Do congenitally blind people have a stria of Gennari? First *in vivo* insights on a subcortical level

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Introduction: In neuroscience it is important to establish some correspondence between the functional organization of the neocortex and its microstructure. Use of very high resolution MRI, feasible at high field strengths such as 7 Tesla, has enabled the reliable observation of cortical layer structures *in vivo*, which correspond to details seen in cadaver brain sections that have been stained for myelin. The most easily visualized of these structures is the stria of Gennari, a layer of densely myelinated axons in layer 4C of the primary visual cortex V1. MRI studies have identified the stria of Gennari *in vivo* using T_1, T_2, T_2^* or phase contrast [1-5]. However, the developmental origin and function of the Gennari stripe are not yet well understood. In order to shed some light on this question, we used 7 Tesla MRI to scan congenitally blind people, who have never experienced any visual sensation. If the stria of Gennari develops as a result of visual input, like much of the organization of visual cortex [6], congenitally blind subjects should lack this structure. On the other hand, if we can reliably detect the Gennari stripe in these subjects it must represent an anatomical feature that does not require visual input to develop. For comparison, we scanned sighted subjects using the same experimental parameters.

Method: All experiments were performed on a 7 Tesla whole-body MR scanner (MAGNETOM 7T, Siemens Healthcare Sector, Erlangen, Germany) using a 24 channel phased array head coil (Nova Medical Inc, Wilmington MA, USA). The study was approved by the ethics committee of the local university and informed consent was obtained. 13 congenitally blind subjects (7 female, 21-70 years, 46 years mean) and 15 sighted controls (8 female, 20-31 years, 25 years mean) were included in the study. For positioning of the high resolution sequences, a 3D whole brain data set was acquired using an MP-RAGE sequence (TR = 3 s; TE = 2.6 ms; flip angle = 6°; BW = 260 Hz/Px; isotropic voxels of $(0.8\ mm)^3$). Subsequently, 30 slices were scanned, if possible orthogonal to the calcarine sulcus, using a Turbo Spin-Echo (TSE) sequence (TE = 27 ms; refocusing flip angle = 180°; BW = 80 Hz/Px, isotropic voxels of $(0.5mm)^3$; turbo factor = 2). Because the blind subjects were naïve to MRI, scan time was kept as short as possible. TR varied between 2.1 - 5.7 s depending on the subject-specific SAR (specific absorption rate) limit. When possible, a second set of images was acquired using a different TSE protocol (TR = 3.1 – 5.1 s; TE = 40 ms; BW = 40 Hz/Px; other parameters equal). For quantitative comparison between blind and sighted subjects, several signal intensity profiles were determined across the stria of Gennari at positions where the slice orientation was approximately perpendicular to the calcarine sulcus. The profiles for the blind and the sighted subjects were respectively averaged across subjects. Both profiles were normalized to the signal value of the grey matter on either side of the stria of Gennari. The procedure was separately repeated for the two different imaging protocols.

Results: Fig. 1 shows enlarged sections of the calcarine sulcus demonstrating the stria of Gennari in 3 congenitally blind subjects (Fig. 1A-C) and 3 sighted subjects (Fig. 1D-F). The main reason for image quality variation was subject motion, which can affect the visibility of the stria of Gennari. However, this feature could be reliably identified by visual inspection in all 15 sighted controls and in 11 of the 13 blind subjects. The remaining two blind subjects moved too much and were excluded from further analysis. Quantitative profile-based analysis showed a range of profiles of the primary visual cortex, varying within and across subjects. Fig. 2A shows the average profiles obtained with the first TSE protocol. The differences between the mean of grey matter image intensity within each profile and the Gennari stripe intensity for congenitally blind (CB) and sighted controls (SC), respectively, are shown in Fig. 2B. The asterisk denotes statistical significance ($p < 0.05$). The difference of the Gennari stripes between both groups did not reach statistical significance ($p = 0.5$).

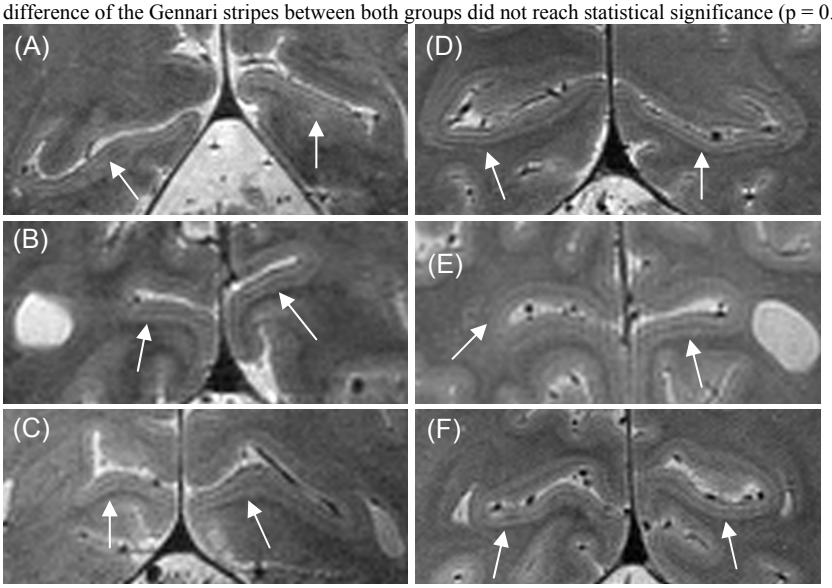

Fig. 1. Visualization of the stria of Gennari (arrows) in 3 blind (**A-C**) and 3 sighted (**D-F**) subjects.

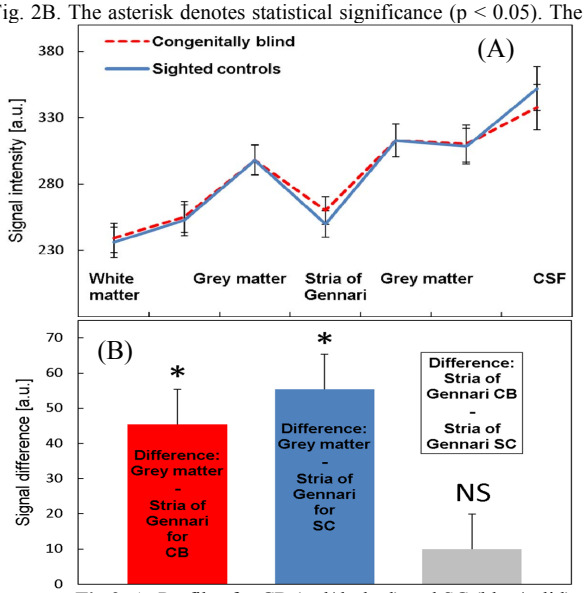

Fig 2. **A**: Profiles for CB (red/dashed) and SC (blue/solid). **B**: Signal differences in and between both groups.

Discussion and Conclusion: Exact quantitative analysis of our data took account of the inter-subject variation in TR needed to minimize SAR, which affected the TSE signal [7,8] as well as the acquisition order of the slices analyzed [9,10]. This effect was minimized by profile normalization. For one subject where two scans with different TR times were acquired, we found a negligible effect on the signal difference between the stria of Gennari and its surrounding grey matter. Profile accuracy was more severely affected by subject motion and imprecision of the angle between the slice and the calcarine sulcus. Thus the slight trend to lower Gennari contrast in congenitally blind subjects shown in Figure 2A may have been due only to greater head motion of the MR-naïve blind subjects.

Many earlier fMRI studies have investigated the functional organization of primary visual cortex [11-14] and a few MRI studies have examined its structure in congenitally blind subjects *in vivo* [15,16]. Here we have demonstrated for the first time that congenitally blind people possess a stria of Gennari which is very similar in appearance in TSE scans to that of sighted controls. This strongly suggests that the Gennari stripe does not form as a result of visual input, nor does it degenerate because of a lack of visual input. Studies of Braille reading in blind subjects show that V1 plays a necessary role in this extreme test of haptic discrimination [e.g. 17], and perhaps it retains its structure in blind subjects because it is put to many other such uses.

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