



# Does the stria of Gennari integrity reflect acquired visual field defects?

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## Abstract

Visual input reaches the primary visual cortex (V1) at the stria of Gennari, a band of highly myelinated fibers at the level of layer IV. Damage to the visual pathways can cause visual field defects (scotomas) that prevent visual input from reaching V1. Here, we evaluate whether the stria of Gennari degrades in the absence of visual input. Using 7 Tesla MRI, we investigate the integrity of the stria of Gennari in case of acquired homonymous visual field defects, in particular hemianopia: the loss of vision in half of the visual field. These visual field defects allow us to compare stria of Gennari integrity between the two hemispheres within the same participant, i.e., the hemisphere that is deprived of visual input (affected hemisphere) versus the hemisphere receiving visual information (unaffected hemisphere). Therefore, we focus on cases of acquired blindness following damage between the optic chiasm and V1. We quantify the stria of Gennari integrity both by measuring the T1-weighted intensity at the middle of cortical depth and using a modeling approach that captures T1-weighted intensity variations across cortical depth. Our results show that the stria of Gennari remains intact in both the affected and unaffected hemisphere, suggesting that the stria of Gennari integrity is not altered in the absence of visual input.

**Keywords** Stria of Gennari · Primary visual cortex · 7 T MRI · Myelin · Visual perception · Acquired blindness

## Introduction

The stria of Gennari is a band of highly myelinated fibers in the primary visual cortex (V1), running parallel to the cortical surface at the level of layer IV (Gennari 1782). Due to the presence of this prominent laminar structure, V1 is also referred to as the striate cortex. The location identified by

the stria of Gennari represents the main input stage reaching V1 from the thalamus (Henschen 1893; Sincich & Horton 2005).

The stria of Gennari has been visualized ex-vivo using myelin-stained sections of the cortex (Annese et al. 2004; Horton & Hocking 1997) and in-vivo using high-resolution MRI, particularly through T1-weighted (T1-w) imaging

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which is sensitive to myelin contrast (Barbier et al. 2002; Fracasso et al. 2016; Glasser & Van Essen 2011). While the stria of Gennari has been extensively studied in both ex-vivo and in-vivo conditions, its integrity following an acquired lack of visual input remains unclear.

Studies on visual system development have shown that V1 retains a normal laminar pattern in enucleated monkeys (Dehay et al. 1989, 1991; Horton & Hocking 1997). This supports the idea that the cytoarchitectonic organization of areas like V1 is pre-determined during embryogenesis, allowing V1 to develop even without retinal input (Rakic 1988; Rakic et al. 1977). Supporting this idea, Trampel and colleagues (Trampel et al. 2011) used 7 Tesla MRI to compare congenitally blind patients with sighted control participants and found that the stria of Gennari was present in both groups. This indicates that visual input is not required for the development of this structure. However, large between-participant variability may obscure the degradation of the stria of Gennari. Furthermore, the preserved stria of Gennari in congenitally blind individuals may undergo cortical reorganization, potentially being recruited by other sensory modalities beyond vision.

**Table 1** Demographics and medical details patients with homonymous visual field defects (*F* Female, *M* Male, *LHH* Left homonymous hemianopia, *RHH* Right homonymous hemianopia, *RHQ* Right homonymous quadrantanopia)

| Patient | Gender | Age | Event causing the visual field defects                                                                 | Visual field defect | Time since event (years) |
|---------|--------|-----|--------------------------------------------------------------------------------------------------------|---------------------|--------------------------|
| P1      | F      | 18  | Intracerebral stroke, epilepsy surgery (V1 partially intact)                                           | LHH                 | 18*                      |
| P2      | M      | 46  | Macroprolactinoma (V1 intact)                                                                          | LHH                 | 9                        |
| P3      | F      | 46  | Vertebral-basilar ischemia (V1 partially intact)                                                       | RHH                 | 5                        |
| P4      | F      | 61  | Stroke posterior cerebellar artery left (V1 partially intact)                                          | RHQ                 | 6                        |
| P5      | M      | 60  | Stroke posterior inferior cerebellar artery left (V1 partially intact)                                 | RHH                 | 5                        |
| P6      | F      | 77  | Ischemia left occipital cortex (V1 partially intact)                                                   | RHH                 | 6                        |
| P7      | M      | 67  | Resection n. acoustic neurinoma, resection glioblastoma parieto-occipital cortex (V1 partially intact) | LHH                 | 15                       |
| P8      | M      | 75  | Intracerebral haematoma right temporo-parietal cortex (V1 intact)                                      | LHH                 | 7                        |

\*intracerebral stroke was present 5 weeks after birth

Here, we aim to assess the presence as well as the integrity of the stria of Gennari after an acquired lack of visual input, using 7 T MRI. We recruited patients with homonymous visual field defects, i.e. hemianopia or quadrantanopia, following damage between the optic chiasm and V1. Importantly, to compare the stria of Gennari integrity, in all cases V1 was either intact or partially intact (2 and 6 patients, respectively), see Table 1, Fig. 3. In order to account for between-participant variations, we compare the integrity of the stria of Gennari at a within-participant level, by comparing the hemispheres affected by the visual scotoma with the unaffected hemispheres that receive normal visual input. In order to account for within-participant variations, we applied both a model-free approach and a novel forward modeling approach. As a model-free approach we measured T1-w intensity at the middle of cortical depth. Additionally, the forward modeling approach captures T1-w intensity variations across cortical depth, and specifically the stria of Gennari integrity. In particular the latter measure may be more independent from both between-participant and within-participant variability as this explicitly models the local laminar profile.

## Methods

### Participants and ethics approval

This study was approved by the ethics committee of the University Medical Center Utrecht (approval number: 09/350), and informed consent was obtained from every participant. All experimental procedures were conducted in accordance with the Declaration of Helsinki (most recently amended in 2008, Seoul).

A total of eleven patients with homonymous visual field defects (hemianopia or quadrantanopia) participated in the study (age range 18–77, Table 1). We studied patients with homonymous visual field defects, as this condition enables a direct comparison of the stria of Gennari integrity in V1 between the affected hemisphere, where visual input is disrupted, and the unaffected hemisphere, which receives normal visual input. Patients with lesions located anterior to the optic chiasm were excluded, as in such cases the segregation of visual input between hemispheres is not preserved. Importantly, to compare the stria of Gennari integrity, in all patients V1 was either intact (P2, P8) or partially intact (P1, P2 to P7).

The selection criteria consisted of a diagnosis of homonymous hemianopia or quadrantanopia with an intact (or partially intact) occipital lobe. Three patients were excluded because of severe damage to the occipital lobe that effectively damaged the calcarine sulcus in its entirety. The event

causing the visual field defect must have happened at least three years prior to scanning. Visual field defects were diagnosed with visual field examination by an experienced ophthalmologist. Demographic and medical details of the eight patients included in the analysis can be found in Table 1. The patients were recruited through contact information stored in databases at several clinics (see author affiliations). Participants received financial reimbursement for participation and travel, gave informed written consent on paper before the experiment, and were debriefed afterwards about the purpose of the study. Eight males (age range 27–43) participated in this study as control participants without known (history of) cerebral disease.

### Image acquisition

Data was acquired using a 7 Tesla MR system (Philips Healthcare, Best, NL; gradient strength 40 mTm, slew rate: 200 T/m/s) with a volume transmit and 32-channel receive head coil (Nova Medical, Wilmington, MA, USA). Whole-brain images were obtained using a 3D T1-weighted (T1-w) magnetization prepared rapid acquisition gradient recalled echo (MPRAGE) sequence to enhance myelin visualization within the cortex, originally developed by Bock and colleagues (Bock et al. 2009). This sequence was further validated with human histological samples and high field (7 Tesla Phillips scanner, see Fracasso et al. 2016). Strong contrast between gray matter (GM) and white matter (WM) was obtained using a time delay (TD) of 6000 ms (approximately 3 times the T1 of GM, allowing full recovery of both GM and WM prior to inversion) and an inversion time (TI) of 1200 ms (yielding GM signal just above zero). At this TI and TD, cerebrospinal fluid (CSF) appears bright in the reconstructed magnitude images. Other parameters were the following: TR/TE: 8/3 ms, flip angle: 8 degrees, adiabatic inversion, voxel size =  $0.5 \times 0.5 \times 0.5 \text{ mm}^3$ , FOV:  $250 \times 250 \times 180 \text{ mm}^3$ , 360 sagittal slices, bandwidth 201 Hz/px, number of excitations per inversion: 300, linear readout, acceleration using SENSE: 2.5 (anterior–posterior)  $\times$  2.5 (right–left). We used an optimized linear sampling scheme over ky and kz provided by the vendor software (commercially termed: *Free factor*), effectively allowing a high number of excitations per inversion in combination with an elliptical k-space shutter. Scan duration was 7.5 min (3–4 repetitions were acquired per MRI session, depending on participant comfort within the bore). A proton density (PD) scan was obtained using the following scan parameters: 3D turbo-field echo, TR/TE: 6/3 ms, FOV:  $250 \times 250 \times 180 \text{ mm}^3$ , voxel size:  $1.0 \times 1.0 \times 1.0 \text{ mm}^3$ , flip angle 1 degree, 180 sagittal slices, BW: 253 Hz/px, SENSE: 1.8 (anterior–posterior)  $\times$  1.8 (right–left), scan duration was 48 s.

### Preprocessing

Whole-brain T1-w images were corrected for head movement between scan acquisitions using the 3dAllineate function in AFNI (<http://afni.nimh.nih.gov>), using 6 degrees of freedom and imposing wsinc5 as the last interpolation step. After motion correction, images were averaged together to increase signal-to-noise ratio (SNR). PD images were resampled to the corresponding T1-w space. T1-w images were divided by the PD images of the corresponding FOV to correct for signal intensity inhomogeneities (Van de Moortele et al. 2009).

### Segmentation

CSF appears bright in the reconstructed magnitude images, as mentioned in the *Image Acquisition* section. Due to this reason, standard whole-brain segmentation packages did not give acceptable estimates of WM and GM. Hence, we developed an algorithm to segment WM and GM tissues from the preprocessed T1-w images. Segmentation was performed on the original acquisition resolution (0.5 mm isotropic). As a first step, the preprocessed T1-w images were co-registered to an atlas (Desikan et al. 2006) and a mask was overlaid to remove the cerebellum and subcortical structures. The preprocessed T1-w images were separated in 6 different sections from posterior to anterior to improve intensity homogeneity and each section was separately used as input for the 3dSeg function in AFNI, to isolate WM. The WM masks obtained from each part were combined together resulting in a whole brain WM mask. The GM segmentation started from the obtained whole brain WM segmentation and an atlas co-registered to the T1-w images to obtain 35 regions of interest (ROIs) per hemisphere (not restricted to the visual cortex, Desikan et al. 2006). Next, a distance map from the WM/GM boundary to the pial surface was built computing the Euclidean distance of each voxel from the WM/GM border. Negative distances were assigned inside WM and positive distances were assigned from WM borders onwards. For each ROI, coordinates were divided into four separate subparts using k-means clustering. This step was needed to work on small portions of the ROI (subparts) with a highly homogeneous T1-w signal. For each subpart, voxels within  $-2 \text{ mm}$  and  $7 \text{ mm}$  from the WM/GM border were selected and their T1-w intensity was stored for further analysis. For each subpart we obtained 10 bins between  $-2 \text{ mm}$  and  $7 \text{ mm}$  from the WM/GM border. For each bin we computed the inter-quartile estimate of T1-w intensity. We calculated the 75% quantile of inter-quartile estimates and computed the associated Euclidian distance from the WM/GM border. This Euclidean distance was taken as the cortical depth associated with the ROI subpart.

To further improve the obtained GM segmentation, the WM and GM masks were fed to the Cortical Reconstruction using Implicit Surface Evolution (CRUISE) algorithm in the Medical Image Processing, Analysis and Visualization (MIPAV) software package in CBS-tools (<https://www.nitrc.org/projects/cbs-tools>). Following this procedure, the quality of the resulting WM and GM segmentation was assessed visually for each participant (Figs. 1, S2, S3).

### Cortical depth analysis

The automatic segmentation of the T1-w images was analyzed with CBS-tools in MIPAV. A volume-preserving distance map was computed between the WM/GM boundary and the GM/CSF boundary (Wachnert et al. 2014) in 20

separate level-set volumes (21 layers). This equi-volume model provides a coordinate system of cortical depth which is independent from local cortical folding (Wachnert et al. 2014), see Fig. 1H,I. Cortical thickness was estimated using CBS-tools. For each voxel within GM, a cortical depth profile of T1-w intensity was generated following the equi-volume metric and stored for subsequent analysis.

### V1 (calcarine sulcus) definition

For patients and controls, we located V1 based on the calcarine sulcus. The calcarine sulcus is an anatomical landmark to define V1, as V1 is located within and around the calcarine sulcus (Stensaas et al. 1974). The calcarine sulcus was manually defined using ItkGray (<https://web.stanford.edu/>

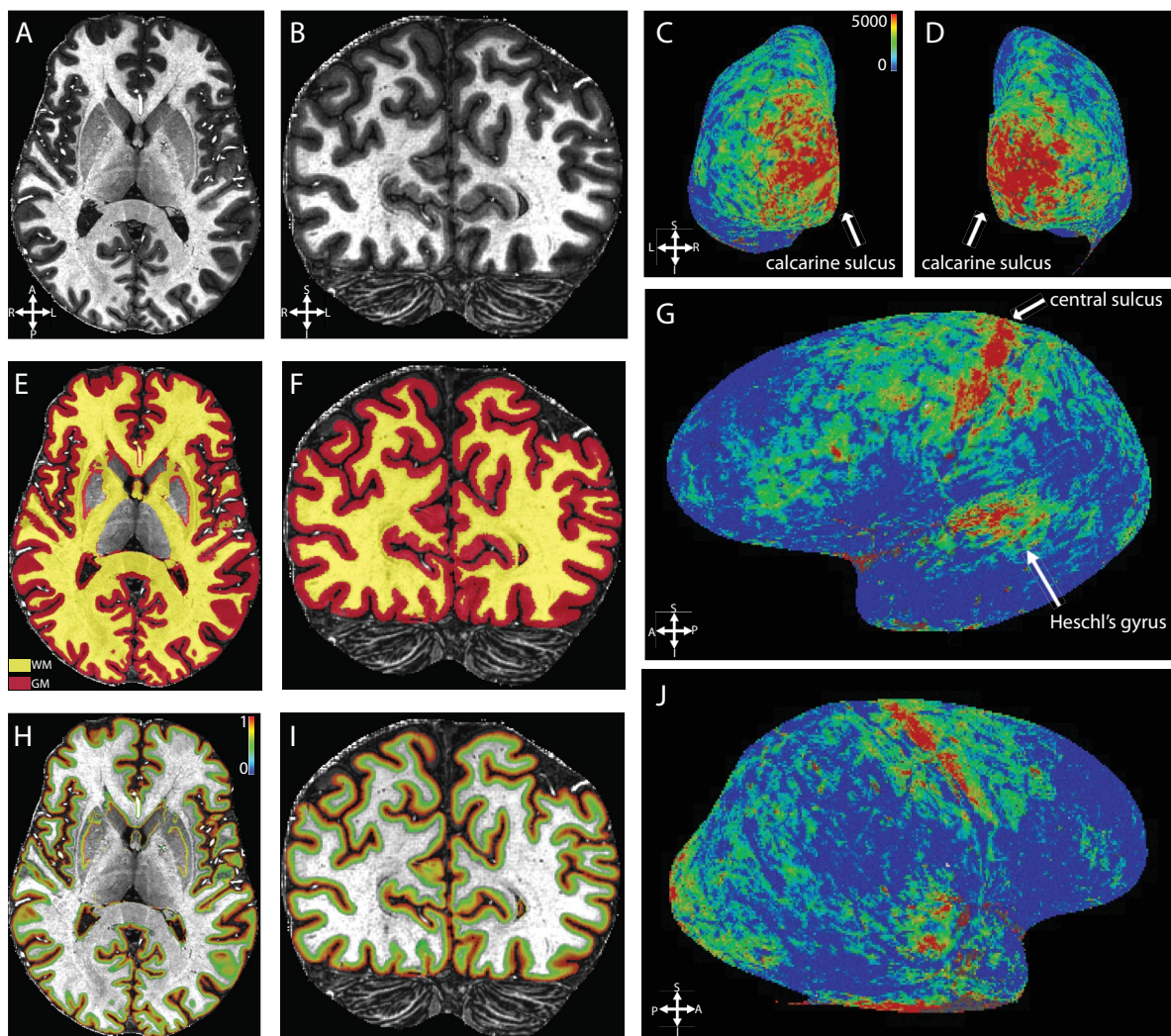


**Fig. 1** A: T1-w anatomy of a control participant, axial view. B: T1-w anatomy of a control participant, coronal view. C: T1-w intensity (middle of cortical depth) plotted on the cortical surface, left hemisphere. D: T1-w intensity (middle of cortical depth) plotted on the cortical surface, right hemisphere. E: T1-w anatomy, segmentation overlaid, axial view. F: T1-w anatomy, segmentation overlaid, coronal view.

G: T1-w intensity (middle of cortical depth) plotted on the cortical surface, left hemisphere. H: T1-w anatomy, depth map overlaid, axial view. I: T1-w anatomy, depth map overlaid, coronal view. J: T1-w intensity (middle of cortical depth) plotted on the cortical surface, right hemisphere

group/vista/cgi-bin/wiki/index.php/ItkGray). We overlaid the segmentation on the T1-w image and manually drew the calcarine sulcus upon the GM for both hemispheres. We moved along the sagittal slices to the most lateral point of the calcarine sulcus and then moved back from the lateral part to the most medial part of the calcarine sulcus.

### Modeling profiles along cortical depth

For each ROI (calcarine sulcus), T1-w signal across cortical depth was modeled using a forward modeling approach. We reasoned that a second order polynomial would capture linear and non-linear low spatial frequency trends across cortical depth, as for example the global decrease in T1-w signal between WM border and GM border. A Gaussian component on the other hand would capture relatively higher spatial frequency trends across cortical depth, an increase in T1-w intensity associated with higher myelin content as for example the stria of Gennari localized within GM.

Each T1-w profile within the left and right calcarine sulcus was modeled with a linear combination of the two components. The second order polynomial across normalized cortical depth (0: WM/GM border and 1: GM/CSF border):

$$I(d) = d^2\beta_2 + d\beta_1 + \beta_0 \quad (1)$$

where  $I$  is the T1-w intensity measured on the single profile across cortical depth,  $d$  is cortical depth and  $\beta$  are the coefficients associated with the quadratic, linear and constant term, respectively (Sprooten et al. 2019). These parameters represent the low spatial frequency component of the T1-w signal across cortical depth, the GM integrity (slope of T1-w signal along cortical depth), and the T1-w signal at the WM/GM boundary (the intercept). The second component was a Gaussian varying in location and width across normalized cortical depth:

$$I(d) = \beta_3 e^{\left(\frac{d-\mu}{2\sigma}\right)^2} \quad (2)$$

where  $I$  is the T1-w intensity measured on the single profile across cortical depth,  $d$  is cortical depth and  $\beta$  is the coefficient associated with the Gaussian component capturing the integrity of the stria of Gennari,  $\mu$  and  $\sigma$  are the Gaussian center and width, respectively.

The Gaussian width was allowed to vary between 0.05 and 1.25 in 14 steps. The Gaussian location parameter was allowed to vary between  $-0.25$  and  $1.25$  in 16 steps. The fit was performed with an iterative procedure for each T1-w profile. On each iteration the Gaussian predictor was built based on the selected width and location parameters. The predictors were set as independent variables of a general linear model and the T1-w profile was the dependent variable

of the model. The model estimated the beta coefficients associated with each predictor, minimizing least squares.

For each iteration we computed the t-statistic associated with each predictor and model goodness-of-fit, as was measured with  $r^2$ . The optimal model parameters for each T1-w profile were found by maximizing  $r^2$  (also see Dumoulin & Wandell 2008), see Fig. 2. Moreover, the linear model returned the t-statistic of each independent predictor, representing the departure of the predictor from 0 (scaled by its standard error). This is a useful measure to assess the importance of a single predictor within the linear model framework.

In the model-based analysis developed here, the estimated parameters (e.g. Gaussian width, location) are connected to local features of the T1-w profile across cortical depth. This approach facilitates the following statistical analysis, allowing to assess the distribution of specific features of the T1-w profiles between the different groups and conditions (see Statistical analysis).

### Removing local curvature contribution

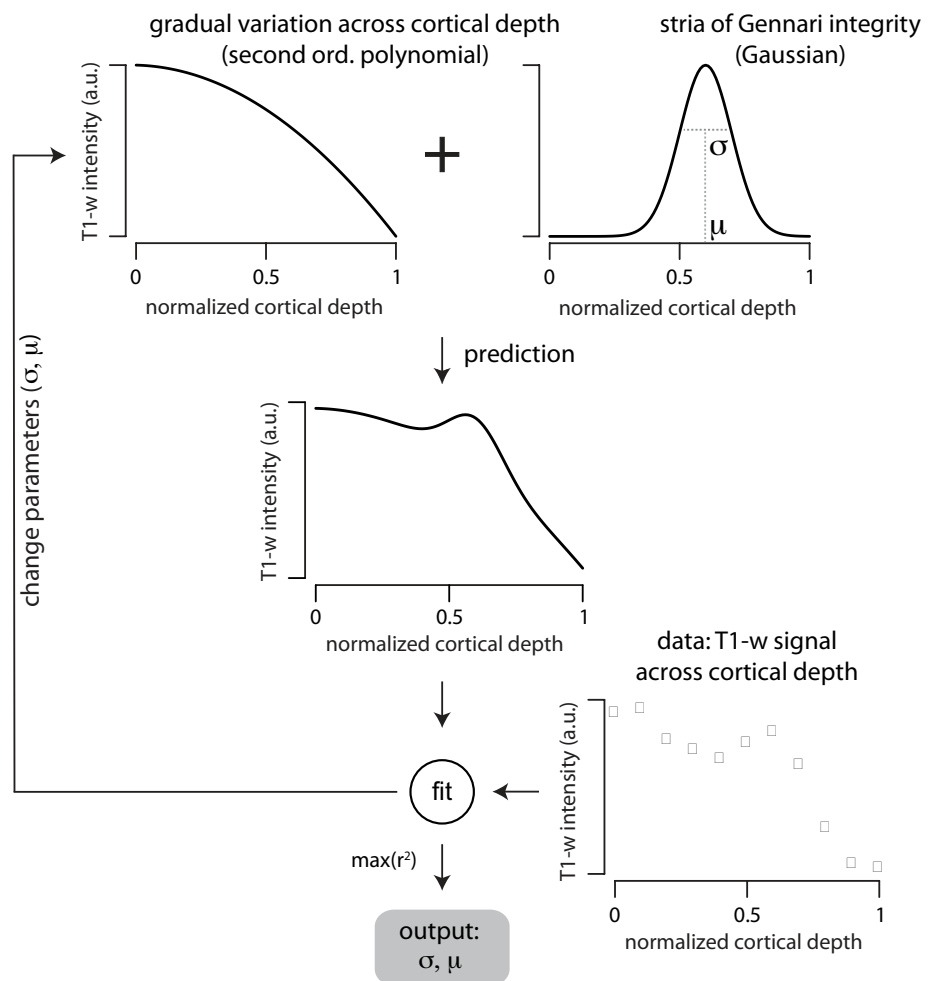
We removed local curvature contributions by regressing out estimates of local curvature from the T1w intensity at the individual voxel level by means of a linear model. We used the residuals of the linear model, adding the estimated intercept to the residual T1-w signal. In this way each cortical depth-dependent profile kept its original offset, while removing the contribution of local curvature (Dalby et al. 2024). This resulted in a separate dataset, corrected for curvature.

### Statistical analysis

We extracted the T1-w intensity profiles for the four middle cortical layers (layer 9–12 of the 21 layers in total). We conducted a Receiver Operating Characteristic (ROC) analysis to test the difference in T1-w intensity between the affected and unaffected hemisphere in each patient (and left versus right hemisphere in each control participant). We used 1000 bootstrapped samples, each containing 5% of the data in the affected and unaffected hemisphere (or left and right hemisphere). We computed the True Positive Rate (TPR) and False Positive Rate (FPR), see Fig. 5. Next, we computed the area under the curve (AUC) for each bootstrapped sample, and the proportion of bootstrapped samples with AUC values below 0.50 of the total number of bootstrapped samples as (two-sided)  $p$  values. We computed the corrected  $p$  values using False Discovery Rate (FDR) to account for multiple comparisons, see Table S1.

Additionally, we extracted the t-statistic associated with the Gaussian of the modeled T1-w intensity profiles from

**Fig. 2** Flow chart describing the fitting procedure adopted to model T1-w signal along cortical depth via a linear combination of a second order polynomial and a Gaussian function. The model is calculated independently for every profile in the calcarine ROI, for details see *Modeling profiles across cortical depth*. Overall, the variance explained of the model was >80%



the calcarine sulcus ROI (t-Gaussian), in the affected and unaffected hemispheres of patients (and left and right hemispheres in control participants). Here, we used the same ROC-analysis as described above to test the ability to distinguish between hemispheres based on the t-Gaussian model parameter representing the stria of Gennari integrity.

## Results

### The stria of Gennari is present in patients and controls

We used a T1-w sequence optimized for myelin visualization (Fracasso et al. 2016; and Figs. 1, 3) and derived T1-w intensity profiles across cortical depth to measure the stria of Gennari in eight patients with homonymous visual field defects (Fig. 3 and Figures S2, S3 for T1-w segmentation).

Next, we compared the stria of Gennari integrity in the affected versus the unaffected hemisphere, and in eight control participants, comparing the left and right hemispheres. We observed the presence of the stria of Gennari in patients

as well as in control participants (Fig. 4, S6). The T1-w intensity profile across cortical depth and the modeled T1-w intensity profile for a specific location are shown in Fig. 4C.

### Similar T1-weighted intensity in stria of Gennari

To quantify the integrity of the stria of Gennari, we extracted the T1-w intensity around the middle of cortical depth (Figs. 5, S4, S6). We compared the T1-w intensity at the middle of cortical depth between the affected and unaffected hemispheres in patients with homonymous visual field defects (and left and right hemispheres in control participants).

There is a large variability in the intensity of the middle layer, i.e., a large between-participant variability. In general, the T1-w intensity at the middle of cortical depth is similar between the affected and unaffected hemispheres in patients (Figs. 5A, S4). In some patients (for example P1, P4, P5), there are overall less T1-w profiles in the affected hemisphere compared to the unaffected hemisphere (Figure S4), due to damage in the calcarine sulcus (Table 1, Fig. 3). Overall, the T1-w intensity of the middle cortical depth is

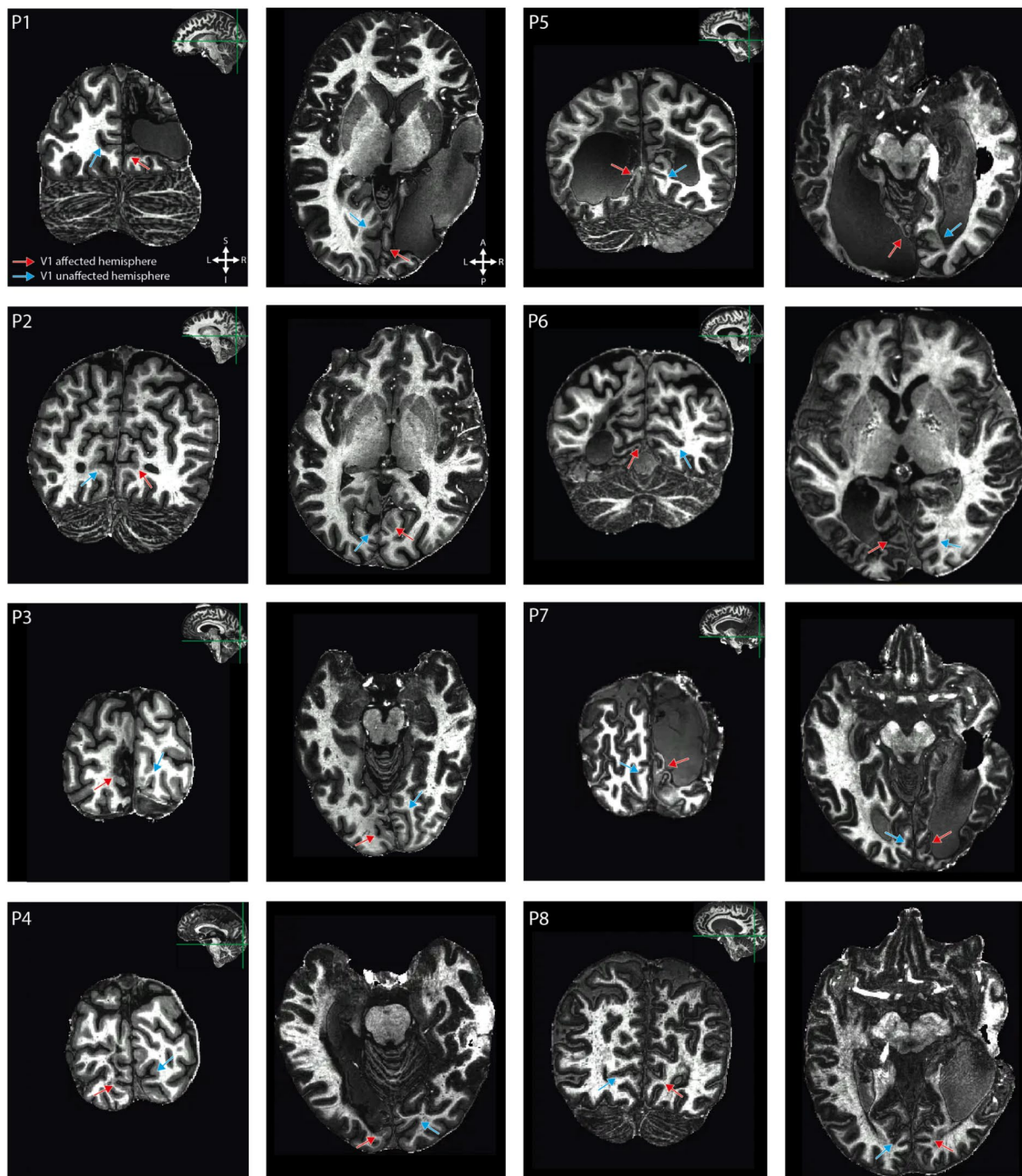


**Fig. 3** T1-w, skull stripped and proton density corrected anatomical images for patients with homonymous visual field defects (P1-P8), coronal view and axial view. Arrows indicate V1 in the affected hemispheres (red) and V1 in the unaffected hemispheres (blue)

similar between the left and right hemispheres in control participants (Fig. 5B).

We conducted an ROC-analysis to test the ability to distinguish between the affected and unaffected hemispheres in patients (and left and right hemispheres in control participants) based on differences in T1-w intensity at the middle of cortical depth, see Fig. 5C. In some patients (P5,

P8) the ROC-curves deviate substantially from chance level (Fig. 5C). The ROC-curve for one patient (P1) extends beyond the range of control participants ( $AUC = 0.79$ ,  $p < 0.001$ , FDR-corrected).

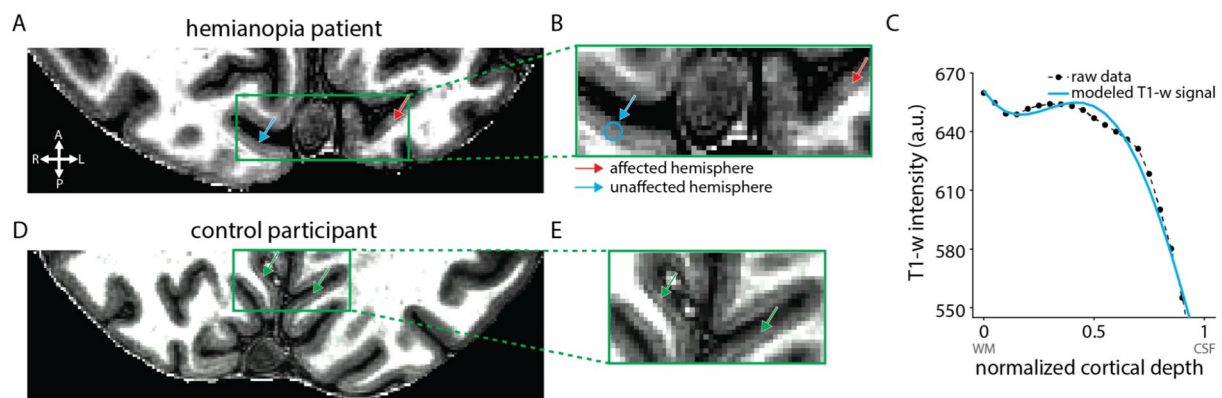


**Fig. 4** Axial sections showing the stria of Gennari. **A, B** Axial sections of T1-w image of a patient (P2). Arrows indicate the presence of the stria of Gennari. **C** Corresponding T1-w profile across cortical depth and the model fit for a specific location in the unaffected hemisphere.

**D, E** Axial sections of T1-w image of a control participant (C5). Arrows indicate the presence of the stria of Gennari. The stria of Gennari is present in both the patient and the control participant

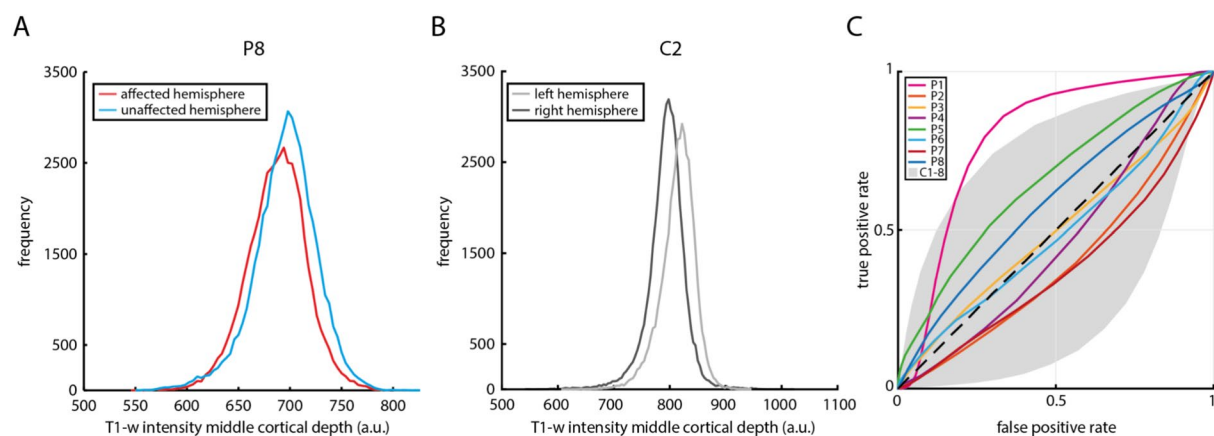


**Fig. 5** T1-w intensity across the middle of the cortical depth between hemispheres. **A** Histogram of the T1-w intensity at the middle of cortical depth, comparing the affected and unaffected hemisphere of a patient (P8). **B** Histogram of the T1-w intensity at the middle of cortical depth comparing the left and right hemisphere of a control participant (C2). The histograms of other patients and control participants are shown in Figure S4. **C** ROC-curve showing the TPR and FPR of the

T1-w intensity at the middle of cortical depth, comparing the affected and unaffected hemispheres in each patient. The grey area represents the range of the control participants, comparing left and right hemispheres on an individual level. The dashed black line represents chance level performance, indicating no difference between hemispheres. See Table S1 for AUC values and  $p$  values, FDR-corrected

### The stria of Gennari integrity is not affected in patients

To further investigate differences in T1-w intensity and specifically the integrity of the stria of Gennari, we modeled T1-w profiles along cortical depth using a second order polynomial and a Gaussian parameter (Fig. 2; Methods, *Modeling profiles along cortical depth*). The Gaussian parameter captures relatively high spatial frequency trends across cortical depth, and has the potential to capture features of the stria of Gennari localized within GM. We extracted the t-statistic associated with the Gaussian parameter of the modeled T1-w profiles (t-Gaussian, from now on referred to as ‘stria of Gennari integrity’) and conducted an ROC-analysis (see Methods, *Statistical analysis*).

In general, the stria of Gennari integrity is similar between the affected and unaffected hemisphere in patients (Fig. 6A, S5). Again, in some patients (for example P1, P4, P5) there are fewer T1-w profiles in the affected hemisphere compared to the unaffected hemisphere (Figure S5) due to damage to the calcarine sulcus (Table 1, Fig. 3). Overall, the stria of Gennari integrity is comparable between left and right hemispheres in control participants (Fig. 6B, S5), suggesting no systematic differences in the stria of Gennari integrity between hemispheres.

We repeated the same ROC-analysis for the model parameter representing the stria of Gennari integrity (see Methods, *Statistical analysis*), to assess the capacity to differentiate between the affected and unaffected hemispheres based on the stria of Gennari integrity in patients (and left and right hemispheres in control participants), see Fig. 6C.

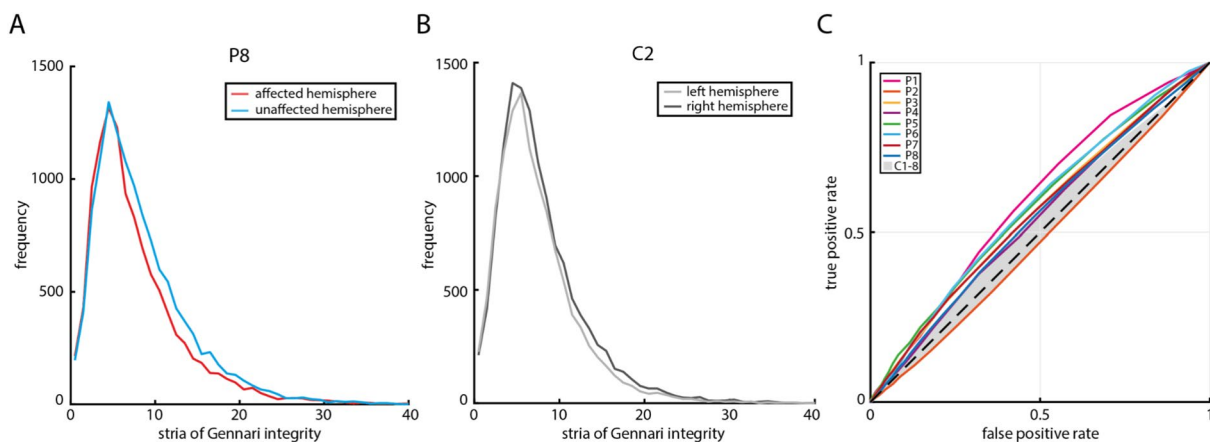


**Fig. 6** Stria of Gennari integrity between hemispheres. **A** Histogram of the stria of Gennari integrity comparing the affected and unaffected hemisphere of a patient (P8). **B** Histogram of the stria of Gennari integrity comparing the left and right hemisphere of a control participant (C2). The histograms of other patients and control participants are shown in Figure S5. **C** ROC-curve showing the TPR and FPR of

the stria of Gennari integrity, comparing the affected and unaffected hemispheres in each patient. The grey area represents the range of the control participants, comparing left and right hemispheres on an individual level. The dashed black line represents chance level performance, meaning no difference between hemispheres. See Table S1 for AUC values and  $p$  values, FDR-corrected

In some patients (P1, P5, P8) the ROC-curves differ from chance level (Fig. 6C). The ROC-curve for one patient (P1) is significantly different from chance ( $AUC = 0.63$ ,  $p < 0.001$ , FDR-corrected). This indicates that for these participants, the stria of Gennari integrity is significantly lower for the affected hemisphere compared to the unaffected hemisphere (see Table S1). However, it is important to note that this difference might be biased by the reduced number of T1-w profiles left over in the affected P1 hemisphere, due to extensive damage to the calcarine sulcus (see Fig. 3). Notably, other patients with a preserved calcarine sulcus that no longer receives visual input (for example P2, P8), show no difference between the affected and the unaffected hemisphere.

Moreover, we observe variability in control participants, with some individuals showing differences in stria of Gennari integrity between the left and right hemispheres ( $AUC > 0.50$ ,  $p$  values  $< 0.050$ , FDR-corrected, see Table S1). While this could be indicative of true differences between the hemispheres, we maintain a more conservative interpretation, suggesting that the observed differences are more likely due to T1-w intensity inhomogeneities between the hemispheres that are not fully accounted for by the proton density correction (Van de Moortele et al. 2009).

We repeated the analysis after regressing out curvature at the individual voxel level, since the T1-w signal is known to vary systematically with cortical curvature, where convex regions tend to be thicker and more myelinated and vice-versa (Sereni et al. 2013). Results are largely indistinguishable from those reported in the present manuscript (Figure S7, Table S2).

## Discussion

In this study, we assessed the presence and integrity of the stria of Gennari following an acquired lack of visual input. We compared the integrity of the stria of Gennari between hemispheres and applied both a model-free approach and a novel forward modeling approach. As a model-free approach we measured T1-w intensity at the middle of cortical depth, while the forward modeling approach captured T1-w intensity variations across cortical depth, specifically targeting the stria of Gennari.

We found that the stria of Gennari was present in both patients with homonymous visual field defects and control participants. The stria of Gennari integrity was investigated by measuring T1-w intensity at the middle of cortical depth. We observed substantial variability in T1-w intensity at the middle of cortical depth between hemispheres and participants in both groups (Fig. 5, S4). The variability in T1-w intensity between participants could be due to biological variations, such as age differences (Grydeland et al. 2013; Pedersini et al. 2025) but also technical variations such as intensity inhomogeneities and motion. The variability between hemispheres could potentially be attributed to local T1-w intensity inhomogeneities not fully accounted for by the proton density correction (Van de Moortele et al. 2009), but not motion.

Additionally, we assessed the integrity of the stria of Gennari using a novel forward modeling approach which captures T1-w intensity variations across cortical depth (Fig. 2). This measure is largely independent from between-participant and within-participant variability, as this models the local T1-w intensity profile across cortical depth. We

found no significant differences in the stria of Gennari integrity within patients, except for patient P1. In P1, the stria of Gennari integrity was significantly lower in the affected hemisphere compared to the unaffected hemisphere. Furthermore, curvature correction had minimal impact on the results, indicating that although the T1-w signal systematically varies with cortical curvature (Sereno et al. 2013), this factor did not substantially influence our findings.

The difference in the stria of Gennari integrity in P1 could stem from either biological or methodological factors. From a biological perspective, the lesion in P1 was present shortly after birth, whereas the lesions in the other participants were acquired during adulthood. The early-onset damage might have triggered cortical reorganization processes in P1, which are less likely in the other patients with lesions acquired in adulthood. Methodologically, the observed difference could be due to a reduced number of T1-w profiles in the affected hemisphere, attributed to extensive damage to the calcarine sulcus (Fig. 3). In contrast, other patients (e.g., P2, P8) had a preserved calcarine sulcus that no longer receives visual input, resulting in a comparable number of T1-w profiles in both hemispheres. Here, we did not find a difference in the stria of Gennari integrity. Therefore, we believe our results suggest that the stria of Gennari integrity is not affected by the loss of visual input in case of acquired blindness in adulthood such as in homonymous visual field defects.

Trampel et al. (2011) demonstrated the presence of the stria of Gennari in congenitally blind individuals. Here, we investigated both the presence and the integrity of the stria of Gennari using two different measures. Additionally, we extended the observations from Trampel et al. (2011) in cases of acquired blindness, confirming its presence in control participants and both hemispheres in patients (Fig. 3). Importantly, our within-participant design minimizes confounding factors inherent to between-participant comparisons, such as between-participant variations in stria of Gennari thickness, myelination, age-related differences, and demographic variability. Additionally, this approach reduces potential methodological concerns, such as motion artefacts in the MRI-scanner, which can impair the resolution of the stria of Gennari. Furthermore, participants with congenital blindness in Trampel et al. (2011) were experienced Braille readers, a factor known to drive reorganization in the visual cortex (Burton et al. 2002). This raises the possibility that the integrity of the stria of Gennari in congenitally blind individuals may be preserved due to compensatory plasticity.

There are a few methodological considerations. First, the exact location of the stria of Gennari along normalized cortical depth can vary, a known phenomenon observed in previous studies (Wachnert et al. 2016). For instance,

differences in the position of laminar structures have been reported between the sulcal crown and fundi of the cortex. This variability influences the T1-w profiles along cortical depth. In this study, we used the equi-volume model, which provides a more accurate metric of normalized cortical depth compared to equi-distance and Laplace approaches (Wachnert et al. 2014). However, it remains susceptible to errors at acquisition resolutions of 0.5 mm isotropic, as used here. Specifically, this approach tends to overestimate cortical depth in sulcal fundi and underestimate the crowns, leading to an apparent shift in laminar features (Wachnert et al. 2016). A potential solution would be to acquire data at higher spatial resolutions (e.g., 0.2 mm isotropic), but this would introduce challenges related to feasibility, lower signal-to-noise ratio, and increased motion artifacts. Second, most patients with homonymous visual field defects had significant unilateral occipital cortex loss due to stroke or other neurological events (Fig. 3). This cortical asymmetry resulted in fewer T1-w profiles in the affected hemisphere compared to the unaffected side, introducing variability that could reduce sensitivity or introduce bias in our comparisons. Segmentation errors could potentially influence the resulting T1-w profiles. However, due to both automatic and manual segmentation, we believe this had a minimal impact on our analysis. The quality of the segmentation outcome can be appreciated on each single individual (Figures S2, S3, S6) and the same segmentation approach was applied uniformly across the whole brain, minimizing the likelihood of hemispheric bias.

In sum, our findings indicate that the stria of Gennari remains structurally intact despite the loss of visual input in cases of acquired blindness. This suggests that the presence of the stria of Gennari is not dependent on visual experience and does not undergo degradation following a lack of visual input in the case of homonymous visual field defects.

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**Data availability** The data are considered personal data pursuant to the General Data Protection Regulation (GDPR) and can only be shared based on and subject to the policies of the Royal Netherlands Academy of Arts and Sciences (KNAW). The datasets are available from the corresponding author on request. Considering the requirements imposed by law and the sensitive nature of personal data, any requests will be addressed on a case-by-case basis, subject to a data usage agreement.

## Declarations

**Conflict of interest** The authors declare no competing interests.

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