Object-Based Cognitive Map in the Human Hippocampus and Medial Prefrontal Cortex

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Summary

A cognitive map, representing an environment around oneself, is necessary for spatial navigation. However, compared with its constituent elements such as individual landmarks, neural substrates of the coherent spatial information remain largely unknown. The present study investigated how the brain codes map-like representations in a virtual environment specified by relative positions of three objects. Representational similarity analysis revealed the object-based spatial environment in the hippocampus (HPC) when participants located their self-positions within it, while the medial prefrontal cortex (mPFC) represented it when they recollected a target object's location relative to their self-body. During the recollection, task-dependent functional connectivity increased between the two areas implying exchange of self- and target-location signals between HPC and mPFC. Together, the coherent cognitive map may be recruited in HPC and mPFC for complementary functions when we relate ourselves with a target object including person for navigation, and presumably for social interactions.

Key words: cognitive map, spatial navigation, episodic memory, memory-guided decision making, social interaction, hippocampus, medial prefrontal cortex, default mode network, representational similarity analysis.

Introduction

During navigation, it is necessary to locate our self-position in the current spatial environment as well as to locate the objects relative to the self-body (i.e., egocentric location). To conduct each of the two mental operations, we need map-like representations, called "cognitive map" in our brain (Tolman, 1948). After the discovery of "place cells," the hippocampus (HPC) of the medial temporal lobe (MTL) has been considered responsible for the cognitive map (Buffalo, 2015), and crucial contributions of the HPC to spatial memory have also been reported by animal model studies that evaluated behavioral patterns of rodents with an inactivated HPC using the Morris water maze and cross-maze (Nakazawa et al., 2002; Packard and McGaugh, 1996; Redish and Touretzky, 1998) as well as human studies that demonstrated the relationship between HPC volume in individual subjects and their amounts of experience exploring spatial environments (Woollett and Maguire, 2011; Schinazi et al., 2013, e.g., London taxi drivers). However, it remains largely unknown how neural substrates of the cognitive map are involved in the two mental operations required for the recollection of an egocentric location of a target object. One possible reason for the difficulty in addressing this question is that despite extensive studies on the spatial elements related to the cognitive map (e.g., self-location, head-direction etc.) (O'Keefe and Dostrovsky, 1971; Vass and Epstein, 2013; Chadwick et al., 2015; Buffalo, 2015; McCormick et al., 2018;), there is still a lack of sufficient isolation and characterization of the neural signal of the cognitive map under the previous research paradigms.

In addition to the HPC, the role of the medial prefrontal cortex (mPFC) in goal-directed planning during navigation was demonstrated by a previous human fMRI study that showed increased connectivity between the HPC and mPFC (Brown et al., 2016). The mPFC has been long considered as a member of the core-brain system in the retrieval of episodic memory (Konishi et al., 2000; Eichenbaum, 2017; McCormick et al., 2018), which is an

autobiographical memory consisting of spatial, object, and temporal information (Suzuki and Naya, 2011; Naya and Suzuki, 2011; Squire and Wixted, 2011). Schacter et al. (2007) suggested an involvement of the mPFC in future-simulation processing and recollection of past episodes, which depend on mnemonic information stored as declarative memory including both episodic and semantic memory. Recently, they also showed increased connectivity between the HPC and mPFC during future simulation (Campbell et al., 2018). This preceding literature suggests that the HPC and mPFC, which belong to the default-mode network, work together when remembering stored information (e.g., cognitive map) and construct the mental representation of goal-directed information (e.g., target-location) from mnemonic information with the current context (e.g., self-location) (Schacter, 2012). However, the specific functional role of each of HPC and mPFC during the construction process (McCormick et al., 2018; Campbell et al., 2018) remain elusive, presumably because the construction of goal-directed information (e.g., spatial navigation) includes at least two mental operations described above (i.e., locating self and locating the target relative to self-location), and the previous experimental paradigms mostly unseparated them.

To address these issues, we aimed to devise a novel 3D spatial-memory task with spatial environments defined by objects, which would enable us to identify the representation of the cognitive map and to investigate how it is related to the two mental operations (Fig. 1). We used the same stimulus set consisting of three different human characters through the entire experiment, while the spatial configuration of the three characters was changed trial-by-trial. The spatial configuration pattern was referred to as a *"map"* in the present study (Fig. 1b). In each trial, participants encoded a *map* from the first-person's view by walking toward the characters in one of four fixed walking directions (walking period, Fig. 1c, see Methods). Following the walking period, one human character (facing object) was presented on a virtual-environment background with other characters being invisible, which gave the

participants a feeling of facing the presented character in the virtual environment (i.e., facing period). After a short delay, one of the two remaining characters (targeting object) was presented without the virtual environment background, and the participants were required to remember the location of this second human character relative to their self-body (i.e., targeting period). Thus, the two mental operations were separated into two periods within a single trial. This task design allowed us to detect the brain regions that distinguished the spatial configurations of the objects (i.e., *map*) around the participants during the facing period and targeting period separately. The results of the representational similarity analysis (RSA; see Methods for details) (Kriegeskorte et al., 2012; Kriegeskorte et al., 2008) showed that the spatial environment defined by the three objects were represented in the HPC during the facing period, while it was represented in the vmPFC during the targeting period, suggesting different contributions of the object-based cognitive map to the recollection between the two brain areas of the default mode network.

Results

The experiment was conducted in two days with 19 participants. On the first day, the participants were familiarized with the 3D virtual environment and the three human characters through a head-nodding detection (HND) task (Fig. S1a). In this task, the participants had the same walking experience as in the spatial-memory task but were subsequently asked to indicate whether a character in a photo nodded its head during the walking period. On the second day, the participants performed the spatial-memory task under scanning. To prevent voluntary memorization of the spatial relationship of the human characters during the walking period, the HND trials were pseudo-randomly mixed with the spatial-memory trials at the ratio of 1:10, and the participants were instructed to focus on head-nodding of the human characters during the walking period in all trials. All participants exhibited a top-ceiling performance with a 93.6% ± 0.02% correct rate (mean ± SE, n = 19) for the spatial-memory task and no significant difference was found among each of the task parameters (e.g., maps, walking directions) (Fig. S1c). All participants showed an accuracy that was significantly higher than chance level (50%) in both the head-nodding and no head-nodding trials (Fig. S1a). Attempts to memorize the spatial arrangements of the human characters during scanning were examined using post-scanning questionnaires. All participants reported that they did not make any voluntary effort to memorize the spatial relationship of the three human characters nor utilize any special strategy for memorizing it (Table S2). It should be noted that no participant was able to recall the number of map patterns they experienced in the experiment even though only three of the six possible patterns of maps were repeatedly presented to each participant. In addition, no significant changes in performance was found across four experimental sessions (Fig. S1b; $F(3,72) = 0.38$, $P < 0.001$), suggesting that the participants performed the spatial-memory task with high-performance from the beginning and did not learn to use a systematic strategy to

124 improve their performance during the sessions. These behavioral results guarantee that the
125 participants automatically encoded maps during the walking period when viewing the human
126 characters attentively to detect head-nodding.
127
128 **Neural representation of the cognitive map during locating self-position**
129 We first assessed the map representation during the facing period (4.0 s including the
130 subsequent delay; Fig. 2a), in which the participants oriented themselves to a presented
131 human character in the 3D environment. To decode the map information across the whole
132 brain, we conducted searchlight-based RSA, which compared the multi-voxel pattern
133 similarities of the "same map" and "different map" between trial pairs across each brain
134 voxel by drawing a 6 mm radius sphere with each voxel in the spherical center. Map
135 information was decoded regardless of other task parameters such as the walking direction or
136 the identity of the facing character (see Methods for details and Table S1 for the regressor list
137 and the averaged r^2 among the regressors in each GLM). We found a cluster located in the
138 left middle HPC (mHPC; Fig. 2b, $P < 0.01$, voxel-wise threshold; $P < 0.05$, cluster-
139 corrected), suggesting that the map defined by multiple objects is represented in the HPC. In
140 addition to the mHPC, the searchlight-based RSA revealed clusters in the insula, angular
141 gyrus, and superior temporal cortex (Fig. S2b, $P < 0.01$, voxel-wise threshold; $P < 0.05$,
142 cluster-corrected; see discussion). To validate the searchlight-based RSA result showing that
143 the left mHPC represents map information, we manually segmented the sub-regions in the
144 MTL in each participant's native space (Fig. S4, left panel) and conducted an independent
145 RSA within each anatomical mask (see Methods for details). The region of interest (ROI)-
146 based result also showed that only the left mHPC had a significantly higher pattern similarity
147 to "same maps" relative to "different maps" among the MTL sub-regions (Fig. S5a; $t(18) =$
148 2.94, $P = 0.004$, Bonferroni corrected for multiple comparisons, alpha < 0.05).

149 To examine possible signal input from the MTL sub-regions to the left mHPC for the
150 map construction, we examined the neural representation of the facing-character identity and
151 walking direction that the participants perceptually and/or mentally re-experienced during the
152 facing period based on the post-scanning test (Table S2; Fig. S3a). Searchlight-based RSA
153 revealed that the bilateral perirhinal cortex (PRC) encoded character identity (Fig. S3b; $P <$
154 0.001, initial threshold; $P < 0.05$, cluster-corrected) (Naya et al., 2001; Suzuki and Naya,
155 2014), while the parahippocampal cortex (PHC) and left retrosplenial cortex (RSC) encoded
156 the walking directions reflecting the spatial layout of one empty and three occupied positions
157 perceived by the participants during the walking period (Fig. 1c). In the HPC, the left
158 posterior HPC (pHPC) selectively represented the spatial layout but not the character identity,
159 while the bilateral anterior HPC (aHPC) revealed clusters for both character identity and
160 spatial layout (Fig. S3b). These results were consistent with the notion of the "two cortical
161 systems" model that suggests that object identity and spatiotemporal context are processed in
162 two separate neural systems with the PRC and PHC-RSC as the core brain regions, with the
163 two different information domains interacting in the HPC (Ranganath and Ritchey., 2012).
164 Together, the RSA analyses demonstrated that the MTL is crucial for representing the spatial
165 environment in the following ways**:** elements such as each object identity and spatial layout
166 were represented by extrahippocampal areas while the relative relationship between multi-
167 objects was represented in the HPC, suggesting cognitive map representation in the HPC.
168

169 **Cognitive map during localizing target**

170 In contrast to locate self-position, a clear difference was found in brain regions responsible
171 for the map representations when the participants remembered the location of a target
172 character relative to their self-body (egocentric target location). In contrast to the facing
173 period, clusters representing the map information were revealed mainly in the Rectus and

174 Brodmann area 10 of the vmPFC (Peak coordinates: 4, 50, -18; t value: 5.62), rather than in
175 the HPC, during the targeting period. We confirmed that no cluster was found in the MTL
176 even though a more liberal threshold was used ($P < 0.01$, voxel-wise threshold, uncorrected).
177 To validate this result, we conducted an independent RSA using frontal sub-regions of the
178 automated anatomical labeling (AAL, Fig. S4, right panel) template as well as manually
179 segmented MTL sub-regions as ROIs. The result confirmed that the map information was
180 represented in the rectus of the prefrontal region (Fig. S5a, $t(18) = 4.64$, $P = 0.0001$,
181 Bonferroni corrected for multiple comparisons, alpha < 0.05), while no MTL sub-regions
182 revealed map representation significantly during the targeting period. Together with the
183 facing period results, these results revealed a double dissociation of MTL and mPFC function
184 in the map representation between the task demands, implying that the mPFC, rather than the
185 MTL, carried the map information during the generation of the egocentric location signal of a
186 target character but during self-body locating. Our results indicate that the HPC and mPFC
187 operate in a complementary manner, supporting the notion of the "parallel, but interactive
188 cognitive map" between the two brain structures (Wikenheiser and Schoenbaum., 2016).
189 Outside of the vmPFC, we found clusters in the precuneus and middle temporal gyrus, and
190 the inferior frontal cortex (Fig. 2c, Fig. S2c; $P < 0.001$, voxel-wise threshold; $P < 0.05$,
191 cluster-corrected). These three brain regions have been consistently reported to be involved in
192 scene construction during recalling of past experience and imagination of new experiences
193 (Hassabis and Maguire, 2007; Bird et al., 2010; Gaesser et al., 2013), which is consistent with
194 the post-scanning report showing that all participants recalled and also imagined the
195 egocentric positions of the three human characters during the targeting period.
196 As with the facing period, we examined neural representation of targeting character
197 identity and walking direction during the targeting period and found that the PRC stably
198 represented character identity (Fig. S3b; $P < 0.001$, initial threshold; $P < 0.05$, cluster-

199 corrected), while we did not find clusters for the spatial layout depending on the walking
200 direction. These results suggested that the HPC did not construct the map information from
201 its constituent elements during the targeting period.
202
203 **Current self-orientation on the map**
204 To compute the egocentric location of a target object (e.g., left, right, or back), information
205 on the current self-position/orientation on the map is necessary (Fig. 3a). Therefore, we
206 examined which brain regions were involved in representing such allocentric "heading-
207 direction" signals (Hargreaves et al., 2005; Wang et al., 2018). Interestingly, while no
208 significant cluster was revealed during the facing period (facing character; Fig. 3b and
209 Supplementary Fig. S5b), robust clusters were revealed during the targeting period (Fig. 3b, P
210 < 0.001, voxel-wise threshold; P < 0.05, cluster-corrected). These clusters were located in the
211 ERC, bilateral HPC, and PHC inside the MTL as well as in the lateral occipital cortex,
212 parietal cortex, precuneus, and anterior cingulate cortex outside the MTL (Fig. 3b, P < 0.001,
213 voxel-wise threshold; P < 0.05, cluster-corrected). These results suggested that a self-
214 orientation signal was induced during the targeting period, presumably because of the
215 necessity to compute the egocentric target location. This interpretation is consistent with the
216 post-scanning report in which participants reported imagining their self-orientation on the
217 map only during the targeting period.
218 To further evaluate the role of the MTL in informational representation, we conducted
219 a ROI-based RSA that computed the averaged pattern similarity among MTL sub-regions for
220 four spatial parameters (cognitive map, walking direction, character identity, and self-
221 orientation). The result revealed that the map and walking direction were represented in the
222 MTL during the facing period (Fig. 3c, cognitive map: t(18) = 2.519, P = 0.01; walking
223 direction: t(18) = 5.134, P = 3.48 x 10-5) followed by an attenuated-representation during the

224 targeting period (cognitive map: $t(18) = 1.312$, $P = 0.1$; walking direction: $t(18) = 2.302$, $P =$
225 0.02); in contrast, self-orientation was represented in the targeting period only (facing period:
226 $t(18) = -2.256$, $P = 0.98$; targeting period: $t(18) = 7.11$, $P = 6.28 \times 10^{-7}$); Notably, the MTL
227 showed significant representation for character identity in each period (facing period: $t(18) =$
228 7.732, $P = 1.98 \times 10^{-7}$; targeting period: $t(18) = 6.687$, $P = 1.42 \times 10^{-6}$). These results
229 demonstrated that MTL encoded or reinstated the information of an external world around the
230 participants which were necessary for determining an egocentric target location.
231
232 **Remembering the egocentric location of a target object**
233 Next, we examined which brain regions signaled the egocentric location (left, right, or back
234 relative to self-body) of a target object (Fig. 4a). The results revealed robust clusters in both
235 the mPFC and MTL (Fig. 4a, $P < 0.001$, voxel-wise threshold; $P < 0.05$, cluster-corrected). In
236 the mPFC, we identified the rectus, medial/superior orbitofrontal cortex, and olfactory cortex.
237 In the MTL, clusters were found in the anterior HPC. Apart from the mPFC and MTL,
238 clusters were also found in the lateral occipital cortex, inferior parietal cortex, anterior
239 temporal lobe, premotor cortex, and lPFC (middle and superior PFC). We also found clusters
240 in the precuneus and posterior parietal cortex, which were previously reported to represent
241 the egocentric location (Chadwick et al., 2015). The widely distributed clusters may indicate
242 that the brain regions representing the egocentric target locations can be involved in either
243 generation of the egocentric-target-location information from multiple pieces of information
244 (cognitive map, self-orientation, and target character identity) or its maintenance while
245 preparing for the following response. These distinct functions might be supported by three
246 different large-scale brain networks: the dorsal attention network, frontoparietal control
247 network, and default mode network (Spreng and Schacter., 2011). In contrast to the robust
248 signal observed across different brain networks for egocentric target-location, no cluster was

249 revealed for allocentric target location relative to the spatial layout of the characters (Fig. 4b,
250 $P < 0.001$, voxel-wise threshold; $P < 0.05$, cluster-corrected), which implies that the target
251 location may be directly retrieved in the form of egocentric coordinates rather than via its
252 allocentric representation.
253
254 **Increased default-mode network connectivity while locating a target compared with**
255 **self-locating**
256 The present results showed that the MTL and mPFC signaled a coherent map coding a spatial
257 relationship of the three human characters during the different time periods in which different
258 task demands were required (i.e., self-locating and target-locating). In addition, the MTL and
259 mPFC signaled the different location information even during the same targeting period;
260 MTL areas tended to represent allocentric self-location while the mPFC tended to represent
261 egocentric target location. To investigate how the different functional contributions of the
262 MTL and mPFC were substantiated by whole brain large-scale networks, we conducted a
263 task-based functional connectivity analysis using MTL and mPFC sub-regions as seeds (six
264 and five, respectively). For each seed, the mean regional time course was extracted and
265 correlated with each voxel's time course outside the seed, generating seed-based connectivity
266 maps for each facing and targeting period. Then, we compared the connectivity between the
267 two periods using a permutation test (see Methods for details).
268 First, the task-based functional connectivity analysis indicated significantly larger
269 connectivity between the MTL and mPFC in the targeting period relative to the facing period
270 ($t(18) = 2.95$, $P = 0.009$). We next examined the connectivity of the MTL and mPFC to the
271 three large-scale brain networks. Both the MTL and mPFC showed significantly larger
272 connectivity to brain areas that belong to the frontoparietal control network during the facing
273 period relative to the targeting period (Fig. 5a, $P < 0.01$, voxel-wise threshold; $P < 0.05$,

274 cluster-corrected). In contrast, the default mode network and dorsal attention network showed
275 significantly larger connectivity to the MTL and mPFC in the targeting period compared to
276 the facing period (Fig. 5b, $P < 0.01$, voxel-wise threshold; $P < 0.05$, cluster-corrected). These
277 results suggest that both the MTL and mPFC changed their connectivity to the three
278 functional networks across the two task periods. We next evaluated the task-based functional
279 connectivity during each task period based on the three functional network masks (Fig. 5a, b).
280 This ROI analysis revealed that the default mode network was positively correlated with the
281 MTL ($t(18) = 9.42$, $P < 0.001$) and mPFC ($t(18) = 10.63$, $P < 0.001$) for both time periods
282 with a significant increase in the targeting period (Fig. 5c & Fig. S6, top panel; $F(1,72) =$
283 4.63, $P = 0.03$), regardless of the seeds (MTL or mPFC; $F(1,72) = 0.24$, $P=0.62$). These
284 results suggest that the default mode network contributes more to the retrieval of the target
285 location than the self-location to an external reference during the facing period. In contrast,
286 the frontoparietal control network showed significantly negative connectivity with the MTL
287 ($t(18) = -9.12$, $P < 0.001$) and mPFC ($t(18) = -10.43$, $P < 0.001$) during both task periods,
288 indicating that the frontoparietal control network works competitively with MTL and mPFC
289 areas of the default mode network. This competitive effect was stronger during the targeting
290 period (Fig. 5c & Fig. S6, middle panel; $F(1,72) = 5.82$, $P = 0.02$). Interestingly, despite both
291 the MTL and mPFC being part of the default mode network, they showed opposite
292 connectivity patterns to the dorsal attention network during both periods (Fig. 5c & Fig. S6,
293 bottom panel; $F(1,72) = 46.72$, $P < 0.001$); the MTL positively with the network while the
294 mPFC negatively correlated with it. The connectivity between the MTL and the dorsal
295 attention network increased from the facing to targeting period ($t(18) = 4.31$, $P = 0.0004$).
296 These results demonstrated that the dorsal attention network, which contains the superior
297 parietal lobule (SPL) that represented egocentric target location (Fig. 4a), showed increased
298 coupling with the MTL during the targeting period. On the other hand, the mPFC only

attenuated its amplitude of anti-correlated connectivity with the dorsal attention network, which may suggest that egocentric target location represented in the mPFC was not directly transmitted to the dorsal attention network. Considering the increased coupling between the mPFC and default mode network including MTL areas during the targeting period (Fig. 5b&c), we hypothesize that the egocentric target location might be transferred from the mPFC to the SPL via the MTL.

305 **Discussion**

306 In this study, we examined neural representations of space defined by three objects and found
307 that both the HPC and mPFC represented the object-based space around the participants.
308 Interestingly, the HPC represented the object-based map when the participants locate their
309 self-body in the environment constructed by the three objects, while the mPFC represented
310 the map when the participants remembered the location of a target object relative to the self-
311 body. These results suggest that the cognitive maps in different brain regions play different
312 functional roles. In addition, during the targeting period, we found different preference in
313 spatial element representation between the MTL and mPFC, more MTL regions reinstated
314 allocentric self-location, while more mPFC regions represented egocentric target location
315 relative to self-location. Increased functional connectivity was observed between the MTL
316 and mPFC under the necessity of the retrieval of the target location from the stored memory
317 (targeting period) compared to when they actually faced the reference object to locate their
318 self-body (facing period). These results suggest that mental representations of the external
319 world formed by the coherent space and its constituent elements may be shared in the default
320 mode network including the MTL and mPFC. The special role of the mPFC in this scheme
321 may be to select the object location based on the mnemonic information including the
322 cognitive map and current self-location on it, which may be propagated from the MTL.

323 For the detection of "*map*" effect (Fig. 1b), the present task was designed to cancel
324 out effects of a particular encoding experience related with the walking direction as well as a
325 particular object identity that the participants viewed during the facing and targeting periods
326 in each trial by balancing number of trials with each of those confounding factors in each
327 map (see Methods). Therefore, the neural representation of the map information revealed by
328 the RSA cannot be explained by individual perceived information in the present study.
329 Moreover, the participants always stood on the center of the virtual environment during the

330 facing and targeting periods, during which the map effect was examined. Because of this task
331 design, the map information does not directly indicate self-location information like place
332 fields of place cells in the HPC (O'Keefe and Dostrovsky, 1971). On the other hand, the
333 representations of place-fields are reportedly influenced by the animal's cognitive map, and
334 the existence of cognitive maps could be most clearly demonstrated by a phenomenon known
335 as "remapping", which reportedly occurs in populations of place cells in the rodent HPC
336 (Moser et al., 2017). Therefore, it might be reasonable to interpret the map representations in
337 the left mHPC during the facing period as experimental evidence of "remapping" of place
338 cells in the human HPC even though the participants stood on the same position. However,
339 holding this interpretation predicts that human place cells are localized in the left mHPC.
340 This prediction is against consistent evidence from previous human studies that reported that
341 the right HPC was more involved in encoding and retrieving spatial information than the left
342 HPC (Abrahams et al., 1997; Maguire et al., 1997; Ekstrom et al., 2003; Doeller et al., 2008;
343 Schinazi, 2013). The other possible interpretation for the map representation in the left
344 mHPC is that it may encode an allocentric spatial relationship of the three objects itself. This
345 interpretation is consistent with previous human imaging studies reporting contributions of
346 the left HPC to the imagination of visual scenes, which could be constructed from multiple
347 spatial elements (Addis et al., 2007; Bird et al., 2010). The specific role of the left HPC in
348 relational memory was also reported in non-spatial information domains, including
349 associative learning (Kumaran et al., 2009; Suarez-Jimenez et al., 2018) and social
350 interactions (Tavares et al., 2015;). Taken together, it might be more reasonable to interpret
351 that the clusters in the left mHPC represented a coherent space constructed by the multiple
352 objects rather than its influence on representations of individual spatial elements such as self-
353 location or head direction. RSA also revealed the involvement of the PRC and PHC in MTL
354 signaling the object identity and egocentric view of their spatial layout, respectively, which

355 might be used for constructing the coherent map from its constituents in the left mHPC.
356 Future studies should address how the coherent map can be constructed by multiple objects in
357 the MTL.

358 In contrast to the facing period, during the targeting period, the representation of the
359 map information was found in the mPFC but not in the HPC. In addition, the mPFC signaled
360 the egocentric location of a targeting object, while the MTL concurrently signaled the
361 allocentric self-location. Involvement of the mPFC in constructing goal-directed information
362 in the current context is consistent with accumulating evidence showing that the mPFC
363 contributes to decision making or action selection (Saxena et al., 1998; Gallagher et al., 1999;
364 Feierstein, 2006; Spiers and Maguire, 2007; Kable and Glimcher, 2009; Young and Shapiro,
365 2011; Balaguer et al., 2016; Yamada et al., 2018). These previous studies consistently
366 supported the notion that the mPFC function becomes obvious when an appropriate selection
367 requires mnemonic information in addition to incoming perceptual information (Bradfield,
368 2015). In this study, together with perceptual information responsible for target object
369 identity, mnemonic information such as the map information and allocentric self-location was
370 required to solve the task. Considering that the MTL could provide all the necessary
371 mnemonic information, a reasonable interpretation is that the mPFC was involved in the
372 selection of one egocentric location among alternative locations rather than the recollection
373 or generation of location information of a target object.

374 In addition to the HPC and mPFC, the map information has been observed in other
375 brain areas such as the angular gyrus (Seghier, 2013; Price et al., 2016), lateral temporal
376 gyrus (Karnath, 2001; Himmelbach et al., 2006), and precuneus (Cavanna and Trimble, 2006)
377 that also belong to the default mode network. The brain areas in the default mode network,
378 particularly the MTL sub-regions except for the PRC represented allocentric self-location

379 during the targeting period. On the other hand, RSA analysis showed that widely-distributed
380 brain regions were involved in the representation of the egocentric target object location not
381 only in the default mode network but also in the dorsal attention network and frontoparietal
382 control network. The positive and negative functional connectivity between the dorsal
383 attention network and the MTL and mPFC suggest that the egocentric target location signal is
384 transmitted from the mPFC to the brain regions of the dorsal attention network, such as the
385 SPL (Evans et al., 2016), via the MTL, which implies a pivotal functional role of MTL as a
386 hub of mental representation of object signals.

387 Interestingly, the frontoparietal control network showed a strong negative correlation
388 with both the MTL and mPFC during both periods, although the lPFC in the frontoparietal
389 control network represented both the map information and egocentric direction during the
390 targeting period. In addition, the lPFC represented walking direction as well as character
391 identity during both the facing and targeting period. These results suggest that the lPFC
392 computes the target location independently of the default mode network. The parallel
393 contributions of the lPFC and MTL-mPFC in choosing the target location may reflect their
394 different cognitive functions (Jimura et al., 2004). lPFC has long been considered as a center
395 of executive functions (Funahashi, 2017; Miller et al., 2018) equipped with working memory
396 (Andrews et al., 2011; Barbey et al., 2013; Brunoni and Vanderhasselt, 2014; Funahashi,
397 2017). In human fMRI studies, the lPFC has been shown to contribute to the retrieval of task-
398 relevant information from spatial memory when more systematic thinking is required
399 (Epstein et al., 2017; Javadi et al., 2017). In this study, the behavioral task was designed to
400 ensure participants neither actively maintained a spatial configuration of the human
401 characters during the walking period nor any systematic strategy to solve the task, which was
402 confirmed by the post-scanning test results. The greater signal for the cognitive map and the
403 egocentric target location in the mPFC than that in the lPFC may indicate that the current task

404 was easy enough to allow participants to depend only on memory to exhibit top-ceiling
405 performance (Epstein et al., 2017; Javadi et al., 2017).
406 In contrast to previous memory/navigation studies, which examined brain functions
407 using spatial environments consisting of immobile landmarks (e.g., stores) and/or landscapes
408 (e.g., mountains) (Bird et al., 2010; Woollett and Maguire, 2011; Schinazi et al., 2013;
409 Chadwick et al., 2015; Brown et al., 2016), the present study used a spatial environment
410 constructed by only mobile objects that could become targets and references of self-location
411 as well as determine the space (i.e., map) around oneself. This task design allowed us to
412 extract a mental representation of the spatial environment consisting of the minimum
413 essential constituents. This reductionist method could be useful for future studies
414 investigating the construction and functional mechanisms of a cognitive map because of its
415 simplicity. One critical concern might be whether the findings discovered by this reductionist
416 method can be applied to a more complicated cognitive map consisting of large numbers of
417 immobile spatial elements, which could be learned through extensive explorations over a
418 long time period (e.g., the city of London) (Woollett and Maguire, 2011). Another related
419 concern might be whether our brain system holds only one cognitive map or multiple ones at
420 a time (Meister and Buffalo, 2018). For example, we may hold an object-based cognitive map
421 consisting of relevant mobile objects such as same species, predators, and foods, while we
422 may also hold the other cognitive map consisting of landmarks, landscapes and other
423 immobile objects such as trees. Future studies should address the relationships of different
424 types of cognitive maps (e.g., mobile vs immobile, short-term vs. long-term) and their
425 underlying neural mechanisms.
426 The present study discovered neural representations of the space specified by objects
427 around us. This object-based cognitive map seems to interact with representation of self-
428 location in HPC and mediate a selection of egocentric target-location in mPFC, which would

serve for leading us to the goal position. In addition to the spatial navigation, an existence of the object-based cognitive map may equip us with a space representation for persons separately from the background, which may serve for our social interactions (Damasio et al., 1994; Stolk et al., 2015) as well as the encoding and retrieval of episodic memory (Tulving, 2002; Squire and Wixted, 2011).

Supplemental Information

Supplemental Information includes six figures, two tables and two videos. The videos contain trial examples for Day 1 and Day 2. In the video of day 1, please note we only used examples of correct trials in which a green photo border was shown as feedback after response was made. File size: 21.5 MB; Video duration: 1.23 minute; File format: .mp4; Video codec: H.264; Aspect ratio: 1024 x 768.

Author Contributions

B.Z. and Y.N made the experimental design; B.Z. conducted all experiments and data analysis under supervision of Y.N.; B.Z. and Y.N. wrote the paper.

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Main figures

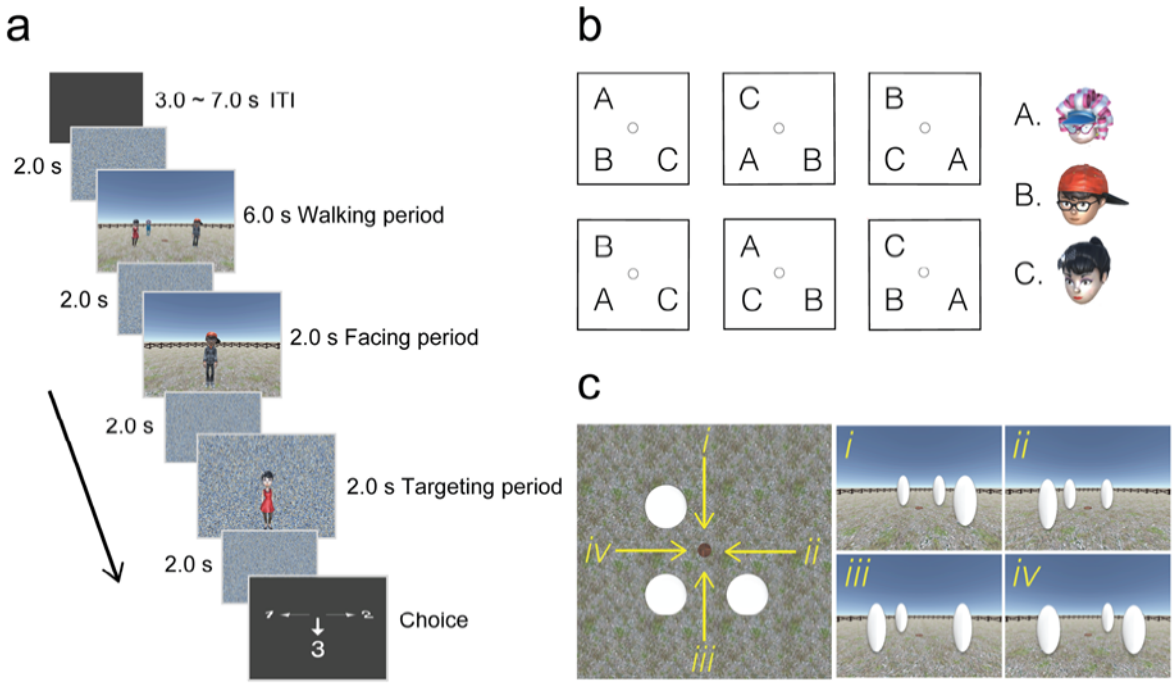

Figure 1: Task design. (a) spatial-memory task. Each trial consisted of three periods. In the walking period, participants walked toward three human characters using the first-person perspective and stopped on a wood plate. In the facing period, one of the human characters was presented, indicating the participant's current self-orientation. In the targeting period, a photo of another character was presented on the scrambled background. The participants chose the direction of the target character relative to their body upon presentation of a response cue. (b) Maps were defined by the relative position of the three human characters, while the unfilled dot represents the wood plate. (c) The walking directions were defined by the spatial layout of the three human characters from the participant's first-person perspective.

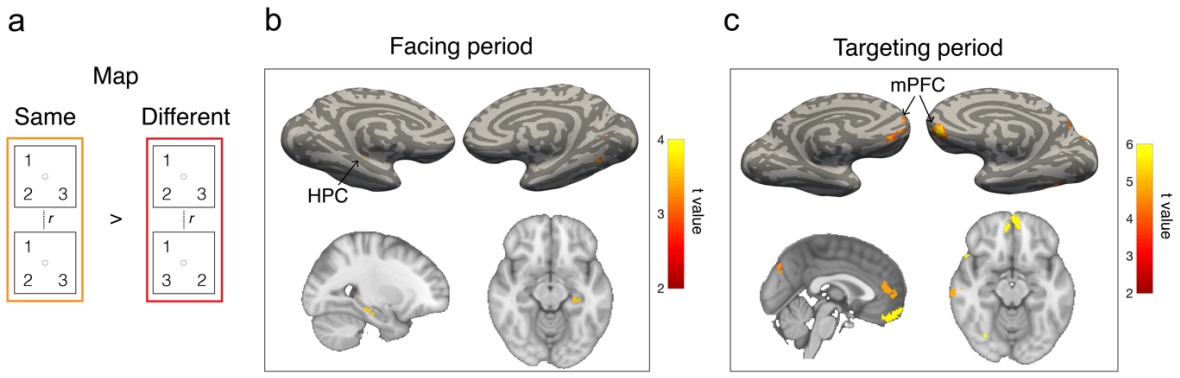

Figure 2: Neural representation of the map information in MTL and mPFC. (a) Schematic representation of decoding the cognitive map using RSA. (b) In the facing period, RSA revealed a cluster in the left middle HPC (mHPC; MNI coordinates: -28,-27,-16; shown on sagittal and transverse section) within the MTL ($P < 0.01$, initial threshold; $P < 0.05$, cluster-corrected; shown on surface). (c) In the targeting period, clusters were revealed in the mPFC but not in the MTL ($P < 0.001$, initial threshold; $P < 0.05$, cluster-corrected). A peak was revealed in the rectus within the mPFC (t value: 5.62; MNI coordinates: 4, 50, -18).

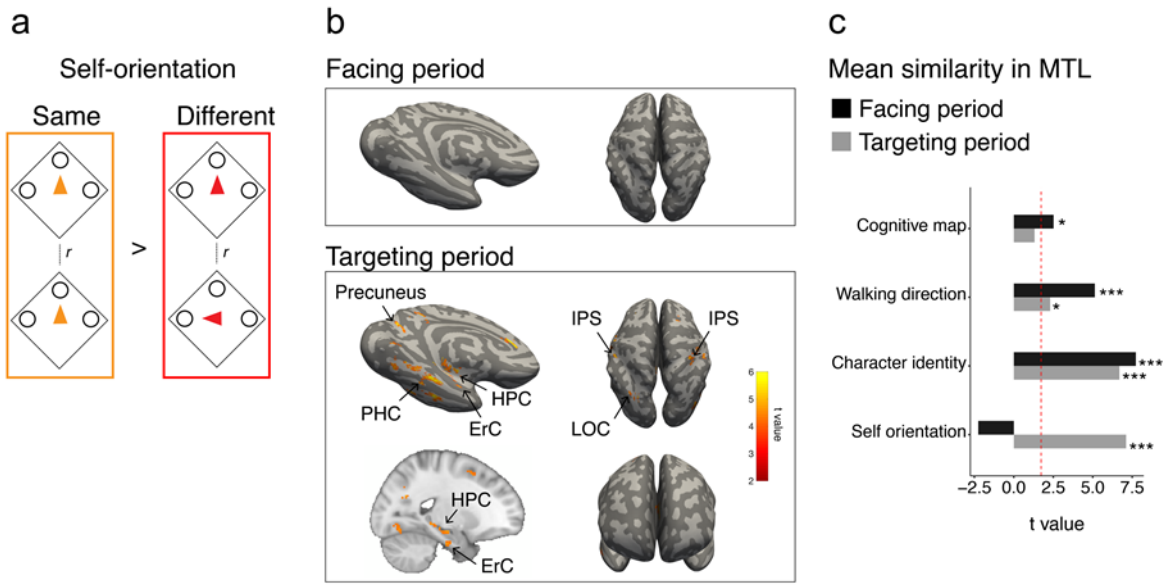

Figure 3: Neural representation of self-orientation on cognitive map. (a) Schematic representation of decoding participants' self-orientation. (b) In the facing period, no cluster was revealed even with the use of a more liberal threshold ($P < 0.01$, initial threshold; $P < 0.05$, cluster-corrected). In the targeting period, clusters were revealed in the MTL (bilateral HPC, PHC, and left ErC) and self-motion areas (inferior parietal cortex, RSC, and lateral occipital cortex). (c) The averaged multi-voxel pattern similarities of the MTL sub-regions (bilateral HPC, PHC and left ErC) based on four spatial parameters. Group level statistics were assessed using the one-tailed t-test. Red dashed line indicates the $p < 0.01$ threshold. * indicates $P < 0.01$, *** indicates $P < 0.001$.

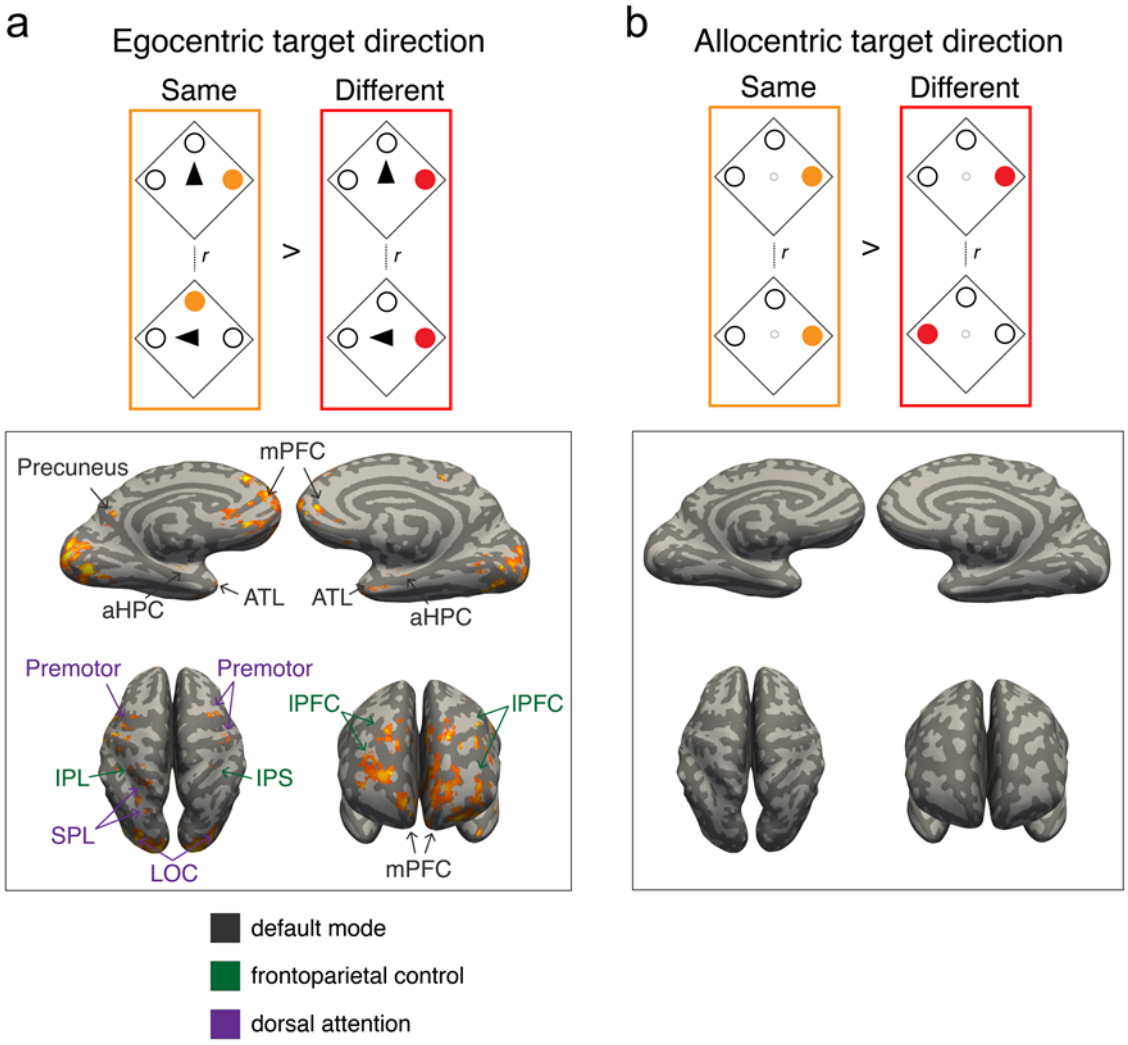

Figure 4: Neural representation of retrieved egocentric target location. (a) Top panel: Schematic representation of decoding the allocentric direction of a target character. Bottom panel: No clusters were revealed even with the use of a liberal threshold ($P < 0.01$, initial threshold; $P < 0.05$, cluster-corrected). (b) Top panel: Schematic representation of decoding the egocentric direction of a target character. Bottom panel: Clusters were revealed across a wide range of brain areas ($P < 0.001$, initial threshold; $P < 0.05$, cluster-corrected). Many of the clusters belonged to one of the following three functional networks: the default mode network, frontoparietal control network, and dorsal attention network.

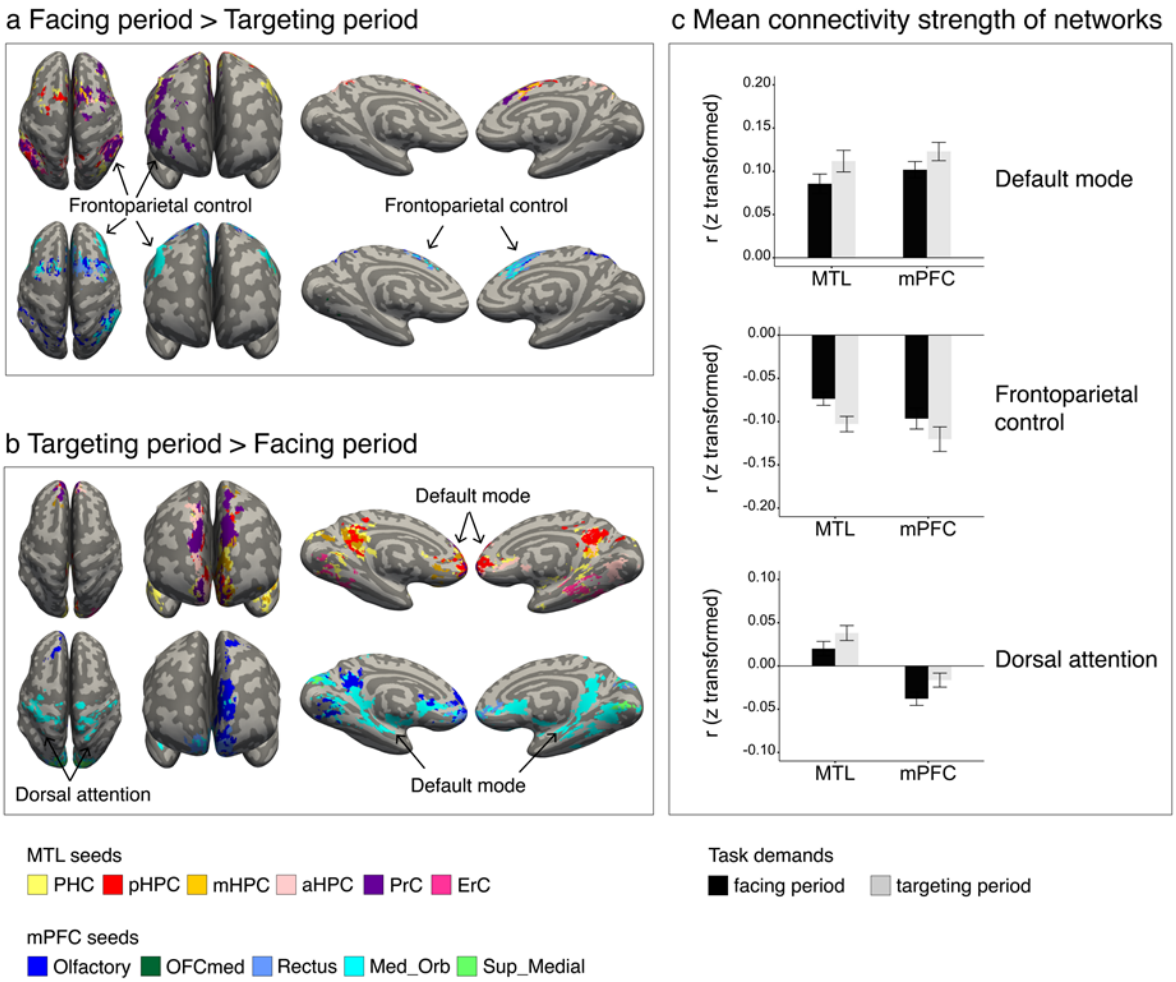

Figure 5: Increased default-mode network connectivity while locating a target compared with locating oneself. Six MTL sub-regions and five mPFC sub-regions were used as anatomical seeds that were highlighted by different colors. All the connectivity brain maps overlapped and were projected on the brain surface. (a) The frontoparietal control network showed enhanced connectivity strength with the MTL and mPFC in the facing period compared to the targeting period ($P < 0.01$, initial threshold; $P < 0.05$, cluster-corrected). (b) The default mode network and dorsal attention network showed enhanced connectivity strength with the MTL and mPFC in the targeting period compared to the facing period ($P < 0.01$, initial threshold; $P < 0.05$, cluster-corrected). (c) The mean connectivity strength of MTL and mPFC sub-regions with three networks, respectively. Note that the two default model network masks were made with the MTL and mPFC excluded, respectively. The masks were used to examine the

connectivity between the MTL and mPFC with the remaining areas of the default mode network.

Methods

Participants

Nineteen right-handed university students with normal or corrected-to-normal vision were recruited from Peking University (12 females, 7 males). The average age of the participants was 24.9 years (range: 18–30 years). All participants had no history of psychiatric or neurological disorders and gave their written informed consent prior to the start of the experiment, which was approved by the Research Ethics Committee of Peking University.

Task design

Virtual environment. We programmed a 3D virtual environment using Unity software (Unity Technologies, San Francisco). The environment was designed with a circular fence as a boundary (48 virtual meters in diameter), a flat grassy ground, a uniform blue sky, and with a wood plate surrounded by four vertices of a square placed in the center (Fig. 1b, 4.7 virtual meters for side length). Three human characters (Mixamo, San Francisco, https://www.mixamo.com) were placed on three of the vertices in each trial. A map was defined by the relative relationship of the three human characters (Fig. 1b). From the six possible maps, three of them were pseudo-randomly selected for each participant, and were the only environmental cues relevant to the task requirement, no distal cues were used outside the boundary. Participants performed the task using the first-person perspective with a 90° field of view (aspect ratio = 4:3), they had never seen a top-down view of the virtual environment.

Walking period. Participants walked from one of four starting locations near the circular boundary (4 virtual meters from the boundary) toward the human characters (Fig. 1c) and stopped on the wood plate. The visual stimuli (spatial environment viewed from first-person

530 perspective) were determined by the combination of the map and walking direction, in other
531 words, each map was presented by four different visual stimuli that were determined by the
532 starting position (Fig. 1c). Importantly, participants were blinded to the map concept
533 throughout the task. The walking period lasted for 6.0 s, during which each character had a
534 20.6% probability of nodding its head at a random time point between the start and end of
535 walking. There was a 50%, 38.9%, 10.2%, and 0.9% probability for 0, 1, 2, and 3 characters
536 to nod head in each trial; we subjectively selected a 20.6% head-nodding probability for each
537 character to ensure an approximately equal number of trials with head-nodding and no head-
538 nodding. During the walking period, participants were required to pay attention to the heads
539 of the human characters rather than to memorize their spatial arrangement. The height of the
540 participants was 1.8 virtual meters from the ground, which was the same as that of the human
541 characters. No response was required during the walking period.

542 Two tasks were completed in two consecutive days. On day 1, the participants
543 performed an HND task that did not include spatial-memory trials. On day 2, participants
544 performed a spatial-memory task that included 90% of spatial-memory trials and 10% of
545 HND trials under MRI scanning. Both tasks contain a walking period at the beginning of
546 each trial; therefore, it was impossible to predict the trial-type. Participants were told that
547 remuneration depended only on the performance in the HND trials but were encouraged to
548 perform both trial-types as best as they could (videos of trial examples are available online
549 for both tasks).

550 *Head-nodding detection (HND) task.* Participants performed 144 randomly ordered HND
551 trials in a behavioral experimental room. In each trial, a photo of one of the characters was
552 presented on a screen after the walking period, and participants were asked to indicate
553 whether the character nodded its head or not (Fig. S1a). For this task, there was a 50% chance
554 that the character in the presented photo nod head. Feedback was given after the participants

555 had responded with either green (correct) or red (incorrect) photo border. The stimuli were
556 rendered on a PC and presented on a 27-inch LCD monitor (ViewSonic XG2730) with a
557 screen resolution of 1024 x 768. The HND task was used to examine whether participants
558 paid attention to head-nodding rather than memorizing the spatial arrangement of the
559 characters, which would be indicated by high success rates in the head-nodding test.

560 *Spatial-memory task.* During this task, participants performed 144 spatial-memory trials
561 (90%) and 16 HND trials (10%) that lasted ~ 70 min in an MRI scanner. In each trial,
562 participants experienced a "facing period" and a "targeting period" sequentially after the
563 walking period. In the facing period, their self-orientation was changed immediately to one of
564 the human characters (facing-character) without viewpoint transition, and a character with the
565 environment background was presented for 2.0 s with the other two characters being
566 invisible, the participants were instructed to face the character. In the targeting period, a
567 photo of another character (targeting-character) was presented as a target on a scrabbled
568 background for 2.0 s. Each of the three experimental periods was followed by a 2.0-s delay
569 (noise screen). At the end of each trial, participants indicated the direction of the target
570 character relative to their self-body by pressing a button when a cue presented on the screen;
571 no feedback was shown for both trial-types (Fig. 1a). The spatial-memory task contained four
572 experimental sessions, each containing a spatial information combination of 3 maps x 4
573 walking directions x 3 facing-character identities in each session, with targeting-characters
574 balanced across sessions. After scanning, all participants completed a post-scanning
575 interview and reported the strategy they used to perform the task (Table. S2).
576

577 **fMRI data acquisition**

578 Imaging data were collected using a 3T Siemens Prisma scanner equipped with a 20-channel
579 receiver head coil. Functional data were acquired with a Multi-band Echo Planer imaging

580 (EPI) sequence (TR = 2000 ms, TE = 30 ms, matrix size: 112 × 112 x 62, flip angle: 90°, gap
581 = 0 mm; resolution: 2 × 2 × 2.3 mm^3, number of slices: 62, slice thickness: 2 mm, slice
582 orientation: transversal). A high-resolution T1-weighted three-dimensional anatomical data
583 set was collected to aid in registration (MPRAGE, TR = 2530 ms, TE = 2.98 ms, matrix size:
584 448 x 512 x 192, flip angle: 7°, resolution: 0.5 × 0.5 × 1 mm^3 , number of slices: 192, slice
585 thickness: 1 mm, slice orientation: sagittal). During scanning, experimental stimuli were
586 presented through a Sinorad LCD projector (Shenzhen Sinorad Medical Electronics) onto a
587 33-inch rear-projection screen located over the subject's head with a resolution of 1024 x 768
588 and viewed with an angled mirror positioning on the head coil.
589
590 **fMRI preprocessing**
591 Functional data for each session were preprocessed independently using FSL FEAT
592 (FMRIB's Software Library, version 6.00, https://fsl.fmrib.ox.ac.uk/fsl/fslwiki; Woolrich et
593 al., 2001; Woolrich et al., 2004). For each session, the first three functional volumes were
594 discarded to allow for T1 equilibration, and the remaining functional volumes were slice-time
595 corrected, realigned to the first image, and high-pass filtered at 100 s. For group-level
596 statistics, each session's functional data were registered to a T1-weighted standard image
597 (MNI152) using FSL FLIRT (Jenkinson and Smith, 2001), and this procedure also resampled
598 the functional voxels into a 2 x 2 x 2 mm resolution. For RSA, data were left unsmoothed to
599 preserve any fine-grained spatial information (Chadwick et al., 2012). For functional
600 connectivity analysis, data were smoothed using a 5 mm FWHM Gaussian kernel and were
601 high-pass filtered at 0.01 Hz to remove low-frequency signal drifts.
602
603 **Anatomical masks**

604 We manually delineated the MTL, including the HPC, PHC, PRC, and ERC on each
605 participant's native space using established protocols (Insausti et al., 1998; Pruessner et al.,
606 2000; Pruessner et al., 2002; Duvernoy, 2005), as well as a delineating software ITK-SNAP
607 (www.itksnap.org). The HPC was further divided into its anterior, middle, and posterior parts
608 using anatomical landmarks of each participant given the anatomical and functional
609 variability along the HPC long axis (Poppenk et al., 2013). For PFC sub-regions, we used the
610 AAL template (Rolls et al., 2015), and selected five mPFC sub-regions for ROI-analysis,
611 which included the rectus, medial orbital gyrus (OFCmed), medial orbital frontal gyrus
612 (Med_Orb), superior medial frontal gyrus (Sup_Med), and olfactory cortex. All ROIs were
613 resampled and aligned with the functional volumes, and voxels outside of the brain were
614 excluded.
615
616 **Representational similarity analysis (RSA)**
617 Task-relevant information was decoded using RSA. We tried to dissociate the neural effect of
618 facing and targeting period based on 4 s duration from each period onset to the end of
619 following noise period (Zeithamova et al., 2017). First, the trial-based multi-voxel activity
620 patterns of two periods were obtained by creating two separate univariate general linear
621 models (GLM). In each GLM, the 4 s blood-oxygen-level-dependent (BOLD) signals of 36
622 trials (a session) were modeled using boxcar regressors. In addition to the 36 trial-based
623 regressors of interest, nuisance regressors were included, which included twelve regressors
624 for modeling the visual patterns of the walking period determined by the maps and walking
625 directions, three for modeling the character identities in the remaining period (for example, in
626 the facing period GLM, three targeting characters were specified as nuisance regressors
627 rather than the facing characters), four for modeling head-nodding detection trials, three for
628 modeling 3 directional cues in the response period, and six motion parameters. This

procedure generated 36 trial-based multi-voxel patterns in participant's native space (2 x 2 x 2.3 mm voxels) for each period, those multi-voxel patterns were normalized prior to subsequent analysis by subtracting the grand mean pattern of the 36 multi-voxel patterns for each session (Vass and Epstein, 2013).

Searchlight-based RSA. Next, we computed the representational similarity for each spatial information based on the multi-voxel patterns using a searchlight-based RSA (Libby et al., 2014; Chadwick et al., 2015), which was conducted using custom Matlab (version R2018b, www.mathworks.com/matlab/) scripts. In detail, a sphere with a 6 mm radius was constructed (85 voxels per sphere) for each brain voxel, and the spheres near the edge of the brain with fewer than ten voxels were excluded from the analysis. The activity parameters within each sphere were extracted from each of the 36 multi-voxel patterns, resulting in a 36-column by n-row (number of voxels within the sphere) matrix. The pattern similarity was then calculated between each column-by-column pair using Pearson's correlation, and was normalized using Fisher's r-to-z transformation. This procedure finally generated a 36-by-36 correlation matrix for each period in each brain voxel. Next, given that a multi-voxel pattern contains the combination of multiple spatial information, we conducted a GLM for each correlation matrix by specifying multiple categorical regressors to rule out potential influences. Each spatial representation represented specific spatial information and used either indicator "1 (same)" or " 0 (different)" that corresponded with the correlation coefficient of a given column-to-row cell of the correlation matrix. For the facing period, the GLM contained five categorical regressors, which included the (1) "map", (2) "walking direction", and (3) "facing-character identity". Since the participants reported thinking about their bodies rotating between the walking direction and self-orientation relative to the environment, we also added the (4) "rotation angle" (turn left/right 45°, turn left/right 135°), and (5) their "self-orientation" into the GLM. For the targeting period, seven regressors were

654 built, which included: (1) “map”, (2) “walking direction”, (3-4) participants’ “rotation angle”
655 and “self-orientation”, (5) “targeting-character identity”, and (6-7) “egocentric and allocentric
656 position of target-character”. It is important to note that the “facing-character identity” was
657 not included in the targeting period GLM since the effect of each facing character was
658 regressed out in the GLM computing of multi-voxel activity patterns. r^2 was computed and
659 ranged from 0 to 0.03 for the facing period GLM, and 0 to 0.04 for the targeting period GLM
660 (Table S1). Each regressor’s parameter was then assigned to the center voxel of each sphere
661 so that a whole-brain statistical parametric mapping could be generated for each spatial
662 information for each period, with those spatial representations being finally averaged across
663 the four scanner sessions. By using this method, spatial information should be successfully
664 decoded if the regressors stably predict the correlation coefficients in any voxels. A
665 permutation test was used to examine the spatial representation stability across the subjects
666 (Nichols and Holmes, 2002; Winkler et al., 2014).
667 *ROI-based RSA*. To validate the spatial representations, we further conducted an
668 independent RSA using anatomical ROIs of MTL and PFC sub-regions. We reasoned that
669 since searchlight analysis identifies the spatial representations as clusters in small portions of
670 anatomical regions, if those representations are stable enough, the corresponding anatomical
671 regions, on average, should show a clear increasing tendency in similarity when spatial
672 information between trial-pairs are similar compared to different such that matching to the
673 searchlight results. To test this, we separated each ROI into the left and right hemispheres and
674 generated 22 anatomical masks (12 for the MTL and 10 for the mPFC). The mPFC masks
675 were normalized into the participants’ native space. The RSA procedure for each ROI was
676 similar to searchlight analysis, which produced a 36-by-36 correlation matrix for each period.
677 Next, for each spatial information, the correlation matrix elements were binarized into “same
678 (1)” and “different (0)” conditions. A discrimination score was computed by comparing the

difference in the means of two conditions, and thus all matrix elements were used. It is important to note that this procedure is different from the previously reported method where the irrelevant information was controlled. Nevertheless, the aim of our analysis was to maintain an efficient number of samples when computing the correlation mean due to the complex nature of the task. The discrimination scores were averaged across the sessions and were submitted to one-tailed one-sample t-tests against change (zero).

Functional connectivity (FC) analysis

To investigate the functional networks for different task demands, we examined the whole-brain FC using each MTL and mPFC sub-region as seed. In detail, based on the preprocessed functional data, we further removed the nuisance covariates by creating a GLM that specified the signal averaged over the lateral ventricles, white matter, and whole brain, six motion parameters, and their derivatives as regressors. The residual signal was bandpass-filtered, leaving signals within the frequency range 0.01 to 0.1 Hz, and was shifted by two TR intervals (4 s) for subsequent analysis (Ranganath et al., 2005; Tompary and Davachi, 2017). Next, for each anatomical mask, a regional time course was computed by extracting and averaging signals over the mask from each facing and targeting period. We then correlated the time course with every voxel in the rest of the brain, resulting in a whole-brain correlation map for each period. The correlation maps were averaged across four scanning sessions and were eventually submitted to a one-tailed t-test for group level statistics.

Statistics

The significance of group level statistics was assessed by performing a one-tailed one-sample t-test. For searchlight-based RSA, we used an initial threshold of $p < 0.001$. If no clusters were revealed, a more liberal threshold of $p < 0.01$ was used. For FC analysis, an initial

threshold of $p<0.01$ was used to identify robust network patterns. The reliability of significant effects was examined using a non-parametric statistical inference that does not make assumptions about the distribution of the data, the test was conducted with the FSL randomise package (version v2.9, http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Randomise)(Winkler et al., 2014) using 5000 random sign-flips and threshold-free clustering. We then reported voxels that were significant at $p < 0.05$ after correcting for multiple comparisons across the entire brain. For other analyses, data distributions were assumed to be normal without formal tests. Analysis of variance (ANOVA) was used to test the difference between experimental conditions; the one-tailed t test was used to test the significance of each anatomical mask in ROI-based RSA.

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