

Aging and Spatial Navigation: What Do We Know and Where Do We Go?

Scott D. Moffat

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Abstract Spatial navigation is a complex cognitive skill that is necessary for everyday functioning in the environment. However, navigational skills are not typically measured in most test batteries assessing cognitive aging. The present paper reviews what we know about behavioral differences between older and younger adults in navigational skill and reviews the putative neural mechanisms that may underlie these behavioral differences. Empirical studies to date clearly identify navigation as an aspect of cognitive function that is vulnerable to the aging process. The few functional and structural neuroimaging studies that speak to neurological correlates of these age-related differences point to the hippocampus, parahippocampal gyrus, posterior cingulate gyrus (retrosplenial cortex), parietal lobes and pre-frontal cortex as structures critically involved in age effects on navigation. Outstanding issues in the field are addressed and productive avenues of future research are suggested. Among these outstanding issues include the necessity of performing longitudinal studies and differentiating between hippocampal and extra-hippocampal contributions to aging in navigation. The field may also be advanced by empirical assessment of navigational strategies and investigations into the multisensory nature of navigation including assessing the relative contributions of visual, vestibular, and proprioceptive function to age differences in navigational skill.

Keywords Cognitive aging · Navigation · Spatial memory · fMRI · Virtual environment · Hippocampus · Frontal lobe

Older age is associated with functional decline in selective aspects of cognitive performance and brain function and anatomy. Cognitive skills that are known to decline with age include component processes of executive function, attention, verbal and visual explicit memory, working memory and processing speed, while more experienced-based cognitive abilities such as semantic memory as assessed by general fund of knowledge, comprehension, and vocabulary can remain stable or even improve with age (Park 2000).

The majority of studies of human cognitive aging focus on age-related differences in psychometric measures of cognition. While this has been, and still is, a very fruitful approach, it has also led to limitations in the understanding of cognitive aging in specific cognitive domains. In particular, when specialists in cognitive aging measure visual memory, the emphasis tends to be on memory for recent displays of static two-dimensional scenes or of complex line drawings (e.g. Rey-Osterrieth Complex Figure) (Osterrieth 1944). Spatial cognition is a domain that receives less attention in studies of cognitive aging and when spatial cognition is measured at all, it is typically evaluated using pencil and paper or computerized tests requiring the mental manipulation of static objects (e.g. mental rotation tests).

Although, these cognitive tasks assess critical human faculties, it could be argued that this method of cognitive testing overlooks the dynamic nature of spatial cognition as it is utilized on a daily basis by most people. Arguably, the most important manner in which our spatial cognitive systems are challenged is during navigation where we must maintain a constant representation of our position in the

S. D. Moffat (✉)
Institute of Gerontology, Wayne State University,
87 E. Ferry Street,
Detroit, MI 48202, USA
e-mail: moffat@wayne.edu

S. D. Moffat
Department of Psychology, Wayne State University,
Detroit, MI, USA

three-dimensional world. Our navigation systems are used whenever we follow a route to a familiar location, learn a route to a new goal or locate an object in an environment in which the object cannot be directly observed. Although there may be several important differences between traditional psychometric measures and navigational or route-finding measures of spatial cognition, the most obvious is that the latter requires physical movement through space (and concomitant dynamic visual processing), whereas paper and pencil tests require no such translocations of the self.

It could be further argued that the neglect of spatial navigation assessments in cognitive aging has hampered a truly comparative approach to cognitive aging. There is a rich literature of cognitive and brain aging in non-human species and neuroscientists studying human cognitive aging make frequent reference to this literature. However, spatial memory in nonhuman species is typically assessed by quantifying performance in a variety of maze-learning tasks that require the animal to actually navigate and remember a route or place in novel environment (e.g. Barnes 1979; Ingram 1988; McLay et al. 1999). Despite the fact that actual movement through the three-dimensional world may require different visual computations than imaginary object rotations or manipulations, it often is taken for granted that studies investigating spatial navigational behaviors in animals are pertinent to our understanding of the mechanisms subserving human spatial memory. For a coherent cross-species understanding of both the behavioral and neural mechanisms of cognitive aging, it would be desirable to assess aging in human and non-human species using comparable paradigms.

There is a steadily accumulating literature investigating age-related navigation differences in humans. This paper reviews the extant literature on how human navigation is affected by the aging process and the neural mechanisms that may subserve these behavioral age differences. Further, it proposes areas of research in which our knowledge is limited and explains how further research could advance our understanding of how age affects this critical cognitive domain.

Aging and Spatial Navigation: What Do We Know?

Behavioral Studies of Age-Related Differences in Spatial Navigation

Age-related deficits in spatial navigation have been studied extensively in non-human species. For example, older rats are generally impaired on a wide variety of navigation tasks, including the Morris Water Task, T-maze, and the Barnes circular platform maze and corridor mazes (Barnes

1979; Ingram 1988; McLay et al. 1999). The Morris Water Task (MWT) in particular has been used extensively in studying cognitive aging in animals in part because of its known dependence on the hippocampal formation (Morris et al. 1982). Briefly, this task requires an animal to locate a platform which is hidden beneath the surface of an opaque pool of water. Surrounding the pool are visual cues which aid the animal in pin-pointing the location of the platform. Over successive trials the animal typically comes to learn the location of the platform as revealed by faster escape latencies and shorter path lengths to the target. Age-related deficits have been reported in that older animals take longer to find the hidden platform, travel a longer distance in locating the platform, and may require more trials before reaching a designated criterion performance (Begega et al. 2001; Gallagher and Pelleymounter 1988; Lukoyanov et al. 1999).

There is now an accumulation of studies that systematically examine age-related vulnerability in route/place learning or large scale spatial memory in humans. Survey research indicates that elderly individuals self-report deficits in navigation and often avoid unfamiliar routes and places (Burns 1999). For example, elderly individuals report avoiding driving to unfamiliar locations. Direct assessments of navigational/route finding skills in non-demented elderly adults provide evidence of age-related differences in these skills. One approach to the study of spatial navigation in the elderly has been to assess navigation in “real-world” settings such as supermarkets, hospitals or manufactured environments. Kirasic (1991) assessed the navigational skills of young and elderly women in novel and familiar supermarket environments and found that younger women acquired the spatial information in the environment faster than did their elderly counterparts (Kirasic 1991).

In another study involving navigation through the real world, Wilkniss and colleagues required participants to navigate through the hallways of a hospital after being presented with a map of the environment and route that they were required to follow. They found that older adults took longer to navigate through the hospital than younger adults, and that the older adults made more frequent turning errors. Interestingly, older adults recalled objects which were encountered along the route just as well as younger subjects, but compared to their younger counterparts, they were deficient at placing those objects in their proper temporal sequence (Wilkniss et al. 1997).

One study has replicated the Morris Water Task on a human scale by requiring older and younger adults to remove, then repeatedly replace a pole in a circular enclosure which was surrounded by visual cues. Across a series of learning trials, older adults showed greater displacement error in replacing the pole (as assessed by

measuring the distance between the subject placement of the pole and the correct location of the pole) compared to younger adults demonstrating age-related deficits in place learning in older humans (Newman and Kaszniak 2000).

One of the reasons that researchers have neglected navigational skill in studies of cognitive aging is that its evaluation is complicated by the fact that human navigation occurs in large-scale space. That precludes tight experimental control, which is necessary for the systematic evaluation of the phenomenon. The development of virtual environment (VE) technology has helped to alleviate that problem. Several groups have successfully applied VE spatial learning tasks to the study of age differences in spatial navigation among both healthy and demented elderly. The results of these studies demonstrate that VE technology can be used to accurately assess spatial learning in elderly individuals.

In one of the first studies to adapt VE navigation to the assessment of age differences, younger and older individuals were confronted with a computer-based route learning task in which several winding and intersecting corridors ultimately led to a goal point (Moffat et al. 2001). Participants were instructed to find a goal point and remember the route. An important distinction in scoring was made between “information errors” (the first visit to an error location in which the subject had no previous knowledge that a corridor did not lead to the goal) and spatial memory errors (repeat visits to error locations that they should have remembered did not lead to the goal). It was found that elderly subjects made more spatial memory errors and traveled a longer linear distance in solving the virtual route learning task (Moffat et al. 2001). Importantly, the older individuals did not make more information errors than their younger counterparts indicating that elderly individuals differed only in their tendency to revisit error location suggesting that the age difference was not a simple result of older individuals being generally deficient at using a computer or using a joystick.

One limitation of this type of route-learning task is that because it requires participants to navigate from the same starting location to the same goal location over several trials, it is possible for participants to use egocentric or logical solution strategies rather than allocentric spatial processing strategies. An egocentric strategy is one in which an individual uses a frame of reference centered on the self, for example remembering left and right turns whereas, an allocentric strategy requires an organism to know its position based on an external reference system. It is thought that the Morris Water Task lends itself to allocentric processing by virtue of having to locate a goal platform from multiple locations and with reference to the platform’s position relative to objects or cues throughout the room.

Moffat and Resnick (2002) developed a virtual MWT (vMWT) for human application and had younger and older adults learn the location of a hidden platform over six learning trials. Cues available to assist navigation were objects of fixed position placed around the room. Asymmetrically-designed walls were also available as distal geometric room cues. The results of their study confirmed substantial age effects on virtual environment place learning. Older individuals traversed a longer linear distance in solving the learning trials of the vMWT. In addition, on a probe trial, considered to be a measure of retention of spatial location, younger individuals spent more time in the vicinity of the platform and had more frequent platform intersections than older subjects (Moffat and Resnick 2002). These findings indicated that younger individuals had retained more accurate knowledge of platform location than their older counterparts. These basic age differences in a virtual MWT have subsequently been replicated and extended by other authors (Deshmukh et al. 2009; Driscoll et al. 2005).

One of the limitations of using VE presentations of navigation tasks is that it deprives the participant of vestibular and proprioceptive feedback that is normally available in real world navigation tasks. Lovden et al. (2005) investigated the effect of age on spatial navigation through virtual museums using an interface that provided participants with the visual image of the environment and required participants to walk on a treadmill to initiate movement through the environment, thus providing proprioceptive feedback. Participants completed the task under two conditions; one in which they were provided with walking support (holding on to a handrail) and another in which no support was provided. These authors found that providing walking support on the treadmill attenuated (but did not eliminate) the age differences in navigation accuracy (Lovden et al. 2005). This study suggests that there are important interactions between cognitive and sensorimotor components of navigation that are relevant to the magnitude of the age difference observed in a given study. The issue of vestibular and proprioceptive contributions to age differences in navigation will be discussed in more detail below.

Another approach to the examination of age differences in navigation has been to quantify the ability of younger and older individuals to develop and use a cognitive map of the environment. A second component of the study by Moffat and Resnick (2002) described above required participants to draw a freehand map of the vMWT environment and to designate the platform location on the map. In addition, they were subsequently shown experimenter-provided maps of the environment and asked to mark an “X” where they believed the platform to be located. Older individuals showed evidence of impairment in cognitive mapping, as revealed by their poorer map

constructions of the environment and their impaired ability to locate the platform on the experimenter-provided maps of the environment. Interestingly, there was no age effect on the recall of the object cues present in the environment. Consistent with the results of Wilkniss et al. (1997), older individuals appear to have comparatively spared object/item memory but are deficient at using those objects to assist in navigational behavior.

Sjolinder et al. (2005) administered a virtual navigation task to a sample of young and older participants and replicated the basic findings of impaired performance in older participants and impaired configural representation of the environment. They also provided all participants with an overhead map of the environment to investigate the effects of navigational aids on the age differences. Sjolinder found that older participants did not benefit more from an overview map than younger subjects. Although the older participant subjectively felt more secure with the map, it did not improve efficiency in navigating the environment (Sjolinder et al. 2005). Similar results were obtained in another VE study of cognitive mapping which showed that older participants required more time to form a cognitive map of the environment than young individuals and required more time and made more errors when subsequently using the map for orientation (Iaria et al. 2009). The results of these studies of cognitive mapping in the elderly clearly point to decreased efficacy among the elderly in generating cognitive maps and using navigational aids to assist in wayfinding.

Navigation tasks are also now being used in clinical populations, particularly in evaluating early stage dementia and mild cognitive impairment. Clinically relevant impairments in navigational skills (“getting lost” and “wandering”) are often apparent in the early stages of Alzheimer’s disease, sometimes even before the well-known verbal memory deficits. In many cases, reports of impaired spatial behavior are a major trigger to the diagnosis and may serve as an indicator to family members that something is wrong with their relative (Klein et al. 1999).

In an assessment of the application of navigation testing to clinical populations, Zakzanis et al. (2009) used a head-mounted goggle display to show a path through a virtual city which then had to be navigated as quickly and as accurately as possible. Their results showed that young adults navigated more accurately than older participants. Compared to older controls, participants with Alzheimer’s disease (AD) made more errors on a subsequent recognition task and were more likely to affirm having seen an element when it was a foil (Zakzanis et al. 2009). This study suggests that spatial navigation is susceptible to the effects of normal aging and AD.

Two well-designed studies have investigated both the effects of AD on navigation skill and whether virtual and

real-world navigation tasks elicit similar findings. Kalova et al. (Kalova et al. 2005) studied navigation in participants with early AD, and non-AD aged controls. An important element in the design of this study was that the researchers used both a real world environment and virtual replication of this real world setting. Their real world navigation task required participants to locate unmarked goals in an arena. The AD group was severely impaired relative to controls in navigation to a hidden goal which was located in eight rotated positions. Importantly, these authors reported that the results from navigation in a real world and a computer version of the tests yielded similar results.

In another study investigating the effects of age and dementia status on spatial navigation, Cushman et al. (2008) obtained virtually identical results. These researchers observed navigational deficits that increased across groups from young normals to older normals, to MCI, and to early AD. Importantly, these researchers found the identical pattern of results and close correlations ($R^2=.73$) between real-world and virtual tasks strongly suggesting that VE testing provides a valid assessment of navigational skills (Cushman et al. 2008).

Navigation as Complex Multi-Sensory Cognitive Skill

An important issue in spatial navigation research is the recognition that it is a complex, multi-sensory cognitive process that requires the contributions of multiple cognitive and perceptual modules. Under real world conditions, information about one’s own movement is obtained through the integration of three major sources of sensory input: vestibular sense (awareness of changes in body orientation and motion), proprioceptive sense (awareness of the body, limb, and joint position via feedback from muscles and joints), and vision (particularly, the visual displacement across the retina known as “optic flow”). This highlights a major limitation of the VE approach to navigation studies; it effectively eliminates or creates a mismatch between visual information and vestibular and proprioceptive signals. On the other hand, VE tasks can now be used to isolate the visual contribution to navigation that was not heretofore possible. It will be important for future studies to investigate the separate contributions of each of these sources of sensory input to the expression of age differences in navigation-related processes.

Duffy and colleagues have performed a series of well-designed studies demonstrating that AD, and to a lesser extent normal aging, is associated with deficits in optic flow perception. Optic flow describes the flow of stimuli through the visual field that occurs during self motion (or during simulated motion in computerized tasks) giving one the perception of movement through the world. These researchers studied the ability of young normal subjects,

elderly normal subjects, and AD patients to interpret the radial motion of optic flow. They also tested spatial navigation by asking questions about a recently traveled path. They found that AD patients showed impaired optic flow perception which was associated with poor performance on the spatial navigation test, even though their perception of simple moving patterns was relatively preserved (Tetewsky and Duffy 1999). In other studies, this group has found that deficits in optic flow perception are correlated with orientation deficits in AD (O'Brien et al. 2001), and that poor heading discrimination (impaired ability to determine direction of simulated movement) was primarily attributed to attentional deficits in normal elderly and to visual motion perception deficits in AD patients (Mapstone et al. 2008). As visual self motion cues, particularly optic flow, provide some of the basic input to navigation systems, these findings demonstrate the key contribution made by high level visual processes which feed forward to navigation systems and likely contribute to age differences in navigational competence.

Mahmood et al. (2009) utilized a VE to investigate age-related differences in 'path integration,' the ability to determine linear distances, angular rotations, and angular displacement exclusively from self motion (in this case, visual self motion cues). Participants passively viewed linear and rotational motion and were required to reproduce, with a joystick, the distance or rotation that they just experienced. Results indicated that older and younger adults were equivalent in their ability to use optic flow to estimate short distances but older individuals became progressively less accurate as the distance increased. Interestingly, there were no age differences in estimating angular rotations which involves the perception of left/right rather than radial motion. This study demonstrated age-related deficits in the ability to use visual input alone to estimate distance traveled and suggests one way in which elderly navigation performance may be compromised.

Other studies have focused on and tried to isolate the *non-visual* contributions to age differences in navigation. Allen et al. (2004) blindfolded younger and older subjects and had them perform a "triangle completion task", in which they were led along two legs of a triangle and were then required to rotate themselves and move back to the origin of their movement. This was done in a blind-folded walking condition and a wheelchair condition to examine the contribution of vestibular and proprioceptive feedback to navigation in the absence of visual input. These authors found that there was no difference in accuracy between the walking and wheelchair condition in the younger adults, whereas, for the older adults, both distance traveled and angle turned were less accurate in the wheelchair condition compared to the walking condition. Specifically, older adults over-rotated small angles and undershot long

distances. These results suggest that older adults may rely more on proprioceptive signals than young adults for task performance in navigating.

In summary, there is now a developing literature assessing the effects of age and cognitive/dementia status on navigation-specific tasks. Despite variability in specific tasks and procedures, the results are highly consistent. When navigating in unfamiliar environments, older individuals generally perform more poorly than younger participants and those elderly with early stage dementia perform more poorly than both normal older and younger participants. They also have considerable difficulty in developing cognitive maps of space and in using experimenter-provided maps to aid navigation.

Strengths and Weaknesses in VE Testing

The greatest advantage afforded by VE testing is that it gives the experimenter unlimited control over the visual features and complexity of the environment, allows detailed recording of behavioral responses to be automated, and allows landmark and route manipulations which could not be accomplished in the real world. However, the question arises as to what extent VE testing simulates real world navigation and depends upon similar behavioral and neural mechanisms. Clearly the greatest drawback of desktop VE testing is that it does not involve actual movement through space. Computer displays restrict coverage of the visual field and deprive the participant of vestibular, kinesthetic and proprioceptive cues which are used to help maintain course in the real world (Berthoz and Viaud-Delmon 1999; Ohmi 1996). VE testing assesses only that component of navigation or route learning which is visually-based with an absence of sources of input from other sensory systems.

Despite these limitations, recent studies suggest that the spatial knowledge acquired through learning in a VE transfers well to subsequent navigation in the real world (Arthur et al. 1997; Witmer et al. 1996). For example, training participants on a virtual version of the Kiel locomotor maze enhanced subsequent acquisition of the actual maze (Foreman et al. 2000). Participants made accurate and confident responses in the real maze as a consequence of having received training in virtual space. Moreover, Ruddle et al. (1997) found that participants develop 'cognitive maps' in a VE that are similar to the maps derived from exploration of the real world (Ruddle et al. 1997). Most importantly, as noted above, studies of cognitive aging have incorporated parallel forms of real and virtual navigation assessments and have generated virtually identical results (Cushman et al. 2008; Kalova et al. 2005), raising confidence that VE navigation assessments are measuring something essentially similar to real-world assessments in cognitive aging.

There are, however, special considerations in using a VE approach in older participants since there are a number of non-navigation parameters, such as low vision and motor impairment, that may differentiate performance between older and younger adults and may affect interpretation of results. Methodological “good practices” include providing extensive practice to older adults to familiarize them with the computer display, assessing age differences in experience using computers and playing video games and including multiple measures of visual (e.g. visual acuity, color vision, contrast sensitivity) and motor function that may impair the ability of elderly individuals to see or interact with the display. In addition, it is essential to include some kind of control task that requires the same sensorimotor components as the navigation task but does not require spatial navigation. Examples of this include trials in the vMWT in which the platform is visible above the surface of the water or joystick control tests in which a participant might maneuver through a winding corridor but does not have to make wayfinding decisions or remember the route. In short, every effort should be made to ensure close equivalence between older and younger individuals in sensorimotor characteristics. This can include exclusion of older participants who do not meet cutoffs for critical sensorimotor skills, as well as incorporating residual age differences in these factors as covariates in statistical models.

Another major advantage of VE navigation tasks is that it allows for the systematic study of the neural mechanisms of navigation in the neuroimaging environment which is clearly not possible in real world navigation. The next section reviews the possible brain bases of the age-differences in spatial navigation.

Neural Mechanism of Age-Related Differences in Spatial Navigation

The neural mechanisms underlying these spatial navigation differences remain unclear. One of the distinct advantages of VE is that it makes many complex tasks MRI-compatible and thus creates opportunities for examination of their brain substrates. Indeed, neuroimaging and lesion studies in younger subjects have identified a network of structures that are involved in spatial navigation. These structures include the hippocampus, parahippocampal gyrus, cerebellum, parietal cortex, posterior cingulate gyrus and retrosplenial cortex (Aguirre et al. 1996; Barrash 1998; Gron et al. 2000; Katayama et al. 1999; Maguire et al. 1998).

Contribution of the Hippocampus and Parahippocampal Regions

It is noteworthy that the medial temporal region shows atrophy with aging and is one of the first affected in AD

(Jack et al. 1998; Raz et al. 2004; West et al. 1995; but see Sullivan et al. 2001, 2005). It seems plausible that age-related alterations in hippocampal and other neural circuitry may manifest as deficiencies in spatial processing, consequently impairing both virtual and real world navigation and possibly altering the cognitive strategies used by the elderly in solving navigational tasks.

Meulenbroek et al. (2004) had younger and older participants learn the layout of a virtual house by viewing and remember a sequence of turns through the house. Compared to older adults, younger subjects showed stronger activations in the supramarginal gyrus and posterior fusiform/parahippocampal areas. In addition, younger subjects showed weaker anterior parahippocampal activity during route recognition compared to the older group. They suggested that age-related navigational memory deficits might be caused by less effective route encoding based on reduced posterior fusiform/parahippocampal and parietal function (Meulenbroek et al. 2004).

Moffat et al. (2006) investigated the neural mechanisms of age differences in spatial navigation in a fMRI study (Moffat et al. 2006). Fifty one healthy individuals (30 young; 21 old) were scanned while performing a VE navigation task and a control task that provided the same visual and motor stimulation but did not require navigation. The task differed from the Meulenbroek study in that participants actively navigated through the environment using a joystick and were encouraged to develop an allocentric representation of the environment. The results of the study demonstrated substantial age-related alteration in the neural networks supporting allocentric navigation. Compared to their younger counterparts, elderly adults showed reduced activation in the posterior hippocampus, parahippocampal gyrus and retrosplenial cortex. Elderly subjects also showed greater frontal lobe activation during encoding of the environment as compared to the younger subjects. This study also demonstrated that increased activation in hippocampus/ parahippocampal gyrus was associated with more accurate navigation. Because elderly participants had reduced activation in these regions, it suggests that the decreased hippocampal involvement in navigation may, in part, underlie the navigation deficit in older individuals.

A recent fMRI study by Antonova et al. (2009) provides converging evidence that the parahippocampal cortex may be a major component of the age differences in navigational performance. As with virtually all navigation studies, these authors report a widespread neural network comprising frontal, parietal, occipital, thalamic, and cerebellar regions being activated in young and older adults. In addition, they report that only young adults significantly activated bilateral hippocampus and left parahippocampal gyrus, as well as right frontal pole and dorso-lateral prefrontal cortex

during encoding. Older adults showed no activation of the hippocampal/ parahippocampal region (Antonova et al. 2009).

Of particular importance in these functional imaging studies of navigation and aging is the consistent observation of reduced activation in the elderly in the hippocampal/ parahippocampal complex and in the retrosplenial cortex of the posterior cingulate. These areas play a critical role in spatial navigation in both human and non-human species (Barnes et al. 1983; Barnes et al. 1997; Shen et al. 1997; Tanila et al. 1997). In particular the hippocampal/parahippocampal area has been hypothesized to act as a cognitive map (O'Keefe and Nadel 1978), receiving egocentric and motion derived information from other cortical regions and converting this input into an allocentric representation of the environment. This suggests a divergence in the neural systems devoted to spatial navigation in young and elderly participants. It will be important for future studies to try to understand both the mechanisms and implications of the reduced medial temporal contribution to navigation in the elderly.

Among the possible cellular mechanisms underlying these findings are substantial age-related differences in the properties of hippocampal place cells (Barnes et al. 1983). Place cells are those neurons that respond when an animal is in a particular physical location in an environment (O'Keefe and Nadel 1978). These cells are highly plastic, change their firing characteristics in response to manipulations of external cues, and in combination with hippocampal grid cells are thought to be a key component of the cognitive mapping function of the hippocampus (Moser et al. 2008). Among the age-related alterations that have been reported in aged rats are that place cells fail to change firing patterns in response to being placed into a novel environment (Wilson et al. 2003); may switch between different spatial firing patterns upon repeated exposure to the same environment (Barnes et al. 1997); or may be delayed, relative to younger animals, in linking external environmental cues to spatial locations in a new environment (Rosenzweig et al. 2003). These observations, combined with the demonstration of the existence of human hippocampal place cells (Ekstrom et al. 2003), suggests that age-related differences in the cellular properties of the hippocampus/parahippocampal complex may play a role in age-related declines in navigational skill. Furthermore, both mesial temporal structures and the posterior cingulate region are affected early in the course of Alzheimer's disease (de Leon et al. 2001; Jack et al. 1997; Minoshima et al. 1994; Silverman 2004 but c.f. Sullivan et al. 2005), and reduced temporal and posterior cingulate metabolism are associated with the Apolipoprotein E epsilon 4 risk factor for AD (Reiman et al. 2001; Small et al. 2000) demonstrating that these regions are particularly vulnerable in neurodegenerative diseases associated with aging.

There is only very limited evidence from human research that specific age-related alterations in hippocampal neurochemistry may be relevant to understanding age differences in spatial navigation abilities. In a magnetic resonance spectroscopy study, it was found that the performance of older adults in a vMWT was associated with decreased NAA/Cre (N-acetyl-aspartate/creatine) ratios, a marker that is thought to reflect neuronal integrity (Driscoll et al. 2003). This study suggests that the biochemistry of the hippocampus may be an important component of age-related navigation decline and this warrants further investigation in future studies.

Extra-Hippocampal Contributions to Age Differences in Navigation

As the above review indicates, most attention in research on age differences in human navigation has focused on the role of the hippocampus and associated structures. This focus is justified in light of the prominent place of the hippocampus in models of human spatial and episodic memory and in animal models of spatial navigation. However, examination of findings from numerous neuroimaging studies reveals that navigation elicits activations in widespread regions of the cortex outside of the hippocampus. Currently, we know very little about the contributions of these extra-hippocampal regions. Behaviorally, it could be argued that navigation contains considerable executive and strategic demands in that successful navigation requires the selection of appropriate search strategies and also depends on appropriate behavioral monitoring and alterations of searching behavior if the selected path proves unsuccessful.

In addition, several behavioral observations suggest that the age-related behavioral deficits observed in the human analogs of the MWT cannot be fully accounted for by models of performance focusing exclusively on spatial memory. In particular, some studies have observed that healthy elderly perform more poorly than their younger counterparts *even on the first trial* (Driscoll et al. 2005; Moffat and Resnick 2002), which does not depend on memory for platform location. It could be hypothesized that the deficits observed among elderly participants in navigational behavior may be partially attributed to impaired executive and strategic functions which manifest as inefficient search strategies early in navigation performance tasks.

One structural neuroimaging study investigated correlations between grey and white matter volumes in several brain regions and performance on a vMWT in younger and older adults (Moffat et al. 2007). This study found that larger volumes of the lateral prefrontal cortex grey matter and white matter and caudate nucleus were positively associated with navigational skill. Interestingly, hippocam-

pal volume was positively correlated with navigational competence only in the young but not in the old, a finding which is supportive of the observations from fMRI studies showing reduced or completely absent hippocampal activation among the elderly (Antonova et al. 2009; Meulenbroek et al. 2004; Moffat et al. 2006).

Cumulatively, these studies strongly suggest that successful navigation in humans requires substantial contribution from prefrontal circuits and associated cognitive systems. Indeed, studies in non-human species confirm important contributions from pre-frontal systems in solving the MWT. One approach to investigating the respective roles of the frontal cortex and hippocampal system have been delineated by adopting both the place and response versions of the MWT. In the former, the platform remains in the same position while the starting location varies, thus requiring a place strategy for successful solution. In the latter, both the platform and starting location vary from trial to trial such that the spatial relationship between both the starting and goal locations are held constant (e.g. a fixed distance to the right). Several studies have reported double dissociations with hippocampal and or fimbria/fornix lesions impairing place learning in the MWT and frontal cortex lesions impairing response learning (de Bruin et al. 2001; de Bruin et al. 1997). A comparable study has not been done in humans, but these data illustrate one way in which an animal model could be applied to directly address an issue in the cognitive neuroscience of human aging.

In addition to contributions from prefrontal cortex to age differences in spatial navigation, the caudate nucleus also plays a critical role. Moffat et al. (2007) found that larger caudate nucleus volume was associated with better spatial performance in both young and old subjects. The caudate nucleus plays an important role in learning and spatial memory and is often activated in young subjects during virtual navigation tasks in functional imaging studies (Iaria et al. 2003; Maguire et al. 1998; Moffat et al. 2006). Because of its extensive connections with the pre-frontal cortex and hippocampus (Alexander et al. 1986) the caudate is a part of distributed fronto-striatal and striato-hippocampal systems, which are vulnerable to aging (Raz 2000; Raz et al. 2003). Studies investigating contributions of the caudate to human spatial navigation suggest that it may work in concert with hippocampal systems (Voermans et al. 2004) and may play a role in non-spatial or procedural response components of spatial behavior (Hartley et al. 2003; Iaria et al. 2003).

Navigation is clearly a complex cognitive skill that likely depends on other cognitive domains such as working memory, processing speed, and cognitive control. Thus, it is not surprising that both structural and functional imaging studies support a distributed network underlying performance. As more data accumulate, it will be critical to more

specifically identify the role that each neural structure or region plays in navigation and to further delineate how changes in these neural systems may manifest in the specific components and sub-processes responsible for age-related differences in spatial navigation.

Aging and Spatial Navigation: Where Do We Go?

The above review evaluated the evidence that aging is associated with declines in navigational ability and highlights what we know about the neural underpinnings of that decline. However, the field is still in its infancy in humans and there are several avenues of inquiry that could advance the field considerably. The next section outlines some of the major gaps in the literature and suggest ways in which these gaps may be filled.

Longitudinal Studies

The first and most obvious need in the field is for longitudinal research. As of this writing, there appears to not be a single longitudinal study published in the field. The existing cross-sectional studies produce large effect sizes and are highly consistent across studies and laboratories. Nevertheless, within the framework of a cross-sectional study it is impossible to discern the influence of life-long individual differences in brain and cognitive variables from true longitudinal declines. As well, a common observation in studies of navigation is that when sex differences are observed, men tend to outperform women (Astur et al. 1998; Driscoll et al. 2005; Moffat et al. 1998). Studies of sex differences have been done primarily in younger adults but it raises the issue of possible differential aging by sex. Cross sectional studies in older populations allow for a snapshot of sex differences but cannot resolve the issue of whether men and women may manifest different *rates* of navigation decline.

Strategies as Modifiers of Performance and Activation Patterns

As reviewed above, an important area of inquiry is to continue to understand hippocampal and extrahippocampal contributions to spatial navigation. One approach which is likely to lead to progress in this area is the consideration of participant *strategies* for solving navigation tasks. Two individuals with equivalent performance may reach a navigational goal through different ‘routes.’ Moreover, some navigation tasks clearly lend themselves to different solution strategies. Although researchers have described navigation strategies using variable nomenclature, the most common are egocentric, allocentric and possibly “non-

spatial.” Non-spatial strategies often act as a ‘catch-all’ classification for strategies that are otherwise unclassifiable. Examples of this might include circling or ‘zig-zagging’ through an environment to locate a goal.

Iaria et al. (2003) performed a well-designed study in which they investigated the effect of strategy on brain activation in fMRI in solving a place learning task. Only younger volunteers were used in this study. Participants were trained to use either spatial landmarks or a non-spatial strategy to navigate. Participants using a landmark-based strategy showed activation in the hippocampus while those using a non-spatial strategy showed activation in the caudate nucleus (Iaria et al. 2003). This study illustrates how individuals solving the same navigation task may show differential brain activation depending on the strategy adopted or required to solve the task. At present, there have been no studies in humans showing unequivocally that older individuals use different strategies in solving navigation tasks. However, the findings from neuroimaging studies have led to speculation that this is what underlies the differences in brain activation between younger and older adults. The absence of hippocampal and parahippocampal activation reported in older subjects (Antonova et al. 2009; Meulenbroek et al. 2004; Moffat et al. 2006) suggests that perhaps older subjects are not using hippocampal-dependent (i.e. allocentric) strategies.

Animal studies suggest that there are prominent age differences in preferred strategies. Barnes et al. (1980) performed an elegant strategy assessment in younger and older rats. Using a three-armed t-maze, rats were trained to locate a goal for reward. There were multiple ways in which the rat could learn the location of the reward. One possibility was an egocentric strategy in which the rat always turned left while another possibility was an allocentric strategy in which the rat moved to the same absolute location designated by external room cues. Barnes and colleagues tested this by rotating the maze following training and starting the rats in a different arm. Barnes et al. (1980) found that older rats were more likely to use an egocentric strategy to solve the maze while younger rats were more likely to use an allocentric strategy.

As noted above, there are currently no published studies empirically demonstrating that older human subjects actually do use different strategies. However, two published studies provide suggestive data. One study simply asked younger and older human participants how they solved a navigation task and found that self-reported allocentric strategy decreased with age (Driscoll et al. 2005). Although it is not ideal to use self report as it requires insight into one's own cognitive processes (i.e., metacognition) which itself decreases with age (Isingrini et al. 2008), this study suggests that older participants may adopt different strategies. In another indirect assessment of strategy in cognitive

mapping, it was found that age differences in a cognitive mapping task were maximal when objects were not present on the map and age differences were eliminated whenever proximal objects were present. This suggests that older participants may disregard distal geometric information in an environment and focus more on objects to guide navigation (Moffat and Resnick 2002). Interestingly, hippocampal lesions in rats result in impaired use of distal but not proximal landmarks (Save and Poucet 2000), raising the possibility that age differences in the human hippocampal activity may underlie age-related shifts in cue-use strategies.

Somewhat paradoxically, one logical possibility that emerges from the perspective that older participants prefer egocentric and/or non-spatial strategies is that navigation tasks may not be as hippocampally-dependent or sensitive in older adults as is presumed. Another important consideration is that if, in fact, older subjects do show age-related shifting of navigation strategies (and concomitant neural activations), it will be important to determine whether these alterations are adaptive and compensatory or suboptimal strategies that result in reduced performance.

Physiologic, Genetic and Other Modifiers of Performance

Among possible modifiers of age-related differences in spatial navigation that have been investigated are the effects of hypertension and other vascular risk factors. One study reported a statistical trend for normotensive older adults to outperform hypertensive older adults in the vMWT (Moffat et al. 2007). Similarly, a recent study found significantly poorer performance among older individuals with a diagnosis or history of hypertension compared to those without such a history (Deshmukh et al. 2009). This study further reported that those individuals with both hypertension and a genetic vascular risk factor associated with increased levels of homocysteine (T allele in a C677T variant in methylenetetrahydrofolate reductase (MTHFR) gene) performed more poorly than all other participants at all ages. These studies highlight the need to investigate vascular risk factors as modifiers or even a component of the causal mechanisms of age-related differences in spatial navigation.

In another study investigating physiologic factors that may modulate navigation performance, Driscoll et al. (2005) investigated the correlation between circulating testosterone levels and performance in a vMWT. They found that higher circulating T concentrations were associated with better performance among men but not women. There are numerous physiologic, metabolic, genetic and other factors that could potentially be used to predict navigation performance, and age-related changes in these factors could underlie the age-related navigation impairments.

Conclusions

In summary, there is good experimental evidence from both human and non-human species indicating robust age-differences in navigational skill. The neural systems activated by spatial navigation are widespread and constitute some of the neural systems that are affected earliest in both normal aging and in the neuropathology of Alzheimer's disease. The assessment of spatial navigation in the elderly may serve as a basis for early prediction of disease and may be a useful measure for assessment of outcomes of pharmacologic and/or behavioral intervention studies for cognitive impairment. Spatial navigation is a complex cognitive skill that depends on multiple cognitive processes including spatial skills, explicit memory, working memory and executive processes. However, the existence of head direction, place and grid cells strongly suggests that it also adds a unique assessment feature to the cognitive aging toolbox. It also assesses an important aspect of human cognitive function that has traditionally been neglected in studies of cognitive aging. Because the field is in a relatively early stage of development, there are many areas of research that could advance the field. Moreover, much of what we know about the neuroscience of cognitive aging comes from the use of animal models where behavioral assessments typically include measures of spatial navigation. Incorporation of navigational models into the evaluation of human cognitive aging provides a sound behavioral and neurological foundation to facilitate comparative research and ultimately aid in the development of advanced cross-species models of cognitive aging.

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