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Visual imagery and functional connectivity in blindness: a single-case study

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Abstract

We present a case report on visual brain plasticity after total blindness acquired in adulthood. SH lost her sight when she was 27. Despite having been totally blind for 43 years, she reported to strongly rely on her vivid visual imagery. Three-Tesla magnetic resonance imaging (MRI) of SH and age-matched controls was performed. The MRI sequence included anatomical MRI, resting-state functional MRI, and task-related functional MRI where SH was instructed to imagine colours, faces, and motion. Compared to controls, voxel-based analysis revealed white matter loss along SH's visual pathway as well as grey matter atrophy in the calcarine sulci. Yet we demonstrated activation in visual areas, including V1, using functional MRI. Of the four identified visual resting-state networks, none showed alterations in spatial extent; hence, SH's preserved visual imagery seems to be mediated by intrinsic brain networks of normal extent. Time courses of two of these networks showed increased correlation with that of the inferior posterior default mode

network, which may reflect adaptive changes supporting SH's strong internal visual representations. Overall, our findings demonstrate that conscious visual experience is possible even after years of absence of extrinsic input.

Keywords

Adulthood; Blindness; Neuroplasticity; Visual system

Introduction

Long-term blindness can be regarded as one of the most tremendous adaptive challenges, given that one-third of the brain is dedicated to vision. Hence, interesting neuroscientific questions about adult neuroplasticity arose when SH, a 70-year old lady, who had been totally blind for 43 years, reported to rely heavily on her internal visual imagery in everyday life. Although structural and functional changes after deafferentation of both the maturing and mature brain have been investigated extensively, we are not aware of a study on such a constellation in human adulthood. Hence, SH provided a unique window of opportunity for a case study to address basic questions on adult neuroplasticity within the human visual system by means of anatomical and functional magnetic resonance imaging (MRI). Has atrophy of visual cortical areas developed, although mental imagery still takes place? Which areas are activated during visual imagery? How does long-standing blindness affect the visual resting-state networks?

Methods

Participants

SH, a 70-year old woman, was presented to us because of transient hypoesthesia of her left arm. After pertinent tests, no causes could be identified. However, medical history was remarkable. At the age of 27, she got involved in a car accident. Although she did not lose consciousness, glass fragments injured both eyes so severely that she immediately lost sight completely with no light perception remaining bilaterally. Hence, she has not had any light perception for 43 years. Yet, she reported having very vivid visualisations and claimed these visual experiences to be extremely important to her. We decided to perform a case study, as we regarded the constellation at hand exceedingly rare. Our assumption was based on the fact that blindness was complete, bilateral, and acquired after the end of the critical period for visual development (i.e., in adulthood) in the absence of brain pathology.

Given that external visual stimulation was impossible, we performed structural MRI, i.e., voxel-based morphometry (VBM), task-related functional MRI (fMRI) involving visual imagery, and resting-state (rs) fMRI. For VBM, the control group included 30 healthy participants (20 women; 10 men). The mean age was 67.5 (range 46–85) years. For task-related fMRI, no control group was available, so that different conditions were compared at the single-subject level. For rs-fMRI, the control group consisted of 20 healthy participants (12 women; 8 men). The mean age was 70 (range 60–90) years. No significant differences in

age were found between SH and controls. No significant correlations were found between age and gender. Controls had no history of ophthalmological or neurological problems.

Data sets of healthy controls were taken from control groups of different neuroimaging studies at our institution. The study conformed to the tenets of the Declaration of Helsinki.

Data acquisition

All MR images were acquired on the same 3-Tesla scanner (Achieva Philips, Eindhoven, Netherlands) using a standard 8-channel SENSE head coil. The 3-D high-resolution structural images were acquired using a gradient echo T1-weighted magnetisation sequence (TE = 4 ms, TR = 9 ms, TI = 100 ms, flip angle = 5°, FoV = 240 × 240 mm², matrix = 240 × 240, 170 slices, voxel size = 1 × 1 × 1 mm³). Functional MRI data were collected using a gradient echo-planar imaging sequence (TE = 35 ms; TR = 2000 ms; flip angle, 82°; FoV = 220 × 220 mm²; matrix = 80 × 80; 32 slices; slice thickness, 4 mm with 0 mm inter-slice gap).

Structural data—Pre-processing of the structural images was done through the VBM8 toolbox (<http://dbm.neuro.uni-jena.de/vbm8>), which is an extension of the SPM8 software (<http://www.fil.ion.ucl.ac.uk/spm>). Images were spatially normalised ('high-dimensional warping') into the stereotactic space of the Montreal Neurological Institute (MNI), segmented into grey matter (GM) and white matter (WM), and modulated. The resulting GM and WM images were smoothed with a Gaussian kernel of 8 × 8 × 8 mm³ and 4 × 4 × 4 mm³, respectively.

Statistical analysis included voxel-wise Crawford's modified *t* test for single-subject assessment (Crawford and Howell 1998), which can be easily implemented as a general linear model in SPM8 by changing the default option to 'equal variance' (Mühlau et al. 2009). Age and gender were included in the statistical model as covariates.

Task-related functional MRI—We used a block design to study three conditions of visual imagery (faces, colour, motion) by fMRI. These conditions were chosen together with SH after exploring categories of her vivid visual imaginations. For each category, we agreed upon several items that SH could easily imagine (e.g., for colours: red flowers, green meadow, blue sky, brown field; for faces: people SH knew; for motion: a car passing by). Instructions were given via headphones. Each condition contained 3 blocks pseudo-randomised across the experiment. Each block started with 5 s of instructions (e.g. 'Please, now imagine colours!'), followed by 30 s, in which an item was announced every 5 s. Blocks of the control condition (baseline) were of the same duration and were presented in an alternating way after each of the task-related conditions. At the beginning of the baseline condition, SH was asked to relax and no further clues were given. Pre-processing and data analysis at the first level were performed with SPM8.

Resting-state functional MRI—All participants (SH and 20 controls) underwent 10 min of rs-fMRI with the instruction to keep their eyes closed and not to fall asleep. SPM8 was used for motion correction, spatial normalisation into the MNI stereotactic space and spatial smoothing with an 8 × 8 × 8 mm³ Gaussian kernel. The resting-state data were processed by

independent component analysis (ICA) as described earlier (Manoliu et al. 2013). In short, pre-processed data were decomposed into 75 spatial independent components and resulted in a spatial z-map reflecting each component's functional connectivity pattern across space (intra-independent functional component, IFC) and an associated time course reflecting the component's activity across time. To identify components reflecting networks of interest in an automated and objective way, we selected from the T-maps presented in Allen et al. 2011 (available online: http://mialab.mrn.org/data/hcp/RSN_HC_unthresholded_tmaps.nii) those representing visual networks and subsystems of the default mode network (DMN). This resulted in 4 components of the visual network, and 3 components of the DMN. To analyse differences between SH and the control group, SH's spatial maps were compared to the controls' maps by voxel-wise application of Crawford's modified t test (Crawford and Howell 1998; Mühlau et al. 2009). To statistically evaluate inter-iFC between selected ICNs, subject-specific ICN time courses were detrended, despiked, filtered by a fifth-order Butterworth low-pass filter with a high frequency cut-off of 0.15 Hz, and correlated in a pair-wise manner by Pearson's correlation coefficient (Allen et al. 2011; Jafri et al. 2008; Manoliu et al. 2013). To assess differences between SH and controls, correlation coefficients were transformed to z-scores using Fisher's z-transformation and entered into two-sample t tests (Crawford and Howell 1998), assuming equal variance across the whole group ($p < 0.05$, Bonferroni-corrected for multiple, i.e. 12, comparisons).

Results

Vision loss

SH lost sight completely and immediately at age 27 with no light perception bilaterally. This was documented in several ophthalmological reports ("nulla lux"). No signs of residual vision were reported.

Structural MRI

SH's cortical atrophy along the calcarine sulci was evidenced from T1-weighted structural imaging (Fig. 1a). VBM revealed significant differences between SH and the control group restricted to the visual pathway. GM decrease was detected along the calcarine sulcus (Fig. 1b), where we found a single large cluster at a height threshold (voxel level) of 0.05, which survived family-wise error (FWE) correction for multiple statistical tests at the cluster level (FWE-corrected p value 0.004). When analysing WM (Fig. 1c), we detected a single cluster at the same height threshold (FWE-corrected p value < 0.001) comprising all structures of the visual pathway: the proximal part of the optic nerve, chiasm, optic tract, and optic radiation.

Task-related fMRI

Comparing all visual imagery conditions to baseline (Fig. 2), we detected activation in extrastriate visual areas as well as in some residual regions of V1 despite structural atrophy in this region (Fig. 1b). However, we were unable to demonstrate domain-specific activity when comparing different visual imagery conditions (colours, faces, motion).

Resting-state fMRI

ICA revealed 7 components of interest in each individual, spatially consistent across groups. The visual networks were represented in 4 components (Fig. 3): inferior posterior visual network (ipVIS) (corresponding to Allen-IC46), medial visual network (mVIS) (corresponding to Allen-IC64), anterior visual network (aVIS) (corresponding to Allen IC67), and lateral visual network (latVIS) (corresponding to Allen IC48). The DMN was captured in 3 components (Fig. 3): anterior DMN (aDMN) (corresponding to Allen IC25), inferior posterior DMN (ipDMN) (corresponding to Allen IC53) and superior posterior DMN (spDMN) (corresponding to Allen IC50) (Allen et al. 2011). Regarding the functional connectivity within networks of interest (intra-IFC), comparisons between SH and controls yielded no significant differences in the networks' spatial extent even at very liberal statistical thresholds. Regarding the functional connectivity between networks of interest (inter-IFC), SH demonstrated increased inter-IFC between mVIS and ipDMN as well as between latVIS and ipDMN (Fig. 4), indicating an increased connectivity between visual networks and DMN ($p < 0.05$, Bonferroni-corrected for multiple comparisons).

Discussion

We investigated the consequences of complete long-lasting visual deafferentation in adulthood in a single-case study by exploring the structural and functional changes in SH's brain in comparison to a normal control group with matched age. Despite striking structural changes along the visual pathway and especially in primary visual cortex, we found largely intact networks of intrinsic functional connectivity. We will discuss these results with regard to the extent of anterograde degeneration at the cortical level, the role of V1 for visual imagery, and the adaptive capacity of cortical networks. Overall, our results add evidence to the concept that neuroplasticity exists after the critical period of visual system development (Calford et al. 2005).

Our findings of decreased WM within the visual pathway and decreased GM restricted to V1 are in line with other studies on degenerative changes resulting from several visual disorders at a later age in humans. These studies have demonstrated that disruption of visual input can lead to atrophic changes including the visual pathway and early visual cortical areas, whereas the spread of atrophy to higher cortical areas has not been demonstrated consistently (Boucard et al. 2009; Chan et al. 2004; Hernowo et al. 2011; 2013; Kitajima et al. 1997; Mendola et al. 2005; Parravano et al. 1993; Plank et al. 2011; von dem Hagen et al. 2005). These extrastriate areas could provide the main substrate for visual imagery in SH.

There is an ongoing debate on the role of V1 for visual imagery. In a meta-analysis, studies with conflicting results were discussed (Kosslyn and Thompson 2003). The authors suggest that imagery of high-resolution detailed objects requires activity of V1; however, visual experience—in both imagery and perception—is unlikely to arise directly from activation of early visual cortex alone but rather from (the effects of such activation on) areas downstream. In line with this notion, visual imagery in SH evoked the strongest activation in visual association areas that did not show GM loss. Further, we observed residual activation in V1 indicating that, although atrophied, this area may still be functional to a certain extent and, hence, could still play a role for some of the more detailed aspects of imagery. This

raises the question of whether atrophy within V1 may primarily comprise layer IV, which is deafferented the most, while relatively sparing supra- and infragranular layers. This may translate into GM loss measurable by means of VBM on the one hand but preserved function with regard to visual imagery on the other hand. However, layer IV of V1 may not depend as much on visual input. A recent paper reported the stria of Gennari to be visible on high-resolution 7-Tesla MRI of congenitally blind subjects independent of their having intact eyes or optic nerves (Trampel et al. 2011). Hence, even layer IV could possess remaining functionality in SH, providing a basis for experiencing visual imagery. Finally, findings from brain-lesioned patients challenge the notion that V1 constitutes a mandatory prerequisite for visual imagery (Bartolomeo 2008; Bridge et al. 2012).

Another question arising is whether resting-state networks change after disruption of direct visual input and consecutive degeneration of the visual pathway. Structural and functional connectivity are believed to be correlated in healthy brains (Greicius et al. 2009). However, normal interactions in common networks have been observed in cases of anatomical disconnection (Tyszka et al. 2011; Uddin et al. 2008). On the other hand, recent evidence suggests a role of brain functional network connectivity for restoration of visual function in blindness (Bola et al. 2014). In SH, the visual networks identified during the resting state did not differ in spatial extent from those in controls, suggesting that, once established, resting-state networks remain robust. Nevertheless, a significantly higher connectivity was found between the inferior posterior DMN (ipDMN) and two of the visual networks in SH (Fig. 4). Evidence exists that this increase in connectivity may underlie SH's robust visual imagery in the absence of any visual input. Laird et al. (2011) studied the relation between resting-state networks and task-related functional activation to elucidate the functional role of resting-state networks (Laird et al. 2011). They found that the mVIS network (ICN 12 in Laird 2011), which we found to have a significantly higher connectivity with the ipDMN, was related to perception of simple visual stimuli. Similarly, the network we defined as ipDMN appears very similar to ICN 13, the DMN linked, among others, to episodic recall and imagined scenes (Laird et al. 2011). Taking into account the functional characteristics of these two significant higher order networks, it is conceivable that SH's visual experience is mediated by default mode properties facilitating the imagination of scenes and episodic recall from long-term memory. Likewise, the most similar network to our latVIS network (i.e. ICN 10) was found to be related to viewing complex, often emotional, stimuli such as faces, as well as action observation, and visuospatial tasks such as tracking of moving objects, mental rotation and spatial localization (Laird et al. 2011). All these are highly important tasks to the blind. A higher connectivity between latVIS and ipDMN could reflect SH's ability to recall and recognise faces, determine her location in space and estimate the movement of objects in her vivid visual experience of the world. In a nutshell, enhanced connectivity between DMN and visual networks may provide the basis for SH to internally 'see' the world despite her blindness.

In conclusion, we have observed that, despite severe atrophic consequences in early visual cortical areas, visual imagery in a blind patient activates higher visual areas, and visual brain networks remain spatially intact. More effective connectivity between the DMN and two visual networks may underlie SH's robust visual imagery. These findings, along with the fact that vivid visual experiences are indeed possible in an individual who suffered from

complete visual deafferentation decades ago, support the idea that adaptation to such extreme environmental challenges in adulthood is implemented by changes in the interaction of intrinsic brain networks (Raichle 2010).

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Fig. 1.

SH's atrophy along visual brain structures. **a** Axial slice of SH's T1-weighted image: cortical atrophy along the calcarine sulci is evident. For better visualisation, the image was bias-corrected and affinely transformed. **b** Voxel-based morphometry of *grey matter*: atrophy within SH's primary visual cortex compared to 30 controls (threshold at uncorrected at $p < 0.05$ and delimited to a cluster threshold of $p < 0.05$ corrected) is displayed on axial ($x = -2$) and sagittal ($z = 0$) planes of the SPM template. **c** Voxel-based morphometry of *white matter*: Atrophy along SH's visual pathway compared to 30 controls (threshold at $p < 0.05$ uncorrected and delimited to a cluster threshold of $p < 0.05$ corrected) are displayed in four different axial planes showing diffuse atrophy along the visual fibres including the proximal optic nerves ($z = -23$), chiasm ($z = -20$), optic tracts ($z = -14$) and optic radiations ($z = 0$). On the glass brain, note how the atrophy comprises a sole cluster clearly indicating degeneration along the visual pathway

Fig. 2.

SH's brain activity during visual imagery. Activation related to all visual imagery conditions (colours, faces, motion) compared to *baseline*. Despite intense structural atrophy in primary visual cortex (Fig. 1b), the visual imagery task evoked activation in extrastriate visual areas as well as in residual parts of V1. For better visualisation, activation patterns are displayed twice at different thresholds. **a** Sagittal and axial planes of the activation pattern at $p < 0.05$ FWE corrected. **b** Sagittal and axial planes of the activation pattern at $p < 0.001$ uncorrected

Fig. 3.

Sagittal and axial planes of the four visual and three default mode networks in SH and the control group. The visual networks were represented in four components: inferior posterior visual network (ipVIS) (corresponding to Allen-IC46), medial visual network (mVIS) (corresponding to Allen-IC64), anterior visual network (aVIS) (corresponding to Allen IC67) and lateral visual network (latVIS) (corresponding to Allen IC48). The default mode network was captured in three components: anterior DMN (aDMN), inferior posterior DMN (ipDMN) and superior posterior DMN (spDMN). For both SH and the control group, all seven networks were masked by the corresponding ICNs of interest for all participants ($p < 0.05$, FWE corrected)

Fig. 4.

Between-group differences of inter-network intrinsic functional connectivity. Based on the network time courses, inter-network intrinsic functional connectivity (inter-iFC) was calculated individually and compared between SH and the control group. Compared to controls, SH demonstrated increased strength of inter-iFC between mVIS and ipDMN as well as between latVIS and ipDMN (red arrows). Axial slices were taken from the ICNs of interest of all participants ($p < 0.05$, FWE corrected)