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Structural neuroplasticity of the superior temporal plane in early and late blindness

Hicret Atilgan [b], Olivier Collignon [a], Uri Hasson [b,*]

[a] Institute of research in Psychology (IPSY) & Institute of Neuroscience (IoNS), University of Louvain (UCL), Belgium
[b] Center for Mind/Brain Sciences (CIMeC), University of Trento, Italy

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ABSTRACT

Blindness is associated with well-documented changes to the morphometry and function of the occipital cortex. By comparison, its impact on the perisylvian regions in the superior temporal plane (STP) is poorly understood, with many studies reporting null findings on this issue. Here we re-approach this question using a morphometric analysis that relied on fine-scale, manual annotation of 13 sub-regions within the STP and that quantified both univariate and multivariate differences in morphometry. We applied these analyses to both cortical thickness (CT) and surface area (SA) data from congenitally and late blind, as compared to two matched sighted control groups. The univariate analyses indicated that for CT, no region differentiated blind from sighted, and for SA, two regions showed lower values for congenitally blind. Moreover, the multivariate analyses identified more robust signatures of plasticity in blindness. Specifically, pairwise regional correlations of CT values between contralateral regions were significantly higher for both blind groups as compared to sighted controls. A similar pattern for SA data was found for congenitally blind alone. Our findings indicate that blindness strongly impacts STP, resulting in a more coordinated pattern of interhemispheric morphometric development. We discuss implications for theories of language plasticity and models of neuroplasticity in the blind.

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1. Introduction

Studying the neuroplasticity of perisylvian regions that mediate speech, audition and lower-level language processing clarifies the dimensions on which the neurobiology of language develops and organizes. At its core, the underlying question is conceptually straightforward – which features of language organization are relatively fixed in the face of experience, and which aspects are flexible and change with experience?

There are not many human models for investigating experience-dependent neuroplasticity of language or speech functions on a life-long scale. For instance, extended musical training (e.g., Herholz & Zatorre, 2012) or multi-year verbal mnemonic training (Hartzell et al., 2016) are known to impact the morphology of the lateral temporal-lobe, and are associated with changes to cortical thickness (CT) and grey-matter density. Yet, such morphometric changes arise from acquiring a body of structured acoustic/verbal knowledge, and so in such cases, perisylvian regions may simply be (re)used for accommodating an additional auditorily-communicated meaning-based system. Similarly, for deaf individuals, changes in morphometry of auditory cortex likely arise from absence of normal function. An interesting exception is that of perinatal focal brain injury, a condition not typically associated with marked negative impact on language function (as opposed to the typical aphasia symptoms that arise for comparable injuries in adults). The functional neuroimaging literature suggests that reorganization after perinatal stroke manifests in more bilateral activity profiles during language comprehension (for review, see Levine, Beharelle, Demir, & Small, 2015). In particular, Dick, Raja Beharelle, Solodkin, and Small (2013) found that in this population, better receptive language performance associates with stronger inter-hemispheric (cross-lateral) functional connectivity of posterior superior temporal gyrus during story comprehension. This suggests that one aspect of language reorganization is not a shift to right-hemisphere activity but potentially increased coordination between the hemispheres.

Another life-long situation that strongly impacts auditory and language processing is blindness. For blind individuals, the need to compensate for the absence of visual input in order to efficiently interact with the world typically leads to enhanced abilities in the remaining senses. With respect to audition, a large number of studies have documented enhanced abilities in blind individuals, including pitch discrimination (Gougoux et al., 2004), auditory spatial processing (Lessard, Pare, Lepore, & Lassonde, 1998; Roder

* Corresponding author at: Center for Mind/Brain Sciences, Via delle Regole, 101, Mattarello (TN), Italy.
E-mail address: uri.hasson@unitn.it (U. Hasson).

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et al., 1999; Voss et al., 2004), auditory motion discrimination (Lewald, 2013) and ultra-fast speech processing (e.g., Dietrich, Hertrich, & Ackermann, 2013). A large body of neurobiological research suggests that in the blind, the occipital cortex supports auditory and higher-level language functions, at the sublexical (Arnaud, Sato, Menard, & Gracco, 2013) and post-lexical levels (Amedi, Floel, Knecht, Zohary, & Cohen, 2004; Amedi, Raz, Pianka, Malach, & Zohary, 2003; Bedny, Pascual-Leone, Dodell-Feder, Fedorenko, & Saxe, 2011; Bedny, Richardson, & Saxe, 2015), including auditory spatial processing (Collignon et al., 2011).

In stark contrast to such multiple demonstrations of large-scale reorganization (both functional and anatomical) within the blind's occipital cortex, there is little evidence for reorganization in auditory and speech-related systems within the superior temporal plane (STP), with some conflicting results as we detail below. This could perhaps explain why, to date, research on blindness has yet to strongly impact neurobiological models of language plasticity (for instance, in a recently published Encyclopedic volume on Neurobiology of Language [Hickok & Small, 2016], the term *Blindness* does not appear in the Index).

Some neuroimaging work (Stevens & Weaver, 2009) suggests that early blind exhibit altered auditory processing, as seen in reduced BOLD responses to tonal stimuli and reduced spatial extent of lateral temporal cortex showing tonotopic responses in the blind. In contrast, an MEG study (Elbert et al., 2002) of this issue concluded that in these regions there exists a more extensive tonotopic representation for the blind. Another study (Coullon, Jiang, Fine, Watkins, & Bridge, 2015) found that for blind, thalamic middle geniculate nucleus responses are equally strong for ipsilateral and contralateral auditory stimuli (as opposed to the typical contralateral bias in sighted), suggesting changes in cortico-thalamic communication. Lane et al. (2016) found stronger bilaterality for language processing in congenitally blind, documenting a significantly reduced left-lateralized response for sentential stimuli (though that study examined lateralization in a network consisting of both inferior frontal regions and regions outside STP). Finally, it has been suggested that changes to auditory processing are not specifically linked to changes within perisylvian regions, but to the way auditory/language functions merge with visual cortex, and some findings (Schepers, Hipp, Schneider, Roder, & Engel, 2012) suggest that auditory inputs produce stronger gamma-band synchronization between auditory and visual cortices in blind.

With respect to potential anatomical reorganization of STP in blind, to our knowledge, no prior study has conducted a detailed examination of this topic, and few have documented morphometric changes in this area. These null findings are not due to a lack of investigation into this question, as almost all prior studies that examined structural changes in occipital cortex in the blind had also probed for morphometric changes in auditory cortex. Voss and Zatorre (2012) conducted a whole brain analysis of CT and did not document differences in auditory regions, and similar null results were reported by Jiang et al. (2009) and Anurova, Renier, De Volder, Carlson, and Rauschecker (2015). Modi, Bhattacharya, Singh, Tripathi, and Khushu (2012) conducted a whole brain voxel-based morphometry (VBM) analysis, which did not implicate either STP or the superior temporal gyrus (STG). Lepore et al. (2010) reported large reductions of volume in occipital cortex but none in the temporal lobe. A study examining thalamic and mesencephalic structures in blind (Cecchetti et al., 2015) largely supported the null findings above: thalamic subregions linked to visual afference/efference in the lateral geniculate nucleus showed marked reductions in volume for the blind, whereas thalamic subregions linked to auditory/motor processing in middle geniculate nucleus did not show any signs of change. An exception to these null findings is a study by Park et al. (2009); they conducted a whole brain analysis using CT, cortical surface and VBM and reported reduced CT in a small section of right posterior STG (congenitally blind < sighted) and left posterior STG (late blind < sighted).

We note however that whole-brain analyses may be particularly underpowered for documenting structural differences in STP. Within that region, auditory areas with highly different anatomical and functional features (e.g., primary and secondary cortices) are arranged in close physical proximity, and in a manner that may result in patchy results. For instance, the secondary association cortices in planum polare (PP) and planum temporale (PT) are divided by a primary auditory region in the transverse temporal gyrus and sulcus. Consequently, any morphometric differences may be limited to small patches of cortex that will not survive typical whole-brain cluster-based corrections (where clusters need to exceed a certain size). Another limitation of prior research is that all prior studies had examined data that are essentially *uni*variate, i.e., single-voxel or single-region morphometry. As we detail below, our current study addressed both these limitations: (i) we examined univariate features at a regional scale with higher resolution, and (ii) we considered multivariate covariance in morphometric features among regions, which is a method that offers a unique insight into processes of neural plasticity. Our analyses focused on STP, which incorporates the primary and secondary auditory association cortices in the human brain. Its main subsections are the PT and PP – the posterior and anterior auditory association cortices – and the transverse temporal gyrus and sulcus (TTG, TTS). We delineated these regions manually on the single participant level, and within them we further differentiated the lateral and medial aspects of TTG and TTS, as well as the posterior, middle and anterior sections of PT. We further included the posterior aspect of the Sylvian fissure (lateral sulcus) as another region of interest, itself divided into anterior and posterior sections. In addition, given the importance of STG for speech processing, we considered this area, dividing it into posterior, middle and anterior sections. In all, we defined 13 subsections per hemisphere, manually parcellated per each individual (see Fig. 1 for schematic). After delineating these regions, we examined their morphometric features for congenitally blind, late blind, and two age-matched control groups.

To address the univariate measures, we first evaluated regional differences in magnitudes of cortical thickness and surface area within STP regions. Our second aim was to determine covariation patterns in morphometry of STP. Covariance analyses (also termed 'structural correlations'; Alexander-Bloch, Giedd, & Bullmore, 2013) quantify the degree to which any two brain regions show covariance in morphological features (e.g., CT, SA) across individuals. These pair-wise regional correlations contain meaningful functional information, in that networks constructed from these produce partitions that are similar to functional ones (e.g., between auditory and visual systems; Chen, He, Rosa-Neto, Germann, & Evans, 2008). In a prior study (Hasson, Andric, Atilgan, & Collignon, 2016) we studied whole-brain structural connectivity of CT networks in congenitally blind and sighted, using a gross regional parcellation suitable for deriving whole-brain networks (specifically, all STP subregions as well as the STG were treated as a single region). We documented changes to the partition structure of whole-brain structural networks in congenitally blind, pointing to a stronger "merging" of areas involved in language and visual functions within shared modules. We did not however examine STP in detail, and the covariance-related changes we documented could, in the limit, have resulted from changes restricted to occipital regions without concomitant changes in the structure of STP.

The goals of our current study were to determine whether there is any specific change to STP morphometry in the blind, relying on both univariate and multivariate features of this region. Departing

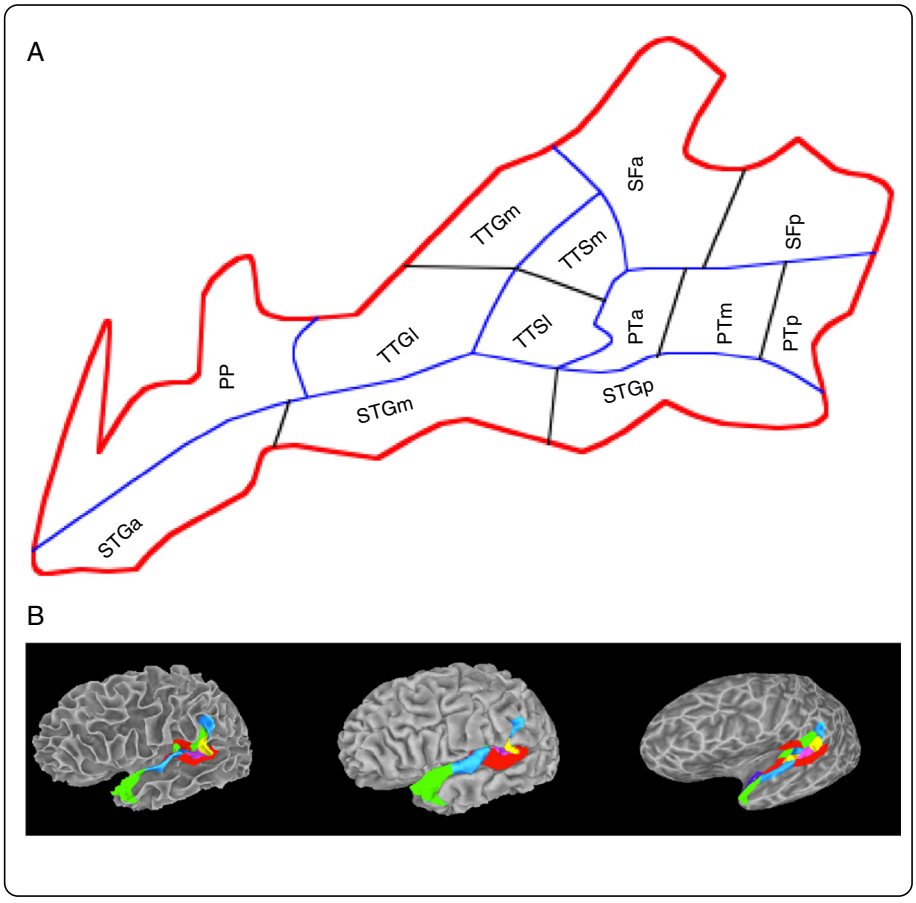

Fig. 1. Manual parcellation of superior temporal plane. Panel A: Schematic parcellation of SRP. suffixes 'a', 'm', 'p' for STG PT and SF indicate anterior, middle and posterior. The suffixes 'l' and 'm' for TTG and TTS indicate lateral and medial. Panel B: A depiction of the sub-regional parcellation projected on a cortical surface of a sample participant. The leftmost view shows the location of the 13 regions projected on a white-matter surface projection. The middle view is a projection on the pial surface, and shows (in green, blue, and red) the 3 subsections of STG. The rightmost image shows all 13 regions on an inflated surface. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

from our prior work, we focused on STP regions, relied on a finer parcellation described above, and examined both CT and SA patterns, as these have been shown to load on different latent factors in auditory cortex (Meyer, Liem, Hirsiger, Jancke, & Hanggi, 2014). In addition, we studied both congenitally and late blind participants (vs. two matched control groups). Given Lane et al.'s (2016) findings of more bilateral language activation in blind, we studied structural co-variance patterns both ipsilaterally (intra-hemispheric) and contralaterally (inter-hemispheric). In all, these analyses allowed drawing conclusions about any blindness-related changes in structural features of STP, a region previously considered as showing limited reorganization in the blind. To foreshadow our results, we found a few univariate differences, but much stronger differences in multivariate organization.

2. Methods

2.1. Participants

The Blind participant groups consisted of 18 congenitally blind (CB: 7 female, mean age: 44.1 ± 13.7 [SD here and in all other reports of dispersion]; 11 male, mean age: 42.45 ± 12.44) and 10 late blind (LB: 7 female, mean age: 52.0 ± 6.8; 3 male, mean age: 53.0). Two control groups (N = 18, N = 10) matched to the CB and LB groups on age and gender distribution (mean age for; CB-male controls: 40.0 ± 6.9; CB-female controls: 45.6 ± 14.6; LB-male controls: 51.6; LB-female controls: 51.6 ± 7.45). All participants in the two control groups were right handed. Of the early blind, 16 were right handed and 2 were potentially ambidextrous (though not left handed). Of the late blind, 9 of the 10 were right handed. Blindness etiology is given in Appendix.

2.2. Acquisition and preprocessing pipeline for structural Images

Structural data used in this study were collected at the functional neuroimaging unit (UNF) of the University of Montreal, Canada. Images were obtained using a 3T TRIO TIM system (Siemens, Erlangen, Germany) equipped with a 12-channel head coil. Anatomical data was acquired using a T1-weighted 3D magnetization prepared rapid acquisition gradient echo sequence (MPRAGE) with the parameters: voxel size $1 \times 1 \times 1.2\ mm^3$; matrix size 240×256; TR 2300 ms; ET 2.91 ms; TI 900 ms; FoV 256; 160 slices.

Processing of structural data was performed using Freesurfer version v5.3.0 (Massachusetts General Hospital, Harvard Medical School). The pre-processing pipeline (Dale, Fischl, & Sereno, 1999; Fischl, Sereno, & Dale, 1999) consisted of non-brain tissue removal, Talairach transformation, white matter and grey matter segmentation, intensity normalization, topology correction, surface inflation, atlas registration, and parcellation of the cerebral cortex. Each of these automatically executed steps was followed by quality control assessments implemented jointly by H.A and U.H. Interventions based on this quality control step consisted of:

(1) replacing low quality structural scans with better alternate scans (3 sighted; 1 blind), (2) manual Talairach alignment (n = 2; both blind), (3) manual adjustment of the skull stripping procedure to assure that dura matter or meninges were not falsely recognized as grey matter or white matter (9 sighted; 6 blind), (4) correction of missed labelling of white matter (2 sighted; 2 blind), and (5) use of control points to correct the intensity normalization of white matter (2 sighted; 3 blind). Scans defined as low quality were subjectively defined when extensive motion artifacts were noted. The manual edits were performed in a manner that was partially agnostic to group assignment. Author H.A who was aware of group membership conducted an initial-pass edit. Next, author U.H who examined each dataset and specified further edits (or changes to prior edits) was blind to group membership.

2.3. Regions of interest

The final FreeSurfer output was exported to GIFTI format and processed in SUMA, part of the AFNI software suit where we performed a manual region-of-interest annotation. We defined our ROIs according to procedures previously used in our lab for parcellation of STP (Tremblay, Baroni, & Hasson, 2013), which consists of marking 13 subregions in STP and STG. The manual annotation proceeded as follows: from the automatic FreeSurfer parcellation we obtained an initial delineation of planum temporale, transverse temporal sulcus, transverse temporal gyrus, planum polare (PT, TTS, TTG, PP), STG and the caudal segment of the Sylvian fissure. We manually corrected the boundaries of these regions in all cases. Then, we further split several of these regions into approximately equally sized region: STG into an anterior, middle and posterior segment (STGa, STGm, STGp), TTG and TTS into lateral/medial segments (TTGl, TTGm, TTSl, TTSm), PT into an anterior, middle and posterior segment (PTa, PTm, PTp), and the caudal segment of the Sylvian fissure was itself divided into 2 units (termed SFa and SFp). Fig. 1 shows a schematic of this parcellation.

The protocol for delineating PP, PT, TTS, TTG, SF and STG has been detailed in our prior work (Tremblay et al., 2013) and for this reason is not re-reported here. We were particularly concerned with delineation of TTG, a gyrus that shows considerable morphological variability across participants, frequently presenting either a partial or complete duplication, where the two gyri are separated by an intermediate sulcus (of Beck). In cases of a single gyrus, primary auditory cortex (PAC) is thought to reside in the medial part of TTG (Da Costa et al., 2011). Da Costa et al. (2011) further present data indicating that in cases of a split, PAC subsumes both anterior and posterior TTG. To define TTG and TTS areas we therefore followed the protocol defined in study by Marie et al. (2013) and Da Costa et al. (2011). Duplications were defined by the presence of an intermediate sulcus, which runs parallel to TTS and divides the TTG, either partially or completely. In cases of such splits we defined both anterior and posterior aspects as TTG proper. The mean CT in each manually annotated region, as well as the region's overall surface area were extracted per each participant, and formed the core data of the study.

2.4. Consideration of covariates and normalization for univariate and multivariate analyses

Age related changes to CT are extensive and well documented (Giedd, 2004; Gogtay et al., 2004), and some prior studies of CT covariance had partialed age-related variance prior to calculating CT covariance patterns (Chen et al., 2008; Lerch et al., 2006). Yet, it is also known that in adults, not all brain regions show a linear relation between age and CT (e.g., Thambisetty et al., 2010). For this reason, and given that we tightly controlled for age across sighted and blind, we report analyses with the variance attributed to age not partialed from CT or SA data. None of the reported results, either univariate or multivariate, were altered when age was partialed out. Also, due to the age difference of the congenitally and late-blind groups, we established separate control groups for each, as patterns of structural covariance can also change with age (e.g., Montembeault et al., 2012).

We also had to decide whether to perform the univariate and multivariate analysis on CT and SA values normalized by whole brain volume or SA. Given that the blind may have lower mean whole-brain SA due to the massive reduction of SA in occipital regions (Park et al., 2009), we were concerned that normalizing each region's SA value by whole-brain SA could artificially bias comparisons of SA values in STP regions: all else being equal for STP regions, normalization could wrongly suggest greater (normalized) SA for blind.

All analyses were corrected for multiple tests using FDR correction. In addition, to allow comparing our results to some prior reports that did not use FDR correction we also note those tests that were statistically significant prior to, but not after FDR correction.

2.5. Covariance analyses

When evaluating correlations between cortical thickness values in each region against all other regions we conducted two types of analyses. The first considered the covariance of the entire set of regions (both ipsi- and contra-lateral). The second analysis first considered contralateral connects, where participants' CT (or SA) values for each region was correlated with that of all contralateral regions, and then ipsilateral connections, where CT of each region was correlated with that of all ipsilateral regions.

For the CT covariance analysis we used the detailed 13-region manually annotated parcellation. For the SA covariance analysis we however used FreeSurfer's 6-region parcellation (PP, PT TTG, TTS, STG and posterior SF), after manual corrections of these regions' boundary when needed. This was due to the fact that by splitting some of these regions into equally-sized subregions (as described in our protocol) we would necessarily introduce (spurious) correlations among these subregions when correlation is calculated across participants. To illustrate, dividing TTG into medial and lateral sections necessarily induces (across participants) two very similar SA vectors whose correlation will approach unity. Note this is not a concern for CT as there is no mathematical necessity that CT in subdivisions would be highly similar (this is indeed one of the questions addressed by the covariance analysis).

2.6. Group prediction from morphometric patterns

To determine whether the spatial distribution of CT (or SA) values differentiated blind from sighted we used Partial Least Squares (PLS) approach, which is a multivariate method that evaluates to what extent latent factors in a predictive datasets (a matrix) can account for variance in a variable of interest (for review, see Krishnan, Williams, McIntosh, & Abdi, 2011). Here we evaluated to what extent morphometric patterns in STP (either CT or SA, coded in a [Participants $\times$ Regions] table) co-varied with group membership; i.e., blind or sighted. We derived the root-mean-square error of prediction (RMSEP) that existed in the data, and evaluated that value against a sampling distribution derived from 5000 permutations. In each permutation the group-membership labels (blind/sighted) were resampled and the permutation-related RMSEP value saved. Importantly, prior to implementing PLS we mean-normalized the regional morphometric values within each participant. This means that prediction could not be driven by absolute differences in morphometric values between the groups (which we tested in the univariate analyses) but could only reflect

relative differences in values within the topography of STP. The RMSEP of the actual data needed to be lower than the 5th percentile value of the sampling distribution in order to be considered statistically significant.

3. Results

Our analyses included both univariate analyses on the regional level and multivariate analyses examining the magnitude and structure of correlation patterns in STP for blind and sighted. Table 1 provides a qualitative summary of the findings that are then reported in detail.

3.1. Whole-brain mean CA and SA values

For the CB vs. CBctrl contrast we found no difference for whole-brain mean CT. For LB vs. LBctrl we found greater CT for LBctrl in both left hemisphere (2.38 ± 0.09 vs. 2.28 ± 0.11, $t_{(18)} = 1.94$, $p = 0.034$) and right hemisphere (2.38 ± 0.09 vs. 2.28 ± 0.10, $t_{(18)} = 1.85$, $p = 0.04$). A converse finding was found for SA. As expected, whole-brain SA was lower for CB than CBctrl in both hemispheres: left (85,057 ± 6620 vs. 78,578 ± 7626, $t_{(34)} = 2.45$, $p = 0.01$); right (85,875 ± 6740 vs. 78,916 ± 7416, $t_{(34)} = 2.67$, $p = 0.005$). The LB vs. LBctrl tests produced null results ($ps > 0.5$).

3.2. Cortical thickness

3.2.1. Differences in cortical thickness within STP

There were no statistically reliable differences in CT, for any STP subregion, for either the CB or LB group vs. their matched controlled groups. This was evaluated via a series of 2 (Group: Blind vs. matched-control) × 2 (hemisphere: Left, Right) ANOVAs for each of the 13 regions. For the analyses of CB vs. CBctrl, none of the effects survived FDR correction (for ANOVA main effect and interaction tests in 13 regions = 26 tests in all). For the analysis of LB vs. LBctrl, ANOVAs revealed only a main effect of group for STGa ($p = 0.003$ *un*corrected) that was not significant after FDR correction; LB showed reduced CT (M = 2.99 mm vs. 3.22 mm in LBctrl). We also conducted an omnibus analysis collapsing across all regions' CT per participant. Student's *T*-tests indicated no difference in mean CT of STP regions between CB and CBctrl or LB and LBctrl. To conclude, we found little evidence for local changes in absolute CT values, for either CB or LB.

3.2.2. CT covariance patterns

We first examined the entire CT cross-correlation matrix that consisted of 26 regions (13 in each hemisphere; see Fig. 2). We then separately examined ipsilateral and contralateral correlations. Prior to evaluating differences in correlation strength, correlation values were Fisher-Z transformed to normalize the distribution.

Examining the entire (26 × 26 region) CT matrix we found a moderate and statistically significant correlation between the regional covariance structure found for CB and CBctrl, Pearson's $R = 0.29$, $t_{(323)} = 5.30$, $p < 0.001$. In contrast, there was no significant similarity between the covariance structure of the LB and LBctrl groups, Pearson's $R = -0.06$, $t_{(323)} = -1.2$, ns.

We then examined the actual magnitude of correlation values. When computed for the entire covariance matrix, correlations were significantly higher for CB than CBctrl ($t_{(324)} = 3.26$, $p < 0.001$, mean difference of Fisher-Z values = 0.054). Correlations were also significantly higher for LB than LBctrl ($t_{(324)} = 10.00$, $p < 0.001$, mean difference of Fisher-Z values = 0.30).

We then divided this analysis to examine correlation values separately for contralateral and ipsilateral sets of regions. *Contralateral correlations* (between each region and each of the contralateral regions; see Section 2) were stronger for CB than CBctrl (Mean difference of Fisher-Z values = 0.08, $t_{(168)} = 3.56$, $p < 0.001$). Contralateral correlations were also stronger for LB vs. LBctrl (Mean difference of Fisher-Z values = 0.29, $t_{(168)} = 6.69$, $p < 0.00001$).

Ipsilateral correlations were stronger for LB than LBctrl (Mean difference of Fisher-Z values = 0.32, $t_{(155)} = 7.5$, $p < 0.0001$). However, these connections were *not* stronger for CB than CBctrl ($t_{(155)} = 1.04$, p = 0.297). To summarize, as compared to control groups, LB showed both stronger ipsilateral and contralateral correlations, whereas CB only showed stronger contralateral correlations. This was accompanied by a more similar covariance matrix structure for CB than LB.

3.3. Surface area

3.3.1. Differences in surface area within STP

A set of ANOVAs (2 Group [Blind vs. matched control] × 2 Hemisphere) conducted for each of the 13 regions identified two areas where SA was greater for CBctrl (FDR corrected for 13 tests of Group main effect and 13 interaction terms). These were lateral TTG, $F(1,34) = 11.42$, $p = 0.0018$ (M = 282 ± 82 vs. 218 ± 57), and PP, $F(1,34) = 17.23$, $p < 0.001$ (M = 466 ± 87 vs. 370 ± 81). Interaction terms with Hemisphere did not approach significance. Several other regions also showed a main effect of Group – all with greater SA for CBctrl – but did not survive FDR correction: middle STG, $F(1,34) = 5.86$, $p = 0.02$, anterior STG, $F(1,34) = 5.93$, $p = 0.02$, anterior SF, $F(1,34) = 4.21$, $p = 0.05$. Overall, the surface area for all STP regions was higher for CBctrl, $t_{(32)} = 3.58$, $p = 0.001$.

When comparing SA for LB vs. LBctrl we did not find any region where the Group effect approached significance. There was a single region showing a Group x Hemisphere interaction but this did not survive FDR correction for 26 comparisons. There was no significant difference between the overall surface area of the LB and LBctrl groups (p = 0.7). To conclude, there were a few regions where SA was greater for CB than CBctrl. A partial-least-squares

Table 1
Summary of main findings.

Morphometric measure	Congenitally blind		Late blind	
	CT	*SA*	*CT*	*SA*
Whole brain	–	CB < CBctrl	LB > LBctrl	–
Regional differences in STP	–	✓	–[a]	–
Group prediction from normalized regional values	–	–	–	–
Similarity of entire covariance matrix to controls	Moderate	Moderate	Minimal	Minimal
Correlation strength				
For entire covariance matrix	CB > CBctrl	CB > CBctrl	LB > LBctrl	–
For contralateral connections only	CB > CBctrl	CB > CBctrl	LB > LBctrl	–
For ipsilateral connections only	–	CB > CBctrl	LB > LBctrl	–

[a] One region significant prior to FDR correction.

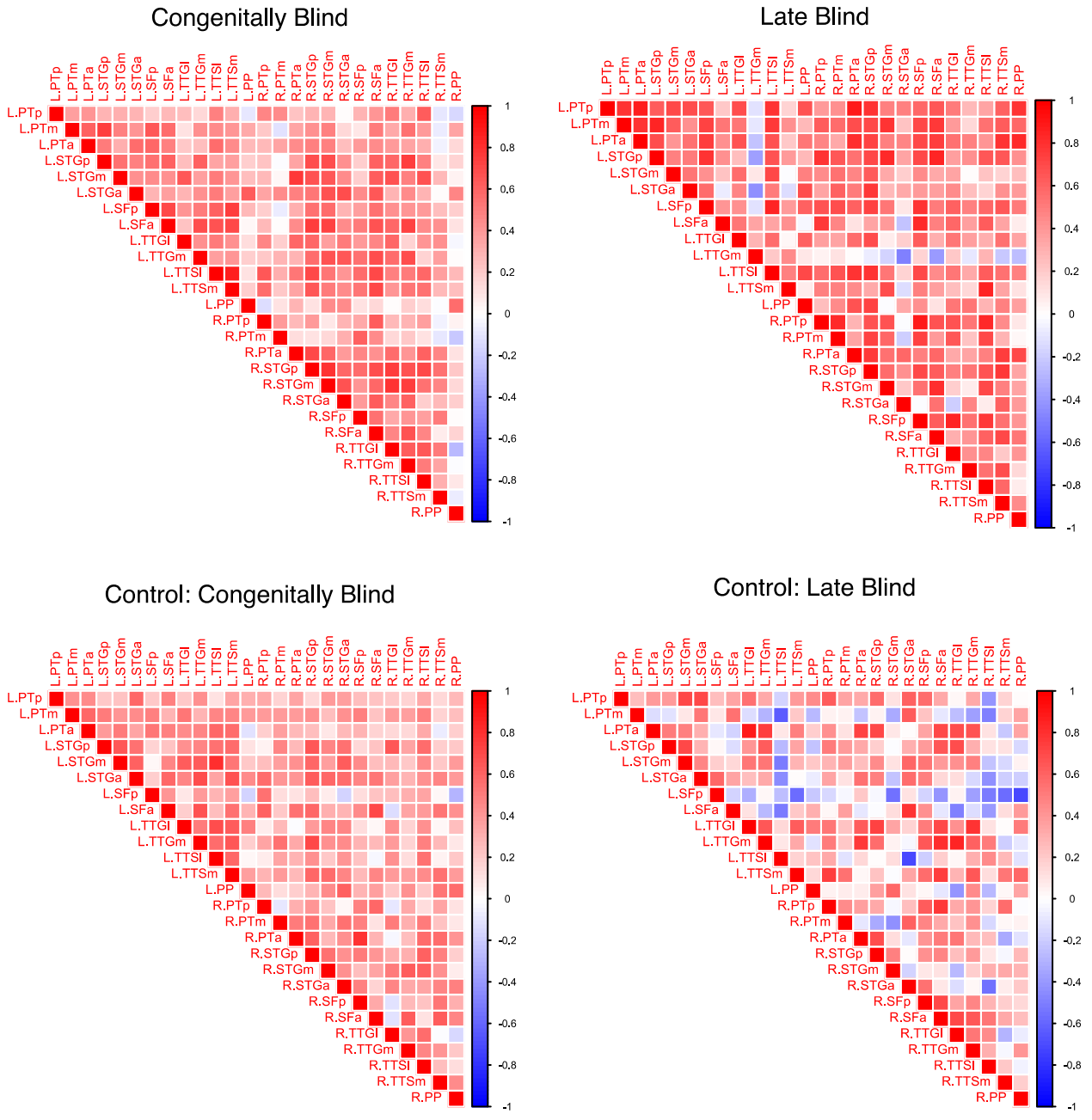

Fig. 2. Covariance matrices for cortical thickness.

regression conducted on mean-normalized SA values in STP subregions could not discriminate neither the congenitally nor late blind from the matched control groups.

3.3.2. SA covariance patterns

For the SA covariance analyses we used the manually-corrected 6-region FreeSurfer parcellation: PP, PT, TTG, TTS, STG and posterior SF rather than the more detailed partitioning (see Section 2).

Considering the entire 12 × 12 covariance matrix (see Fig. 3), there was moderate similarity between the SA covariance patterns for CB and CBctrl ($t_{(64)} = 2.65$, $R = 0.31$, $p = 0.01$). There was however no significant similarity between the covariance structure of LB and LBctrl, Pearson's $R = 0.16$, $p = 0.19$).

We then examined the actual magnitude of correlation values. Considering the entire 12 × 12 covariance matrix, correlations were significantly higher for CB than CBctrl ($T_{(65)} = 4.53$, $p < 0.001$, mean differences = 0.17). There was no significant difference in correlation strength between LB and LBctrl ($p = 0.07$).

As we had done for the CT values, we conducted further analyses of covariance magnitude between contralateral sets of regions and ipsilateral sets. *Contralateral correlations* were stronger for CB vs. CBctrl (Mean difference of Fisher-Z values = 0.18, $t_{(35)} = 3.24$, $p < 0.003$). No significant difference was found for LB vs. LBctrl. *Ipsilateral correlations* were stronger for CB than CBctrl (Mean difference of Fisher-Z values = 0.16, $t_{(29)} = 3.19$, $p = 0.003$). However, these connections were again not stronger for LB than LBctrl ($p = 0.59$).

4. Discussion

Our results point to two facets of structural reorganization of STP morphometry in blind. First, on the single-region level, uni-

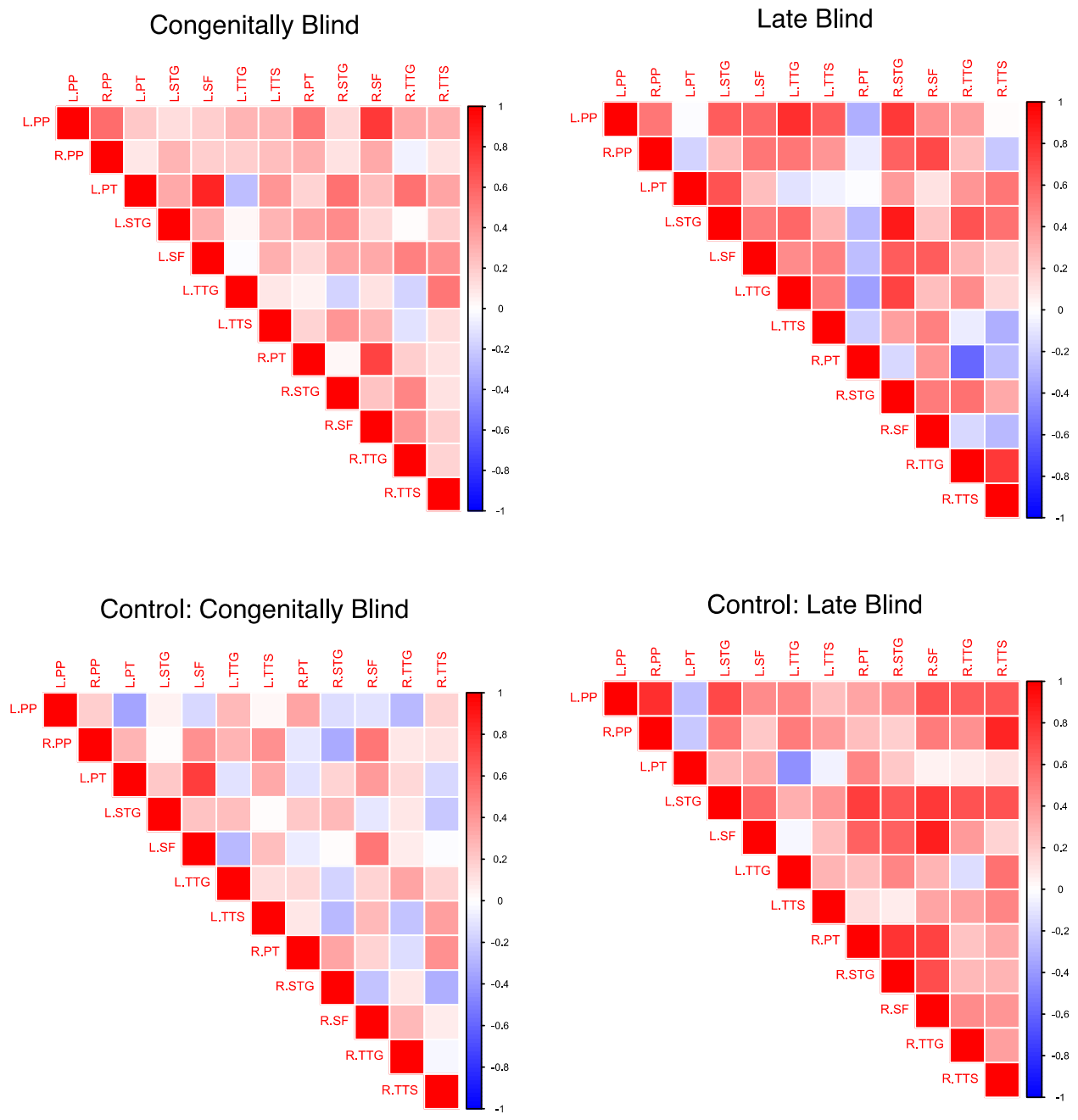

Fig. 3. Covariance matrices for surface area.

variate analyses indicated significant reduction in surface area of lateral TTG and PP for congenitally blind. No differences were found for cortical thickness on the single-region level. For all these single-region analyses, no differences were found for the late blind group.

Second, much more robust differences were seen in multivariate parameters reflecting the correlation among cortical thickness in subregions of STP. For CT, the overall similarity structure of the correlation matrices was moderate for CB vs. matched controls, and extremely low for LB vs. matched controls. The exact same pattern was found for the correlation matrices derived from surface area covariance. This suggests that late blindness alters the correlation structure of both cortical thickness and surface area. Changes to the structure of the covariance matrix were further accompanied changes to the strength of correlations: regional pair-wise correlations were consistently stronger in the two blind groups. Specifically, for CT we found that (as compared to controls) contralateral (inter-hemispheric) CT correlations were stronger for both blind groups, and the LB also showed stronger ipsilateral correlations. For SA we found that both ipsi- and contralateral correlations were stronger for CB than controls, but there was no difference in the magnitude of correlations for LB. In what follows below we discuss the implications of these findings for theories of reorganization of auditory and language processing and for theories of structural neuroplasticity in the blind.

4.1. Relation to theories of neuroplasticity of language

It is useful to discuss our findings in relation to one of the better-studied models of language-related neuroplasticity – that

of Aphasia – particularly concerning left hemisphere inferior frontal, premotor and superior temporal regions. As noted in earlier neuropsychological reviews (Thompson, 2000), functional recovery of language in aphasia demonstrates two strong signatures: homologue area adaptation where right hemisphere regions become more involved in language processing, and map extension, where a larger number of regions become involved in language functions. Later work has treated such changes within a theory of large-scale network reconfigurations that may themselves flexibly change over time. For instance, Saur et al. (2006) showed that within 2 weeks after a left hemisphere stroke there is a strong increase in right hemisphere activity (maximally in right IFG, right SMA), but this imbalance disappears within a year post-stroke. Given the timescale of these processes it is therefore possible that greater reliance on the auditory system and perisylvian regions in both early and late blindness leads to more coordinated use of right hemisphere regions mediating auditory and speech functions. This would be consistent with recent work documenting less left-lateralized responses for sentence processing in congenitally blind (Lane et al., 2016). One possibility is that such coordinated inter-hemispheric activation results in more coordinated changes in CT between the hemispheres (for review, see Herve, Zago, Petit, Mazoyer, & Tzourio-Mazoyer, 2013).

An alternative explanation is one based on a complementary aspect of plasticity, which is pruning of unnecessary connections. This process can account for why the congenitally blind show stronger contra-lateral correlations. As reviewed by Blumstein and Amso (2013), the initial network-level configuration subserving language processing undergoes substantial reconfiguration with development. Newborns show less lateralized task-induced activation, as well as stronger interhemispheric functional connectivity between areas subserving adult language comprehension (Perani et al., 2011). This more symmetric profile appears to maintain until early childhood: using seed-based functional connectivity (seed region in STS), Friederici, Brauer, and Lohmann (2011) showed that 6 year-olds display stronger bilateral correlations than do adults. This pattern, of increased inter-hemispheric coordination in functional activity in early childhood which is followed by greater asymmetry appears to be general and not limited to language functions (Herve et al., 2013). Inter-hemispheric resting-state functional connectivity of temporal-lobe regions in typically developing individuals is stronger than that seen for individuals born pre-term, and in the latter population, stronger bilateral connectivity patterns are positively associated with a behavioral measure of verbal comprehension (Wilke, Hauser, Krageloh-Mann, & Lidzba, 2014). This latter finding is consistent with the finding of Dick et al. (2013) where greater inter-hemispheric connectivity between superior temporal regions during story comprehension was associated with greater receptive language performance in children with perinatal focal brain injury. All these studies point to an initial state of greater coordination between bilateral temporal regions, which is naturally substituted for a lateralized profile in typical development, but which can still improve function in particular conditions.

To conclude, the stronger bilateral correlations in CT and SA profiles we find for the blind could reflect a combination of two processes: coordinated involvement of bilateral temporal regions in similar language computations (consistent with findings of Lane et al., 2016) that results in coordinated bilateral development, or alternatively, maintenance of an initial, more bilateral coordinated state of the language system that is typically seen in children but lost in adults. Clearly both these explanations apply to the congenitally blind group. However, for the late blind, the first is more feasible as these individuals had spent their early years as seeing individuals. These explanations are clearly speculative at this point, and make several assumptions regarding patterns of synchronized neural activity (in blind vs. sighted) and their potential relation to synchronized neural development. However, one mechanism that may mediate them is the increased activity in the superior colliculus (SC) that has been documented for the blind. Animal studies have shown that deafferentation of the visual system produces expansion of descending projections to SC (Lesicko & Llano, 2016), and functional neuroimaging has shown the blind show stronger SC responses and more bilateral MGN responses to auditory inputs (with indications for more bilateral A1 activity; Coullon et al., 2015).

Regarding method, we note that inter-regional correlation of morphometric features (also referred to as 'structural connectivity') is a well-established method that has been used to address typical whole-brain organization, experience-dependent plasticity and clinical conditions (Alexander-Bloch, Raznahan, Bullmore, & Giedd, 2013; Alexander-Bloch et al., 2013; Chen et al., 2008; Evans, 2013). Our findings show how this method can shed light on experience-dependent neuroplasticity of language and auditory regions. As opposed to univariate measures that quantify neuroplasticity for any given metric by establishing the value of that metric per each participant, structural connectivity analyses establish the degree of correlation in morphometric measures and are therefore independent of whether any univariate measure differs between populations. For instance, cortical thickness may be identical for Region A and Region B in two populations, but yet the correlation between the values of the two regions may be much stronger for one population, suggesting there exists a difference in the factors that organize development of that feature across groups.

4.2. Relation to theories of neuroplasticity of language system in blind

As reviewed in the introduction, a central tenet of current neurobiological and functional approaches to neuroplasticity in blind is that occipital cortex takes on computations related to language processing. Recent reviews (Kupers & Ptito, 2014; Renier, De Volder, & Rauschecker, 2014) emphasize the following aspects: for early blind, visual cortex is multisensory and activated by sound and touch, and maintains its original roles (e.g., what/where distinction) for nonvisual senses. Conjointly, other, supramodal regions maintain their general functionality even in absence of visual input (Ricciardi, Bonino, Pellegrini, & Pietrini, 2014).

In an early review, Bavelier and Neville (2002) already noted the marked absence of data speaking to neuroplasticity of the preserved auditory cortex in human blind, which stands in contrast to findings in animal models where blindness has been linked to hypertrophy of auditory cortex. For instance, lack of visual exposure in cats produces an increased proportion of auditory cortex neurons with spatial tuning (Korte & Rauschecker, 1993). As we outlined in the Introduction, there exists a wealth of null-results regarding morphometric changes in the auditory and language systems of blind. A near exception is a study by Park et al. (2009) that examined CT and SA values using whole-brain regional parcellation. They defined a single 'superior temporal' region and reported lower CT for blind (uncorrected for multiple comparisons), and no differences for SA. Our findings contribute to this literature as they document a marked reduction in surface area for congenitally blind in lateral TTG and PP (with no interaction with hemisphere).

Neuroimaging studies have provided inconsistent findings with respect to the impact of blindness on STP activity. Some studies suggest that during auditory processing, blind and sighted show similar activation patterns in auditory regions, though the blind show greater activity in visual cortex, frontal, and parietal regions (Bedny, Konkle, Pelphrey, Saxe, & Pascual-Leone, 2010; Collignon et al., 2011; Tao et al., 2015). However, evidence for changes in processing within STP was reported in an fMRI study (Jiang, Stecker, &

Fine, 2014) that used patterns classifiers to show that the right planum temporale (auditory association cortex) codes information about auditory motion features in sighted but not in early blind. Dormal, Rezk, Yakobov, Lepore, and Collignon (2016) reported similar results but bilaterally. This suggests a change in functional characteristics of auditory cortex in blind. Other studies show that blind show particular modes of functional connectivity between auditory and occipital regions (Klinge, Eippert, Roder, & Buchel, 2010; Schepers et al., 2012). We note that prior neuroimaging work has also shown that early and late blind show different patterns of functional connectivity between occipital and auditory cortex (Collignon et al., 2013) and such differential changes are consistent with some of the patterns we found here. While we did not contrast the CB and LB groups directly due to age differences, the contrasts against controls suggested limited changes in surface area for LB, but stronger ones for the CB group. This might indicate a more fundamental reorganization of STP for congenitally blind, but we are cautious in interpreting these differential effects as the late blind were substantially older, and naturally occurring age-related morphometric changes may lead to more similar data patterns for LB and their controls.

Our own prior work (Hasson et al., 2016) on whole-brain structural connectivity in the blind (using a 74-region parcellation) examined the modular arrangement of cortical thickness networks and concluded that the structure of these networks differs significantly for blind and sighted. It also documented a pattern of "multisensory merging" in the blind where perisylvian and visual-cortex regions more frequently share same structural modules. That study however lacked the higher resolution manual annotation that we implemented in the current study, did not perform surface-area analyses, did not study a late blind group and was not focused on reorganization of STP. Still, the changes it documented are consistent with the idea that the structural connectivity of STP is altered in congenitally blind and sighted.

While the changes to structural covariance we document are consistent with a different mode of auditory function in the blind, it is still possible that these changes are *un*related to auditory function in blind, but reflect Braille reading ability or other capacities developed over long periods. Yet, the behavioral evidence for improved auditory and speech-processing functions in blind (e.g., Dietrich et al., 2013; Gougoux et al., 2004; Lessard et al., 1998; Lewald, 2013; Roder et al., 1999; Voss et al., 2004), taken together with the functional neuroimaging results reported above, are highly consistent with changes to STP structure in blind. Future work can address this issue by obtaining detailed inter-individual variability measures of auditory or speech performance for blind and sighted. That would allow to partial out from the cortical thickness (or surface area) data any variance related to behavior, and then re-constructing morphological covariance from the residual values. Any substantial changes to the covariance results after partialling out behavioral or functional covariates would directly link co-variance measures to functional signatures.

4.3. Summary

Our study indicates there are strong alterations in the morphometry of the superior temporal plane, in both congenitally and late blind. We found statistically significant, but relatively few indications in the univariate measures, but strong indications in multivariate measures relying on structural connectivity. Our findings indicate that blindness is associated with a more symmetric morphometric organization. This pattern is consistent with several prior reports of a shift towards a more bilateral organization in clinical populations, and with recent demonstrations of more bilateral functional activity profile in congenitally blind during language comprehension (Lane et al., 2016). Most generally, our findings suggest that structural connectivity, particularly when relying on relatively fine-scale anatomical parcellation, is a sensitive method for studying experience dependent plasticity of language systems, in both clinical and normally developing populations. Its use, in combination with rich inter-individual descriptors offers multiple avenues for future work.

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Appendix A. Blind etiology

Number	Age at testing	Gender	Handedness	Light perception	Onset (years)	Etiology
Early blind						
EB1	45	M	R	Diffuse light	0	Retinopathy of prematurity
EB2	62	M	R	Diffuse light	0	Congenital cataracts
EB3	55	M	R	No	0	Electrical burn of optic nerve bilaterally
EB4	28	M	R	No	0	Retinopathy of prematurity
EB5	57	F	R	No	0	Chorioretinal atrophy associated to toxoplasmosis
EB6	31	M	R	No	0	Leber's congenital amaurosis
EB7	54	M	R	No	0	Glaucoma
EB8	23	M	R	Diffuse light	0	Glaucoma and microphtalmia
EB9	43	M	R	No	0	Retinopathy of prematurity
EB10	44	M	R	Diffuse light	0	Leber's congenital amaurosis
EB11	31	F	R/A	No	0	Retinopathy of prematurity
EB12	60	F	R	No	0	Retinopathy of prematurity
EB13	33	F	R	No	0	Glaucoma
EB14	58	F	R	No	0	Retinopathy of prematurity
EB15	51	M	R/A	No	0	Major eye infection (Thalidomide victim)
EB16	36	F	R	No	0	Bilateral Retinoblastoma

(*continued on next page*)

Appendix A (*continued*)

Number	Age at testing	Gender	Handedness	Light perception	Onset (years)	Etiology
EB17	51	M	R	No	0	Glaucoma
EB18	48	M	R	No	0	Glaucoma
Late blind						
LB1	53	M	L	No	51	Diabetic Retinopaty
LB2	52	M	R	Diffuse light	25	Detachment of Retinas due to accident
LB3	54	M	R	No	44	Diabetic Retinopaty
LB4	54	F	R	No	9	Aniridia
LB5	61	F	R	No	52	Steven Johnston Syndrome + Sulfonamide
LB6	42	F	R	Diffuse light	30	Microphtalmia + Cataract
LB7	47	F	R	Diffuse light	44	Glaucoma + Cataract
LB8	48	F	R	No	20	Diabetic Retinopaty
LB9	53	F	R	Diffuse light	27	Retinitis Pigmentosa
LB10	59	F	R	No	11	Retinitis Pigmentosa

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