A study of brain white matter plasticity in early blinds using tract-based spatial statistics and tract statistical analysis

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Early blind individuals are known to exhibit structural brain reorganization. Particularly, early-onset blindness may trigger profound brain alterations that affect not only the visual system but also the remaining sensory systems. Diffusion tensor imaging (DTI) allows in-vivo visualization of brain white matter connectivity, and has been extensively used to study brain white matter structure. Among statistical approaches based on DTI, tract-based spatial statistics (TBSS) is widely used because of its ability to automatically perform whole brain white matter studies. Tract specific analysis (TSA) is a more recent method that localizes changes in specific white matter bundles. In the present study, we compare TBSS and TSA results of DTI scans from 12 early blind individuals and 13 age-matched sighted controls, with two aims: (a) to investigate white matter alterations associated with early visual deprivation; (b) to examine the relative sensitivity of TSA when compared with TBSS, for both deficit and hypertrophy of white matter microstructures. Both methods give consistent results for broad white matter regions of deficits. However, TBSS does not detect hypertrophy of white matter, whereas TSA shows a higher sensitivity in detecting subtle differences in white matter colocalized to the posterior parietal lobe. *NeuroReport* **26:1151–1154 Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.**

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Introduction

Blind individuals are subject to functional and anatomical reorganization in the brain in response to the absence of visual inputs [1–11]. For example, a PET study revealed specific activation patterns of the visual cortex during Braille reading in congenital blind individuals [2]. A functional MRI study reported that brain regions involved in visuospatial processing in sighted individuals were remarkably activated in auditory-spatial processing tasks in congenital blind individuals [10]. Furthermore, a structural MRI study found that volume gains in non-occipital areas are more widespread in early-onset individuals than in late-onset blind individuals based on whole brain tensor-based morphometry [6]. A more complete review of brain alterations in blindness can be found, for example, in the study by Collignon *et al.* [8].

With the advent of diffusion tensor imaging (DTI), microscale white matter integrity can be analyzed non-invasively, thus facilitating the in-vivo detection of white matter connectivity alterations in the human brain [12]. Among dimensionality reduction methods, tract-based spatial statistics (TBSS) [13] is widely used because it automatically projects results on white matter tracts. In particular, Shu *et al.* [5] looked at individuals with early visual deprivation using TBSS, and reported significant white matter impairments in geniculocalcarine tract and its adjacent regions, whereas no white matter hypertrophy was mentioned. Wang *et al.* [14] found both decreases and increases on the brain white matter skeleton of the blind individuals' brain using TBSS, although the *P*-values for the increased changes were not corrected. These inconsistencies in reported results highlight the need for further investigation with higher detection power in this area.

Tract specific analysis (TSA) [15,16] is a more recent semiautomated method that quantifies white matter changes in specific white matter bundles. Instead of looking at the whole brain white matter at once, TSA zooms in on specific white matter bundles, thereby improving localization of the results [16]. Second, whereas the TBSS algorithm registers the low-dimensional fractional anisotropy (FA) map, TSA uses DTI-ToolKit [17] to register the whole diffusion tensors. Another advantage of TSA is that while with TBSS a precise segmentation of the template is needed to determine specific locations of changes, with bundle specific approaches such as TSA the tract is manually defined and thus more anatomically correct. In the

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present study, we hypothesize that the improved registration and localization in TSA will also lead to increased statistical detection power.

In this paper, we compare the white matter alterations in early blind individuals, which were found using the TBSS and TSA approaches. Our purposes are two-fold: first, to explore the deficits and gains in white matter associated with early blindness; second, to examine the sensitivity of TSA, compared with the more standard TBSS, for both deficit and hypertrophy of white matter microstructures.

Materials and methods

Our dataset consisted of 12 early blind individuals (age: 40.1 ± 10.2 years; eight males, four females) and 13 age-matched (age: 38.5 ± 9.4 years; eight males, five females) sighted controls. Brain DTI scans of the recruited individuals were acquired using a Siemens (Avanto, Montreal, Quebec, Canada) 1.5 T scanner, single-shot echo-planar diffusion tensor sequence, with an acquisition time of $\sim$8–12 min and 12 gradient directions. Imaging parameters were as follows: TR = 8000 ms, TE = 92 ms, 2.5 mm interslice distance and four averages.

DTI data from all the recruited individuals were first preprocessed [including skull stripping, eddy current correction in FSL (created by the Analysis Group, FMRIB, Oxford, UK) and tensor estimation in MedInria (developed within the Ascleplos research project, Inria Sophia Antipolis, France)], and were then registered to a consistent template – the IXI adult template – through DTI-ToolKit [17]. The same processing steps and the use of the IXI adult template were meant to improve consistency [18]. Subsequently, statistical analyses on FA values were performed using TBSS and TSA. For TBSS, statistics were carried out on the skeletonized mean FA image as a whole. For TSA, we focused on six major tracts: the corpus callosum (CC), corticospinal tract (CST), inferior fronto-occipital, inferior longitudinal fasciculus, superior longitudinal fasciculus and uncinate. In all cases, *P*-values were corrected for multiple comparisons using 10 000 permutations, and the significance thresholds were set to P less than 0.01.

Results

Statistical comparison of FA between early blind and sighted groups using TBSS and TBA approaches are shown in Fig. 1. Both methods detected decreased FA in early blind individuals in widespread areas of the brain white matter, including but not limited to the occipital lobe. These were consistent with the findings in the study by Büchel and colleagues [2,6,14,19,20].

On the other hand, under the hypothesis of FA greater in blind than sighted, no significant difference was detected using TBSS, whereas significantly increased white matter integrity was detected using TSA in parts of the CC and CST connecting to the posterior parietal lobe. These were consistent with the tractography-based findings of significantly increased mean FA of CST [19] and increased white matter volume in subcortical parietal lobe [6] in these individuals.

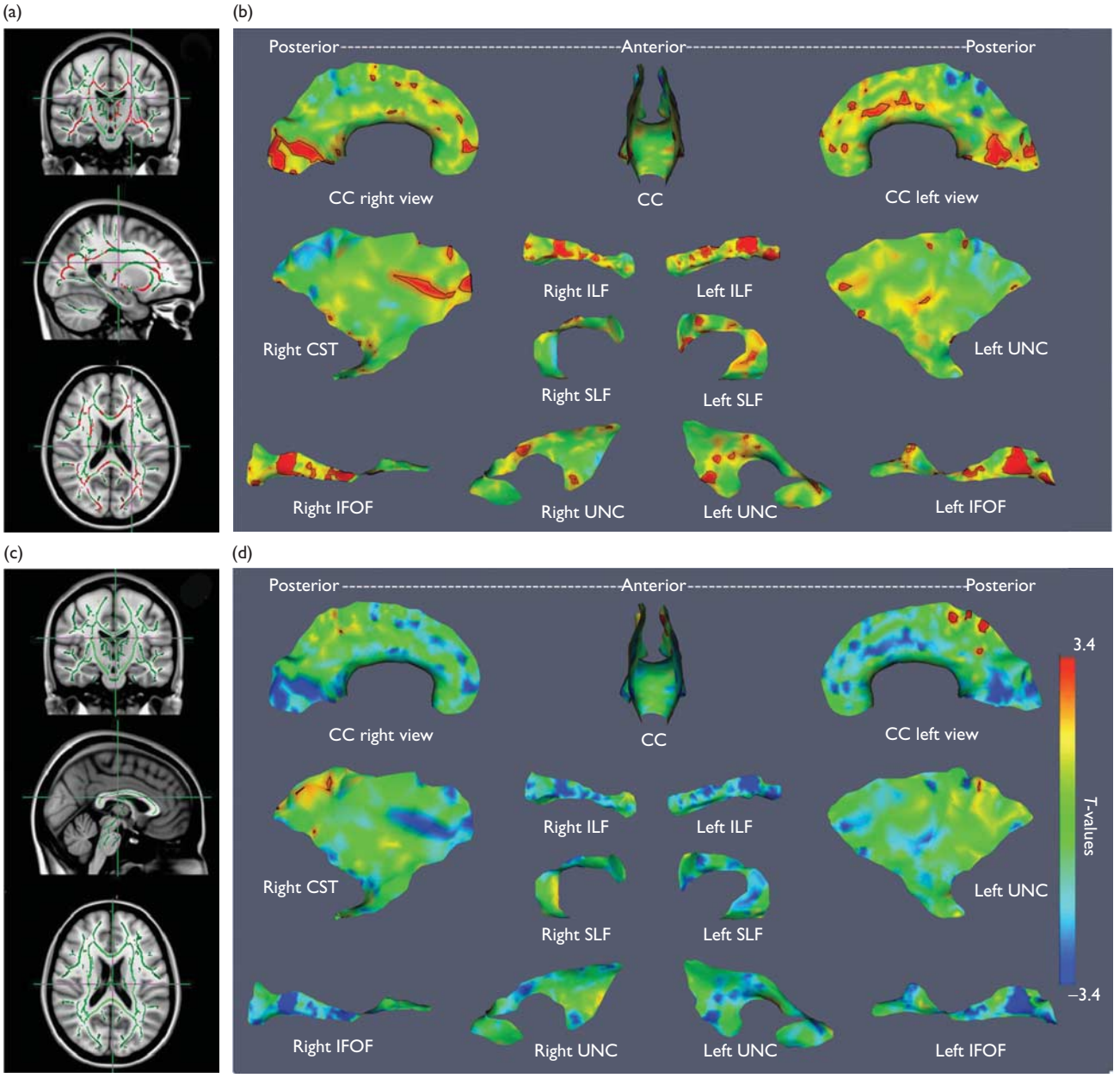
Discussion and conclusion

In the present study, we found significant alterations in white matter microstructure in several brain regions between early blind and sighted group using TSA, which was consistent with the TBSS results. White matter deficits were detected using both TBSS and TSA in the congenital blind individuals in broad brain regions, mainly distributed in the frontal and the occipital lobe. These were consistent with previous findings of impaired white matter integrity secondary to early visual deprivation, which extensively affects optic nerves and neuroconnections typically involved in visual processing [2,6, 14,19,20]. On the other hand, white matter alterations resulting from central nervous system adaptation are much more subtle and thus require more sensitive approaches of analysis. In our experiment settings, TSA successfully pinpointed significantly strengthened white matter in the CC and CST, colocalized to the posterior parietal lobe, whereas TBSS failed to identify the alteration.

Blind plasticity in early-onset blind individuals is well accepted as a means of reassigning functions of the visual system [2,3]. A few structural and diffusion MRI studies further confirm the brain structural alterations in the congenital blind brain in response to visual deprivation. For instance, Lepore *et al.* [6] looked at structural MRI scans of early blind individuals, and reported regional hypertrophy using tensor-based morphometry. Yu *et al.* [19] calculated the FA values over the entire tractography derived cortical spinal tracts, and found significant higher FA values in early blind individuals compared with normal controls. Wang *et al.* [14] reported more extensive white matter impairments in late blind individuals than in congenital blind individuals using both TBSS and VBA, and found a trend of increased FA in bilateral CST using TBSS, with uncorrected *P*-values in these two groups compared with sighted controls. Here, the white matter hypertrophies detected by TSA were consistent with previous findings [1,6,14,19]. Moreover, for the first time, white matter alterations were specifically located in the posterior parietal lobe – a region reported to be involved in route planning [21–23].

In the human brain, visual information is processed and integrated through two separate pathways: a 'ventral-what' stream that involves the occipital-temporal lobes and is in charge of recognizing objects, and a 'dorsal-where' stream that involves the occipital-parietal lobes and participates in identifying the spatial location of the object [23]. In particular, the posterior parietal cortex, which receives the visual inputs from dorsal visual

Fig. 1



Statistical analysis of FA using TBSS (a, c) and TSA (b, d). For TBSS, results are shown as mean FA skeleton maps. Significant areas with $P < 0.01$ are marked in red. For TSA, results are shown for the bilateral corticospinal tract (CST), inferior fronto-occipital tracts (IFO), inferior longitudinal fasciculus tracts (ILF), superior longitudinal fasciculus tracts (SLF), uncinate tracts (UNC), and the corpus callosum (CC). Significant areas with $P < 0.01$ are encircled with black boundaries. (a, b) Results under the hypothesis of blind < sighted. (c, d) Results under the hypothesis of blind > sighted. FA, fractional anisotropy; TBSS, tract-based spatial statistics; TSA, tract specific analysis.

stream, has long been viewed as an essential part for spatial processing and navigation [22,23].

Brain functional studies have observed substantial recruitment of the visual cortex in the processing of nonvisual inputs in blind individuals [2,3,7,10,11]. In congenitally blind individuals, increased functional connectivities between occipital areas and the parietal cortex have been reported [2,10,11]. For example, in a study comparing the activation patterns of pitch and spatial properties of sounds, auditory-spatial processing regions in congenital blind individuals overlapped with visuo-spatial processing regions in sighted controls [11]. In the present study, the strengthened connectivity implied by significantly increased FA in white matter tracts towards the posterior parietal cortex further confirms brain cross-

modal plasticity in response to the deprivation of sight, possibly because of enhanced auditory aspects of spatial perception rather than deprived visual stimuli [7,10,11]. This may form new neurosubstrate for the compensatory adjustment in congenital blind individuals in the absence of visual inputs. In the future, we would like to further strengthen the conclusion using a larger group of individuals, and correlate results with different factors such as education, occupation, and IQ. In addition, it will be helpful to zoom into the auditory tracts by comparing it with olfactory tracts. However, auditory nerves have intricate pathways crossing other white matter fibers, which are better identified by HARDI data [24,25]. In addition, olfactory tracts comprise decussating anterior commissure fibers, which are hard to model using a medial plane. Therefore, our current data and methods do not provide valid and reliable analyses of auditory and olfactory fiber integrity. As a result, we will study auditory and olfactory areas using HARDI and functional MRI data in the future, to further investigate the alterations of these systems in early blind individuals. We expect that these analyses will enrich our understanding of brain plasticity.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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