Effects of visual deprivation on the organization of the semantic system

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Summary

Early onset blindness provides a lesion model to investigate whether experience-dependent mechanisms subside the functional anatomy of semantic retrieval. In particular, visual deprivation might alter the neural systems underlying retrieval of semantic information that is acquired via visual experience. Using functional MRI, we demonstrate that both early blind and sighted subjects activate a left-lateralized fronto-temporal ‘core’ semantic retrieval system and show common effects for retrieval of visually experienced semantic information. However, irrespective of the type of semantics, blind subjects activate additional extrastriate regions, which are coupled with frontal and temporal semantic regions. The resilience of semantic retrieval responses to visual deprivation suggests a considerable degree of innate and epigenetic specification of the semantic system. In contrast, the exuberant functional connectivity between extrastriate and ‘core’ semantic retrieval regions might be explained by abnormal pruning processes during early neurodevelopment.

Keywords: blindness; cortical plasticity; functional imaging; semantic organization

Abbreviations: BOLD = blood oxygenation level dependent; fMRI = functional MRI; LPMT = left posterior middle temporal region; SPM = statistical parametric mapping

Introduction

Early onset blindness allows one to study the effects of visual deprivation on the neuro-development of remaining sensory modalities and higher cognitive systems. Visual deprivation induces abnormal developmental neuroplasticity due to lack of visual experience and altered cross-modal integration among the spared sensory modalities (Rauschecker, 1995; Lessard et al., 1998; Roder et al., 1999; Bavelier and Neville, 2002). Previous studies have demonstrated that this leads to developmental changes in polymodal association and primary cortices of the visual and spared modalities. In animal studies, visual deprivation results in cross-modal reorganization of extrastriate cortex (Hyvarinen et al., 1981; Heil et al., 1991), primary visual areas (Hubel and Wiesel, 1977; Price et al., 1994) and hypertrophy of auditory cortex (Gyllensten et al., 1966; Kyugo et al., 1975). Similarly, functional imaging studies in humans have reported extrastriate activation bilaterally for tactile discrimination relative to a non-discrimination task (Sadato et al., 1996, 1998) and in the right hemisphere (Brodman area 18) for location of sounds relative to rest (Weeks et al., 2000). Developmental changes in higher cognitive systems have been investigated through functional imaging studies of Braille reading. In blind subjects, additional extrastriate and inconsistently primary visual activation was observed for Braille reading relative to rest (Cohen et al., 1999; Melzer et al., 2001; Sadato et al., 2002), tactile non-discrimination tasks (Sadato et al., 1996, 1998), auditory processing (Buchel et al., 1998a, b) and reading non-lexical Braille strings (Burton et al., 2002).

The present study investigated the effects of visual deprivation on the neural systems underlying semantic retrieval. Basically, two types of semantic processes can be distinguished, which might be affected differentially by visual deprivation. First, semantic retrieval involves general stimulus-driven or executive semantic processes that are invoked irrespective of the type of semantic information retrieved. Visual deprivation might affect these non-specific semantic retrieval processes vicariously by altering related systems (e.g. access to the semantic system from Braille orthography). Secondly, semantic retrieval involves processes that depend on the specific content of semantic information that is retrieved. Visual deprivation might alter retrieval of semantic information related to colour, form, action and motion, which is learnt via visual experience, while sparing semantic information related to sounds, which
is acquired predominantly via the auditory sense. There are several accounts of how semantic information might be represented in the human brain. Amongst them, the ‘sensorimotor theory’ hypothesizes that semantic features (e.g. visual, auditory, action) are represented close to the sensory (or motor) areas which are active when the features (e.g. motion, colour) are experienced (Allport, 1985; Warrington and McCarthy, 1987; Damasio et al., 1996; Martin et al., 2000; but also see Caramazza and Shelton, 1998; Tyler and Moss, 2001). Thus, the functional anatomy of semantic memory is predicated on the organization of sensory systems. From this perspective, one might expect that sensory deprivation that leads to the restructuring of sensory systems will also modify the neural systems underlying semantic representations.

Functional imaging studies of the sensorimotor theory have primarily investigated whether the neural correlates of visual and action semantics are anatomically segregated. With respect to visual semantics, functional imaging has produced inconsistent results. While some studies have associated visual semantics with a left fusiform region that is anterior and lateral to the fusiform area involved in colour perception (Martin et al., 1995; Chao and Martin, 1999), others have not replicated this effect (Vandenberghe et al., 1996; Mummery et al., 1998; Noppeney and Price, 2002b; Phillips et al., 2002). Moreover, left anterior fusiform activation has also been shown for blind subjects reading abstract words in Braille (Buchel et al., 1998b). In contrast, action semantics (i.e. how you manipulate an object) has most consistently been associated with increased activation in a left posterior middle temporal region (LPMT) that is lateral and anterior to motion area V5/MT (Martin et al., 1995; Phillips et al., 2002a, b). LPMT activation has been reported for: (i) observation of actions relative to static images (Rizzolatti et al., 1996; Grezes et al., 1999; Perani et al., 2001); (ii) pictures or sentences with implied motion relative to similar stimuli that do not imply motion (Kourtzi and Kanwisher, 2000; Senior et al., 2000; Ruby and Decety, 2001); and (iii) the written names of tools relative to the written names of animals or fruit (Martin et al., 1996; Mummery et al., 1998; Chao et al., 1999; Phillips et al., 2002). The action-selectivity of LPMT may thus be engendered by its functional relation to action/motion perception mediated by afferents from area V5/MT (Martin et al., 2000). Therefore, the question arises whether visual deprivation, which enforces action experience via somatosensorimotor associations, rather than visual motion perception, reduces the action-selective response in LPMT.

The present study investigated the effect of visual deprivation on semantic processes that are (i) invoked irrespective of, or (ii) dependent on, the semantic content of stimuli. For this, blind and sighted subjects made semantic decisions on heard words referring to auditory, visual, hand action and body motion features. In baseline conditions, they performed an auditory decision on reversed words that had no lexical or semantic content. Differences in neurophysiological correlates of semantic processing were measured with functional MRI (fMRI). We characterized differences in the functional anatomy of semantic retrieval in two ways. First, by comparing regional activations (i.e. group × condition interaction) and secondly, in terms of effective connectivity using psychophysiological interactions (i.e. group × semantic activation). The psychophysiological analyses represent a natural way to characterize differences in functional architecture in the brain, because they refer explicitly to changes in coupling between classical semantic and visual regions that may reflect differences in developmental plasticity.

In summary, we used early onset blindness as a lesion model that selectively alters experience-dependent developmental plasticity to ask whether ‘experience-dependent’ mechanisms specify the functional anatomy of semantic retrieval. Within this general question, we embedded a more focused one: ‘If experience-dependent mechanisms do play a role, is this more pronounced in parts of the semantic system that depend on visual experience?’ On the basis of previous neuroimaging results, we hypothesized that LPMT responds selectively to action features in sighted but not in blind subjects, i.e. action-selectivity of LPMT depends on visual experience. Conversely, if semantic responses are not affected by experience-dependent plasticity, we can infer that the organization of the semantic system is innate and specified epigenetically.

Subjects and methods

Subjects

Eleven blind (six male, five female; mean age 50 years, range 23–69) and 12 sighted control (eight male, four female; mean age 23.5 years, range 20–30) subjects participated in the study. Four subjects were congenitally blind and six were blind before the age of 2 years (early onset). One subject had very weak residual light perception. The causes of blindness were peripheral and included retinopathy of prematurity, retinoblastoma, anophthalmos and injury. Apart from one ambidextrous blind subject, all subjects were right-handed. All subjects had English as their first language and no history of further neurological or psychiatric disorder. Each gave informed consent to participate in the study, which was approved by The National Hospital for Neurology and Neurosurgery and the Institute of Neurology joint research committee.

Experimental design

During the activation conditions, blind and sighted subjects listened to words with four different types of meaning and performed a semantic decision task that explicitly directed their attention to the semantic content of each word (see Appendix for more details):

(i) Words referred to hand actions. Subjects decided whether the hand action involved a tool.
(ii) Words referred to body motion. Subjects decided whether the body movement was slow/involved jumping.

(iii) Words referred to visual features. Subjects decided whether the visual form was curved/dark.

(iv) Words referred to auditory features. Subjects decided whether the sound was usually loud/quiet.

For each semantic condition, there was a matched baseline condition that employed the same recorded stimuli after digital reversal, to remove lexical and semantic content. Subjects decided whether they were recorded in a male voice. For all eight (four semantic and four baseline) conditions, one-third of the stimuli were targets (i.e. the correct response was yes). All stimuli were presented at a rate of one every 4 s, with five stimuli per block (20 s per block), and each block was preceded by a short instruction period (5 s). Yes/no responses to all conditions were indicated (as quickly and as accurately as possible) by a two-choice key press. The order of semantic conditions was counterbalanced within and across subjects, and each semantic condition was followed or preceded by its matched baseline condition.

**Data acquisition**

A 2 T Siemens Vision system was used to acquire both T₁ anatomical volume images and T₂*-weighted echoplanar images [echo time (TE) = 40 ms, 38 slices, distance factor 0.67, slice thickness 1.8, repetition time (TR) 2.9 s] with blood oxygenation level-dependent (BOLD) contrast. There were two sessions, with a total of 250 volume images per session. The first six volumes were discarded to allow for T₁ equilibration effects.

**Data analysis**

The data were analysed with statistical parametric mapping (using SPM99 software from the Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk/spm). Scans from each subject were realigned using the first as a reference, spatially normalized into a standard space (Talairach and Tournoux, 1988) and spatially smoothed with a Gaussian kernel of 8 mm FWHM (full-width half maximum). Data were highpass filtered to 1/100 Hz and were globally normalized with proportional scaling. The conditions were modelled in an event-related fashion, with regressors entered into the design matrix after convolving each event-related stick function with a canonical hemodynamic response function. In addition to modelling each condition, the statistical model included instructions and errors. Nuisance covariates included the realignment parameters (to account for motion artefacts) and reaction times that were modelled in an event-related fashion separately for (i) all activation conditions and (ii) all control conditions (to account for differences in reaction times across conditions). Condition-specific effects for each subject were estimated according to the general linear model (Friston et al., 1995) and passed to a second-level analysis as contrasts. This involved creating contrast images for each subject and a second-level ANOVA (analysis of variance), which modelled the group effect (sighted or blind) on the contrast of interest. Inferences were made at the second level to emulate a random effects analysis and allow generalization to the population (Friston et al., 1999).

Analysis of the data tested for: (i) general semantic effects: semantic decision on words > auditory decision on reversed words; (ii) specific semantic effects: (a) hand action relative to all other semantic conditions (and vice versa), (b) body motion relative to all other semantic conditions (and vice versa), (c) visual relative to all other semantic conditions (and vice versa), and (d) auditory relative to all other semantic conditions (and vice versa).

Our analysis of specific semantic effects was restricted to voxels that were activated in the semantic condition relative to its baseline (P < 0.001).

At the second level, we tested whether (i) general or (ii) specific semantic effects were common to both groups (conjunction of blind and sighted) or dependent on group (i.e. by testing for a significant condition by group interaction). Unless otherwise stated, we only discuss activations that are significant after correction for the entire brain volume.

**Regression analysis testing for psychophysiological interactions**

To investigate whether regions from the semantic retrieval system were differentially connected to brain areas in blind and sighted subjects, a psychophysiological analysis (Friston et al., 1997) was performed where the BOLD signal time-course in one semantic region was the physiological factor and the group was the psychological factor. For this, we first identified one left temporal (peak coordinates: −54, −54, −18) and one frontal reference region (peak coordinates: −45, 18, 27) that were activated for semantic relative to baseline tasks in both groups. For each subject, we created a new statistical model that used the BOLD signal timecourse of this frontal (or temporal) region as a regressor in a first level analysis, while not modelling the condition effects.

For each subject, one contrast image (positive regression slope) was entered into a second level ANOVA that modelled the group effect (blind versus sighted). At the second level, we tested for a psychophysiological interaction by simply comparing the regression slopes between blind and sighted subjects. A significant difference reflects changes in coupling or effective connectivity between the semantic system and the region identified.

**Results**

**Behavioural data (Table 1)**

The mean and standard deviation of reaction times and the number of errors for sighted and blind subjects are displayed in Table 1.
General semantic retrieval effects

Common to blind and sighted subjects. In blind and sighted subjects, semantic decisions relative to baseline activated an extensive left-lateralized fronto-temporal system encompassing the left inferior and middle frontal, the middle and inferior temporal gyri, intraparietal sulcus, the paracingulate, and the cerebellum.

Differences between blind and sighted subjects (condition by group interaction). A direct comparison of the differences between the semantic and auditory conditions for the two groups revealed stronger activation for the blind in visual association areas including the left fusiform, middle and superior occipital gyri (see Fig. 1). These activation differences are unlikely to be due to age effects because: (i) an additional analysis that modelled the age effect as a covariate in addition to the group effect (sighted or blind) confirmed the enhanced extrastriate activation in the blind subjects; and (ii) previous studies have shown increased extrastriate activation during similar tasks for blind relative to control subjects even when age was controlled (De Volder et al., 2001; Roder et al., 2002).

There were no areas where sighted subjects showed greater activation than blind subjects.

Specific semantic effects

Common to blind and sighted subjects. For hand action relative to other semantic types, both blind and sighted subjects activated the LPMT, which has previously been associated with action retrieval relative to all other semantic types (see Fig. 2). Notably, this effect was present in congenitally blind, early blind subjects and the patient with very weak residual light perception. For visual relative to other semantic types, blind and sighted subjects activated the left inferior temporal gyrus and the cerebellum. There were no other significant effects.

Differences between blind and sighted subjects (condition by group interaction). There were no brain areas where sighted subjects showed greater or less activation than the blind subjects for one semantic type relative to others.

Psychophysiological interaction

The characterization of visual association cortex responses during semantic processing was finessed in a psychophysiological interaction analysis: in the blind subjects relative to the controls, the BOLD signal time-courses of the left inferior frontal (or temporal) region showed higher correlations with those in several primarily left-hemispheric occipital regions, including the lateral occipital sulcus and the lingual gyrus. These results demonstrate that frontal as well as temporal regions from the common semantic retrieval system exerted a stronger influence on, or were more strongly coupled with, regions in the occipital cortex in the blind than in the sighted subjects. The results of the psychophysiological interaction analysis, using the left frontal region, are shown in Fig. 1 (bottom) at a threshold of P < 0.05 (corrected). Note the similarity of these results with the regions identified by the conventional group by condition interaction in Fig. 1. Equivalent results were seen for the temporal psychophysiological interaction (results not shown).

Discussion

The current study investigated how early visual deprivation affects the brain systems involved in semantic processing. First, we examined the effect of visual deprivation on the responses that were common to all types of semantic features and primarily reflect semantic retrieval processes. Secondly, we investigated whether the selectivity of brain responses to one specific semantic type (e.g. action) is modulated by or is dependent on early visual experience.
In brief, semantic retrieval evoked left-lateralized fronto-temporal activations in both blind and sighted subjects with activation in the blind group extending beyond the normal semantic retrieval regions to encompass extrastriate regions. To our surprise, selective responses to semantics that are normally learnt with visual experience were not affected by blindness. The remarkable resilience of LPMT action-selectivity to profound perturbation of visual experience suggests a considerable degree of innate and epigenetic specification of the semantic system.

The differences in non-specific semantic activations and the preservation of action semantic selectivity can be reconciled by noting the differences were only expressed in extrastriate visual regions. These can be understood, most simply, from the perspective afforded by the psychophysiological interaction analysis. In short, blind subjects expressed exuberant effective connectivity between the semantic and visual regions. This overexpressed coupling is consistent with the abnormal pruning of synaptic connections during neurodevelopment that depends on experience (Huttenlocher et al., 1982; Huttenlocher, 1990; Burkhalter, 1993; Price et al., 1994; Batardiere et al., 2002). This pruning normally leads to sparser connectivity, a more refined architecture and a greater degree of functional specification.

**The ‘core’ semantic retrieval system**

In both blind and sighted subjects, semantic retrieval commonly activated a widespread, predominantly left-lateralized neuronal system encompassing the inferior/middle frontal and temporal gyri, the intraparietal sulcus, the paracingulate and the cerebellum. In addition to this well-
Fig. 1 Top: general semantic activations (i) common to blind and sighted subjects (red), and (ii) increased for blind subjects (green) are rendered on an averaged normalized brain. Height threshold = $P < 0.05$ corrected. Middle left: general semantic activations for blind subjects only on sagittal and axial slices of an echoplanar image created by averaging the normalized mean images from all 23 subjects. Height threshold = $P < 0.05$ corrected. Middle right: parameter estimates for semantic decision relative to baseline for control (black) and blind (white) subjects at $x = -36, y = -63, z = -18$. Bottom: psychophysiological interaction results using the left inferior frontal region as a reference region on sagittal and axial slices of the average echoplanar image from all 23 subjects. Height threshold = $P < 0.05$ corrected. L = left; R = right.

documented semantic retrieval/executive system (Petersen et al., 1990; Vandenberghe et al., 1996; Fiez, 1997; Price et al., 1997; Binder et al., 1997; Noppeney and Price, 2002a), blind subjects activated left hemispheric visual association areas that extended into the left fusiform and inferior/middle occipital gyri. Previously, left hemispheric occipito-temporal activation in blind subjects has been demonstrated for: (i) reading Braille (Sadato et al., 1998, 2002) relative to rest; (ii) tactile discrimination relative to a non-discrimination task (Sadato et al., 1996, 1998); and (iii) sound imagery relative to listening to noise stimuli (De Volder et al., 2001) and other verbal tasks such as verb generation and future experiments using transcranial magnetic stimulation (TMS) with blind and control subjects would be required (for related TMS experiments on tactile perception and Braille reading see Cohen et al., 1997, 1999).

The functional role of the visual association cortex in blind subjects may depend on its task-dependent connections with other brain regions. This was characterized by the psychophysiological interaction analysis (Friston et al., 1997) using, as reference regions, the frontal and temporal areas that were identified as the key players during semantic retrieval. This analysis revealed a significant interaction between the physiological factor, the left prefrontal/temporal activation, and the psychological factor, blindness. An interaction of this sort can be construed as (i) a contribution to extrastriate responses from the prefrontal/temporal regions that is augmented by blindness, or (ii) group differences in extrastriate responses that are enhanced by prefrontal/temporal activation. From a neurobiological perspective, the first interpretation is consistent with the notion that backwards connections from higher order fronto-temporal brain areas to extrastriate areas have greater efficacy in the context of visual deprivation. In other words, it characterizes extrastriate brain areas as regions that are more tightly coupled with higher order fronto-temporal regions in blind subjects. This may reflect a recruitment of extrastriate regions into the semantic retrieval system. The second, complementary interpretation implies that—possibly due to crossmodal reorganization (Rauschecker, 1995; Bavelier and Neville, 2002)—the extrastriate cortex response is enhanced in the blind when prefrontal/temporal activation is high.

Semantic activation related to semantic content
Consistent with previous studies investigating retrieval of action knowledge (Martin et al., 1995; Phillips et al., 2002), our results demonstrate that a posterior middle temporal region responds more during semantic decisions on hand action than semantic decisions on visual, sound or motion knowledge. However, contrary to our hypothesis, we did not observe a significant interaction between LPMT action-selectivity and early onset blindness. Instead, an action-selective LPMT response was observed for both blind and sighted subjects. This surprising resilience of LPMT action-selectivity to visual deprivation might rely on its multimodal function, mediating between semantic aspects learnt from several modality-specific experiences of hand actions (e.g. visual, auditory, somatosensory and motor). LPMT is thus integrating converging inputs from many regions, so that its
response properties might not be altered substantially by the absence of visual input. However, as blind subjects experience actions predominantly via somatosensorimotor associations, action-selective responses in the blind subjects would be expected in several other regions (e.g. anterior intraparietal sulcus) that integrate somatosensory input and motor output. Alternatively, in both blind and sighted subjects, the LPMT response might primarily be driven by connections from areas involved in hand actions. However, this is unlikely given the close anatomical and potential functional relation between LPMT and V5/MT. Therefore, we suggest that LPMT action-selectivity might be engendered by innately specified neurobiological mechanisms in addition to experiential factors. In short, the consistent LPMT action-selectivity in blind and control subjects indicates a considerable degree of epigenetic specification of the semantic system.

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## References


Appendix: example stimuli

Sound
Is it usually quiet/loud?, Bark, Bang, Siren, Whisper

Visual
Is it always curved?, Angle, Cone, Pyramid, Oval, Is it usually dark?, Brown, Dusk, Glow, Flash

Motion
Is it a jumping movement?, Leap, Swimming, Climb, Springing, Is it a slow movement?, Tiptoeing, Dawdle, Gallop, Run

Hand action
Is it a hand action with/without a tool?, Chisel, Knit, Tapping, Ticklem