routes) but gave intact directions on how to navigate from the start to the end locations in their verbal descriptions of routes. Even when probed for additional information, the three patients had difficulty describing landmarks. Their descriptions were often vague, whereas control participants would often describe several additional, more detailed, aspects of the probed landmarks, such as color and size.

To compensate for less vivid details within the descriptions, amnesic participants may have relied to a greater extent than controls on spatial references that may be based on schematic representations. By contrast, like K.C., E.P., S.B., and T.T., the amnesic cases provided accurate judgments of distance and direction



D.G.'s City S sketch map



Control comparison City S sketch map

**FIGURE 9.1.** Sample sketch maps of home neighborhood produced by amnesic case D.G. and a control participant familiar with D.G.'s city, showing an intact basic schematic representation of home environments but fewer landmarks and street segments for the amnesic cases compared to controls. From Herdman et al. (2015).

between well-known landmarks on a vector mapping task, which is thought to depend on a context-free allocentric representation of the environment conducive to allocentric spatial representations. Nevertheless, recognition of the visual appearance of landmarks, especially those that might constitute perceptual details that are not essential to navigation, was also compromised in the amnesic participants. The authors concluded that the hippocampus is needed for representing detailed spatial features to enable rich reexperiencing of an environment, but not for schematic representations of spatial relations. The results suggest a role for the hippocampus in representing spatial details contained within cognitive maps, and possible interactions with episodic reexperiencing.

The amnesic cases' difficulties retrieving detailed visual-perceptual representation of space may reflect other, nonmnemonic difficulties experienced by hippocampal/medial temporal lobe amnesics, such as discriminating spatial scenes and binding information into a unified percept (Erez, Lee, and Barense 2013). The results are also consistent with research showing that the hippocampus plays a role in recognition memory specifically when a stimulus must be remembered to occur in a particular place (Barker and Warburton 2011). The landmark recognition task explicitly examined this type of memory, as the experiment asked participants to decide whether each landmark presented could be found in their preexperimentally familiar environment.

## Insights from Studying Rodents

One factor that is difficult to control, and often impossible to verify, in naturalistic studies of remote spatial memory is the encoding episode—when a memory was first formed. Specifically, the circumstances surrounding its formation and the precise contents of the memory, if occurring at a remote time point, may never be possible to reconstruct accurately. One way around this issue is to track the learning experience from the time of first exposure until the memory is presumably well established and remote. This is not generally feasible in humans, because it would likely take years before a memory has reached that level of stability. However, in other species like rats, the process should take no longer than weeks to months. Similar to the idea of "dog years," rats mature at a rapid pace relative to humans, reaching puberty at 6 weeks, which is thus seen as equivalent to 12 to 13 human years.

The idea, then, is to train rats in a maze for several weeks, and once a rat has mastered, and perhaps overlearned, navigation within the maze, the hippocampus is selectively disrupted with very precise chemical lesions. In this way, researchers create a model of retrograde amnesia that is immune to individual differences in lesion size and location that are often seen in amnesic patients (Rosenbaum, Winocur, and Moscovitch 2001; Frankland and Bontempi 2005). While we have discussed some of the caveats regarding differences in human versus rat spatial navigation (see chapter 4), there is no strong reason to think familiarity itself will differ strongly between the species. Thus, it is reasonable to consider these manipulations of familiarity in such rodent models.

Researchers have attempted to study these overlearned memories acquired weeks before, using a variety of mazes and tasks, including the Morris water maze, the radial arm maze, contextual fear conditioning, and a nonspatial socially acquired food preference task, where a rat learns to select one food over another based on the odor within the breath of a "friendly" rat, signaling that the food is safe to eat (Galef, Wigmore, and Kennett 1983; Winocur 1990). However, the results have been mixed, even when comparing studies that use the same task, with a few studies showing the temporal gradient in retrograde amnesia, as seen in human amnesic patients like K.C. and E.P., but more studies typically showing a flat gradient (equally poor recent and remote memory; Mumby et al. 1999). There are several ways to account for discrepancies among animal studies, but one possible explanation for the discrepancy between previous animal studies and human studies is that the environments are not equated in terms of complexity. A neighborhood in which humans live is rich in landmarks, street networks, texture of landscape and nonspatial features, opportunities to interact with people and objects, and so on. Mazes that are typically used to test animals, in contrast, may be considered impoverished and relatively unstimulating.

Inspired by findings in K.C. and other amnesic patients of intact navigation within their home neighborhoods, Gordon Winocur and colleagues built a complex maze to more closely resemble the complex street network navigated by humans (Winocur et al. 2005). They affectionately referred to it as the "village" maze to reflect its complexity and human-like qualities compared to typical mazes used with rats (figure 9.2; Winocur et al. 2005). What was special about this maze was that it was a large, two-story apparatus containing corridors baited with food or a potential mate and including a running wheel, in addition to being surrounded by visually distinct posters external to the maze to be used as distal cues. In contrast

**FIGURE 9.2.** "Village Maze" used by Winocur et al. (2005) to simulate a complex, enriched environment that could be experienced extensively by rats from a young age until later in life, when they would undergo surgical ablation of the hippocampus. The maze was inspired by findings reported in Rosenbaum et al. (2000) of intact navigation by an amnesic person with extensive bilateral hippocampal lesions when the environment is highly familiar.

to the strict conditioning protocols that are often imposed on rats in the learning phase of an experiment, rats in the village maze experiments were free to explore the environment at will over a long period of time.

Winocur et al. found that the rats' ability to rely on their remote memory to navigate the maze was impaired after hippocampal lesions unless the rats had extensive premorbid experience with the environment prior to the time of the hippocampal lesion. If they did experience it premorbidly, then after the lesion, rats navigated normally in that environment, although the routes they took to their goal if the shortest route was blocked were more circuitous than that of controls and errors in route choices persisted over time (Winocur et al. 2005; Winocur, Moscovitch, and Bontempi 2010). Winocur et al. used a series of probe trials that included rotating the floor of the maze, distorting the relationship between the maze and distal cues, and moving the maze to a different room, to show that the rats relied on an allocentric spatial representation to perform the task. Thus, this study showed that when the conditions for the rats and humans are more similar, more equivalent patterns of behavior in a remote memory task emerge.

## Remote Spatial Memory and the Debate about the Role of the Hippocampus in Navigation

The overall findings in humans and rats suggest only partial dependence of remote spatial memory on the hippocampus, findings that neither cognitive map theory nor standard consolidation theory can fully accommodate. One recently suggested alternative that attempts to account for these discrepancies is *multiple trace theory* (MTT), which directly addresses the relationship between hippocampal function and remote spatial memory (Moscovitch et al. 2005; Moscovitch et al. 2006). According to MTT, a new trace element is added each time a memory is retrieved, serving to strengthen the memory. Most often, only fairly general information (termed *gist*) memory is reactivated. This repetition of gist-like memories means that neocortical traces become strengthened and, as a result, are less vulnerable to disruption. This mechanism whereby gist, or schematic, types of memories form in neocortex contrasts with episodic or detailed information, which MTT postulates always relies on the hippocampus, regardless of the age of the memory (Moscovitch et al. 2005; Moscovitch et al. 2006).

To accommodate findings of dissociations in spatial memory in amnesic patients with hippocampal/MTL damage, an extension of MTT involved *trace transformation theory*. Trace transformation theory was built on findings that healthy older individuals and cases of hippocampal amnesia like patient K.C. have difficulty representing detailed features of well-known environments that they can otherwise navigate in their imagination and in the real world (Rosenbaum et al. 2000; Rosenbaum et al. 2012). This theory predicts that all relational/declarative memories, including spatial, initially depend on the hippocampus but with time and experience can exist independently of the hippocampus within neocortical regions, if they lose their detailed contextual features. Within spatial memory, this would include coarse, schematic, gist-like information, such as well-known landmarks and the approximate relations between them. Fine, detailed information about an environment, in contrast, would continue to rely on hippocampal function, similar to detailed episodic representations, regardless of how long ago that information was acquired. An important addition to MTT is that the transformed memory is not believed to replace the initial, more detailed memory but rather the two representations can coexist and even interact when the situation requires it (Rosenbaum, Winocur, and Moscovitch 2001).

## Hippocampus as a "Jack-of-All-Trades" in Memory and Perception

While much of the research we discussed in rats in chapter 3 focused on a primary role for place cells in the hippocampus in spatial navigation, work on the human hippocampus has revealed a far more diverse set of functions, as we have discussed previously. The hippocampus is one of a host of primarily posterior brain structures that support the many ways in which an environment is represented in terms of its spatial and visual-perceptual properties. This network bears a striking resemblance to the network involved in remembering details of personal experiences in episodic memory, imagining and planning future personal experiences that have not yet occurred via "mental time travel," and forming a theory of mind to process other people's mental states. Some theories (such as *scene construction theory* [Hassabis and Maguire 2007]) hypothesize such a central role for the hippocampus that they postulate it would be better conceived of as having a role in assembling and imagining new scenes. Indeed, there is now substantial evidence that the hippocampus, together with the medial temporal cortices surrounding it, is involved in nonmemory functions that range from perceptual processing to language and problem-solving. At least some of these activities seem to occur when a person is not engaged in any particular task and instead is in a restful, mind-wandering state—what has become known as a *default mode*. While there is little doubt that the hippocampus is probably best conceived of as a "hub" that connects many other brain regions for cognitive function (see chapter 8), it is not clear that we should dismiss the idea that the hippocampus plays an important role in navigation and memory.

Given its unique positioning, structure, cellular properties, and connectivity, we argue that there is still reason to assign a special status to the hippocampus within a larger network, one that may be particularly well suited to processing navigation and related spatial information, although it is not exclusively dedicated to this. With these attributes, the hippocampus would seem to be well-suited as a brain structure devoted to the formation and temporary storage of memories, specifically those that are considered "explicit" or "declarative" in nature, meaning that the content of the memory can be accessed within one's conscious awareness, with spatial memory as an example (Squire 1992; Teng and Squire 1999). When we consider the many other roles that the hippocampus might play in language, future thinking, perception, and rumination, it is also noteworthy that attempts to find common ground among these varied abilities have typically referred back to the spatial-perceptual qualities of the representations and relational or binding properties of the hippocampus (Cohen and Eichenbaum 1993 and Eichenbaum 2001; see chapter 3 for a description of relational memory theory). In this way, we can think of the hippocampus as a more general "hub" for a variety of cognitive processes with its integrative capacities particularly well suited to memory and navigation.

In support of this idea, representations of the external world rely on domain-specific neocortical operations, at least as much as they do on hippocampal ones. By *domain-specific*, we mean regions of the brain dedicated to processing a specific type of information within a specific perceptual modality like vision or audition. For example, as discussed in chapter 8, neurons within the fusiform face area appear dedicated to processing faces and those within the lingual gyrus appear dedicated to representing landmarks. The encoding, storage, and recovery of spatial memories, though, depends on multifaceted information requiring polymodal and association neocortex that was involved in the perceptual and conceptual processing of the original input. Loss of one or more of these neocortical components should affect the memory in terms of one or more of its defining features, reflected in focal impairments, such that those features coded by any remaining neocortex are spared. This follows from fundamental differences between the hippocampus and neocortex in terms of organizational structure. Whereas the hippocampus collates a complex of unrelated features in a distributed manner, neocortical organization appears to be guided by regularities shared among concepts or processes, with a tendency for those having the most features in common to cluster together to form a neocortical module (Sigala and Logothetis 2002). In this way, it is easy to see the hippocampus as an integrator for cortical representations important to memory and navigation, a jack-of-all-trades of sorts, rather than a structure uniquely devoted to one cognitive process (Moscovitch et al. 2006).

## How Remote Spatial Memories Are Represented in the Brain with No Hippocampus

Models of memory consolidation are typically vague about which brain regions might be responsible for consolidation of memories from the hippocampus, often stating that memories are strengthened over time in the *neocortex* (Squire, Stark, and Clark 2004). There are two reasons for this vagueness. One reason is that little research has explored this topic, particularly at the cellular level. The second reason is that consolidation is often argued to involve strengthening in sensory-specific regions of cortex, with audio-visual areas of the brain storing long-term audio-visual memories. For example, face processing regions of the brain come to represent knowledge about who a person is from seeing that person, and initially require the hippocampus for retrieval. However, over time the hippocampus is no longer needed to support the retrieval of the person's identity. The story is more complex for spatial memories because they are, in essence, multimodal and complex, and spatial regions of the brain are diverse.

Consolidation of some remote spatial memories may not even involve neocortex. When memory involves an egocentric sequence of turns during a route, termed *response learning*, evidence indicates that this type of route memory is dependent on the striatum (see chapter 6) and the parietal cortex (see chapter 8). Indeed, patients with hippocampal damage can recall more than the procedural memory for how to follow an overlearned route. Specifically, K.C., whose head injury affected not only his hippocampus but also his striatum, had no difficulty navigating and representing spatial relations contained within his home neighborhood, based on a remotely formed representation. Thus, other brain regions likely supported this form of egocentric long-term knowledge.

fMRI studies of remote spatial memory in healthy adults and the amnesic case K.C. have revealed several other candidate regions, including posterior parietal cortex, known for its role in egocentric processing and imagery; retrosplenial cortex, involved in map learning, heading direction, and/or translation between egocentric and allocentric representations; and parahippocampal cortex, required for acquisition of new landmarks. These same regions were reviewed in chapter 8 as part of a taxonomy proposed by Aguirre and D'Esposito (1999) that supports topographical orientation in both new and old environments. Interestingly, K.C. showed activation of these regions in the right hemisphere in relation to intact performance on the various mental navigation tasks administered to him in the scanner (Rosenbaum et al. 2007), whereas healthy adults recruited these regions in both hemispheres (Rosenbaum et al. 2004; figure 9.3). This suggests the possibility that compensatory changes can occur even following lesions, suggesting again that areas outside the hippocampus can support some forms of complex spatial memory (see also chapter 8). But is it possible that these areas were involved because the familiar environments had simply been consolidated?

To answer this question, let's focus on one brain region in particular that could support memory for routes, the posterior parietal cortex. As we argued in chapter 8, according to the Aguirre and D'Esposito taxonomy, this area supports egocentric forms of spatial memory. For example, in a study that we discussed previously, Bisiach and Luzzati asked patients to recall the locations around the Piazza del Duomo, a main square in their hometown of Milan, Italy, from a perspective of looking at the main cathedral on the opposite side of the square (Bisiach and Luzzatti 1978). Consistent with their hemispatial neglect, the patients neglected the left side of space when recalling the town square from memory. However, when they were asked to recall the town square as it would look with their back to the cathedral (that is, when facing the opposite direction as before), they neglected to recall

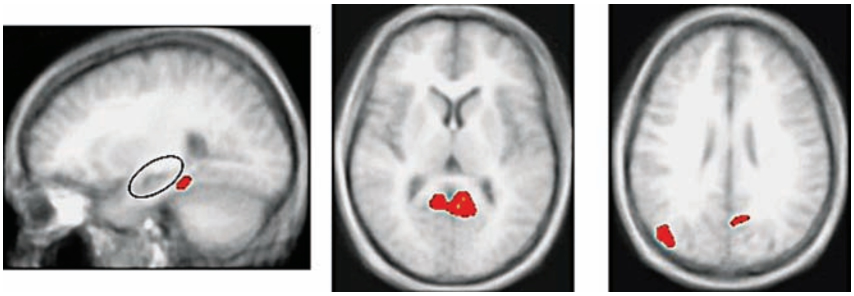


**FIGURE 9.3.** A network of brain regions that are activated across a wide range of remote spatial memory tasks (judgments of distances, directions, routes, and landmark identity) in healthy young adults. Areas of activity common across tasks included right parahippocampal gyrus (left image), left retrosplenial cortex (middle image), and right superior occipital cortex (right image). The hippocampus (open circle in left image) was not significantly activated in any task. Reproduced from Rosenbaum et al. 2004.

places on the right side of the square, places they had previously remembered. Thus, the patients' remote memory for the square was intact, but their ability to process it was disrupted by parietal damage. This, combined with other evidence, leads to the view that the posterior parietal cortex is not needed for storing long-term remote spatial memories, but it may be needed for retrieving them from a particular viewpoint (Spiers and Maguire 2007). This perspective, though, conflicts with the standard model of consolidation.

If the posterior parietal cortex is not the locus of long-term memories, where and how are long-term memories represented? The parahippocampal cortex and retrosplenial cortex are two other key areas of the human brain known to be important for spatial processing and might help to maintain long-term memories. Preliminary evidence suggests that patients with parahippocampal damage are able to recall remote spatial memories as tested by map drawing, albeit with less accuracy than control participants (Epstein et al. 2001). While patients with retrosplenial damage do show deficits in remote spatial memory, such deficits can disappear over time, raising the possibility that other regions of the human brain may serve as the long-term repository (Spiers and Maguire 2007). Thus, these findings suggest that certain parts of the neocortex are better thought of for their specific role in processing remote spatial information rather than storing these memory traces specifically. But if this is the case, what brain regions do represent remote spatial memories?

As suggested by work in rodents, regions of the prefrontal cortex may be a candidate structure (Ding, Teixeira, and Frankland 2008). However, the recruitment of the prefrontal cortex may relate to the greater difficulty associated with recalling memories for events that occurred in the remote past (Rudy, Biedenkapp, and O'Reilly 2005). Another possibility is that the anterior temporal lobe, owing to its role in storing semantic knowledge, is the "seat" of long-term memories (Patterson, Nestor, and Rogers 2007). Little work has explored the impact of damage to the temporal pole on remote spatial memory. It may be important for storing facts about how a remotely learned environment was arranged, but it seems unlikely that the anterior temporal lobe would be a key region for allowing someone to mentally orient within space. Overall, it remains unclear which brain regions, or groups of brain regions, are responsible for coarse-grained remote spatial memories, and more research in this area is clearly needed to determine the answer to this question.

## Summary

As discussed earlier, the study of remote spatial memory is of theoretical importance, but it is also of practical importance. From a theoretical perspective, we have described the ways in which spatial memories behave like other types of declarative memories in terms of how long they rely on the hippocampus for their representation, and how other parts of the brain continue to support spatial memories once the memories are more established and presumably integrated with preexisting information. From a practical standpoint, it is important to predict spatial disorientation not only in novel environments, which has been the focus of much of this book, but also in well-known places following hippocampal damage. As discussed in chapter 7, the hippocampus changes in structure and function as part of the typical aging process. It is also highly vulnerable to brain injury and to a wide array of diseases, some relating to advanced age and others owing to the status of the hippocampus as a “watershed” region with its unique vasculature as well as position, cellular structure, and neurochemistry. Overall, though, the position we advance here is that the hippocampus plays a role in a variety of different cognitive functions, and its role as an integrator “hub” seems particularly well suited to dealing with the complex, multimodal forms of information typical of episodic memories and navigation.

## CHAPTER 10

# CONCLUSION

We started our discussion by considering a frequently asked question to those who research spatial navigation: Why do many of us rate ourselves as below average navigators (Hegarty et al. 2006)? On first pass, we might not choose to take this question seriously. After all, studies of people's self-assessments suggest that they are often unreliable (Alicke and Govorun 2005; Connolly, Kavanagh, and Viswesvaran 2007). Is it just that we tend to get frustrated easily when we get lost, and thus remember these experiences better compared to the typical experience, in which we find our way (Tversky and Kahneman 1973)?

As our discussion starting in chapter 1 revealed, the human species, as a whole, has many examples, both historical and current, of individuals with unprecedented and unparalleled navigational skills. Indeed, in the same study that suggested that about half of participants rated themselves as below average navigators, about the same number rated themselves as above average (Hegarty et al. 2006). In fact, there are numerous examples of highly skilled navigators among our species. One example we have discussed is the Puluwat sailors of the south Pacific, who start their navigational training at a young age and learn to navigate between islands in the open ocean, in some cases covering distances of nearly one thousand kilometers (Gladwin 1970).

What is so striking about these navigators is that they do so with no mechanical aids, traveling even in complete darkness using their fine-tuned path integration systems. As we discussed in chapter 1, the Puluwat go through an extensive apprenticeship in which they learn from an older experienced navigator, perfecting both their path integration system and their internal representations of the locations of islands, which we termed their *cognitive map*. The Puluwat thus also use many other sources of information to estimate their distance and direction, including the speed and direction of waves, the constellations, and cues about the positions of different islands from seabirds. Together, these combine to form a highly developed and honed navigational system, either aspect of which provides a backup and redundant checks for the other, which contributes to their incredible and unparalleled ability to navigate.

Despite what may seem like incredible navigational abilities, the same brain systems that the Puluwat employ to navigate are also present in our brains, as we hope we have convinced you in this book. In particular, our path integration system involves a variety of egocentric cues related to turn and distance, which can be combined to provide a sense of distance and direction. This system, which is well established in humans (as shown by the experiments of Jack Loomis that we discussed in chapter 2), is well developed, and over short distances it operates with little error. The exact neural basis of this system remains debated, but as we discussed in chapter 3, the path integration system likely involves a combination of head direction input from areas like the retrosplenial cortex and grid cell input from the entorhinal cortex, which together form a foundation for how we navigate.

As we mentioned in chapters 1, 2, and 4, however, the path integration system accumulates errors. As the Puluwat travel across the ocean, they must also rely on some knowledge of the relative positions of islands, thus using their cognitive map in order to navigate allocentrically. We have talked in numerous places about the importance of cognitive maps to navigation, particularly in chapter 3 with regard to place cells and in chapter 6 with regard to place strategies for navigation. In many ways, map-based approaches to navigation, which rely heavily on our memory for the relative positions of landmarks when we navigate, and for which the Puluwat train by practicing drawing islands in the sand, is a second critical component of how we figure out our location.

Of course, as we discussed in chapter 5, navigation must also involve a goal. Neural representations in the entorhinal cortex and hippocampus contain codes not only for specific goals but also for our relative distance from these goals. In this way, the path integration system provides a representation of distance and direction from the start point, the cognitive map provides information about how one is situated in one's current location, and the goal system provides information about the future—for example, how far are we from our desired goal?

Other groups of skilled navigators that we have discussed in this book and learned from are people like Frank Worsley, who helped lead Ernest Shackleton's expedition to safety over thousands of kilometers of open ocean; the Inuit people, who travel in darkness using snowdrifts and stars; and taxi drivers, who navigate novel, often complex routes routinely as part of their job. Both Western sailors and taxi drivers share quite a few things in common: unlike the Puluwat, they do study maps and often use mechanical devices like compasses to navigate. In the case of Worsley, though, when he navigated between Elephant Island and the Georgia Islands, as described in chapter 1, he had few navigational devices available to him because of their circumstances (being marooned and in extremely inclement weather). Similarly, although taxi drivers, particularly London taxi drivers, study maps as part of their apprenticeship, they must pass an exam showing that they know London streets from memory, and they typically navigate without such aids.

In this way, Worsley and taxi drivers give us insight into individuals with a high degree of navigational expertise who, while not as incredible as the Puluwat in terms of navigating with no aids, are still highly skilled navigators. Worsley in particular demonstrates the importance of vision and the cognitive map to spatial navigation. As we discussed in chapter 1 and then returned to in chapter 4, navigation involves a high degree of visual imagery, particularly in humans, supported by inputs from highly developed visual areas. This allowed Worsley to picture the positions of islands, along with his current bearing and position, based on his memory of a cartographic map of the Antarctic. As discussed in chapter 5, another important component for Worsley was estimating how far it was to the Georgia Islands, his intended goal. This was critical, because if he wandered off course, his crew would quickly become lost in open ocean.

Similarly, taxi drivers must imagine both their current position and their intended goal to navigate quickly and efficiently. After all, for a taxi driver—unlike the Puluwat—time is money, and thus taxi drivers have a strong incentive to navigate efficiently. In all these cases—the Puluwat, Worsley, the Inuit, and taxi drivers—where they started from, their current position, their visualization of the relative allocentric positions of other landmarks, and their knowledge of the distance to their goal are all critical parts of their ability to successfully navigate. These in turn, as we have discussed throughout the book, are supported by brain areas like the hippocampus for position, the retrosplenial cortex for current heading direction (for example, north/south), the parietal cortex for egocentric bearing, and the entorhinal cortex for estimates of distance traveled and distance to goal.

Our discussion of taxi drivers then led to a discussion of two specific taxi drivers who, as a result of a stroke, essentially lost the ability to navigate. In the case of one taxi driver we discussed in chapter 7, a stroke affecting his retrosplenial cortex led to complete disorientation when driving, even though he knew the names of landmarks. A second driver, T.T., experienced damage to his medial temporal lobes from viral encephalitis, leading to a higher reliance on navigational paths that involved major, likely more familiar roads. We also discussed cases of patients who, though they had no obvious neurological condition, have extremely impaired navigational skills. These patients, termed *developmental topographical disorientation* (DTD) patients, can become lost in their own neighborhoods. Interestingly, their pattern of deficit does not involve focal brain damage but rather a pattern of impaired communication between two important regions for memory and decision making, the hippocampus and prefrontal cortex.

In chapter 8, we attempted to take what we have learned from patients with focal damage to their brains and their specific navigational impairments to suggest a taxonomy for the neural basis of human spatial navigation. The four key regions we discussed were the retrosplenial cortex for allocentric heading direction, the parietal cortex for egocentric heading direction, the lingual gyrus for landmark identification, and the hippocampus for encoding new topographical information. This division fits nicely with the cellular distinctions we discussed in chapter 3. Namely, the retrosplenial cortex contains neurons that code for head direction (egocentric knowledge) in allocentric space—in other words, based on landmarks that might identify various directions. We also suggested that the hippocampus contains place cells that code location and might be expected to be important to any map, or place-based, coding strategy, which would be consistent with the typical impairments in spatial precision accompanying such lesions. Similarly, the lingual gyrus shows strong activation for viewing landmarks compared to other objects, and other, neighboring areas we discussed, like the parahippocampal gyrus, contain neurons that increase their spiking rate when viewing landmarks. Thus, this taxonomy fits nicely with what we know from the results of focal damage in the brain, cellular recordings in humans and rats, and fMRI data.

Our discussion of DTD, though, revealed some potential limitations with this model, and, as we have explored throughout this book, the idea of the cognitive map, and the accompanying taxonomy for navigation discussed in chapter 8, cannot explain all of the varied phenomena observed in human spatial navigation. In particular, as we discussed as early as chapters 2 and 6, egocentric and allocentric navigational strategies are not as cleanly separable as we might think. Instead, it is fairer to say that they form a continuum of possible forms of representations, with most navigational situations involving mixtures of these two different methods of representing space while navigating. This led us to the idea that perhaps the brain regions involved in navigation are not so cleanly separated either. For example, in chapter 8, we discuss the newly emerging idea that the neural basis of navigation might be better conceptualized as an interacting network, where no one process can be isolated to one brain region. This model helps us to better understand the egocentric/allocentric continuum, DTD, the fact that lesions to multiple brain regions can often result in similar impairments to navigation, and the idea that communications and interactions between brain regions might be as important as the computations they perform individually.

Similarly, another way of thinking about different navigational strategies, in this case place versus response strategies, provides quite a bit of traction in terms of understanding how we navigate and why we get lost. As we discussed in chapter 6, place and response strategies are governed, in part, by two brain systems operating in parallel, the hippocampus and caudate nucleus. The hippocampus favors map-based place strategies, and the caudate nucleus favors well-worn, habitual routes involving sequences of turns or simply following a landmark to the goal. This dichotomy helps us understand why we might take a habitual route over a new one, in that our caudate nucleus and hippocampus often compete for navigational precedence. It also provides us with novel insight into neurological conditions like Alzheimer's disease, which may lead to a differential emphasis on response strategies.

As we discussed in chapters 8 and 9, though, like the egocentric versus allocentric dichotomy, the place versus response strategy dichotomy also has limitations. Specifically, as we described in chapter 9, the hippocampus has significant memory functions unrelated to any direct role in navigation, and recasting it as a brain area involved in memory rather than navigation helps us to understand its function in navigating familiar versus novel environments. Damage to the hippocampus seems better linked to amnesia than to gross navigational impairments, as evidenced by the fact that many amnesics have good general memories for routes and cities that they have navigated in the past (see chapters 7 and 9). In this view, thinking of the hippocampus as purely a spatial brain structure is a mistake and does not encapsulate its true diversity of functions. Additionally, *strategy use* does not always map cleanly in a "one function, one structure" type of way. For example, a place strategy involves several different cognitive operations, such as recognizing landmarks, remembering a specific goal, and using the relative positions of landmarks to compute a trajectory based on a new start location (see an interesting discussion of this issue in Wang 2017). Overall, it is more accurate to consider how navigational functions emerge based on interactions across a range of functions than computations in a single brain region.

Last, a topic that we have returned to again and again in this book, but focused on particularly in chapters 4 and 8, is that human spatial navigation has its own unique features that differ from those of any other species on earth. As valuable as animal models have been to understanding the neural basis of spatial navigation, human spatial navigation displays fundamental differences. In particular, our high-resolution visual system confers advantages not available to any other species, like the ability to use a cartographic map to navigate. In addition, our language capability allows us to use codes and communicate directions in a way that directly accesses navigational representations unlikely to be present in any other species. These differences, in turn, point to important differences in the neural basis of navigational systems that we are just beginning to appreciate and shed light on. Human spatial navigation is a discipline in its own right, and it is wrong to think that we can learn everything we know about how we navigate solely from studying rats, as we hope we have demonstrated here.

Overall, we hope that the reader has come away with a new appreciation for not just navigation but, more specifically, human spatial navigation. As navigators, human beings may not seem nearly as interesting or noteworthy as desert ants, sea turtles, rats, or bees. However, we believe that human navigation is a fascinating area of study in its own right, with its own set of highly complex and evolved possibilities, and we have tried to do justice to the wealth of different ideas in the literature about the neural basis of human spatial navigation. As we hope is obvious, there is no single consensus for how things work, and there remain many issues to be resolved. The brain systems that underlie navigation may ultimately prove to be far more complex than any of our current models would indicate. Undoubtedly, there are exciting roads ahead of us that we will need to explore in order to arrive at a better understanding of human spatial navigation.

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