Neuroanatomical changes in patients with loss of visual function

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Conclusions

My thesis described research on the association between ocular pathology and anatomical changes in the brain. My aim was to discover which mechanisms underlie this association. To do so, I studied brain changes in a variety of patient groups: AMD, JMD, monocular blindness, and POAG with a monocular field defect, using structural magnetic resonance imaging (MRI) of the brain. My assumption was that by assessing and comparing the results over these different groups, we could determine the contributions of functional deprivation, anterograde transsynaptic degeneration, and general neurodegenerative mechanisms to the association between ocular pathology and neuroanatomical changes.

In **Chapter 2**, I found grey and white matter volumetric reductions throughout the visual pathways in AMD and JMD patients, compared to age-matched healthy controls. Additionally, AMD patients also showed decreased white matter volume outside of the visual pathways, specifically in the frontal lobe. I suggested the latter finding to be the possible neural correlate that reflects a previously described association between AMD and mild cognitive impairment and Alzheimer's disease. In **Chapter 3**, I found marked differences in the cortical thickness, surface area and grey matter volume of the areas V1 and V2 in JMD patients, compared to their age-matched healthy controls. Specifically, the posterior parts of V1 and V2 were more extensively affected than the anterior parts. This reflects retinotopic-specific neuronal degeneration of the visual cortex. In AMD patients, I only found a thinner cortex in V2, whereas V1 did not show any differences. This implies that the volumetric differences found with VBM (chapter 5) in the visual cortex of AMD patients are less apparent than those in JMD patients.

The anatomical changes found in both AMD and JMD in chapter 2 and 3 are generally consistent with both functional deprivation and transsynaptic degeneration. The binocular overlapping central visual field defects lead to decreased activity in the visual pathways. Due to the retinotopic organisation of the visual cortex, a part of the visual pathways will have been deprived of visual input for a long period of time, which may lead to neuroanatomical changes. Finding degeneration in all structures along the entire pathway also suggests that transsynaptic degeneration could explain the degeneration. Given the wide-spread frontal white matter volumetric reductions observed in AMD, also a more general neurodegenerative process may have contributed to the neuroanatomical changes in AMD.

In **Chapter 4**, I found a loss of white matter volume in monocularly blind patients in the optic nerve on the side of the blind eye, in the chiasm and in the bilateral optic tracts, compared to age-matched healthy controls. This white matter volumetric loss in the pregeniculate structures is most consistent with a direct degeneration of the axons that originate from the blind eye. I did not find any anatomical changes in the early visual cortex, which suggests that anterograde transsynaptic degeneration did not play any major role. Furthermore, I found grey matter volumetric loss in the bilateral superior lateral occipital cortices. The superior lateral occipital cortices are located in

the dorsal visual cortex, which is involved in the perception of stereoscopic depth. Therefore, the grey matter volumetric loss in the superior lateral occipital cortices of monocularly blind patients is consistent with functional deprivation caused by their loss of stereopsis. Generalizing from these findings, I deduce that functional deprivation causes anatomical changes, and that transsynaptic degeneration plays no or only a minor role.

In **Chapter 5**, I found neuroanatomical changes in volume and cortical thickness throughout the visual pathway in POAG patients with a monocular visual field defect compared to age-matched healthy controls and age-matched monocularly blind controls. Considering that the visual field defect only existed monocularly, visual function is still supported by the other eye, and stereopsis is mostly preserved. Therefore, these changes can neither be fully explained by functional deprivation nor by transsynaptic degeneration. Furthermore, the brain was more affected in POAG with a monocular visual field defect than in monocular blindness. Hence, this suggests that in POAG also a more general neurodegenerative disorder may contribute to the visual pathway changes.

To conclude, I studied neuroanatomical changes in various ocular diseases that cause visual deprivation. I found evidence for a role of functional deprivation in monocular blind patients. Generalizing, this mechanism presumably plays an important role in all cases in which loss of visual function is associated with neuroanatomical changes. In monocular blindness, I found no indication that transsynaptic degeneration plays any major role, suggesting that this process plays no important role in causing neuroanatomical changes in ocular pathology in general. Furthermore, in both AMD and POAG, I found neuroanatomical changes that could not be explained by functional deprivation. This suggests that in both AMD and POAG more general neurodegenerative processes contribute to the neuroanatomical changes.