Neuroanatomical changes in patients with loss of visual function
Prins, Doety

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2016

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

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CHAPTER 4

Loss of binocular vision in monocularly blind patients causes selective degeneration of the superior lateral occipital cortices

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Submitted
Abstract

Introduction. Chronic ocular pathology, such as glaucoma and macular degeneration, is associated with neuroanatomical changes in the visual pathways. It is a challenge to determine the mechanism responsible for these changes. This could be functional deprivation or transsynaptic degeneration. Acquired monocular blindness provides a unique opportunity to establish which mechanism underlies neuroanatomical changes in ocular pathology in general, since the loss of input is well defined, and it causes selective functional deprivation due to the loss of stereopsis.

Methods. High-resolution T1-weighted MR-images were obtained in 15 monocularly blind patients and 18 healthy controls. We used voxel- and surface-based morphometry to compare grey and white matter volume, cortical thickness, mean curvature, and surface area between these groups.

Results The grey matter volume in the bilateral superior lateral occipital cortices was decreased in the monocular blind patients. We found no volumetric differences in their early visual cortex.

Discussion. The volumetric decrease in the superior lateral occipital cortices is consistent with specific functional deprivation, as the superior lateral occipital cortices play an important role in depth perception. Moreover, in the absence of differences in the early visual cortex, the decrease is inconsistent with transsynaptic degeneration propagating from the degenerated retinal axons.
4.1 Introduction

Treatment of blindness is the ultimate challenge in ophthalmology; it has motivated the development of various vision restoration therapies, including retinal implants, stem-cell derived retinal pigment epithelium, and gene-therapy. (da Cruz et al. 2013, MacLaren et al. 2014, Stingl et al. 2010, Van Zeeburg et al. 2012) The potential success of such future treatments will depend to a great extent on the capacity of the brain to guide and process the new input following vision restoration. Previous studies found evidence for neuroanatomical changes in patients with various eye diseases, such as glaucoma, macular degeneration, and amblyopia. (Barnes et al. 2010, Boucard et al. 2009, Hernowo et al. 2011, Hernowo et al. 2014, Mendola et al. 2005, Plank et al. 2011, Prins, Hanekamp and Cornelissen 2016, Xiao et al. 2007, Xie et al. 2007) Due to such changes, the brain may no longer be able to optimally process new input from a retinal implant. As for a truly successful treatment it needs to be able to do so, it is important to precisely understand the mechanism underlying the association between prolonged partial blindness and neuroanatomical changes.

Three mechanisms may explain the association between loss of visual input and neuroanatomical changes. First, in functional deprivation a permanent loss of visual input leads to decreased activity in the visual pathways, which – in turn – leads to neuroanatomical degeneration. Second, in transsynaptic degeneration, the degenerating axons originating from the eye provoke degeneration of more posterior parts of the visual pathways. Distinguishing between the contributions of these two mechanisms has been problematic as neural and functional visual losses are usually highly correlated and difficult to characterize precisely. Third, there are indications that degenerative eye diseases, such as macular degeneration and glaucoma, are associated with general neurodegenerative diseases. (Cumurcu et al. 2013, Ghiso et al. n.d., Janssen et al. 2013, Sivak 2013, Tamura et al. 2006, Wostyn, Audenaert and De Deyn 2010) As such, the neuroanatomical changes might not exclusively be caused by functional deprivation or transsynaptic degeneration, but could be due to the general neurodegenerative character of the disease.

Studying patients with previously healthy eyes who became monocularly blind – due to for example an eye trauma – provides a unique opportunity to disentangle the possible causes of the association between altered visual function and neuroanatomical changes. Unlike in chronic ocular pathology, in this group the reduction of visual input is well defined. Moreover, monocular blindness causes a loss of binocular vision and stereopsis, resulting in a highly selective functional deprivation. Finally, there is no association with neurodegenerative diseases. If we can determine whether and where neuroanatomical changes occur in monocularly blind patients, we would gain more insight into the etiology of neuroanatomical changes associated with visual loss in general. As such, monocularly blind patients can also serve as a reference group for studies in patients with various eye diseases.

The aim of our study was to determine whether and how monocular blindness affects the neuroanatomical properties of the visual pathways. Such neuroanatomical properties were defined by grey and white matter volume, cortical thickness, surface area, and mean curvature. In our study, we used voxel-based morphometry (VBM) and surface-based morphometry (SBM) to compare the abovementioned neuroanatomical properties between monocularly blind patients without a chronic or degenerative ocular disease and age-matched healthy controls. Using region of interest (ROI) analysis, we specifically assessed the visual pathways.

4.2 Materials and methods

4.2.1 Ethics statement

The Medical Ethical committee of the University Medical Center Groningen approved this study. The study conformed to the tenets of the Declaration of Helsinki. All subjects gave their written informed consent before participating in the study.

4.2.2 Subjects

We included 33 subjects in this study: 15 monocularly blind patients and 18 healthy age-matched controls. The inclusion criteria for the monocularly blind patients were the following. They had to be unilaterally light-perception negative for at least five years, due to a trauma (n = 11, in 11 patients the eye was removed) or after surgery for a tumor (n = 4, in 3 patients the eye was removed). The contralateral eye had to have a good visual acuity (0.8 or better) and an intact visual field. Healthy age-matched controls had to have a good visual acuity and intact visual field in both eyes. None of the subjects had previously been diagnosed with neurological disorders, psychiatric disorders, or any degenerative ocular disease.

The monocularly blind patients had a mean age of 63 years (range 54 – 72 years); 47% of them were males. The healthy controls had a mean age of 62 years (range 53 – 75 years); 61% of them were males. In the group of monocularly blind patients, seven patients were blind in their right eye, and eight were blind in their left eye.
4.2.3 Data acquisition
MR images of all subjects were obtained on a 3.0 Tesla MRI scanner (Philips Intera, Eindhoven, the Netherlands) at the Neuroimaging Center of the University Medical Center Groningen. Whole brain T1-weighted images with a voxel dimension of 1 x 1 x 1 mm were acquired using a sequence of T1W/3D/FFE, 30° flip angle, repetition time 25 ms, matrix size 256 x 256, and field of view 256 x 160 x 204, yielding 160 slices.

The visual acuity was measured with a Snellen chart with optimal correction for the viewing distance. The visual field was tested with frequency doubling technology (FDT; C20-1 screening mode).

4.2.4 Data analysis
We analyzed the anatomical properties of the visual pathways using VBM and SBM. VBM was used to study the volumes of the grey and white matter; SBM was used to study the cortical thickness, gyrification pattern, and surface area.

VBM analysis
We performed VBM analysis of the grey matter and white matter volume using the FMRIB Software Library (FSL) analysis tools (version 5.0.6, available at: http://www.fmrib.ox.ac.uk/fsl).(Jenkinson et al. 2012, Woolrich et al. 2009) First, we applied nonlinear noise reduction using Smallest Unvalue Segment Assimilating Nucleus (SUSAN). Second, we segmented the brain from non-brain tissue, using the Brain Extraction Tool (BET). (Smith 2002) Subsequently, we performed bias field correction and segmented the brain into grey matter, white matter and cerebrospinal fluid with the FMRIB Automated Segmentation Tool (FAST) from the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain .(Zhang, Brady and Smith 2001) We registered all the images to the template of the Montreal Neurological Institute (MNI template) with the FMRIB Linear Image Registration Tool (FLIRT) and the FMRIB Non-linear Image Registration Tool (FNIRT), and applied the registration to the grey and white matter segments.(Jenkinson et al. 2002, Jenkinson and Smith 2001) Using the FSL ‘randomise’ analysis tool, we performed nonparametric permutation tests on our data.(Winkler et al. 2014)

SBM analysis
We performed SBM analysis of cortical thickness, mean curvature, surface area, and grey matter volume using Freesurfer (version 5.3.0, available at: http://surfer.nmr.mgh.harvard.edu/). We digitally removed the non-brain tissue (Ségonne et al. 2004), and performed automated Talairach transformation and intensity normalization.(Sled, Zijdenbos and Evans 1998) Subsequently, tessellation of the grey/white and grey/cerebrospinal fluid boundaries and automatic correction of topologic inaccuracies was performed, which we customized by setting the value for the lower threshold of the white matter to an appropriate value for our dataset.(Fischl, Liu and Dale 2001,

**ROI analysis**

In the ROI-based analyses, we used masks of the various grey and white matter structures of the visual pathways. Figure 4.1 presents the ROIs: the pregeniculate structures, which contains the optic nerves, chiasm and optic tracts, the lateral geniculate bodies, the optic radiations, the calcarine region, the occipital pole, the inferior lateral occipital cortices, and the superior lateral occipital cortices. The masks for the pregeniculate structures were created manually, and adjusted to match the structures in each individual subject if needed. The masks for the lateral geniculate bodies and for the optic radiations were obtained from the Jülich histological atlas(Bürgel et al. 2006, Bürgel et al. 1999). The masks for the calcarine region, the occipital pole, the inferior lateral occipital cortices, and the superior lateral occipital cortices were obtained from the Harvard-Oxford cortical structural atlas.(Desikan et al. 2006) In all these ROIs, we analyzed the volume of the grey matter and white matter using VBM. In the calcarine region, the occipital pole, the inferior lateral occipital cortices, and the superior lateral occipital cortices, we also analyzed cortical thickness, gyrification, and surface area using SBM.

**Figure 4.1.** Regions of interest along the visual pathway. Pink – pregeniculate structures; dark green – lateral geniculate bodies; red – optic radiations; lighter green – pericalcarine cortices; dark blue – occipital pole; lighter blue – inferior lateral occipital cortex; yellow – superior lateral occipital cortex. The Talairach position of the slices is given by their “x”, “y”, and “z” values.

**Statistics**

We examined differences between monocularly blind patients and healthy controls using multivariate analysis of covariance (MANCOVA) (IBM SPSS Statistics software
package, version 20). The white matter volume, grey matter volume, cortical thickness, gyrification pattern, and surface area for each ROI were included as dependent variables, and the subject groups were entered as a fixed factor. We added age as a covariate in the analysis. The threshold for significance in the ROI analyses was set to a $p$-value of 0.05 (uncorrected).

**ROI-analysis of optic nerves**

Since not all monocularly blind patients had their blind eye on the same side, we performed the ROI analyses in two stages. In the first analysis, we compared the volumes of the optic nerves between monocularly blind patients and healthy controls. This analysis was done separately for the monocularly blind patients with a blind right eye and for the monocularly blind patients with a blind left eye, in both cases comparing them to all the healthy controls.

**ROI-analysis of post-chiasmal structures**

The nerve fibers that carry the information from the homonymous hemifields of both eyes to the visual cortex are combined after the chiasm. Hence, no detectable volumetric differences in the post-chiasmal structures were expected between the monocularly blind patients with a blind right eye and those with a blind left eye. Therefore, in a second analysis, we compared the visual pathway structures onwards from the optic chiasm to the posterior parts of the visual pathways, this time for the entire group of monocularly blind patients and again comparing them to the healthy controls.

**Exploratory whole-brain analysis**

To determine the presence of unexpected differences in the neuroanatomy between monocularly blind patients and healthy controls, we performed additional exploratory whole-brain analyses using both VBM and SBM. With VBM, we compared grey and white matter volume, while with SBM, we compared the cortical thickness and mean curvature across the entire brain. In both cases, age was added as a covariate. Comparisons were made after applying a family-wise error correction for multiple comparisons.

### 4.3 Results

In summary, in monocularly blind patients – compared to age-matched controls – we found a significantly smaller volume of the optic nerve on the side of the blind eye, of the optic chiasm, of the bilateral optic tracts, and of the bilateral superior lateral occipital cortices. We will describe these results in more detail below.
4.3.1 ROI analyses

VBM ROI analysis of the optic nerves

To compare the white matter volume of the optic nerves of the monocularly blind patients to that of the healthy controls, we performed VBM analyses in two subgroups. Table 4.1 lists the results of these analyses. On the one hand, in the patients with a blind right eye, the right optic nerve showed a significant decrease in volume, whereas the left optic nerve did not. On the other hand, in the patients with a blind left eye, the left optic nerve showed a significant decrease in volume, whereas the right optic nerve did not. Figure 4.2 visualizes the location of these volumetric differences in the optic nerves for the patients with either a blind right eye (Figure 4.2a) or a blind left eye (Figure 4.2b).
VBM ROI analysis of the visual pathways from the optic chiasm towards the visual cortex
This time including the entire group of monocularly blind patients, we performed ROI analyses of the optic chiasm, the optic tracts, the lateral geniculate bodies, the optic radiations, the calcarine region, the occipital pole, the inferior lateral occipital cortices, and the superior lateral occipital cortices. Table 4.2 and the first row of Table 4.3 show the results of these analyses, and highlight the ROIs for which we find significant reductions in white or grey matter volume: the optic chiasm, the bilateral optic tracts, and the bilateral superior lateral occipital cortices. We did not find any significant differences in grey matter volume in the pericalcarine region and the occipital pole. Figure 4.3 visualizes the volumetric differences in the optic tracts (Figure 4.3a) and the visual cortex.
Figure 4.3. Volumetric differences in the optic chiasm, the optic tract, the optic radiation, and the visual cortex ROIs

a. The areas in blue highlight where the monocularly blind patients show significantly lower volume in the ROIs in the optic chiasm and the optic tracts (see figure 4.1) than the age-matched healthy controls. b. The areas in blue highlight where the monocular blind patients show significantly lower grey matter volume in the ROIs in the visual cortex than the age-matched healthy controls. The red-yellow areas highlight where the monocular blind patients show significantly higher white matter volume in the ROIs of the optic radiations than the age-matched healthy controls. Talairach position of the slices is given by their “x,” “y” and “z” values. ROIs are defined in figure 4.1.

(Figure 4.3b). Grey matter volume was significantly reduced bilaterally in the superior lateral occipital cortices. We found no evidence for a reduced white matter volume of the optic radiations. However, within the optic radiations we did find –relatively small– sections of significantly increased white matter volume.

SBM ROI analysis of the visual cortex

We performed SBM analyses in the ROIs of the pericalcarine cortices, the occipital pole, the inferior lateral occipital cortices and the superior lateral occipital cortices. Table 4.3 indicates that in none of these ROIs, cortical thickness, mean curvature or surface area (2nd, 3rd, and 4th row of Table 4.3, respectively) differed significantly between the...
## Table 4.3.

ROI morphometric values of the pericalcarine cortices, occipital pole, and the inferior and superior lateral occipital cortices.  

ROI - region of interest; $\mu$ - mean; $\sigma_\mu$ - standard error of the mean; df – degrees of freedom.  

<table>
<thead>
<tr>
<th></th>
<th>Pericalcarine cortices</th>
<th>Occipital pole</th>
<th>Inferior lateral occipital cortices</th>
<th>Superior lateral occipital cortices</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume (mm³)</strong></td>
<td>Monocular blind</td>
<td>15691 ± 408</td>
<td>31119 ± 831</td>
<td>30860 ± 955</td>
</tr>
<tr>
<td></td>
<td>Healthy controls</td>
<td>15669 ± 402</td>
<td>32288 ± 719</td>
<td>32634 ± 648</td>
</tr>
<tr>
<td></td>
<td>f-value (df = 1,30)</td>
<td>0.000</td>
<td>1.352</td>
<td>2.894</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.985</td>
<td>0.254</td>
<td>0.099</td>
</tr>
<tr>
<td><strong>Cortical thickness (mm)</strong></td>
<td>Monocular blind</td>
<td>3.03 ± 0.03</td>
<td>2.99 ± 0.03</td>
<td>3.30 ± 0.04</td>
</tr>
<tr>
<td></td>
<td>Healthy controls</td>
<td>3.02 ± 0.05</td>
<td>2.98 ± 0.03</td>
<td>3.25 ± 0.04</td>
</tr>
<tr>
<td></td>
<td>f-value (df = 1,30)</td>
<td>0.015</td>
<td>0.017</td>
<td>0.865</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.902</td>
<td>0.897</td>
<td>0.360</td>
</tr>
<tr>
<td><strong>Mean Curvature (mm⁻¹)</strong></td>
<td>Monocular blind</td>
<td>0.15 ± 0.002</td>
<td>0.16 ± 0.003</td>
<td>0.15 ± 0.002</td>
</tr>
<tr>
<td></td>
<td>Healthy controls</td>
<td>0.15 ± 0.003</td>
<td>0.16 ± 0.003</td>
<td>0.15 ± 0.003</td>
</tr>
<tr>
<td></td>
<td>f-value (df = 1,30)</td>
<td>0.062</td>
<td>1.090</td>
<td>0.240</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.805</td>
<td>0.305</td>
<td>0.628</td>
</tr>
<tr>
<td><strong>Surface area (mm²)</strong></td>
<td>Monocular blind</td>
<td>6838 ± 275</td>
<td>12387 ± 496</td>
<td>15093 ± 678</td>
</tr>
<tr>
<td></td>
<td>Healthy controls</td>
<td>7112 ± 202</td>
<td>12510 ± 338</td>
<td>14737 ± 399</td>
</tr>
<tr>
<td></td>
<td>f-value (df = 1,30)</td>
<td>0.651</td>
<td>0.045</td>
<td>0.213</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.426</td>
<td>0.834</td>
<td>0.648</td>
</tr>
</tbody>
</table>

* Significant difference between the patient group and control group.
monocularly blind patients and the age-matched healthy controls.

4.3.2 Exploratory whole-brain analyses
Using whole-brain analyses, we examined whether unexpected neuroanatomical differences might be present beyond the previously examined visual pathways ROIs. However, we found no significant differences in either the grey or the white matter, or in cortical thickness or mean curvature.

4.4 Discussion

We find that binocular vision loss – as a result of acquired monocular blindness – is associated with a reduced volume of the superior lateral occipital cortices. Functionally, the location of this degeneration is consistent with the loss of binocular vision and stereopsis in the monocularly blind patients. Moreover, in the absence of accompanying volumetric reductions of the optic radiations and the early visual cortex, this implies that the cortical degeneration can only be explained by functional deprivation and not by propagated transsynaptic degeneration that originated at an earlier stage along the visual pathway.

4.4.1 Volumetric loss in the dorsal visual stream is consistent with functional deprivation due to loss of stereopsis

We found grey matter volumetric decreases in the bilateral superior lateral occipital cortices. The superior lateral occipital cortices are located in the dorsal visual stream, which processes information about the location of objects in space. Stereopsis is needed to perceive depth and to precisely localize objects in space. Several fMRI studies have shown that dorsal visual areas are involved in stereoscopic depth perception, specifically the dorsal V3. (Backus et al. 2001, Baecke et al. 2009, Ban et al. 2012, Brouwer, van Ee and Schwarzbach 2005, Goncalves et al. 2015, Ip et al. 2014, Minini, Parker and Bridge 2010, Neri, Bridge and Heeger 2004, Rutschmann and Greenlee 2004, Welchman et al. 2005) Furthermore, the area in which we found the grey matter volumetric decrease extends to the posterior part of the intraparietal sulcus, which has been implicated in visual attention and eye movements. (Culham and Kanwisher 2001) Since monocularly blind patients can only scan the outside world using one eye, they may have adjusted to a different pattern of eye movements. Therefore, the decrease in grey matter volume in the superior lateral occipital cortices in monocularly blind patients might be explained by both the loss of stereopsis as well as accompanying changes in oculomotor behavior. Irrespective, this volumetric decrease in the superior lateral occipital cortices is particularly significant, as we found no evidence for neuroanatomical changes in the early visual cortex. This implies that the observed differences in the dorsal stream are the exclusive result of functional deprivation rather than transsynaptic degeneration.
4.4.2. No anatomical differences in the postgeniculate pathways

If transsynaptic degeneration would play a significant role in causing anatomical changes, we would have expected to find degeneration of the postgeniculate pathways, in particular given the extensive pregeniculate degeneration. The absence of evidence for degeneration in the postgeniculate pathways suggests that transsynaptic degeneration played no role in causing anatomical changes higher up in the visual hierarchy.

4.4.3 Volumetric loss in pregeniculate structures is consistent with degeneration of the axons from the blind eye

We found a volumetric decrease of the optic nerve ipsilateral to the blind eye, the optic chiasm and the bilateral optic tracts. These volumetric losses are consistent with a degeneration of the axons from the removed blind eye. Such degeneration in the pregeniculate structures has been observed previously in a pathohistological study in a single patient that underwent enucleation of one eye 40 years prior to the study, in which evidence was found for axonal degeneration in the ipsilateral optic nerve relative to the blind eye, in both optic tracts, and in the neuronal laminae corresponding to the enucleated eye in both lateral geniculate nuclei.(Beatty et al. 1982) Our study shows that the results of Beatty et al. are common to monocularly blind patients. However, in contrast to Beatty et al. we did not find any differences in the lateral geniculate bodies. It could be that Beatty’s finding was specific to their patient, or that the differences in the lateral geniculate bodies were too small or variable to be detected by MRI analysis.

4.4.4 Occipital white matter volumetric increase might reflect neural remodeling to compensate for the loss of stereopsis

We found a few small sections of increased white matter within the optic radiations, predominantly in the right optic radiation, located close to the region of grey matter volumetric reduction in the superior lateral occipital cortices. The areas of white matter volumetric increase were located within our masks of the optic radiation. However, since the configuration of the largest cluster of increased white matter is oriented vertically rather than horizontally, this cluster might also be part of the vertical occipital fasciculus, which connects the dorsolateral and ventrolateral visual cortices, as recently rediscovered by Yeatman et al.(Yeatman et al. 2014) Using diffusion tensor imaging (DTI), a number of studies showed that white matter fractional anisotropy increased in various brain areas after learning a specific skill.(Fields 2010, Schlegel, Rudelson and Tse 2012, Scholz et al. 2009) Therefore, the increase in white matter we found might indicate neural remodeling in monocularly blind patients due to their learning to rely on alternative cues for estimating depth, for example based on parallax or familiar size, or also adjusted eye-movement patterns.
4.4.5 Comparison with previous visual deprivation studies

Compared to our study, previous structural MRI studies in bilateral blind subjects found more widespread neuroanatomical changes. (Jiang et al. 2009, Leporé et al. 2010, Noppeney 2007, Noppeney et al. 2005, Pan et al. 2007, Park et al. 2007, Park et al. 2009, Ptito et al. 2008, Schoth et al. 2006, Shimony et al. 2006, Shu et al. 2009, Wang et al. 2013, Zhang et al. 2012) This is to be expected, as in bilateral blind subjects there is a complete lack of visual input, whereas in monocularly blind subjects visual input from the healthy eye sustains largely normal visual functioning. However, in bilateral blind cases, it is much harder to establish the selectivity of functional deprivation, whereas in our study we could. Moreover, previous studies in glaucoma and macular degeneration found neuroanatomical changes along the entire visual pathway, including the early visual cortex. (Boucard et al. 2009, Chen et al. 2013, Hernowo et al. 2011, Hernowo et al. 2014, Li et al. 2012, Plank et al. 2011, Williams et al. 2013) This is consistent with the fact that these studies examined patients with binocular visual field defects that overlapped thus causing complete functional deprivation of a region of visual cortex. Therefore, we can conclude that structural changes in the early visual cortex can be caused by functional deprivation but require a complete absence of signals due to either blindness or overlapping bilateral visual field defects.

4.4.6 Limitations

The reduced grey matter volume that we found in the lateral occipital cortex is consistent with a loss of stereopsis and binocular function. While we can be completely certain about the absence of these functions in the monocular blind patients, we could not verify their presence prior to the trauma or operation. However, there is no reason to assume that the (low) incidence of absence of stereopsis would have been higher in the – now monocular blind – patients than in the normal population.

Furthermore, the lateral occipital cortex is quite a large region in which – amongst depth perception – also other functions are represented. Functional studies have shown that depth perception specifically involves dorsal V3. (Baecke et al. 2009, Goncalves et al. 2015, Ip et al. 2014) Therefore, a more accurate linkage of the anatomical changes to the functional deprivation would require an analysis specifically of this area. This, in turn, would require exact localization of this area in individual observers using retinotopic mapping and localizer studies. However, these were not performed in the current observers.

The finding of decreased grey matter density in the superior lateral occipital cortices could also partly reflect the increased white matter volume in adjacent areas. If the nerve fibers extend from the white matter into the cortex, this might interfere with the grey matter analyses. In this case, the changes in grey matter in the superior lateral occipital cortices might not only represent a decrease in grey matter volume, but also a change in the ratio of grey and white matter in this specific area.
The abovementioned volumetric differences were obtained using VBM. With SBM, we found no differences in either the ROI or the whole-brain analysis. Such discrepancies between VBM and SBM results have been observed before. In accordance with our results, in most of these studies SBM showed no changes in cortical anatomical properties in areas where VBM found differences in grey matter volume. (Bridge et al. 2012, Hernowo et al. 2014, Lyoo et al. 2006, Palaniyappan and Liddle 2012, Prins et al. 2016, Voets et al. 2008, von Glehn et al. 2014, Whitwell et al. 2013) This suggests that VBM may be a more sensitive method to discover neuroanatomical differences than SBM.

4.4.7 Conclusion
In this study in monocularly blind patients, we established that the volumes of bilateral superior lateral occipital cortices are reduced, which is most likely caused by the loss of binocular vision, stereopsis and/or altered eye movement patterns. Importantly, we found no evidence for degeneration of the optic radiations and early visual cortex. This indicates that the volumetric reductions in the postgeniculate visual pathways are caused by a selective functional deprivation of the affected areas, rather than by transsynaptic degeneration originating from degenerated axons of the ganglion cells from the blind eye.