The medial occipital longitudinal tract supports early stage encoding of visuospatial information

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Visuospatial learning depends on the parahippocampal place area (PPA), a functionally heterogeneous area which current visuospatial processing models place downstream from parietal cortex and only from area V4 of early visual cortex (EVC). However, evidence for anatomical connections between the PPA and other EVC areas is inconsistent, and these connections are not discussed in current models. Through a data-driven analysis based on diffusion MRI tractography, we present evidence that the PPA sits at the confluence of two white matter systems. The first conveys information from the retrosplenial complex to the anterior PPA and runs within the cingulum bundle. The second system connects all peripheral EVC areas to the posterior PPA and corresponds to the medial occipital longitudinal tract (MOLT), a white matter pathway that is distinct from the cingulum and that we describe here in detail. Based on further functional connectivity analysis and meta-analytic data, we propose that the MOLT supports early stage encoding of visuospatial information by allowing direct reciprocal exchange between the PPA and EVC. Our findings may improve symptom interpretation in stroke and tumour patients with damage to the medial occipito-temporal region and call for revisiting current visuospatial processing models.

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Multiple streams of research into rodents, non-human, and human primates have identified several brain regions that contribute to the complex ability of visuospatial learning. Although the hippocampal formation is a key player in this cognitive domain, several reports suggest that the more posterior parahippocampal gyrus (PHG) lodges cortical areas more vital for specific types of visuospatial learning, including configuration learning and its identification in early tractography studies. Here, we propose the definition of two white matter systems: a dorso-medial system comprising the PPA, sits at the confluence of two white matter systems: a dorso-medial system stemming from the PHG and a ventromedial system stemming from EVC. Anatomically, both systems merge with the posterior collateral sulcus and this may have prevented their identification based on clustering analysis of structural connectivity tractography studies. Here we propose the separation of the ventral EVC-PPA system from the cingulum, and its identification as a distinct pathway that we refer to as the medial occipital longitudinal tract (MOLT).

Results
The PPA sits at the confluence of two white matter systems. As a first step, we sought to study the general connectivity pattern between the MTL and two sets of regions. The first set, based on the revised dual-stream model, included the RSC and additional surrounding regions from the MTL (RSC/MTL region in Fig. 1). The second set of regions was defined to fully cover EVC within the occipital lobe. This set of regions in each hemisphere. On one hand, there is a clear trend where the posterior MTL receives the majority of EVC connections, followed by a sharp decrease moving toward the anterior MTL. This trend is statistically significant according to a Spearman rank correlation: left hemisphere, \( r_s = -0.72, p < 0.001 \); right hemisphere, \( r_s = -0.67, p < 0.001 \). On the other hand, the RSC/MTL connections show prominent peaks in both the posterior and anterior MTL, resulting in a non-significant trend overall: left hemisphere, \( r_s = 0.35, p = 1.00 \) (n.s.); right hemisphere, \( r_s = 0.39, p = 1.00 \) (n.s.). In both cases, the zone with the highest density coincides with the location of the PPA but the density of these connections within the PPA is not homogeneous. For the EVC connections,
the highest density is observed in the posterior half of the PPA, with a decline to near-zero density towards its anterior border (Fig. 1). However, the density of RSC/MPC connections is negligible in the posterior half of the PPA and sharply rises to its highest peak in the anterior PPA. These findings point to a topographic correspondence, within the PPA, between functional gradients\(^ {17,18}\) and hodological segregation based on the two anatomical systems stemming from EVC and RSC/MPC.

**Clustering analysis of the PPA’s connections.** To better understand how the two observed white matter systems interact structurally and functionally within the PPA, we resorted to a data-driven clustering analysis. To this end, we first combined the EVC and RSC/MPC regions into a single large ROI, and filtered the structural connectivity matrices to only keep connections between the PPA on one end and this combined ROI on the other end. Next, we used principal component analysis (PCA) to only retain the main features that represent these connections. In both hemispheres, PCA yielded three principal components which explained 89.1\% (LH) and 89.8\% (RH) of the variance in the connectivity profile of the PPA to the target ROI (Fig. 2).

We then applied a hierarchical clustering analysis to extract distinct connectivity-based clusters within the PPA based on the identified principal components (Fig. 2). We used the separation vs. spread (SS) index\(^ {38}\) to determine the clustering’s optimal granularity. In both hemispheres, a granularity of three clusters yielded the highest SS index: \(SS_{\text{max}} = 2.71\) (LH); \(SS_{\text{max}} = 3.01\) (RH). This indicates that the PPA is best subdivided into three clusters based on its structural connectivity to the region encompassing EVC, RSC, and the MPC.

In Fig. 3, the structural connectivity of the three PPA clusters to EVC and RSC/MPC is shown and compared to their functional connectivity, which is based on an average resting-state fMRI connectivity map obtained from an HCP dataset of 812 subjects (analysed and released by the HCP; see “Methods” section). On one hand, the anterior cluster (aPPA) is mainly connected to the RSC/MPC according to both structural and functional connectivity. A Spearman rank correlation confirmed the agreement between the two methods: \(r_s = 0.57, p < 0.001\) (LH); \(r_s = 0.72, p < 0.001\) (RH). On the other hand, the posterior cluster (pPPA) is mainly connected to peripheral visual representations in EVC areas V1, V2 and V3, with a strong agreement between structural and functional connectivity: \(r_s = 0.61, p < 0.001\) (LH); \(r_s = 0.65, p < 0.001\) (RH).

Although there is strong agreement between structural and functional connectivity for the anterior and posterior clusters, with a clear distinction between the two clusters, the correspondence between structural and functional connectivity of the lateral cluster (lPPA) is more ambiguous. While it shows preferential structural connectivity to area V4 of EVC, its functional connectivity appears more similar to that of the pPPA. This ambiguity is captured by the weakest agreement between structural and functional connectivity for this cluster: \(r_s = 0.45, p < 0.001\) (LH); \(r_s = 0.51, p < 0.001\) (RH). An in-depth discussion of this finding and further statistical comparisons are available in Supplementary Note 1 (also see Supplementary Figs. 1, 2 and 3).

**From connectivity to functional specialisation.** The results of the structural and functional connectivity analyses indicate that the RSC/MPC and EVC anatomical systems feed into the anterior and posterior PPA, respectively. This suggests that the functional specialisation within the PPA should reflect the distinct roles of RSC/MPC and EVC in the encoding and retrieval of visuospatial information\(^ {39}\). To address this point, we resorted to a meta-analysis\(^ {40}\) of PPA activations for the terms ‘encoding’ and ‘retrieval’ obtained from NeuroSynth (https://neurosynth.org/).

Figure 4 shows the distribution of the maximum z-score attributed to each of the terms ‘encoding’ and ‘retrieval’ along the posterior-anterior axis of the PPA. In the left hemisphere, encoding and retrieval show a similar trend: both have a low load posteriorly (z-score < 2) and an increasingly higher load...
moving anteriorly. However, while both encoding and retrieval are associated with the anterior PPA in the right hemisphere, only encoding shows a high peak in the posterior PPA (z-score > 2 starting at $y = -60$ mm) and its overall load in the right PPA is much higher. These results are in line with previous functional imaging studies and meta-analyses.

White matter bundle connecting the PPA to EVC. The connectivity analyses and the meta-analytic results point to the existence of at least two anatomical systems converging within the PPA. While the PPA’s connections to the RSC/MPC have been well characterised and described within the posterior cingulum bundle and are well discussed in current models, the anatomy of the connections between the PPA and EVC is less understood. On that account, we performed semi-automatic tractography dissections of the latter connections in the 200 HCP datasets using the ROIs described in the Methods section (see also Supplementary Fig. 4). The ROIs were delineated to dissect streamlines that terminate in the region surrounding the PPA on one end, and in the medial occipital lobe (cuneus and lingual gyrus) on the other end. These dissections confirmed the existence of a

![Fig. 2 Clustering analysis of the PPA reveals multiple anatomical subunits.](image)

Data-driven clustering of the parahippocampal place area (PPA) based on average structural connectivity in 200 subjects. **a** Principal component analysis (PCA) based on the PPA’s connectivity to a region encompassing early visual cortex (EVC), the retrosplenial complex (RSC), and medial parietal cortex (MPC) (yellow tint) resulted in three principal components. **b** Hierarchical agglomerative clustering grouped PPA surface vertices with similar PCA coefficients. **c** The highest separation vs. spread (SS) index objectively determined the optimal number of clusters. **d** The resulting anterior, posterior, and lateral PPA clusters are shown on the inflated brain surface.

![Fig. 3 PPA clusters share similar structural and functional connectivity profiles.](image)

Structural and functional connectivity of the three parahippocampal place area (PPA) clusters. The anterior cluster (aPPA) is preferentially connected to retrosplenial complex and corresponds to the parieto-medial-temporal branch of the dorsal visual stream. The posterior cluster (pPPA) is preferentially connected to the anterior medial occipital lobe, i.e., peripheral representations within early visual cortex (EVC). The lateral cluster (IPPA) is more ambiguous but is preferentially connected to EVC. This is discussed in detail in Supplementary Note 1 (also see Supplementary Figs. 1-3).
large, coherent white matter bundle connecting EVC in the medial occipital lobe to the posterior MTL. On one end, most of the streamlines of this bundle project in the anterior portions of areas V1, V2, and V3 within the occipital lobe. On the other end, most streamlines terminate within the posterior portion of the PPA.

Figure 5 shows the 3D reconstruction of this bundle, within the brain surface of an example HCP participant. After leaving the anterior peri-calcarine cortex with a lateral course, fibres emerging from the cuneus (Cu) and lingual gyrus (LG) merge into a single bundle. This bundle continues anteriorly toward the temporal lobe and terminates in the region that overlaps the anterior tip of the LG and the posterior PHG. The entire course of this bundle is infero-medial to the occipital horn and atrium of the lateral ventricles. We chose to label this bundle as the medial occipital longitudinal tract (MOLT) owing to its location and anatomical course. Further visual representations of the MOLT are available in Supplementary Fig. 5, and descriptive statistics are presented in Supplementary Table 1.

The distribution of the MOLT’s projections within the occipital lobe suggests the existence of two components within this bundle, and their further anatomical characterisation may provide insight into the MOLT’s functional role. For this reason, we used three tractography-based metrics to assess the macrostructure and microstructure of the Cu and LG components of the MOLT and their interhemispheric laterisation. The first metric was tract volume measured as the total volume of voxels intersected by streamlines (i.e., spatial occupancy) for each of the Cu and LG components in the two hemispheres. The second metric was the surface area of their cortical projections within EVC. The third metric was the hindrance modulated orientational anisotropy (HMOA), which is a proxy for the microstructural measure of fibre density. For each metric, we calculated a (Cu − LG)/(Cu + LG) ratio within each hemisphere, and a (RH − LH)/(RH + LH) ratio for each component (Fig. 6). Full descriptive statistics of these metrics and comparisons are reported in Supplementary Tables 2 and 3, and more details about these comparisons are available in the “Methods” section.

The comparison between the MOLT components within each hemisphere revealed that the LG component is larger in size and targets a larger surface area within EVC compared to the Cu component. The LG component also has lower HMOA values, which
possibly indicates a lower axonal cohesion and/or density compared to the Cu component. The inter-hemispheric comparison revealed that both Cu and LG components of the MOLT are larger in size, project to a larger surface area within EVC, and have higher HMOA values in the right hemisphere. Overall, these results indicate that the MOLT may carry more visual information about the upper visual field and have a higher information capacity in the right hemisphere.

**Discussion**

Current models of visuo-spatial processing\(^1\)\(^,\)\(^2\)\(^\text{a}\)\(^,\)\(^2\)\(^\text{b}\) focus on input to the MTL via multiple routes. Input that is specific to the PPA seems to arise mainly from indirect parietal projections relayed via the RSC/MPC, or from direct projections from area V4 of EVC. This view does not disagree with our findings that different sub-zones within the PPA receive information via separate anatomical pathways. On one hand, we observe that the anterior zone (aPPA) is strongly connected to the RSC/MPC, which is a connectivity profile that closely agrees with the descriptions of the parieto-medial-temporal branch of the dual-stream model\(^2\)\(^1\)\(^,\)\(^3\)\(^\text{a}\) and previous functional connectivity analyses of this pathway.\(^4\)\(^,\)\(^5\)\(^\text{a}\) On the other hand, the posterior zone (pPPA) is strongly connected to the anterior-most portions of the Cu and LG, overlapping peripheral visual field representations within EVC. This observation challenges the current view that EVC projections to the PPA mainly arise from V4, and instead suggests that earlier visual areas contribute directly to PPA afferents.

The idea that the PPA contains multiple subunits with different connectivity profiles has already been alluded to in the literature. Cytoarchitectonic data suggests that TFO, the posterior-most area of the macaque PHG, has a prominent layer IV and a general laminar profile more akin to the profiles of visual areas than to those of its anterior neighbours TF and TH.\(^6\)\(^\text{a}\)\(^,\)\(^6\)\(^\text{b}\) Further, evidence from task fMRI studies of the human brain suggests that, within the PPA, the posterior portion exhibits stronger functional coupling with peripheral representations within EVC, while the anterior portion shows a strong coupling with an extended fronto-parietal network.\(^7\)\(^,\)\(^8\)\(^\text{a}\)\(^,\)\(^8\)\(^\text{b}\) Additionally, the pPPA contains two distinct retinotopic maps of the visual field, PHC1 and PHC2, which do not extend to its anterior-most border defined by anatomo-functional approaches.\(^9\)

This view of the PPA might seem different from its original description as a cortical region which shows greater functional responses to images of scenes compared to those of isolated faces or objects.\(^1\)\(^\text{a}\) Yet, the two views go together given that the main features in a visual scene are its space-defining borders and the spatial configuration of its constituent elements.\(^1\)\(^\text{a}\)\(^,\)\(^1\)\(^\text{b}\)\(^,\)\(^1\)\(^\text{c}\) Additionally, the PHG plays a general role in processing contextual associations, with spatial associations activating the pPHG and non-spatial associations activating the anterior PHG.\(^1\)\(^\text{d}\)\(^,\)\(^1\)\(^\text{e}\)\(^,\)\(^1\)\(^\text{f}\)

In our analysis of 200 HCP subjects, we consistently replicated a coherent white matter bundle that runs between the peripheral visual representations within EVC and the PPA. Considering its medial location and course along the posterior-anterior axis, we refer to this pathway as the medial occipital longitudinal tract (MOLT). The MOLT has a dorsal (Cu) and a ventral (LG) component that both project onto the same zone in the posterior PPA. Fibres of the MOLT were identified in early tractography studies but considered as part of the ventral cingulum and inferior longitudinal fasciculus.\(^1\)\(^\text{g}\) The existence of a direct connection between EVC and posterior PHG as a separate tract from the cingulum was presented by Catani and indicated with the descriptive term ‘Sledge Runner’ fasciculus. Recent post mortem dissection and in vivo tractography studies confirmed the existence of the ‘Sledge Runner’ fasciculus but they limited its occipital terminations to the most dorsal portion of the cuneus.\(^1\)\(^\text{h}\)\(^,\)\(^1\)\(^\text{i}\)\(^,\)\(^1\)\(^\text{j}\) Therefore, we believe that the ‘Sledge Runner’ fasciculus should only be considered as the dorsal-most component of the MOLT, possibly projecting onto dorsal V2 and V3.

This distinction becomes more important when we consider that the MOLT mediates a stronger overall connectivity between the PPA and ventral EVC (LG, upper visual field) compared with dorsal EVC (Cu, lower visual field). This imbalance is in line with a functional bias within the PPA which contains a larger representation of the upper visual field.\(^1\)\(^\text{k}\)\(^,\)\(^1\)\(^\text{l}\)\(^,\)\(^1\)\(^\text{m}\) The MOLT also exhibits a right hemisphere lateralisation, which is an observation that fits existing literature reporting such a hemispheric bias in the spatial learning functions supported by the parietal lobe and MTL.\(^1\)\(^\text{n}\)\(^,\)\(^1\)\(^\text{o}\) Further, this
lateralisation may explain the higher frequency of visuospatial learning deficits following posterior right hemisphere lesions56. Axonal tracing reports in the macaque using anterograde tracer injections in EVC, specifically in peripheral visual field representations in V2, lead to traces in the posterior PHG31. Other reports using anterograde injections in the PHG itself show traces in the peri-calcarine occipital region32. This suggests that bidirectional information exchange takes places between the posterior PHG and EVC in the macaque. Therefore, the MOLT likely represents reciprocal anatomical connections between EVC and the PPA in the human brain.

According to clinical reports, lesions affecting the posterior PHG and anterior tip of the LG (coinciding with the posterior PPA cluster) lead to a deficit known as landmark agnosia in which patients are "unable to represent the appearance of salient environmental stimuli"56. Conversely, lesions to more anterior MTL regions and/or RSC lead to anterograde disorientation, meaning that patients are "unable to create new representations of environmental information"56. This suggests that the posterior cortical regions are more important for encoding the local space, while the anterior regions are involved in placing and retrieving this information within the context of existing knowledge. Indeed, through the use of meta-analytic maps associated with these two terms, we found that the posterior PPA is more involved in encoding, while retrieval is only present in the anterior PPA, in line with previous reports24,39,41.

Our view is that the MOLT carries ‘raw’ visual information from EVC which the PPA requires, in combination with higher-order spatial information stemming from the parietal lobe, to fully map the visual scene. In other words, afferents from EVC and from RSC/MPC must work in tandem to allow the PPA to fully carry out its role. In this context, the MOLT may carry feedforward and feedback spatial information between EVC and the PPA, thereby serving as a role. In this context, the MOLT may carry feedforward and feedback spatial information stemming from the parietal lobe, to fully map the EVC which the PPA requires, in combination with higher-order spatial information from the parietal lobe to the MTL according to the dual-stream hypothesis and that no artefactual boundaries are created.

Defining cortical ROIs. In preparation for the connectivity analyses in the following sections, several regions of interest were defined using published cortical atlases.

First, an ROI was defined to cover EVC and included the following labels from the multimodal parcellation (MMP) atlas64: V1, V2, V3, V4, V3A, and V6. This effectively covered the Cu, LG, and occipital pole, and included all eccentricity volumes and non-diffusion-weighted volumes. For this study, only data from the b = 2000 s/mm² shell were used as this b-value offers a good compromise between signal-to-noise ratio and high angular resolution, especially at high spatial resolution66.

The data were obtained from the HCP database in pre-processed form following the HCP minimal pre-processing pipelines65. Briefly, correction for motion and eddy current distortion was performed using eddy with outlier slice replacement62,63. Correction of susceptibility distortions was incorporated into this step by means of an off-resonance field estimated using topup64. Diffusion MRI data were then corrected for gradient non-linearity and finally aligned to the structural space using a boundary-based registration66.

Tractography was computed using FMRIB’s Diffusion Toolbox (https://www.fmrib.ox.ac.uk/fsl/). Streamline tractography used a spherical representation of each fibre cross-section and a threshold for streamline termination. Streamlines were considered to be terminated when they reached an ROI or intersected a boundary. A second ROI was defined to cover the entire length of the MTL and included the hippocampal formation, and more distant frontal regions21,28,32,56.

Here, we applied a multimodal investigation to a large cohort of healthy participants. It remains important to list some limitations and suggestions for future investigations. First, neuroimaging methods, including fMRI and diffusion tractography, rely on models to produce results. Although these depend on data quality and choice of processing pipeline, we used high resolution data processed according to best practices to minimise such biases. Second, future investigations aiming to ascertain the role of the MOLT in the spatial learning domain would benefit from including specific testing for its putative function along with imaging investigation within the same cohort. Finally, the data we used is from a young adult cohort, so future investigations of the MOLT’s developmental trajectory may offer insights into the development of visuospatial learning abilities across the lifespan.

Based on converging evidence from structural and functional connectivity, and from the distribution of the encoding and retrieval systems within the PPA, we believe that the MOLT serves as a ventral white matter pathway that carries information crucial for visuospatial learning.

Methods

MRI data. DWI data from 200 healthy participants (100 females; age = 29.16 ± 3.73 years) were obtained from the Human Connectome Project (https://www.humanconnectome.org). As this study only used fully anonymised data from a public dataset, no ethical approval was required according to the guidelines of the King’s College London, Ethics Committee and the objects right-handed as determined by a score of 50 and above on the Edinburgh handedness questionnaire59.

Diffusion MRI data of the HCP were acquired on a 3 T Siemens ‘Connectome Skyra’ using a spin-echo EPI sequence (TR = 3520 ms; TE = 89.5 ms; matrix of 168 x 144 x 117 slices with a thickness of 1.25 mm; multiband factor = 3). Three diffusion-weighted shells were acquired (b = 1000, 2000, and 3000 s/mm²) with two opposite phase-encoding directions (L>R and R>L). Each shell consisted of 90 diffusion-weighted directions and six non-diffusion-weighted volumes. For this study, only data from the b = 2000 s/mm² shell were used as this b-value offers a good compromise between signal-to-noise ratio and high angular resolution, especially at high spatial resolution66.

The data were obtained from the HCP database in pre-processed form following the HCP minimal pre-processing pipelines65. Briefly, correction for motion and eddy current distortion was performed using eddy with outlier slice replacement62,63. Correction of susceptibility distortions was incorporated into this step by means of an off-resonance field estimated using topup64. Diffusion MRI data were then corrected for gradient non-linearity and finally aligned to the structural space using a boundary-based registration66.

Tractography was computed using FMRIB’s Diffusion Toolbox (https://www.fmrib.ox.ac.uk/fsl/). Spherical deconvolution was based on a damped version of the Richardson-Lucy algorithm63,64 with the following parameters: fibre response a = 1.8, number of iterations = 300; amplitude threshold q = 0.0020; geometric regularisation p = 12. Fibre tracking was then performed using the multi-fibre Euler-like algorithm with the following parameters: minimum HMOA threshold = 0.0033; step size 1.0 mm; maximum angle threshold = 45°; minimum fibre length = 20 mm; maximum fibre length = 300 mm.

Building vertex-wise connectivity matrices. The whole-brain tractogram of each subject was converted to a vertex-wise structural connectivity matrix. For each subject, this approach was based on the native space midthickness cortical mesh, vertex-matched to the ‘32k FS Surface’ template using the multimodal surface matching (MSM) method65,66. These surfaces have the advantage of maintaining the native anatomy of the brain while offering a vertex-level matching between subjects. As a result, information from multiple subjects can be directly compared at each vertex.

The end points of each tractography streamline were projected to the nearest vertex on the midthickness surface, with a maximum allowed distance of 4 mm. Only streamlines that resulted in two cortical targets (one for each end point) survived this step. Due to the sparse distribution of streamlines near the cortical surface, this approach would result in a patchy representation of cortical targets which is problematic for group-level analysis. To compensate for this and for tractography’s uncertainty near grey matter56, a geodesic Gaussian kernel (FWHM = 2.5 mm) was applied to each target independently. The connectivity information resulting from each streamline was used to populate a 32492 x 32492 sparse matrix representing all vertices of the cortical surface. Each subject’s matrix was then normalised by its highest value before the group-level mean connectivity matrix was computed.
Connection density in the MTL. The aim of this analysis was to assess the spatial distribution of the density of connections stemming from the EVC and RSC/MPC ROIs, and projecting within the MTL. To this end, the vertex-wise connectivity matrices previously computed were filtered to only keep connections between the MTL and either of these ROIs. The obtained values for the MTL vertices were then sorted according to the position of each vertex along the y-axis and grouped into 1 mm bins. The connectivity value was first computed for each subject separately in each bin, then the group mean and standard deviation were calculated. This effectively allowed for the assessment of the relationship between the location of an MTL vertex along the anterior-posterior axis and the strength of its connectivity to the EVC or RSC/MPC ROIs. A Spearman rank correlation was finally computed to assess the relationship between projection density and position along the y-axis.

PPA clustering and connectivity analysis. The aim of this analysis was to assess whether the PPA contains multiple sub-units with different anatomical connectivity. First, the values of the subject-level connectivity matrices previously computed were converted to z-scores, and the mean z-matrix was computed. This matrix was then filtered to only retain the connections between the PPA on one end, and both the EVC and RSC/MPC ROIs on the other end. The mean z-matrix was entered into a principal component analysis (PCA). In this context, the z-matrix acted as a large dataset where the PPA vertices represented variables and the EVC/RSC/MPC vertices represented observations of these variables. This approach was blind to the locations of vertices on the brain surface and was thus completely driven by the connectivity profile of each PPA vertex. A scree plot was used to determine the number of components to retain within the PCA. A higher SS index means that the variability of observations between clusters is greater than the variability within clusters. Therefore, the number of clusters was chosen to correspond to the highest SS index. The mean structural connectivity of each resulting cluster was then obtained from the mean connectivity matrix previously computed. Additionally, the mean functional connectivity of each cluster was calculated based on the average group dense resting-state functional connectome released by the HCP as part of the ‘HCP-S1200_GroupAvg_v1’ dataset (https://www.humanconnectome.org/study/hcp-young-adult/document/extensively-processed-fmri-data-documentation). Tract-based connectivity values, which follow a heavily skewed distribution compared to functional connectivity, were log-transformed. Spearman rank correlations (one-tailed) were then computed between tract-based and functional connectivity measures for each cluster to assess the degree of agreement between the two modalities.

Functional meta-analysis. Two association test maps were generated for the terms ‘encoding’ and ‘retrieval’ following a meta-analytic approach using NeuroSynth (https://neurosynth.org/). For each voxel, these maps contain a z-score from a two-way ANOVA that indicates how consistently that voxel is activated in studies that mention the key term compared with studies that do not. These maps are corrected for multiple comparisons using a false discovery rate of 0.01. Each map was projected to the surface of the MNI brain, allowing us to use the PPA mask as an ROI for the analysis. The maximum z-score for each coordinate along the PPA’s anterior-posterior axis was plotted for each of the two maps, allowing us to compare their distribution along the PPA.

Virtual dissections. Virtual dissections were performed in TrackVis (http://trackvis.org/) to extract the anatomical bundle that gave rise to the observed connectivity patterns between the posterior PPA cluster and the EVC in the clustering analysis. MegaTrack42, a supervised semi-automatic group-level approach, was used to objectively determine the optimal number of clusters. A higher SS index means that the variability of observations between clusters is greater than the variability within clusters. Therefore, the number of clusters was chosen to correspond to the highest SS index. These links defined ROIs that were visualized in TrackVis, and custom scripts were used to generate the final meta-analysis maps.

Assessment of lateralisation and vertical bias in the disected tracts. Hemispheric lateralisation for each of the dorsal and ventral components was assessed according to the following formula:

\[
\text{lateralisation} = \frac{\text{value}_{\text{right}} - \text{value}_{\text{left}}}{\text{value}_{\text{right}} + \text{value}_{\text{left}}} \quad (1)
\]

where value represents one of the following metrics: (1) tract volume; (2) surface area of connected EVC cortex; (3) hindrance modulate orientational anisotropy (HMOA). In this way, a lateralisation toward the right hemisphere would lead to positive values, and left lateralisation would lead to negative values.

Additionally, given that each PPA contains a substantially larger representation of the upper visual field\(^{25}\), the connectivity between the PPA and ventral EVC (LG, representing the upper visual field) was expected to be stronger than that with dorsal EVC (Cu, representing the lower visual field). This vertical bias was assessed following a similar approach to the one used for laterisation, according to the following formula:

\[
\text{vertical bias} = \frac{\text{value}_{\text{Cu}} - \text{value}_{\text{LG}}}{\text{value}_{\text{Cu}} + \text{value}_{\text{LG}}} \quad (2)
\]

where value also represents one of the previously described metrics, and where a dominance of the Cu component would result in positive values and a dominance of the LG component would result in negative values.

For each of these comparisons, statistical significance was determined through a one sample t-test (two-tailed) performed on the resulting bias index. The Bonferroni corrected significance level was set to 0.0042.

Statistics and reproducibility. This study used MRI data from 200 subjects. All statistical analyses were conducted in MATLAB using built-in functions (such as pca and pdist), and custom scripts to build on those functions. Where appropriate, Bonferroni correction was used to control for FWE in multiple comparisons. For hemisphere or tract component comparisons, two-tailed paired samples t-tests were conducted in MATLAB.

Reporting summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability. The pre-processed diffusion MRI data and structural surface models used in this study were obtained from the Human Connectome Project (HCP) database (https://db.humanconnectome.org). The resting-state functional connectivity dataset was obtained from a processed release of HCP data (https://www.humanconnectome.org/study/hcp-young-adult/document/extensively-processed-fmri-data-documentation). The meta-analysis voxel-wise maps were obtained from NeuroSynth (https://neurosynth.org). Population atlas maps of the MOLT are available through the MegaTrack Atlas (http://megatrackatlas.org). Source data underlying main figures are presented in Supplementary Data 1–4.

Code availability. The analyses performed here are based on MATLAB built-in functions. Wrapper scripts written for this paper are available upon request from the corresponding author.

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A.B. conceptualisation, methodology, software development, investigation, resources, writing original draft. F.D.A. conceptualisation, methodology, software development, investigation, resources. D.C. methodology, software development. F.D.R. methodology, software development. D.F. conceptualisation, methodology, investigation. M.C. conceptualisation, methodology, investigation, resources, writing original draft, funding acquisition. All authors reviewed and approved the submitted manuscript.

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The authors declare no competing interests.

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