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The mid-fusiform sulcus: A landmark identifying both cytoarchitectonic and functional divisions of human ventral temporal cortex

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Abstract

Human ventral temporal cortex (VTC) plays a pivotal role in high-level vision. An under-studied macroanatomical feature of VTC is the mid-fusiform sulcus (MFS), a shallow longitudinal sulcus separating the lateral and medial fusiform gyrus (FG). Here, we quantified the morphological features of the MFS in 69 subjects (ages 7–40), and investigated its relationship to both cytoarchitectonic and functional divisions of VTC with four main findings. First, despite being a minor sulcus, we found that the MFS is a stable macroanatomical structure present in all 138 hemispheres with morphological characteristics developed by age 7. Second, the MFS is the locus of a lateral-medial cytoarchitectonic transition within the posterior FG serving as the boundary between cytoarchitectonic regions FG1 and FG2. Third, the MFS predicts a lateral-medial functional transition in eccentricity bias representations in children, adolescents, and adults. Fourth, the anterior tip of the MFS predicts the location of a face-selective region, mFus-faces/FFA-2. These findings are the first to illustrate that a macroanatomical landmark identifies both cytoarchitectonic and functional divisions of high-level sensory cortex in humans and have important implications for understanding functional and structural organization in the human brain.

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Keywords

cytoarchitectonics; fusiform gyrus; mid-fusiform sulcus; eccentricity bias; Fusiform Face Area

Introduction

Human ventral temporal cortex (VTC) plays a pivotal role in perceptual and cognitive tasks spanning high-level vision (Haxby et al., 2000; Tarr and Gauthier, 2000; Malach et al., 2002; Martin, 2007; Op de Beeck et al., 2008; Weiner and Grill-Spector, 2013), memory (Wagner et al., 1999; Henson et al., 2000), and multi-sensory integration (Amedi et al., 2002; James et al., 2002; Kitada et al., 2009). One of the most replicable organizational features of human VTC documented by functional magnetic resonance imaging (fMRI) is a large-scale lateral/medial functional distinction. For instance, inanimate (Martin, 2007; Mahon and Caramazza, 2009), place (Aguirre et al., 1998; Epstein and Kanwisher, 1998; Nasr et al., 2011), and peripherally-biased (Levy et al., 2001; Hasson et al., 2002; Malach et al., 2002) representations are located in medial VTC encompassing the medial FG and collateral sulcus (CoS), while animate (Martin, 2007; Mahon and Caramazza, 2009; Connolly et al., 2012), face (Kanwisher et al., 1997), and foveally-biased (Levy et al., 2001; Hasson et al., 2002; Malach et al., 2002) representations are located in lateral VTC, encompassing the lateral fusiform gyrus (FG) and occipito-temporal sulcus (OTS). Intriguingly, in addition to this lateral/medial functional distinction, a lateral/medial cytoarchitectonic distinction has recently been identified (Caspers et al., 2012). Using novel tools detecting transitions in both cell density and layering across gray matter, Caspers and colleagues (2012) reported two cytoarchitectonic regions in the posterior aspect of VTC: FG1 and FG2. Macroanatomically, FG1 is located on the medial FG extending into the CoS, while FG2 is located on the lateral FG extending into the OTS. Cytoarchitectonically, FG1 displays a columnar arrangement of small pyramidal cells, while FG2 contains large pyramidal cells in layer III and a prominent layer IV, but no columnar arrangement. If and how these functional and cytoarchitectonic parcellations are related to one another is presently unknown.

A major obstacle preventing the full understanding of cytoarchitectonic and functional correspondences in VTC is that macroanatomical structures are yet to be fully characterized. For instance, an often over-looked feature of VTC is that the FG is divided longitudinally by a minor sulcus referred to as the mid-fusiform sulcus, or MFS (Puce et al., 1996; Nobre et al., 1998; Allison et al., 1999; Weiner and Grill-Spector, 2010; Weiner et al., 2010; Nasr et al., 2011; Weiner and Grill-Spector, 2012, 2013). Indeed, although the MFS was first labeled as such in the late nineties (Puce et al., 1996; Nobre et al., 1998; Allison et al., 1999), it has been mentioned in the literature less than ten times (Schultz et al., 2003; Weiner and Grill-Spector, 2010; Weiner et al., 2010; Nasr et al., 2011; Davidenko et al., 2012; Parvizi et al., 2012; Weiner and Grill-Spector, 2012, 2013). Despite the paucity of studies mentioning the MFS, recent research in adults provides insight into how incorporating the MFS into functional neuroimaging might enhance the understanding of VTC functional organization. Specifically, these studies show that the MFS serves as a lateral-medial functional boundary dividing face-selective regions (Weiner and Grill-Spector, 2010; Weiner et al., 2010; Nasr et al., 2011; Davidenko et al., 2012; Parvizi et al., 2012; Weiner and Grill-Spector, 2012, 2013) from place-selective regions (Nasr et al., 2011), and also dissociates differential repetition suppression mechanisms (Weiner et al., 2010). However, it is unknown (1) if the morphology of the MFS is stable across development, (2) if the MFS is coupled with cytoarchitectonic partitions of VTC, (3) whether the MFS predicts additional lateral-medial functional gradients in VTC such as

eccentricity bias representations, and (4) if the MFS also predicts the fine-scale clustering of face-selective regions.

To address these questions, we conducted four separate studies. First, we characterized the morphology of the MFS in 69 subjects (ages 7-40), determining the developmental and stable features of the MFS in children, adolescents, and adults. Second, we examined the relationship between the MFS and cytoarchitectonic regions FG1 and FG2 using an independent set of 10 postmortem brains. Third, using a novel classification approach, we tested if the MFS serves as a functional boundary separating the large-scale eccentricity bias map (Levy et al., 2001; Hasson et al., 2002; Malach et al., 2002) in 36 subjects (ages 7-40). We chose eccentricity bias measurements because they show a medial-lateral gradient across VTC and constitute a large-scale category-independent representation. Fourth, we tested if the MFS serves as a functional landmark identifying the fine-scale functional organization of face-selective regions pFus-faces/FFA-1 and mFus-faces/FFA-2 (Weiner and Grill-Spector, 2010) using high-resolution fMRI (HR-fMRI) in 14 adult subjects. To our knowledge, this is the first in depth analysis of human high-level visual cortex spanning cytoarchitectonics, macroanatomy, and functional organization at multiple spatial scales. We demonstrate that the MFS is a stable macroanatomical feature across development, as well as a crucial landmark identifying both cytoarchitectonic and functional divisions of VTC.

Materials and Methods

We describe the methods in two sections, one for the anatomical and functional MRI scans and a separate section for the cytoarchitectonical analysis.

Participants

To obtain macroanatomical data, 69 subjects participated in an anatomical MRI session. Subjects included 20 children (ages 7-11, 7 females), 14 adolescents (ages 12-17, 8 females), and 35 adults (ages 18 – 40, 18 females), all of whom were healthy with no report of neurological or psychiatric disease. To obtain data on the functional organization of VTC, 36 (12 children, 12 adolescents, and 12 adults) of these 69 subjects also participated in an fMRI session. Written consent was obtained from each subject. Procedures were approved by the Stanford Internal Review Board on human subjects research.

Data Acquisition and Analysis

Anatomical Scans and Analysis

Scanning: All subjects were scanned on a GE 3-Tesla Signa scanner at Stanford University. A high-resolution anatomical volume of the whole brain was acquired with a whole head coil using a T1-weighted SPGR pulse sequence (TR = 1000 ms, flip angle = 45°, 2 NEX, FOV = 200 mm, resolution of 0.78 × 0.78 × 1.2 mm).

Data Analysis: Data were analyzed with MATLAB (MathWorks) using the mrVista toolbox (<http://white.stanford.edu/software>).

Cortical surface reconstruction: Anatomical volumes were aligned to the AC-PC plane and resampled to 1mm isotropic voxels. Using a combination of automated (FreeSurfer: <http://surfer.nmr.mgh.harvard.edu>) and manual segmentation tools (ITK-SNAP: <http://white.stanford.edu/itkgray>), each anatomical volume was segmented to separate gray from white matter, from which we reconstructed the cortical surface for each subject (Wandell et al., 2000).

Identification of the MFS on single slices and cortical surface reconstructions: The MFS is a longitudinal sulcus dividing the FG into lateral and medial partitions as viewed on the cortical surface (Figure 1). Here, we determined the identifying features of the MFS relative to surrounding sulci on single sections in order to define the MFS consistently on anatomical MRIs as well as in single histological sections. As illustrated in Figure 1, the MFS is positioned between the OTS and CoS on the cortical surface (Figure 1a), resulting in a distinct omega (ω) pattern on single coronal slices (Figure 1b). This ω pattern (red outline in Figures 1-2) is a characterizing feature of the MFS despite differences in how it may appear on the cortical surface.

Sulcal length measurements: Lines were manually drawn along the fundus of the MFS on the cortical surface for each subject and hemisphere. The length of this line was determined using a modified version of Dijkstra's algorithm (as in Wandell et al., 2000). As the cortical surface reconstruction is composed of a series of connected vertices, the algorithm computes the length by determining the shortest path between endpoints on the line taking into consideration their actual distance in gray matter. When the MFS was fractionated into more than one component (Table 1, Figure 2, and **Results**), the total length was based on the sum of the independent sulcal components excluding the interspersed gyral components. We repeated the length measurement including the intergyral components, which were on average 5.26 ± 0.22 mm long, but it minimally affected MFS length measurements as these occur in less than 30% of hemispheres (length with intergyral: 29.2 ± 13.5 mm, without intergyral: 27.3 ± 10.8 mm). To further relate these measurements to stereotaxic space, we calculated the Talairach coordinates of the anterior and posterior extents of the MFS in the 70 adult hemispheres (Table 2).

Sulcal depth measurements: Lines were manually drawn from the lateral lip to the medial lip of each sulcus of interest (MFS, OTS, and CoS) on the cortical surface (dotted lines on the cortical surface and corresponding coronal slices in Figures 1-2). The distance of this line was first determined using the same algorithm as the length measurements and then divided by two to transform these width measurements into depth measurements. To test the validity of this approach, we also measured sulcal depth in coronal slices – evaluating the distance between the fundus of a sulcus (the MFS, CoS, or OTS) to the morphologically closed border of the cerebrum in the 35 adult subjects. In a two-way repeated measures ANOVA with factors method (cortical surface and coronal slices) and sulcus (MFS, CoS, and OTS), there was no significant main effect of method, no main effect of subject, and no significant interaction ($p > .54$). Thus, we report depth measurements from the cortical surface.

fMRI Scans and Analysis

Large-scale functional-structural correspondence: To test if the MFS reliably delineates lateral-medial functional divisions of VTC across development, we examined 12 children (ages 8-11), 12 adolescents (ages 12-16), and 12 adults (ages 18-40) using fMRI. During fMRI, subjects viewed images of faces and houses presented either centrally spanning 3° or peripherally in a ring whose inner radius was 7° and outer radius was 14° . Stimuli in the periphery were scaled in size to account for lower acuity in the peripheral visual field and their diameter was $\sim 6^\circ$. Subjects participated in 2 runs of this experiment where each run was 384 seconds long containing four, 12-second blocks of each condition. Subjects were instructed to fixate on a central dot and to indicate with a button press when the fixation color changed.

Acquisition: We acquired 32 slices at a resolution of $3.125 \times 3.125 \times 3$ mm mm using a two-shot T2*-sensitive spiral acquisition sequence (Glover, 1999) (FOV = 200 mm; TR=2

seconds, TE=30 ms, and flip angle = 77°) on a 3T GE scanner. Inplane anatomical scans were acquired with the same prescription using a two-dimensional RF- spoiled GRASS (SPGR) sequence (TE = 1.9 ms, flip angle = 15°, bandwidth=15.63 kHz).

Time series processing: Functional data of each session were motion corrected using an affine transformation (Nestares and Heeger, 2000). Time series data were filtered using a temporal high-pass filter with a 1/20 Hz cutoff and then converted to percentage signal change by dividing the time series of each voxel by its mean intensity. We estimated the blood oxygen level dependent (BOLD) response amplitudes for each condition using a general linear model (GLM) applied to the time series of each voxel using as predictors the experimental conditions convolved with the hemodynamic impulse response function used in SPM5. Data were not spatially smoothed.

Anatomical ROIs: Lateral and medial anatomical VTC regions of interest (ROIs) were defined on the cortical surface of each subject and hemisphere, blind to functional data. The anterior and posterior boundaries of each ROI were the anterior and posterior extents of the MFS, respectively. Lateral VTC was defined as the region between the lateral lip of the MFS and OTS. Medial VTC was defined as the region between the medial lip of the MFS and CoS (Figure 7a). The average sizes of lateral and medial anatomical ROIs were similar across age groups (children: 2600 mm³ ± 158 mm³; adolescents: 2580 mm³ ± 151 mm³; adults: 2380 mm³ ± 126 mm³; no significant effect of age, $p = .47$).

Linear discriminant analysis (LDA) of functional-structural correspondence: To test if the MFS serves as a functional landmark in VTC, we conducted a linear discriminant analysis (LDA) to examine if the *anatomical* location of each voxel (i.e. whether it belonged to the lateral or medial VTC) in one subject's brain could be classified from the *functional* data in other subjects' brains. For each ROI and hemisphere, we used 500 voxels whose time series were best fit by the GLM. This voxel selection criterion was implemented to be independent of stimulus condition and to exclude voxels with excessive noise. Within-group classification was conducted with a leave-one-subject-out procedure. Across-group classification was conducted by training on one age group and testing on subjects from another age group. The training set consisted of eccentricity bias values measured at the level of each voxel (t -value of fovea - periphery, collapsed across stimulus categories) labeled as belonging to either the lateral or medial VTC ROIs. We used an LDA to derive a linear boundary separating these t -values based on their anatomical classification. The test set consisted of functional t -values from voxels with an unknown anatomical location from a subject not used in the training. Using the boundary derived from the training set, we classified the test set voxels either the lateral or medial VTC ROI. Classification performances on test sets were evaluated by comparing the classification results to the actual anatomical location of each voxel, and then calculating the percentage of voxels classified correctly. Since there was no effect of hemisphere on classification performance ($p=.23$), data were concatenated across hemispheres resulting in 1000 voxels from each subject used for classification.

Distance between eccentricity bias boundary and the MFS fundus: Following the classification analyses, which were blind to the functional data, we measured the distance along the cortical surface between each point of the eccentricity bias boundary in VTC (defined as the transition between foveally-biased and peripherally-biased voxels) and the MFS fundus, and calculated the average distance in each hemisphere. Unlike the classification analysis, this analysis included voxels within the MFS itself to measure the exact position of the functional transition within the MFS. In Figure 8, we show the average

distance between the eccentricity bias boundary and the MFS fundus collapsed across hemispheres and subjects for each age group.

Fine-scale functional-structural correspondence: To examine the MFS-functional coupling in the anterior-posterior dimension, 14 of the 35 adults were scanned with high-resolution fMRI (HR-fMRI) during a block design experiment while viewing images of different categories including faces, limbs, objects, houses and texture patterns as described in prior studies (Weiner and Grill-Spector, 2010; Weiner et al., 2010; Weiner and Grill-Spector, 2011; Parvizi et al., 2012). HR-fMRI improves localization of functional regions and improves measurements of the anterior portion of the MFS, where tSNR is often low due to the ear canal susceptibility artifact (Weiner and Grill-Spector, 2013).

Acquisition: Data were collected on a 3T GE scanner with either a 32-channel surface coil, EPI sequence, and 1.8mm isotropic voxels (FOV = 192 mm; TR=2 seconds, TE=30 ms, and flip angle = 77°, 28 slices; 7 subjects) or 8-channel surface coil, spiral acquisition sequence, and 1.5 × 1.5 × 3mm voxels (FOV = 192 mm; TR=2 seconds, TE=30 ms, and flip angle = 77°, 12 slices, 7 subjects). As there was no effect of acquisition on the MFS-functional coupling reported in Figures 9-10 (1-way ANOVA with factor of acquisition; $p = .71$), we report results averaged across all 14 subjects.

Analysis: To determine the structural-functional coupling between the MFS and face selectivity using HR-fMRI, we defined anatomical, Talairach, and functional regions of interest (ROIs) for each subject and hemisphere. *Anatomical ROIs:* 1cm disk ROIs were placed on the anterior and posterior extents of the MFS extending laterally into the FG (Figure 10). *Talairach ROIs:* 1cm disk ROIs were centered on the Talairach coordinates of FFA-1 and FFA-2 from prior studies (Pinsk et al., 2009). *Functional ROIs:* pFus-faces/FFA-1 and mFus-faces/FFA-2 were defined as voxels in the FG responding more to faces > nonfaces, $t > 3$, voxel level, uncorrected (see Weiner and Grill-Spector, 2010; Weiner et al., 2010; Weiner and Grill-Spector, 2011; Davidenko et al., 2012; Parvizi et al., 2012; Weiner and Grill-Spector, 2013). We examined the percentage overlap between these anatomical and functional ROIs as well as Talairach and functional ROIs in each subject.

Postmortem Data Acquisition and Analysis

To examine the relationship between the MFS and cytoarchitectonic divisions of the FG, 10 postmortem (PM) brains were studied. These brains were from adults (ages 37-85, 5 females) with no history of neurological or psychiatric disease (with the exception of one individual with transitory motor disease. See Table 1 from Amunts et al., 2000; Rottschy et al., 2007; Caspers et al., 2012). All 10 PM brains came from the body donor program of the Institute of Anatomy, University of Dusseldorf, all procedures were approved and in alignment with the program guidelines (Amunts et al., 2000).

Scanning—Postmortem brains were scanned on a Siemens 1.5T Scanner (Erlangen, Germany) after being removed from the subject's skull 8-24 hours after death.

Anatomical brain volumes—A high-resolution anatomical volume of the whole brain was acquired using a T1-weighted 3D-FLASH sequence (TR = 40 ms, flip angle = 40°, TE=5ms; resolution of 1 × 1 × 1mm) before histological processing and after fixation in 4% formalin or Bodian's fixative for at least 6 months.

Cortical surface reconstruction—Detailed methods of histology and 3D reconstruction have been described previously (Amunts et al., 1999; Zilles et al., 2002; Amunts et al., 2005). The fixated brains were embedded in paraffin, serially sectioned in coronal sections

(20 microns thick), and stained with the Merker-method for cell bodies (Merker, 1983). This method yields a high contrast between cell bodies (black) and the neuropil (unstained). 3D reconstructions were computed using (a) the 3D-MRI volume of each brain, (b) images of the paraffin block face for precise alignment of the histological sections, and (c) digitized images of the cell body-stained sections (Amunts et al., 2004). For direct comparison to the 69 subjects, brains were also manually segmented to separate gray from white matter using ITK-SNAP (<http://white.stanford.edu/itkgray>), from which we reconstructed the cortical surfaces (Figure 6a).

Detection of FG1 and FG2 boundary—A detailed description for defining cytoarchitectonic areas of FG1 and FG2 is given elsewhere (Amunts et al., 2000; Amunts and Zilles, 2001; Caspers et al., 2012). Briefly, the border between FG1 and FG2 was defined (Caspers et al., 2012) using a statistically testable, quantitative, and observer-independent cortical parcellation technique (Schleicher et al., 1999; Amunts et al., 2000; Zilles et al., 2002; Schleicher et al., 2005). Specifically, gray-level indices (GLI) were determined in digitized histological sections as a measure of the volume proportion between cell bodies and the neuropil. GLI profiles were calculated along curvilinear trajectories oriented perpendicular to the cortical layers, thus measuring the GLI from the superficial to the innermost layer in cortical regions of interest. The shape of GLI profiles was determined based on ten features: the mean GLI value, the position of the center of gravity on the profile curve (cortical depth), the standard deviation of the mean GLI (indicating the variability of the GLI throughout all layers), skewness and kurtosis of the profile curve, and the respective features from the profile's first derivative (Schleicher et al., 1999). The borders between areas were determined based on the cortical position of the greatest difference between neighboring GLI profiles quantified by the Mahalanobis distance and tested for significance (Figure 4; Hotelling's T^2 test; Bonferroni-corrected). Areal borders are expected at positions along the cortical ribbon showing a great dissimilarity in laminar patterns between adjacent blocks of profiles. To assure that the areal boundary was not dependent on the block size, the procedure was titrated for block sizes ranging from 8 to 24 profiles per block. Cortical borders were confirmed if they were consistently positioned in adjacent histological sections and across several block sizes (Figure 4).

Distance between the FG1/FG2 boundary and the MFS—In all 20 hemispheres, we measured the distance along the cortical surface between each point of the FG1/FG2 boundary and the nearest point on the MFS in a given hemisphere. We used the average distance for each subject in each hemisphere as our measure of the distance between the FG1/FG2 boundary and the MFS and report the mean distance across subjects. In the 18 hemispheres within which the cytoarchitectonic boundary between FG1 and FG2 occurred in the MFS, we also measured the percentage of the MFS containing the FG1/FG2 boundary (Figure 6b) and the average distance of this boundary from the fundus of the MFS (Figure 6c).

Relationship between Talairach coordinates and the FG1/FG2 boundary—Using the average Talairach coordinates of the MFS from our independent adult sample (Table 2), we compared the ability of Talairach coordinates to predict the FG1/FG2 boundary relative to the actual MFS coordinates. In all 20 hemispheres, we drew a line between the anterior and posterior points of the MFS as predicted by Talairach coordinates. We then measured the average distance between this line and the FG1/FG2 boundary and compared this metric to the distance between the FG1/FG2 boundary and the MFS as described in the above section.

Results

Incidence, Morphology, and Development of the Mid-Fusiform Sulcus (MFS)

The MFS displays four morphological patterns and is identifiable in every hemisphere—We first examined the incidence and morphological features of the MFS on the cortical surface and single coronal slices in 138 hemispheres across three age groups: children, adolescents, and adults. Although the MFS is a minor sulcus and not mentioned in the most commonly used human neuroanatomical atlases from the last century (Brodmann, 1909; Talairach and Tournoux, 1988; Ono et al., 1990; Evans et al., 1992; Duvernoy, 1999), it was identifiable in all 138 hemispheres, and is best described as a longitudinal sulcus dividing the FG into lateral and medial partitions (Figure 1) with a distinctive “ ω ” pattern on single coronal slices (red outline in Figures 1-2).

The organization of the MFS relative to surrounding sulci exhibited two characteristic pattern types (Type I and Type II) that were evident when viewing the cortical surface. In Type I patterns, the MFS appeared as a distinct sulcus separate from the OTS and CoS. In Type II patterns, the MFS intersected with either the OTS or CoS. Both Type I and Type II patterns were further classified based on whether the MFS was continuous (subtype A) or fractionated (subtype B). Thus, the features of the different MFS patterns are defined as follows:

Type IA: a single longitudinal sulcus, distinct from the OTS and CoS (Figure 2, **far left**).

Type IB: a fractionated longitudinal sulcus, distinct from the OTS and CoS (Figure 2, **middle left**).

Type IIA: a single longitudinal sulcus, sharing a sulcal bed with the OTS or CoS (Figure 2, **middle right**).

Type IIB: a fractionated longitudinal sulcus, with at least one component sharing a sulcal bed with the OTS or CoS (Figure 2, **far right**).

These morphological patterns occurred with similar frequencies across hemispheres, genders, and age groups tested (Table 1). Type I MFS patterns (manifesting as a distinct sulcus) were the most common, occurring in about two thirds (68%) of hemispheres. Type II MFS patterns occurred in about a third of hemispheres (32%) and were distinct from the recently described lateral branches of the CoS (Huntgeburth and Petrides, 2012). Further, unfractionated A patterns were about two times as frequent as fractionated B patterns (ratio: 2.5 for Type I; 1.9 for Type II) and fractionated B patterns were most frequently composed of two components (34/42; 81%). Thus, the MFS is a stable anatomical landmark on the FG with four typical morphological patterns that are common across hemispheres, genders, and age groups.

Characteristic feature of the MFS: Half as deep as the OTS and CoS—The average depth of the MFS was 6.13 ± 1.53 mm in children, 6.0 ± 0.91 mm in adolescents, and 6.57 ± 1.67 mm in adults (Figure 3). There was no difference in depth (a) across hemispheres within any of the age groups (all p s $>.67$; paired t-tests), (b) across groups (1-way ANOVA; $F(2,68)=.94$, $p=.39$), or (c) across genders (1-way ANOVA, $F(1,68)=.31$, $p=.58$). There was also no correlation between age and MFS depth in either hemisphere (all r s $<.16$, all p s $>.2$).

The MFS exhibited two features distinguishing it from the OTS and CoS. First, the MFS was significantly more shallow than both sulci (1-way repeated measures ANOVA:

$F(2,206)=562, p<10^{-10}$; Figure 3). In fact, the OTS and CoS were more than two times as deep as the MFS (average ratio OTS/MFS=2.13, and CoS/MFS= 2.16). Second, depth measurements of the MFS in one hemisphere were correlated with depth measurements in the other ($r = .28, p < .02$, collapsed across groups), which was not the case for the OTS or CoS (all $r_s < .11$, all $p_s > .35$). Taken together, the shallowness of the MFS relative to the OTS and CoS is a stable measurement across subjects and is predictable across hemispheres within a given subject.

Length of the MFS is consistent across age groups and hemispheres—The length of the MFS was on average 25.7 ± 8.0 mm in children, 28.8 ± 6.0 mm in adolescents, and 27.5 ± 10.3 mm in adults. There were no differences in MFS length (a) across hemispheres within age group (all $p_s > .28$; paired t-tests), (b) across groups (1-way ANOVA: $F(2,68)=.51; p=.60$), or (c) across genders (1-way ANOVA, $F(1,68)=.02, p = .89$). Furthermore, there was no correlation between age and MFS length in either hemisphere (all $r_s < .16$, all $p_s > .2$), or between MFS length in the right and left hemisphere ($r = .02, p = .88$).

In contrast to the MFS depth, there was significant variability across subjects in the length of the MFS, ranging from 2.0 mm to 56.3 mm. This variability is consistent with prior reports (8 mm to 54 mm in 17 subjects; Nasr et al., 2011). Morphologically, this variability in length affected the posterior, but not anterior, limit of the MFS, where the anterior tip of the MFS was a stable macroanatomical landmark situated about halfway between the tips of the temporal and occipital poles (Figure 2). However, the posterior extent of the MFS varied substantially across subjects. Indeed, the largest variability among Talairach coordinates of the MFS occurs in the y-dimension of the posterior MFS (Table 2).

Cytoarchitectonics

The boundary between cytoarchitectonic regions FG1 and FG2 occurs within the MFS—We next examined the location of the MFS relative to two cytoarchitectonic divisions of the FG, FG1 and FG2, in 10 postmortem (PM) brains whose cytoarchitectonics were defined previously (Caspers et al., 2012). The border between FG1 and FG2 was determined based on the cortical position of the greatest difference between neighboring GLI profiles quantified by the Mahalanobis distance and tested for significance (Materials and Methods; Figure 4). It is important to note that these cytoarchitectonic boundaries were defined using observer independent methods, and were made prior to characterizing the MFS, as the ω pattern (Figure 1) used to localize the MFS on single histological sections was unknown at the time of the original FG1/FG2 identification (Caspers et al., 2012).

We identified the presence of the MFS on digitized images of histological sections (20 microns thick), using the typical ω pattern of the MFS relative to the OTS and CoS. The difference in depth between the MFS relative to the CoS and OTS producing the ω pattern is a robust metric, where the CoS and OTS were two times as deep as the MFS (CoS/MFS: 2.12 ± 0.2 and OTS/MFS: 2.13 ± 0.3), similar to our in-vivo measurements (2.16 and 2.13, respectively). Thus, we were able to identify the MFS in the single histological sections in all (20/20) hemispheres. Figure 4 (left) shows example histological sections zoomed on the MFS. These data illustrate that the cytoarchitectonic boundary between FG1 and FG2 occurs within the MFS. The reliability of this cortical border between FG1 and FG2 was determined by titrating the number of GLI profiles used in each block used for calculating the Mahalanobis distance function (Materials and Methods). These analyses indicate that the positioning of the FG1/FG2 boundary within the MFS was consistent across block sizes (Figure 4, right). These two slices are indicative of the general trend as the FG1/FG2 boundary occurred within the MFS in 90% (18/20) of hemispheres. To illustrate both the

consistency and variability of these cortical borders across subjects, we show coronal histological sections from eight additional hemispheres (Figure 5). In each case, the boundary between FG1 and FG2 is located in the MFS.

To further examine the link between the MFS morphology and the FG1/FG2 boundary, we generated cortical surface reconstructions for each subject (Figure 6a). The morphological pattern types of each hemisphere in the post-mortem sample was representative of those documented in our in-vivo sample (Table 1) where Type 1 patterns occurred 60% of the time (12/20) with A patterns about 1.5 times as frequent as B patterns (1.4 for Type 1; 1.67 for Type II). We then projected FG1 and FG2 from the digitized histological sections onto the brain volume and cortical surface to precisely quantify where the microanatomical transition between FG1 and FG2 occurs within the MFS (Figure 6). This approach yielded three important findings. First, the cytoarchitectonic transition between FG1 and FG2 occurred within the posterior aspect of the MFS irrespective of morphological differences (Figure 6a). Second, not all of the MFS contains the FG1/FG2 boundary. Indeed, quantifying the percentage of the MFS containing this FG1/FG2 boundary reveals more overlap within the left ($60.0 \pm 6.5\%$) than the right ($33.4 \pm 7.2\%$) hemisphere (Figure 6b). Third, though the extent of the MFS containing the FG1/FG2 boundary varies across hemispheres, the cytoarchitectonic transition occurs in a comparable position within its depth across hemispheres, just 3-4mm from the fundus (left: $3.00 \pm 0.42\text{mm}$; right: $3.71 \pm 0.58\text{mm}$; Figure 6c). Notably, the distance between the entire FG1/FG2 boundary (not just the portion within the MFS as in Figure 6b) and the MFS in all 20 hemispheres, is on the order of 5mm (L: $5.75 \pm 3.11\text{mm}$; R: $5.07 \pm 1.07\text{mm}$), which is twice as precise as that predicted by Talairach coordinates (L: $11.35 \pm 1.51\text{mm}$; R: $11.65 \pm 2.59\text{mm}$; $p < 10^{-3}$). Taken together, these analyses reveal that in 90% of hemispheres, nearly half of the FG1/FG2 boundary occurs within the MFS less than 4mm from the fundus, illustrating a tight correspondence between a microanatomical transition and a macroanatomical landmark within the posterior FG.

Function

The MFS identifies a lateral-medial transition in the eccentricity bias map across age groups

While cytoarchitectonic analyses offer unprecedented precision of micron level measurements elucidating the fine-scale anatomical structure within the shallow MFS, fMRI offers the opportunity to examine the relationship between the MFS and the large-scale functional structure surrounding it. For instance, prior studies show that the MFS separates face-selective regions in lateral VTC from place-selective regions in medial VTC (Weiner et al., 2010; Weiner and Grill-Spector, 2010; Nasr et al., 2011). Given this structural-functional relationship, and the present findings indicating the stability of the MFS across development and its consistent relation to cytoarchitectonic partitions of the FG, we hypothesized that a) the location of the MFS will predict additional functional differentiations between lateral and medial VTC, and b) this relationship will be stable across development.

We tested this hypothesis with eccentricity bias measurements, which show a lateral-medial functional gradient in VTC (Levy et al., 2001; Hasson et al., 2002) and are thought to reflect a general organizing principle of human high-level visual cortex (Malach et al., 2002). Blind to the functional data, we first defined lateral and medial anatomical VTC ROIs guided by the MFS morphology in each subject and hemisphere (Materials and Methods). We then used a linear discriminant classifier within and across age groups to determine if the *anatomical* location of VTC functional voxels in one subject's brain could be predicted from learning the structural-functional relationship between anatomy and eccentricity bias in other subjects' brains. Results show that the classifier predicted the anatomical location of

voxels significantly above chance in all age groups (all $t_s > 45.4$, $p_s < 10^{-13}$, Figure 7b). The percentage voxels classified correctly was $80.2 \pm 6.1\%$ (std) in children, $79.5 \pm 5.6\%$ in adolescents, and $80.4 \pm 5.3\%$ in adults, with no significant differences across age groups (1-way ANOVA, $F(2,35)=.09$, $p=.92$). Intriguingly, anatomical classification across age groups was also significantly above chance (all $t_s > 19.84$, $p_s < 10^{-10}$) with the average correct classification ranging between $77.3 \pm 4.8\%$ and $81.5 \pm 5.6\%$ (Figure 7c). This across age group classification was strikingly similar to within age group classification where a 2-way ANOVA using training age group and testing age group as factors showed no main effect of testing age group ($p=.33$), no main effect of training age group ($p=.18$), and no interaction ($p=.99$). These data reveal a tight structural-functional coupling relative to the MFS across age groups.

To verify the classification results, we projected the eccentricity map of each subject onto their corresponding cortical surface reconstruction. Even though the MFS was not used in the classification analyses, we include the MFS in the visualizations to relate to the distance measurements in Figure 8, lower right. Consistent with the classification results, there was a clear eccentricity gradient arranged in a reliable manner relative to the MFS. In children, adolescents, and adults, a majority of voxels medial to the MFS showed a clear peripheral bias (cool colors in Figure 8) and a majority of voxels lateral to the MFS showed a more foveal eccentricity preference (warm colors in Figure 8). A minority of voxels showed the reverse preference (e.g. voxels with a peripheral bias laterally and a foveal bias medially) in lateral and medial VTC, which explains why the classifier misidentified about 20% of the voxels across age groups (Figure 7b-c). Intriguingly, the transition of the eccentricity bias map oftentimes occurs within or on the outer lips of the MFS itself (Figure 8). Measuring the distance between the MFS fundus and the foveal-peripheral transition of the VTC eccentricity bias map (Figure 8, lower right) reveals that this distance is only 4.1-4.6 mm across age groups (mean and SEM: kids: $4.17\text{mm} \pm 0.36\text{mm}$; adolescents: $4.58\text{mm} \pm 0.51\text{mm}$; adults: $4.10\text{mm} \pm 0.49\text{mm}$), which is comparable to the distance between the MFS fundus and the FG1/FG2 cytoarchitectonic transition. Together, these results indicate a stable structural-functional relationship between the MFS and a large-scale functional map extending from lateral to medial VTC across ages (from 7 to 40, the youngest and oldest subjects in our fMRI study, respectively).

Fine-scale: The anterior tip of the MFS identifies mFus-faces/FFA-2

Can the MFS identify fine-scale functional clusters in addition to transitions in large-scale functional maps?: Prior HR-fMRI studies report two separate face-selective regions along the length of the MFS where one overlaps anterior portions of the MFS extending into the lateral FG (mFus-faces/FFA-2) and another overlaps the posterior portion of the MFS and lateral FG extending into the OTS (pFus-faces/FFA-1) adjacent to a body part-selective region (OTS-limbs/FBA: Weiner and Grill-Spector, 2010; Weiner et al., 2010; Weiner and Grill-Spector, 2011, 2012, 2013; Figures 9-10). However, the exact correspondence of mFus-faces/FFA-2 and pFus-faces/FFA-1 with respect to the morphological features of the MFS (Figures 1-2) has not been quantified. We examined two possible outcomes. One possibility is that there is a direct relationship between the morphological features of the MFS and the location of face-selective regions, suggesting that their location will be determined by the anterior and posterior ends of the MFS, respectively. Alternatively, given the greater variability in the posterior than anterior aspect of the MFS (see *Results-Morphology*), there may be a stronger coupling between the anterior tip of the MFS and mFus-faces/FFA-2 than between the posterior tip and pFus-faces/FFA-1.

In order to quantify the structural-functional coupling between the MFS and face-selective regions, we positioned 1cm disks at the anterolateral and posterolateral limits of the MFS in

each hemisphere and determined the amount of overlap between these disks and face-selective ROIs (Figure 9; Materials and Methods). Our measurements reveal that the strongest functional-structural coupling occurs between the anterolateral tip of the right MFS and right mFus-faces/FFA-2 (Figure 9). Strikingly, $83\pm 7\%$ of the right mFus-faces/FFA-2 is located within a 1cm anatomical disk located on the anterior tip of the MFS (left: $66\pm 7\%$; significantly less than right $t(13)=2.4$, $p<.03$). Notably, and in support of the second hypothesis, the coupling between the anterolateral tip of the MFS and mFus-faces/FFA-2 is significantly stronger than the coupling between the posterolateral tip of the MFS and pFus-faces/FFA-1 which is about 50% (left: $50\pm 9\%$; right: $48\pm 9\%$; two-way repeated measures ANOVA with factors region and hemisphere revealing a significant main effect of region $F(1,13)=10.74$, $p < .006$). Critically, identifying the functional-structural coupling between face-selective regions and the MFS is more than twice as effective compared to the coupling of face-selective regions with Talairach coordinates. That is, repeating the same analysis with 1cm disk ROIs placed on the published Talairach coordinates of FFA-1 and FFA-2 (Pinsk et al., 2009) produces an average coupling of only $18\pm 4\%$ with each functional ROI (dashed lines in Figure 9). Thus, MFS-functional coupling is significantly better than Talairach-functional coupling (two-way repeated measures ANOVA using as factors ROI type (anatomical vs. Talairach) and hemisphere, showing a significant main effect of ROI type: $F(1,13)=31.04$, $p < .0001$). Together, these results reveal that irrespective of MFS type or length, the MFS is a stable identifier for mFus-faces/FFA-2, less so for pFus-faces/FFA-1, and both significantly better than Talairach coordinates.

To link these measurements to MFS morphology and the location of these regions relative to other macroanatomical landmarks such as OTS, CoS, and ptCoS, we illustrate four example hemispheres with various MFS morphological patterns (Figure 10; IOG-faces/OFA and OTS-limbs/FBA are also included to anchor the reader). Despite differences in morphological patterns, the anterior tip of the MFS (white in Figure 10) is coupled with mFus-faces/FFA-2. In the case of pFus-faces/FFA-1, the relation is less salient. In some brains the posterior tip of the MFS aligns with pFus-faces/FFA-1 (Subjects 1 and 3). However, in brains with a short MFS, the posterior tip of the MFS does not align with pFus-faces/FFA-1 (Subject 2). These data indicate that the anterior extent of the MFS is a stable macroanatomical landmark predicting the location of mFus-faces/FFA-2, but the morphological patterns of the MFS do not directly influence the cortical positioning of mFus-faces/FFA-2 or pFus-faces/FFA-1.

Discussion

The present findings provide empirical evidence demonstrating that the mid-fusiform sulcus (MFS) is a key macroanatomical landmark identifying both cytoarchitectonic and functional divisions of human ventral temporal cortex (VTC). Macroanatomically, the MFS is a shallow sulcus dividing the fusiform gyrus (FG) longitudinally and appears as one of four morphological patterns irrespective of age, gender, or hemisphere (Figures 1-3). Identifying the MFS in histological sections illustrates that the boundary between two cytoarchitectonic regions, FG1 and FG2, occurs within the sulcal bed of the posterior MFS (Figures 4-6). Additionally, the MFS shows tight structural-functional coupling at both large and fine spatial scales. At a large-scale, the MFS is a landmark identifying a lateral-medial functional transition in the eccentricity bias map in children, adolescents, and adults (Figures 7-8). At a fine-scale, the MFS identifies an anterior-posterior anatomical differentiation of two fusiform face-selective regions where the anterior tip of the MFS most tightly couples with mFus-faces/FFA-2 (Figures 9-10). In the sections below, we discuss how the correspondence of a macroanatomical landmark with both cytoarchitectonic and functional parcellations may develop in high-level sensory cortex and the implications of this correspondence for future research.

Stable morphological features of the MFS across children, adolescents, and adults

In the original observation of the MFS in modern writing, Puce and colleagues (1996) reported, “The fusiform gyrus often is divided by a longitudinal sulcus that can be confused with the collateral sulcus in isolated coronal slices” (p. 5207). Seventeen years later, our findings clarify the morphology of the MFS, identifying its shallowness as its hallmark morphological feature which discriminates it from the surrounding OTS and CoS. The difference in depth among these three sulci generates a distinctive “ω” pattern on coronal slices, which is identifiable from age 7 to 85 (the youngest and oldest subjects of our four studies, respectively). The stability of the MFS morphology across development makes it a particularly useful landmark to incorporate into studies examining the functional properties of the FG across age groups and populations (Golarai et al., 2006; Golarai et al., 2007; Scherf et al., 2007; Grill-Spector et al., 2008; Peelen et al., 2009; Golarai et al., 2010b; Golarai et al., 2010a; Cantlon et al., 2011), as well as histological studies across typical (Caspers et al., 2012) and atypical (Courchesne et al., 2005; van Kooten et al., 2008) populations. It would be particularly interesting to investigate if the MFS is present in newborns and if the structural-functional coupling we report here is already evident at birth. Importantly, identifying the MFS may (1) increase the precision of anatomical registration across subjects by increasing the inter-rater reliability of manual identification of sulci, which is lowest in VTC (Sowell et al., 2002), (2) improve the alignment among brains in atlasing projects using large cohorts of subjects (Van Essen et al., 2012a; Van Essen et al., 2012b), and (3) aid investigations of functional-structural correspondences using cortex based alignment methods (CBA; Frost and Goebel, 2012, 2013). While present studies applying CBA report substantial variability in the cortical positioning of functional regions along the length of the lateral FG (Frost and Goebel, 2012, 2013), inclusion of the MFS in future CBA techniques may substantially reduce this variability.

The MFS is a landmark identifying cytoarchitectonic and functional divisions of VTC

Understanding the morphology of the MFS allowed us to link cortical folding patterns to both cytoarchitectonic and functional divisions of the FG. Interestingly, both the cytoarchitectonic division between FG1 and FG2 and the functional division among peripheral and foveal representations occur along a medial-lateral axis relative to the MFS. That is, FG1 and peripherally biased voxels are located within the medial aspect of the MFS extending into the medial FG and CoS, whereas FG2 and foveally biased voxels are located within the lateral aspect of the MFS extending into the lateral FG and OTS. Given that cytoarchitectonic (FG1/FG2) and functional representations (peripheral-bias/foveal-bias) occupy the same macroanatomical expanse on either side of the MFS, and both within comparable distances from the MFS fundus on the order of 4mm within the MFS itself, our results suggest that differential neural hardware may implement differential computations on medial and lateral aspects of VTC. Our findings also raise new questions regarding the relationship between the underlying neural architecture with the functional properties of these regions. For instance: *Is the peripheral bias in medial VTC an outcome of the defining features of FG1, such as its columnar organization? How is the foveal bias in lateral VTC associated with the defining features of FG2, such as its lack of a columnar organization and increased neuronal density compared to FG1?*

From structure to function: Implications for cytoarchitectonic-functional coupling in VTC

Linking between cytoarchitectonic and functional divisions of VTC through their correspondence to the MFS is not limited to foveal and peripheral biases, but may extend to other large-scale maps and fine-scale clusters identified in VTC. For instance, recent fMRI studies in adults show that face- and place-selective regions are also reliably separated by the MFS (Weiner and Grill-Spector, 2010; Weiner et al., 2010; Nasr et al., 2011) indicating

the generality of the MFS as a functional landmark in VTC. In addition to eccentricity bias and category selectivity, lateral-medial functional gradients have also been found for animacy (Martin, 2007; Kriegeskorte et al., 2008; Mahon et al., 2009; Connolly et al., 2012), real-world object size (Konkle and Oliva, 2012), semantics (Huth et al., 2012), and retinotopy (Brewer et al., 2005; Arcaro et al., 2009; Kolster et al., 2010). Since the boundary of FG1 and FG2 occurs within the MFS, we predict that a functional component of each of these maps will align with respect to the MFS, which can be directly tested in future studies.

While our data suggest differential neural architectures on separate sides of the MFS, we caution that the correspondence between cytoarchitectonic and functional divisions are likely not one-to-one. First, while all of the maps mentioned above display a similar lateral-medial gradient, these maps are not identical in their spatial organization across the cortical sheet. For example, though the cortical representations differentiating faces from scenes and foveal from peripheral biases both illustrate a lateral-medial gradient, respectively, they do not overlap entirely (Hasson et al., 2002; Levy et al., 2001, 2004; Malach et al., 2002). Second, within these large-scale maps, the MFS-functional coupling may be different for fine-scale clusters. In the present study, we illustrated this with face-selective regions where there is a tighter correspondence between the MFS and mFus-faces/FFA-2 than for pFus-faces/FFA-1 (Figure 9). However, there are additional fine-scale clusters in both lateral VTC (e.g. for limbs, words, and objects: Grill-Spector, 2003; Peelen and Downing, 2007; Yeatman et al., 2012; Weiner and Grill-Spector, 2013) and medial VTC (e.g. several retinotopic maps: Brewer et al., 2005; Arcaro et al., 2009), making it highly probable that FG1 and FG2 each contain several fine-scale functional regions. Future research will determine how these many large-scale maps and fine-scale clusters tile cytoarchitectonic regions, as well as directly relate their overlapping and non-overlapping portions to the specific neural hardware of FG1 or FG2. Recent methodological advancements in non-invasive quantitative measurements of cortical anatomy, such as myeloarchitecture (Glasser and Van Essen, 2011; Dick et al., 2012; Sereno et al., 2012; Mezer et al., 2013), and subvoxel fMRI acquisitions (Zimmermann et al., 2011), might make this possible and may allow researchers to directly relate microarchitectural and functional boundaries within the same subjects.

What mechanisms may generate the cortical folding of the MFS and its correspondence with cytoarchitectonic and functional parcellations of VTC?

Several hypotheses (Zilles et al., 2013) have been proposed to explain the formation of cortical folding, including cell migration (Rakic, 1995, 2009), inhomogeneous cell growth across cortical layers (Richman et al., 1975), and tension generated by axonal connectivity in white matter (Van Essen, 1997). Interestingly, the tension-based hypothesis (Van Essen 1997) suggests that strongly connected regions will be located on different sides of a gyrus and that sulci may form from region-specific tensions pulling in opposite directions. Since both cytoarchitectonic regions FG1 and FG2 (as well as peripherally- and foveally-biased representations as measured in the present study) wrap around separate gyral components flanking the MFS, the tension-based hypothesis predicts higher connectivity within than between FG1 and FG2, which in turn generates a pull forming the MFS. Likewise, the model predicts higher connectivity within peripherally-biased representations medial to the MFS than between foveally- and peripherally-biased representations on different sides of the MFS. According to this scenario, the cortical folding of the MFS is a consequence of an interplay among cytoarchitectonic, connectivity, and functional demands. As the aforementioned theories of cortical folding (Richman et al., 1975; Rakic, 1995; Van Essen, 1997; Rakic, 2009) are not mutually exclusive (Zilles et al., 2013), future work is needed to shed light on how combinations of these proposed mechanisms may explain differing

relationships of macroanatomical landmarks with cytoarchitectonic and functional parcellations throughout the cerebral cortex.

Summary

In conclusion, the present study implemented a novel multimodal approach, combining measurements across macroanatomics, cytoarchitectonics, as well as both standard and high-resolution fMRI for the first time in human VTC. This unique method revealed that the mid-fusiform sulcus (MFS) is a macroanatomical landmark in human VTC identifying 1) a cytoarchitectonic lateral-medial division between areas FG1 and FG2, 2) a functional lateral-medial transition in a large-scale eccentricity bias map across age groups, and 3) a posterior-anterior discrimination of mFus-faces/FFA-2 from pFus-faces/FFA-1. We hypothesize that the lateral-medial cytoarchitectonic transition within the MFS provides a mechanistic explanation for the pervasive lateral-medial functional divisions of VTC more generally. Future studies will determine if other sensory and non-sensory cortical regions also exhibit a similar relationship among macroanatomical, cytoarchitectonics, and functional organization, or if this correspondence is specific to human ventral temporal cortex.

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Highlights

1. MFS identifies cytoarchitectonic and functional divisions of the fusiform gyrus.
2. MFS identifies the division between cytoarchitectonic areas FG1 and FG2.
3. MFS predicts functional transition in eccentricity bias map across age groups.
4. Structural-functional coupling between anterior MFS and mFus-faces/FFA-2.

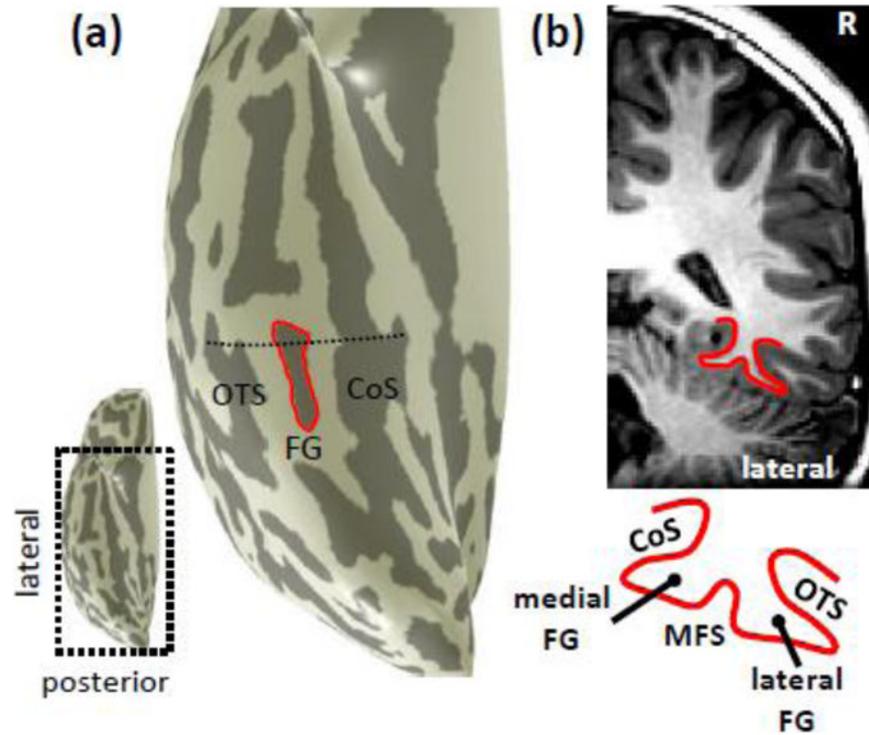


Figure 1. The mid-fusiform sulcus (MFS). Example right hemisphere from a ten-year old male
 (a) Inflated cortical surface with sulci illustrated in dark gray. The MFS (outlined in red) is a longitudinal sulcus dividing the fusiform gyrus (FG) into lateral and medial partitions, flanked by the occipito-temporal sulcus (OTS) laterally and the collateral sulcus (CoS) medially (inset for location of zoomed portion). (b) The MFS, OTS, and CoS have a distinctive ω pattern on single coronal slices where the MFS is the shallower sulcus flanked by the much deeper CoS and OTS. Top: Example coronal slice from the position of the dotted line in (a). Bottom: Schematic of the ω pattern of the MFS, OTS, and CoS.

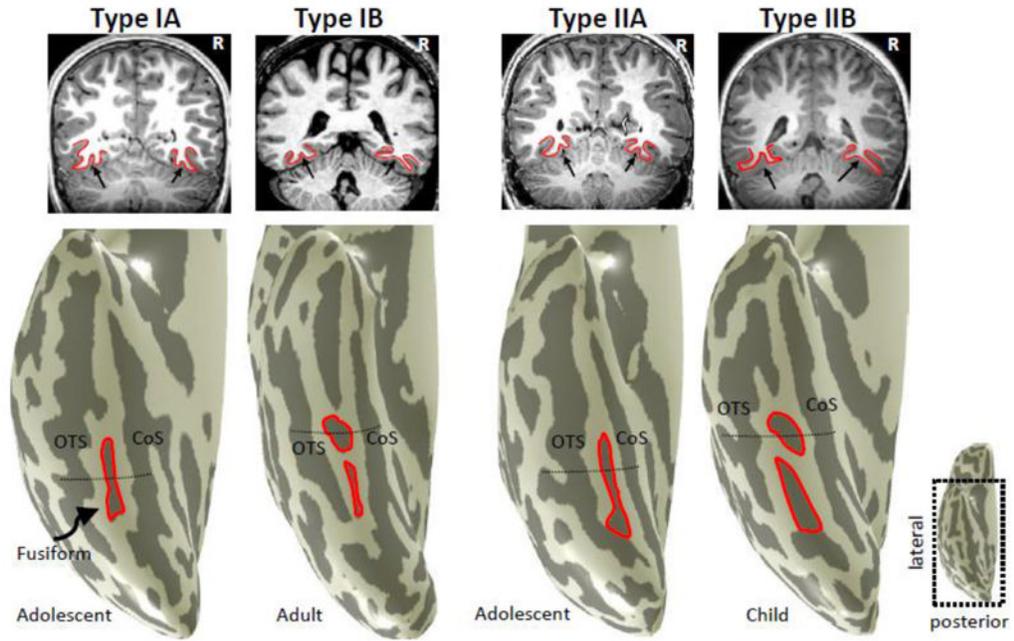


Figure 2. The four morphological patterns of the MFS

The MFS is outlined in red in both single coronal slices (top) and corresponding inflated hemispheres (bottom). Dotted lines indicate the location of the coronal slice. Note that the ω pattern described in Figure 1 persists on single coronal slices despite differences in fractionation and/or contiguity with surrounding sulci on the cortical surface. All patterns are equally likely across ages and hemispheres (Table 1). CoS: collateral sulcus; OTS: occipito-temporal sulcus.

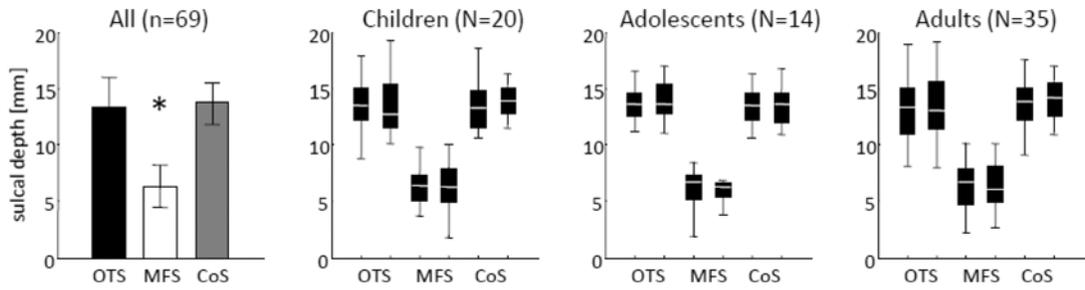


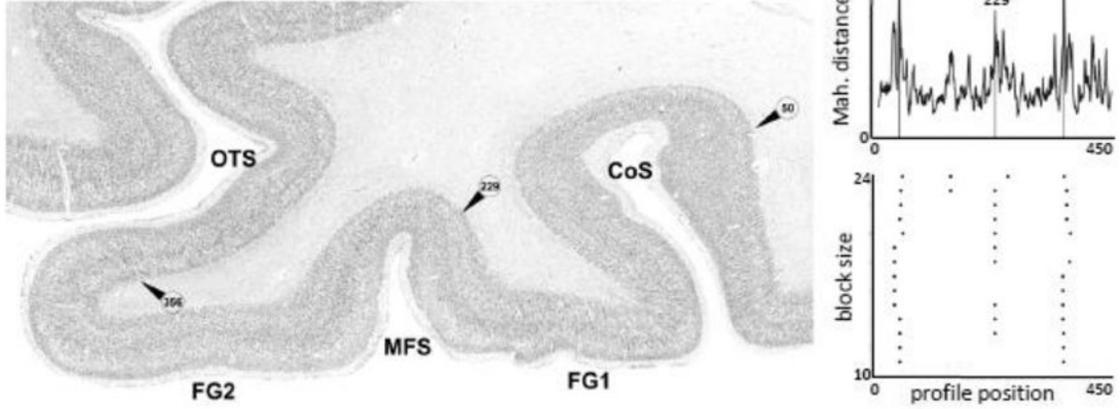
Figure 3. The CoS and OTS are more than two times as deep as the MFS

Leftmost panel: Each bar (+/-std) represents data averaged across hemispheres and subjects.

The MFS is significantly more shallow than either the OTS or CoS, * $p < 10^{-38}$.

Right panels: Boxplots of MFS depth indicating median, 25% and 75% percentiles, as well as range of minimum and maximum values separately for each age group. In each pair, the right hemisphere measurements are presented on the right.

Brain 6



Brain 3

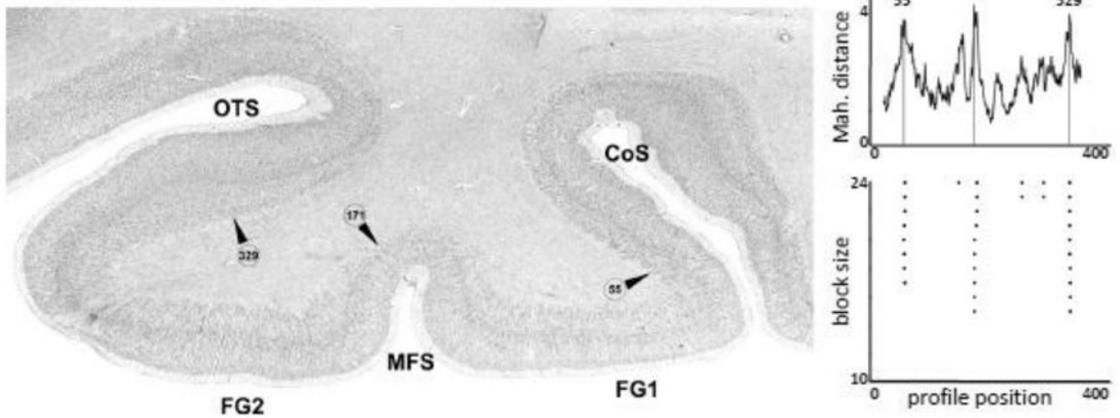


Figure 4. Cell body stained histological coronal sections through the fusiform gyrus of two different adult brains show that the boundary between FG1 and FG2 is in the MFS. Arrowheads with numbers indicate the positions of the cytoarchitecturally defined borders between FG1 and FG2 as well as between these areas and the surrounding cortex. The course of the Mahalanobis distance along the cortical ribbon is shown by the black curves on the right side of the figure. The respective graphs below the Mahalanobis curves demonstrate the independence of the position of the three significant Mahalanobis distances from the block size comprising immediately neighboring laminar profiles (for details of the observer-independent detection of areal boundaries see Materials and Methods: *Detection of FG1 and FG2 boundary*). Acronyms: CoS: collateral sulcus; FG1 and FG2 are cytoarchitectonical areas; MFS: mid-fusiform sulcus; OTS: occipito-temporal sulcus.

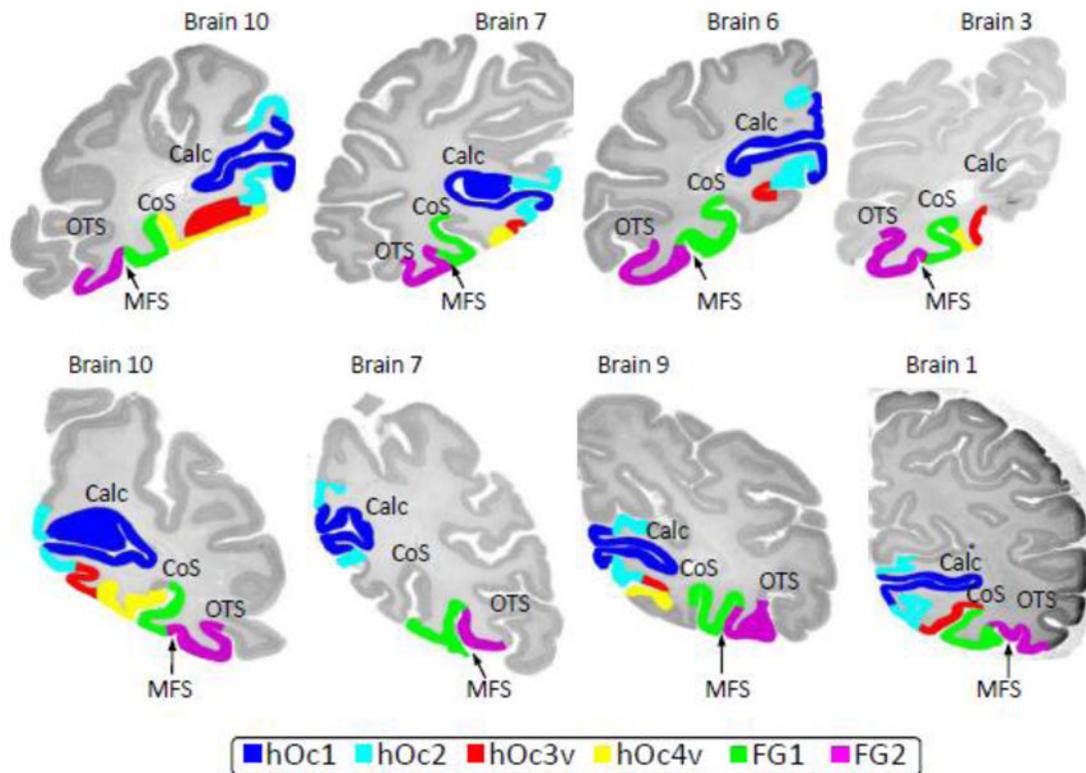


Figure 5. The MFS identifies the cytoarchitectonic boundary between FG1/FG2

8 example histological sections from 6 of the 10 brains within which FG1 and FG2 have been defined. Arrows indicate location of the MFS. Legend indicates color code for cytoarchitectonically defined regions hOc1, hOc2, hOc3v, hOc4v, FG1, and FG2. hOc1 and hOc2: from Amunts et al., 2000. hOc3v and hOc4v: from Rottschy et al., 2007. FG1 and FG2: from Caspers et al., 2012. h indicates that the area is defined in the human brain, and Oc indicates that it is in the occipital lobe. Calc: calcarine sulcus; CoS: collateral sulcus; FG: fusiform gyrus; MFS: mid-fusiform sulcus; OTS: occipito-temporal sulcus.

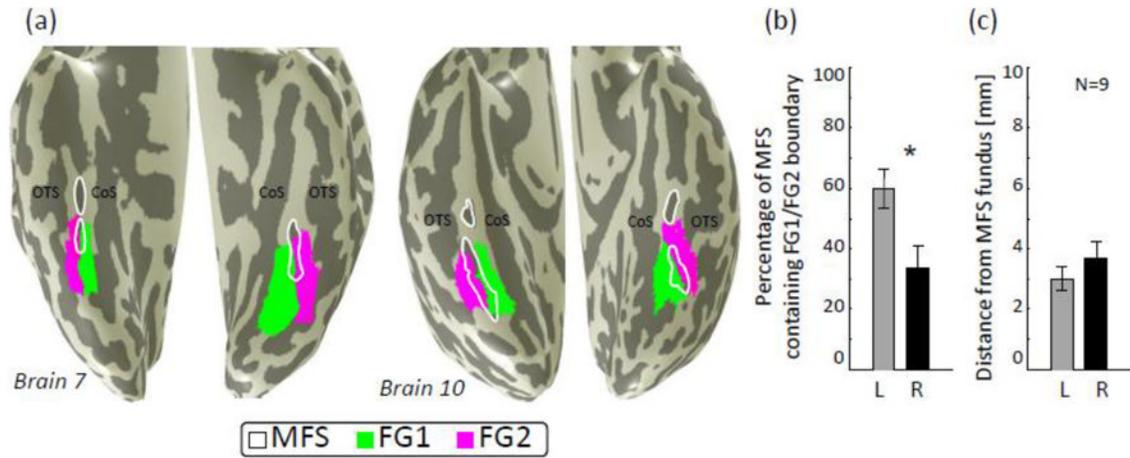


Figure 6. The boundary between FG1/FG2 occurs within the posterior extent of the MFS less than 4mm from the fundus

(a) Inflated cortical surfaces from two example postmortem brains showing the entire surface of VTC as well as the FG1 and FG2 cytoarchitectonic regions. *White*: MFS; *Green*: FG1; *Magenta*: FG2. (b) Percentage of the MFS containing the FG1/FG2 boundary; Asterisk: Left > Right, $p < .01$. (c) Average distance of the FG1/FG2 boundary from the MFS fundus. CoS: collateral sulcus; MFS: mid-fusifiform sulcus; OTS: occipito-temporal sulcus.

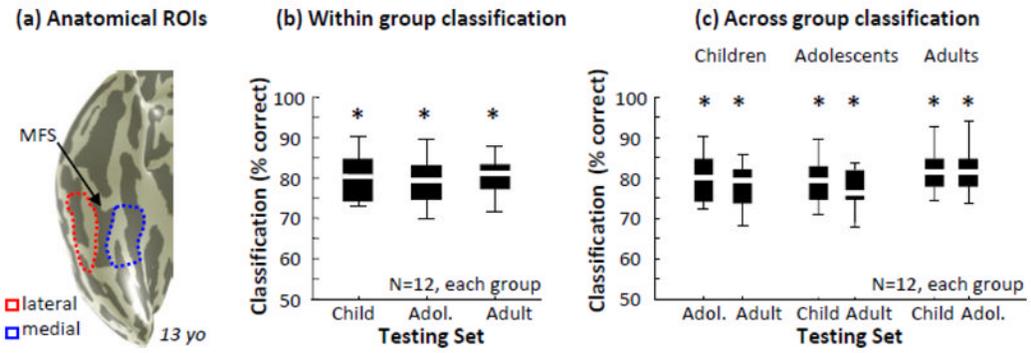


Figure 7. Classifying structural-functional relationships across age groups

(a) Inflated right hemisphere from an example subject. Blind to functional data, anatomical ROIs were defined lateral and medial to the MFS. (b) Within-group classification performance using a linear discriminant analysis (LDA) with a leave-one-out procedure. Within each age group, classification performance was significantly greater than chance (50%; $p < 10^{-13}$). (c) Across-group classification performance. The LDA was conducted by training on data from one age group and testing with data from each subject in the other age groups. Testing performance was above chance ($p < 10^{-10}$) for all classifications.

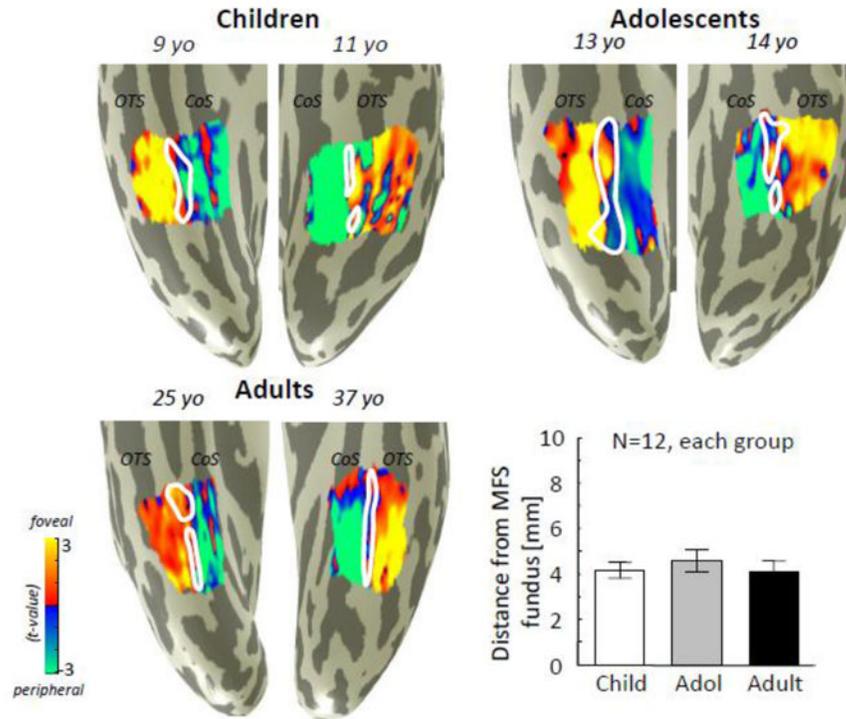


Figure 8. The MFS identifies a large-scale division in eccentricity bias representations across age groups where the transition from foveal- to peripheral-biased voxels occurs 4mm from the MFS fundus

Eccentricity bias measurements within the lateral and medial anatomical ROIs were mapped to the cortical surface to visualize the functional distinctions learned by the classifier. As illustrated in example right and left hemispheres from each age group, a majority of voxels lateral to the MFS (white outline) illustrates a foveal bias (warm colors), while a majority of voxels medial to the MFS illustrates a peripheral bias (cool colors). *Lower right:* Average distance between the MFS fundus and transition of eccentricity bias map averaged across subjects and hemispheres. CoS: collateral sulcus; MFS: mid-fusiform sulcus; OTS: occipito-temporal sulcus.

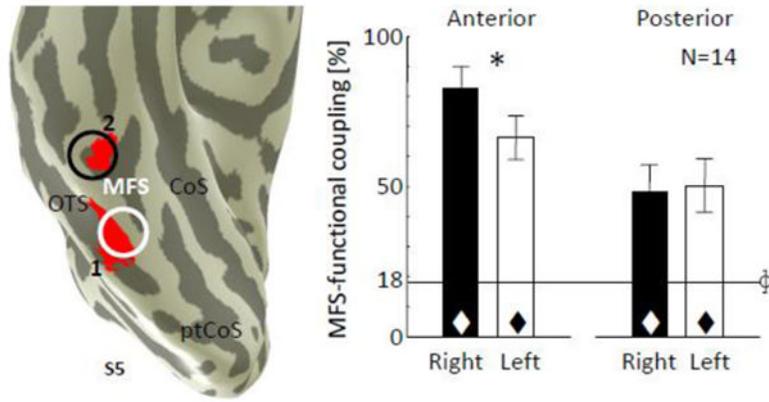


Figure 9. Structural-functional coupling is highest in the anterior tip of the MFS

Left: Inflated right cortical surface from one example subject. Red illustrates face-selective voxels corresponding to mFus-faces/FFA-2 (2) and pFus-faces/FFA-1 (1). Disks illustrate positioning of anatomical ROIs. Each disk was 1cm in diameter and positioned at the anterolateral (black) or posterolateral (white) tip of the MFS extending to the lateral FG. *Right: Bars:* Proportion of face-selective voxels that are contained within the anatomical disk ROIs described in image at left. *Dashed line:* Proportion of face-selective voxels that are contained within Talairach-defined disks centered on the coordinates of FFA-1 and FFA-2 from Pinsk et al., 2009. *right > left, $p < .03$. ◆ MFS-functional coupling > Talairach-functional coupling, $p < .02$.

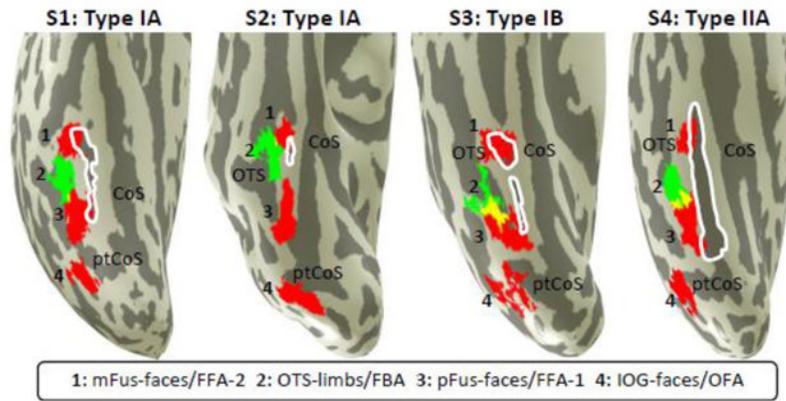


Figure 10. The MFS identifies a fine-scale division of face-selective regions irrespective of morphology

Face- (red) and limb-selective (green) parameter maps, as well as their overlap (yellow), as measured with high-resolution fMRI on four example right hemispheres with three different MFS morphological patterns. Irrespective of type or length in a given hemisphere, the MFS divides mFus-faces/FFA-2 from pFus-faces/FFA-1 along the length of the FG, where the anterior portion of the MFS tightly couples with mFus-faces/FFA-2 across subjects. CoS: collateral sulcus; OTS: occipito-temporal sulcus; ptCoS: posterior transverse collateral sulcus; MFS outlined in white. Red: faces > nonfaces, $t > 3$; green: limbs > nonlimbs, $t > 3$; yellow: overlap.

Table 1

Incidence characteristics of the mid-fusiform sulcus (MFS) in the right (RH) and left (LH) hemispheres.

	Child RH	Child LH	Teen RH	Teen LH	Adult RH	Adult LH	Total	Total %
<i>Type IA</i>	9/20	10/20	8/14	2/14	20/35	18/35	67/138	48.55%
<i>Type IB</i>	5/20	5/20	3/14	2/14	5/35	7/35	27/138	19.57%
<i>Type IIA</i>	5/20	3/20	2/14	6/14	7/35	6/35	29/138	21.01%
<i>Type IIB</i>	1/20	2/20	1/14	4/14	3/35	4/35	15/138	10.87%

Table 2

Talairach coordinates of the anterior and posterior tips of the MFS in the adult brain (n =35).

anterior	x	y	z
<i>Right (ave ± std)</i>	32 (3.79)	-41 (6.40)	-16 (4.19)
<i>Left (ave ± std)</i>	-31 (3.50)	-40 (6.18)	-17 (3.76)
posterior	x	y	z
<i>Right (ave ± std)</i>	28 (4.61)	-59 (8.38)	-13 (5.46)
<i>Left (ave ± std)</i>	-30 (3.94)	-62 (7.88)	-15 (3.74)