Neuroscience Research on Human Visual Path Integration: Empirical
Overview and Strategic Considerations

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Foreword / Disclaimer

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Abstract

Over the past two decades, many neuroimaging studies have attempted to uncover the brain regions and networks involved in path integration and identify the underlying neurocognitive mechanisms. Although these studies made inroads into the neural basis of path integration, they have yet to offer a full disclosure of the functional specialization of the brain regions supporting path integration. Henceforth, this paper reviewed notable neuroscientific studies on visual path integration (i.e., path integration based on information from visual/optic cues) performed with human subjects, identified the commonalities and discrepancies in their findings, and incorporated fresh insights from recent path integration studies. Specifically, this review paper presented neuroscientific studies performed with virtual reality (VR) variants of the triangle/path completion task and addressed whether or not the hippocampal formation is necessary for human path integration. Drawing upon a sizeable pool of empirical evidence showing (i) individual differences in path integration strategy use, (ii) critical roles of the hippocampus and entorhinal cortex in spatial computation and cognition, and (iii) complicated methodological issues in neuropsychological studies that can either credit or discredit medial temporal lobe (MTL) involvement in path integration, this paper proposes that the use of different path integration strategies may determine the extent to which the hippocampus and entorhinal cortex are engaged during path integration. To this end, recent studies that investigated the impact of different path integration strategies on behavioral performance and functional brain activity were discussed. Methodological concerns were raised with feasible recommendations for improving the experimental design of future strategy-focused path integration studies. Such studies can cover cognitive neuroscience research on age-related differences in the role of the hippocampal formation in path integration and Bayesian modelling of the interactive roles of landmark and self-motion cues. The practical value of investigating different path integration strategies was also discussed briefly from a biomedical perspective. Overall, this paper aims to educate and generate higher awareness among spatial cognition and navigation researchers about the most crucial cognitive and brain mechanisms supporting path integration, and the practical steps that can be done to further investigate such mechanisms from a strategic perspective.

Keywords: neuroscience, cognitive neuroscience, neuroimaging, fMRI, EEG, hippocampus, entorhinal cortex, path integration, spatial navigation, strategies

1 Introduction

2
3 In everyday contexts, whenever we have a destination in mind we want to travel to, we
4 rely on our innate adeptness for navigation, as typified by our cognitive ability to reason in
5 space, plan, and execute a path to our desired location [1]. Navigation generally occurs in the
6 presence of external cues that present themselves ubiquitously in the form of stationary
7 landmarks in our everyday environments but can also proceed when only internal bodily cues
8 are available (i.e., during non-visual self-locomotion) [2,3]. The process of estimating distance
9 and directional changes relative to a starting position and integrating such displacements with
10 self-motion cues to compute and update a homing vector is called *path integration* (also known
11 as *dead reckoning*) [1,4-10].

12 Path integration was first postulated to apply to humans by Darwin (1873) [11], who
13 recounted the remarkable feat in which the natives of North Siberia were able to chart direct
14 courses of return after meandering through icy plains without relying on any visible cues at sea
15 or in the sky, concluding that:

16
17 “We must bear in mind that neither a compass, nor the north star, nor any other such sign, suffices to
18 guide a man to a particular spot through an intricate country, or through hummocky ice, when many
19 deviations from a straight course are inevitable, unless the deviations are allowed for, or a sort of ‘dead
20 reckoning’ is kept.”

21 Darwin (1873, p. 418)

22
23 Subsequent empirical studies showed that this special “dead reckoning” ability is present
24 in a wide variety of animals, encompassing insects (e.g., honey bees, Saharan desert ants),
25 spiders, birds (e.g., pigeons, geese), and mammals (e.g., golden hamsters, gerbils, dogs, humans)
26 [1, 4, 5, 6, 7, 8, 10]. In the animal kingdom, the perfect example of the “path integrator” is
27 perhaps the Saharan desert ant, *Cataglyphis fortis*, which is capable of returning in a straight-line
28 path back to its nest after tracking a tortuous outbound path in a featureless landscape to find
29 food [9,12,13] (**Figure 1**). Based on the ant’s foraging and homing behavior, path integration
30 was proposed to enable the navigating animal to compute its movement changes continuously
31 along each step of its outbound journey and integrate such changes with idiothetic signals

(derived from the vestibular and proprioceptive systems) to update a *homing vector* (i.e., a representation of distance and directional estimates from a point of origin) (9).

To date, research on path integration continues to draw the attention of many researchers in spatial cognition due to the possibilities it offers for a better understanding of the basic neurocognitive processes or mechanisms that are involved in spatial perception and cognitive mapping [14-16]. Over the past two decades, many neuroimaging studies (fMRI, EEG) have attempted uncover the neural substrates or networks involved in path integration and pinpoint its underlying neural mechanisms. Although these studies made inroads into the neural basis of path integration, they have yet to offer a full disclosure of the functional specialization of the brain regions supporting path integration. Therefore, this paper aims at reviewing these neuroimaging studies on visual path integration (i.e., path integration based on information from visual/optic cues), identify the commonalities and discrepancies in their findings, and incorporate fresh insights from related research in spatial navigation to render an improved understanding of the brain mechanisms of path integration. Specifically, this review shall largely cover studies involving college-aged participants who performed virtual reality (VR) variants of the triangle completion task – a task that has been widely used to assess path integration in humans. It shall elucidate the methods and findings from notable studies, reveal the brain regions and networks that are commonly involved in visual path integration, and examine contentious pieces of evidence concerning medial temporal lobe (MTL) involvement in path integration. Drawing upon a sizeable pool of empirical evidence showing (i) individual differences in path integration strategy use, (ii) critical roles of the hippocampus and entorhinal cortex in spatial computation and cognition, and (iii) complicated methodological issues in neuropsychological studies that can either credit or discredit MTL involvement in path integration, this paper centrally proposes that the hippocampus and entorhinal cortex have important roles to play in the computation of homing vectors during path integration. Toward its end, recent fMRI findings were introduced to support this proposal that the differential involvement of these two brain regions in path integration could be influenced by the use of different spatial strategies, along with recommendations for methodological improvements in future attempts at investigating strategic influences on hippocampal and entorhinal activations (73). In addition, ideas for future neuroimaging research on visual path integration involving age group comparisons and a Bayesian modelling of visual and self-motion cues were also introduced. Overall, this paper aims

at generating awareness of the huge inroads made by neuroimaging research at giving us an understanding of the brain regions supporting path integration, and the practical steps we can do to further explore the brain mechanisms underlying path integration.

Figure 1. Path integration in *Cataglyphis fortis*. An ant's tortuous outbound path (from N to F) and straight homeward path (from F to N, in bold) recorded in a featureless salt pan [Source: Figure 1.1 in [12]. Reproduced with permission.]

Methods

Assessing Path Integration in Humans

The traditional behavioral paradigm used for studying path integration in humans is the path- or triangle-completion task [2,3,17-19]. The path completion task, originally developed by Klatzky et al. (1990) [2], requires a participant, donning blindfolds and headphones, to walk two or more straight segments with one or more turns in between under the guidance of the experimenter, and to walk back (or point back) to the origin on his/her initiative at the end of the outbound journey. Triangle completion (**Figure 2**) is the popular derivative of this path completion paradigm and refers to participants' attempts at returning to the origin (or pointing toward it) after traversing two straight segments with one turn (i.e., the whole trajectory forms a

triangle) [3,18-20]. Importantly, the donning of blindfolds and headphones throughout the task blocked out visual and auditory cues that could facilitate the updating of positional estimates and obliged the participant to attend to idiothetic cues from vestibular and proprioceptive systems (e.g., efferent motor commands, kinesthetic feedback from the musculature, acceleratory signals from the vestibular system) for a moment-to-moment updating of the perceived home or target location.

Figure 2. In a trial of the conventional triangle completion task, the participant traverses an outbound path (shown by dark arrows) and then attempts to walk back to the starting position with visual and auditory cues occluded (the dotted line segment shows the ideal/perfect path of return). Apart from walking responses, pointing or heading responses toward the point of origin have also been applied.

In the first extensive study that applied the triangle completion task, Loomis et al. (1993) showed that sighted participants who were blindfolded performed as well as their congenitally and adventitiously blind counterparts when walking back to the starting position at the end of outbound travel. No group showed particularly good performance and analyses of the distance and turning responses revealed *systematic errors* that depended on the types of path parameters. On average, the participants tend to over-rotate when small turns to the origin were required and to under-rotate when large turns were required (**Figure 3**). Similarly, the average participant also overshoot and undershot small and large return distances to the origin respectively. These regular patterns of errors have been found in numerous triangle completion studies conducted in both real-world [2,3,18,19, 21] and virtual reality settings [20,22-27].

Figure 3. Depictions of the triangular paths used by Loomis et al. (1993) [3] (A). X represents the origin of travel and the large dots (A, B) represent the termini of the two-legged outbound paths, each being 2, 4, or 6 m. The turn varied between 60, 90, and 120 degrees. Average performance of Loomis et al.'s (1993) participants (B). Small dots represent the centroids of the stopping points of 37 participants. The majority of these centroids did not coincide with X. [Adapted from Figure 5.3 in [5]. Reproduced with permission.]

The classical *configural encoding model* [28] explains these systematic errors of return as arising out of difficulties in generating a configural mental representation of the outbound path, and *not* when participants executed their homeward responses. An alternative mathematical model — the *leaky path integration model* [29-31] — proposes that the representation of distance is affected by two parameters: a (i) *leak rate* and a (ii) *gain rate*. The leak rate reflects the extent to which an integrated distance estimate decays over the length of locomotion whereas the gain rate describes the amount of distance that is added to the integrated distance estimate with each single step. Mathematically, as shown by Lappe and colleagues, all these can be formulated in the form of a differential equation and a function for a path-integrated distance $p(x)$:

$$\frac{dp}{dx} = -\alpha p + k \quad (1)$$

$$p(x) = \frac{k}{\alpha} (1 - e^{-\alpha x}) \quad (2)$$

In equation (1), dp denotes the change in the current perceptual position (i.e., change in the perceived distance travelled away from a point of origin), dx denotes the change of a subject's position along a path of travel. In equation (2), p denotes a path-integrated distance (i.e., a

perceived or estimated distance of travel) and x denotes the true or actual distance of travel. In both equations, α denotes the leak rate and k denotes the gain rate. With larger leak rates, the perceived distance p will become smaller than the true distance x , leading to an underestimation of distance travelled away from a point of origin, a well-known phenomenon that has been demonstrated experimentally [30,31].

Together, the leak and gain rate parameters in these two equations are critical for explaining the underestimation and overestimation of traveled distances [29-31]. When $k = 1$, optic flow information is transformed perfectly into the instantaneous travel distance. When $k < 1$ and $k > 1$, the length of the current step is underestimated and overestimated, respectively, in relation to the perceived visual information [31]. The leak rate α affects how much of the path-integrated distance is lost during movement along a path and tends to become progressively larger with longer distances away from a point of origin, leading to the underestimation of return distances after traversing relatively long outbound paths during triangle completion [25].

Notable Neuroimaging Studies on Visual Path Integration in Humans

Over the past two decades, there have been a series of neuroimaging studies that investigated the neural correlates of human path integration through virtual reality forms of the triangle completion task (for fMRI studies, see [23,27]; for EEG studies, see [32-36]). Unlike the behavioral studies on human path integration that excluded the availability of visual cues, participants performing virtual triangle completion in neuroimaging experiments receive full exposure to visual cues in the form of optic flow at the cost of having no proprioceptive or kinesthetic feedback due to the testing constraints of neuroimaging experiments that prevent locomotion. Consequently, participants performing triangle completion in virtual environments rely primarily on optic flow information when computing their homing responses at the end of outbound paths. Therefore, the performance of path integration in virtual reality (or in any desktop virtual environment) has been called *visual path integration* (24).

The common feature of all these virtual triangle completion tasks was the presentation of open plains [23,27] (**Figure 4**) or passageways [32-36] (**Figure 5**) that lacked any salient landmark or object cues. In such virtual environments, the perception of optic flow was rendered through experimentally controlled translations and rotations. In a typical path integration trial,

142 the participants experienced animated/passive travel either along the outbound path of a
143 triangular trajectory comprised of two straight segments with a turn in between [27,32-36] or
144 along the entire three segments of the triangular trajectory comprised of a homebound path in
145 addition to the outbound path [23]. The homing responses generally involve: (i) pointing back to
146 the starting position by deflecting the joystick [27], (ii) pressing buttons to adjust 3D homing
147 arrows [32, 33, 34, 35, 36], or (iii) pressing buttons to indicate whether or not they have
148 successfully returned to their starting position [23]. As for fMRI-based control trials, they varied
149 across studies from passive travels along straight paths [23,34-36] to along winding paths with
150 turns that differed from the turns in the test trials [27,33-35].

Figure 4. A ground-level view of the featureless virtual plain used by Wolbers et al. (2007) [27] and a schematic diagram of the outbound paths with turns that varied systematically in increments of 30° from 30° to 120° in both clockwise and anticlockwise directions. Each of the eight outbound paths were presented five times. The second segment after the turn was varied in length to keep the animation within a suitable temporal range for functional scanning. The participants pointed back to the perceived starting position at the end of travel along each outbound path. [Adapted from Figure 1 in [27]. Reproduced in compliance with the terms of Creative Commons Attribution License supported by *The Journal of Neuroscience* and the *Society for Neuroscience*.]

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Figure 5. The virtual tunnel task originally used by Gramann et al. (2005) [24] showing: (A - C) the first-person scenes during a typical tunnel passage along a straight segment along with a schema of the allocentric and egocentric return bearings, and (D, E) the two types of homing vectors that can be specified based on adjusting the 3D homing arrows at the end of the tunnel passageway. Panels F and G show the schematics of the mental representations of the allocentric and egocentric homing vectors.

[Retrieved from: <http://scn.ucsd.edu/~klaus/images/Description%20Strategy.pdf> (Reproduced with permission). To download an animation clip of a sample virtual tunnel trial, go to: http://scn.ucsd.edu/~klaus/download/tunnel_cat.mpg]

152

153 Distinct types of data analyses were applied to the respective neuroimaging studies. In the
 154 first fMRI study on visual path integration, Wolbers et al. (2007) [27] contrasted functional
 155 activity between path integration test and control conditions, followed by investigating how this
 156 contrast-based brain activation was modulated parametrically by homeward pointing responses.

In that study, the researchers devised a featureless plane with no objects set against a dark backdrop in a virtual environment. In the path integration trials, the participants were presented with eight outbound paths that varied according to turning direction after an initial forward translation (left vs. right) and rotational angle (30°, 60°, 90°, 120°) (**Figure 4**). The translation along the first segment of the outbound path was animated and fixed at the same distance across all trials (8.5 m). Similarly, the rotational movement and the translation along the second segment was animated. However, the translational distance of the second segment varied according to the time it took for the turn. This variability in the latter half of the outbound path was done to ensure each trial was performed within a fixed timeframe (11.9 sec). At the end of each animated path, the participants were instructed to make a directional decision that points back to the origin using a joystick within an interval of 5 seconds. Their responses were recorded in terms of pointing errors in degrees. Before the start of the path integration trials, participants performed training trials that resembled the path integration trials apart from an adjustment of the four angles of rotation to ensure a discrepancy in the required homing responses.

In the control task condition, identical visual stimulation were introduced to the exclusion of performing path integration, the participants were presented with trials with displays of arrows pointing 90° leftwards or rightwards for four seconds at the start of each control trial. They were instructed to memorize them and reproduce the directional response at the end of each outbound path (same as those used in the path integration trials) within 5 seconds. The directional arrows were made to always coincide with the body-centered direction back to the origin. To minimize the possibility that the participants engaged in path integration during the control task, the path integration and control trials were presented in equal proportions over two separate scanning sessions.

Behavioral findings from the path integration trials showed that participants tended to over-turn and under-turn small and large required pointing angles respectively. More pointing errors were committed in path integration trials than control trials. Interestingly, the pointing errors attributed to a turning angle of 120° (linked to a required pointing response of 103°) was particularly high. According to the authors, this probably reflects the participants' high uncertainty about the large rotation of 120° for estimating relatively accurate pointing responses.

As for fMRI findings, blood oxygen level-dependent (BOLD) contrast maps showed activations in the precuneus, subdivisions of the intraparietal sulcus, posterior middle temporal

gyrus, and superior frontal gyrus. Brain-behavior correlations showed negative correlations between pointing errors and activations in the right hippocampus and bilateral medial prefrontal cortex (BA9) during encoding of the outbound paths across subjects. Specifically, it is worth noting that the pattern of negative correlation found between absolute pointing errors and right hippocampal activation levels was unaffected by general performance levels, applying to both good and poor performers in visual path integration.

As for the EEG studies on visual path integration, they were mostly conducted using a virtual tunnel task that was proposed to be valid for assessing individual proclivities in the use of either an allocentric reference frame (akin to taking a third-person perspective that focuses on the processing of object-to-object spatial relations) or an egocentric reference frame (akin to taking a first-person perspective that focuses on the processing of self-to-object spatial relations) [24]. The virtual tunnel showcases animated motion from the first-person perspective through a dimly lit tunnel that contains one to three turns separated by straight segments of equal lengths. The angles of each tunnel turn were made to vary in a systematic fashion in order to chart out a predetermined set of eccentricities of tunnel end position relative to the start position. These eccentricities refer the bearing of the tunnel's ending position relative to the vertical north-bound axis passing through the starting position; they normally range between 15° to 90° in increments of 15° [24]. No proximal or distal landmarks were shown in the tunnel and the tunnel passage was intended to provide the navigator with sparse optic flow information that involved translational and rotational changes, and the rate of turning (**Figure 5A**). Similar to the animated motion clip presented by Wolbers et al. (2007) [27] in their triangle completion task, the absence of landmarks compelled participants to rely on optic flow to update their position and orientation and in the eventual computation of a homing vector. At the end of a tunnel passage in the experimental phase (**Figure 5C**), participants were shown a backward-pointing 3D arrow mounted on a cross and they have to rotate the vertical axis of the cross (i.e., by using the mouse) to indicate the angle of return to the starting point (**Figure 5D-E**). The response is recorded to the nearest degree and compared to the expected correct response (i.e., the accurate turning angle calculated by the experimenter) to derive the pointing error.

Depending on the reference frame that a participant adopted for the spatial representation of the tunnel passage, this backward-pointing response can vary between left and right quadrants. For instance, in a tunnel with a single turn to the right (**Figure 5a-c**), if a navigator engaged in

the egocentric reference frame to visualize the turn and subsequently imagined his bodily motion along the segment after the turn, he would represent the starting point as being behind him and to the right side of his body. Under this scenario, he would direct the apex of the 3D homing arrow *rightwards* according to an estimated angle that his body would need to turn in order to return (**Figure 5E**). However, if the navigator imagined the turn from an allocentric perspective, he would not have updated his bodily coordinates during the turn, and instead imagined the passage from an overhead view curving to the right. In this case, his final orientation at the tunnel's end would have remained unchanged and aligned with his orientation at the entrance of the tunnel, and he would imagine the starting point to be located in a southwest section of his third-person mental map. Therefore, he would direct the apex of the backward-pointing 3D arrow *leftwards* according to a Euclidean vector computed from Cartesian coordinates (**Figure 5D**).

EEG data collected from the virtual tunnel task were generally analyzed based on: (i) EEG current density reconstruction [34], and (ii) EEG independent component analysis (ICA) – a spatio-temporal filtering method that separates the far-field EEG potentials arising from synchronized cellular assemblies into spatially fixed but temporally separated processes [32-36] (for technical details of ICA, see [37-39]). Based on these EEG analysis techniques, a common set of brain regions was observed to be activated during virtual triangle completion across these studies; namely, the precuneus (BA 7), the retrosplenial cortex (RSC) [BA 29/30], and the middle frontal cortex (BA 6, BA 9). The precuneus was demonstrated to be more activated [as assessed through EEG source density and alpha desynchronization (i.e., decreased oscillation of the alpha frequency band, 8 – 13 Hz)] *before* and *during* the turning phase(s) of the outbound path among participants who preferred an egocentric/body-centered frame of reference for estimating their positional changes (“Turners”, **Figure 5G**) than among participants who preferred an allocentric/environment-centered frame of reference for estimating their positional changes (“Non-Turners”, **Figure 5F**) [32-36]. These findings implicated the precuneus as a key site for attending to optic flow information and integrating it with egocentric positional estimates. Conversely, when Non-Turners were compared with Turners, higher alpha desynchronization in the right precuneus/posterior parietal cortex was observed during the turning phase of an outbound route [33,35]. This suggested that the right precuneus/posterior parietal cortex could also be involved in directing information about egocentric directional changes to the construction of an allocentric representation of the outbound path [33].

Similarly, Lin et al. (2015) [33] showed that alpha desynchronization in the RSC was higher in Non-Turners than in Turners *before* and *after* the turning phase, whereas alpha power increases in the RSC was higher in Turners than in Non-Turners during the turning phase. Crucially, the researchers showed that RSC event-related spectral perturbations (ERSPs) [i.e., power frequencies of brain waves] during separate path integration phases covaried differently with the pointing errors committed by Non-Turners. Specifically, Non-Turners' pointing errors covaried negatively with the ERSPs recorded before and after the turn but positively with the ERSPs recorded during the turn. Based on these findings, the RSC was proposed to be involved in two types of cognitive processes: (i) the integration of ego-motion information with allocentric reference frames (e.g., boundaries of the virtual environment) during forward translations (before and after the turn), and (ii) the computation and tracking of allocentric headings during turns. The second part of this proposal was supported by subsequent fMRI findings showing that the RSC played a specific role in processing rotational changes during virtual motion [40].

Unlike the precuneus and RSC whose activations are influenced by the type of spatial reference frame that one prefers, activation in the middle frontal cortex (BA 6 and/or BA 9) has consistently been found to occur during the turning phase of the outbound path regardless of the preferred type of spatial reference frame (for variation in EEG current densities, see [34]; for variation in theta band synchronizations (4 – 8 Hz ERSPs), see [32-36]). These findings suggested that a principal role of the middle frontal cortex in visual path integration lies in monitoring changes in virtual movements [35,36]. This interpretation paralleled Wolbers et al.'s (2007) view that the medial prefrontal cortex is crucially involved in maintaining spatial information in working memory for the subsequent computation of homing responses [27].

Involvement of the Hippocampus in Path Integration: Contentious Findings from Rats and Humans

The hippocampus is a key component of the medial temporal lobe (MTL) that has long been seen as being functionally relevant for cognitive mapping [41] and the strategic control of attention and memory processes in spatial navigation [42]. More specifically, the hippocampus is made up of two parts: the hippocampus proper, which comprises four *Cornu Ammonis* (CA) subfields, and the dentate gyrus [42]. These two parts, together with the subiculum,

presubiculum, parasubiculum, and the entorhinal cortex, constitute the *hippocampal formation* [43].

Positive Findings

Behavioral neuroscience studies on the foraging behavior of rats have generally linked the hippocampus to path integration [44-46]. Notably, Whishaw et al. (1997) [45] argued that one of the specialized functions of the hippocampus pertains to coding for idiothetic information (e.g., efferent signals to the musculature, afferent proprioception from the muscles and joints) and channeling such information toward the optimal processing of allothetic information (e.g., visual, auditory, olfactory cues). Specifically, the relevance of the hippocampus for path integration was demonstrated by random and inaccurate homing responses of rats with fornix-fimbria lesions [47-50]. Unlike the control rats (with intact hippocampus) who found their way back to home locations under both light and dark (or blindfolded) conditions, fornix-fimbria lesioned rats returned home successfully only when allothetic cues were available (e.g., in a lighted room with visual cues). In addition, fornix-fimbria lesioned rats became disoriented or took suboptimal return paths when restricted to idiothetic cues [47,48], and perseverated in returning, under both light and dark conditions, to a refuge location that was used for training purposes [49,50]. Overall, these findings gave the earliest support for the pertinence of the hippocampus for path integration. Ostensibly, lesions to the fornix-fimbria fibers impaired spatial learning that came under the influence of idiothetic signals from the vestibular and proprioceptive systems.

As for human subjects, the aforementioned fMRI findings by Wolbers et al. (2007) [27] showing negative correlation between visual path integration pointing errors and right hippocampal activation implied that the hippocampus was involved in integrating distance and direction signals for updating the coordinates of the starting position during spatial displacements. Subsequent region-of-interest (ROI) analysis performed by Chrastil et al. (2016) [40] focusing on the hippocampus supported this interpretation by showing that bilateral activation in the anterior hippocampus (in the same areas as those found by 27) correlated positively with the magnitudes of translations and rotations that were encoded accurately during virtual motion episodes.

Furthermore, several neuropsychological studies showed that epileptic patients with right hippocampal resections demonstrated deficiencies in path integration with regard to estimating (i) the distances from the starting position during blindfolded walking [51] and (ii) the angle-of-return (i.e., homing vector) during triangle completion [52]. In addition, recent research on wayfinding (i.e., goal-directed navigation to places that are beyond the sensory horizon, see [53], for a review) in virtual environments implicated that the hippocampus was involved in: (i) a continuous tracking of distances to a goal location as perceived from the egocentric/first-person perspective [54,55], (ii) navigating to previously observed targets under the influence of salient optic flow information and top-down signals from the medial frontal cortex [56], and (iii) flexible navigational decision-making at intersecting hallways [57]. Altogether, these findings support the notion that the hippocampus is a key brain region involved in path integration and common spatial navigation activities.

Negative Findings

Despite these positive findings, there were several notable studies that showed findings negating the relevance of the hippocampus for path integration [23, 58-60]. Alyan & McNaughton (1999) [58] showed that hippocampectomized rats with lesions in the dorsal and ventral regions of the hippocampus could perform a path integration task as well as healthy control rats. Likewise, neuropsychological studies involving human subjects showed that amnesic patients with lesions in the hippocampus and adjacent regions in the MTL performed as well as healthy control subjects in a blindfolded return-to-origin task [59], and in a pointing-back-to-the-start task at the end of an outbound path [60].

Moreover, an fMRI study by Arnold et al. (2014) [23] that required participants to estimate return/homebound path distances during virtual triangle completion showcased activations over a wide range of brain regions that excluded the hippocampus. The authors attributed the lack of hippocampal involvement to the possibility that the hippocampus may be more relevant for tracking the starting position prior to return than for tracking the entire triangular route, and that hippocampal activation may be more influenced by directional estimates than distance estimates. Regardless of the reason for the absence of hippocampal involvement in path integration, all of these studies suggested that the hippocampus is *not*

essential for determining homing responses, and that extrahippocampal areas and neural circuits involved in cognitive control, spatial attention, and working memory are more likely to constitute a neural system that supports path integration.

Re-examining the Contentious Findings over Hippocampal Involvement in Human Path Integration

Due to these contentious findings over the involvement of the hippocampus in human path integration, differences in methodology, framed in terms of experimental design and subject characteristics, must be considered. Starting with Arnold et al.'s (2014) study [23], the participants experienced animated motion along all three legs of a triangular path and were instructed to decide whether the return path's distance was more (or less) than its actual distance based on one of two button presses. Unlike the traditional triangle completion task which involved either walking or pointing back to the origin, each of which generated a continuous measure of accuracy, Arnold et al.'s (2014) path integration task involved a binary decision-making of the return path distance – whether it matched (or mismatched) with their estimated return distance (**Figure 6**). This characteristic makes it hard for one to infer whether or not the judgment of the return vector is comparable to the spatial processes involved in a mental updating of the starting position during travel along the outbound path. This spatial updating mechanism in visual path integration was originally proposed by Wolbers et al. (2007) to represent the function of the right hippocampus [27]. It is likely that the transformation of the original triangle completion paradigm into a task wherein the participant had *no control* over the trajectory of the return path diminished the amount of cognitive effort directed toward the spatial updating of the starting position, culminating in the absence of hippocampal activation.

Figure 6. (A) A first-person view of the featureless virtual plain implemented by Arnold et al. (2014) [23] for triangle completion. (B) The participants performed estimations (E) of the return distance to the start (S) based on three categories of triangular paths reflecting an overshoot, undershoot, and matching of the estimated endpoint in relation to the starting position. The participants pressed one of two buttons indicating whether the animated return path's distance matched (or mismatched; either overshoot or undershot) their estimated return distance. [Adapted from Figure 1 in [23]. Reproduced in compliance with the terms of Creative Commons Attribution License supported by Frontiers Media SA.]

In the two neuropsychological studies that called into question the involvement of the hippocampus in path integration [59,60], memory-impaired patients and healthy control subjects were tested under blindfolded condition using path integration tasks that required walking back to the starting position after a self-directed search of target objects (i.e., tiles on the floor) [59], and pointing back to the starting position after traversing outbound paths with one or two turns [60]. In view of non-significant group differences in performance, the authors of both studies stressed the importance of working memory for carrying out the essential spatial computations during path integration and proposed that the MTL may be more involved in converting information from spatial perception into long-term memory than in processing information directed to path integration *per se*.

However, a detailed examination of the patient profiles suggested caveats to this conclusion. Although all patients experienced large degrees of hippocampal volume loss that reflected a substantial depletion of hippocampal neurons, lesions to the adjacent entorhinal cortex or subiculum was not common to all [59,60]. The entorhinal cortex is a vital subregion of the hippocampal formation that was found to contain grid cells with hexagonally arranged firing fields that topographically map onto the geometric surface of the environment in both rats [61, 15, 16] (**Figure 7A**) and humans [62,63] (**Figure 7B**). Crucially, these grid-like firing patterns were proposed to be coincident with an online computation of positional and directional estimates during events involving path integration [64], wayfinding [54,65] and spatial orientation [66]. Compared with severely amnesic patients that have more than 90% reductions

in hippocampal and parahippocampal volumes (one patient in [59] and two patients in [60s]), three moderately amnesic patients in Shrager et al.'s (2008) study [60] had bilateral hippocampal volume reductions of 46%, 48%, and 49%, respectively, and four moderately amnesic patients in Kim et al.'s (2013) study [59] had bilateral hippocampal volume reductions of 35%, 46%, 48%, and 49%. Interestingly, based on a cross-species comparison, these magnitudes of volumetric reduction are comparable with those in hippocampectomized rats that demonstrated similar levels of path integration performance as healthy control rats [58]. The brain lesioned rats had their dentate gyri and CA3 regions spared compared with the wild-type control rats.

More importantly, it is worth noting that all moderately amnesic patients in both Shrager et al.'s (2008) and Kim et al.'s (2013) studies did *not* have large bilateral reduction that are more than 50% of the volume of the parahippocampal gyrus, a region whose rostral part comprises the entorhinal cortex. Compared with healthy controls, the patients experienced between 5% to 17% reduction in the volumes of their parahippocampal gyri. Therefore, it is very likely that large parts of the entorhinal cortex remained intact in these patients, and that might have enabled them to generate relatively accurate directional [60] and Euclidean distance-to-goal estimates [59].

Figure 7. (A) Firing fields of a cell recorded in layer II of the dorsocaudal region of the medial entorhinal cortex (dMEC) in a rat during 30 min of running in a 2 m wide circular enclosure. ‘t’ represents ‘tetrode’ while ‘c’ represents ‘cell’. Left panel: Locations where neuronal spikes were recorded (red), superimposed over the rat’s trajectory (black). Middle panel: Color-coded firing rate map. Red indicates peak firing while dark blue indicates zero firing. Right panel: Spatial autocorrelation of the cell’s firing activity. Color ranges from blue ($r = -1$) to green ($r = 0$) to red ($r = 1$). [Adapted from Figure 1 in [15]. Reproduced with permission.] **(B)** The activity of a cell in the left entorhinal cortex of a human subject. Left panel: Overhead view of the environment, with color representing the firing rate (in Hz) at each virtual location. Middle panel: Spatial autocorrelation of the cell’s firing activity. Peaks in the autocorrelation function determined the spacing and angle of the fitted grid, which was then used to plot the estimated grid peaks (white cross) across the entire environment. Right panel: Neuronal spike waveform. [Adapted from Figure 2 in [63]. Reproduced with permission.]

Moreover, Shrager et al. (2008) [60] encouraged their participants to actively maintain the outbound path in mind during each trial – a potential strategy-inducing procedure that was *not* attempted in any previous studies on path integration [2,3,5,18,20,51,52]. This led to two

severely amnesic patients (with an average bilateral volume reduction in the hippocampus and parahippocampal gyrus that exceeded 90%) and four control participants reporting attempts to continuously track their position and update it relative to the starting position as they moved. The two severely amnesic patients performed as well as the four control subjects when pointing back to their starting positions immediately at the end of outbound travel. However, these two patients performed significantly poorer than the control subjects after a period of distraction; this suggested that an intact MTL might be necessary for long-term maintenance and retrieval of path integration-related spatial information.

On the other hand, neuropsychological studies which supported the involvement of the hippocampus in human path integration [51,52] recruited epileptic patients that had resections of the entire entorhinal cortex and amygdala, and resections of approximately half [51] to two-thirds [52] of the hippocampus. Apart from the removal of brain areas that exceeded the extent of lesioned sites in the memory-impaired patients tested by Shrager et al. (2008) [60] and Kim et al. (2013) [59], Philbeck et al. (2004) [51] and Worsley et al. (2001) [52] also recruited relatively more patients that counterbalanced the number of control subjects. Specifically, Worsley et al. (2001) [52] tested 33 patients (16 with right temporal lobectomy; 17 with left temporal lobectomy) versus 16 control participants. Likewise, Philbeck et al. (2004) [51] tested 18 patients (10 with right temporal lobectomy; eight with left temporal lobectomy) versus 10 control participants. In general, the findings showed that epileptic patients with right temporal lobectomy were the poorest performers in the path integration tasks.

Specifically, in the path integration task whereby participants have to walk blindfolded to a previously seen target object (i.e., a cone) placed 5 m away from the starting position, Philbeck et al. (2004) [51] showed that right temporal lobectomy patients overshot the target location to a significantly larger extent than both left temporal lobectomy patients and control participants. Likewise, in a triangle completion task, Worsley et al. (2001) [52] showed that right temporal lobectomy patients overshot the required return distance and exhibited bigger angles-of-return than both left temporal lobectomy patients and control participants. Unlike Shrager et al.'s (2008) experimental protocol [60], no instructions were given to the patients about keeping the outbound path in mind as they walked. Overall, both studies by Philbeck et al. (2004) [51] and Worsley et al. (2001) [52] were similar in: (i) testing patients with resections of both the hippocampus and the entorhinal cortex, (ii) having a relatively large and balanced ratio of

patients and controls, and (iii) having no instructions that could unexpectedly induce the use of specific strategies. Thus, one could argue that their findings offered a more convincing picture of MTL's role in path integration.

Clarifying the Roles of the Hippocampus and Entorhinal Cortex in Human Path Integration through the Use of Different Strategies

The empirical literature discussed thus far provided pieces of evidence that both supported and negated the relevance of the hippocampus for human path integration – and this begs the question of whether or not activation in the hippocampus and entorhinal cortex could be induced using different path integration strategies. In the context of the wider spatial navigation literature, I associate the term “strategy” with the cognitive style or mental imagery technique a moving agent utilizes when deciding on and travelling to a destination in mind [21,67-71]. In view of past findings showing that different types of navigation strategies predisposed their users to acquire different kinds of cognitive maps from the first- (egocentric) and third-person (allocentric) perspectives [67-70], and that a plethora of perceptual and cognitive subprocesses (or “sub-strategies”) composed the statistical dimension representing a particular strategy type [67-70], I propose that the study of different navigation strategies can offer spatial navigation researchers better clues for understanding individual differences in hippocampal or MTL engagement during path integration.

To my knowledge, as of now, there has only been three studies to date that investigated path integration strategies in the context of the triangle/path completion paradigm [21, 72, 73]. All three studies investigated path integration in the form of two types of spatial updating strategies that differ in the computational timing of the homing vector. Specifically, these two strategies refer to: a (i) *continuous updating strategy* focusing on keeping track of the start position at all times along the outbound path (i.e., moment-to-moment updating) in order to maintain a constantly updated homing vector (for more details, see [21]); and a (ii) *configural updating strategy* focusing on encoding the shape of the outbound path and computing homeward responses based on the encoded mental image. Based on the conceptual framework set forth by Wiener et al. (2011) [21], continuous updating is an *online* process whereby the homing vector is computed continuously during navigation to the exclusion of a need for visualizing the shape of the outbound path, while configural updating is an *offline* process

whereby the homing vector is computed at the end of the outbound path based on an encoded representation of the path. In the sections below, the experimental design and results from the two behavioral studies conducted by Wiener et al. (2011) [21] and He and McNamara (2018) [72] are discussed first prior to those from an fMRI study done by Zhong (2019) [73], as the latter was inspired by the implications derived from these two earlier works.

Results

Behavioral Findings of Wiener et al. (2011) [21], He and McNamara (2018) [72]

Based on a real-world triangle completion task, Wiener et al. (2011) [21] instructed their participants ($n = 15$) to apply the continuous and configural updating strategies *in sequence* over two counterbalanced blocks of outbound paths (**Figure 8A**). This means that a fully within-subjects design was used that same group of participants were tested in the use of both strategies. The differences in homing performance arising from the use of these two strategies were exhibited in terms of head orientation and corresponding path integration errors. When the participants applied configural updating, they showed little head movements when traversing both segments of the outbound path. By contrast, when they applied continuous updating, they were strongly biased to turning their heads in the direction of the starting position as they walked along the second segment of the outbound path after the turn. Regardless of the length of the outbound path, the participants took longer time in attempting to return to the perceived starting position when they applied configural updating than when they applied continuous updating. However, path length mattered with regard to distance and angular measures. After traversing longer outbound paths (mean length = 15.3 m, mean turning angle = 148°), the participants committed lower magnitudes of direction errors, distance errors, and homing errors (**Figure 8B**) when they applied configural updating than when they applied continuous updating. The differences in the commission of errors between the two strategy conditions were smaller after traversals on shorter outbound paths (mean length = 8.3 m, mean turning angle = 101°) than after traversals on longer outbound paths. Overall, these findings showed that the use of two different path integration strategies generated contrasting patterns of path integration performance.

Figure 8. (A) A schematic diagram of the real-world outbound paths used in the triangle completion task of Wiener et al. (2011) [21]. (B) Three path integration error variables used by Wiener et al. (2011): (i) *Direction error*: the difference between the expected and actual angle-of-return; (ii) *Distance error*: the difference between the expected and actual linear distance/path of travel; and (iii) *Homing error*: the Euclidean distance between the starting and stopping position. [Adapted from Figure 1 in [21]. Reproduced with permission.]

499

500 To confirm the findings of Wiener et al. (2011) [21], He and McNamara (2018) [72]
 501 performed a VR study that combined self-locomotion in both real-world and virtual
 502 environments (i.e., updating of VR scenes in a head-mounted display with each forward leg
 503 movement in real physical space) and extended the differential application of these two strategies
 504 to judgments of relative directions (JRDs) between virtual objects arranged in a geometrically
 505 regular layout. Unlike Wiener et al. (2011), who instructed each participant on both strategies,
 506 the researchers tested two groups of participants, each instructed in the use of one strategy only.
 507 Configural updating strategy users were instructed to “mentally draw” out a path that connected
 508 three virtual posts whereas continuous strategy users were instructed to update their position and
 509 orientation continuously with respect to a red virtual post appearing close to the starting position.
 510 Results showed that configural updating strategy users committed significantly *fewer* errors
 511 when their final heading directions (i.e., head orientation at the end of the outbound path when
 512 facing a third virtual post) were aligned a North-to-South principal reference axis that aligned
 513 with their initial heading direction than when their heading directions were misaligned with this

514 reference axis (**Figure 9**). This behavioral pattern did not apply to the continuous strategy users,
515 who demonstrated comparable levels of pointing errors regardless of whether or not their final
516 heading directions were aligned with the principal reference axis. These findings suggested that
517 configural updating strategy users retrieved information about spatial locations with referral to an
518 allocentric reference frame that organized objects in a North-to-South orientation that paralleled
519 their initial heading direction. By contrast, continuous strategy users were inattentive to the
520 allocentric layout of the virtual objects and most likely depended on egocentric cues or reference
521 frames when making their pointing responses.

Figure 9. A schematic diagram of the locations of the virtual posts used by He and McNamara (2018) [72] in their immersive virtual environment. Configural updating strategy users committed significantly lower degrees of pointing errors when their final heading direction at end of outbound travel ran parallel to the North-to-South reference axis (compare black dashed line and red arrow) than when their final heading direction was misaligned with the same reference axis (compare black dashed line with blue arrow). Dashed grey lines show the pointing directions back to the first virtual post (no. 9) from the final virtual posts (nos. 8 and 12) reached by a moving participant. Note that the examples given here are for an illustration of concepts and did not reflect two actual experimental trials. [Adapted from Figure 2 in [72]. Reproduced with permission. Lines and arrows were added by the author.]

522

523 Implications

524

525 In retrospect, by comparing Wiener et al.'s findings with the neuropsychological studies
 526 conducted by Shrager et al. (2008) [60] and Kim et al. (2013) [59], it seems possible that their
 527 amnesic patients might have preserved the ability to implement some form of spatial strategy
 528 resembling the continuous updating strategy. As moderately amnesic patients from both studies
 529 were reported to have largely intact entorhinal cortices, Zhong (2019) [73] hypothesized the
 530 entorhinal cortex as the key MTL region associated with continuous updating strategy use. This

proposal was supported by previous studies implicating that the entorhinal cortex is involved in the online computation of: (i) Euclidean distances toward distal locations [54, 65], (ii) linear distances toward a point of origin [74], and (iii) intended geocentric directions to target objects [66]. Most probably, these online vector computations are dependent on the spatially stable firing patterns of entorhinal grid cells [15,61,63,75,76]. With firing fields that represent the vertices of tessellating triangles arranged in a hexagonal lattice, a common spatial metric with the same scale and orientation is maintained across the geometric surfaces of different environments [15, 77]. This uniform distribution of firing fields of grid cells can be conceived as neuronal nodes in a mapping of topographical space to mediate the continuous updating of positional or locational changes [77]. Importantly, the multi-peaked firing pattern exhibited by grid cells does *not* need reciprocal inputs from the hippocampus to maintain the number of firing peaks and the size or scale of the firing field, implicating that spatial information about self-movements can be expressed primarily by the entorhinal cortex [61]. This might explain why Shrager et al.'s (2008) amnesic patients (with largely intact entorhinal cortices) can perform as well as the control subjects despite experiencing hippocampal atrophy [60].

On the other hand, MTL resections in the epileptic patients [51, 52] might have abolished or complicated the use of a path integration strategy resembling configural updating strategy. This could be seen from the finding of Shrager et al.'s (2008) amnesic patients being unable to conduct homeward pointing as well as the controls after a period of distraction (see Experiment 5 in [60]), which implicated certain deficits in encoding or accessing offline representations of outbound paths. Putatively, such mental representations can be formed in an allocentric format, as shown by He and McNamara (2018) [72], and it is possible that these amnesic patients encountered difficulties in the configurational learning of outbound paths. As such, Zhong (2019) [73] hypothesized the hippocampus as the key MTL region associated with configural updating strategy use. The basis for this hypothesis is also supported by O'Keefe & Nadel's (1978) cognitive map theory [41], which proposed the hippocampus as the neural substrate for storing an allocentric spatial representation of the environment, as well as by numerous empirical findings that posited a pivotal role of the hippocampus in cognitive mapping and spatial memory formation [50,78-82].

fMRI Findings of Zhong (2019) [73]

Set on the aims of testing the hypotheses mentioned above, Zhong (2019) [73] conducted an fMRI experiment using a virtual path integration task that was programmed with animated outbound paths that presented the participant with passive traversals of short routes (**Figure 10**). At the end of such passive travels, the participant maneuvered a joystick and attempted to find a direct path back to the starting position within a short period. This phase pertained to homebound travel and path integration error variables identical to those used by Wiener et al. (2011) [21] (**Figure 8B**) were automatically recorded at the end of the homebound path.

Prior to the fMRI experiment, path integration practice and test/training sessions were held for 50 college-aged participants in an experimental lab (Study 1 in [73]). These participants were separated into two groups taught to use continuous updating and configural updating strategies, respectively, based on detailed instructions provided by the experimenter. In brief, 24 continuous updating strategy users (11 females) were taught to continuously monitor their changing positions relative to the starting positions whereas 26 configural updating strategy users (11 females) were taught to visualize the overall shape of the traveled path from an aerial perspective. Each group of participants practiced using the learned strategy in the vicinity of the lab as well as on the computer. On the computer, practice trials of the virtual path integration task featured arrows on the ground that pointed out the paths of travel and an orange cone that marked the starting position (**Figure 10B**). These navigational cues were programmed to vanish successively over the trials (for details, see Methods of Study 1 in [73]). Overall, the practice task served the important purpose of familiarizing participants with the challenging demands of visual path integration – ensuring that they had some experience with strategy practice in the absence of navigational cues prior to formal strategy testing/training.

In the strategy test/training session that followed, the biological sex of the participant was found to be a significant moderator of strategy use, with male configural updating strategy users scoring significantly lower homing, absolute direction, and signed distance mean errors than female configural updating strategy users. Strategy group differences in performance were found only among the female participants, with female continuous updating strategy users scoring significantly lower homing and signed distance mean errors than female configural updating strategy users.

592

Figure 10. (A) A schematic diagram of the animated outbound paths designed for the path integration trials in Zhong's (2019) fMRI experiment [73]. These outbound paths differed from those used in pre-fMRI strategy training. Simple paths (one turn each; 1a to 1d) are colored in red whereas complex paths (two turns each; 2a to 2d) are colored in blue. Paths 2a and 2b depict unidirectional complex paths (two turns in the same direction) while paths 2c and 2c depict the bidirectional complex paths (two turns in opposite directions). Passive travel over the simple and complex paths each lasted 8.0 and 10.0 seconds. Homebound travel in compound trials lasted 10.0 seconds at the end of each outbound path (Source: Figure 6D in [73]).s **(B)** First-person screenshots of the practice and test environments set in a virtual desert-like plain with a starry night sky. Overhead recordings of the animated outbound path and the homebound path travelled by each participant was automatically registered at the end of each trial. [Image accessible at: <https://www.silc.northwestern.edu/virtual-path-integration-task/> Reproduced with permission.]

A **B**

593

594 In the fMRI experiment that commenced after the completion of in-lab strategy practice
 595 and testing (Study 2 in [73]), a separate set of outbound paths (**Figure 10A**) differing in the
 596 length of the first path segment and turning magnitudes were used. 38 participants who

completed in-lab strategy practice and testing were involved in this experiment. There were 19 participants per strategy group. Trial presentation was different from that used in pre-fMRI testing such that it followed an event-related *partial trial design* (for details of how it was modeled and used previously, see [83-85]) featuring *compound trials* with both outbound and homebound paths (like the regular in-lab test trial) and *partial trials* featuring outbound paths only. The mixing of compound and partial trials in a 3:1 ratio and with jittered inter-trial intervals allowed a close examination of the brain regions activated during separate phases of outbound and homebound travel.

Region-of-interest (ROI) analysis circumscribed within the anatomical boundaries of hippocampus and entorhinal cortex showed significant activation in the left entorhinal cortex among continuous updating strategy users based on a linear subtraction of homebound BOLD activation coefficients of simple paths (each featuring one turn in the outbound phase, **Figure 10A**) from those of complex paths (each featuring two turns in the outbound phase, **Figure 10A**) [complex - simple] (**Figure 11**). Based on this contrast, marginally significant homebound activations in the left hippocampus in both strategy groups were also found (**Figure 12**). During the homebound phase of simple paths, whole-brain analysis showed that the two groups of strategy users exhibited common patterns of activations – in the left parietal cortex – and deactivations – in the parts of the default mode network that comprised the medial PFC and lateral temporal lobe. Brain-behavior correlational analysis further associated individual variation in path integration performance with functional activity changes in the occipito-parietal and inferior frontal regions, but *not* in the hippocampus or the entorhinal cortex. In addition, it must be noted that like the pre-fMRI test results, there was no significant main effect of strategy use. This null effect paralleled the absence of any significant differences in BOLD activation levels (both phase-specific and contrast-related) between the two groups of strategy users.

Figure 11. Significant activation in the left entorhinal cortex (28 voxels) among continuous updating strategy users based on a contrast of activations between simple and complex homebound phases [complex - simple]. Cross hairs were centered on the peak voxel of activation [$x = -18$, $y = -18$, $z = -26$]. The ROI-based activation map was overlaid on a high-resolution Montreal Neurological Institute (MNI) anatomical template. L = left hemisphere; R = right hemisphere. [Adapted from Figure 15 in [73]. Image is a higher-resolution version of the original.]

Continuous Updating Strategy Users

Figure 12. Marginally significant clusters of activation in the left hippocampus among (A) continuous updating strategy users (17 voxels) and (B) configural updating strategy users (18 voxels) based on a contrast of activations between simple and complex homebound phases [complex - simple]. Cross hairs were centered on the peak voxel of activation in each group of strategy users [continuous updating strategy: $x = -24$, $y = -12$, $z = -20$; configural updating strategy: $x = -30$, $y = -12$, $z = -14$]. The ROI-based activation map was overlaid on a high-resolution Montreal Neurological Institute (MNI) anatomical template. L = left hemisphere; R = right hemisphere. [Adapted from Figure 16 in [73]. Image is a higher-resolution version of the original.]

Continuous Updating Strategy Users

A

Configural Updating Strategy Users

B

More Implications

The detection of significant contrast-related activation in the left entorhinal cortex during continuous updating strategy use in the homebound phase was suggested to reflect a metabolic manifestation of underlying changes in the firing patterns of entorhinal grid cells in response to an alteration of homing responses between simple and complex paths [64,86,87]. Specifically, Zhong (2019) [73] speculated that attention to the demands of continuous updating strategy might have induced a rescaling of grid cell firing fields or phases when switching between

exposures to simple and complex outbound paths, and this neurophysiological change might have manifested itself hemodynamically in the form of greater entorhinal activation during the complex homebound phase than during the simple homebound phase.

As regards to the presence of hippocampal activations in both groups of strategy users, they showed that the involvement of the hippocampus was not specific to the use of only one type of path integration strategy. As these activations were not fully significant at the cluster-wise threshold of $p = .05$, the findings were interpreted to suggest that the hippocampus harness the potential of being involved in detecting variations in homing responses between simple and complex paths.

Rather than showing the hippocampus as the lead actor in successful path integration performance, the findings generally showed that extrahippocampal processes related to executive functioning, attention, and perception – brought forth by functional activity changes in the anterior cingulate gyrus, inferior frontal gyrus, precuneus, and cuneus (see also [71], for other relevant extrahippocampal brain regions) – were of higher priority in contributing to accurate visual path integration performance.

Discussion

Future Directions

Methodological Concerns and Suggested Improvements

To date and to my knowledge, Zhong's (2019) fMRI experiment [73] was the first neuroimaging attempt at investigating the impact of two types of spatial strategies on visual path integration. The presence of contrast-based activations in the left entorhinal cortex (in continuous updating strategy users) and left hippocampus (marginal significant in each group of strategy users) suggested that these two MTL regions may have pivotal roles to play in detecting switches in homing decisions or responses after traversing outbound paths of different complexity. As the original aims were to uncover whether these two MTL regions were activated during two specific path integration phases (outbound and homebound), the contrast-related findings were quite unexpected. To clarify that path complexity is indeed an important variable of concern for entorhinal and hippocampal engagement, future fMRI studies can consider assessing the extent

to which activation in these two MTL regions can be modulated parametrically by paths of increasing complexity. To ensure a detailed inspection of such functional changes, future studies would need to involve more categories of outbound paths (> 2) that vary systematically with respect to designated path parameters (e.g., number of path segments, outbound and homebound path distances, turning magnitudes). Here, when designing such novel paths, it is important to keep in mind extant research evidence showing the existence of hippocampal “time cells” that can code differentially for time and distance [88-90]. Due to the fact that a large distance can be covered over a short time span with a fast movement speed, the time spent to traverse an outbound (or homebound) path cannot be treated as a veridical representation of the actual distance covered. Consequently, future fMRI studies can consider employing experimental manipulations (e.g., a systematic variation of movement speeds over different path segments) that help to distinguish between measures of elapsed time and distance, and use them as separate variables during fMRI data analysis (e.g., during brain-behavior analysis) for a detailed inspection of hippocampal activation.

Another important consideration for future fMRI investigations concern the use of functional connectivity analysis. The form of analysis can pinpoint the degree of temporal correlations between brain voxels and ROIs of choice and can offer a more detailed “brain map” than the co-activations of discrete brain regions shown by Zhong (2019) [73]. An analysis of functional connectivity between the entorhinal cortex and hippocampus (chosen as seed voxels or ROIs) and extrahippocampal voxels and regions can be done using Zhong’s (2019) dataset but was not performed by the author in his initial round of data analysis because of two reasons: (i) the verification of the study hypotheses did not require this sophisticated form of analysis, and (ii) there was not a substantial number of significant phase-specific clusters of activations that can uncomplicate the selection of seed coordinates. The relatively small number of significant brain clusters highlighted another possibility that task-based brain activations might have been attenuated by pre-fMRI strategy testing/training in the lab, which featured more trials than the ones participants experienced in the fMRI scanner. Moreover, the in-lab test trials did not differ drastically from the fMRI trials, so some degrees of learning and familiarity effects might have “spilled over” from the in-lab test session to the fMRI session. Henceforth, it may be highly advisable for future studies to avoid extensive strategy testing/training prior to neuroimaging and to use sets of outbound paths that differ dramatically between the two sessions.

With the right improvisations to the Zhong's (2019) experimental design, future studies can explore the patterns of functional connectivity between hippocampal formation and extrahippocampal regions under different conditions of path integration strategy use to give a more nuanced insight into the dual roles of the entorhinal cortex and hippocampus. A recent fMRI study by Izen, Chrastil, and Stern (2018) [91] showed that functional connectivity between MTL regions (i.e., posterior hippocampus, parahippocampal cortex, entorhinal cortex) and resting state activations in the fronto-parietal and default mode networks increased with path integration accuracy on a loop closure task (different from the triangle/path completion task). The fronto-parietal and default mode networks involve wide swaths of the lateral and medial prefrontal cortices, respectively, which serve key regions for executive functioning and working memory processing, and hence future fMRI studies can examine the varying degrees to which MTL regions are connected to them under the influence of differential path integration strategy use. Contingent on the research question and experimental design, such connectivity studies can be done on fMRI data collected from either resting state or task-based brain scans.

Together with all these fMRI-related concerns, there is another pertinent concern on the environmental context under which different path integration strategies are executed. The most noticeable difference between the behavioral findings of Zhong (2019) [73] and those of Wiener et al. (2011) [21], and He and McNamara (2018) [72], was that Zhong (2019) [73] failed to find any main performance effect posed by the two strategies while the previous two studies did. Considering the fact that the previous two studies involved physical walking in real-world space and that Zhong's (2019) path integration task was conducted with vision serving as the primary source of sensory information in the absence of any physical walking, it is not far-fetched to speculate that kinesthetic sensory information (i.e., vestibular, proprioceptive) has some roles to play when implementing different types of path integration strategies. As noted by Zhong (2019) in his pre-fMRI strategy training study (Study 1 in [73]), the absence of kinesthetic cues and proprioceptive feedback might have contributed to the salient difficulties female participants experienced in carrying out an effective use of the configural updating strategy relative to their male counterparts. This interpretation was backed up by a recent study by Coutrot et al. (2019) [92] that compared path integration performances between real-world and virtual environments. The authors showed that real-world path integration (walking involved) generated smaller sex differences, suggesting that a dual combination of kinesthetic and visual information might be

required for women to perform as well as men during navigation. This interpretation supports past findings of sensory integration and enhancement, in which stimulation of a particular sensory modality increases an individual's sensitivity to the discrimination of stimuli processed by another modality [93,94], and implies that in order to elicit the best performance possible, path integration may be best assessed under naturalistic environments which allows a multimodal processing of sensory inputs. To verify this possibility in relation to path integration strategy use, future behavioral studies of path integration can examine how male and female users of different strategies perform under test conditions in which varying amounts of visual and kinesthetic cues are available (e.g., walking versus moving on a wheelchair versus staying stationary and performing the task on screen).

Further Investigations of Cognitive Aging Effects on Visual Path Integration

So far, the research studies presented above elucidated the neurocognitive processes involved in visual path integration among college-aged young adults. As research into how spatial navigation ability deteriorates with advancing age is a popular topic in the aging neuroscience literature [71,95], it is worthwhile to investigate the neurocognitive processes involved in visual path integration in older adults and how these processes differ between different age groups.

To date, the majority of studies which highlighted age group differences in visual path integration were behavioral in nature [22,25,26,96]. Based on assessments of visual path integration through the virtual triangle completion task performed on desktop computers, older adults have been shown to commit more distance [22,25,26] and rotation errors [22,25] than younger adults when walking back to their starting positions. Specifically, for outbound paths eliciting large distances and angles of return, older adults were found to travel shorter distances and turn less than younger adults when returning to the starting position, with a restriction in the range of homing distances being particularly prominent [25]. This common tendency to underestimate relatively long homing distances by older adults has been suggested to reflect an age-related decline in executive, working memory, and spatial imagery resources allocated to path integration [22, 96]. This interpretation corresponds well with numerous neuroimaging studies in wayfinding that showed age differences in the brain regions supporting environmental

learning [97-100]. For instance, Moffat et al. (2006) [99] showed that young and older adults showed noticeably different patterns of brain activations when learning the layout of a virtual maze. During this navigational learning phase, when compared to young adults, older adults exhibited lower levels of activations in the hippocampus, parahippocampal gyrus, medial inferior parietal lobe, and retrosplenial cortex, but higher activations in the anterior cingulate gyrus and medial frontal gyrus. Lower activations in the hippocampal formation were proposed to reflect an age-related impairment in generating an allocentric representation of the environment while higher activations in the frontal regions were proposed to reflect an age-related *compensatory shift* in spatial memory performance toward prefrontal regions, away from medial temporal and posterior regions (see also [71, 101], for recent experimental findings supporting this compensatory shift hypothesis).

Moreover, structural MRI studies have shown that volume reductions in the hippocampi of older adults were associated with poorer performance in wayfinding [98], place learning in a virtual water maze (i.e., learning the location of a hidden platform) [96,100], and episodic recall of stories and name-picture associations [102]. Despite these neuroimaging evidence showing the negative impact of age-related changes in the hippocampus on spatial navigation among older adults, there has not been many studies that associated structural or functional changes in the hippocampus (or adjacent MTL regions like the entorhinal cortex) to age-related impairments in path integration. To my knowledge, there are two fMRI-based aging neuroscience studies to date by Stangl et al. (2018) [76] and Bierbrauer et al. (2020) [103] that linked lower degrees of grid-cell-like representations (as measured by a parametric variable) in the entorhinal cortices of mentally healthy older adults with poorer path integration performance in the form of larger homing errors in path integration tasks that mainly involved self-motion (i.e., physical walking involved) [76] or visual cues (done on a computer, no walking involved) [76, 103]. Among the two fMRI studies, the one by Bierbrauer et al. (2020) [103] went a step further by performing genetic testing for the presence of the $\epsilon 4$ allele of the apolipoprotein E (APOE) gene, which have had been shown to be a potent genetic risk factor for late-onset Alzheimer's disease (AD). Specifically, among APOE $\epsilon 4$ carriers, which comprised both young and older adults, Bierbrauer et al. (2020) [103] associated higher visual path integration performance in the absence of any landmark cues with greater strength of grid-like cell representations in the posterior-medial entorhinal cortex (pmEC), implying that a disruption of normal grid-cell functions can serve as a

reasonable mechanistic explanation of path integration deficits in such carriers. Keeping this kind of finding in mind, future studies can investigate whether an age-related decline in path integration performance can be explained on the basis of similar or related mechanistic changes in the hippocampus, as well as in extrahippocampal regions that are found to be relevant for path integration (e.g., precuneus, retrosplenial cortex, medial prefrontal gyrus). Linking up with the discussion of path integration strategies above, it shall be highly interesting to see how the use of different strategies can be related to such variations in brain functions and structures in both young and older adults.

From a biomedical standpoint, making these efforts to investigate the neurobiological changes that underlie age-related decline in path integration will offer us greater insights into the brain-related factors contributing to the onset of AD, considering the fact that age-related decline in spatial navigation ability continues to remain as one of the most noticeable trends marking the onset of AD and related types of dementia [95,104,105].

Further Investigations of Interactive Roles of Landmark and Self-motion Cues

In addition to the aforementioned studies that assessed visual path integration in virtual environments which are either featureless or without distinctive landmarks, some studies implementing the triangle completion task in virtual environments have added landmark cues to the periphery of their paths for an investigation of the interaction between idiothetic (i.e., kinesthetic, proprioceptive) and allothetic (i.e., visual) cues in the framework of Bayesian theory [106, 107, 108, 109]. These behavioral studies showed that both types of cues could be represented mathematically in the form of Bayesian weights that reflected their use when one attempted to return to the starting position after traversing an outbound path. Initially conceived by Chen and McNamara (2014) [106], Bayesian modelling in the context of path integration works by computing the Bayesian weight (w) associated with the use of idiothetic and allothetic cues as:

$$w_{idiothetic} = \sigma_{allothetic}^2 / (\sigma_{idiothetic}^2 + \sigma_{allothetic}^2) \quad (3)$$

$$w_{allothetic} = \sigma_{idiothetic}^2 / (\sigma_{idiothetic}^2 + \sigma_{allothetic}^2) \quad (4)$$

, where σ^2 represents the response variance related to the use of either cue. The response variances associated with these two weights can be integrated to produce a combined estimate:

$$\sigma_{combined}^2 = \sigma_{idiothetic}^2 * \sigma_{allothetic}^2 / (\sigma_{idiothetic}^2 + \sigma_{allothetic}^2) \quad (5)$$

A cue reliability measure (r), linked to the use of either one of these two cues or their combined form, is computed based on $r = 1/\sigma^2$, giving rise to alternative representations of equations (3) to (5) in the form of:

$$w_{idiothetic} = r_{idiothetic} / (r_{idiothetic} + r_{allothetic}) \quad (6)$$

$$w_{allothetic} = r_{allothetic} / (r_{idiothetic} + r_{allothetic}) \quad (7)$$

$$\sigma_{combined}^2 = 1 / (r_{idiothetic} + r_{allothetic}) \quad (8)$$

As r is inversely proportional to response variance, higher values always imply greater attention to and reliance on a particular cue, be it in single or combined format. For a more detailed elucidation of the formulas above and associated formulas, the reader is advised to refer to the methods and results sections of Chen and McNamara (2014) [106].

Experimentally, the aforementioned cue integration was found to occur under conditions when the landmarks were not shifted or shifted slightly (15°) away from their original locations when one is carrying out a homing response [106, 107]. However, under situations in which the landmarks were shifted by a large degree from their original location ($\geq 90^\circ$) at the end of outbound path travel, participants were found to conduct cue integration less and to rely more on self-motion cues (representative of path integration per se) for directing themselves back to the starting position [107, 108].

Notably, Zhao & Warren (2015) [109] showed that after prolonged exposure to stable landmarks (i.e., landmarks that remain in fixed positions) in a virtual environment, homing based on reference to landmark cues (i.e., landmark-based navigation) was promoted whereas path integration (based on sensitivity towards self-motion cues) was undermined. Perhaps surprisingly, path integration was shown to be neither a back-up system (responsible for homing in the absence of landmarks) nor an automatic reference system (responsible for detecting the changes in the locations of the surrounding landmarks; for details of these two systems, see Experiments 1 and 2 in [109]). However, when the landmarks were designed to have chronically unstable locations over multiple trials and stable/unchanging locations on only a few “catch” trials, homing responses were shown to be less modulated by landmark navigation and more dependent on path integration-related self-motion cues (see Experiment 3 in [109]). The presence of large conflicts between landmark and self-motion cues produced by large and random landmark shifts suppressed the use of landmark cues and compelled a reliance on self-motion

cues. However, what remains unknown is the extent to which different path integration strategies play in affecting homing responses over sequences of trials that presented identical versus different configurations of landmark cues. To my knowledge, there has yet to be a neuroimaging study that applied a virtual triangle/path completion task with landmarks appearing in different locations over separate trials, and thus it will be intriguing for future studies to investigate the brain regions involved in the relative use of landmark and self-motion cues with respect to an appropriate Bayesian model of path integration.

Conclusion

Research on path integration has come a long way since the early days when path integration was first discovered from the navigational behavior of animals (e.g., desert ants [12], gerbils [7]). In this paper, we saw that virtual simulations of the triangle/path completion task, a task originally designed to assess the homing behavior of humans based on idiothetic cues [Klatzky, 1990, 3], have been used widely by many neuroscience researchers over the past two decades. Their research highlighted the neural substrates and networks that subserve visual path integration, as well as engendered skepticisms about the pertinence of the hippocampus and entorhinal cortex for visual path integration. The comparisons of the studies showing support for and opposition to the involvement of the MTL in path integration revealed potential complications in the participant recruitment [59, 60] and testing procedures [23]. These studies called into question the involvement of the MTL in path integration and whether the use of different types of path integration strategies have the potential to elicit different levels of activations in the hippocampus and entorhinal cortex. So far, Zhong (2019) [73] conducted the first fMRI study that sought to clarify this question, showing that significant activation in the entorhinal cortex occurs in the comparison of complex and simple paths during the homebound phase of visual path integration. In the discussion of this study and related works, methodological concerns were raised, and feasible steps were suggested to improve the experimental design for future studies. At the same time, this endeavor to study different path integration strategies was also suggested to be relevant for future cognitive neuroscience research on age-related differences in the role of the hippocampal formation in path integration, and Bayesian modelling of the interaction between landmark and self-motion cues.

This strategy-focused approach is also supported by the large pool of pre-existing neuroimaging findings which showed that distinct brain regions, namely the precuneus and the retrosplenial cortex, were differentially involved during path integration through the adoption of different frames of reference [32-36, 55]. Such findings suggested the use of different spatial visualization strategies for cognitive mapping and spatial memory formation. Currently, only two types of spatial visualization strategies for path integration were discussed – continuous updating and configural updating – and future studies can investigate other types of path integration strategies, which do not have to be spatial in nature. For instance, an egocentric pace- or step-counting strategy that makes use of the number of counted steps taken over an outbound path to estimate the length of the homebound path can be used for visual path integration [73]. Instead of controlling for this strategy as a potential confound [26,73], participants can be taught to use this strategy and then be compared with other groups of participants using other strategy types. This approach shall provide more experimental data and a better understanding of how different path integration strategies compare and contrast against each other with respect to behavioral performance and brain functions.

Moreover, from an applied biomedical perspective, understanding the behavioral and neurobiological impact of a wider variety of path integration strategies can inform the design of better navigational software (e.g., “Sea Hero Quest” [92]) and artificial intelligence (AI) algorithms [110,111] for assessing and training navigational skills for different population groups. For instance, achieving a potential finding from future studies showing that a particular kind of path integration strategy can mitigate further age-related declines in general spatial navigation ability can help to inform the programming of appropriate AI algorithms and software for training older adults in the most effective use of that strategy.

Together with this behavioral approach to training one’s spatial navigation ability (or spatial ability in general), findings from experimental and clinical trial studies demonstrating the selective enhancing effect of pharmacological drugs on specific brain areas should also be noted. For instance, in a randomized, double-blind, placebo-controlled, and crossover design, Apud et al. (2007) [112] evaluated the effects of tolcapone, a central nervous system penetrant specific catecholamine-O-methyltransferase (COMT) inhibitor, on measures of cognitive function and prefrontal cortical information processing in healthy human participants stratified by the COMT (val158met) genotype. They found significant drug effects on measures of executive function

and verbal episodic memory and a significant drug by genotype interaction on verbal episodic memory, such that participants on tolcapone with val/val genotypes showed improved memory performance whereas participants on tolcapone with met/met genotypes showed lower memory performance. An fMRI experiment further showed a significant tolcapone-induced improvement in the efficiency of information processing in prefrontal cortex during a working memory test, demonstrating that prefrontal executive functioning in normal human subjects can be enhanced with a non-stimulant drug having COMT inhibitory activity. Such studies and findings suggest that human cognition, of which spatial navigation ability is a part of, can be enhanced through non-invasive drug or chemical interventions, and raises the possibilities for biomedical researchers to test and administer newly designed drugs that can either enhance spatial navigation ability among healthy adults or ameliorate age-related spatial ability declines among older adults at risk of getting AD or other types of dementia.

In sum, the advent of neuroimaging research on visual path integration has greatly improved our understanding of its underlying brain regions and networks, yet much remains to be explored about the relative involvement of MTL regions like the hippocampus and the entorhinal cortex in visual path integration. By identifying the need to do so in the context of path integration strategies, this paper presented an overview of the most important works in the cognitive neuroscience literature on visual path integration, and introduced feasible ideas to set neuroscience researchers on higher grounds for further investigations into the behavioral and brain mechanisms of path integration.

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Conflicts of Interest

The author declare that he has no affiliations with or involvement in any organization or entity that has financial or non-financial interest in the subject matter discussed in this manuscript.

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