RESEARCH ARTICLE

Distinct gradients of cortical architecture capture visual representations and behavior across the lifespan

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This **valuable** study draws on large-scale multimodal MRI measurements of human brain structure across the lifespan to offer a new perspective on visual cortex architecture. The data provide **compelling** evidence for two cortical architectural gradients that show distinct functional, cytoarchitectural, behavioural, and lifespan profiles. One gradient captures a broad early-to-higher-level visual cortical hierarchy in which cortical thickness tissue density covary; the other reflects more localised divergence from this relationship, notably predicting putative anterior temporal visual field representations that have not previously been described.

Abstract The microstructure of cells within the human cerebral cortex varies across the cortical ribbon, where changes in cytoarchitecture and myeloarchitecture are thought to endow each region of the cortex with its unique function. While fine-scale relative to a cell, these changes at the population level impact architectural properties of the cortex measurable in vivo by noninvasive MRI, such as the thickness and myelin content of the cortex. This raises the question of whether or not we can use these in vivo architectural measures to understand cortical organization, function, and development more broadly. Using the human visual cortex as a test bed, we demonstrated two architectural gradients, one in which cytoarchitecture and myeloarchitecture converge and another in which they diverge. These two gradients underlie the structural and functional topography of the visual cortex, even predicting the presence of new visual representations. Moreover, the two gradients show distinct visual behavior relevance and lifespan trajectory. These findings provide a more general framework for understanding the human cortex, showing that architectural gradients are a measurable fingerprint of functional organization and ontogenetic routines in the human brain.

Introduction

A fundamental goal of brain science is to elucidate the functional properties of the structural elements of the brain, at an appropriate organizational scale. Classical architectural brain maps, including

cytoarchitectonic (**Brodmann, 1909**; **Brodmann and Gary, 2006**) and myeloarchitectonic (**Vogt and Vogt, 1919**) maps, derived from postmortem brain sections, have revealed strong correspondence with the functional properties of the cerebral cortex (**Amunts and Zilles, 2015**; **Amunts et al., 2020**). Recent observations of spatial gradients in gene expression across the human cortex (**Burt et al., 2018**; **Gomez et al., 2019b**), especially in genes controlling the shape and distribution of dendrites and myelin, also suggest that functional differences across the cortex are linked to broad changes in architectural properties (**Glasser et al., 2016a**). However, these architectural maps are often examined in isolation, lacking interrogation across different maps and individuals. It remains uncertain whether any common or distinct patterns exist among these maps, and if they can offer more reliable and sensitive indicators of functional, behavioral, and developmental relevance. Technological advances in MRI have made it possible to map architectural correlates in the human cortex in a noninvasive and individual-specific way, and to test whether any key architectural features of the cortex reflect its functional organization (**Lerch et al., 2017**; **Sebenius et al., 2023**; **Genon et al., 2022**). Leveraging the field's deep understanding of the functional organization of the visual cortex relative to cortical folding (**Grill-Spector and Weiner, 2014**; **Witthoft et al., 2014**; **Dumoulin et al., 2000**; **Gomez et al., 2019a**; **Konkle and Caramazza, 2013**; **Wandell and Winawer, 2011**; **Benson and Winawer, 2018**; **Konen and Kastner, 2008**), we focus here on the visual cortex as a test bed to understand how the architectural patterns of the cortical mantle relate to changes in function. More explicitly, to what extent do individuals demonstrate shared architectural features of the visual cortex which could be derived from multiple kinds of architectural measurements; and how might these structural patterns differ in development and capture differences in visual function and behavior (**Genon et al., 2022**)?

Answering such a question would require a large-scale, multimodal MRI dataset to appropriately capture the architectural variations at the level of the population. To that end, we combine three datasets from the Lifespan Human Connectome Project (HCP), which together sample the human lifespan from 5 to 100 years of age (**Bookheimer et al., 2019**; **Van Essen et al., 2013**; **Somerville et al., 2018**), and ask if there are shared motifs in architectural features of the cortex across individuals and development. Based on T1-weighted (T1w) and T2-weighted (T2w) images, we produce for each individual two distinct maps: a map of cortical thickness (**Fischl and Dale, 2000**) and a map of the T1w/T2w signal ratio (**Glasser and Van Essen, 2011**). While the thickness map is thought to be attributable to the organization of neuronal, glial, and neuropil tissue (**Carlo and Stevens, 2013**; **Huttenlocher and Dabholkar, 1997**; **Natu et al., 2019**; **Bo et al., 2023**), the ratio map is thought to be sensitive to the density of myelinated and neurite structures (**Glasser and Van Essen, 2011**; **Preziosa et al., 2021**), which we refer to more broadly as tissue density. In the case of visual cortex, general trends along the cardinal axes have been observed in architectural features such as myelination and cortical thickness in adults and infants (**Miller et al., 2021**; **Grotheer et al., 2022**; **Sowell et al., 2004**), as well as functional properties of neurons such as receptive field size (**Wandell and Winawer, 2015**; **Gomez et al., 2018**) and temporal sensitivity (**Stigliani et al., 2015**; **Hasson et al., 2008**). A model explicitly linking these architectural and functional variations across the cerebrum, one that can generalize to yet-mapped regions of cortex as well as explain behavior and dynamics across the lifespan, would be a steppingstone toward bridging structural and functional properties of the living human brain.

Results

To extract the latent spatial patterns underlying cortical architecture across both properties and individuals, the thickness and tissue density maps from each hemisphere are concatenated across individuals to perform a spatial principal component analysis (PCA) (**Hong et al., 2020**; **Lever et al., 2017**) in which participants are features and cortical vertices are samples. As a result, the concatenated maps were linearly decomposed into a collection of orthogonal principal components (PCs), consisting of spatial maps (i.e., scores) and individual weights (i.e., loadings) in pairs. The former explains how the architectural properties change across the cortical sheet on each component and the latter describes how individuals' maps contribute to each component (**Figure 1a**). The resulting first two PCs describe over 50% of architectural variance across the cortical sheet (**Figure 1b**). Because they are very similar across the two hemispheres (**Figure 1—figure supplement 1**), only data from the right hemisphere are presented here for clarity. The contributions of thickness and tissue density indicate that each PC relied on an integration of the two architectural measures at a given spatial location (**Figure 1c**), rather

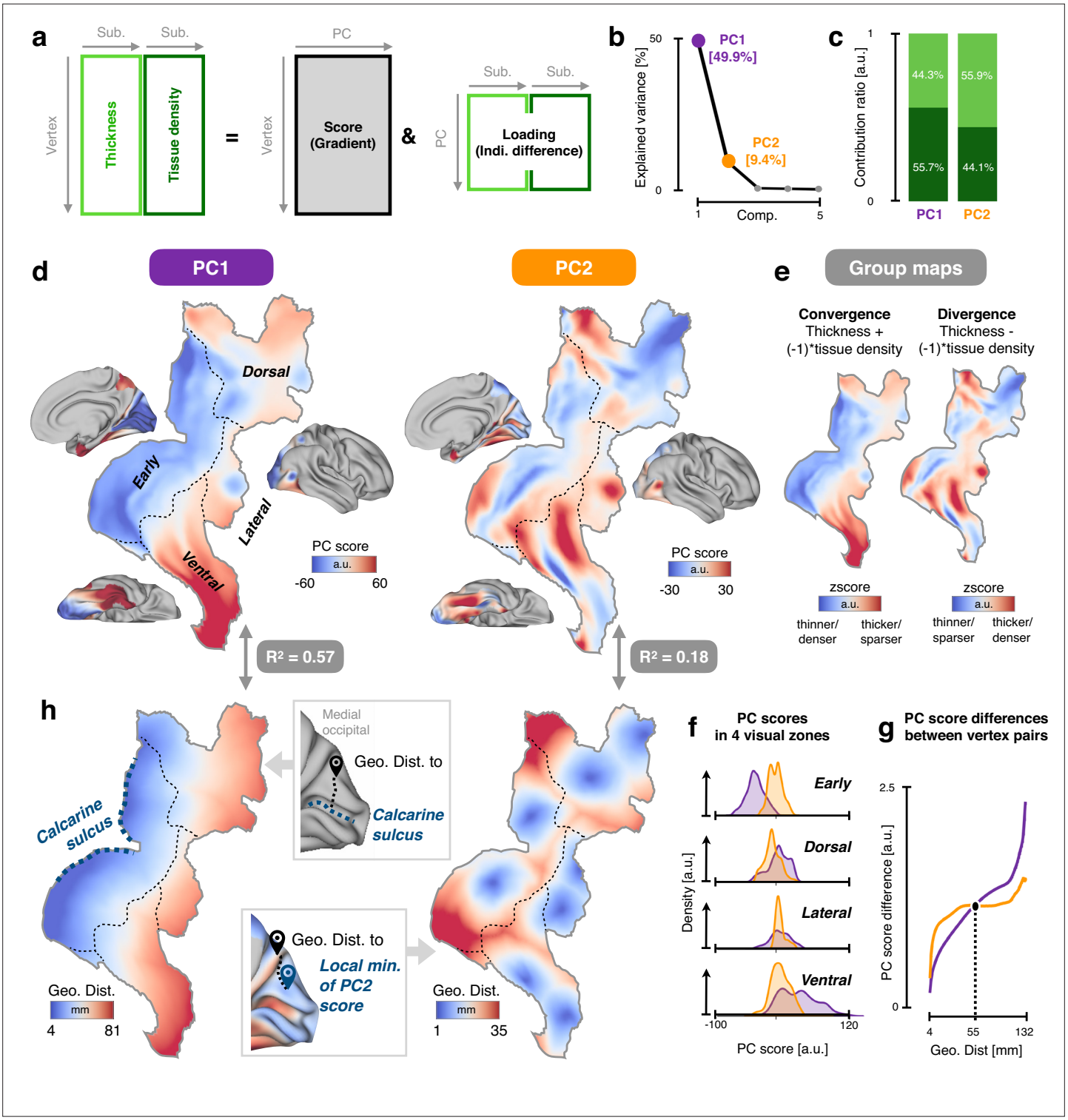


Figure 1. Two architectural gradients scaffold human visual cortex. (**a**) Principal component analysis on the concatenated cortical thickness and myelin/neurite density maps from all participants in HCP-YA to extract architectural gradients of human visual cortex produced a collection of orthogonal principal components (PCs), consisting of spatial maps (i.e., scores) and individual weights (i.e., loadings) in pairs. (**b**) The explained variance ratio of the top 5 PCs. The first two PCs (i.e., gradients 1 and 2) dominate the explainable variance. (**c**) Contributions of the two architectural measures (thickness and density) to the two gradients. (**d**) Topographic patterns of the two gradients on a flattened cortical surface. Gradient 1 (PC1) displays roughly monotonic change from negative to positive scores across visual cortex, emanating from primary visual cortex V1, while gradient 2 (PC2) showed repeated representation in four localities, mirroring the four visual streams (early, dorsal, lateral, and ventral). Black dotted lines: borders where the different visual

Figure 1 continued on next page

Figure 1 continued

streams meet, defined using HCP MMP label boundaries. A.U. is arbitrary units. (**e**) The convergence and divergence between the group average map of thickness and tissue density. (**f**) Histogram depicting gradient scores in the four visual stream regions. Gradient 1 is a large-scale gradient increasing from early to ventral, for example. Gradient 2 is a fine-scale gradient sampled evenly within an individual visual stream. (**g**) The dependence of gradient value differences on geodesic distance is different for the two gradients. Gradient 1 shows larger changes across vertices separated by a long distance, whereas gradient 2 shows larger changes for short distances. (**h**) Geometric models of the two architectural gradients, which were constructed using the geodesic distance of each vertex of visual cortex to specific anatomical landmarks as anchors. The calcarine sulcus and eight local minima of gradient 2 were used as anchors to model gradients 1 and 2, respectively.

The online version of this article includes the following figure supplement(s) for figure 1:

Figure supplement 1. The two hemispheres have very similar architectural gradients in visual cortex.

Figure supplement 2. The principal component analysis (PCA) on the concatenated cortical thickness and tissue density maps can exploit the concurrent spatial changes of the two measurements and thus extract more meaningful architectural gradients than PCA on a single architectural measurement.

Figure supplement 3. Principal component analysis (PCA) and the convergent and divergent patterns between group average maps of cortical thickness and tissue density.

Figure supplement 4. Split-half cross-validation of PC2 maps demonstrates reliable geometric features underlying visual cortex organization.

than a single feature, thus revealing architectural patterns of visual cortex (i.e., score maps) not visible through a single measure alone (***Figure 1—figure supplement 2***).

Thickness and density maps showed a robust anti-correlation both at the coarse across-area level based on an independent parcellation (***Abdollahi et al., 2014***) and at the finer within-area level, except in primary regions (***Figure 1—figure supplement 3a, b***). Given the notable anti-correlation, along with the strong inter-individual correlations within these two sets of architectural maps (***Figure 1—figure supplement 3c***), it is anticipated that the first two PCs (***Figure 1d***) would capture the convergent and divergent patterns between group average maps of cortical thickness and tissue density (***Figure 1—figure supplement 3d***). We confirmed this by performing a correlation analysis between PC1 and convergent pattern (thickness map + inversed tissue density map), and between PC2 and divergent pattern (thickness map − inversed tissue density map). As illustrated in ***Figure 1e***, the converging/diverging maps of the group average thickness and inversed density maps are highly correlated with the PC1/2 maps across the visual cortex (both rs = 0.997, ps < 0.001). Within-area analyses further confirmed that PC1/2 represent the consistent/deviating components of the thickness–density anti-correlation at finer scales (***Figure 1—figure supplement 3e***). This indicates that the PCs have a straightforward and intuitive interpretation. Specifically, PC1 effectively captures the convergence of cortical thickness and tissue density (i.e., how they vary together), while PC2 represents the spatial divergence from this commonality.

Looking into the spatial topography of the two PCs, both PC1 and PC2 maps form spatial gradients whose values change smoothly as one traverses the cortical surface (***Figure 1d***). Specifically, gradient 1 (i.e., PC1 map) shows an increase in value as one travels from the fundus of the calcarine sulcus (CS) either dorsally toward the intraparietal sulcus or ventrally into the anterior temporal lobe. Higher PC1 vertex values correspond to lower tissue density and a thicker cortical sheet (***Figure 1—figure supplement 3d***). Interestingly, gradient 2 demonstrates an alternating pattern that fluctuates across cortex. Positive (negative) PC2 scores correspond to higher (lower) thickness or tissue density than expected from PC1 (***Figure 1—figure supplement 3d***). Gradient 2 seems to be broadly organized into four distinct zones, mirroring the visual cortex's division from early visual field maps (***Wandell et al., 2007***) into the ventral, lateral, and dorsal processing streams of the visual cortex (***Pitcher and Ungerleider, 2021***; ***Weiner and Gomez, 2021***; ***Ungerleider and Haxby, 1994***; ***Goodale and Milner, 1992***). Quantitatively, the distribution of values for gradient 1 shifts across the four processing streams while the value distributions of gradient 2 are evenly sampled within each processing stream (***Figure 1f***). Furthermore, gradient 2 exhibits a higher spatial frequency in the distribution of its values across cortex. That is, for a given pair of vertices separated by a short distance, gradient 2 tends to show a larger difference in values compared to the more spatially homogeneous gradient 1 (***Figure 1g***). It should be noted that maps of cortical thickness had any variance explainable by curvature removed to account for known thickness differences between gyri and sulci, ruling out the possibility that the alternating architectural pattern was caused by the folding of the underlying cortical sheet. Collectively, these findings demonstrate that gradient 1 forms a large-scale, low-spatial-frequency gradient

spanning the entire visual cortex, whereas gradient 2 exhibits a fine-scale, high-spatial-frequency gradient across subregions of the visual cortex.

To get a deeper understanding of the shape of these topographies, we produced simulated models using cortical geometry for the two spatial gradients. For gradient 1, the CS was used as the fiducial line, and vertices of the cortical surface were assigned values based on their minimal geodesic distance to the CS. This simple simulation was able to capture 57.1% of the explainable variance in the topography of gradient 1 (***Figure 1h***, left), similar to prior distance-based models of this well-known gradient (***Burt et al., 2018***). Gradient 2, which was more complicated in shape, could nonetheless be simulated using anchor points positioned at local minima within each visual processing stream (***Figure 1h***, right), and vertices of the cortical surface were assigned values based on their minimal geodesic distance to these anchor points. This map of geometric distance also captured a sizeable portion of the variance (17.7%) within the gradient 2 map. A split-half cross-validation (CV) yielded similar results, with anchor points and geodesic distances derived from one half of the sample successfully predicting PC2 in the other half (***Figure 1—figure supplement 4***), indicating reliable geometric features underlying the spatial organization of PC2. These simulation results again highlight the large-scale and fine-scale characteristics of the two gradients.

Given that gradient 1 values show smooth changes as one travels from early to high-level visual cortex, we hypothesize that it will recapitulate the hierarchical organization of functional features across visual cortex. To test this, we examined the spatial similarity between the architectural gradients and the population receptive field (pRF) properties as measured by the HCP 7T retinotopy dataset (***Benson et al., 2018***). The pRF represents the portion of visual space in which a stimulus evokes a response in a given voxel, and pRF size increases along the visual processing hierarchy (***Dumoulin and Wandell, 2008***; ***Amano et al., 2009***; ***Harvey and Dumoulin, 2011***). We found that gradient 1 was highly correlated with pRF size (***Figure 2a***) and the known ranking of visual field maps across cortex (***Figure 2b***), while gradient 2 was not. Strikingly, gradient 1 explains functional features of visual cortex (receptive field size, hierarchical rank) better than the gradient derived from resting-state functional connectivity (RSFC) within visual cortex (***Figure 2—figure supplement 1a–c***). Further evidence for this hypothesis can be found when examining temporal properties of visual cortex function. It is widely recognized that the frequency at which the BOLD signal fluctuates during resting-state functional MRI (rs-fMRI; ***Hasson et al., 2008***; ***Shmuel and Leopold, 2008***; ***Sydnor et al., 2023***) is different in distinct regions of cortex. This temporal property of the BOLD signal, quantified as a fractional amplitude of low-frequency fluctuation (fALFF) (***Zou et al., 2008***), correlates well with temporal properties of receptive fields in visual cortex (***Stigliani et al., 2015***; ***Hasson et al., 2008***; ***Stigliani et al., 2017***). Here, we find that this temporal gradient as measured by fALFF is well-described by gradient 1 in a simple regression analysis (***Figure 2c***).

Thus, the convergence relationship between cortical thickness and density across visual cortex appears related to broad changes in functional features. In contrast, gradient 2 appears to act more locally, showing greater spatial inhomogeneity with interdigitating peaks and valleys of scores within individual visual streams. We hypothesized that these local deviations from the canonical thickness and density of cortex underlie the finer-scale division of visual cortex into categorically distinct regions. That is, does the arealization of cortex into distinct regions involve these regions becoming more distinct from a typical cortical sheet (i.e., gradient 1)? To test this, we hypothesize that gradient 2, when combined with gradient 1, will improve the differentiation of cortical regions as defined by the HCP multimodal parcellation (MMP; ***Glasser et al., 2016a***). Through a classifier-based analysis, regional classification was significantly higher when gradient 2 is combined with gradient 1 (***Figure 2c***). Additionally, the two architectural gradients outperform the first two gradients derived from rs-fMRI in a similar classification approach (***Figure 2—figure supplement 1d***).

Lastly, if the two architectural gradients truly relate to the functional organization of visual cortex in distinct ways, then these differences should be mirrored in the way cytoarchitecture contributes to each structural gradient. Based on the BigBrain dataset (***Amunts et al., 2013***), we extracted cell body density (CBD) data for each of the six cortical layers to produce six structural maps projected onto the cortical surface. For gradient 1, we find that changes in its structural features correlate strongly with cell density of layers III and IV, where the pronunciation of layer IV decreases with increasing distance from the CS. Gradient 2 was most correlated with cell density of layer I, with positive scores overlapping cortex with thicker superficial layers of cortex (***Figure 2d***). Because layers III and IV are

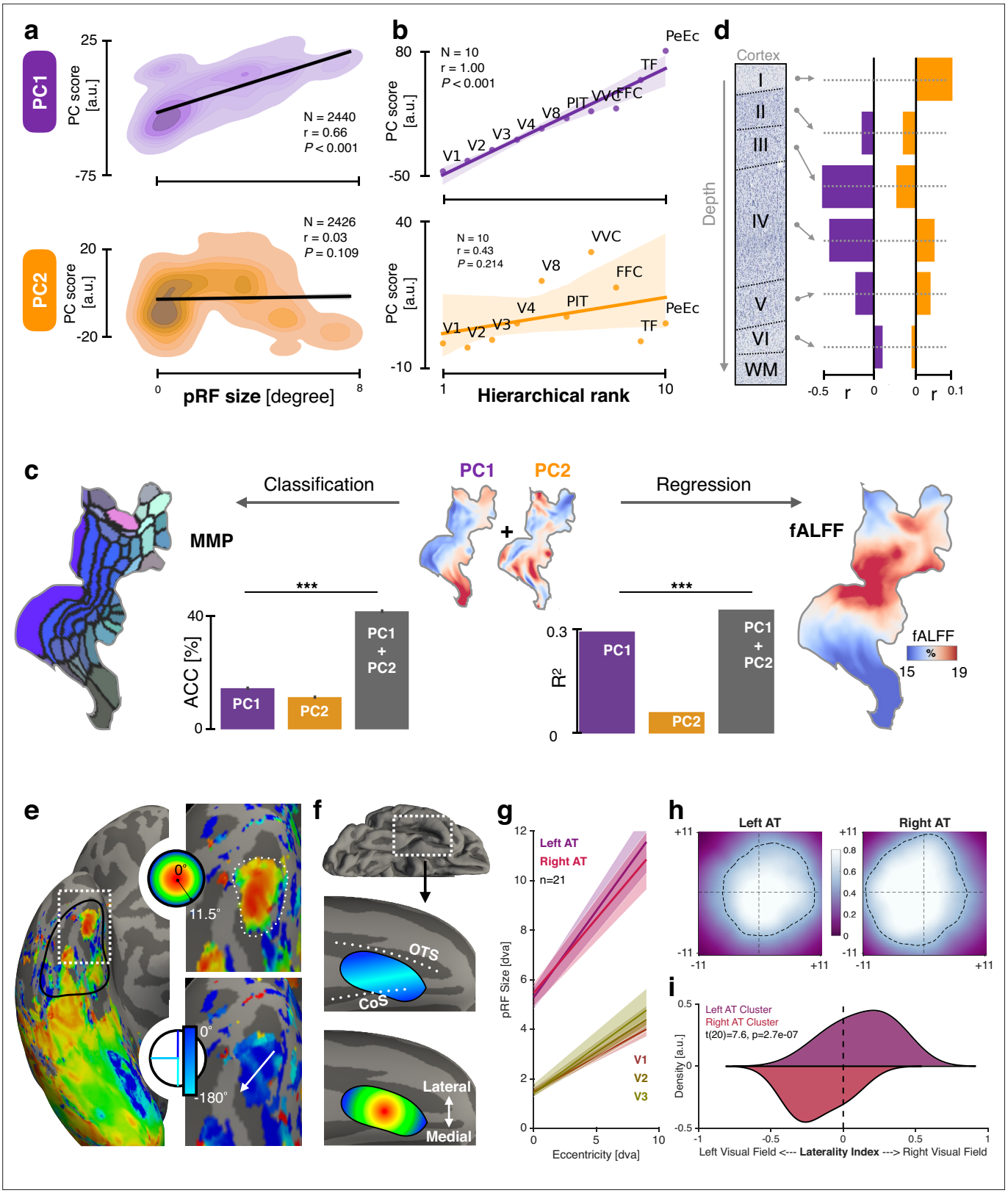


Figure 2. The functional and microstructural properties of the two architectural gradients. (**a**) Gradient 1 was highly correlated with the population receptive field (pRF) size (r = 0.66), while gradient 2 was not (r = 0.03). (**b**) Gradient 1 was perfectly correlated with the hierarchical rank of the 10 visual areas within the ventral visual stream (Spearman rank ρ = 1.00), while gradient 2 was not. (**c**) The functional significance of the architectural gradients was evaluated by measuring to what extent each gradient is related to areal differentiation of the visual cortex (left) and the global functional organization

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measured by fractional amplitude of low-frequency fluctuation (fALFF) from resting-state fMRI (right). The combination of gradients 1 and 2 greatly improved the predictive power of classifying visual areas compared to using either gradient alone. However, gradient 1 contributes more than gradient 2 in predicting the large-scale functional organization (i.e., fALFF map). (**d**) Cell body density from the BigBrain dataset is quantified for each cortical layer at each vertex and correlated with each gradient map. Gradient 1 was mainly correlated with cell body density in layers III and IV, while gradient 2 was mainly correlated with cell body density in layer I. (**e**) The architectural gradient 2 predicts the presence of novel visual representations in the anterior temporal lobe. Left: example participant with the pRF eccentricity map displayed on the inflated cortical surface. The highlighted region (white dotted line) is the subject of the zoomed insets on the right. The black outline delineates the anatomical region from which pRF data was extracted. The putative visual representation cluster is outlined on the insets, showing a radial eccentricity representation and a perpendicular representation of polar angle traveling roughly medio-anterior to latero-posterior as indicated by the white arrow. (**f**) Illustration on an inflated cortical surface illustrating that the AT-cluster of retinotopic maps is located near the anterior intersection of the occipitotemporal (OTS) and collateral sulci (CoS). The AT-cluster representations demonstrate perpendicular representations of pRF eccentricity and polar angle. (**g**) In all 21 participants, pRF size and eccentricity from all above-threshold vertices within the anatomically defined region (black solid line from panel e) are extracted, binned by eccentricity, averaged across participants, and then lines of best fit are modeled across the averaged data. Shaded regions represent bootstrapped 68% confidence intervals. (**h**) Average visual field coverage maps of left and right AT voxels. Lighter colors represent higher coverage density, black outline denotes 50% pRF density compared to maximum. Value of 1 denotes all participants had maximum pRF coverage at that point in space. (**i**) Kernel density histogram denoting laterality index across participants. Value adjusted such that +1 denotes purely right visual field coverage across an individual's pRF fits, −1 denotes purely left laterality, and 0.5 is bilateral coverage.

The online version of this article includes the following figure supplement(s) for figure 2:

Figure supplement 1. The architectural gradients derived from the principal component analysis (PCA) on the mesoscale structural measurements are more functionally relevant than the gradients from resting-state functional connectivity (RSFC).

Figure supplement 2. Anterior temporal visual representation clusters in all participants.

primarily involved in feedforward connections, whereas layer I plays a predominant role in feedback projections, this finding might suggest that gradient 2 is a structural fingerprint of differential feedback connectivity in visual cortex.

Given the relatively tight correspondence between these architectural gradients and the functional organization of visual cortex, can this structural–functional coupling generalize to regions of visual cortex that have not yet been mapped? Upon examination of the topology of gradient 2, a pattern emerges between the gradient and retinotopic representations. While most of the anchor points for the gradient 2 map simulation correspond to visual field map clusters which share a foveal representation (V1–V4, VO1–2, IPS0–1, IPS2–3, and TO1–2) (***Wandell et al., 2007***; ***Brewer et al., 2005***), one additional anchor appeared in the anterior temporal lobe near the location where the occipitotemporal sulcus (OTS) merges with the collateral sulcus (CoS) more medially (***Figure 1d, h***). If we assume a correspondence between gradient 2 anchors and visual field map clusters, then this anterior-most anchor would suggest an additional cluster of visual field maps in the anterior temporal lobe, one which has not yet been described in the literature. To test this hypothesis, and potentially demonstrate the predictive power of these architectural gradients to unmapped cortex, we performed pRF mapping (***Dumoulin and Wandell, 2008***) on 21 participants with high-contrast, socio-ecological images to better drive neurons of high-level visual cortex often tuned for such complex objects (***Finzi et al., 2021***).

We indeed find a cluster of visually responsive pRFs in the anterior temporal lobe located medially, overlapping the CoS and extending laterally toward the OTS usually just beyond the anterior tip of the fusiform gyrus but sometimes overlapping it (***Figure 2e***). This location is consistent with a previous report of face-selectivity in the anterior temporal lobe (***Finzi et al., 2021***) and is located within perirhinal cortex and approximately located at the border between Brodmann areas 35 and 36 (***Xie et al., 2017***; ***Ding and Van Hoesen, 2010***). These maps were observable in the majority of hemispheres (see ***Figure 2—figure supplement 2***). This cluster of maps shows a clear radial representation of pRF eccentricity, with voxels near the center of the cluster sampling central visual space, and those near the outer boundary of the cluster sampling peripheral visual space. Perpendicular to this radial eccentricity representation was a representation of polar angle, with two upper visual field representations separated by a shared lower visual field representation, usually oriented at an oblique angle to the CoS but sometimes parallel with it (***Figure 2e, f***). A hallmark feature of visual pRFs is that they increase in size as one ascends the visual processing hierarchy, and the positive relationship between pRF eccentricity and size tends to become more dramatic as well (***Wandell and Winawer, 2015***; ***Dumoulin and Wandell, 2008***; ***Amano et al., 2009***; ***Harvey and Dumoulin, 2011***). To test this,

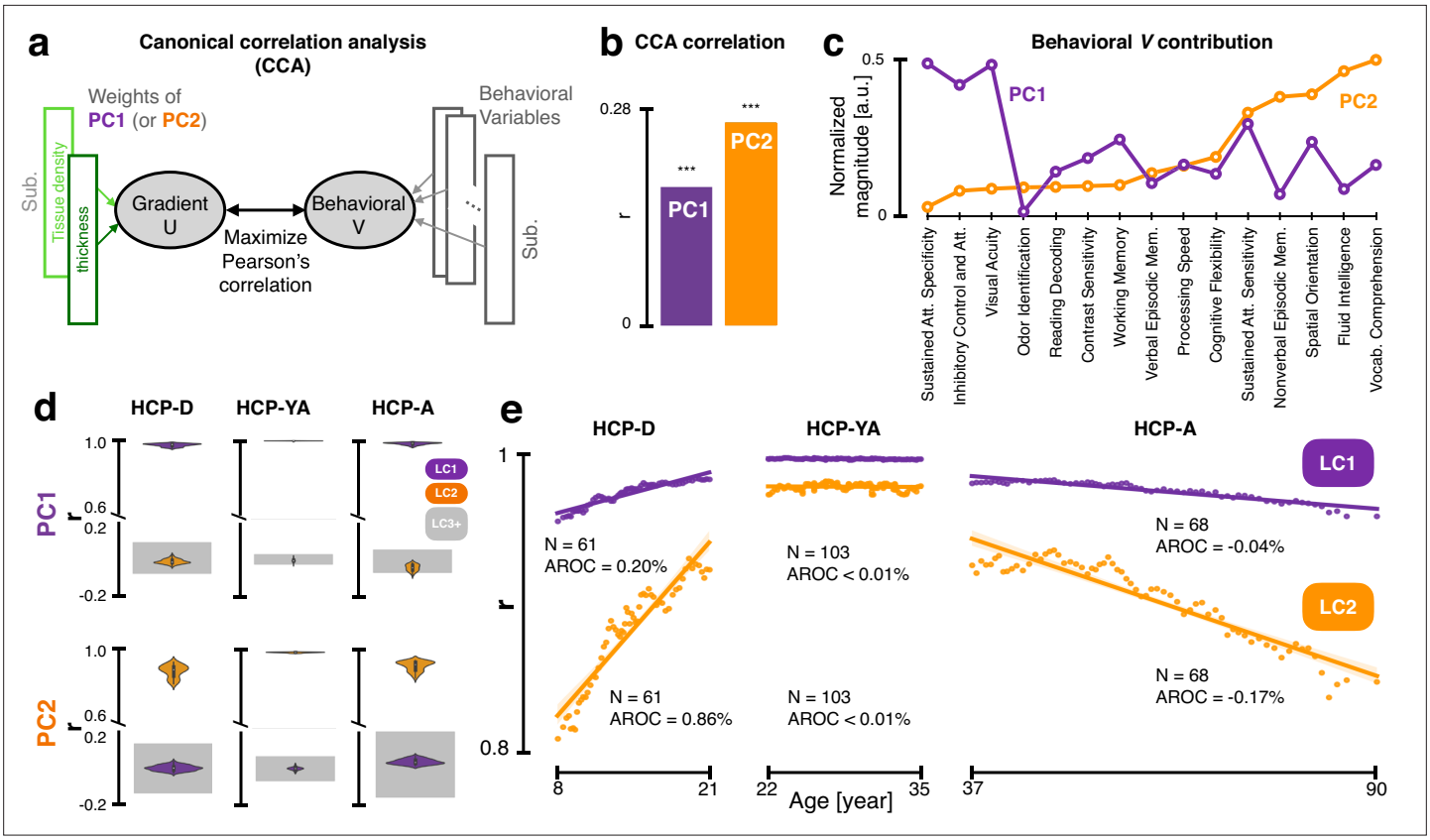


Figure 3. The relevance of the architectural gradients to visual behavior, development, and degeneration across the lifespan. (**a**) Canonical correlation analysis (CCA) was used to associate multiple vision-related tasks with the two weight-vectors of each architectural gradient in the HCP-YA. CCA finds the linear combination of variables that best associate measures from the two data domains across participants. (**b**) Both architectural gradients can significantly predict individual visual ability. However, gradient 2 showed stronger correlation with visual behaviors than gradient 1. (**c**) The normalized magnitude of behavioral factor weights from CCA indicates that gradient 1 was correlated more with low-level visual abilities, while gradient 2 was correlated more with higher-level visual abilities. (**d**) Sliding-window spatial principal component analysis (PCA) was performed across the lifespan (PCA on a given age-bin results in 'lifespan component', LC) to compare how the patterns of gradient 1 and 2 change with age. The top two LCs (i.e., spatial maps) extracted from each age window correlate strongly with their respective component from the HCP-YA, confirming that the architectural gradients can be observed across the lifespan. (**e**) Correlations between LCs and PCs reveal that gradient 2 shows more development and degeneration across childhood and aging, compared to gradient 1.

we extract pRF fits from vertices with variance explained greater than 10%. We find that consistent with its high position within the processing hierarchy, pRF sizes are significantly larger than in earlier visual field maps V1 through V3, and the linear function relating pRF eccentricity and size yielded larger slopes compared to V1–V3 (***Figure 2g***). Consistent with spatial computations in earlier visual field maps, these anterior temporal (AT) representations display pRF coverage that mainly samples the contralateral visual field (***Gomez et al., 2019a***; ***Gomez et al., 2018***; ***Amano et al., 2009***), although it was not uncommon for pRF centers to sample ipsilateral visual space (***Figure 2h***). To quantify if the visual field sampling in each AT representation was significantly contralateral, we derived a laterality index (***Sheremata and Silver, 2015***) for each individual left or right AT cluster and display the histogram of indices (***Figure 2i***). We find a significant difference in laterality indices between left and right AT pRFs (paired-samples *t*-test, $t(20) = 7.6$, $p = 2.7 \times 10^{-7}$).

If these architectural gradients are capable of extrapolating to functional representations in visual cortex, to what extent can they also describe the behaviors supported by visual cortex? In addition to providing spatial maps of scores, the PCA provides a weight or sense of fit describing how a given participant relates to a given gradient. To answer the question above, a canonical correlation analysis (CCA) (***Wang et al., 2020***) was performed to examine how individual participant weights for the two gradients can predict the individual behavioral performance from 15 vision-related behavioral tasks (***Barch et al., 2013***; ***Figure 3a***). As shown in ***Figure 3b***, both gradients show significant correlation

with visual ability. However, in comparison to the architectural convergence pattern (gradient 1), the divergence pattern (gradient 2) demonstrates a stronger correlation with visual behaviors. Moreover, the two gradients are associated with distinct and unrelated behavioral profiles (***Figure 3c***): Behavioral variables related to attention, visual acuity, and inhibitory control are more closely associated with gradient 1, while vocabulary comprehension, fluid intelligence, spatial orientation processing ability, and nonverbal episodic memory ability are more strongly linked to gradient 2. The distinct behavioral mapping profiles of the convergence and divergence gradients further underscore each architectural gradient's unique contribution to brain function and highlight the cognitive importance of the architectural gradients.

If these architectural gradients across the cortical sheet correspond to differences in cortical tissue content, brain function, and behavior, as evidenced above, then they should also change across the lifespan, given that behavior and neocortical tissue structure develop dramatically during childhood across visual cortex (***Natu et al., 2019***; ***Sowell et al., 2004***; ***Gomez et al., 2017***). The two spatial gradients described above were derived from the young adult dataset (HCP-YA). We can therefore repeat the spatial component analysis at various stages of the lifespan. We can ask if the first two principal gradients replicate in these separate stages, and determine how they may change, if at all, across the lifespan using HCP development (HCP-D) and aging (HCP-A) datasets (***Harms et al., 2018***). We binned participants in equal-sized windows of increasing age, deriving within each window the top PCs and correlating their score maps with that from the young adult dataset. To distinguish the PCs of each age window from the PCs of the young adult dataset, we referred those derived from developmental age bins as lifespan components (LCs). We found that LC1 and LC2 from the developmental (n = 652 participants, 351 females, ages 5–21), adult (n = 1070, 586 females, ages 22–37), and aging (n = 725 participants, 406 females, ages 36–100) data at every age bin show a high correspondence to gradients 1 and 2 from the young adult data, respectively, compared to other LCs (***Figure 3d***). This demonstrates that the two gradients derived from lifespan data at each window replicate those of the young adult dataset, allowing us to trace their developmental trajectories.

Examining the correlation between the young adult gradient and LC within each developmental window, we first found that LCs, as expected, are stable during young adulthood (***Figure 3e***, middle). However, we found a linear change across childhood, with the topography of LC1 and LC2 becoming more adult-like with maturation (***Figure 3e***, left). The trajectory of each LC was unique, with a significant age × LC interaction ($F_{1,118}$ = 257.01, p < 0.001). LC2 showed a significantly larger developmental effect than LC1, with an annualized rate of change (AROC) four times that of LC1 (0.86% vs 0.20%). Finally, if gradients solidify their structural topography across childhood and adolescence, do they show degeneration in later adulthood? We can make two a priori hypotheses here: first, that both LCs will show linear loss of their adult-like topographies and second, that LC2 will show more rapid degeneration than LC1, consistent with the developmental retrogenesis trends observed in white matter development (***Yeatman et al., 2014***). As shown in ***Figure 3e*** (right panel), the sliding-window gradient analysis on the aging dataset revealed that both hypotheses are supported, LC1 and LC2 both show linear loss of their topographies with LC2 showing more dramatic degeneration than LC1 (LC1 AROC = −0.04%; LC2 AROC = −0.17%; age × LC interaction $F_{1,132}$ = 263.85, p < 0.001).

Discussion

Overall, we provide evidence for two architectural gradients across human visual cortex, each of which captures a distinct relationship between the thickness and tissue density of the cortical sheet. While the first gradient captures a relationship in which thickness and density measures vary in agreement with one another, the second captures a relationship in which these two features diverge from one another. The convergence pattern, arising from the negative correlation between thickness and density, is consistent with previous findings (***Maingault et al., 2021***; ***Sereno et al., 2013***; ***Shafee et al., 2015***) and may support the balloon model, whereby cortical thinning is associated with tangential stretching due to myelination (***Seldon, 2005***). In terms of cortical spatial organization, the convergence map scaffolds the cortex into a processing hierarchy, while the divergence map between these features appears to contribute to the finer-scale arealization of the cortex into distinct regions. These two architectural gradients together describe well the broader functional landscape and seem to relate to unique aspects of cytoarchitecture across cortex. Where the first gradient correlates strongly with pRF size of the visual system, and is capable of ranking regions into their ground-truth hierarchical ordering,

the second gradient appears to differentiate visual cortex into distinct zones within a hierarchical level. The second gradient not only predicted the location of a new contralateral visual representation in anterior temporal cortex, but also demonstrated more dynamic changes across the lifespan which may correlate with visual behavior development.

These data would suggest that gradient 2 tracks the functional differentiation of visual cortex into unique regions, wherein regions occupying the same hierarchical level within gradient 1 show distinct values in gradient 2. The current data offer strong evidence in this regard through two separate observations. First, adding the divergent gradient into a classifier along with the convergent gradient significantly improved classification performance of cortical region labels (***Figure 2c***). Second, cortical regions where divergent gradient scores transitioned from positive to negative values appeared to be spatially related to the location of shared foveal representations in visual field map clusters. We observed such a transition zone in the structural measures of the divergent gradient in anterior temporal cortex. Consistent with this structure–function coupling, we observed a novel, contralateral visual field representation with a clear radial eccentricity and largely perpendicular polar angle transitions (***Figure 2e–i***). The organization of polar angle in anterior temporal cortex was not as orderly as earlier visual cortex, but consistent with disorderly polar angle representations in higher-level dorsal visual cortex (***Mackey et al., 2017***). Thus, whether these representations constitute formal visual field maps will require higher-resolution pRF mapping, but their observed location provides strong empirical evidence for the predictive power of our cortical model on the functional topography of the brain. These new contralateral visual representations also provide greater context for previous observations of a face-selective region in the anterior temporal lobe (***Axelrod and Yovel, 2013***), which may neighbor or overlap these novel AT pRF clusters. This relationship would be consistent with previous work showing that face-selective regions on the fusiform gyrus neighbor foveal representations of nearby visual field map clusters in more posterior portions of ventral occipitotemporal cortex (***Winawer and Witthoft, 2015***; ***Weiner and Grill-Spector, 2010***).

Given that gradient 2 shows the strongest relationship to behavior and tracks developmental changes across the lifespan, it might suggest that the differential development between cortical regions during childhood more strongly drives maturation of visual behavior, compared to broader-scale structural changes. Indeed, previous work has shown that divergent developmental trajectories between category-selective regions of high-level visual cortex underlie behavioral maturation of high-level visual abilities (***Gomez et al., 2017***) and that a disruption in this differential structural development may underlie disorders of high-level vision (***Gomez et al., 2015***). Future work can examine if functional arealization at earlier developmental timepoints, as in infancy (***Wang et al., 2023***), follows this prediction.

Likewise, our results hold implications for understanding human neurodevelopment. The nearly mirror symmetric development and degeneration of these architectural gradients between childhood and later adulthood offer strong evidence that gradient 2 follows the pattern of retrogenesis (***Reisberg et al., 1999***) across the lifespan. It is presently unclear if the changes in cortical tissue during childhood that drive the developmental emergence of gradient 2 are the same tissue compartments which degenerate later in life (***Figure 3e***). Indeed, while our current analyses focus on cortex, the expanse of visual cortex described here is innervated by several major white matter pathways such as the vertical occipital (***Takemura et al., 2016***), the inferior longitudinal (***Catani et al., 2003***), and the arcuate fasciculi (***Catani and Mesulam, 2008***), all of whose development has been shown to be behaviorally relevant (***Gomez et al., 2015***; ***Oishi et al., 2018***; ***Song et al., 2015***; ***Thomas et al., 2009***; ***Tavor et al., 2014***). Therefore, the extent to which these architectural changes reflect local tissue structure versus connectomic features (***Sarwar et al., 2021***) should be clarified in future work. Furthermore, while gradient 1 described a typical relationship between the thickness and density of tissue in the cortical sheet, gradient 2 captures how these two features diverge from this canonical relationship and exhibits greater behavioral relevance across a range of visual behaviors. This might suggest that the patterning of cortex into distinct cortical regions necessitates deviation from a canonical cortical sheet, reminiscent of the protocortex hypothesis of gestational neurodevelopment in which largely similar progenitor cells in the primordial cortex differentiate as a result of distinct thalamic inputs across cortex (***O'Leary, 1989***; ***López-Bendito and Molnár, 2003***; ***Appan et al., 2023***). The morphological changes during gestation that lead to arealization of cortex into distinct regions are certainly distinct from the childhood structural measures quantified here through MRI, but may nonetheless suggest

that the ontogenetic routines which serve to differentiate cortex into cytoarchitectonically distinct zones during gestation likely have long-term influences on the postnatal development observed here.

It is worth emphasizing that while classical cortical parcellation emphasizes sharp cytoarchitectonic boundaries (***Brodmann, 1909***), the gradients identified here—derived from interindividual variability in microstructural features—do not contradict this view but instead provide complementary information that may capture supra-areal organizational principles describing how distinct cortical regions relate to one another across the cortical sheet.

These findings offer evidence that there are architectural gradients, measurable with MRI, that are shared across individuals. These shared patterns of cortical sheet morphology track the functional organization and computations of the underlying cortical sheet across the human lifespan. These findings provide a normative benchmark for future work examining how deviations from these shared mesoscale architectural patterns underlie neurological disorders.

Methods

HCP data

The publicly available data from the HCP-YA (***Van Essen et al., 2013***; ***Glasser et al., 2013***), HCP-D, and HCP-A (***Harms et al., 2018***) were used in the study. The three large-scale brain imaging studies collect behavioral and multimodal MRI data in healthy participants from 5 to 100 years of age, and thus provide us with opportunities to characterize brain changes across the human lifespans. Only structural MRI, resting-state fMRI and behavioral data were used in the study. The use and analyses were approved by the Institutional Review Boards of Beijing Normal University (No. ICBIR_A_0111_001) and Princeton University (No. 13074).

After excluding participants with invalid MSM-All registration and those without any rs-fMRI data, we obtained multimodal MRI and behavioral data for 1070 HCP-YA participants (586 females, ages 22–37, S1200 release). For each participant, T1w and T2w structural images (0.7 mm isotropic voxels) and functional images (2 mm isotropic voxels; TR = 720 ms) were acquired on the HCP's customized 3-Tesla Siemens Skyra scanner using a 32-channel head coil. The rs-fMRI paradigm included two sessions, each session itself including two runs with opposite phase-encoding directions (R/L and L/R, each 15 min long). All the structural and functional MRI data were preprocessed using the HCP minimal preprocessing pipelines, and more information regarding data acquisition and preprocessing is available from previous work (***Glasser et al., 2013***; ***Van Essen et al., 2012***; ***Glasser et al., 2016b***).

The HCP-D and HCP-A datasets were acquired on a 3T Siemens Prisma scanner with similar protocol as the HCP-YA data (***Bookheimer et al., 2019***; ***Somerville et al., 2018***). Structural MRI data (0.8 mm isotropic) from 652 HCP-D participants (351 females, ages 5–21) and 725 HCP-A participants (406 females, ages 36–100) were used in this study (Lifespan HCP release 2.0). Preprocessing of these two datasets was nearly identical to that of the HCP-YA with small adaptations to account for the variability of the wider age range (***Harms et al., 2018***). The HCP data used in this study were in fsLR_32k cortical space based on the MSM-All registration (***Robinson et al., 2018***), and cortical thickness data used in the study have been regressed out to exclude the linear effect of cortical curvature.

BigBrain data

The BigBrain dataset is a volumetric reconstruction (20 μm isotropic) of a histologically processed postmortem brain of a human male 65 years of age. Sections were stained for cell bodies, imaged, and digitally reconstructed into 3D volume (***Amunts et al., 2013***). The white and pial surfaces of the BigBrain were extracted at the gray–white matter boundary and gray matter/cerebrospinal fluid boundary (***Wagstyl et al., 2018***), respectively. The 3D laminar atlas, including six cortical layers, was also derived at 20 μm isotropic resolution (***Wagstyl et al., 2018***; ***Wagstyl et al., 2020***). Based on the surface registration to the MRI-based MNI152 template surface, the cytoarchitectural information from each layer of the BigBrain can be linked to in vivo neuroimaging data.

pRF experiment

We performed pRF mapping on 21 participants with high-contrast, ecological images to better drive neurons of high-level visual cortex often tuned for such complex objects. We adapted the experiment used in the HCP 7T Retinotopy Dataset (***Benson et al., 2018***). Stimuli consisted of slowly moving

bar-shaped apertures of 2° width filled with a dynamic colorful texture. Textures presented within the bar aperture were updated at a rate of 7 Hz. Textures included randomly presented cartoon scenes depicting people, animals, characters, text, limbs, and objects evenly spanning the width of the stimulus aperture. Participants were asked to fixate on a central dot while attending to the bar, monitoring it for the random appearance of a target cartoon stimulus (a grid of wiggling bumblebees) which appeared for a 500ms duration, 10 times during the experiment. Each run lasted 300 s, and participants completed 3–4 runs.

Data analysis

Definition of human visual cortex

Human visual cortex was defined by grouping the 44 visual areas from the HCP MMP atlas (***Glasser et al., 2016a***). All of these areas located in the occipital, parietal, and temporal cortices and show a significant BOLD response to visual objects. According to the well-established model of the visual cortex, these areas are grouped into four visual processing streams: early stream (V1, V2, V3, and V4); lateral stream (V3CD, LO1, LO2, LO3, V4t, FST, MT, MST, and PH); dorsal (V3A, V3B, V6, V6A, V7, IPS1, LIPv, VIP, MIP, 7Am, 7PL, 7Pm, IP0, IP1, DVT, ProS, POS1, POS2, and PCV); and ventral (V8, VVC, PIT, FFC, VMV1, VMV2, VMV3, PeEc, PHA1, PHA2, PHA3, and TF). Please see supplementary information for the detailed descriptions of these areas (***Supplementary file 1A***).

Extracting architectural gradients of human visual cortex

The thickness of cortex, and the density of neurite and myelin content (referred to here as tissue density), are two widely used mesoscale in vivo architectural measures derived from structural MRI and were used to extract architectural gradients of human visual cortex. Cortical thickness was measured as the shortest distance between each vertex on the white matter surface and the pial surface (***Fischl and Dale, 2000***), while cortical tissue density was measured by the ratio of T1w to T2w (***Glasser and Van Essen, 2011***). For each hemisphere, individual cortical thickness and T1/T2-weighted ratio maps from all HCP-YA participants—each represented as an $M \times N$ matrix, where M is the number of cortical vertices (samples) and N is the number of participants (features)—were concatenated along the column dimension, resulting in a combined matrix of shape $M \times 2N$. Prior to conducting PCA, we applied Z-score normalization across vertices, thereby centering and scaling each feature to unit variance. PCA was then performed on this normalized matrix, treating cortical vertices as samples and the concatenated participant features as input variables. This decomposition produced a set of orthogonal PCs, consisting of spatial maps (i.e., PC scores) and corresponding participant-wise contributions (i.e., PC loading or individual weights) in pairs. The score map explains how the structural properties change across the cortical sheet on each component and the individual weights describe how individual cortical thickness and tissue density maps contribute to each component. The PCs are sorted in decreasing order according to the amount of variance explained by each of the components. The contribution ratio of density or thickness for a given PC was calculated by the ratio of the sum of absolute values of weights of the loading matrix from each measure to the sum of absolute values of weights from both measures.

The global hierarchy of architectural gradients

Two metrics which index the visual cortical functional hierarchy were used to validate the global hierarchy of the architectural gradients.

1. pRF size: It is widely known that pRF size progressively increases as one ascends the processing hierarchy from V1 to high-level visual cortex (***Wandell and Winawer, 2015***; ***Dumoulin and Wandell, 2008***; ***Amano et al., 2009***). We first validated the global hierarchy of the architectural gradients by measuring if the gradients show similar spatial pattern to the pRF size across visual areas. Specifically, we calculated the Pearson correlation coefficients between architectural gradients and pRF size from the HCP's 7T retinotopy dataset (***Benson et al., 2018***). Only the vertices whose eccentricity of pRF within 8° were used because retinotopic mapping stimuli were constrained to a circular region with a radius of 8°.
2. Hierarchical rank: As the hierarchical level of the visual areas within the ventral stream has been widely studied and relatively clear, we reviewed literature describing the hierarchical relationships of 10 visual areas within the ventral stream (***Gomez et al., 2019b***; ***Glasser et al., 2016a***;

Abdollahi et al., 2014; ***Beauchamp et al., 2008***; ***Felleman and Van Essen, 1991***; ***Hadjikhani et al., 1998***; ***Haxby et al., 2000***; ***Kolster et al., 2010***; ***Larsson and Heeger, 2006***; ***Moreno-Ortega et al., 2019***; ***Nunn et al., 2002***; ***Orban et al., 2004***; ***Sellal, 2022***; ***Tootell et al., 1997***; ***Tootell et al., 2003***; ***Weiner et al., 2014***) and ranked them into a hierarchy from lowest-level to high: V1, V2, V3, V4, V8, PIT, VVC, FFC, TF, and PeEc, with cortical regions defined using labels of the HCP multimodal atlas (***Glasser et al., 2016a***). Spearman's rank correlation coefficients were then computed between the mean gradient score and the hierarchical rank of the areas.

Geometric models of the architectural gradients

The geometric models of the architectural gradients were constructed by the geodesic distance of each vertex to a set of specific references (***Figure 1h***). The primary gradient was modeled as the geodesic distance of each vertex of visual cortex to the CS anchor. The secondary gradient was modeled as the minimum geodesic distance from each vertex on the visual cortex to the eight anchors dispersed among four visual processing streams, which consisted of two local minima in the early visual cortex, two local minima in the dorsal visual stream, two local minima in the lateral visual stream, and two local minima in the ventral visual stream (please see supplementary information for details, ***Supplementary file 1B***).

The gradient differences between vertices with different spatial distance

The gradient differences for each pair of vertices were calculated as the absolute difference between their gradient scores. The spatial distance between each pair of vertices was measured by the geodesic distance separating them on the cortical surface. The gradient differences between pairs of vertices were then sorted into 100 groups according to their spatial distance. The mean gradient differences and geodesic distances were then computed for each group and plotted against each other to evaluate how the gradient differences depend on spatial distance.

Functional significance of the architectural gradients

We characterized the functional significance of the architectural gradients by measuring to what extent each gradient is related to areal differentiation of the visual cortex (***Glasser et al., 2016a***) and the fALFF from resting-state fMRI (***Zou et al., 2008***).

1. Predicting visual areas based on the architectural gradients: Logistic regression classifiers were trained on the architectural gradients to predict visual cortical areas. Specifically, the vertices from the visual cortex, with the architectural gradients as features, were used as the samples and the 44 visual cortical areas from the HCP MMP were used as the true class labels (i.e., 44-class classification). The areas with more vertices were down sampled to have the same number of vertices as the smallest areas to keep the number of samples with each class constant and thus avoid the imbalance of sample number across different visual areas. Logistic regression classifiers were trained and tested on each downsampled data using a fivefold CV procedure. 100 random downsamples were performed and the averaged accuracy was used to measure the classification accuracy.
2. Predicting fALFF based on the architectural gradients: The fALFF is calculated as the ratio of the power spectrum of low-frequency modulations to that of the entire frequency range and is indicative of the magnitude of spontaneous brain activity (***Shmuel and Leopold, 2008***; ***Zou et al., 2008***). For each rs-fMRI run, the time series of each vertex was Fourier transformed to a frequency domain without band-pass filtering, and the square root of the power was calculated at each frequency within the spectrum. fALFF was then computed by dividing the sum of amplitudes across a low-frequency band of the spectrum (0.01–0.1 Hz) by the sum of amplitudes across all frequencies up to the Nyquist frequency (0–0.625 Hz). The group fALFF map was calculated by averaging individual fALFF across all valid rfMRI runs within each participant and then across participants. 100 linear regression analyses using the fivefold CV procedure were performed and the averaged R^2 was used to characterize to what extent the two architectural gradients are related to spontaneous functional activity characterized by fALFF.

Laminar cytoarchitecture underlying the architectural gradients

The BigBrain cortical surfaces registered to standard surfaces, the surfaces of borders of the six cortical layers in BigBrain histological space, and the CBD data at 40 μm resolution were used together to

extract laminar cytoarchitecture of the visual cortex. Specifically, for each of six cortical layers (***Wagstyl et al., 2018***), we first generated 10 surfaces based on the equivolumetric principle between its inner and outer borders (***Waehnert et al., 2014***) to extract 10 CBD maps in the BigBrain space. Next, the CBD data from the BigBrain space were resampled to the fsLR_32k space, and then the 10 CBD maps were averaged to obtain an averaged CBD map for the layer. Finally, the spatial similarity between the architectural gradients and the averaged CBD map from each of the six cortical layers was measured with Pearson correlation coefficients.

pRF mapping

Functional images were preprocessed using a similar pipeline to the HCP data, including motion-correction, slice-timing correction, and phase-encoding distortion correction, and then aligned to each participant's native cortical surface through FreeSurfer's FS-FAST pipeline (***Fischl, 2012***). The preprocessed data from multiple runs from each participant were averaged to increase signal-to-noise ratio. The data were finally analyzed by a pRF model implemented in the VISTA Lab toolbox (github.com/vistalab; ***Legarreta Gorroño, 2026***), with additions for compressive nonlinearity (cvnlab.net/analyzePRF). The model predicts fMRI time series as the convolution of the stimulus-related time series and a canonical hemodynamic response function. The stimulus-related time series are in turn generated by computing the dot product between the stimulus apertures and a 2D isotropic Gaussian, scaling and applying a static power-law nonlinearity (***Kay et al., 2013***). Several parameters of interest are produced from the pRF model for each vertex, including phase angle, eccentricity, and pRF size. Vertices entered into any analyses presented in ***Figure 2*** were only included if there was at least 10% variance explained by the model-fit.

To produce maps of visual field coverage (***Figure 2h***) similar to previous work (***Gomez et al., 2018***), each participant's pRF fits from the AT region were simulated as 2D Gaussians and plotted on the visual field with a maximum value of 1, summing across pRFs within a participant without allowing values at any given point in the visual field to exceed 1. pRF fits with sigma values smaller than 0.5 or eccentricity values larger than the stimulus-mapping field of view (11.5° of visual angle) were excluded. The coverage map for a given participant's AT region was bootstrapped 1000 times, plotting 75% of pRF fits on each iteration, then averaged across bootstraps. Coverage maps were then averaged across participants to produce ***Figure 2h***.

To quantify whether there is a left–right contralateral bias in the sampling of visual space (and to test whether such a bias is significantly different in each hemisphere), we calculated for each pRF a laterality index as previously defined by ***Sheremata and Silver, 2015*** according to the following equation:

$$\left[\frac{1}{\sqrt{\pi}}\int_{\frac{x_0}{\sqrt{2}\sigma}}^{+\infty} e^{-t^2}\,dt\right],$$

where resulting values of 1 mean the pRF is contralateral, 0.5 is no laterality bias, and 0 is ipsilateral bias. Additionally, we input pRF sigma values that were adjusted for the nonlinearity exponent as defined by ***Kay et al., 2013***. For the purposes of visual comparison, we subtracted 0.5 from index values so that resulting laterality scores were relative to 0 to represent the center of the visual field, and then values were inverted with a −1 scalar so that left hemisphere pRF laterality index values are plotted on the right side of space, and the right hemisphere on the left, as shown in ***Figure 2i***. The laterality index was calculated for each pRF for a given participant and then averaged within that participant to result in a single mean laterality index for the left hemisphere pRFs and a single index for their right hemisphere pRFs. The histograms illustrated in ***Figure 2i*** depict the density of participants (kernel smoothed).

Behavioral relevance of the architectural gradients

The behavioral significance of the architectural gradients was examined by measuring how the individual weights from PCA can account for the individual variation in behavioral performance on related visual tasks. The HCP-YA dataset includes behavioral tasks of a range of motor, sensory, cognitive, and emotional processes. Because our architectural gradients cover the entire visual cortex and may involve

a variety of cognitive and behavioral abilities, a total of 15 vision-related or vision-based behavioral tasks (***Barch et al., 2013***), designed to measure nonverbal episodic memory ability, cognitive flexibility, inhibitory control and attention ability, fluid intelligence, reading decoding skill, general vocabulary knowledge, speed of processing, spatial orientation processing ability, sensitivity of sustained attention, specificity of sustained attention, verbal episodic memory ability, working memory ability, odor identification ability, visual acuity, and contrast sensitivity, were selected to examine the behavioral relevance of the gradients (Please see supplementary information for details, ***Supplementary file 1C***).

For the two sets of individual weights (i.e., myelin/neurite density weights and cortical thickness weights) associated with each architectural gradient, we carried out a single integrated multivariate analysis using CCA (***Wang et al., 2020***), to simultaneously co-analyze the two sets of weights along with 15 behavioral variables from all participants. CCA aims to identify symmetric linear relations between the two sets of variables. That is, we used CCA to find components that relate the two sets of weights from each gradient to 15 sets of participants' behavioral measures. Each CCA component identifies a linear combination of two weights and a linear combination of behavioral variables, where the variation in strength of involvement across participants is maximally correlated. The normalized magnitude of behavioral weights, obtained by dividing each squared behavioral weight by the total sum of all squared weights, was used to characterize the behavioral profile of an architectural gradient and reveal how the two gradients are different in predicting the same set of behavioral variables.

The development of the architectural gradients across the lifespan

We divided HCP-D, HCP-YA, and HCP-A participants into different age windows (subgroups) in ascending order of age. Among them, the participants of HCP-D and HCP-A were sorted by their age in months, while HCP-YA was sorted in years because no month information was provided. Each window consisted of 50 participants and had a step size of ten. As a result, there are 61, 103, and 68 age windows generated for HCP-D, HCP-YA, and HCP-A data, respectively. To characterize the changes of the architectural gradients across the human lifespan, we conducted PCA on the stacked tissue density and thickness maps of each window as we did in the whole HCP-YA data. We label the PCs from each age window as LCs to differentiate them from the original PCs derived from the HCP-YA dataset. To determine if the observed LCs were similar to the PCs from the HCP-YA data, we calculated the Pearson's correlation coefficients between the HCP-YA PCs and the top ten LCs for each window. The LC which shows the strongest correlation with a PC was considered to be the correspondence LC to the PC in that age window. Lastly, how the observed gradients from each age window change relative to the gradient from the HCP-YA was measured by the Pearson's correlation coefficient between their score maps. The changes along age were then charted (i.e., developmental trajectories). A linear model was then constructed to characterize the developmental trajectory within each of the three datasets. The slope of the linear model was defined as the AROC in the architectural gradients.

Ethical compliance

Data analyzed from the Human Connectome Project follows all necessary privacy and security guidelines. Data collected from participants at Princeton University followed all Institutional Review Board ethics and guidelines (protocol number 13074), and all safety regulations set forth by the Scully Center for the Neuroscience of Mind and Behavior. Informed consent was collected from every participant involved in this study, and all were reimbursed for their time.

Code availability

The HCP data were preprocessed using the HCP-Pipeline analyses (https://github.com/Washington-University/HCPpipelines, ***Brown et al., 2026***). Custom code for gradient analysis can be found at https://github.com/BNUCNL/VisualCortexGradient (copy archived at ***Chen, 2026***). Code to reproduce pRF mapping figures can be found at https://github.com/gomezj/entorhinal_prf (copy archived at ***Gomez, 2023***).

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Author contributions

Xiayu Chen, Xingyu Liu, Data curation, Formal analysis, Visualization, Methodology, Writing – original draft, Writing – review and editing; Patricia Maria Hoyos, Edan Daniel Hertz, Jewelia K Yao, Formal analysis; Zonglei Zhen, Jesse Gomez, Conceptualization, Resources, Supervision, Funding acquisition, Writing – original draft, Project administration, Writing – review and editing

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Ethics

Only structural MRI, resting-state fMRI, and behavioral data were used in the study. The use and analyses were approved by the Institutional Review Boards of Beijing Normal University (No. ICBIR_A_0111_001) and Princeton University (No. 13074).

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Additional files

Supplementary files

Supplementary file 1. Tables A–C. **Table A:** Detailed descriptions of the 44 visual areas from the HCP multimodal parcellation (MMP) atlas, related to ***Figure 1***. **Table B:** Location information of anchors of the secondary gradient's geometric model, related to ***Figure 1***. **Table C:** Detail information of 15 vision-related or vision-based behavioral tasks selected from HCP-YA dataset, related to ***Figure 3***.

MDAR checklist

Data availability

The HCP datasets supporting this study are publicly available. HCP-YA (S1200) data are accessible via ConnectomeDB powered by BALSA (https://db.humanconnectome.org). Open-access data can be downloaded directly after creating a free ConnectomeDB account and accepting the Data Use Terms; no application, research proposal, or committee review is required. The HCP-D and HCP-A data (Lifespan HCP Release 2.0) are publicly available through the NIMH Data Archive (NDA) at https://nda.nih.gov (HCP-D: Collection 2846; HCP-A: Collection 2847). Detailed access instructions are provided in the Lifespan HCP Release 2.0 Data Access Instructions (https://www.humanconnectome.org/storage/app/media/documentation/LS2.0/LS_Release_2.0_Access_Instructions_June2022.pdf).

References

Abdollahi RO, Kolster H, Glasser MF, Robinson EC, Coalson TS, Dierker D, Jenkinson M, Van Essen DC, Orban GA. 2014. Correspondences between retinotopic areas and myelin maps in human visual cortex. *NeuroImage* **99**:509–524. DOI: https://doi.org/10.1016/j.neuroimage.2014.06.042, PMID: 24971513

Amano K, Wandell BA, Dumoulin SO. 2009. Visual field maps, population receptive field sizes, and visual field coverage in the human MT+ complex. *Journal of Neurophysiology* **102**:2704–2718. DOI: https://doi.org/10.1152/jn.00102.2009, PMID: 19587323

Amunts K, Lepage C, Borgeat L, Mohlberg H, Dickscheid T, Rousseau M-É, Bludau S, Bazin P-L, Lewis LB, Oros-Peusquens A-M, Shah NJ, Lippert T, Zilles K, Evans AC. 2013. BigBrain: an ultrahigh-resolution 3D human brain model. *Science* **340**:1472–1475. DOI: https://doi.org/10.1126/science.1235381, PMID: 23788795

Amunts K, Zilles K. 2015. Architectonic mapping of the human brain beyond brodmann. *Neuron* **88**:1086–1107. DOI: https://doi.org/10.1016/j.neuron.2015.12.001, PMID: 26687219

Amunts K, Mohlberg H, Bludau S, Zilles K. 2020. Julich-Brain: a 3D probabilistic atlas of the human brain's cytoarchitecture. *Science* **369**:988–992. DOI: https://doi.org/10.1126/science.abb4588

Appan D, Hsu SM, Hsu WH, Chou SJ. 2023. Patterning the cerebral cortex into distinct functional domains during development. *Current Opinion in Neurobiology* **80**:102698. DOI: https://doi.org/10.1016/j.conb.2023.102698, PMID: 36893490

Axelrod V, Yovel G. 2013. The challenge of localizing the anterior temporal face area: a possible solution. *NeuroImage* **81**:371–380. DOI: https://doi.org/10.1016/j.neuroimage.2013.05.015, PMID: 23684864

Barch DM, Burgess GC, Harms MP, Petersen SE, Schlaggar BL, Corbetta M, Glasser MF, Curtiss S, Dixit S, Feldt C, Nolan D, Bryant E, Hartley T, Footer O, Bjork JM, Poldrack R, Smith S, Johansen-Berg H, Snyder AZ, Van Essen DC, et al. 2013. Function in the human connectome: task-fMRI and individual differences in behavior. *NeuroImage* **80**:169–189. DOI: https://doi.org/10.1016/j.neuroimage.2013.05.033, PMID: 23684877

Beauchamp MS, Yasar NE, Frye RE, Ro T. 2008. Touch, sound and vision in human superior temporal sulcus. *NeuroImage* **41**:1011–1020. DOI: https://doi.org/10.1016/j.neuroimage.2008.03.015

Benson NC, Jamison KW, Arcaro MJ, Vu AT, Glasser MF, Coalson TS, Van Essen DC, Yacoub E, Ugurbil K, Winawer J, Kay K. 2018. The Human Connectome Project 7 Tesla retinotopy dataset: description and population receptive field analysis. *Journal of Vision* **18**:23. DOI: https://doi.org/10.1167/18.13.23, PMID: 30593068

Benson NC, Winawer J. 2018. Bayesian analysis of retinotopic maps. *eLife* **7**:e40224. DOI: https://doi.org/10.7554/eLife.40224, PMID: 30520736

Bo T, Li J, Hu G, Zhang G, Wang W, Lv Q, Zhao S, Ma J, Qin M, Yao X, Wang M, Wang G-Z, Wang Z. 2023. Brain-wide and cell-specific transcriptomic insights into MRI-derived cortical morphology in macaque monkeys. *Nature Communications* **14**:1499. DOI: https://doi.org/10.1038/s41467-023-37246-w, PMID: 36932104

Bookheimer SY, Salat DH, Terpstra M, Ances BM, Barch DM, Buckner RL, Burgess GC, Curtiss SW, Diaz-Santos M, Elam JS, Fischl B, Greve DN, Hagy HA, Harms MP, Hatch OM, Hedden T, Hodge C, Japardi KC, Kuhn TP, Ly TK, et al. 2019. The lifespan human connectome project in aging: an overview. *NeuroImage* **185**:335–348. DOI: https://doi.org/10.1016/j.neuroimage.2018.10.009, PMID: 30332613

Brewer AA, Liu J, Wade AR, Wandell BA. 2005. Visual field maps and stimulus selectivity in human ventral occipital cortex. *Nature Neuroscience* **8**:1102–1109. DOI: https://doi.org/10.1038/nn1507, PMID: 16025108

Brodmann K. 1909. *Vergleichende Lokalisationslehre Der Großhirnrinde: In Ihren Prinzipien Dargestellt Auf Grund Des Zellenbaues*. Johann Ambrosius Barth.

Brodmann K, Gary LJ. 2006. *Brodmann's Localisation in the Cerebral Cortex: The Principles of Comparative Localisation in the Cerebral Cortex Based on Cytoarchitectonics*. New York, NY: Springer. DOI: https://doi.org/10.1007/b138298

Brown TB, Coalson T, Harms M, Repovš G. 2026. HCPpipelines. 6d69580. Github. https://github.com/Washington-University/HCPpipelines

Burt JB, Demirtaş M, Eckner WJ, Navejar NM, Ji JL, Martin WJ, Bernacchia A, Anticevic A, Murray JD. 2018. Hierarchy of transcriptomic specialization across human cortex captured by structural neuroimaging topography. *Nature Neuroscience* **21**:1251–1259. DOI: https://doi.org/10.1038/s41593-018-0195-0, PMID: 30082915

Carlo CN, Stevens CF. 2013. Structural uniformity of neocortex, revisited. *PNAS* **110**:1488–1493. DOI: https://doi.org/10.1073/pnas.1221398110, PMID: 23297199

Catani M, Jones DK, Donato R, Ffytche DH. 2003. Occipito-temporal connections in the human brain. *Brain* **126**:2093–2107. DOI: https://doi.org/10.1093/brain/awg203

Catani M, Mesulam M. 2008. The arcuate fasciculus and the disconnection theme in language and aphasia: history and current state. *Cortex* **44**:953–961. DOI: https://doi.org/10.1016/j.cortex.2008.04.002

Chen X. 2026. VisualCortexGradient. swh:1:rev:5544d589dd0f8ed23b33c6b612cdc1653e6465fc. Software Heritage. https://archive.softwareheritage.org/swh:1:dir:bd0ac250b178d39d1a7b6457a57083dbc83eab2e;origin=https://github.com/BNUCNL/VisualCortexGradient;visit=swh:1:snp:497dff69559e8b98c86c4654c6665a504c27bc70;anchor=swh:1:rev:5544d589dd0f8ed23b33c6b612cdc1653e6465fc

Ding S-L, Van Hoesen GW. 2010. Borders, extent, and topography of human perirhinal cortex as revealed using multiple modern neuroanatomical and pathological markers. *Human Brain Mapping* **31**:1359–1379. DOI: https://doi.org/10.1002/hbm.20940, PMID: 20082329

Dumoulin SO, Bittar RG, Kabani NJ, Baker CL Jr, Le Goualher G, Bruce Pike G, Evans AC. 2000. A new anatomical landmark for reliable identification of human area V5/MT: a quantitative analysis of sulcal patterning. *Cerebral Cortex* **10**:454–463. DOI: https://doi.org/10.1093/cercor/10.5.454, PMID: 10847595

Dumoulin SO, Wandell BA. 2008. Population receptive field estimates in human visual cortex. *NeuroImage* **39**:647–660. DOI: https://doi.org/10.1016/j.neuroimage.2007.09.034, PMID: 17977024

Felleman DJ, Van Essen DC. 1991. Distributed hierarchical processing in the primate cerebral cortex. *Cerebral Cortex* **1**:1–47. DOI: https://doi.org/10.1093/cercor/1.1.1-a, PMID: 1822724

Finzi D, Gomez J, Nordt M, Rezai AA, Poltoratski S, Grill-Spector K. 2021. Differential spatial computations in ventral and lateral face-selective regions are scaffolded by structural connections. *Nature Communications* **12**:2278. DOI: https://doi.org/10.1038/s41467-021-22524-2, PMID: 33859195

Fischl B, Dale AM. 2000. Measuring the thickness of the human cerebral cortex from magnetic resonance images. *PNAS* **97**:11050–11055. DOI: https://doi.org/10.1073/pnas.200033797, PMID: 10984517

Fischl B. 2012. FreeSurfer. *NeuroImage* **62**:774–781. DOI: https://doi.org/10.1016/j.neuroimage.2012.01.021, PMID: 22248573

Genon S, Eickhoff SB, Kharabian S. 2022. Linking interindividual variability in brain structure to behaviour. *Nature Reviews. Neuroscience* **23**:307–318. DOI: https://doi.org/10.1038/s41583-022-00584-7, PMID: 35365814

Glasser MF, Van Essen DC. 2011. Mapping human cortical areas in vivo based on myelin content as revealed by T1- and T2-weighted MRI. *The Journal of Neuroscience* **31**:11597–11616. DOI: https://doi.org/10.1523/JNEUROSCI.2180-11.2011, PMID: 21832190

Glasser MF, Sotiropoulos SN, Wilson JA, Coalson TS, Fischl B, Andersson JL, Xu J, Jbabdi S, Webster M, Polimeni JR, Van Essen DC, Jenkinson M, WU-Minn HCP Consortium. 2013. The minimal preprocessing pipelines for the Human Connectome Project. *NeuroImage* **80**:105–124. DOI: https://doi.org/10.1016/j.neuroimage.2013.04.127, PMID: 23668970

Glasser MF, Coalson TS, Robinson EC, Hacker CD, Harwell J, Yacoub E, Ugurbil K, Andersson J, Beckmann CF, Jenkinson M, Smith SM, Van Essen DC. 2016a. A multi-modal parcellation of human cerebral cortex. *Nature* **536**:171–178. DOI: https://doi.org/10.1038/nature18933, PMID: 27437579

Glasser MF, Smith SM, Marcus DS, Andersson JLR, Auerbach EJ, Behrens TEJ, Coalson TS, Harms MP, Jenkinson M, Moeller S, Robinson EC, Sotiropoulos SN, Xu J, Yacoub E, Ugurbil K, Van Essen DC. 2016b. The human connectome project's neuroimaging approach. *Nature Neuroscience* **19**:1175–1187. DOI: https://doi.org/10.1038/nn.4361, PMID: 27571196

Gomez J, Pestilli F, Witthoft N, Golarai G, Liberman A, Poltoratski S, Yoon J, Grill-Spector K. 2015. Functionally defined white matter reveals segregated pathways in human ventral temporal cortex associated with category-specific processing. *Neuron* **85**:216–227. DOI: https://doi.org/10.1016/j.neuron.2014.12.027, PMID: 25569351

Gomez J, Barnett MA, Natu V, Mezer A, Palomero-Gallagher N, Weiner KS, Amunts K, Zilles K, Grill-Spector K. 2017. Microstructural proliferation in human cortex is coupled with the development of face processing. *Science* **355**:68–71. DOI: https://doi.org/10.1126/science.aag0311, PMID: 28059764

Gomez J, Natu V, Jeska B, Barnett M, Grill-Spector K. 2018. Development differentially sculpts receptive fields across early and high-level human visual cortex. *Nature Communications* **9**:788. DOI: https://doi.org/10.1038/s41467-018-03166-3, PMID: 29476135

Gomez J, Drain A, Jeska B, Natu VS, Barnett M, Grill-Spector K. 2019a. Development of population receptive fields in the lateral visual stream improves spatial coding amid stable structural-functional coupling. *NeuroImage* **188**:59–69. DOI: https://doi.org/10.1016/j.neuroimage.2018.11.056, PMID: 30508682

Gomez J, Zhen Z, Weiner KS. 2019b. Human visual cortex is organized along two genetically opposed hierarchical gradients with unique developmental and evolutionary origins. *PLOS Biology* **17**:e3000362. DOI: https://doi.org/10.1371/journal.pbio.3000362

GomezJ. 2023. Entorhinal_prf. swh:1:rev:6d64d29d02d09ef5c536998b4d1e6147380d7390. Software Heritage. https://archive.softwareheritage.org/swh:1:dir:cef1cdeb1be3c95252e5c99cc70676b2941ede25;origin=https://github.com/gomezj/entorhinal_prf;visit=swh:1:snp:cb99517122596941e2edb660ffe07d0c7d167351;anchor=swh:1:rev:6d64d29d02d09ef5c536998b4d1e6147380d7390

Goodale MA, Milner AD. 1992. Separate visual pathways for perception and action. *Trends in Neurosciences* **15**:20–25. DOI: https://doi.org/10.1016/0166-2236(92)90344-8, PMID: 1374953

Grill-Spector K, Weiner KS. 2014. The functional architecture of the ventral temporal cortex and its role in categorization. *Nature Reviews. Neuroscience* **15**:536–548. DOI: https://doi.org/10.1038/nrn3747, PMID: 24962370

Grotheer M, Rosenke M, Wu H, Kular H, Querdasi FR, Natu VS, Yeatman JD, Grill-Spector K. 2022. White matter myelination during early infancy is linked to spatial gradients and myelin content at birth. *Nature Communications* **13**:997. DOI: https://doi.org/10.1038/s41467-022-28326-4, PMID: 35194018

Hadjikhani N, Liu AK, Dale AM, Cavanagh P, Tootell RB. 1998. Retinotopy and color sensitivity in human visual cortical area V8. *Nature Neuroscience* **1**:235–241. DOI: https://doi.org/10.1038/681, PMID: 10195149

Harms MP, Somerville LH, Ances BM, Andersson J, Barch DM, Bastiani M, Bookheimer SY, Brown TB, Buckner RL, Burgess GC, Coalson TS, Chappell MA, Dapretto M, Douaud G, Fischl B, Glasser MF, Greve DN, Hodge C, Jamison KW, Jbabdi S, et al. 2018. Extending the human connectome project across ages: imaging protocols for the lifespan development and aging projects. *NeuroImage* **183**:972–984. DOI: https://doi.org/10.1016/j.neuroimage.2018.09.060, PMID: 30261308

Harvey BM, Dumoulin SO. 2011. The relationship between cortical magnification factor and population receptive field size in human visual cortex: constancies in cortical architecture. *The Journal of Neuroscience* **31**:13604–13612. DOI: https://doi.org/10.1523/JNEUROSCI.2572-11.2011, PMID: 21940451

Hasson U, Yang E, Vallines I, Heeger DJ, Rubin N. 2008. A hierarchy of temporal receptive windows in human cortex. *The Journal of Neuroscience* **28**:2539–2550. DOI: https://doi.org/10.1523/JNEUROSCI.5487-07.2008, PMID: 18322098

Haxby JV, Hoffman EA, Gobbini MI. 2000. The distributed human neural system for face perception. *Trends in Cognitive Sciences* **4**:223–233. DOI: https://doi.org/10.1016/S1364-6613(00)01482-0

Hong SJ, Xu T, Nikolaidis A, Smallwood J, Margulies DS, Bernhardt B, Vogelstein J, Milham MP. 2020. Toward a connectivity gradient-based framework for reproducible biomarker discovery. *NeuroImage* **223**:117322. DOI: https://doi.org/10.1016/j.neuroimage.2020.117322, PMID: 32882388

Huttenlocher PR, Dabholkar AS. 1997. Regional differences in synaptogenesis in human cerebral cortex. *The Journal of Comparative Neurology* **387**:167–178. DOI: https://doi.org/10.1002/(sici)1096-9861(19971020)387:2<167::aid-cne1>3.0.co;2-z, PMID: 9336221

Kay KN, Winawer J, Mezer A, Wandell BA. 2013. Compressive spatial summation in human visual cortex. *Journal of Neurophysiology* **110**:481–494. DOI: https://doi.org/10.1152/jn.00105.2013, PMID: 23615546

Kolster H, Peeters R, Orban GA. 2010. The retinotopic organization of the human middle temporal area MT/V5 and its cortical neighbors. *Journal of Neuroscience* **30**:9801–9820. DOI: https://doi.org/10.1523/JNEUROSCI.2069-10.2010

Konen CS, Kastner S. 2008. Representation of eye movements and stimulus motion in topographically organized areas of human posterior parietal cortex. *The Journal of Neuroscience* **28**:8361–8375. DOI: https://doi.org/10.1523/JNEUROSCI.1930-08.2008, PMID: 18701699

Konkle T, Caramazza A. 2013. Tripartite organization of the ventral stream by animacy and object size. *The Journal of Neuroscience* **33**:10235–10242. DOI: https://doi.org/10.1523/JNEUROSCI.0983-13.2013, PMID: 23785139

Larsson J, Heeger DJ. 2006. Two retinotopic visual areas in human lateral occipital cortex. *The Journal of Neuroscience* **26**:13128–13142. DOI: https://doi.org/10.1523/JNEUROSCI.1657-06.2006, PMID: 17182764

Legarreta Gorroño JH. 2026. Vistasoft. 73378f4. GitHub. https://github.com/vistalab/vistasoft

Lerch JP, van der Kouwe AJW, Raznahan A, Paus T, Johansen-Berg H, Miller KL, Smith SM, Fischl B, Sotiropoulos SN. 2017. Studying neuroanatomy using MRI. *Nature Neuroscience* **20**:314–326. DOI: https://doi.org/10.1038/nn.4501, PMID: 28230838

Lever J, Krzywinski M, Altman N. 2017. Principal component analysis. *Nature Methods* **14**:641–642. DOI: https://doi.org/10.1038/nmeth.4346

López-Bendito G, Molnár Z. 2003. Thalamocortical development: how are we going to get there? *Nature Reviews. Neuroscience* **4**:276–289. DOI: https://doi.org/10.1038/nrn1075, PMID: 12671644

Mackey WE, Winawer J, Curtis CE. 2017. Visual field map clusters in human frontoparietal cortex. *eLife* **6**:e22974. DOI: https://doi.org/10.7554/eLife.22974, PMID: 28628004

Maingault S, Pepe A, Mazoyer B, Tzourio-Mazoyer N, Crivello F. 2021. Characterization of late structural maturation with a neuroanatomical marker that considers both cortical thickness and intracortical myelination. *bioRxiv*. DOI: https://doi.org/10.1101/2021.02.24.432645

Miller JA, Voorhies WI, Lurie DJ, D'Esposito M, Weiner KS. 2021. Overlooked Tertiary Sulci serve as a meso-scale link between microstructural and functional properties of human lateral prefrontal cortex. *The Journal of Neuroscience* **41**:2229–2244. DOI: https://doi.org/10.1523/JNEUROSCI.2362-20.2021, PMID: 33478989

Moreno-Ortega M, Prudic J, Rowny S, Patel GH, Kangarlu A, Lee S, Grinband J, Palomo T, Perera T, Glasser MF, Javitt DC. 2019. Resting state functional connectivity predictors of treatment response to electroconvulsive therapy in depression. *Scientific Reports* **9**:5071. DOI: https://doi.org/10.1038/s41598-019-41175-4, PMID: 30911075

Natu VS, Gomez J, Barnett M, Jeska B, Kirilina E, Jaeger C, Zhen Z, Cox S, Weiner KS, Weiskopf N, Grill-Spector K. 2019. Apparent thinning of human visual cortex during childhood is associated with myelination. *PNAS* **116**:20750–20759. DOI: https://doi.org/10.1073/pnas.1904931116, PMID: 31548375

Nunn JA, Gregory LJ, Brammer M, Williams SCR, Parslow DM, Morgan MJ, Morris RG, Bullmore ET, Baron-Cohen S, Gray JA. 2002. Functional magnetic resonance imaging of synesthesia: activation of V4/V8 by spoken words. *Nature Neuroscience* **5**:371–375. DOI: https://doi.org/10.1038/nn818, PMID: 11914723

Oishi H, Takemura H, Aoki SC, Fujita I, Amano K. 2018. Microstructural properties of the vertical occipital fasciculus explain the variability in human stereoacuity. *PNAS* **115**:12289–12294. DOI: https://doi.org/10.1073/pnas.1804741115, PMID: 30429321

O'Leary DDM. 1989. Do cortical areas emerge from a protocortex? *Trends in Neurosciences* **12**:400–406. DOI: https://doi.org/10.1016/0166-2236(89)90080-5

Orban GA, Van Essen D, Vanduffel W. 2004. Comparative mapping of higher visual areas in monkeys and humans. *Trends in Cognitive Sciences* **8**:315–324. DOI: https://doi.org/10.1016/j.tics.2004.05.009, PMID: 15242691

Pitcher D, Ungerleider LG. 2021. Evidence for a third visual pathway specialized for social perception. *Trends in Cognitive Sciences* **25**:100–110. DOI: https://doi.org/10.1016/j.tics.2020.11.006, PMID: 33334693

Preziosa P, Bouman PM, Kiljan S, Steenwijk MD, Meani A, Pouwels PJ, Rocca MA, Filippi M, Geurts JJG, Jonkman LE. 2021. Neurite density explains cortical T1-weighted/T2-weighted ratio in multiple sclerosis. *Journal of Neurology, Neurosurgery, and Psychiatry* **92**:790–792. DOI: https://doi.org/10.1136/jnnp-2020-324391, PMID: 33436500

Reisberg B, Franssen EH, Hasan SM, Monteiro I, Boksay I, Souren LE, Kenowsky S, Auer SR, Elahi S, Kluger A. 1999. Retrogenesis: clinical, physiologic, and pathologic mechanisms in brain aging, Alzheimer's and other dementing processes. *European Archives of Psychiatry and Clinical Neuroscience* **249 Suppl 3**:28–36. DOI: https://doi.org/10.1007/pl00014170, PMID: 10654097

Robinson EC, Garcia K, Glasser MF, Chen Z, Coalson TS, Makropoulos A, Bozek J, Wright R, Schuh A, Webster M, Hutter J, Price A, Cordero Grande L, Hughes E, Tusor N, Bayly PV, Van Essen DC, Smith SM, Edwards AD, Hajnal J, et al. 2018. Multimodal surface matching with higher-order smoothness constraints. *NeuroImage* **167**:453–465. DOI: https://doi.org/10.1016/j.neuroimage.2017.10.037, PMID: 29100940

Sarwar T, Tian Y, Yeo BTT, Ramamohanarao K, Zalesky A. 2021. Structure-function coupling in the human connectome: a machine learning approach. *NeuroImage* **226**:117609. DOI: https://doi.org/10.1016/j.neuroimage.2020.117609, PMID: 33271268

Sebenius I, Seidlitz J, Warrier V, Bethlehem RAI, Alexander-Bloch A, Mallard TT, Garcia RR, Bullmore ET, Morgan SE. 2023. Robust estimation of cortical similarity networks from brain MRI. *Nature Neuroscience* **26**:1461–1471. DOI: https://doi.org/10.1038/s41593-023-01376-7, PMID: 37460809

Seldon HL. 2005. Does brain white matter growth expand the cortex like a balloon? Hypothesis and consequences. *Laterality* **10**:81–95. DOI: https://doi.org/10.1080/13576500342000310, PMID: 15841825

Sellal F. 2022. Anatomical and neurophysiological basis of face recognition. *Revue Neurologique* **178**:649–653. DOI: https://doi.org/10.1016/j.neurol.2021.11.002, PMID: 34863530

Sereno MI, Lutti A, Weiskopf N, Dick F. 2013. Mapping the human cortical surface by combining quantitative T_1 with retinotopy. *Cerebral Cortex* **23**:2261–2268. DOI: https://doi.org/10.1093/cercor/bhs213, PMID: 22826609

Shafee R, Buckner RL, Fischl B. 2015. Gray matter myelination of 1555 human brains using partial volume corrected MRI images. *NeuroImage* **105**:473–485. DOI: https://doi.org/10.1016/j.neuroimage.2014.10.054, PMID: 25449739

Sheremata SL, Silver MA. 2015. Hemisphere-dependent attentional modulation of human parietal visual field representations. *The Journal of Neuroscience* **35**:508–517. DOI: https://doi.org/10.1523/JNEUROSCI.2378-14.2015

Shmuel A, Leopold DA. 2008. Neuronal correlates of spontaneous fluctuations in fMRI signals in monkey visual cortex: Implications for functional connectivity at rest. *Human Brain Mapping* **29**:751–761. DOI: https://doi.org/10.1002/hbm.20580, PMID: 18465799

Somerville LH, Bookheimer SY, Buckner RL, Burgess GC, Curtiss SW, Dapretto M, Elam JS, Gaffrey MS, Harms MP, Hodge C, Kandala S, Kastman EK, Nichols TE, Schlaggar BL, Smith SM, Thomas KM, Yacoub E, Van Essen DC, Barch DM. 2018. The lifespan human connectome project in development: a large-scale study of brain connectivity development in 5–21 year olds. *NeuroImage* **183**:456–468. DOI: https://doi.org/10.1016/j.neuroimage.2018.08.050

Song S, Garrido L, Nagy Z, Mohammadi S, Steel A, Driver J, Dolan RJ, Duchaine B, Furl N. 2015. Local but not long-range microstructural differences of the ventral temporal cortex in developmental prosopagnosia. *Neuropsychologia* **78**:195–206. DOI: https://doi.org/10.1016/j.neuropsychologia.2015.10.010, PMID: 26456436

Sowell ER, Thompson PM, Leonard CM, Welcome SE, Kan E, Toga AW. 2004. Longitudinal mapping of cortical thickness and brain growth in normal children. *The Journal of Neuroscience* **24**:8223–8231. DOI: https://doi.org/10.1523/JNEUROSCI.1798-04.2004, PMID: 15385605

Stigliani A, Weiner KS, Grill-Spector K. 2015. Temporal processing capacity in high-level visual cortex is domain specific. *The Journal of Neuroscience* **35**:12412–12424. DOI: https://doi.org/10.1523/JNEUROSCI.4822-14.2015, PMID: 26354910

Stigliani A, Jeska B, Grill-Spector K. 2017. Encoding model of temporal processing in human visual cortex. *PNAS* **114**:E11047–E11056. DOI: https://doi.org/10.1073/pnas.1704877114, PMID: 29208714

Sydnor VJ, Larsen B, Seidlitz J, Adebimpe A, Alexander-Bloch AF, Bassett DS, Bertolero MA, Cieslak M, Covitz S, Fan Y, Gur RE, Gur RC, Mackey AP, Moore TM, Roalf DR, Shinohara RT, Satterthwaite TD. 2023. Intrinsic activity development unfolds along a sensorimotor-association cortical axis in youth. *Nature Neuroscience* **26**:638–649. DOI: https://doi.org/10.1038/s41593-023-01282-y, PMID: 36973514

Takemura H, Rokem A, Winawer J, Yeatman JD, Wandell BA, Pestilli F. 2016. A major human white matter pathway between dorsal and ventral visual cortex. *Cerebral Cortex* **26**:2205–2214. DOI: https://doi.org/10.1093/cercor/bhv064

Tavor I, Yablonski M, Mezer A, Rom S, Assaf Y, Yovel G. 2014. Separate parts of occipito-temporal white matter fibers are associated with recognition of faces and places. *NeuroImage* **86**:123–130. DOI: https://doi.org/10.1016/j.neuroimage.2013.07.085, PMID: 23933304

Thomas C, Avidan G, Humphreys K, Jung K, Gao F, Behrmann M. 2009. Reduced structural connectivity in ventral visual cortex in congenital prosopagnosia. *Nature Neuroscience* **12**:29–31. DOI: https://doi.org/10.1038/nn.2224, PMID: 19029889

Tootell RBH, Mendola JD, Hadjikhani NK, Ledden PJ, Liu A, Reppas JB, Sereno MI, Dale AM. 1997. Functional analysis of V3A and related areas in human visual cortex. *The Journal of Neuroscience* **17**:7060–7078. DOI: https://doi.org/10.1523/JNEUROSCI.17-18-07060.1997

Tootell RBH, Tsao D, Vanduffel W. 2003. Neuroimaging weighs in: humans meet macaques in "primate" visual cortex. *The Journal of Neuroscience* **23**:3981–3989. DOI: https://doi.org/10.1523/JNEUROSCI.23-10-03981.2003, PMID: 12764082

Ungerleider LG, Haxby JV. 1994. 'What' and 'where' in the human brain. *Current Opinion in Neurobiology* **4**:157–165. DOI: https://doi.org/10.1016/0959-4388(94)90066-3

Van Essen DC, Ugurbil K, Auerbach E, Barch D, Behrens TEJ, Bucholz R, Chang A, Chen L, Corbetta M, Curtiss SW, Della Penna S, Feinberg D, Glasser MF, Harel N, Heath AC, Larson-Prior L, Marcus D, Michalareas G, Moeller S, Oostenveld R, et al. 2012. The human connectome project: a data acquisition perspective. *NeuroImage* **62**:2222–2231. DOI: https://doi.org/10.1016/j.neuroimage.2012.02.018

Van Essen DC, Smith SM, Barch DM, Behrens TEJ, Yacoub E, Ugurbil K. 2013. The WU-Minn human connectome project: an overview. *NeuroImage* **80**:62–79. DOI: https://doi.org/10.1016/j.neuroimage.2013.05.041

Vogt C, Vogt O. 1919. *Allgemeine Ergebnisse Unserer Hirnforschung*. JA Barth.

Waehnert MD, Dinse J, Weiss M, Streicher MN, Waehnert P, Geyer S, Turner R, Bazin PL. 2014. Anatomically motivated modeling of cortical laminae. *NeuroImage* **93 Pt 2**:210–220. DOI: https://doi.org/10.1016/j.neuroimage.2013.03.078, PMID: 23603284

Wagstyl K, Lepage C, Bludau S, Zilles K, Fletcher PC, Amunts K, Evans AC. 2018. Mapping cortical laminar structure in the 3D BigBrain. *Cerebral Cortex* **28**:2551–2562. DOI: https://doi.org/10.1093/cercor/bhy074, PMID: 29901791

Wagstyl K, Larocque S, Cucurull G, Lepage C, Cohen JP, Bludau S, Palomero-Gallagher N, Lewis LB, Funck T, Spitzer H, Dickscheid T, Fletcher PC, Romero A, Zilles K, Amunts K, Bengio Y, Evans AC. 2020. BigBrain 3D atlas of cortical layers: cortical and laminar thickness gradients diverge in sensory and motor cortices. *PLOS Biology* **18**:e3000678. DOI: https://doi.org/10.1371/journal.pbio.3000678, PMID: 32243449

Wandell BA, Dumoulin SO, Brewer AA. 2007. Visual field maps in human cortex. *Neuron* **56**:366–383. DOI: https://doi.org/10.1016/j.neuron.2007.10.012, PMID: 17964252

Wandell BA, Winawer J. 2011. Imaging retinotopic maps in the human brain. *Vision Research* **51**:718–737. DOI: https://doi.org/10.1016/j.visres.2010.08.004

Wandell BA, Winawer J. 2015. Computational neuroimaging and population receptive fields. *Trends in Cognitive Sciences* **19**:349–357. DOI: https://doi.org/10.1016/j.tics.2015.03.009, PMID: 25850730

Wang H-T, Smallwood J, Mourao-Miranda J, Xia CH, Satterthwaite TD, Bassett DS, Bzdok D. 2020. Finding the needle in a high-dimensional haystack: Canonical correlation analysis for neuroscientists. *NeuroImage* **216**:116745. DOI: https://doi.org/10.1016/j.neuroimage.2020.116745, PMID: 32278095

Wang F, Zhang H, Wu Z, Hu D, Zhou Z, Girault JB, Wang L, Lin W, Li G. 2023. Fine-grained functional parcellation maps of the infant cerebral cortex. *eLife* **12**:e75401. DOI: https://doi.org/10.7554/eLife.75401, PMID: 37526293

Weiner KS, Grill-Spector K. 2010. Sparsely-distributed organization of face and limb activations in human ventral temporal cortex. *NeuroImage* **52**:1559–1573. DOI: https://doi.org/10.1016/j.neuroimage.2010.04.262, PMID: 20457261

Weiner KS, Golarai G, Caspers J, Chuapoco MR, Mohlberg H, Zilles K, Amunts K, Grill-Spector K. 2014. The mid-fusiform sulcus: a landmark identifying both cytoarchitectonic and functional divisions of human ventral temporal cortex. *NeuroImage* **84**:453–465. DOI: https://doi.org/10.1016/j.neuroimage.2013.08.068

Weiner KS, Gomez J. 2021. Third visual pathway, anatomy, and cognition across species. *Trends in Cognitive Sciences* **25**:548–549. DOI: https://doi.org/10.1016/j.tics.2021.04.002, PMID: 34024730

Winawer J, Witthoft N. 2015. Human V4 and ventral occipital retinotopic maps. *Visual Neuroscience* **32**:E020. DOI: https://doi.org/10.1017/S0952523815000176, PMID: 26241699

Witthoft N, Nguyen ML, Golarai G, LaRocque KF, Liberman A, Smith ME, Grill-Spector K. 2014. Where is human V4? Predicting the location of hV4 and VO1 from cortical folding. *Cerebral Cortex* **24**:2401–2408. DOI: https://doi.org/10.1093/cercor/bht092

Xie L, Pluta JB, Das SR, Wisse LEM, Wang H, Mancuso L, Kliot D, Avants BB, Ding S-L, Manjón JV, Wolk DA, Yushkevich PA. 2017. Multi-template analysis of human perirhinal cortex in brain MRI: explicitly accounting for anatomical variability. *NeuroImage* **144**:183–202. DOI: https://doi.org/10.1016/j.neuroimage.2016.09.070, PMID: 27702610

Yeatman JD, Wandell BA, Mezer AA. 2014. Lifespan maturation and degeneration of human brain white matter. *Nature Communications* **5**:4932. DOI: https://doi.org/10.1038/ncomms5932, PMID: 25230200

Zou Q-H, Zhu C-Z, Yang Y, Zuo X-N, Long X-Y, Cao Q-J, Wang Y-F, Zang Y-F. 2008. An improved approach to detection of amplitude of low-frequency fluctuation (ALFF) for resting-state fMRI: fractional ALFF. *Journal of Neuroscience Methods* **172**:137–141. DOI: https://doi.org/10.1016/j.jneumeth.2008.04.012