Supplemental Materials

Imaging acquisition

Image acquisition was performed using a 3T Siemens Trio scanner (Erlangen, Germany) equipped with a standard 12-channel head coil. A high-resolution structural scan was acquired using a 3-dimensional sagittal T1-weighted magnetization-prepared rapid gradient echo (MPRAGE, echo time [TE] = 16 msec, repetition time [TR] = 2,400 msec, inversion time [TI] = 1,000 msec, flip angle = 8°, 256 × 256 acquisition matrix, 1×1×1mm voxels). This scan was used for atlas registration. High-resolution 2-D multislice oblique axial spin density/T2-weighted fast spin echo (FSE) structural images were also acquired using slice tilts and positions computed by slice preregistration (TE=455 msec, TR = 3,200 msec, 256 × 256 acquisition matrix, 1 acquisition, 1×1×1mm voxels). These T2-weighted FSE data were used for rs-fcMRI atlas registration. rs-fcMRI scans were collected using a gradient spin-echo sequence (TE = 27 msec, TR = 384 msec, field of view = 256 mm, flip angle = 90°, 4mm isotropic voxels) sensitive to blood oxygen level dependent (BOLD) contrast. Complete brain coverage was obtained using 36 contiguous slices acquired parallel to the anterior commissure/posterior commissure plane. Two six minute rs-fcMRI runs (164 volumes per run) were acquired during which participants were asked to fixate on a visual cross-hair and not fall asleep.

Pre-processing of rs-fMRI

Initial preprocessing of rs-fMRI data followed conventional methods as previously described. Generic preprocessing of fMRI data included correction for slice-dependent
intensity differences related to interleaved acquisition (debanding)\textsuperscript{6}, rigid body correction for head movement within and between fMRI runs, and atlas transformation. Volumes strongly contaminated by head movement\textsuperscript{7} were removed and voxelwise replaced with linearly interpolated values\textsuperscript{8}. Frame censoring was computed using the root mean difference of the BOLD intensity image across subsequent frames (DVARS) measure\textsuperscript{9} modified to include a 10mm full width at half maximum (FWHM) Gaussian spatial pre-blur. N.B.: This pre-blur was used only to calculate DVARS and was not carried forward. The frame exclusion threshold was set at 0.7% rms BOLD signal change over successive frames, counting only voxels within the brain. Only subjects with fewer than 40\% of frames excluded were passed on to the next stage of processing. Signals of non-interest were extracted from white matter, ventricles, and the global signal averaged over the whole brain.\textsuperscript{10} These time-series along with movement time-series and their first temporal derivatives were regressed from the BOLD time-series. The residual BOLD time-series was then low-pass filtered to retain frequencies below 0.1Hz and spatially smoothed with Gaussian blur (6mm FWHM in each direction). The linearly interpolated volumes were excluded in all subsequent analyses.

\textit{Quality Assurance}

Image intensity temporal standard deviation (s.d.) was evaluated voxelwise over the whole brain. One ON patient was excluded due to excess motion resulting in insufficient usable BOLD frames.

\textit{Visual outcome Measures}
We divided the visual metrics into those obtained at the nadir of visual function and those obtained either at baseline examination (defined as partial or complete recovery) or at the time of the rs-fMRI. The rationale for this decision was that some patients were examined after they had begun to recover their visual function, and we were interested in determining whether visual function at nadir would correlate with changes in functional connectivity. Visual function at nadir was defined as the worst documented visual function within two weeks of onset of visual loss, the timeframe during which a typical episode of ON might progress, and when most patients reach their nadir. For some patients, this information was extracted from the referring ophthalmologist’s or optometrist’s records. Most subjects (n = 13) underwent automated perimetry testing with Humphrey Visual Field Analyzer, using the 24-2, Swedish Interactive Threshold Algorithm (SITA)-standard program. Visual field mean deviation was used for analysis. For subjects with visual acuity < 20/200, Goldmann kinetic perimetry was performed. These subjects were assigned a value of -30 decibels (dB) for the purposes of analysis. A majority of patients (n=11) underwent optical coherence tomography (OCT) testing using the Cirrus Spectral Domain OCT. The fast retinal nerve fiber layer thickness (rNFL) program was used. Average rNFL thickness and quadrant rNFL thickness, including temporal rNFL thickness, were recorded for analysis. Although all patients underwent complete examination at baseline, SLCLA, VFQ-25, and OCT were performed in those eligible at the time of the rs-fMRI scan.
References


