Pituitary adenoma is the third most common primary intracranial neoplasm with an annual incidence of 0.8–8 per 100,000.17 One of the clinical manifestations of this tumor is visual deterioration stemming from compression of the anterior visual pathway. 6 The classic teaching has been that compression of the optic chiasm by pituitary tumors is associated with reversible bitemporal hemianopia. Anecdotal evidence, however, has suggested a large variability in the range of preoperative visual dysfunction and the recovery these patients may experience. To optimize the clinical management and surgical decision making for patients with pituitary adenomas, we need a better understanding of the relationship between the effects of compression on neural activity in the visual cortex and the decline, and eventual recovery, of visual function. Previous studies have not followed this patient population longitudinally with functional neuroimaging to assess how decompression of the visual pathway can affect the neuronal reorganization in the context of recovering neurological function.

A number of studies have used functional neuroimaging to examine the relationship between visual field defects due to various etiologies and the neural activity in the visual cortex.8 Many, however, have not used standard retinotopic procedures16 to map out systematically how different parts of the retina are represented in corresponding portions of the primary visual cortex. Instead, most have used alternative paradigms such as presenting

Retinotopic organization of the visual cortex before and after decompression of the optic chiasm in a patient with pituitary macroadenoma

Case report

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Compression induced by a pituitary tumor on the optic chiasm can generate visual field deficits, yet it is unknown how this compression affects the retinotopic organization of the visual cortex. It is also not known how the effect of the tumor on the retinotopic organization of the visual cortex changes after decompression. The authors used functional MRI (fMRI) to map the retinotopic organization of the visual cortex in a 68-year-old right-handed woman before and 3 months after surgery for a recurrent pituitary macroadenoma. The authors demonstrated that longitudinal changes in visual field perimetry, as assessed by the automated Humphrey visual field test, correlated with longitudinal changes in fMRI activation in a retinotopic manner. In other words, after decompression of the optic chiasm, fMRI charted the recruitment of the visual cortex in a way that matched gains in visual field perimetry. On the basis of this case, the authors propose that fMRI can chart neural plasticity of the visual cortex on an individual basis and that it can also serve as a complementary tool in decision making with respect to management of patients with chiasmal compression.

doi:10.3171/2012.4.JNS112158

Key Words • retinotopy • primary visual area • primary visual cortex • optic chiasm • pituitary macroadenoma • pituitary surgery • transnasal transsphenoidal resection

Abbreviations used in this paper: fMRI = functional MRI; V1 = primary visual cortex.
flashing stimuli in various parts of the visual field. It is often difficult with these paradigms to map out the full extent (and organization) of retinal representations in the V1. Nonetheless, there have been a few studies that have compared visual field defects and retinotopic organization of the V1 using standard retinotopic procedures. For example, Furuta et al.\(^2\) compared visual field loss as assessed on the Humphrey automated perimeter and retinotopic activation in the V1 in several patients after trauma, hemorrhage, and infarction. This study showed that V1 retinotopy correlated with the visual field perimeter in each patient. Nielsen et al.\(^10\) further demonstrated that the visual field loss in a patient with a pituitary macroadenoma compressing the optic chiasm was closely correlated with V1 retinotopy. However, these 2 studies did not examine changes in visual defects over time. To our knowledge, there has been no longitudinal investigation that has used standard fMRI retinotopic mapping to chart the effects of tumor compression and decompression on the optic chiasm. The ability to examine changes in V1 retinotopy in patients with pituitary tumors before and after transnasal transsphenoidal surgery has the potential to provide new insights into V1 plasticity. Such studies could also provide an opportunity to evaluate the contribution that fMRI has to offer in clinical decision making.

Case Report

This 68-year-old woman presented with ophthalmological symptoms due to a recurrent pituitary macroadenoma. The patient complained of left retroorbital pressure, difficulty with focusing, and diplopia. The Humphrey automated perimetry detected a left visual field defect (Table 1 and Fig. 1). The MRI examination confirmed upward compression of the left anterior portion of the optic chiasm as well as the left optic nerve from the tumor (Fig. 2A). The tumor measured 3.4 cm (craniocaudal) × 3.1 cm (transverse) × 3.5 cm (antero-posterior). The patient had previously undergone subtotal debulking of the tumor 3 years prior to her recent presentation with complete normalization of the visual fields after the initial surgery. She then underwent a second transnasal transsphenoidal debulking of the tumor, which was confirmed to be a recurrent null cell pituitary adenoma. After surgery, the visual fields normalized, and the MRI study demonstrated substantial debulking of the tumor without any ongoing compression of the optic chiasm (Fig. 2B). An fMRI study was performed before and 3 months after the patient’s second surgery. Specifically, we examined the retinotopic organization of the primary visual cortex and compared these results with those of the automated Humphrey visual field test (Carl Zeiss Meditec) using program 30-2. Ethics approval for this study was granted by the University of Western Ontario’s Health Sciences Research Ethics Board. Written consent was obtained from the patient before the start of the fMRI investigation.

### Retinotopic Stimulation

Similar to standard retinotopic procedures for polarmapping,\(^16\) the stimulus consisted of a high-contrast checkerboard wedge back-projected on a screen located at the back of the bore of the fMRI scanner. The display was viewed using a mirror. During fMRI, one eye was always patched, and each eye was tested separately. The wedge subtended 14° of visual angle from a red fixation circle, had an angular width of 30°, rotated around central fixation for 16 cycles with 13 steps and 26.0 seconds per cycle, and flickered at a rate of 4 Hz. The starting position for the rotating wedge began from the upper vertical meridian and rotated either counterclockwise for polar mapping of the left visual field (with the left eye open and the right eye patched) or clockwise for polar mapping of the right visual field (with the right eye open and the left eye patched). Eccentricity mapping was not performed so that we could keep the scanning sessions at a reasonable duration for the patient. The patient was instructed to fixate her gaze on the fixation circle at all times. Because the Humphrey automated perimetry indicated that the visual deficit was largely restricted to the left lower visual field, this area was scanned. We modified the protocol of previous studies to keep the stimulation time manageable.

<table>
<thead>
<tr>
<th>Date</th>
<th>Visual Acuity</th>
<th>Visual Field</th>
<th>Other Ophthalmological Findings</th>
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<tr>
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<td>20/20</td>
<td>20/30</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>perimetry)</td>
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<tr>
<td>November 2006</td>
<td>20/20</td>
<td>20/25</td>
<td>full (Goldmann perimetry)</td>
</tr>
<tr>
<td>April 2008</td>
<td>20/20</td>
<td>20/25</td>
<td>full (Humphrey perimetry)</td>
</tr>
<tr>
<td>October 2008</td>
<td>20/20</td>
<td>20/25</td>
<td>full (Humphrey perimetry)</td>
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<tr>
<td>October 2009</td>
<td>20/20</td>
<td>20/30</td>
<td>It temporal field defect (Humphrey perimetry)</td>
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<td>20/20</td>
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</tr>
<tr>
<td>October 2010</td>
<td>20/20</td>
<td>20/25</td>
<td>full (Humphrey perimetry)</td>
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* The patient’s first surgery was performed in September 2006, and the second surgery was performed in February 2010. Abbreviations: Dx = diagnosis; NA = not available.
Neural plasticity in a patient with chiasmal compression

Scanning was performed using a 3-T Tim Trio MRI system with a 32-channel head coil (Siemens). An anatomical image was obtained, encompassing the entire brain. This was achieved by collecting 192 1-mm-thick slices using a 3D T1-weighted acquisition sequence (T1 900 msec, TE 2.98 msec, TR 2300 msec, flip angle 9°). The in-plane resolution of the anatomical images was 256 × 240 pixels. To collect the functional data, we used a T2*-weighted echo planar imaging sequence (TE 30.0 msec, TR 2000 msec, flip angle 90°) for blood oxygen level–dependent acquisition. The field of view was 24.0 × 24.0 cm with an in-plane matrix size of 80 × 80 pixels. Each image covered the entire brain and consisted of 36 horizontal slices that were collected in an interleaved order (isotropic voxel size 3.0 mm). There were no gaps between slices.

SPM8 (Statistical Parametric Mapping software, University College of London, United Kingdom; available at http://www.fil.ion.ucl.ac.uk/spm) was used to preprocess and analyze the data. The functional data were realigned to the mean image of all the functional data. The first 2 volumes in each run were excluded because they may not be representative of steady state. A slice-time correction algorithm was used to correct for differences in acquisition times between slices by resampling all slices to match the first slice. Anatomical MRI studies were transformed into standardized space using the template brain from the Montreal Neurological Institute (McGill University, Montreal, QC, Canada). The functional data were then coregistered to the anatomical MRI studies in standardized space and resampled at an isotropic voxel size of 1 mm. Although retinotopic data are typically analyzed in the patient’s own native space, the transformation of the functional data into standardized space provided us with a much better coregistration between the pre- and postsurgery sessions than coregistering the functional data between sessions in native space. Drift was removed with a high pass filter (cutoff 128 seconds), and the data were spatially smoothed with a 2.5-mm full-width half-maximum Gaussian filter to help improve the signal-to-noise ratio.

**Statistical Analysis**

For statistical analyses, the retinotopic stimulation was modeled as 2 regressors (sine and cosine functions with the same frequency as the rotating wedges) in a general linear model and the relative phase of the response at each voxel was calculated from the arctangent of the ratio of the parameter estimates (that is, beta weights) for the sine and cosine regressors. The resulting phase maps were masked to select all voxels responding to the retinotopic stimulation using a voxel-wise F-test thresholded at p < 0.001 and superimposed on an inflated reconstruction of the brain in Freesurfer (Martinos Center for Biomedical Imaging, Harvard University, Cambridge, MA; available at http://surfer.nmr.mgh.harvard.edu). Representations of the V1 for the lower and upper visual fields were manually labeled by defining the vertical (as assessed by reversals in the phase map) and horizontal (as assessed by changes in polarity in the phase map) meridians. The volume of activated gray matter was then calculated for each region by counting the number of 1-mm cubic voxels within a label that responded significantly to the retinotopic stimulation.

**Results**

Examination of the patient’s T1-weighted MRI studies showed compression of the left anterior portion of the optic chiasm and the left optic nerve before the patient’s operation and a decompression of these structures after the surgery (Fig. 2). Inspection of the functional data revealed that head movements were within an acceptable range never exceeding 2 mm in translation and 1° in rotation.
mated perimetry, which adjusts for the effects of age and any overall changes in the height of the measured hill of vision, are shown in Fig. 1. Before the operation, there was a clear visual defect located primarily in the patient’s left lower visual field when the left eye was tested, and there were no indications of any defects in the right visual field when the right eye was tested (Fig. 1A and B). After the operation, the patient made a meaningful recovery with respect to her vision; no detectable visual field defects were observed after the surgery (Fig. 1C and D). Her fMRI results corresponded well with these visual field measurements (Figs. 3 and 4). Namely, most of her left V1 responded to retinotopic stimulation in her right visual field (Fig. 3A), but a large portion of her right V1 did not respond to retinotopic stimulation in her left visual field (Fig. 3B). In addition, her right V1 representation of the left lower visual field was more affected than her right V1 representation of the left upper visual field (Fig. 3B). After her surgery, the fMRI results showed a recovery in the right V1’s responsiveness to retinotopic stimulation in the left visual field, particularly for the lower part of the visual field (Fig. 3D). A total of 886 mm$^3$ of the V1 responded to retinotopic stimulation in the left lower visual field after the operation compared with 314 mm$^3$ before the operation. This represents a 282% increase of the V1 recruited for the left lower visual field.

To further underscore agreement between the Humphrey and fMRI examinations, we performed a Pearson correlation between the intensity of light that was detected by the patient in the visual quadrants of each eye during the Humphrey automated perimetry (in dB) and the volume of activated V1 gray matter (in mm$^3$) in the corresponding regions of the contralateral hemisphere before and after the operation. This analysis yielded a correlation that was significant ($r_{(6)} = 0.82$, $p < 0.05$; Fig. 4C). An additional Pearson correlation between improvements in the Humphrey automated perimetry ($\text{dB}_{\text{after}} - \text{dB}_{\text{before}}$) and the change in the amount of V1 recruitment ($\text{mm}^3_{\text{after}} - \text{mm}^3_{\text{before}}$) showed a similar relationship that almost reached statistical significance ($r_{(2)} = 0.95$, $p = 0.05$; Fig. 4D).

**Discussion**

We examined the retinotopic organization of the
Neural plasticity in a patient with chiasmal compression

V1 in a patient with visual field defects before and after transnasal transsphenoidal resection of a pituitary tumor that was compressing the left anterior portion of her optic chiasm and her left optic nerve. The patient’s perimetry on the Humphrey examination indicated primarily a left lower visual field defect before the surgery. Her left visual field returned to normal after the surgery, and the results of the fMRI retinotopy corresponded well with this recovery. Namely, the surface area of retinotopic activation in the right V1 for the left lower visual field was diminished before surgery, and there was a 282% increase in cortical representation for this visual quadrant after surgery. Pearson correlations between the Humphrey automated perimetry and fMRI retinotopic activation further revealed that improvements in her visual field were accompanied by a corresponding increase in the amount of activation in the corresponding V1 retinotopic map.

Although the Humphrey automated perimetry provides a useful measure of visual field defects and is a useful screening tool for assessing compression of the optic chiasm, the observed deficits do not always coincide with expected deficits from a particular compression. Visual field defects can differ from one individual to another with similar types of compression. The reasons for this are not yet clear, but there are a number of possible explanations. First, retrograde tracing studies in the monkey revealed that the retinotopic organization of the optic nerve is not as clear cut as we often assume it to be. In fact, this literature has shown that there is quite a bit of scatter in the retinal organization of the optic nerve. Second, the size of the fibers in the optic nerve differs depending on whether they are part of the magnocellular or parvocellular pathways. Fibers from the magnocellular pathway tend to be larger in diameter, whereas fibers from the

Fig. 3. Retinotopic results. The retinotopic activation is superimposed on a reconstructed cortical surface viewed from the back for the left V1 representing the right visual field before surgery (A), the right V1 representing the left visual field before surgery (B), the left V1 representing the right visual field after surgery (C), and the right V1 representing the left visual field after surgery (D). Also displayed for illustrative purposes are the results from the Humphrey automated perimetry (in db) after a cubic spline was used for data interpolation. The activation is color coded such that cool colors represent the lower visual field (dark blue to light blue: the vertical meridian to the horizontal meridian) and warm colors represent the upper visual field (red to yellow: the vertical meridian to the horizontal meridian).
parvocellular pathway tend to be smaller in diameter.\textsuperscript{13} It is still unclear as to how these pathways may be affected differently by tumor compression.\textsuperscript{3,12} Third, it has been argued that the vulnerability of the optic chiasm to compression may also relate to vascular supply, which varies from one individual to another.\textsuperscript{2} Given that similar forms of compression can yield different visual field defects across individuals, it would be important to develop tools that would allow one to examine the neural consequences of chiasmal compression on an individual basis. As demonstrated in our study, fMRI retinotopy has the power to chart these effects in the V1 as well as how the brain responds after decompression on an individual basis.

Our testing paradigm specifically assessed how chiasm compression and decompression potentially impacts V1 organization. By studying how the V1 might reorganize after compression on the optic chiasm, one might gain insight as to why some patients do not show visual field defects in the setting of chiasm compression and why other patients do not respond to decompression. For example, Ryu et al.\textsuperscript{14} documented over time how slow-growing tumors can compress the optic chiasm approximately 1 cm upward without causing any disruption in visual field perimetry. Clearly, in these cases, compensatory or repair mechanisms are at play. Compensation might occur through parallel pathways in which fibers that are unaffected by the compression compensate for loss of function by the compressed fibers. However, in the setting of rapid tumor growth, irreversible damage from either pulling on the optic disc or nerve sheering, could occur before compensation can develop. In addition, not all patients undergoing transnasal transsphenoidal resection of a pituitary tumor will make a meaningful recovery. Powell showed that visual field defects do not improve in approximately 11% of patients after this surgery.\textsuperscript{11} The reason for this is thought to be due to irreversible damage of the optic fibers from either rapid or prolonged compression of the optic chiasm. Functional MRI might potentially be more sensitive to detect visual field defects caused by physical damage on optic fibers before these defects are manifested behaviorally on the Humphrey automated perimetry.

Functional MRI also offers other advantages over the Humphrey automated perimetry. The Humphrey automated perimetry is more subjective because it requires patients to actively indicate on each trial whether they see a light. In fact, a previous report has shown that the Humphrey automated perimetry cannot differentiate between reliable and unreliable patients.\textsuperscript{3} Depending on patient cooperation, false positives and false negatives can oc-

**Fig. 4.** Bar graphs showing the changes in fMRI retinotopy and changes in the Humphrey automated perimetry. The graphs demonstrate the amount of gray matter activation in V1 representation for different visual fields (VFs) (A), the intensity of light detected during the Humphrey automated perimetry in different visual fields (B), the correlation between the intensity of light during the Humphrey automated perimetry and the amount of gray matter V1 across different visual fields before and after the operation (C), and the correlation between differences (Diffs) in the Humphrey automated perimetry and the amount of V1 recruitment (D). Each circle represents a different visual field quadrant.
cur with the Humphrey automated perimeter, which can lead to misinterpretations in visual field defects. The Humphrey automated perimeter is also prone to learning effects, which can further lead to misrepresentations in how visual fields change over time. In contrast, retinotopic examination using fMRI is passive and, as a consequence, more objective. However, fMRI should not be seen as a replacement for the Humphrey automated perimeter but rather as a complementary tool for decision making. Functional MRI has its unique set of challenges, the foremost being that patients should be compliant with its constraints. Patients must remain still because head movements contaminate the fMRI signal. Moreover, it is important that levels of attention are equated between sessions to generate meaningful longitudinal assessments, given that the blood oxygen level–dependent signal, particularly in visual areas, is modulated greatly by levels of attention. One solution to this problem might be to combine retinotopic procedures with an attentional task such as indicating with a button press whether a central fixation cue changes color. The button pressing data could enable one to assess the degree to which patients attend to the stimuli.

Conclusions

To our knowledge, this is the first fMRI study to demonstrate retinotopic reorganization of the V1 before and after transnasal transsphenoidal chiasmal decompression. As one would expect, the primary visual cortex was recruited after the surgery in a manner that coincided with gains in visual field perimetry. Given these results, we believe that fMRI has the potential to serve as a complementary tool in decision making with respect to management of patients with chiasmal compression.

Disclosure

This work was supported by a postdoctoral fellowship award from the Ontario Mental Health Foundation to P.A.C., a Natural Sciences and Engineering Research Council of Canada postdoctoral fellowship award to C.L.S., an Ontario Ministry of Research and Innovation postdoctoral award to I.S., and a research-operating grant from the Canadian Institutes of Health Research to M.A.G.

Author contributions to the study and manuscript preparation include the following. Conception and design: Duggal, Striemer, Ryu, Goodale, Rotenberg. Acquisition of data: Striemer, Ryu, Nicolle. Analysis and interpretation of data: Chouinard, Striemer, Sperandio. Drafting the article: Chouinard, Ryu, Sperandio, Goodale. Critically revising the article: Duggal, Chouinard, Striemer, Ryu, Sperandio, Goodale. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Duggal. Statistical analysis: Chouinard, Ryu, Sperandio. Administrative/technical/material support: Chouinard, Striemer, Goodale. Study supervision: Duggal, Goodale.

Acknowledgments

The authors thank Lars Strother for his advice on issues concerning retinotopy and Sandy Goncalves for her administrative assistance.

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Manuscript submitted December 1, 2011. Accepted April 25, 2012.
Please include this information when citing this paper: published online June 8, 2012; DOI: 10.3171/2012.4.JNS112158.
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