# Multi-scale Image Analysis and Prediction of Visual Field Defects after Selective Amygdalohippocampectomy

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## Abstract

Patients with therapy-refractory temporal lobe epilepsy benefit from selective amygdalohippocampectomy, however it can induce Visual Field Defects (VFD). We used whole-brain studies from voxel to network level to describe tissue-specific pre- and postoperative imaging correlates of VFD severity. Pre- and postoperative MRI (T1-MPRAGE and Diffusion Tensor Imaging) as well as kinetic perimetry according to the Goldmann standard were performed on 28 individuals with temporal lobe epilepsy. Using voxel-based morphometry and tract-based spatial statistics, we looked for whole-brain Grey Matter (GM) and White Matter (WM) correlations with VFD. We also performed local and global network studies, as well as reconstructing individual structural connectomes. The postsurgical GM volume decreased with increasing VFD severity in two clusters in the bihemispheric middle temporal gyri (FWE-corrected p 0.05). With increasing severity of VFD in the ipsilesional optic radiation, the fractional anisotropy of a single WM cluster decreased (FWE-corrected p 0.05). Furthermore, patients with VFD had a larger number of postoperative local connectivity alterations than those without. We identified no preoperative associations of VFD severity in the GM, WM, or network measures. Nonetheless, an artificial neural network meta-classifier could predict the occurrence of VFD based on presurgical connectomes above the chance level in an exploratory study.

Keywords: Visual Field Defects • Grey Matter •

White Matter

### Introduction

The most prevalent focal epilepsy is Temporal Lobe Epilepsy (TLE), which affects 25% to 40% of all epilepsy patients. Approximately 40% of TLE patients are pharmacoresistant, and studies have repeatedly demonstrated the superiority of epilepsy surgery over pharmacotherapy. The anterior temporal lobectomy and selective amygdalohippocampectomy are the two most prevalent surgeries (SAH). While multiple studies have found no difference in the number of patients who become seizure-free after surgery, the potential advantage of sAH is the lesser cognitive loss after surgery due to the preservation of the temporal cortex and underlying white matter. A transsylvian or subtemporal method to SAH can be used. When compared to the transsylvian technique, the subtemporal approach has the advantage of avoiding a partial separation of the temporal stem. To gain access to the mesial temporal regions, a piece of the fusiform gyrus is excised. After sAH, between 60% and 80% of patients are seizure-free.

Visual Field Impairments (VFD) have been reported to develop in 15% to 100% of individuals undergoing temporal lobe resective surgery, preventing the ability to drive a car even in people who are seizure-free permanently. The spatial closeness of the Meyer's Loop (ML) to the resection cavity in the temporal lobe causes these VFD, which commonly manifest as contralateral homonymous upper quadrant anopia, sometimes known as 'pie in the sky.' Patients who underwent sAH via a subtemporal route had a lower risk of postoperative VFD than those who underwent SAH via a transsylvian approach, according to reports. With an estimated 100.000 TLE patients potentially susceptible to epilepsy surgery each year in the United States alone, a better knowledge of how damage occurs and how to prevent it during surgery is critical. However, a multi-modal, data-driven strategy to identifying structural underpinnings of perioperative VFD in many tissue types and scales has yet to be explored. We use numerous whole-brain analyses to look for presurgical Grey Matter (GM) and White Matter (WM) predictors of postoperative VFD using imaging and perimetry data from patients undergoing SAH. Furthermore, we want to look into the direct and indirect impacts of the surgical surgery on both voxel and structural connectome levels, as well as how these relate to VFD. We also want to use a mix of structural connectomics and supervised machine learning methods to predict postoperative VFD in an exploratory study.

## Results

### Clinical group differences

In the automated Goldmann perimetry, 21 of the 28 patients in the research showed postsurgical VFD, while the other 7 showed no VFD. Age, gender, epilepsy duration, and surgery-scan interval did not differ significantly between VFD and non-VFD patients (all p > 0.05). The demographic variables listed above did not differ between the subtemporal and transsylvian surgery technique groups (p > 0.05). Patients who had sAH with a subtemporal access, on the other hand, had less severe VFDs (p 0.05). In a regression analysis using VFD as the dependent variable, the extent of the postoperative resection and the preoperative Euclidean distance between the temporal pole and the most anterior region of Meyer's loop were shown to be non-significant (both p > 0.45).

### VLSM results

In the ipsilesional external capsule and the uncinate fasciculus, VLSM analysis of all 28 manual lesion masks revealed a significant correlation between lesioned voxels and postsurgical VFD severity (FWE-corrected p 0.05; volume = 423 mm³). The GM of the ipsilesional temporal pole (FWE-corrected p 0.05; volume = 41 mm³) and the parahippocampal gyrus (FWE-corrected p 0.05; volume = 25 mm³) both had smaller significant clusters.

### VBM results

We discovered a significant decrease in ipsilesional GM volume in our patient cohort using a permutation-based paired t-test comparing pre- and postsurgical T1-weighted scans for the subgroup of patients who underwent a transsylvian surgery operation (n = 18). The largest cluster covered extensive areas of the ipsilesional caudate, putamen, pallidum, and thalamus, as well as other subcortical structures. Aside from subcortical structures, the postsurgical GM reduction cluster also included areas of the insular cortex, as well as the inferior and middle temporal gyrus. A cluster containing the ipsilesional inferior frontal gyrus resulted in the opposite contrast of a postsurgical GM volume increase, although it did not survive FWE-correction (uncorrected p 0.001).

After excluding patients with a surgery-scan gap of more than 12 months, clusters remained significant. In a second analysis, we looked for a linear relationship between the degree of VFD and postsurgical GM volume and found two significant clusters in the posterior divisions of both the ipsi- and contralesional middle temporal gyrus, both of which showed a decrease in GM volume as the degree of VFD increased. For both the transsylvian and subtemporal patient cohorts, this linear relationship may be stated. The presurgical T1 scans were subjected to the opposite contrast as well as the same contrasts, with no notable results.

TBSS results We used a permutation-based paired t-test to compare pre- and postsurgical FA in the transsylvian subgroup, in addition to the VBM analysis. We discovered considerably lower FA-values in vast portions of the ipsilesional temporal and inferior frontal lobe, similar to the GM alterations mentioned above. The inferior and superior longitudinal and fronto-occipital fasciculi, as well as the anterior thalamic radiation and the uncinated fasciculus, were all covered in clusters. In contrast, a large cluster of postsurgically enhanced FA was found in the ipsilesional corona radiata, particularly in the corticospinal tract. This cluster, on the other hand, did not withstand FWE correction (uncorrected p 0.001). After excluding individuals with a surgery-scan interval of more than 12 months, all clusters remained significant. When we looked for a linear link between FA and the severity of VFD, we found a single cluster where FA decreased as the severity of VFD increased. The cluster corresponded to the sagittal stratum's position inside the ipsilesional optic radiation's trajectory, as established by probabilistic tractography. Both the transsylvian and subtemporal patient groups may see the linear relationship. On presurgical DTI scans, the opposite contrast as well as the correlation analysis yielded no significant results.

### Differences in connectivity between groups

When comparing pre- and postsurgical mean connectivity matrices, sAH can be seen in the postsurgical connections that have been negated, such as the amygdala and hippocampus. Apart from this clear finding, both the VFD and no VFD patient groups show a modest decrease in the streamline count of connections inside the ipsilesional hemisphere (upper left quadrant of connectivity matrices). The connection matrices alone, however, do not reveal any significant changes between the two patient groups. In patients with no VFD following SAH, a drop in streamline count of four edges containing six nodes inside the ipsilesional hemisphere was identified using permutation-based paired t-tests between pre- and postsurgical scans. Patients with postsurgical VFD, on the other hand, had severe loss of connectivity in 73 edges involving 28 different brain areas. The ipsilesional temporal lobe, subcortical and prefrontal areas, as well as temporo-occipital connections, were all affected. The superior temporal gyrus, superior frontal gyrus, and pericalcarine cortex were also included, as were three brain regions from the contralesional hemisphere. In the opposite contrary, there was no substantial increase in streamline counts. When the sample was divided into surgical procedures, the pre- and postsurgical connectome comparisons revealed a similar pattern of connectivity differences: after subtemporal SAH, a significant decrease in streamline count was seen in 24 strictly ipsilesional edges spanning 15 nodes, primarily involving the temporal lobe and subcortical brain regions. In comparison, after transsylvian SAH, there was a more wide-spread loss of connectivity, with lower streamline counts in 70 predominantly ipsilesional edges involving 29 brain areas, two of which were on the contralesional hemisphere. The polar opposite did not provide any notable outcomes.

## Discussion

We went attempted to uncover presurgical correlates of postsurgical VFD in this investigation. While we found numerous postsurgical variations between patients with and without VFD in both grey and white matter structures, we were unable to discover any presurgical changes, either at the voxel or structural network level. Despite the lack of statistical significance, supervised machine learning methods might be used to uncover patterns that appear to discriminate these two patient groups solely based on presurgical structural connectomes with above-chance accuracies. Patients receiving temporal lobe resective surgery have had their imaging analysed on a regular basis. This is the first study to link surgery-related grey and white matter consequences to VFD on a worldwide scale. The structural changes found are largely consistent with the findings of prior studies: following epilepsy surgery, both degeneration and neuroplastic reorganisation can occur, which is mirrored by a loss or increase in grey matter volume or fractional anisotropy. White matter abnormalities linked with VFD can be identified using voxel-based lesion-symptom mapping and correlation studies. It should be noted that these findings could reflect VFD correlations or causative relationships. The distinction between causal relationships and correlates, in particular, can only be made using common knowledge of the anatomy and physiology of the visual system. While the changes in the ML are consistent with prior research and to be expected, the bilateral nature of the VBM-cluster in the posterior division of both the ipsi- and contralesional middle temporal gyri is unexpected. This could be explained by diaschisis/secondary degeneration of so-called homotopic connectivity: diaschisis is defined as the post-lesional alteration of brain regions that are distant from but related to the anatomical site of damage.

The particular interconnectivity of mirror parts of the cerebral hemispheres is referred to as homotopic connectivity. As a result, bihemispheric white matter alterations have previously been discovered as a side effect of temporal lobe surgery. However, global network measures based on structural connectomes did not reflect the putative reconfiguration. Another unexpected finding is that the location and shape of the TBSS-cluster are related to the degree of the VFD. The current work is the first to use an objective, ROI-independent approach to show alterations in the path of optic radiation following SAH. However, why this cluster was discovered in the sagittal stratum rather than in the temporal lobe remains a mystery. The anterior region of the ML has a lot of interindividual anatomical variability, which could be one of the reasons. The anatomical distance between the temporal pole and the medial lemniscus (ML) ranges from 22 mm to 37 mm. As a result of the dataset's size and class imbalance, even the best performing classifier in this study's generalizability cannot be guaranteed, and it should be viewed as merely exploratory research that may point to a future predictive approach that needs to be developed in a larger, more balanced sample and validated on yet another, external dataset.