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Physiological correlates and predictors of functional recovery after chiasmal decompression

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Abstract

Background—The intrinsic abilities and limits of the nervous system to repair itself after damage may be assessed using a model of optic chiasmal compression, prior to and following a corrective surgical procedure.

Methods—Visual fields (VFs), multi-focal visual evoked potentials (mfVEP), retinal nerve fiber layer (RNFL) thickness and diffusion tensor imaging (DTI) were used to evaluate a patient before and after removal of a meningioma compressing the chiasm. Normally-sighted individuals served as controls. The advantage of each modality to document visual function and predict post-operative outcome (two years follow up) was evaluated.

Results—Post-surgery visual recovery was best explained by critical mass of normally-conducting fibers, and not associated with average conduction amplitudes. Recovered VF was observed in quadrants in which more than 50% of fibers were identified, characterized by intact mfVEP latencies but severely reduced amplitudes. Recovery was evident despite additional reduction of RNFL thickness and abnormal optic tract diffusivity. The critical mass of normally conducting fibers was also the best prognostic indicator for functional outcome two years later.

Conclusion—Our results highlight the ability of the remaining normally conductive axons to predict visual recovery following decompression of the optic chiasm. The redundancy in anterior visual pathways may be explained, neuro-anatomically, by overlapping receptive fields.

Keywords

Chiasmal decompression; Prognosis; Visual Evoked Potentials; Visual fields

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Acquired optic chiasmal abnormalities usually present with a bitemporal visual field defect. Reversibility of symptoms is often evident following a decompressive surgical procedure (1). This may serve as a suitable in-vivo model for assessing the intrinsic abilities and limits of the nervous system for functional recovery following compressive damage. While various technologies are available to assess the impact of chiasmal compression (2–6), their correlation to functional status and recovery is unclear.

We evaluated a patient before and after removal of a giant meningioma compressing the entire chiasm. Multifocal visual evoked potentials (mfVEP) amplitudes and latencies, retinal nerve fibers layer (RNFL) thickness measured with optic coherence tomography (OCT), and optic tract diffusivity by diffusion tensor imaging (DTI) and fiber tractography were acquired prior and following craniotomy. All measurements were compared to a group of normally-sighted controls. Correlation with functional status as determined with visual fields (VFs) was assessed for each technology. In addition, the distinctive advantage of each tool as a prognostic indicator for visual recovery was determined over two years following surgery.

Methods

Case Report

A 35-year-old man presented with bilateral visual loss, which he noticed six months prior to admission. Apart from VF loss, his ophthalmic examination was intact. Magnetic resonance imaging (MRI) showed a giant tuberculum sellae meningioma compressing the entire optic chiasm. No hormonal abnormalities were found. The patient underwent right fronto-orbital craniotomy and the tumor was completely resected. No neurological complications were reported following the surgery.

Controls—17 normally-sighted individuals aged 24.2 ± 9.1 (mean $\pm$ SD) years underwent DTI scans to obtain normal optic tracts diffusivity measurements. Six separate normally-sighted controls aged 38.7 ± 13.3 underwent mfVEP to obtain normative measurements of MfVEP amplitudes and latencies in each quadrant.

The study has been approved by the Hadassah Hebrew University Medical Center Ethics Committee. Informed consent was obtained from all participants.

Procedures

Visual fields: VFs were tested using the automated perimetry (Humphrey SITA-standard 24–2 protocol with stimulus 3; Carl Zeiss Meditec, Inc., Dublin, CA). We reviewed VFs for the presence of fixation losses and false-positive and false-negative rates. The averaged threshold detected for each spot was calculated separately for the inferotemporal, inferonasal, superotemporal and superonasal VF quadrants (the dimmer the stimuli detected, the higher the threshold number. Therefore, the higher the threshold, the better the patient has performed the test). VFs were measured pre-operatively, immediately post-surgery, 4, 12 and 24 months later. To assess visual outcome in comparison to age-related norms, VFs obtained two years following surgery also were evaluated by means of total deviation. Total

deviation was calculated separately for the inferotemporal, inferonasal, superotemporal and superonasal quadrants.

mfVEP: The mfVEP was performed using the Accumap™ (ObjectiVision, software: Opera, Sydney, Australia). The stimulus consisted of a cortically-scaled dart-board pattern of 58 segments (eccentricity up to 24 degrees). Each segment contained 4 × 4 grid of black and white checks, which reversed patterns, according to a pseudorandom sequence. Recordings were obtained with four electrodes placed over the inion. Mean amplitudes and latencies were calculated for each of the four VFs quadrants. For details see (7); mfVEP was assessed prior to and 2 months following surgery.

OCT: RNFL thickness pre- and post-surgery were recorded on different machines, time (Zeiss Stratus) and spectral (Heidelberg Engineering Carlsbad, CA) –domain OCT, respectively. Recording was done by a trained technician; an expert independently reviewed all scans to check for artifacts that might interfere with RNFL segmentation. OCT was assessed prior to and 4 months following surgery.

MRI scans were acquired on a 3-tesla scanner (Trio; Siemens, Erlangen, German) using 12-channel standard head coil. Anatomical MRI sequences included 3D T1-weighted images (minimum TE, flip angle 9°, TR=2,300 ms, voxel size 1×1×1.1mm).

DTI: DTI data were acquired using diffusion-weighted imaging sequence (single-shot, spin-echo, TE=94ms, TR= 7127–8224 ms). To cover the whole brain, 52–60 axial, 2 mm thick slices (no skip) were acquired for two b-values, b=0 and b=1000 s/mm². The high b-value was obtained by applying gradients along 64 different diffusion directions, including 2 averages. DTI image processing and analysis was performed using the open-source mrVista package <http://vistalab.stanford.edu/software>. Preprocessing included removing Eddy current distortions and subject motion. Each diffusion-weighted image was then registered to the mean of the (motion-corrected) non diffusion-weighted images using a two-stage coarse-to-fine approach that maximized the normalized mutual information. The mean of the non-diffusion weighted images was also automatically aligned to the T1 image using a rigid body mutual information algorithm.

Fiber tractography was used to delineate the optic tracts in each patient, using the Contrack algorithm (8), a probabilistic algorithm designed to identify the most likely pathway between two regions of interest (ROIs). For delineating the optic tracts in control subjects, optic chiasm ROIs were positioned on coronal reformations of T1 maps of each subject, centered on the right and left sides of the pituitary stalk; the volume of these regions were standardized to 485 mm³. Both lateral geniculate nuclei (LGNs) were defined anatomically on the axial and sagittal reformations of T1 maps, and their volumes were standardized to 895 mm³. Since the optic chiasm could not be detected in the patient's scan prior to surgery, pre-operative b=0 maps were registered to the post-operative T1 maps, in which ROIs were described.

ConTrack was set to generate a set of 10,000 candidate pathways between the optic chiasm and the LGN ROIs. The candidate pathways were scored, and the top 10% (1000) scores

pathways were selected as the most likely pathways for connecting the chiasm to the LGN. Diffusivity measurements along the tract were re-sampled at 30 positions, calculating fractional anisotropy (FA) at each of these nodes. In this way, measures throughout the length of the fiber could be combined across different subjects. In order to avoid partial volume averaging with non-white matter (i.e. ventricles or grey matter), diffusion measurements were taken near the dense core of the fibers. Diffusion at the core was estimated by combining data from different voxels in a weighted fashion, assigning greater weight to voxels that are close to the core of the estimated tract (9). DTI was assessed prior to and 4 months following surgery.

RESULTS

Pre-operatively, bitemporal visual field loss was accompanied by major reduction in mfVEP amplitudes, prolongation of mfVEP latencies in the inferior fields, RNFL thinning was present throughout the retina and not confined to the crossing nasal retinal fibers. There was reduced fractional anisotropy (FA) along the optic tracts (12 and 7 points outside the range of $\pm$ one SD from controls' mean in the left and right sides, respectively) (Fig 2).

Post-operatively, there was significant improvement in VFs. Improvement in the left eye was seen immediately and continued in the subsequent months. In the right eye, VFs deteriorated immediately but improved by 4 months; further improvement was evident during the two years follow-up (Fig 1).

Improved VFs were evident despite sustained reduction of mfVEP amplitudes, extending more than 2 SD from controls' mean (and more than 4 SD from controls' mean within the temporal quadrants of both eyes as well as the inferonasal quadrant of the right eye). In contrast to the reduced amplitudes, post-surgical mfVEP latencies were intact in all measurable regions (mfVEP latencies could be measured within quadrants in which more than 50% of the fibers were detected, i.e. mfVEP amplitudes > 0 nV. This was the case in all but the inferotemporal quadrant of the right eye (Fig 1).

Thus, the amount of conducting fibers, rather than the averaged level of conductance, correlated best with VF; function of more than 50% of fibers resulted in overall normal conduction latencies and intact VF. The amount of conducting fibers had also the best prognostic value for VF two years following surgery.

Functional improvement four months post-operatively was not in line with the additional structural damage evident in the right eye RNFL thickness, possibly reflecting surgical injury (Fig 1). While optic tract diffusivity (FA) improved, it did not reach normal levels (7 and 6 points were below controls' mean in the left and right tracts, respectively) (Fig 2).

Discussion

Improvement in visual fields following decompression of the optic chiasm has been reported in large cohorts of patients (10–12). Consecutive measurements suggest two stages of recovery that might stem from different biological mechanisms: a fast early improvement

due to the resolution of conduction block, and late improvement due to restoration of axonal transport, remyelination or remodeling within the anterior visual pathways (12).

Our study further highlights the resiliency of the anterior visual pathways. Major loss of VF, marked reduction in mfVEP amplitude and diffusivity along the optic tracts were not barriers to recovery. This adaptive ability also was supported by the decline in post-surgical RNFL thickness of the right eye.

The presence of conducting fibers in our study was best assessed by the mfVEP technique. The simultaneous recording from multiple locations allowed detection of the number of conducting axons within subsets of the visual field, facilitating threshold detection (13). Reduction in mfVEP amplitude represented loss of anterior visual pathway fibers and thinning of RNFL indicated its irreversible nature.

Visual function, reflected in VF results, could be best explained by a critical mass of remaining normally conducting fibers. The functional improvement following surgery was probably the result of surviving fibers, as indicated by shortening of mfVEP latencies and improved diffusivity. Thus, chiasmal compression produced both permanent damage reducing the amount of fibers and reversible damage to conduction in surviving fibers.

This critical mass of normally conducting fibers (mfVEP amplitude > 0 nV in more than 50% of fibers) was the best prognostic indicator for functional outcome, predicting visual performance two years later.

The importance of a critical mass of normally conducting fibers is supported by previous studies, demonstrating that functional visual deficit [visual acuity (14) and relative afferent pupillary defect (15)] is apparent only after loss of approximately 40–50% of optic nerve axons. This threshold effect is probably related to the redundancy in the anterior visual pathways, which can be explained neuro-anatomically by overlapping receptive fields.

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Figure 1. Testing results over a 2 year period following removal of a tuberculum sellae meningioma. mfVEP, multifocal visual evoked potential; SD-OCT, spectral- domain optical coherence tomography.

Figure 2.

Diffusion tensor imaging and fiber tractography. Left: the optic tracts delineated in the patient pre-operatively and four months following surgery. Right: FA values along the optic tracts in control subjects (n=17, dark blue plots), patient prior to surgery (pale blue plots) and during the post-surgical period (light blue plots). Error bars represent standard deviation. Red dotted line represents the border of the meningioma. FA, fractional anisotropy.