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Congenital blindness is associated with large-scale reorganization of anatomical networks

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ABSTRACT

Blindness is a unique model for understanding the role of experience in the development of the brain's functional and anatomical architecture. Documenting changes in the structure of anatomical networks for this population would substantiate the notion that the brain's core network-level organization may undergo neuroplasticity as a result of life-long experience. To examine this issue, we compared whole-brain networks of regional cortical-thickness covariance in early blind and matched sighted individuals. This covariance is thought to reflect signatures of integration between systems involved in similar perceptual/cognitive functions. Using graph-theoretic metrics, we identified a unique mode of anatomical reorganization in the blind that differed from that found for sighted. This was seen in that network partition structures derived from subgroups of blind were more similar to each other than they were to partitions derived from sighted. Notably, after deriving network partitions, we found that language and visual regions tended to reside within separate modules in sighted but showed a pattern of merging into shared modules in the blind. Our study demonstrates that early visual deprivation triggers a systematic large-scale reorganization of whole-brain cortical-thickness networks, suggesting changes in how occipital regions interface with other functional networks in the congenitally blind.

1. Introduction

Blindness is associated with changes to both the functional and anatomical organization of the brain (e.g., Noppeney, 2007; Voss and Zatorre, 2012b). Most strikingly, occipital regions are involved in and have been causally linked to different non-visual processes in the blind (Amedi et al., 2004; Cohen et al., 1997; Collignon et al., 2007), and there are some suggestions that their recruitment is linked to enhanced abilities in the remaining senses (Amedi et al., 2003; Gougoux et al., 2005). Anatomically, early blindness is accompanied by atrophy of gray matter volume and increased cortical thickness in occipital cortex (Bridge et al., 2009; Jiang et al., 2009; Park et al., 2009; Qin et al., 2013; Voss and Zatorre, 2012a) that may also be related to non-visual behaviors in blind individuals (Voss et al., 2014; Voss and Zatorre, 2012a). In addition, blindness also impacts thalamic subregions involved in visual processing (Cecchetti et al., 2015; Ptito et al., 2008), the shape and volume of corpus callosum (Tomaiuolo et al., 2014), and hippocampal volume (Fortin et al., 2008).

It is still poorly understood whether the specialization for non-visual information in the blind's occipital cortex reflects mostly localized changes, or whether blindness induces a larger-scale reorganization associated with a different mode of global information exchange at the whole-brain level. More specifically, is the occipital cortex re-programmed without affecting the large-scale organization of brain networks, or does re-programming occur at the level of whole-brain networks inducing occipital regions to cluster differently with other regions? An influential view on brain organization suggests that the development of domain selectivity in occipital regions, as well as superior parietal, parahippocampal, and several other brain areas, is independent of visual experience (Dormal and Collignon, 2011; Mahon and Caramazza, 2011; Reich et al., 2012; see Ricciardi et al., 2014 for recent review). On this view, the maintained functional selectivity in occipital regions in early blind would arise from a pre-existing (possibly innate) set of neural connections, which are similar for blind and sighted individuals (e.g., Hannagan et al., 2015; Mahon and Caramazza, 2011; Reich et al., 2011). For example, several studies have documented a maintained pattern of resting-state functional connectivity between functionally specific occipital regions (e.g. the visual word form area, the numerical form area, the parahippocampal place area) across blind and sighted individuals (Abboud et al., 2015; He et al., 2013; Reich et al., 2011).

In addition, several functional neuroimaging studies have pointed to a large-scale reorganization of extended brain networks. Schepers et al. (2012) showed that processing auditory inputs in blind produces

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stronger neural synchronization between auditory and visual cortices in the gamma band and suggested that "the deprived visual cortex is integrated into a larger network related to its new function" (for similar conclusions, see Collignon et al., 2011, 2013; Klinge et al., 2010; Wittenberg et al., 2004). Also, resting-state neuroimaging studies in the blind have revealed stronger connectivity between occipital and frontal or parietal regions (e.g., Deen et al., 2015; see Bock and Fine, 2014 for a recent review). In summary, the extent to which early-acquired blindness may induce large-scale reorganization of brain networks remains controversial.

Our goal here was to determine whether there is large-scale, network-level reorganization of anatomical features in the blind. Voss and Zatorre (2015) showed that anatomical covariance between a specific seed region in occipital cortex and a region in the superior frontal gyrus differs for blind and sighted, but no network-level study has examined the two populations. When evaluated from a graph-theoretic perspective, regional covariation patterns in cortical thickness show a modular network organization (e.g., Chen et al., 2008), and areas within these modules tend to be associated with similar behavioral or cognitive function. Moreover, correlations between distant cortical regions are thought to be signatures of functional integration between different systems (Alexander-Bloch et al., 2013a, 2013b). Therefore, features of these structural networks are taken to reflect the brain's core capacity for information transmission across cortical regions, and the structure of these networks has been shown to differ between clinical and non-clinical populations (for review, see Alexander-Bloch et al., 2013b).

Interestingly, prior work (Chen et al., 2008) has shown that in structural networks of sighted, frontal, lateral–temporal, and occipital regions tend to cluster within separate cliques ("modules" in graph-theoretic parlance). This makes structural networks an interesting target for study in congenitally blind since auditory and language functions have notably been mapped inside occipital structures in this population (e.g., Bedny et al., 2011; Collignon et al., 2011). This raises the general possibility that blindness would be associated with some sort of "multisensory merging" between sensory systems that would be manifested in a weakening of the structural separation between occipital and lateral–temporal regions.

Importantly, blindness has a unique status as a model system for examining the role of experience in anatomical development and functional activity. For this reason, documenting changes in network structure in this population would convincingly substantiate the notion that the brain's core network-level structural organization may undergo neuroplasticity as result of life-long experience.

2. Methods

2.1. Participants

The blind participant group consisted of 18 congenitally blind (7 female, mean age: 44.1 ± 13.7; 11 male, mean age: 42.45 ± 12.44) and the sighted control group (N = 18) matched the CB group on age and gender distribution (7 female controls, mean age: 45.6 ± 14.55; 11 male controls, mean age: 40.0 ± 6.9). Additional characteristics of the blind group are provided in Supplementary Table 1. All procedures involving human participants were approved by the research ethic and scientific boards of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal and the Quebec Bio-Imaging Network.

2.2. Acquisition and preprocessing pipeline for structural images

Structural data used in this study were collected in 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. Data were 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; TE 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 preprocessing pipeline (Dale et al., 1999; Fischl et al., 1999) consisted of non-brain tissue removal, Talairach transformation, white matter and gray matter segmentation, intensity normalization, topology correction, surface inflation, atlas registration, and parcellation of the cerebral cortex according to the Destriux atlas (74 regions per hemisphere, Destrieux et al., 2010). Each of these automatically executed steps was followed by quality control assessments implemented jointly by H. A. and U. H. Interventions in this quality control step consisted of 1) replacing low-quality structural scans of 4 participants with higher quality alternate scans for the same participants; 2) manual Talairach alignment (n = 2); 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 (n = 4); 4) correction for missed labeling of white matter (n = 15); and 5) use of control points to correct the intensity normalization of white matter (n = 5).

2.3. Analysis of cortical thickness at regional level

To evaluate our data against prior results, we conducted a region-based univariate analysis of cortical thickness. For each of the 148 regions automatically parcelated by FreeSurfer, we contrasted the mean cortical thickness of the blind and sighted groups using unpaired T-tests, and controlling for multiple comparisons using FDR correction.

2.4. Partial least squares analysis for group-linked CT covariance

To evaluate whether there is a network-level covariance pattern that discriminates the two groups, we used a partial least squares regression (PLSR) approach (Krishnan et al., 2011; McIntosh and Lobaugh, 2004). In the current implementation, the to-be-predicted variable was the [36 participants × 1] vector coding the participant's group identifier (0.5 for sighted, −0.5 for blind), and the explanatory data were the [36 participants × 148 regions] matrix. We implemented PLSR using the PLS package in the statistical software R (Mevik and Wehrens, 2007), with 2 components analyzed based on an initial evaluation of prediction accuracy profiles as estimated by the RMSEP parameter in a Leave One Out classification scheme. The workflow for evaluating statistical significance followed the one detailed in Krishnan et al. (2011). Specifically, as in previous studies, we used permutations to evaluate whether the fit between participant's scores and the predicted variable exceeded what would be expected by chance. For this purpose, a sampling distribution was constructed from 500 permutations, with each permutation randomly assigning the group labels to participants. To identify regions whose brain scores were systematic across implementations of the PLSR algorithm, we used a bootstrapping procedure that was run 100 times (see McIntosh et al., 1996). In each instance, we bootstrapped, with replacement, rows from the original [36 × 148] CT-value matrix, to populate a proxy [36 × 148] matrix. For each proxy matrix, PLSR was run, and the loadings for the estimated 2 components were retrieved. This loading matrix was rotated to match the direction of the loadings in the original data via a Procrustes Rotation, and the Y-loadings (Brain loadings) for the first component saved. Finally, we calculated the standard deviation of the 100 bootstrap loadings, per region, and then obtained a Z-score per region [region loading/sd(loading)]. Only regions that passed a Z-score of ±2.5 were considered significantly "salient."

2.5. Regression approach to assess bivariate correlations between region-pairs

Our regression approach followed that described by Lerch et al. (2006), and included partialling out the effect of age, followed by FDR