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A Lack of Experience-Dependent Plasticity after more than a Decade of Recovered Sight

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Abstract

Fourteen years ago, MM had monocular vision restored after being blind between age 3 and 46. Tests carried out over two years following the surgery revealed impairments of 3D form, object, and face processing, and an absence of object and face selective BOLD responses in ventral visual cortex. Here we re-examined MM to test for experience-dependent recovery of visual function. Behaviorally, MM remains impaired in 3D form, object, and face processing. Accordingly, we find little to no evidence of the category-selective organization within ventral visual cortex typically associated with face, body, scene, or object processing. We do observe remarkably normal object selectivity within lateral occipital cortex in MM, consistent with his previously reported shape discrimination performance. Together, these findings provide little evidence for recovery of high-level visual function after more than a decade of visual experience in adulthood.

In 1960, at the age of three and a half, MM lost one eye and was blinded in the other due to corneal damage resulting from a chemical explosion. As described previously (Fine et al., 2003), MM had some light perception but no experience of contrast or form over a period of 43 years. He reported no visual memories or imagery, despite one unsuccessful corneal replacement attempt in childhood. In 2000, MM received a corneal transplant and stem cell therapy, which restored monocular vision. In tests carried out over the 1-2 years after surgery MM showed severe amblyopia (an acuity limit of ~ 1.2 cycles per degree, corresponding to Snellen acuity of $\sim 20/500$) and substantial deficits in high-level visual processing (Fine et al., 2003). Here, we used behavioral measures and fMRI to assess whether MM's processing of complex form, objects, and faces has changed after more than ten years of restored sight.

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The period of visually driven normal development differs from both the sensitive period for damage and the sensitive period for recovery, and these developmental windows appear differ substantially across different types of visual processing (Lewis & Maurer, 2005). Moreover, these developmental windows depend on a complex balance between inhibitory and excitatory circuits that are themselves affected by deprivation (Bavelier, Levi, Li, Dan, & Hensch, 2010).

Most cases of early visual deprivation are due to congenital cataracts that are generally diagnosed and removed within the first year of life. Thus, these cases differ substantially from MM, who was blinded at age 3.5, and remained blind until adulthood. Indeed, the period of deprivation is entirely non-overlapping between MM and almost all bilateral cataract cases. Infants treated for congenital cataracts early in life regain useful visual function, though deficits in a variety of low level (Maurer, Mondloch, & Lewis, 2007), mid-level (Ellemberg et al., 2005; Lewis et al., 2002) and high level (Le Grand, Mondloch, Maurer, & Brent, 2004; Robbins, Nishimura, Mondloch, Lewis, & Maurer, 2010) capacities remain. In contrast, some uncertainty exists in the literature as to whether those who have sight restored in adulthood can regain useful vision, and over what timescale such improvement might occur. Previous studies and case reports (Chesselden, 1753; Fine et al., 2003; Gregory & Wallace, 1963; Šikl et al., 2013; Sinha & Held, 2012; Valvo, 1971) suggest that adult sight-recovery subjects tend to find the visual world confusing and difficult to interpret even many months after surgery, although certain visual abilities seem to improve post-surgery (Kalia et al., 2014; Ostrovsky, Meyers, Ganesh, Mathur, & Sinha, 2009), and some spared high-level visual function has been reported in one case of sight-recovery in early adolescence (Ostrovsky, Andalman, & Sinha, 2006).

When tested shortly after surgery, MM had normal perception of color and motion, and only modest deficits in perception of simple form, consistent with the comparatively early sensitive periods proposed for these capacities (Fine et al., 2003). In contrast, MM showed severe deficits in many aspects of complex form, object, and face processing, accompanied by a lack of face or object category-specific responses within ventral visual cortex, as measured using functional magnetic resonance imaging (fMRI). Although these capacities are qualitatively present at the age of 3-4, when MM lost vision, certain aspects of object and face processing continue to develop well into early childhood (Lewis & Maurer, 2005; McKone, Crookes, Jeffery, & Dilks, 2012; Nishimura, Scherf, & Behrmann, 2009), and the degree of plasticity within these areas after early childhood has not yet been established in humans. Thus it remains possible that MM could recover these capacities with sufficient visual experience.

Methods

Subjects

MM and two age and gender-matched controls participated in both the behavioral and fMRI portions of the experiment. Two additional gender and age matched control subjects were excluded from the analysis due to sleeping during the fMRI portion of the experiment. All procedures, including recruitment, consenting, and testing followed the guidelines of the

University of Washington Human Subjects Division and were reviewed and approved by the Institutional Review Board.

Procedure for behavioral experiments

Since MM had studied the original object and face stimuli with feedback after the original experiments, different databases were used in the experiments described here to obtain novel but analogous stimuli. Object identification and emotion classification were tested using gray-scale images of common objects adapted from a standard stimulus set courtesy of Michael J. Tarr, Center for the Neural Basis of Cognition and Department of Psychology, Carnegie Mellon University (<http://www.tarrlab.org/>). Gender classification was tested using stimuli adapted from the Stirling face set, (http://pics.stir.ac.uk/2D_face_sets.htm). To insure that MM was familiar with the objects in our stimuli, we selected common household items to which he was regularly exposed. Novel face stimuli minimized non-configural cues, like eyebrow shape and hair length, which MM previously reported using to discriminate male from female faces.

All stimuli were presented on a large flat-screen monitor, which subtended 56-by-42 degrees of visual angle at a viewing distance of 35 cm. Stimulus images subtended roughly 12 degrees and were presented in gray-scale on plain, achromatic backgrounds. As in our original experiments, MM viewed unblurred stimuli while control subjects viewed stimuli that were convolved with a Gaussian filter centered at 1 cycle per degree to match MM's psychophysically determined acuity (see Supplementary Materials), which has remained stable since initial tests conducted shortly after sight-recovery (Fine et al., 2003; Levin, Dumoulin, Winawer, Dougherty, & Wandell, 2010). The number of trials run per task was chosen prior to the start of data collection to allow presentation of several exemplars from each category while minimizing fatigue in MM, for whom the tasks were challenging.

To assess perception of complex 3D form, we presented subjects with line drawings of cubes that were intact, had a single line missing, or were rearranged to disrupt the 3D structure while preserving local junctions. Subjects completed 32 trials, each containing a 4-second presentation of the stimulus, followed by an unlimited response interval. Subjects were asked to report via key-press whether each image depicted a cube or a jumbled shape.

To further test perception of simple shape and 3D form, we adapted a set of stimuli containing images of 3D forms photographed from various viewpoints spanning a 360-degree rotation (Scharff, Palmer, & Moore, 2013). Subjects reported whether two images, shown simultaneously on the left and right halves of display, contained rotated versions of the same object or different objects. To create a version of the task that did not require interpolation in depth, we modified a subset of the stimuli by tracing their outer contours and then filling with a uniform gray (see Figure 1 for example stimulus images). Subjects then matched these stimuli across 2D rotations (60 to 300 degrees in the XY plane). All subjects completed the 2D version of the task first.

For the object identification task, subjects were asked to name each of 41 unique items, advancing to the next trial by key-press when unsure of an object's identity. Gender and emotion classification were tested via two-alternative (male vs. female) and three-alternative

(happy, neutral, or sad) forced choice. The gender classification task included 40 trials (20 male and 20 female faces) and the emotion classification task included 45 trials (15 individuals displaying each of the 3 emotional expressions). As with the shape stimuli, face and object stimuli were presented individually for 4 seconds at the center of the display, and subjects had unlimited time to respond by key-press.

Procedure for fMRI experiment

Category-selective regions in the ventral visual pathway have been well characterized in normally sighted subjects (Kanwisher & Dilks, 2013). To insure that any absence of this organization in MM could not be attributed to his reduced acuity, control subjects viewed blurred as well as unblurred versions of the stimuli, as described below.

Subjects viewed stimuli presented on a screen at the end of the scanner bore via a mirror attached to the head coil. Cortical category selective BOLD responses were estimated using freely-viewed, colorful, full-screen 3s video clips presented using a block design that alternated between faces, bodies, scenes, objects, and scrambled objects (Julian, Fedorenko, Webster, & Kanwisher, 2012). Face, body, and object videos were recorded against a black background. Scene stimuli consisted mostly of rural locations and included buildings, yards, and forested roads. To create scrambled versions of the object stimuli, each object clip was segmented into a 15 by 15 grid, and spatial locations were shuffled in a pseudorandom order. Example frames are shown in Supplementary Figure 2.

Each block lasted 18 seconds and consisted of six clips. Uniformly colored screens were used as a baseline and were presented at the beginning, middle, and end of each run. The movie clips were presented in palindromic block order (e.g. cFSOBGcGBOSFc)¹. Each subject completed eight 234-second runs. Control participants first completed four runs with an eye-patch over the left eye and stimuli blurred with a Gaussian filter to match MM's psychophysically determined acuity. In the following four runs, control subjects binocularly viewed unblurred stimuli, allowing direct assessment of the effects of blurring and monocular viewing on category selective organization. MM always viewed unblurred stimuli with his remaining (right) eye.

Scanning was performed using a 3 T Allegra scanner with a 32-channel head coil at the Diagnostic Imaging Sciences Center at the University of Washington. High-resolution T1-weighted MPRAGE images were collected in 128 sagittal slices with 1mm isotropic voxels (TR=7.6ms; TE=3.5ms). Blood-oxygen level dependent (BOLD) images were acquired with a gradient-echo EPI sequence: TR=1500ms; TE=25ms; flip angle = 75°; field of view = 220 × 220; voxel size 3mm isotropic. The acquisition window was positioned off axial to include the temporal and occipital lobes.

Structural MRI data were analyzed with FreeSurfer (v5.2) (<http://surfer.nmr.mgh.harvard.edu/>) to construct cortical surface models for each subject. Functional MRI data were processed with FSLFAST (v5.2) (<https://surfer.nmr.mgh.harvard.edu/fswiki/FsFast>). Preprocessing involved motion corrected using

¹F: faces, B: bodies, S: scenes, O: objects, G: grid scrambled objects, c: uniform colored screens

AFNI 3dvolreg (Cox & Jesmanowicz, 1999) and the use of the FSL Brain Extraction Tool (Smith, 2002). Each functional run was then registered to that subject's cortical surface model using boundary-based registration (Greve & Fischl, 2009). A General Linear Model was used to estimate the cortical response to each experimental condition. Statistical contrasts were computed for faces vs. objects, objects vs. scrambled objects, bodies vs. objects and scenes vs. objects. Contrast maps were thresholded at $p < 0.0001$, uncorrected, prior to further analyses, similar to numerous previous studies of the ventral visual stream, (Downing, Jiang, Shuman, & Kanwisher, 2001; Epstein & Kanwisher, 1998; Kanwisher & Dilks, 2013; Kanwisher, McDermott, & Chun, 1997; Malach et al., 1995). No smoothing or normalization to a template was performed.

Results

Results for behavioral experiments

While MM discriminated images of cubes from incomplete and scrambled versions with greater than chance level accuracy, his performance was significantly below that of control subjects, suggesting continued impairment in 3D form perception. Similarly, MM's performance on a simple (2D) shape matching across rotation task was higher than expected from chance alone, but significantly worse than control subject performance. When required to match 3D forms at varying rotations in depth, MM's performance was indistinguishable from chance, and significantly below that of control subjects. MM correctly named several household objects, though significantly fewer than control subjects, for whom the task was trivial. For both the gender and emotion classification tasks, MM's performance was significantly below that of control subjects and not distinguishable from chance. Finally, MM showed no significant improvement in performance between 2003 and 2013 for any of the tasks. See Table 1 for a summary of these results.

Results for fMRI

Responses to monocularly viewed, blurred stimuli in the control subjects were generally qualitatively similar to those obtained using binocularly viewed, un-blurred stimuli (data not shown).

Face and object selectivity—As has been demonstrated for un-blurred stimuli (Kanwisher & Dilks, 2013), subjects showed robust face and object category selective responses within lateral occipital and ventral temporal cortex. Fig. 2A-C shows data from one control subject (4 runs, monocularly viewed and blurred stimuli). As expected, a contrast between faces and objects (Fig 2A) isolated face selective regions in the lateral occipital cortex, superior temporal sulcus, and fusiform gyrus. Similarly, a contrast between objects and scrambled objects revealed a typical pattern of object selective regions (Fig 2B).

In contrast, there was no evidence of face selectivity in MM, even after more than a decade of recovered sight (Fig. 2C). While some regions in ventral temporal cortex responded more to objects than faces, these regions did not show a selective response to objects in a contrast between objects and scrambled objects (Fig. 2D), suggesting that MM also lacks typical high-level object selective cortical responses. With a very lenient threshold, there was some

evidence for a highly attenuated object selective response in the ventral temporal cortex, though this was difficult to differentiate from noise, Supplementary Figure 5.

MM did show object selective activity in the object vs. scrambled object contrast on the lateral surface in a location consistent with the object selective region LOC. Given that MM has no difficulty discriminating different 2D shapes (Fine et al., 2003), this finding is compatible with previous studies suggesting that LOC encodes shape without being involved with matching to stored object representations (Grill-Spector et al., 1999; Kanwisher & Dilks, 2013; Kourtzi & Kanwisher, 2001; Malach et al., 1995), though the caveat should be made that our finding of relatively spared responses in LOC should not be taken as evidence for fully functional shape encoding.

Scene selectivity—The contrast of scenes versus objects did not yield the expected results in our control subjects. Monocular viewing of blurred stimuli produced attenuated responses in the right hemisphere of one subject (Fig. 3B), although this subject had robust response in the parahippocampal cortex in the left hemisphere (see supplementary materials). In a second control subject, we found very little scene selective response for the blurred stimuli (see supplementary materials). Both of these subjects showed typical responses in the unblurred condition. It is possible that the lack of scene selective response, particularly in the parahippocampal place area, results from a high spatial frequency bias in this region (Rajimehr, Devaney, Bilenko, Young, & Tootell, 2011). MM showed no scene selective responses in either the lateral occipital or ventral temporal cortex (Fig. 3D). At a lower threshold, we observed a small region consistent with the Parahippocampal Place Area (PPA) that responded slightly more to scenes than objects, though this was difficult to differentiate from noise, Supplementary Figure 6.

Body selectivity—Control subjects monocularly viewing the blurred stimuli also showed body selective responses in the lateral occipital and ventral temporal cortex (Fig. 3A) which were highly similar to those evoked when binocularly viewing unblurred stimuli (data not shown). While we see little evidence of the typical ventral temporal responses to bodies at a conventional threshold in MM, we did observe a region of body selective responses consistent with the Extrastriate Body Area (Fig. 3C). With a very lenient threshold, we do observe a region in a location consistent with the Fusiform Body Area (FBA) responding more strongly to bodies than objects, Supplementary Figure 6, though these responses were again difficult to differentiate from noise.

Discussion

Visual function continues to develop throughout childhood and into early adolescence, with performance on tasks such as object recognition and face processing reaching adult-like levels between the ages of 5-8 and 4-6, respectively, while remaining sensitive to deprivation for several years afterward (McKone et al., 2012; Nishimura et al., 2009). Subject MM had normal visual development up to age 3.5, followed by an extended period of visual deprivation, with sight-restoration occurring well after adolescence. As such, his case provides a unique opportunity to assess both the limits of plasticity in later adulthood, and the influence of early vision on recovery from long-term blindness.

Tests carried out with MM shortly after surgery suggested normal perception of color and motion, and only modest deficits in perception of simple form. Consistent with his behavioral sensitivity to motion cues, MM shows essentially normal responses in hMT+ for visual motion stimuli (Fine et al., 2003), though these responses seem to co-exist with auditory motion responses not present in sighted individuals (Saenz, Lewis, Huth, Fine, & Koch, 2008). Consistent with MM's ability to interpret simple 2D forms, described first by Fine et al. (2003) and examined further here, we here show relatively normal responses in the cortical region known as the lateral occipital complex (LOC), which has been implicated in the processing of object shape (Grill-Spector et al., 1999). One possibility is that spared perception of color, motion, and shape reflects hard wiring of these faculties; indeed, evidence exists to suggest that this may be the case with basic color processing (Mancuso et al., 2009). Alternatively, preservation of these faculties may indicate that their periods of sensitivity to deprivation end prior to 3.5 years of age.

Several recent studies have suggested that cross-modal responses resulting from early blindness may follow an organization that is analogous to that of least some high-level visual areas in normally sighted individuals. For instance, cortical regions typically associated with visual object processing have been implicated in object size estimation in the congenitally blind (Mahon, Anzellotti, Schwarzbach, Zampini, & Caramazza, 2009), and these regions contain information about similarities in object shape in both sighted and blind participants (Peelen, He, Han, Caramazza, & Bi, 2014). Activity has also been reported in the visual word form area during Braille reading (Buchel, Price, & Friston, 1998; Reich, Szwed, Cohen, & Amedi, 2011), and the emergence of body selective regions in congenitally blind subjects has been reported as a result of training with soundscapes representing bodies (Striem-Amit & Amedi, 2014). Similarly, activation of common regions during visual and haptic recognition of facial expressions in sighted and blind subjects (Kitada et al., 2013) suggests that haptic experience may be sufficient for development of these regions in the absence of visual input.

Although MM was normally sighted until 3.5 years of age, the literature suggests that this is well within the period when some forms of cross-modal plasticity occur (e.g. Burton et al., 2002; Gougoux et al., 2009; Sadato, Okada, Honda, & Yonekura, 2002), and he shows robust cross-modal responses to auditory motion stimuli (Saenz et al., 2008). However, beyond the auditory motion responses in hMT+, we do not know the extent of cortical cross-modal responses in MM. Further, it is unclear whether any existing cross-modal responses would serve to facilitate or interfere with restored visual function. As described above, MM has essentially normal perception of visual motion and robust responses to both visual and auditory motion within hMT+. In contrast, despite several years of early visual experience and more than a decade of recovered sight, MM remains profoundly impaired at interpreting visual facial expressions, suggesting that his haptic experience with faces and/or voice perception (Gougoux et al., 2009) did not lead to the preservation of neural architecture relevant for visual face recognition. Similarly, although we do observe relatively normal selectivity for bodies and objects within lateral occipital cortex, we find little to no evidence of high-level visual responses in ventral temporal cortex selective for face, body, scene or object stimuli in MM.

Shortly after sight recovery, MM showed severe behavioral deficits in high-level visual tasks and our follow-up tests reveal these to be long-standing impairments. When asked about what remained challenging to do with vision in daily life, MM replied “I have learned what works with vision and what doesn't so I really don't challenge my vision much anymore”. MM now uses a combination of vision and other modalities for specific tasks. “This means where motion or color might be clues, I use my vision. Where details might be required, like reading print or recognizing who someone is, I use tactile and auditory techniques.”

In conclusion, MM continues to show severe behavioral impairments in 3D form, object, and face processing with no evidence of improvement of recognition performance even after more than a decade of recovered vision. These behavioral impairments are associated with highly attenuated category selective activity in ventral visual cortex, suggesting that adult high-level vision is based on a visual architecture that is still sensitive to deprivation at age three, and which has only limited plasticity in adulthood.

For example frames from the fMRI video clips, and additional behavioral and BOLD data see Supplementary Materials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Stimuli, tasks and performance on tests of object, face, and shape perception. Stimuli shown to controls were blurred to match MM's visual acuity losses. Where applicable, chance performance is indicated with a dashed line.

Figure 2.

Right hemisphere responses, thresholded at $|p| < 0.0001$. Data is averaged across 4 scans (monocular, blurred stimuli) for the control subject, 8 scans for MM. *Faces vs. Objects* (a, c): The control subject showed a typical pattern of regions giving greater responses to faces than objects in the lateral occipital cortex, STS, and ventral temporal cortex. In contrast, MM lacked category specific responses to the face stimuli. *Objects vs. Scrambled Objects* (b, d): The control subject showed a typical pattern regions responding more to objects than scrambled objects in the lateral occipital and ventral temporal cortex. MM showed a near normal pattern of response on in the lateral occipital cortex, despite almost completely lacking object selective responses on the ventral surface. FuG: Fusiform gyrus; LG: Lingual gyrus; PhG: Parahippocampus gyrus; STS: Superior temporal sulcus; LOG: Lateral occipital gyrus; ITS: Inferior temporal sulcus.

Figure 3.

Right hemisphere responses, thresholded at $|p| < 0.0001$. Data is averaged across 4 scans (monocular, blurred stimuli) for the control subject, and 8 scans for MM. *Bodies vs. Objects* (a, c): The control subject showed a typical pattern of lateral occipital, STS, and ventral temporal regions responding more to bodies than objects. While MM's body selective regions were absent or highly attenuated in the STS and ventral temporal cortex, at least part of the extrastriate body area seems to be present. *Scenes vs. Objects* (b, d): The control subject showed near typical pattern regions responding more to scenes than objects in the lateral occipital and ventral temporal cortex, though the response magnitude was somewhat diminished, especially in the parahippocampal cortex. MM had no discernable category selective responses to scene stimuli. FuG: Fusiform gyrus; LG: Lingual gyrus; PhG: Parahippocampus gyrus; STS: Superior temporal sulcus; LOG: Lateral occipital gyrus; ITS: Inferior temporal sulcus.

Table 1

Behavioral performance of MM compared to chance, average control subject performance, and prior performance, evaluated using a two-proportion z-test. Each cell contains the difference in proportion correct (ranging from -1 to 1) and the corresponding 95% confidence interval. Results marked with a single asterisk are significant at the level of $p < 0.05$. Results marked with a double asterisk are significant at the level of $p < 0.01$.

	Object Recognition	Faces: Gender	Faces: Emotion	2D Shape Constancy	3D Shape Constancy	3D Shape Recognition
MM vs. Chance		0.075 [-0.14, 0.29]	0.11 [-0.085, 0.31]	0.16* [0.035, 0.28]	0.12 [-0.0081, 0.24]	0.33** [0.095, 0.56]
MM vs. Controls	-0.66** [-0.81, -0.51]	-0.43** [-0.58, -0.27]	-0.34** [-0.53, -0.16]	-0.21** [-0.32, -0.11]	-0.20** [-0.31, -0.088]	-0.31** [-0.49, -0.14]
MM 2013 VS. MM 2003	0.067 [-0.15, 0.28]	-0.13 [-0.35, 0.099]	-0.16 [-0.41, 0.082]			