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Combining patient-lesion and big data approaches to reveal hippocampal contributions to spatial memory and navigation

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Summary

Classic findings of impaired allocentric spatial learning and memory following hippocampal lesions indicate that the hippocampus supports cognitive maps of one's environment. Many studies assess navigation in vista-space virtual reality environments and compare hippocampal-lesioned individuals' performance to that of small control samples, potentially stifling detection of preserved and impaired performance. Using the mobile app *Sea Hero Quest*, we examined navigation in diverse complex environments in two individuals with hippocampal lesions relative to demographically matched controls (N = 17,734). We found surprisingly accurate navigation in several environments, particularly those containing a constrained set of sub-goals, paths, and/or turns. Areas of impaired performance may reflect a role for the hippocampus in anterograde memory and more flexible and/or precise spatial representations, even when the need for allocentric processing is minimal. The results emphasize the value of combining single cases with big data and illustrate navigation performance profiles in individuals with hippocampal compromise.

Keywords: spatial memory, hippocampus, amnesia, virtual reality, neuropsychology, big data

Introduction

The view that there are multiple types of memory, each with distinct properties and differentially supported by dissociable brain regions, became a biological reality with the study of impaired and preserved behaviours in amnesic individuals with lesions to the hippocampus¹⁻⁴. Initial discoveries of impaired explicit memory, particularly episodic and spatial memory, in the context of relatively preserved working memory and long-term implicit and semantic memory, exerted a strong influence on memory theory and clinical diagnosis of a wide range of neurological conditions affecting hippocampal function⁵. Here we show how the case study approach can be amplified by combining it with big data to reveal even finer dissociations within spatial memory and navigation.

Like other forms of memory, human spatial memory is multifaceted. Findings in cases of hippocampal damage appear to show that the hippocampus is needed to support allocentric (observer-independent) spatial representations of relations among items contained within an environment⁶⁻¹⁰. By contrast, egocentric (observer-dependent) spatial representations of items in relation to oneself and path integration of one's previous location in relation to both allocentric and egocentric coordinates appear to exist independent of the hippocampus^{7,11-12}. This pattern of impairment and preservation is largely consistent with the predictions of Cognitive Map Theory¹³, which argues that the hippocampus is needed to construct and maintain internal map-like representations of spatial environments.

There are notable exceptions, however, to findings of impaired allocentric spatial learning following hippocampal lesions. The famous amnesic case H.M. was able to reproduce the basic floor plan of a house in which he lived following bilateral resection of his hippocampus¹ and find a hidden sensor from multiple start locations in a human analog of the

Morris Water Maze¹⁴. When deficits do emerge following hippocampal lesions, they tend to occur when working memory is taxed due to the time or distance needed to travel or when the task requires greater precision, such that destinations are reached circuitously, if at all^{7,15-20}. The lack of precision in new spatial learning following hippocampal compromise resembles findings in remote spatial memory, where gist-like representations of environments learned long ago appear to be largely intact in hippocampal amnesia despite the loss of memory for more precise details contained within the same environments²¹⁻²⁸.

Overall, allocentric spatial representations are unlikely to depend only on the hippocampus, and there are other, non-spatial task demands which also may determine hippocampal involvement in spatial memory, resulting in the nature and extent of hippocampal contributions to spatial memory remaining underspecified. Case studies are needed to draw conclusions about the causal relationship between hippocampal function and spatial memory but are severely limited. This approach typically includes individuals who are unlikely to have selective lesions and compares them to a relatively small number of control participants who are not always closely matched on key variables, including age, education, and, in the case of studies on spatial memory, geographic experience. This may lead to overly general or inappropriate interpretations of data. The value of the case study approach should not be diminished by its shortcomings but, rather, elevated, especially given the limitations of averaging group-level performance at the expense of individual-level variability²⁹⁻³⁰. When deep data that are available from extensively studied individuals with amnesia are combined with large, well-matched control samples available in “big data,” results are more likely to advance our understanding of human memory than when either method is used alone.

Here we examine spatial navigation in two well-characterized individuals with hippocampal amnesia and compare their performance to that of a very large number of carefully curated, well-matched controls. The mobile video game Sea Hero Quest (SHQ) has been administered to over 4 million people globally and measures path integration and allocentric mapping abilities across different levels of environmental properties and complexity³¹⁻³⁴. SHQ performance has been found to correlate with real-world navigation³⁵ and shows good test-retest reliability³⁶. Performance is significantly correlated with both gross domestic product (GDP) and gender inequality across nations³¹, and amount of reported sleep³⁷. Performance on the SHQ has also been found to distinguish individuals with traumatic brain injury³⁸ and individuals who based on APOE ϵ 4 status are at a higher genetic risk of developing Alzheimer's Disease (AD)³⁶ and relates to incidence of spatial disorientation in individuals with AD³⁹. These findings further support the view that spatial navigation difficulties hold utility as a marker of hippocampal compromise and may be sensitive to neurodegenerative disease⁴⁰⁻⁴³.

Testing individuals with hippocampal amnesia provides the opportunity to better understand the contribution of the hippocampus and medial temporal lobe (MTL) to spatial navigation. These individuals are well-suited for this aim given their stable memory impairments due to circumscribed lesions secondary to acquired brain injury. Their selective deficits allow for investigation of whether performance on spatial navigation tasks differs based on task demands on precision and anterograde memory. To investigate the influence of anterograde memory, the two individuals tested in this study differ in the nature and severity of their anterograde amnesia, with one individual (D.A.) having more extensive damage to the MTL, including the hippocampus bilaterally, and the other individual (B.L.) having more selective bilateral hippocampal lesions primarily affecting the dentate gyrus. Based on past research, we predicted

that greater MTL damage and anterograde amnesia would result in worse performance and that this would interact with attentional processes through demands on map encoding. By using the SHQ paradigm, results can inform theoretical models of the contribution of the hippocampus to spatial memory and provide guidance for integrating detailed information available in individual cases with data from large, well-matched normative samples. This study also aimed to provide a new standard for clinicians to assess individual performance in more subtle cases of memory decline and in other neurological conditions.

Results

Wayfinding Levels

D.A.'s Performance

Due to his dense anterograde amnesia, D.A. has not effectively learned to use an iPad or computer technology. This resulted in him forgetting the iPad commands (dragging versus swiping his finger) multiple times during testing and, at times, moving forward tightly in one area, unable to effectively maneuver to the precise spot. An experimenter was present to remind D.A. of technology instructions, but he was still less accurate as reflected by longer level durations. Nevertheless, compared to B.L., D.A.'s navigation style was slower and more deliberate, which did not appear to be due to any technical difficulty. On certain levels that were particularly difficult due to technical challenges (levels 7, 13, and 18), indicated in Table 4, duration metrics were excluded from the mean and standard deviation calculations listed below.

D.A.'s performance, when averaged across the 12 available wayfinding levels, was in the average range for distance traveled ($M = 34^{\text{th}}$ percentile, $SD = 26^{\text{nd}}$ percentile) and low-average range for duration or time taken ($M = 16^{\text{th}}$ percentile, $SD = 20^{\text{th}}$ percentile)⁵¹. Level 7 is omitted from calculations due to technical difficulties and level 21 is omitted from calculations because

D.A. quit this level due to significant task and technical difficulties. Wayfinding distance performance did not significantly correlate with level difficulty (as determined by the large control group sample)³⁴, $r_s(10) = 0.42$, $p = 0.18$. See Figure 4 for a graphical depiction.

When considering performance in the context of map visibility, D.A.'s distance performance was worse for partial map ($M = 21^{\text{st}}$ percentile, $SD = 34^{\text{th}}$ percentile) than full map ($M = 45^{\text{th}}$ percentile, $SD = 31^{\text{st}}$ percentile) levels. The data show that duration is also longer in partial map ($M = 1^{\text{st}}$ percentile) than full-map levels ($M = 20^{\text{th}}$ percentile, $SD = 22^{\text{nd}}$ percentile). This latter comparison should be treated with caution, however, as only 2 levels are available for the duration calculation for the partial-map conditions.

D.A.'s performance was variable across levels, however, performance was better than that of 25% of controls on 8 of the 12 wayfinding levels. This calls for greater consideration into the map characteristics that may have contributed to task performance. D.A. appears to have performed best on closed map levels, defined as maps where navigation is occurring in a tight space. First decision point or turn accuracy can also help explain D.A.'s performance. The first decision point choice may be indicative of the level of encoding of the map presented before navigating. D.A. made the correct decision on 3 of the 5 levels that have a clear decision point early in the level (see Table 5).

Another consideration for performance differences is the order of buoys on a wayfinding level. On level 11, D.A. made an incorrect decision at the first decision point and performed much worse than his controls (5th percentile distance, 1st percentile duration). Level 11's buoys are out of order, requiring D.A. to return to a previous location and the first buoy he passed. In contrast, on level 12, he made a correct judgment at the first decision point and did not need to

return to the first buoy that he passed. His performance on this level was in the average range (69th percentile for distance, 53rd percentile for duration).

Overall, it appears that when D.A. must remember and return to the previously visited buoys, he is more likely to perform poorly compared to control participants. This may also relate to more time spent navigating, as levels with buoys out of order are longer and more time passes since map encoding, leading to a greater likelihood of anterograde amnesia impacting performance. For videos highlighting D.A.'s poor performance compared to control participants, see level 22 and 26 at <https://osf.io/s47wa/>.

Additional qualitative scoring information from blinded review of videos is available in Table 6. This includes counts of backtracking, overall navigation ratings, and longest pause. Included in this table are D.A.'s performance, control performance, and calculated Z-scores for each level where available. When Z-score calculations were not possible due to no standard deviation (no variability in controls' performance), a label of 'comparable' or 'elevated' was assigned. Overall, D.A. had a higher incidence of backtracks ($M = 3.17$, $SD = 1.87$) than control participants ($M = 1.53$, $SD = 1.75$). Ratings of overall quality of navigation were also lower for D.A. ($M = 4.39$, $SD = 2.92$) than controls ($M = 8.08$, $SD = 1.22$). D.A.'s longest pauses, calculated in seconds, were also much longer ($M = 31.56$, $SD = 22.43$) than those for control participants ($M = 0.5$, $SD = 0.57$), the majority of whom did not have any pauses during navigation.

B.L.'s Performance

B.L.'s performance was averaged across 14 available wayfinding levels and is presented in Table 5. Performance was in the low-average range for distance traveled ($M = 24^{\text{th}}$ percentile, $SD = 33^{\text{rd}}$ percentile) and duration of navigation ($M = 10^{\text{th}}$ percentile, $SD = 19^{\text{th}}$ percentile)

(Guilmette et al., 2020). Wayfinding distance performance did not significantly correlate with level difficulty (see Yesiltepe et al., 2023) as calculated with a Spearman rank order correlation, $r_s(12) = 0.14, p = 0.62$. See Figure 4 for a graphical depiction.

When considering map visibility, B.L. performed better on the three levels in which maps were partially visible in terms of both distance ($M = 59^{\text{th}}$ percentile, $SD = 38^{\text{th}}$ percentile versus $M = 15^{\text{th}}$ percentile, $SD = 26^{\text{th}}$ percentile) and duration ($M = 54^{\text{th}}$ percentile, $SD = 34^{\text{th}}$ percentile versus $M = 10^{\text{th}}$ percentile, $SD = 19^{\text{th}}$ percentile). See Figure 5 for a comparison of D.A.'s and B.L.'s distance performance by map visibility.

B.L.'s best wayfinding performance was on levels 12, 18, and 22. For a video showing BL's performance on level 22 compared to control participants, see <https://osf.io/s47wa/>. These levels differ in map visibility but share the characteristic of a closed map style. Some other characteristics make navigating these levels easier. Specifically, level 18 has all buoys in order (set sequence), level 22 has an island in the centre that participants can navigate around, and level 12 has both buoys in order and an island in the centre to navigate around. The islands in the centre may offer a cue for navigation in open-map levels. Like D.A., B.L. performs best and more comparably to controls when there is less demand on anterograde memory as he navigates, because he does not have to return to previous locations.

Additional qualitative information from blinded review of videos is available in Table 6. In addition to D.A.'s performance, this table also includes B.L.'s performance, the performance of controls matched to B.L., and calculated Z-scores for each level. When Z-score calculations were not possible due to a lack of variability and no standard deviation in control performance, a label of 'comparable' or 'elevated' was assigned.

Overall, B.L. had a higher incidence of backtracks ($M = 5.11$, $SD = 6.9$) than control participants ($M = 1.50$, $SD = 1.73$) and than D.A. ($M = 3.17$, $SD = 1.87$). For graphical depiction of average number of backtracks for D.A. and B.L. compared to controls, see Figure 6.

Ratings of overall quality of navigation were lower for B.L. ($M = 4.72$, $SD = 3.31$) than controls ($M = 8.11$, $SD = 1.20$). B.L.'s overall navigation was rated as similar to that of D.A. and worse than controls. B.L. had a similar duration of pauses ($M = 0.67$, $SD = 1.03$) as control participants ($M = 0.68$, $SD = 0.93$). His dwell times were comparable to controls and much lower than D.A.'s. This indicates that B.L. has a more direct navigation style than D.A.

Path Integration

Accuracy of D.A.'s, B.L.'s, and matched controls' performance on the 7 path integration levels is presented in Table 7.

D.A. did not navigate directly to the flare on 2 of the 7 levels (44, 49), which are indicated with asterisks in Table 5.6. On these levels, he navigated backwards, seeming to forget the task instructions, performing as if he was on a wayfinding level. D.A.'s performance was accurate on 2 of the 7 (28.57 %) flare levels that he had completed. His performance was accurate on 1 of the 5 (25%) levels where he navigated directly to the flare. Controls matched to D.A. showed higher accuracy on each of the 7 flare levels ($M = 51.49\%$, $SD = 0.05\%$).

B.L. took a direct path on all flare levels. His performance was accurate on 3 of the 7 (42.86 %) levels, whereas controls were slightly more accurate ($M = 58.46\%$, $SD = 0.07\%$).

Discussion

Using the mobile video game SHQ, wayfinding and path integration were examined in two well-characterized individuals with amnesia compared to thousands of closely matched controls to identify the conditions in which the hippocampus contributes to different aspects of

human spatial memory. The amnesic individuals, including D.A. who has extensive lesions affecting his hippocampus bilaterally, performed surprisingly well on several wayfinding levels, indicating that their spatial learning is not universally impaired. Instead, performance differed based on each case's unique clinical profile and on wayfinding level complexity, operationalized by environment characteristics (open versus closed environment) and memory demands (number and order of buoys). Interestingly, performance did not clearly relate to geometric features of wayfinding levels as in healthy controls³⁴, highlighting the impact of anterograde memory on spatial navigation. On path integration levels, D.A., who has more extensive hippocampal and MTL damage, performed worse than controls than B.L., who has more selective bilateral hippocampal lesions largely affecting the dentate gyrus. Results for both the wayfinding and path integration levels expand on research showing preserved spatial learning and memory in individuals with hippocampal amnesia^{11,19,22,52-53}. The results conflict with predictions from theoretical models that argue that the hippocampus is needed for navigation of environments over longer periods of time^{7,11}. Instead, spatial navigation deficits exhibited in hippocampal amnesia appear best explained by general deficits in anterograde memory, as minimal learning demands in an environment did not necessarily interfere with navigation, even on levels that may depend on allocentric spatial learning. The current findings demonstrate the value of combining the patient-lesion method with big data to understand brain-behaviour relations.

The SHQ paradigm used in this study provides greater insight into the spatial navigation abilities of individuals with amnesia in virtual environments varying in memory demands. The results show that D.A. and B.L. performed worse than controls when greater demands were placed on anterograde memory during navigation as suggested by backtracking and a less direct navigation path. Backtracking to previous locations has been examined in studies of sex

differences in virtual and real-world environments, with females showing greater revisiting of previous locations than males⁵⁴⁻⁵⁵. The individuals with amnesia displayed a more extreme nature of the backtracking than that documented in previous studies, which likely reflects rapid forgetting and/or deficient learning of environmental characteristics, consistent with the amnesic individuals' episodic memory deficits⁴. The increased time needed on certain levels may have further exacerbated anterograde memory deficits^{4,56}. In contrast to the backtracking demonstrated by patients in this study, recent research suggests that backtracking improves navigation by resulting in a shorter path to goal and is associated with activity in frontal regions and anterior cingulate cortex⁵⁷. Future research in individuals with different cognitive profiles, including individuals with only executive dysfunction, is needed to understand whether backtracking during navigation is pathognomonic of anterograde memory impairment and not impaired allocentric spatial memory per se.

The SHQ levels also differed in terms of map visibility, allowing for different encoding opportunities of the overall layout of the environment prior to navigation. For these maps to be useful for navigating the wayfinding levels, individuals would also need to translate the encoded maps between a bird's-eye view and ground-level perspective⁵⁸⁻⁵⁹. Overall, control participants generally performed worse on partially visible map trials compared to trials in which completely visible maps were presented, demonstrating how intact memory encoding allows for a benefit of viewing a map of the environment prior to navigating. The amnesic individual with less impaired memory, B.L., performed more similarly to controls on levels with partially visible maps compared to fully visible maps, which may indicate that he is not making effective use of the maps, whether fully or partially available. This may be due to B.L.'s additional cognitive weaknesses in complex attention and processing speed. However, D.A. who has more extensive

memory loss but intact attentional processes, did not show this pattern of performance, suggesting that he may initially benefit from a visible map during navigation. Future work using the SHQ paradigm could assess the effects of time spent encoding and map visibility to investigate if and when it aids or interferes with navigation in individuals with anterograde amnesia with tracking encoding time and inclusion of more map visibility trials.

Qualitative analyses show the influence of individual style of navigation on wayfinding performance. Despite D.A.'s more severe anterograde amnesia, he did not perform much worse than B.L. on wayfinding levels and had fewer instances of backtracking. However, D.A. did pause for longer durations during navigation than B.L., which may be interpreted as a slower and more deliberate navigation style. It is unclear whether D.A. is rehearsing or otherwise using any strategies during this additional time. This difference in navigational style may correspond with D.A.'s subjective report of greater everyday reliance on allocentric strategies and better distance estimation skills compared to matched controls and to B.L.⁶⁰ and intact performance on tests of remote spatial memory²². An important moderator of objective performance on SHQ may be individual navigation style. We encourage future research to integrate systematic analyses of qualitative data given these preliminary findings.

Results from D.A.'s and B.L.'s detailed neuropsychological testing may help explain some of the differences observed in their performance. Compared to D.A., B.L. has a milder memory impairment but greater weakness in processing speed and complex attention, which are linked to his brain injury etiology and areas of damage. Past research has shown that B.L. has difficulty with fine-grained perceptual discrimination, which may be linked to his dentate gyrus and partial CA3 lesions⁴⁸⁻⁴⁹. This difficulty may have contributed to his difficulty learning map details or effectively attending to details when navigating wayfinding levels on the SHQ^{19,53}. It

may also explain his extreme backtracking performance. These findings highlight attentional and perceptual contributions to spatial navigation performance, including the ability to learn from a partially visible map^{17,57,62}. Overall, D.A.'s and B.L.'s navigation styles and different profiles of cognitive deficits may interact to produce differences in navigational performance, which the SHQ paradigm is able to effectively capture.

Both individuals with amnesia performed better on the closed than the open wayfinding levels. On closed levels, D.A. and B.L. were able to stay close to the boundaries and appeared to benefit from the restricted navigation options, with fewer opportunities to make errors. Open levels more closely resemble a Morris water maze-like environment since all buoys are in one space and not located along different paths^{19,36,63-64}. Unlike the Morris water maze, however, none of the SHQ levels have the entire environment visible to participants. Investigating line of sight during navigation may help to explain some differences in performance across closed and open environments, for example due to differences in the visibility of distal cues^{16,66}. It is also plausible that allocentric demands are not as great on the SHQ than on the Morris water maze^{64,65}, even in the open water levels. The latter test requires participants to begin navigating from different start locations and does not include local markers along the way that may be used as proximal cues prior to reaching the goal, which stays hidden for the duration of the trial. It is still conceivable that on the SHQ participants must rely on some type of mental map of the space that includes distal features, particularly when the actual overhead map is not fully visible, but one can reach the goal in a non-allocentric way and in the absence of the ability to use the map flexibly. It follows that areas of impairment exhibited by B.L. and D.A. are unlikely to be solely due to deficits in allocentric processing, as it should have been possible for them to achieve at least near-control-level performance in the open water conditions of the SHQ via non-allocentric

means. The results suggest that the role of the hippocampus in spatial memory is determined by principles that go beyond those proposed within Cognitive Map Theory^{58,63}.

Wayfinding tasks drawing on allocentric spatial relations were traditionally thought to depend on the hippocampus. Findings from the current study show that hippocampal involvement may depend more on anterograde memory demands originating from map characteristics. Other work defines the role of the hippocampus in allocentric spatial relations as linked to precision and/or flexibility of use of allocentric information^{15,18,53,67}. Findings from the current study might also be consistent with previous findings in B.L. of the role of the dentate gyrus in precision, suggested by his difficulties with fine-perceptual discrimination in the context of less severe anterograde amnesia⁴⁹. These results are also not entirely consistent with predictions of Cognitive Map Theory, instead suggesting that the role of the hippocampus may be driven by anterograde memory and precision more than by allocentric spatial processing *per se*.

Path integration, which involves some degree of egocentric-to-allocentric translation, has yielded mixed findings, with some studies showing that the hippocampus relies on the retrosplenial cortex and hippocampus, and other studies showing that path integration remains intact following hippocampal lesions^{12,17,68-72}. The current findings show worse path integration in both D.A. and B.L. compared to each of their control groups. D.A. performed worse than B.L., which may relate to more extensive hippocampal/MTL damage and severe anterograde amnesia. This is consistent with findings of hippocampal contributions to path integration in rodents⁷¹ and in individuals on the AD spectrum^{35,74-75}. It is important to note, however, that the timeframes for each of the path integration levels in this study were likely beyond the limits of working memory, which may explain the performance deficits seen in D.A. and B.L.¹² Interpretation of

path integration performance is more tentative than that for wayfinding given the relatively small number of trials available, though this is offset by the large and well-matched control samples.

Examination of wayfinding and path integration on the SHQ in two individuals with different degrees of anterograde amnesia provides information on the SHQ's sensitivity to memory impairment and encourages future research to assess its clinical utility in assessing the nature of spatial navigation. The data presented in this study provide researchers and clinicians with an in-depth view of spatial navigation integrity on the SHQ in individuals with well-characterized, real-world spatial memory impairment in relation to relatively selective lesions to the dentate gyrus subregion of the hippocampus and to more extensive damage that extends beyond the hippocampus and MTL. These findings, in turn, can be used as a benchmark for assessing spatial learning in milder cases of memory compromise and as a contrast to those who are genetically at risk of developing AD (e.g., Coughlan et al., 2018).

Limitations of the Study

It is important to note that D.A. and B.L. have volume loss outside of the hippocampus and MTL that may have contributed to their task performance, but that is largely unavoidable in patient-lesion research^{2-3,19,44}. Findings of significant overlap in areas of spared and impaired performance despite different locations and extents of extra-MTL volume loss allows for stronger conclusions to be drawn about hippocampal involvement. Importantly, both D.A. and B.L. have seemingly intact structural integrity of other regions known to be necessary for different aspects of spatial memory and navigation, including the striatum, posterior parietal cortex, and retrosplenial cortex^{45,76-80}. To better understand the contributions of the hippocampus, MTL, and extra-MTL regions to spatial navigation, future studies are needed to assess SHQ performance in individuals with focal lesions to these regions and differing cognitive profiles.

Another study limitation is the number of trials available across the different task conditions (i.e., map visibility, environmental layout). Future work with more trials per condition could lead to more certain conclusions, though the large number of control participants for comparisons is a study strength that helps mitigate this limitation.

Conclusion

Taken together, the current investigation of wayfinding and path integration on the SHQ provides a unique approach to understanding the contributions of the hippocampus to spatial navigation by combining in-depth examination of single individuals with “big data.” The results show that hippocampal damage and anterograde (episodic) amnesia do not necessarily translate to an all-encompassing allocentric spatial memory deficit, providing further evidence of differences between episodic and spatial memory⁸¹⁻⁸². Wayfinding is possible in the face of hippocampal compromise, and especially benefits from ‘closed’ environments and fewer demands on anterograde memory. These results expand on past research on the spatial navigation abilities of individuals with amnesia, including anecdotal intact real-world navigation abilities^{28,83}, poor performance on table-top tests of memory⁸⁴⁻⁸⁵, and allocentric spatial tasks in environments with few distal cues and only a single goal^{16,63}. Since the spatial navigation network extends beyond the hippocampus⁸⁶⁻⁸⁷, the results have implications not only for individuals with hippocampal compromise on the AD clinical spectrum^{39,41}, but also for individuals who present with topographical disorientation due to neurological conditions affecting other regions within and beyond the MTL^{38,88-91}. The current work also highlights the utility of the SHQ and identifies task levels that are most sensitive to memory deficits and that may be considered within the context of a more comprehensive assessment of spatial navigation abilities.

Journal Pre-proof

Author Contributions (CRediT)

Sara Pishdadian: conceptualization, data curation, formal analysis, investigation, methodology, project administration, visualization, software, writing- original draft, writing-review, and editing, project administration, supervision

Antoine Coutrot: conceptualization, data curation, formal analysis, methodology, visualization, writing-review and editing

Lauren Webber: investigation, formal analysis, writing-review and editing

Michael Hornberger: conceptualization, funding acquisition, writing-review and editing,

Hugo Spiers: conceptualization, Writing - Original Draft, writing-review and editing, funding acquisition, project administration, supervision

R. Shayna Rosenbaum: conceptualization, funding acquisition, resources, supervision, Writing - Original Draft, writing-review and editing, project administration, supervision

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Declaration of Interests

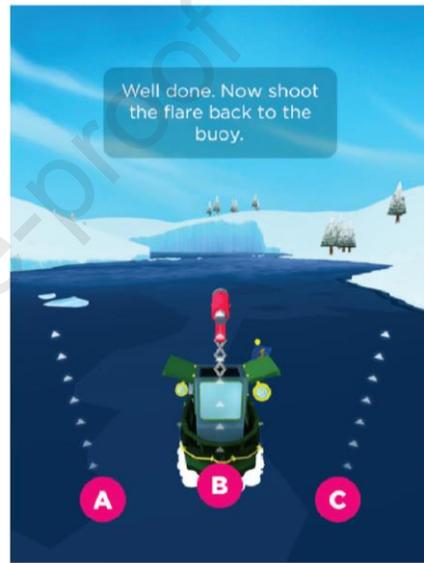
The authors declare no competing interests.

Figure 1***Examples of Gameplay on Sea Hero Quest***

A)

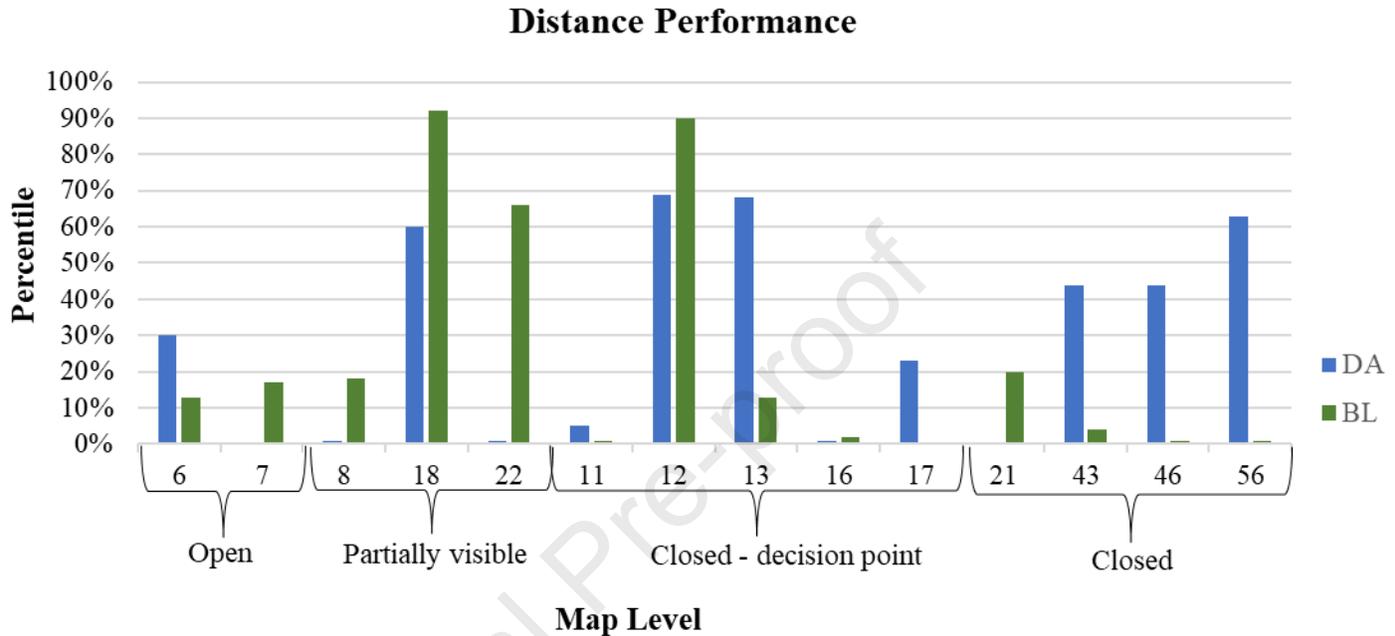


B)



Note. A) Example of gameplay during wayfinding levels. B) Example of gameplay during path integration levels, where participants had to navigate within a maze and when reaching a flare, shoot it back towards the start location. Images from Coutrot et al. (2019)³⁵.

Figure 2

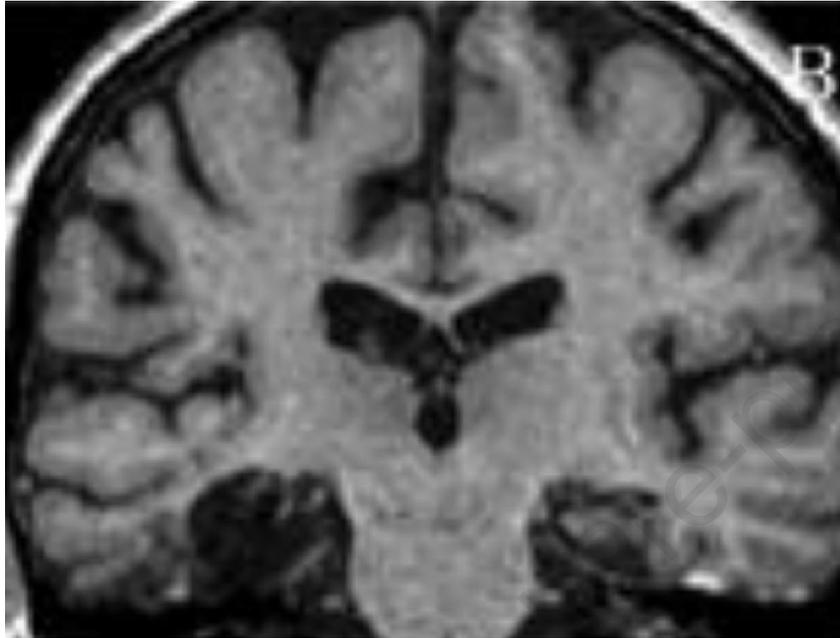
Distance Performance in B.L. and D.A. on Each Level of Sea Hero Quest

Note. Graph depicts distance performance in percentiles for D.A. and B.L. relative to their respective controls for each map level, which vary in difficulty and level characteristics (see Supplemental Table 1 and 2 for images). Higher percentile indicates better performance. Findings show that individuals with amnesia have performance that is comparable to controls when demands on anterograde memory are lower, which differs depending on level characteristics.

Figure 3

Representative MR images of the Medial Temporal Lobe in D.A. and B.L.

A)



B)



A) MR image of D.A.'s medial temporal lobes (MTLs) in a coronal view showing loss of volume bilaterally, most prominently in the right hemisphere. Image adapted from Kwan et al. (2013)⁴⁴. B) MR image of B.L.'s MTLs in a coronal view, with hippocampal segmentation visible to show the greatest volume loss within the dentate gyrus and partial volume loss in the CA3 subfield. Image adapted from Baker et al. (2016)⁴⁸.

Figure 4***D.A.'s and B.L.'s Distance Performance Compared to Controls***

Map difficulty is derived from entropy, geometric and level-specific features (Yesiltepe et al., 2022). Distance percentile is the distance traveled during navigation compared to matched control participants.

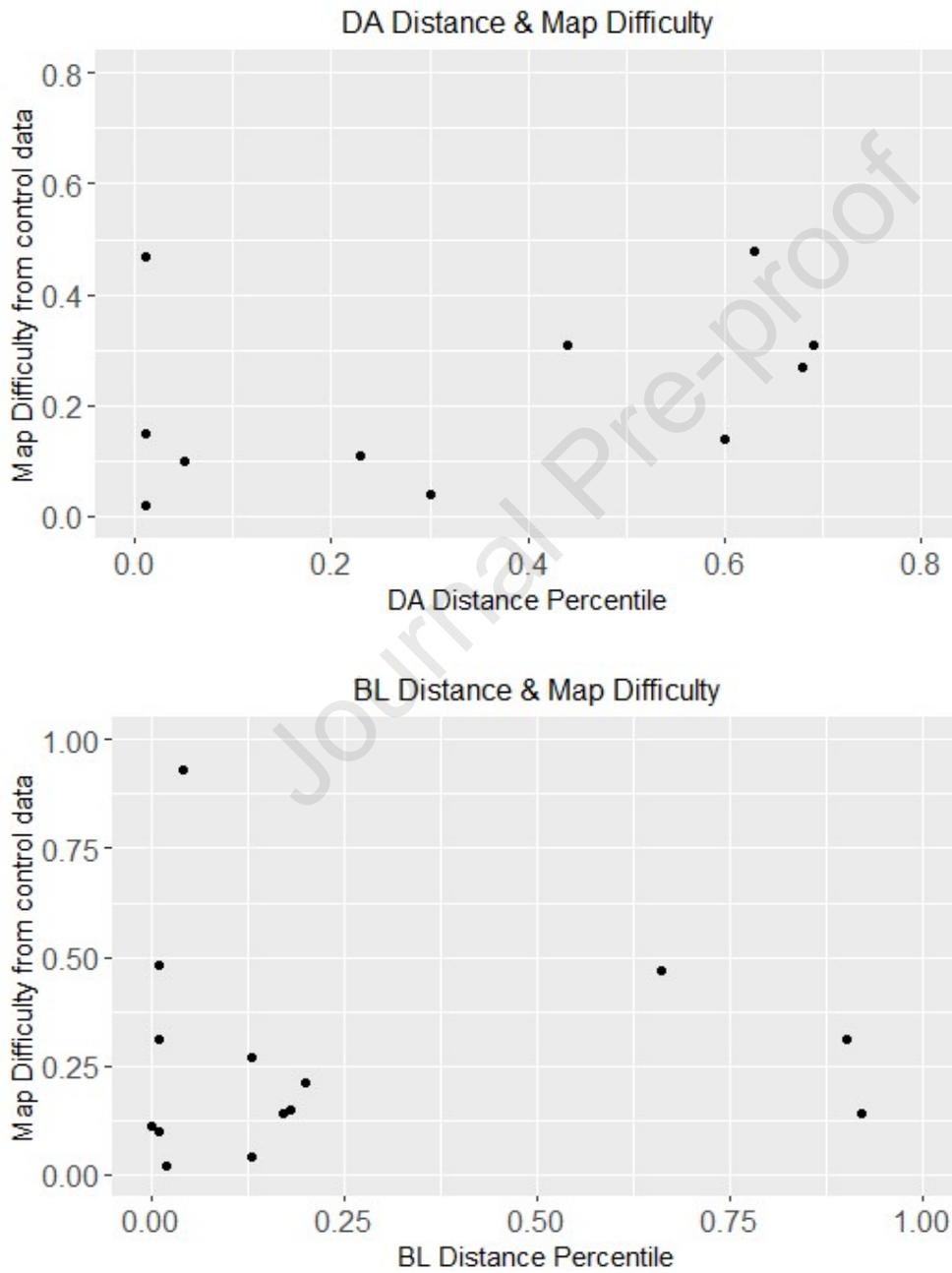
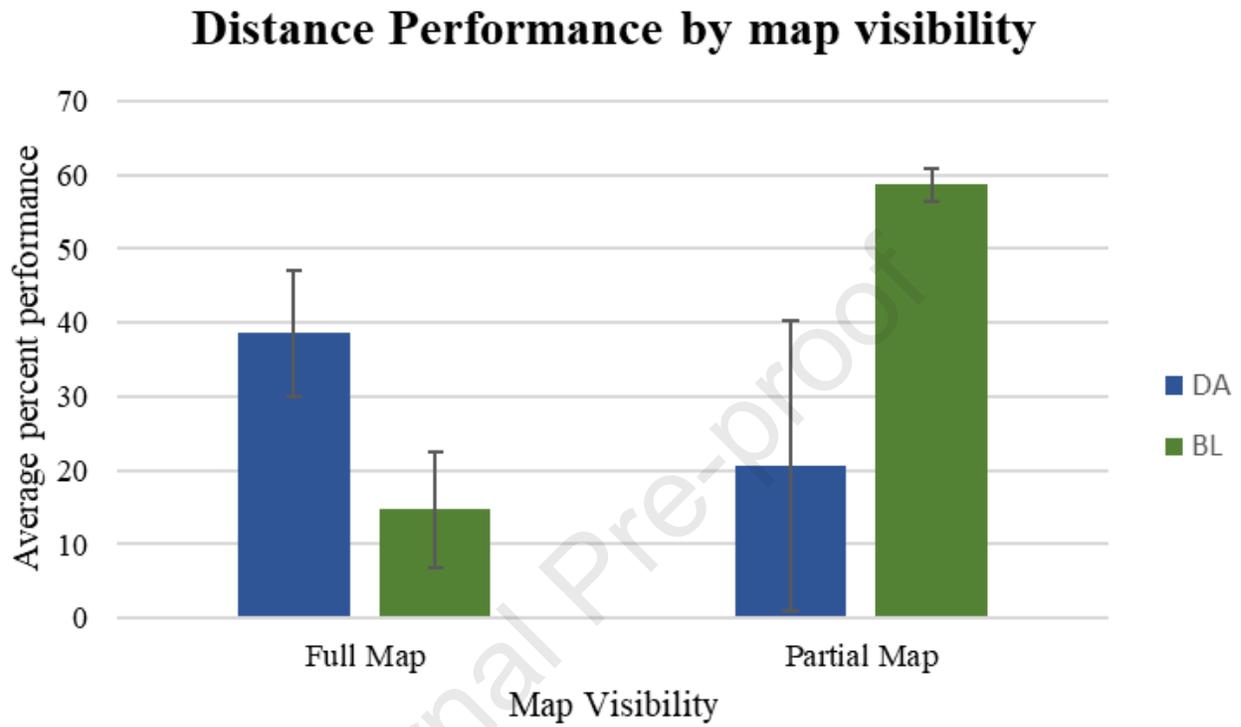
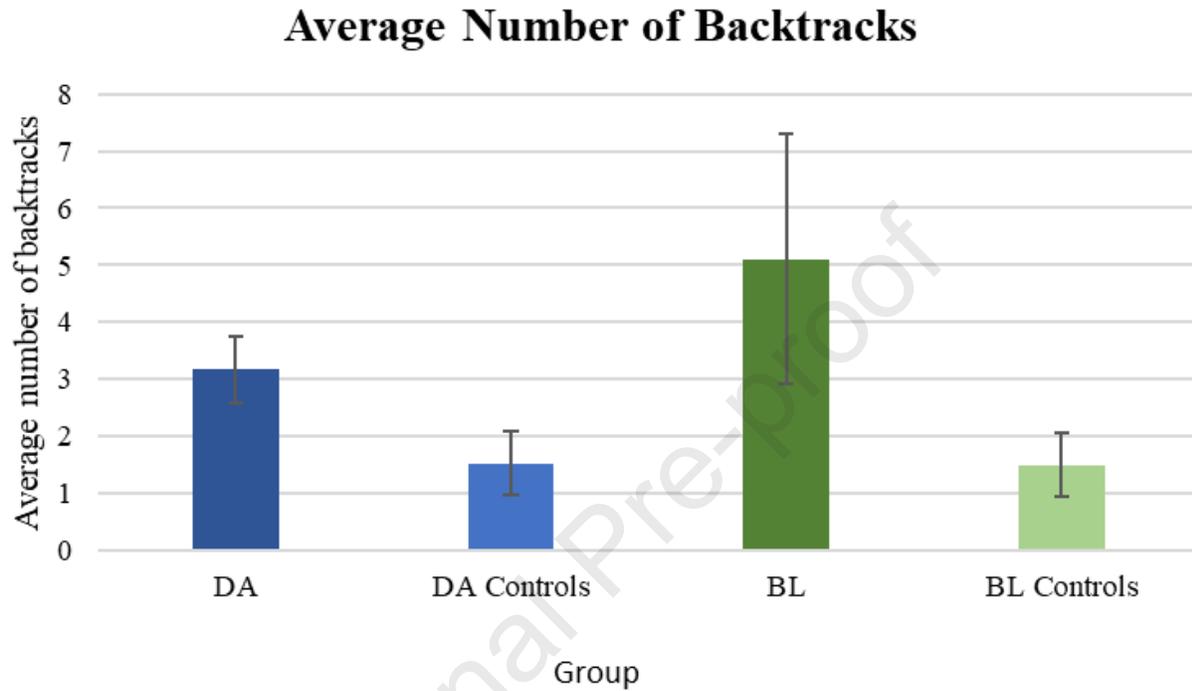


Figure 5*D.A.'s and B.L.'s Distance Performance by Map Visibility*

Note. Data are represented as mean +/- standard error of measurement.

Figure 6

Number of Backtracks by D.A. and B.L. Compared to Controls



Note. Data are represented as mean +/- standard error of measurement.

Table 1***Neuropsychological Test Results for D.A.***

	Scores	Score Label
General Intellectual Functioning		
WAIS-R ^a Full-scale Intellectual Quotient, <i>Standard Score</i>	117	High Average
WAIS-R ^a Verbal Intellectual Quotient, <i>Standard Score</i>	121	Above Average
WAIS-R ^a Performance Intellectual Quotient, <i>Standard Score</i>	106	Average
Attention & Executive Functioning		
WAIS-R ^a Digits, <i>Scaled Score</i>	13	High Average
Wisconsin Card Sorting Test (WCST) Categories, <i>raw score /6</i>	6	Within Normal Limits
WCST Perseverative Responses, <i>Z-score</i>	-0.5	Average
Letter Fluency ^b , <i>Scaled Score</i>	8	Average
Memory		
California Verbal Learning Test (CVLT) Acquisition, <i>T-score</i>	9	Low Average
CVLT Short Delay Free Recall, <i>Z-score</i>	-4	Exceptionally Low
CVLT Long Delay Free Recall, <i>Z-score</i> ,	-4	Exceptionally Low
CVLT Recognition Discrimination, <i>Z-score</i>	-4	Exceptionally Low
WMS-R ^b Logical Memory I, <i>percentile</i>	15 th	Low Average
WMS-R ^b Logical Memory II, <i>percentile</i>	<1 st	Exceptionally Low
Rey Osterrieth Complex Figure Delayed recall, <i>raw score /36</i>	0	Exceptionally Low
Perception/Visuospatial Abilities		
Rey Osterrieth Complex Figure Copy, <i>raw score /36</i>	35	Within Normal Limits
Language		
Boston Naming Test, <i>raw score /60</i>	56	Within Normal Limits
Semantic Fluency ^d , <i>Scaled Score</i>	12	High Average

Note. Score labels were assigned according to Guilmette et al., 2020.

^a Wechsler Adult Intelligence Scale–Revised (WAIS-R)

^b Score is based on the total number of words produced for the letters *F*, *A*, and *S* when given 1 minute for each.

^c Wechsler Memory Scale–Revised (WMS-R)

^d Score is based on the number of animal names produced in 1 minute

Table 2***Neuropsychological Test Results for B.L.***

	Scores	Score Label
General Intellectual Functioning		
WASI-II ^a Similarities Subscale, <i>percentile</i>	53 rd	Average
WASI-II ^a Vocabulary Subscale, <i>percentile</i>	53 rd	Average
WASI-II ^a Matrix Reasoning Subscale, <i>percentile</i>	39 th	Average
WASI-II ^a 2-factor Intellectual Quotient, <i>percentile</i>	45 th	Average
Processing Speed		
WAIS-IV ^b Symbol Search, <i>percentile</i>	9 th , 1 error	Low Average
WAIS-IV ^b Coding, <i>percentile</i>	9 th , 0 errors	Low Average
WAIS-IV ^b Processing Speed Index, <i>percentile</i>	6 th	Below Average
D-KEFS ^c Colour Naming, <i>percentile</i>	5 th , 0 errors	Below Average
D-KEFS ^c Word Reading, <i>percentile</i>	9 th , 0 errors	Low Average
Attention & Executive Functioning		
Wisconsin Card Sorting Test (WCST), <i>Scaled Score</i>	6	Low Average
WAIS-IV ^b Digit span Forward, <i>percentile</i>	50 th	Average
D-KEFS ^c Verbal fluency phonemic, <i>percentile</i>	63 rd , 0 errors	Average
D-KEFS ^c Verbal fluency semantic, <i>percentile</i>	50 th , 0 errors	Average
D-KEFS ^c Colour-word inhibition, <i>percentile</i>	1 st , 0 errors	Exceptionally low
D-KEFS ^c Colour-word switching, <i>percentile</i>	1 st , 0 errors	Exceptionally low
D-KEFS ^c Trails visual scanning, <i>percentile</i>	5 th , 0 errors	Below average
D-KEFS ^c Trails number sequencing, <i>percentile</i>	16 th , 0 errors	Low average
D-KEFS ^c Trails letter sequencing, <i>percentile</i>	2 nd , 0 errors	Exceptionally low
D-KEFS ^c Trails switching, <i>percentile & Time Discontinue errors</i>	<1 st , 2 errors 5 TD ^d errors	Exceptionally low
Memory		
Rey Osterrieth Complex Figure Delayed Recall, <i>Scaled Score</i>	5	Below Average
WMS-IV ^d LM-I, <i>Scaled Score</i>	8	Average
WMS-IV ^d LM-II, <i>Scaled Score</i>	6	Low Average
CVLT-3 ^e Verbal Learning, <i>percentiles (raw score trials)</i>	1 st , (3,5,4,4,5)	Exceptionally Low
CVLT-3 ^e Short Delay Free Recall, <i>percentile</i>	2 nd	Below Average
CVLT-3 ^e Short Delay Cued Recall, <i>percentile</i>	5 th	Below Average
CVLT-3 ^e Long Delay Free recall, <i>percentile</i>	5 th	Below Average
CVLT-3 ^e Long Delay Cued Recall <i>percentile</i>	9 th	Low Average
CVLT-3 ^e Long Delay free recall vs. T5 learning, <i>percentile</i>	25 th	Average
CVLT-3 ^e Recognition Hits, <i>percentile</i>	50 th	Average
CVLT-3 ^e Recognition False Positives, <i>percentile</i>	<1 st	Exceptionally Low

	Scores	Score Label
CVLT-3 ^e Recognition Discriminability (d'), <i>percentile</i>	5 th	Below average
Perception/Visuospatial Abilities		
Rey Osterrieth Complex Figure Copy, <i>Scaled Score</i>	6	Low Average
Judgement of Line Orientation, <i>percentile</i>	11-18 th	Low Average

Note. Score labels assigned according to Guilmette et al., 2020.

^a Wechsler Abbreviated Scale of Intelligence II (WASI-II)

^b Wechsler adult intelligence scale-IV (WAIS-IV)

^c Delis-Kaplan Executive Function System (D-KEFS)

^d Wechsler Memory Scale IV (WMS-IV)

^e California Verbal Learning Test-3 (CVLT-3)

^f TD – time discontinue errors – DKFES

Table 3*Descriptions of Wayfinding Levels from Sea Hero Quest*

Map Level	Difficulty	Map Description	Number of Buoys	Map Visibility
6	0.04	Open	3	Yes
7	0.14	Open-Island	3	Yes
8	0.15	Closed – Decision Point	3	Partial
11	0.10	Closed- Decision Point	3	Yes
12	0.31	Closed	3	Yes
13	0.27	Closed- Decision Point	3	Yes
16	0.02	Closed- Decision Point	3	Yes
17	0.11	Closed- Decision Point	3	Yes
18	0.14	Closed	3- in order	Partial
21	0.21	Closed – 2 islands	3	Yes
22	0.47	Closed – 1 island	3	Partial
43	0.93	Closed	4	Yes
46	0.31	Closed	3	Yes
56	0.48	Closed	5	Yes

Note. Difficulty ratings for each map level are based on Yesiltepe et al. (2023)³⁴.

Table 4***Wayfinding Performance on Sea Hero Quest in D.A. and B.L. vs. Control Participants***

Map Level	D.A. Distance	D.A. Duration	D.A. Number of Controls	B.L. Distance	B.L. Duration	B.L. Number of Controls
Open Level Maps						
6	30%	48%	5389	13%	5%	7978
7	NA	NA – stuck in front of buoy	5060	17%	18%	7647
Partially Visible Maps						
8	1%	2%	4713	18%	17%	7247
18	60%	2% – stuck in one location	1702	92%	84%	2611
22	1%	0%	1327	66%	61%	2006
Closed Level Maps - Decision Point						
11	5%	1%	3745	1%	0%	5774
12	69%	53%	3392	90%	64%	5237
13	68%	1% – stuck in one location	3068	13%	15%	4709
16	1%	0%	1993	2%	2%	3106
17	23%	6%	1869	0%	0%	2875
Closed Level Maps						
21	Quit	Quit	-	20%	3%	2168
43	44%	0%	425	4%	3%	580
46	44%	21%	315	1%	1%	447
56	63%	31%	208	1%	0%	295

Note. Performance indicated by percentiles, with higher numbers representing better performance.

Table 5*First Turn Accuracy on Sea Hero Question in D.A. and B.L.*

Level	Correct decision direction	D.A. Accuracy	B.L. Accuracy
7	Left	No	Yes
11	Left	No	Yes
12	Right	Yes	Yes
13	Right	Yes	Yes
17	Right	Yes	No

Table 6*Qualitative Scores of Performance on Sea Hero Quest in B.L. and D.A. vs. Controls*

Level	Category	B.L.	B.L. Controls	B · L · Z - D.A. s c o r e	D.A.	D.A. Controls	D · A · Z - s c o r e
11	Navigation Rating	1.5	8.15 (2.30)	- 2 · 8 9	2.5	8.7 (1.44)	- 4 · 3 1
	Backtracks	6	0.95 (1.24)	4 · 0 7	3	0.55 (0.83)	2 · 9 5
	Longest Dwell	2	0.95 (2.27)	0 · 4 6	9	0.4 (0.66)	1 3 · 0 3
13	Navigation Rating	7	8.75 (2.14)	- 0 · 8 2	10	7.8 (1.74)	1 · 2 6
	Backtracks	1	0.65 (1.38)	0 · 2 5	0	1.4 (1.58)	- 0 · 8 9
	Longest Dwell	0	0.90 (2.85)	- 0 · 3 2	43.5	0	e l e v a

Level	Category	B.L.	B.L. Controls	B.L. Score	D.A.	D.A. Controls	D.A. Score
16	Navigation Rating	3.5	8.67 (2.00)	2.59	3	9.70 (0.35)	1.94
	Backtracks	3	0.78 (1.46)	1.52	4**	0.10 (0.32)	1.28
	Longest Dwell	1.5	0.28 (0.67)	1.82	25	0.50 (1.27)	1.92
17	Navigation Rating	2.5	9.55 (0.50)	1.19	8	8.65 (1.13)	0.58
	Backtracks	6	0.3 (0.48)	1.18	2	0.85 (0.58)	1.88
	Longest Dwell	0	0	1.0	10	1.7 (5.38)	1.0

Level	Category	B.L.	B.L. Controls	B.L. Score	D.A.	D.A. Controls	D.A. Score
				18.54			
18	Navigation Rating	9.5	8.45 (1.01)	1.5	8.25 (1.34)		
	Backtracks	0	1.1 (1.02)	2.18	0.95 (0.93)		
	Longest Dwell	0	0.1 (0.32)	40.5	0.35 (0.75)		
21	Navigation Rating	3	7.35 (2.02)	2.15	NA	-	
	Backtracks	2	2.55 (2.33)	0.24	NA	-	
	Longest Dwell	1	0	1	NA	-	

Level	Category	B.L.	B.L. Controls	B.L. Z-score	D.A.	D.A. Controls	D.A. Z-score
22	Navigation Rating	9	8.7 (0.68)	0.44	2.5	8.55 (0.80)	7.56
	Backtracks	0	0.75 (0.79)	0.95	4	0.85 (1.03)	3.06
	Longest Dwell	0	0		24	0.3 (0.95)	2.45
43	Navigation Rating	2	6.65 (2.74)	1.70	3	7.45 (1.01)	4.41
	Backtracks	7	2.85 (2.47)	1.68	5	2.9 (1.47)	1.43

Level	Category	B.L.	B.L. Controls	B · L · Z - D.A. s c o r e	D.A.	D.A. Controls	D · A · Z - s c o r e
	Longest Dwell	2.5	2.95 (8.98)	- 0 · 0 5	71.5	0	e l e v a t e d
46	Navigation Rating	6.5	8.4 (0.81)	- 1 · 7 0	6	8.35 (1.65)	- 1 · 4 2
	Backtracks	1	0.45 (0.37)	1 · 4 9	2	0.5 (0.75)	2 · 0 0
	Longest Dwell	0	0.25 (0.79)	- 0 · 3 2	54	1.15 (3.64)	1 4 · 5 2
56	Navigation Rating	1	5.65 (2.43)	- 1 · 9 1	3	5.3 (2.06)	- 1 · 1 2
	Backtracks	22	5.65 (4.03)	4 · 0 6	6	5.7 (4.38)	0 · 0 7

Level	Category	B.L.	B.L. Controls	B · L · Z - D.A. s c o r e	D.A.	D.A. Controls	D · A · Z - s c o r e
	Longest Dwell	0	0.7 (1.27)	- 0 · 5 5	6.5	0.1 (0.32)	2 0 · 0 0

Note. Mean and standard deviation provided for control participants. Qualitative scores of DA's performance on level 21 is unavailable due to inability to complete the level. Asterisk on level 16 indicates that D.A. struggled to use the iPad on this level, requiring him to return to the buoy. Categories: "Navigation Rating" is a rating of navigation effectiveness on a 1-to-10 Likert-scale given by raters unaware of group membership, with 10 as the highest possible rating; "Backtracks" refers to the number of revisits to a previous location which was not relevant to navigation; "Longest Dwell" is the longest duration of a stop or pause during navigation, measured in seconds.

Table 7

Flare Accuracy on Path Integration Levels of Sea Hero Quest

Flare Level	Number of Turns	B.L. Accuracy	B.L. Control Accuracy %	D.A. Accuracy	D.A. Control Accuracy %
4	1	0	70.9 (0.45)	0	55.31 (0.50)
9	1	0	59.7 (0.49)	0	55.89 (0.50)
14	1	1	65.06 (0.48)	0	57.32 (0.49)
24	1	1	52.2 (0.50)	0	47.31 (0.50)
44	2	0	53.3 (0.50)	1*	44.65 (0.50)*
49	2	1	53.49 (0.50)	0*	50.15 (0.50)*
54	2	0	54.57 (0.50)	1	49.81 (0.50)

Note. Each flare level had three possible options. A score of “1” indicates an accurate choice, whereas a score of “0” indicates an inaccurate choice. Asterisks indicate levels on which D.A. did not navigate directly to the buoy.

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STAR Methods

RESOURCE AVAILABILITY

Lead Contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Dr. Sara Pishdadian (sara.pishdadian@camh.ca).

Materials Availability

This study did not generate any new materials.

Data and Code Availability

- Control data is available at <https://shqdata.z6.web.core.windows.net/> and all data will be publicly available as of the date of publication.
- This paper does not report original code.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

Experimental models

- Subjects
- Caucasian
- Mean age
- 100% males

Participants

This study conformed to the guidelines that were approved by the ethics committee at Baycrest Health Sciences. Informed consent was gathered from all study participants. All participants were tested online or through mobile-game technology for this study. Individuals with amnesia were tested online with an experimenter available through video or by phone to assist with instructions.

Amnesic individuals

Two individuals with amnesia, D.A. and B.L., who are well-characterized based on extensive neuroanatomical and neuropsychological assessment, participated in the current study⁴⁴. They differ in the extent of their lesions (see Figure 3) and neuropsychological profiles (see Tables 1 and 2), but both have in common bilateral hippocampal damage and deficits within episodic and spatial memory based on comprehensive testing.

D.A. is a 68-year-old, right-handed male with 17 years of education who developed amnesia as a result of herpes encephalitis in 1993⁴⁴⁻⁴⁵. He has bilateral MTL damage that is more severe in his right hemisphere (see Figure 3) and additional volume reduction in regions of posterior temporal, ventral frontal, and occipital cortex, as well as in the anterior cingulate cortex and posterior thalamus. D.A.'s neuropsychological profile is characterized by high-average intelligence, temporally graded retrograde amnesia, severe anterograde amnesia, deficient episodic details in autobiographical memory, and otherwise intact cognitive functioning⁴⁴⁻⁴⁶. D.A. has previously been shown to have difficulty learning to navigate in newly encountered spatial environments and has a loss of detailed memory but not schematic memory for remotely learned spatial environments, consistent with his hippocampal amnesia^{4,22,47}.

B.L. is a 59-year-old, right-handed male with 13 years of education who experienced anoxia in relation to cardiac arrest following an electrical accident in 1985⁴⁸. He has bilateral loss of the dentate gyrus and, to a lesser extent, CA3 subregion of the hippocampus, and additional volume loss in the left superior parietal lobe and right precuneus⁴⁸ (see Figure 3 for MRI image showing B.L.'s dentate gyrus and partial CA3 lesions). BL's neuropsychological profile is characterized by average intelligence, mild-moderate anterograde amnesia, and weaknesses in processing speed and complex attention⁴⁸⁻⁴⁹. Interviews with B.L. and his care team reveal that BL's navigation is restricted to familiar environments learned long ago, and there have been incidents of disorientation even in these familiar environments.

Controls

Control groups were formed from subsets of the SHQ benchmark data^{31,33,35}. All control participants were matched with either D.A. or B.L. based on practice level performance as well as country of origin (Canada), age (+/-3 years), and reported sex. D.A. was matched with a possible 7,439 controls. B.L. was matched with a possible 10,295 controls. The numbers of participants matched to D.A. and B.L. for each wayfinding level are available in Table 4.

METHOD DETAILS

Wayfinding and path integration ("flare") levels were administered using SHQ^{31,33}. The SHQ paradigm is not publicly available but is available upon request. The individuals with amnesia were tested individually on select SHQ levels on an iPad 11'5" from corner to corner and a 9" screen. Controls were tested independently through SHQ remotely³¹.

SHQ wayfinding levels have different characteristics, which are detailed in Table 3 (see also Figure 1 for gameplay and Figure 2 for graphical depiction). On each wayfinding level,

participants are asked to navigate to a specified number of checkpoint buoys in a particular order and navigation is complete when all buoys have been navigated to. Participants must maintain the order of buoys in their working memory but the total number of buoys and how many buoys participants have already visited is represented visually throughout the level (i.e., stars). The number and order of buoys also varies across wayfinding levels (Table 3). There is a range of 3-5 buoys depending on the level. The ordering and distance between buoys also vary across levels.

Participants are shown a map of each wayfinding level before navigating (images available in Figure 2) and can view these maps for as long as they would like before beginning the level. These maps may fully or partially depict the environment and are always from a bird's eye viewpoint (Table 3). A full map depiction shows the environment outline and the number of buoys, which themselves are numbered. A partial map depiction displays the number and position of buoys but not the entire environmental outline (boundaries of the water to be navigated), which are partially faded.

Wayfinding levels also differ in environmental layout. This includes whether a level contains open or closed paths. An open layout has all buoys in one space (see Figure 2 level 6 for an example) while a closed layout has buoys along different paths. In neither the open nor closed layouts are all buoys visible from any one point of view. Another environmental element that differs across wayfinding levels is whether there is a decision point at the start of navigation or the participants' first turn, that leads to different buoys (see Figure 2 level 11 for an example).

Path Integration Levels

Path integration or "Flare" levels require participants to navigate a level to a single location where a flare is located³¹ (see Figure 1). These levels differ in the number of turns taken

before reaching the flare location. Once participants reach the flare location, they are then asked to send the flare back to the levels' start location. Participants are given three potential directions to choose from and provided with subsequent feedback by seeing the flare sent to the specified location. The number of turns on each flare level is available in Table 7.

QUANTIFICATION AND STATISTICAL ANALYSIS

The data were analyzed using R version 4.2.0 (<https://www.r-project.org/>). Control data is available at <https://shqdata.z6.web.core.windows.net/> and publicly available as of the date of publication. Descriptive statistics were run using the psych package⁵⁰. The performance of individuals with amnesia was compared to that of controls using percentiles for distance traveled and time taken to complete each level (duration), see supplemental tables for a graphical depiction of each level. Performance was also averaged across all levels and divided by whether maps presented prior to each level were fully visible or partially visible (see Table 3 for level descriptions). On appropriate levels, the accuracy (correct or incorrect) of the first decision point was also coded. Path integration levels were coded for accuracy with chance performance at 33% given that there were three options to choose from. The relationship of D.A.'s and B.L.'s performance with previously derived metrics of level difficulty based on entropy, geometric and level-specific features was examined graphically and with correlation analyses³⁴.

To better contextualize amnesic participants' performance on each level, an in-depth qualitative scoring was conducted by two trained research assistants who were blind to group membership (i.e., individuals with amnesia vs. controls). Videos of the amnesic individuals' performance on each level were compared to those of 10 randomly selected age-/gender-matched

controls, for a total of 20 controls. All videos and map levels are available at <https://osf.io/mydwa/>.

Scoring categories included longest dwell time (i.e., pause) on a given level, number of returns to a previous location that is not relevant to the goal of navigation (i.e., backtracking), and an overall qualitative rating of navigation quality. In the case of a discrepancy between scorers, which were few and minor (within one point), participants were given the benefit of the doubt and were not penalized. Given the large number of control participants, whenever possible on wayfinding levels, Z-scores comparing the amnesic individuals to controls were calculated to show relative performance. Specific statistical tests used are described in the results section.

Supplemental

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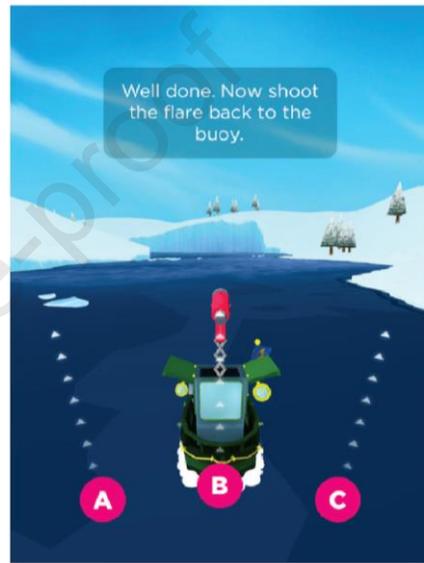
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Figure 1***Examples of Gameplay on Sea Hero Quest***

A)



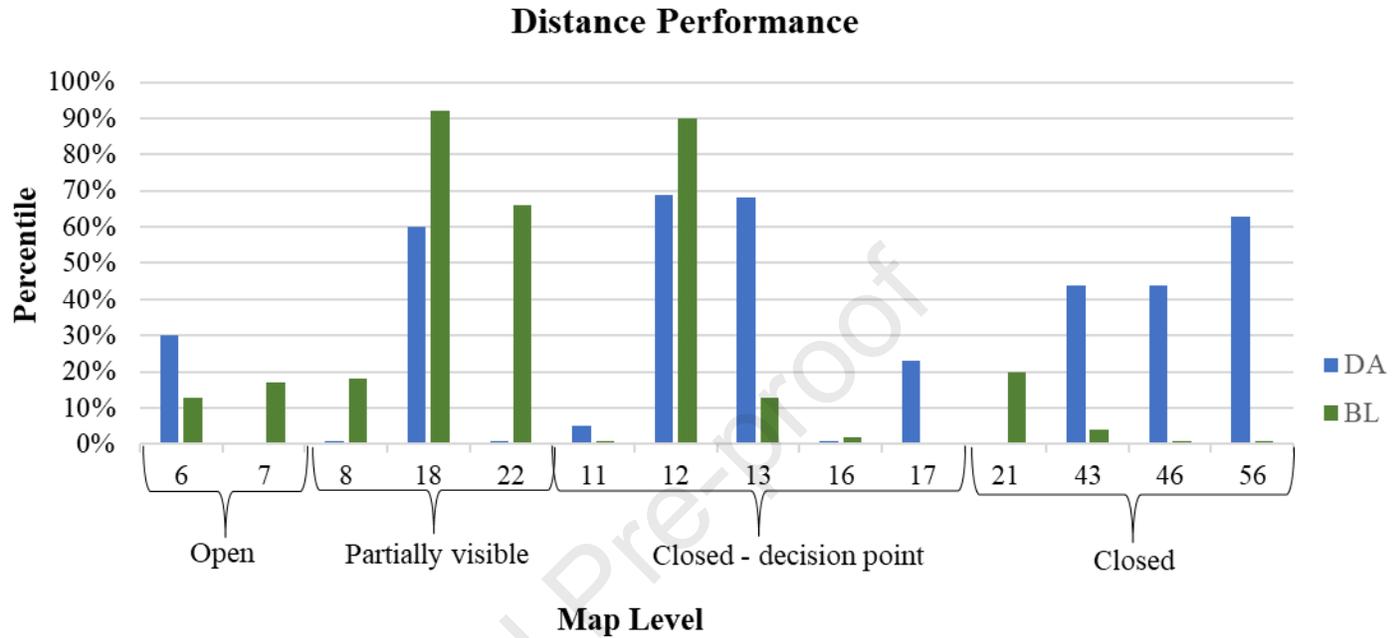
B)



Note. A) Example of gameplay during wayfinding levels. B) Example of gameplay during path integration levels, where participants had to navigate within a maze and when reaching a flare, shoot it back towards the start location. Images from Coutrot et al. (2019)³⁵.

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Figure 2

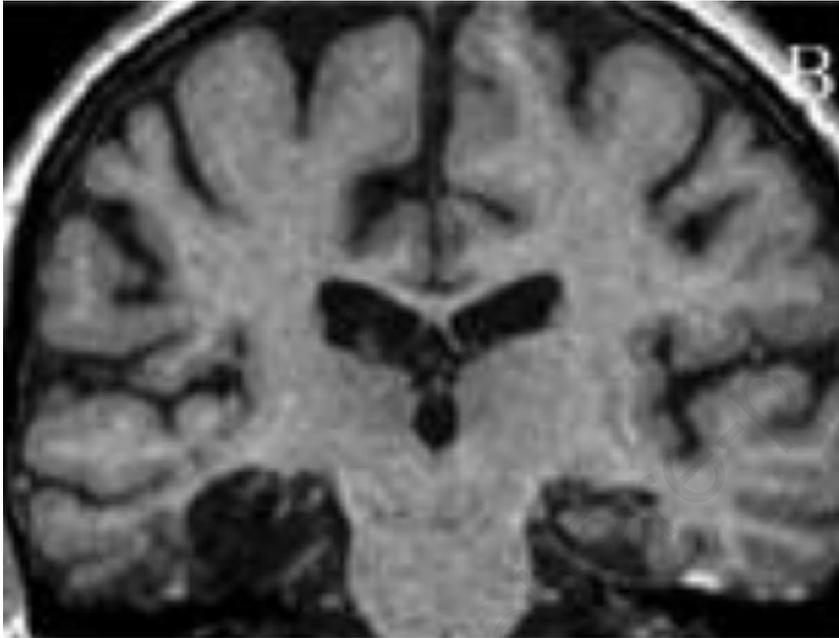
Distance Performance in B.L. and D.A. on Each Level of Sea Hero Quest

Note. Graph depicts distance performance in percentiles for D.A. and B.L. relative to their respective controls for each map level, which vary in difficulty and level characteristics (see Supplemental Figure 1 and 2 for images). Findings show that individuals with amnesia have performance that is comparable to controls when demands on anterograde memory are lower, which differs depending on level characteristics.

Figure 3

Representative MR images of the Medial Temporal Lobe in D.A. and B.L.

A)



B)



A) MR image of D.A.'s medial temporal lobes (MTLs) in a coronal view showing loss of volume bilaterally, most prominently in the right hemisphere. Image adapted from Kwan et al. (2013)⁴⁴. B) MR image of B.L.'s MTLs in a coronal view, with hippocampal segmentation visible to show the greatest volume loss within the dentate gyrus and partial volume loss in the CA3 subfield. Image adapted from Baker et al. (2016)⁴⁸.

Figure 4***D.A.'s and B.L.'s Distance Performance Compared to Controls***

Map difficulty is derived from entropy, geometric and level-specific features (Yesiltepe et al., 2022). Distance percentile is the distance traveled during navigation compared to matched control participants.

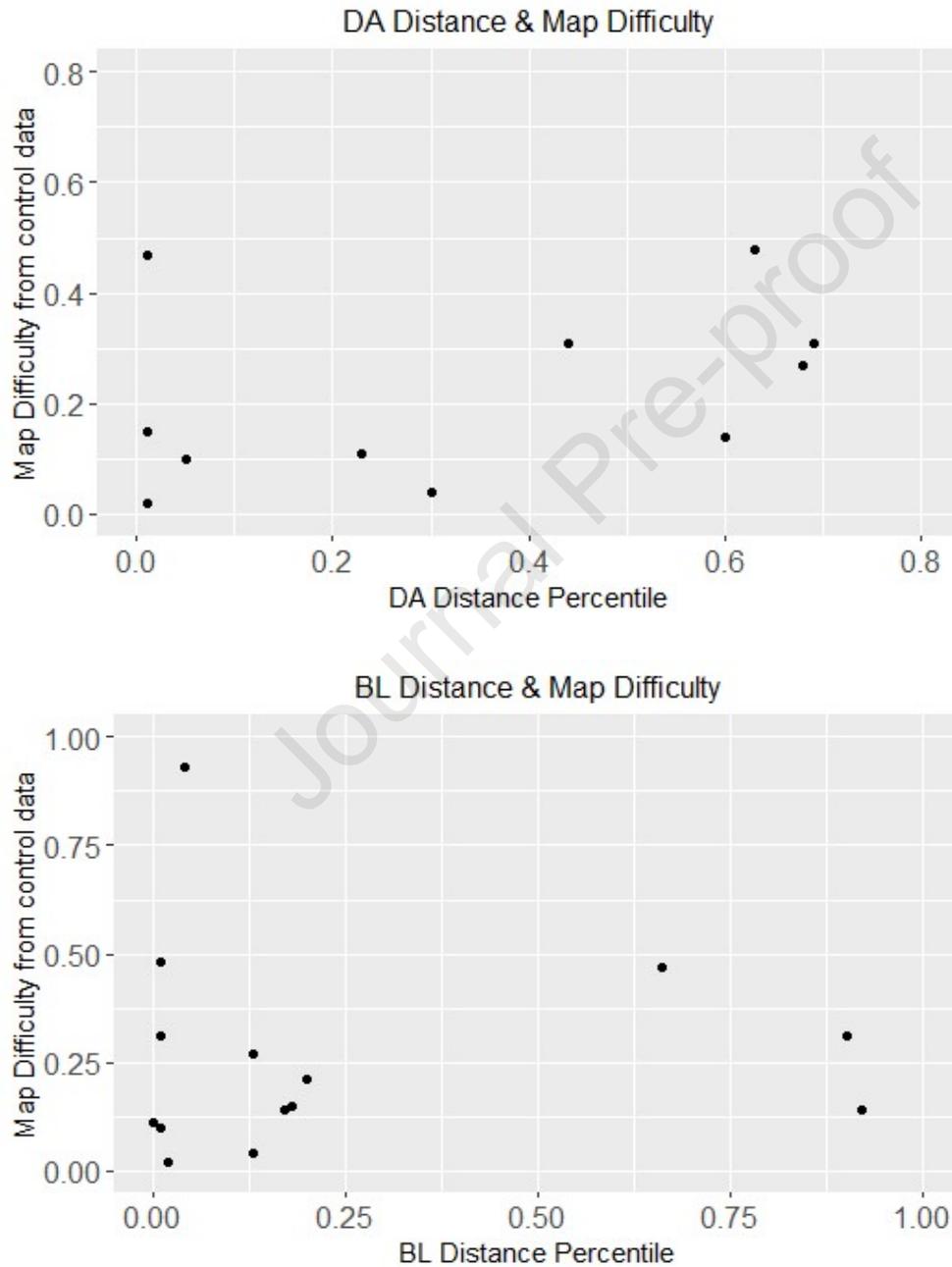
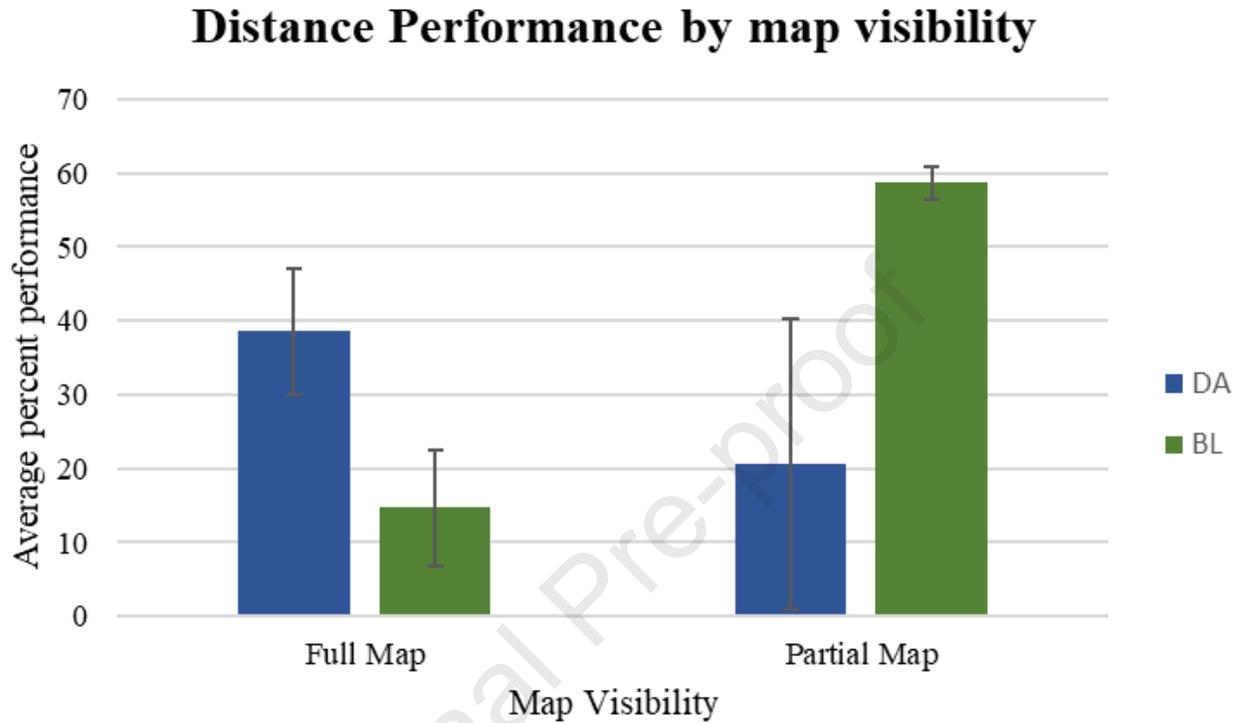


Figure 5

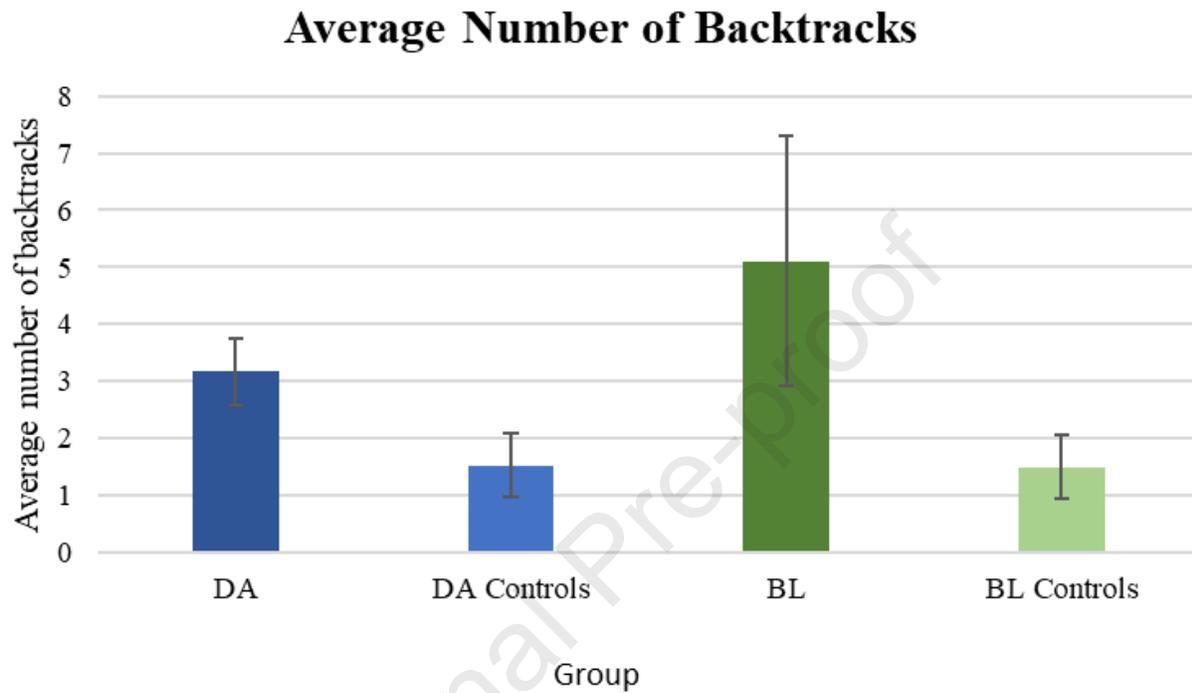
D.A.'s and B.L.'s Distance Performance by Map Visibility



Note. Data are represented as mean +/- standard error of measurement.

Figure 6

Number of Backtracks by D.A. and B.L. Compared to Controls



Note. Data are represented as mean +/- standard error of measurement.

Highlights

- hippocampal amnesia allows for low anterograde memory environmental navigation
- Findings challenge the hippocampus as critical for allocentric navigation
- Single case studies and big data methodology can be complimentary

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TABLE FOR AUTHOR TO COMPLETE

Please do not add custom subheadings. If you wish to make an entry that does not fall into one of the subheadings below, please contact your handling editor or add it under the “other” subheading. ***Any subheadings not relevant to your study can be skipped.*** (NOTE: references should be in numbered style, e.g., Smith et al.¹)

Key resources table

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Bacterial and virus strains		
Biological samples		
Chemicals, peptides, and recombinant proteins		
Critical commercial assays		
Deposited data		
Data set	https://shqdata.z6.web.core.windows.net/	
Experimental models: Cell lines		

Experimental models: Organisms/strains		
Oligonucleotides		
Recombinant DNA		
Software and algorithms		
Other		