New light from the dark: what blindness can teach us about brain function

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Purpose of review

In this review, we discuss findings from some recent brain imaging studies that shed new light on our understanding of the role of visual experience on the development of the brain morphological and functional architecture in humans. To what extent is vision truly necessary to 'see' the world around us?

Recent findings

Congenitally blind and sighted individuals present analogous cognitive and social performances. Findings from structural and functional brain studies in both sighted and congenitally blind individuals have shown the existence of supramodal brain regions able to process external information regardless of the sensory modality through which such an information has been acquired. This more abstract nature of functional cortical organization may enable congenitally blind individuals to acquire knowledge, form mental representations of and interact effectively with an external world that they have never seen.

Summary

Altogether, findings from both behavioural and imaging studies indicate that the brain functional organization is to a large extent independent from visual experience and able to process information in a supramodal fashion. The study of the blind brain is a very powerful approach to understanding not only the cross-modal plastic, adaptative modifications that occur in the 'visual' regions but primarily the functional architecture of the human brain itself.

Keywords

blindness, brain function, cross-modal plasticity, fMRI, supramodality

Introduction

Vision plays a central role in how we represent and interact with the world around us. Individuals who lack vision since birth, however, are able to navigate independently in space, to recognize objects, to learn how to use utensils, to catch other people's intentions and feelings, and to interact socially with others. Blind individuals very often make us notice some specific sensorial aspects that we are simply 'unable to see': a specific timbre of the voice that conveys information of one's feelings, a sudden mild change of temperature while walking around the corner, a peculiar scent in front of a grocery store, an unusual texture of a textile.

These few considerations alone are sufficient to pose some fundamental questions. How do individuals with congenital blindness form a representation of a world that they have never seen? What happens to the 'visual' brain in congenitally blind individuals? How is nonvisual sensory information processed in the brain of sighted and congenitally blind individuals? To what extent is vision really necessary for the human brain to develop and function? Recently, novel behavioural and functional brain studies in sighted and congenitally blind individuals have begun to shed some new light on our understanding of the role of visual experience in brain development and function.

How the brain rewires when vision lacks

Since the first evidence of recruitment of the occipital cortex in congenitally blind individuals during Braille reading [1], it has become clear that early visual brain regions that receive information via direct, or indirect, retinal input undergo a cross-modal plastic functional reorganization in sight-deprived individuals [2,3••]. Thus, if on one side it is undeniable that the lack of visual input leads to significant morphological and functional changes in the visual pathway structures in the brain of blind individuals, including atrophy of grey and white matter [4,5] and increased glucose metabolism at

rest in the occipital areas [6], on the other side a growing body of evidence indicates that the occipital cortex is recruited for a variety of nonvisual perceptual and cognitive tasks, including lexical and phonological processing, verbal memory, memory retrieval, repetition priming, spatial discrimination, object discrimination, auditory discrimination, selective attention, working memory and spatial navigation [2,3**,7,8**,9]. Given that studies in animals show that the loss of a specific sense leads to the invasion of the deprived cortical area by inputs originating from other primary cortical regions, as cross-modal connections between early sensory areas are physiologically present [8**,10], we can expect that the human visual cortex may also be capable of rewiring in order to accommodate nonvisual sensory inputs [3**,9].

Nonetheless, although this functional recruitment of early visual areas has been found to correlate with specific cognitive or perceptual performances [2,11,12], the demonstration of a specialization or segregation of functions, other than an aspecific functional response during nonvisual tasks (especially for the occipital pericalcarine cortex) still remains ill-defined. An efficient functioning of occipital cortex is supported by the observation that higher cognitive and perceptual level tasks – and not merely basic sensorimotor tasks – primarily engage occipital regions in blind individuals, as indicated by the fact that real or 'virtual' [via transcranial magnetic stimulation (TMS)] lesions of occipital cortex impair tactile perception, verb generation and Braille reading [2].

However, recent studies aimed at interpreting this cross-modal and across-tasks responsiveness in the early visual areas of the occipital cortex in visually deprived individuals have reported contrasting findings on the existence of a functional specialization [11,13•–15•]. Indeed, the limitation in disentangling the meaning of the differential combinations of cortical activations/deactivations is mainly related to the difficulty of exploring more than a single perceptual/cognitive function or sensory modality during a single experimental session [2], as well as to the fact that by having to rely on nonvisual stimulation paradigms the functional localization of specialized 'visual' areas in blind individuals is relatively approximate. Nonetheless, we cannot exclude that their recruitment may be, at least in part, the result of an aspecific positive response in congenitally blind individuals, likely related to the sensory deafferentation occurring in blindness.

The blind brain is the key to prove supramodality

Visual perception of faces and other object categories evokes distinct patterns of neural activity in the extrastriate ventral temporal cortex that are widely distributed

Key points

- In spite of the predominant role attributed to vision to acquire a representation of the surrounding world, individuals who are visually deprived since birth show cognitive and social abilities that are comparable to those of sighted individuals.
- Studies in both sighted and congenitally blind individuals have demonstrated that many cortical regions are supramodal in nature, that is, they are able to process external information regardless of the sensory modality through which such information has been acquired, and that vision is not a mandatory prerequisite for the brain to develop its sophisticated functional architecture.
- Visual experience, though, leads to a functional specialization in specific cortical areas and, conversely, lack of vision is followed by cortical functional rewiring through cross-modal plasticity.
- The supramodal nature of functional cortical organization may explain how individuals who have never had any visual experience are able to acquire normal knowledge about objects and their position in space, form mental representations of and interact effectively with the external world.
- The study of blindness is a uniquely enlightening tool to understand the functional organization of the human brain.

and overlapping. This model, named 'object form topography' [16], may explain how a limited portion of the brain, such as the visual cortex in the inferior surface of the temporal lobe, is capable of distinguishing an infinite number of object categories. Following these observations, we designed a functional magnetic resonance imaging (fMRI) study to test the hypothesis that the representations of object categories in ventral temporal cortex are not simply visual but, rather, reflect more abstract, 'supramodal' (or 'metamodal') aspects of object form [17–21]. We also questioned whether visual experience is a necessary prerequisite for this functional organization to develop. In line with our hypothesis, others had shown that both visual and tactile recognition of objects activate a part of the object-responsive cortex, the dorsal part of the lateral occipital complex, named LOtv [22]. This study, however, did not assess the relation between the patterns of neural response elicited by the two sensory modalities, nor did it rule out that the activations in visual cortical area during tactile recognition could be simply due to a visual imagery-based mental representation of the object explored haptically [22]. In our fMRI study, we found that both visual and tactile recognition tasks evoked category-related patterns of response in ventral extrastriate visual cortex in sighted individuals (Fig. 1), that were correlated across the two sensory modalities [21]. Furthermore, blind individuals also showed category-related patterns of response in these

Figure 1 Supramodal organization of the ventral 'what' and dorsal 'where' cortical pathways
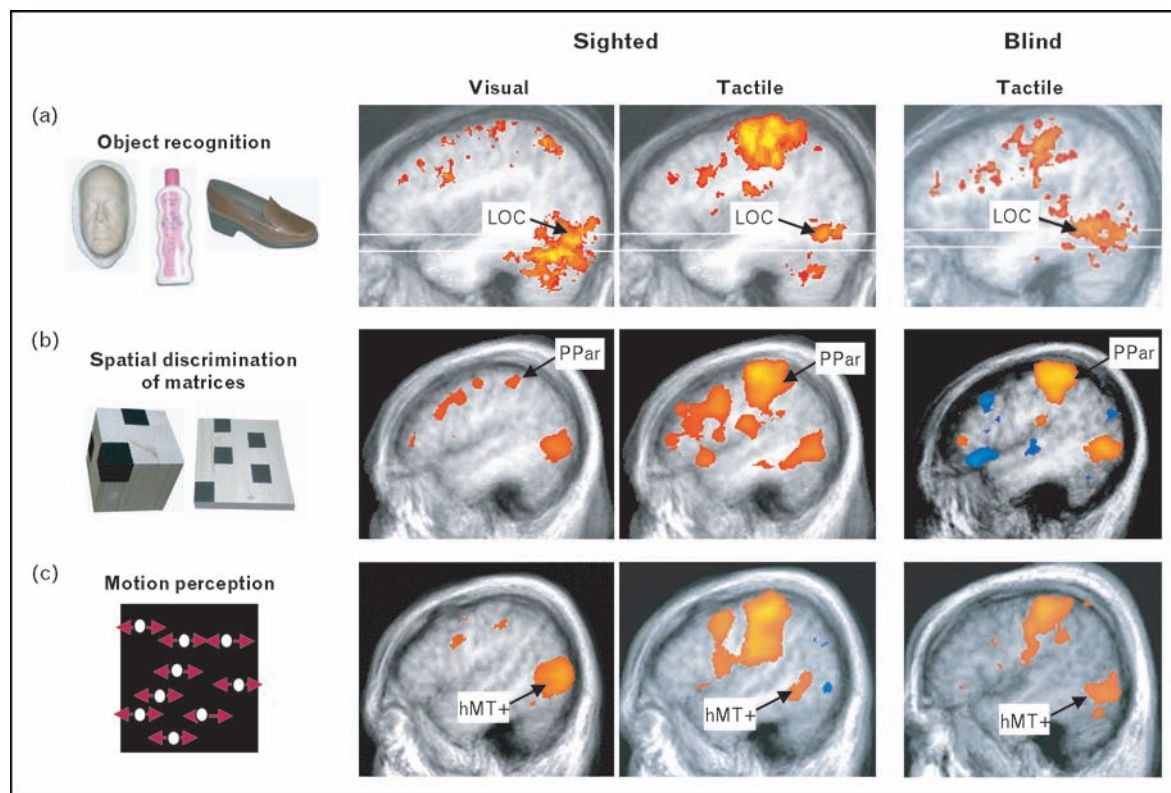
Brain areas that responded during tactile or visual perception in sighted individuals and during tactile perception in blind individuals across different tasks: (a) object recognition, (b) spatial discrimination and (c) motion perception. Sagittal images from group Z-score maps of activated areas are shown for the sighted and blind individuals, and the lateral occipital complex (LOC), the posterior parietal cortex (PPar) and the human middle temporal complex (hMT+) are indicated. Adapted from [21,23,24] with permission.

'visual' areas, implying that these patterns are not due merely to visual imagery and, furthermore, that visual experience is not necessary for these category-related representations to develop (Fig. 1). These findings indicated that a common, more abstract representation of object form is elicited by these two sensory inputs.

Therefore, the supramodal nature of a specific brain region relies on a common, more abstract representation of the perceived stimuli (e.g. of object form for the inferior temporal-ventral occipital cortex), and does not depend uniquely on the contribution of a specific sensory modality, neither to function nor to develop. Indeed, in line with the existence of a supramodal 'object form topography', a recent brain functional study indicated that both sighted and congenitally blind individuals show for aurally presented words of nonliving and living items the same medial-to-lateral bias in the ventral temporal extrastriate cortical regions [25]. In addition, auditory perception of material properties in both sighted and cortically blind individuals elicits a neural response in medial regions of the ventral extrastriate pathway, the same areas recruited for the visual representation of

object properties [26]. Furthermore, a more abstract representation of object form in these cortical regions is supported by the observation that LOtv is activated in both sighted and congenitally blind individuals when information on object form, but not object identity, is conveyed by visual-to-auditory sensory substitution devices [27–29], and shows robust cross-modal (visuo-tactile and audio-visual) adaptation during object recognition in sighted individuals [30●●,31].

Extending supramodality outside of the ventral pathway

These findings in the ventral 'what' pathway prompted us to ask whether a similar supramodal functional organization also existed in the 'where' pathway of the dorsal occipito-parietal stream, involved in spatial processing and imagery. Although through vision one is able to obtain distinctive information regarding the representation of the surroundings and the localization of objects, blind individuals show spatial discrimination and navigational skills that are comparable to those of sighted individuals, even in those cognitive domains that rely

indirectly on mental spatial representation, such as number processing or action planning [7,32–34]. Consistent with these behavioural findings, tactile and auditory spatial localization studies in blind individuals showed a specific recruitment of dorsal occipital and posterior parietal areas (Fig. 1) [35•,36–38], indicating that the activations found in sighted individuals in response to nonvisual spatial discrimination tasks are not merely due to visual imagery (e.g. [39]). Thus, as in the case of the 'what' pathway in the ventral temporal cortex, also these cortical areas appear to be supramodal in nature. Additional evidence in support of this hypothesis comes from the recruitment of dorsal pathway cortical areas, whereas both sighted and congenitally blind individuals perform more complex cognitive tasks that require spatial representation, such as navigation within large-scale environments [40•], numerical cognition [41] and action planning and control [42,43].

The concept of supramodal organization has been extended much beyond the 'what' and 'where' pathways to brain areas associated with other perceptual and cognitive functions: left parietal cortex for representation of tools [44], 'visual' word form area for letter reading [45], superior temporal cortex for processing of vocal stimuli [46], fronto-parietal areas for working memory [23], frontal eye fields for spatial attention orientation [47], and medial prefrontal cortex for self-representation [48].

Furthermore, in line with findings in sighted individuals indicating modality independent, but emotion-specific patterns of neural response in medial prefrontal and superior temporal areas [49], a supramodal organization has been found recently also in those brain areas that modulate affective responses and social interactions [50,51]. Congenitally blind individuals not only showed a selective amygdala response to fearful and angry as compared to neutral voices [52••], but also recruited similar-to-sighted cortical networks that subserve action and behaviour recognition, and understanding of others' intentions (Fig. 2). For instance, we found that a left premotor-temporo-parietal network subserves action perception through hearing in individuals who have never had any visual experience, and that this network overlaps with the left-lateralized 'mirror system' that is activated by visual and auditory stimuli in the sighted [51]. Similarly, the same bilateral network (temporo-parietal junction, medial prefrontal, precuneus, and anterior superior temporal cortex) is recruited in congenitally blind and sighted individuals for reasoning about the mental states of others, that is, for 'theory of mind' processing [50]. Altogether, these findings suggest that visual experience is not necessary for the development of an efficient 'social' brain, and that sensory processing and learning through nonvisual sensory

Figure 2 The supramodal 'social' brain
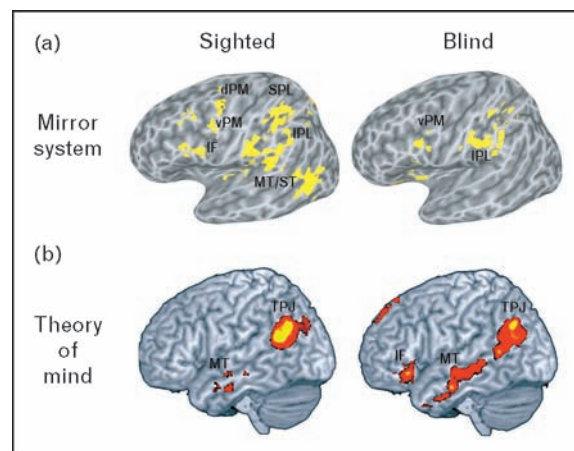
Auditory mirror voxels (a – adapted with permission from [50]) and brain areas subserving theory of mind (b – adapted with permission from [49]) in both sighted and congenitally blind individuals are projected onto a standardized left hemisphere template. Inferior frontal (IF), ventral and dorsal premotor (vPM and dPM), and middle/superior temporal (MT/ST) areas, superior and inferior parietal lobules (SPL and IPL), and the temporo-parietal junction (TPJ) are reported.

experience make it possible to acquire an efficient knowledge and awareness of other persons' beliefs and intentions.

When supramodality meets cross-modal plastic rewiring: the example of motion perception

Whereas sighted and congenitally blind individuals have an essentially similar functional organization within the supramodal cortical areas described above, not surprisingly they also show differences in the extension and magnitude of the activation in the recruited areas [3••,7,18,53] and in the correlations across task-related regions [13•,35•,54,55•]. These differences are the results of the combined effects of the intrinsic supramodal nature on one hand and cross-modal plastic reorganization on the other hand.

An interesting example to illustrate this issue comes from the study of the neural correlates of visual and/or tactile motion discrimination in sighted and congenitally blind individuals. Both visual and nonvisual motion perception share fundamental psychophysical aspects [56], and recruit a specific circuit within the temporo-occipital cortical regions including the middle temporal complex, hMT+, in both sighted [24,57] and congenitally blind individuals [24,58] (Fig. 1). However, visual experience in sighted individuals does lead to a functional segregation within hMT+ into a more anterior subregion, involved in the supramodal representation of motion,

and a posterior subregion that processes visual motion only [24]. In contrast, nonvisual motion activates the full extent of hMT+ in congenitally blind individuals, indicating that the whole hMT+ develops to subserve nonvisual motion perception in the absence of any visual experience [24,58]. In addition, distinct patterns of brain functional correlations originate from hMT+ subregions as a result of supramodal organization and visual experience: whereas the supramodal portion of hMT+ in both sighted and congenitally blind individuals correlates not only within visual occipital cortex but also with areas of sensory integration, such as sensorimotor and posterior parietal regions, the posterior subregion behaves differently in the two groups [55•]. Specifically, in the sighted individuals correlations are restricted within visual cortical areas, whereas in the congenitally blind individuals this portion of hMT+ develops functional correlations also with other sensory integration cortical regions, similarly to what the anterior supramodal portion does [55•].

The fine supramodal nature of hMT+ is further supported by the observation that this cortical area is capable of processing motion-related information *per se*, even when motion stimuli are delivered to body structures, such as the tongue, that are not primarily devoted to the perception of movement, at least in humans [59]. Also, repetitive TMS applied on the more anterior portion of hMT+ led to a significant impairment in accuracy and reaction times, whereas individuals had to detect motion speed changes of rotating plastic dots tactilely, indicating that this cortical area is necessary for nonvisual motion processing [60].

Which neural pathways may subserve these common and differential responses in the 'visual' cortex of congenitally blind individuals? As mentioned before, on the basis of various anatomical and functional studies in both animals and humans, we may hypothesize that nonvisual information reaches the occipital cortex through cortico-cortical connections, such as the parieto-occipital ones [2,3••]. These anatomical connections, viable also in physiological conditions as demonstrated in the brain of blindfolded sighted individuals who perform nonvisual discrimination tasks [19], may then undergo also a cross-modal plastic reorganization and become more robust in those individuals who lose sight at birth or in the early postnatal period [3••,9,61–63]. Indeed, brain functional studies reported a strengthened functional and effective connectivity between 'visual' occipital cortex and the primary nonvisual sensory cortices, via direct or indirect (through multisensory association areas) pathways [54,64]. Nonetheless, a concomitant involvement of subcortical loops between distinct sensory cortical areas also has been proposed [65,66].

Conclusion

Although vision is considered to play a predominant role in acquiring information to form the representation of the surrounding world, individuals who are visually deprived since birth show cognitive and social skills that are substantially comparable to those in sighted individuals [2,3••,7]. Behavioural and functional studies in congenitally blind individuals have provided novel and stimulating insights on many questions regarding not only the cross-modal plastic rearrangements that take place when vision is absent, but primarily the functional development and organization of the sighted brain itself. The recruitment of task-related regions in both sighted and congenitally blind individuals during nonvisual recognition indicates that these different percepts (e.g. object form, motion, spatial localization, words, actions and behaviours, etc.) rely on more abstract, supramodal representations that: (i) are independent from the sensory modality that conveys information to the brain; (ii) do not require visual experience nor visually-based mental imagery to form; and (iii) can be accessed either through bottom-up mechanisms from distinct direct sensory inputs, or through top-down mechanisms from regions subserving higher cognitive functions (as in the case of working memory, attentional modulation, etc.).

A common abstract representation would favour the development of a unique, coherent percept through the integrated processing of distinct pieces of information conveyed by different sensory modalities. This aspect requires distinguishing supramodal from multisensory brain areas. The latter regions mainly refer to cortical and subcortical structures, such as the superior colliculus, superior temporal sulcus or intraparietal cortex, that process multiple stimuli conveyed by different sensory modalities at once, both in space and time [29,67]. From an electrophysiological viewpoint, neurons with different degrees of multisensory responsiveness (from pure unimodal to bi/trimodal neurons) have been reported to have a 'patchy' distribution within these areas in animals [68]. Recent fMRI data suggest a similar distribution in the human brain as well [67]. Less is known on the neuronal characteristics of supramodal cortical areas in humans. Given that fMRI resolution does not allow measurement of activity at the level of single neurons [see Cheng, (pp. 401–408)], overlapping functional activations in a particular brain region elicited by distinct sensory modalities may reflect identical recruitment of individual supramodal neurons, or be due to selective recruitment of unimodal neuronal subpopulation within the same cortical areas. We could certainly accept the idea that, during the multistep and parallel processing of different sensory inputs along early sensory areas, as well as higher order association areas, a continuous interplay and integration may occur between multisensory percepts and supramodal attributes.

How the different pieces of sensory information are functionally unified into a more abstract representation, and whether or not the development of this supramodal functional organization does require a minimal sensory input of any given sensory modality (i.e. supramodal), or not (i.e. amodal), is a matter of speculative debate [32,69]. Notably, Held *et al.* [70••] recently showed that although congenitally/early blind individuals who gained sight after eye surgery did not exhibit an immediate transfer of their tactile shape knowledge to the visual domain, this ability was acquired after a very short time, suggesting the existence of a coupling between the representations of visual and tactile features based on experience.

In summary, the mental representation of the external world is sustained by a cortical functional organization that is largely supramodal in nature and independent from vision. This may explain how individuals who have never had any visual experience are able to acquire normal knowledge about objects and their position in space, and form mental representations of and interact effectively with the external world.

Acknowledgements

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A blind individual that regains sight is not immediately able to visually recognize an object previously known only by touch, but such cross-modal mapping develops rapidly. This is a first attempt answer the famous Molyneux question, but also to address the role of sensory experience in object representation.