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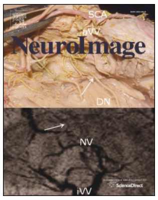

# Top-down influence on the visual cortex of the blind during sensory substitution

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ABSTRACT

Visual sensory substitution devices provide a non-surgical and flexible approach to vision rehabilitation in the blind. These devices convert images taken by a camera into cross-modal sensory signals that are presented as a surrogate for direct visual input. While previous work has demonstrated that the visual cortex of blind subjects is recruited during sensory substitution, the cognitive basis of this activation remains incompletely understood. To test the hypothesis that top-down input provides a significant contribution to this activation, we performed functional MRI scanning in 11 blind (7 acquired and 4 congenital) and 11 sighted subjects under two conditions: passive listening of image-encoded soundscapes before sensory substitution training and active interpretation of the same auditory sensory substitution signals after a 10-minute training session. We found that the modulation of visual cortex activity due to active interpretation was significantly stronger in the blind over sighted subjects. In addition, congenitally blind subjects showed stronger task-induced modulation in the visual cortex than acquired blind subjects. In a parallel experiment, we scanned 18 blind (11 acquired and 7 congenital) and 18 sighted subjects at rest to investigate alterations in functional connectivity due to visual deprivation. The results demonstrated that visual cortex connectivity of the blind shifted away from sensory networks and toward known areas of top-down input. Taken together, our data support the model of the brain, including the visual system, as a highly flexible task-based and not sensory-based machine.

## Introduction

Sensory substitution devices (SSDs) represent one approach to vision rehabilitation for those who have lost sight. These devices use a video camera to take a series of images, convert the images into a cross-modal auditory (Meijer, 1992) or tactile (Bach-y-Rita, 2004) signal, and present this substituting signal in place of direct visual input. SSDs have been shown to impart improved environmental perception in the completely blind (Nau et al., 2013, 2014). The advantages of SSDs include their immediate availability, non-surgical implementation, and relatively accessible cost. Moreover, SSDs have been shown to enable improved function in a wide variety of patients with diverse etiologies in blindness (Lee et al., 2014; Nau et al., 2013, 2014, 2015).

In addition to the potential for functional improvements, SSDs provide a unique tool for investigating functional organization of the visual system, as well as neuroplasticity associated with visual deprivation. In sighted subjects, Renier et al. used an SSD task to demonstrate that regions within the occipital lobe that are involved in depth perception do not require visual input, but are more specific to modeling depth

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*Abbreviations:* Aud/Ins/Lim, auditory/insula/limbic networks; BA, Brodmann area; BOLD, blood-oxygen-level dependent; CSF, cerebrospinal fluid; FC, functional connectivity; fcMRI, functional connectivity magnetic resonance imaging; fMRI, functional magnetic resonance imaging; FDR, false discovery rate; FWE, family-wise error; FWHM, full-width half-maximum; GLM, general linear model; PET, positron emission tomography; ROI, region of interest; SSD, sensory substitution device; SS/M, somatosensory/motor networks; Task−, task-negative networks; Task+, task-positive networks.

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regardless of the mode of sensory input (Renier et al., 2005). Early studies of SSDs using positron emission tomography (PET) and functional MRI (fMRI) revealed that the visual cortex was engaged by the interpretation of cross-modal signals in blind subjects (Arno et al., 2001; De Volder et al., 1999; Merabet et al., 2009; Ptito et al., 2005). Collignon et al. further demonstrated a direct relationship between occipital lobe activation and improved SSD use in blind subjects by demonstrating decreased accuracy when subjects had occipital lobe activity disrupted by transcranial magnetic stimulation (Collignon et al., 2007). More recent studies have utilized SSDs to identify regions of the brain that maintain the functions of higher-order visual processing during analogous sensory substitution tasks even if the subjects have had no prior visual experience (Amedi et al., 2007; Striem-Amit and Amedi, 2014; Striem-Amit et al., 2012a,2012b; Watkins et al., 2013).

While previous work has demonstrated the presence of activity within the visual cortex during SSD use following visual deprivation, the cognitive basis of this activation remains unclear. The classical view of visual processing in healthy, sighted subjects posits a bottom-up flow of information from lower-order visual centers to higher-order centers, where visual information is continually integrated along this pathway. However, each of these bottom-up projections also has a reciprocal top-down projection from the higher-order center back to the lower-order center (Gilbert and Li, 2013). These top-down projections carry information about attention and expectation, and can alter perception of the visual environment by modulating the activity of lower-level visual regions in the brain. To date, the role of these projections in cross-modal activity in the visual cortex following visual deprivation remains incompletely understood. In this study, using fMRI and an auditory sensory substitution task in both blind and sighted subjects who had no prior knowledge of the SSD, we aimed to minimize the training time necessary to observe significantly increased visual cortex activity. In this way, we tested the hypothesis that visual cortex activity in the blind is significantly modulated by cognitive processing that is intrinsically present in the brain before there is further reorganization in functional or structural connectivity from long-term sensory substitution training.

To investigate this aim, we compared functional activation in both blind and sighted subjects in response to an auditory sensory substitution task using fMRI in two conditions separated by just minutes: 1. passive listening with no prior knowledge of the SSD, and 2. active interpretation of same auditory sensory substitution stimuli after a brief training session of approximately 10 min in the MRI scanner. This type of paradigm, which is necessary to measure the proportion of activity specific to top-down input, is not usually possible because subjects will have typically undergone training prior to the functional imaging session. We further supplemented this experiment with a separate functional connectivity MRI (fcMRI) study to investigate changes in the intrinsic functional connectivity measured at rest due to visual deprivation.

## Materials and methods

All studies were approved by the University of Pittsburgh Institutional Review Board.

### *Subject recruitment*

Twenty-two blind subjects and twenty age-matched controls were enrolled from the established research registry of the Sensory Substitution Laboratory at the University of Pittsburgh. Blind subjects were confirmed to have no vision beyond light perception bilaterally by the Freiburg Visual Acuity and Contrast Test (FrACT), and all subjects had no known neurological disorders and were right-handed. Subjects were scanned after obtaining informed written consent. See Table 1 for complete demographic information.

**Table 1**
Subject demographic information.

| Sensory substitution task subjects | | | | | |
|---|---|---|---|---|---|
| Blind group | | | | Sighted group | |
| Age | Gender | Cause | Age of onset | Age | Gender |
| 18 | M | Retinitis pigmentosa | 13 | 25 | F |
| 25 | M | Retinopathy of prematurity | Birth | 27 | M |
| 30 | F | Tumors | 23 | 38 | F |
| 39 | F | Retinopathy of prematurity | 17 | 41 | F |
| 55 | M | Trauma | 35 | 44 | F |
| 56 | M | Unknown | Birth | 55 | F |
| 58 | F | Retinopathy of prematurity | Birth | 56 | M |
| 58 | F | Glaucoma | 46 | 58 | F |
| 58 | M | Encephalitis | 7 | 61 | M |
| 60 | F | Glaucoma | 31 | 70 | F |
| 64 | F | Retinopathy of prematurity | Birth | 74 | M |
| Additional functional connectivity MRI subjects | | | | | |
| Blind group | | | | Sighted group | |
| Age | Gender | Cause | Age of onset | Age | Gender |
| 53 | F | Diabetic retinopathy | 28 | 55 | F |
| 59 | F | Congenital cataracts, aniridia, pediatric glaucoma | 53 | 55 | F |
| 60 | F | Retinopathy of prematurity | Birth | 57 | F |
| 62 | F | Retinopathy of prematurity | Birth | 58 | M |
| 62 | M | Trauma | 51 | 64 | F |
| 63 | M | Retinopathy of prematurity | Birth | 70 | F |
| 64 | M | Detached retinas | 54 | 71 | M |
| 75 | M | Retinitis pigmentosa | 59 | 75 | M |

### *Sensory substitution fMRI experiment*

In order to investigate visual cortex activity arising from top-down input during sensory substitution, we scanned each subject twice while presenting them with a set of “soundscapes” generated by The vOICe sensory substitution transformation (Meijer, 1992). These soundscapes represented white horizontal or vertical bars moving across a black background in one of four directions (up, down, left or right). Each stimulus was 10 s long consisting of 10 concatenated soundscapes. Over those 10 s, the white bar would move across the image from one edge to the opposite edge a single time with constant velocity. The subjects were able to respond any time during those 10 s. Subjects had no prior knowledge of the vOICe device or how to interpret the soundscapes before beginning the experiment. For the first scan, the subjects were presented the soundscapes for passive listening, and were asked to respond with the left arrow on the keypad placed in their right hand whenever they heard a sound to indicate they were able to hear the stimuli. Subjects were instructed to press this button as soon as they heard the soundscapes begin. The subjects then took a short break in the MRI scanner and were provided a brief introduction to The vOICe. This training typically took 10 min, during which we described the image-to-soundscape transformation and discussed examples. The subjects then repeated the scan, but this time we asked them to interpret the soundscapes as images, determine the direction the bar was moving, and respond on the keypad with that direction. Subjects were instructed to respond as soon as they could discern the direction of motion, bearing in mind that they should listen to at least more than one soundscape in order to determine which direction the bar was moving. By holding the bottom-up input constant, we were able to compare activity between the passive listening (pre-training) and active interpretation (post-training) scans to measure activity specific to top-down input. Structural reorganization of the brain was not expected between the pre- and post-training scans because of the short duration