The blind brain: How (lack of) vision shapes the morphological and functional architecture of the human brain

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Abstract

Since the early days, how we represent the world around us has been a matter of philosophical speculation. Over the last few decades, modern neuroscience, and specifically the development of methodologies for the structural and the functional exploration of the brain have made it possible to investigate old questions with an innovative approach. In this brief review, we discuss the main findings from a series of brain anatomical and functional studies conducted in sighted and congenitally blind individuals by our's and others' laboratories. Historically, research on the 'blind brain' has focused mainly on the cross-modal plastic changes that follow sensory deprivation. More recently, a novel line of research has been developed to determine to what extent visual experience is truly required to achieve a representation of the surrounding environment. Overall, the results of these studies indicate that most of the brain fine morphological and functional architecture is programmed to develop and function independently from any visual experience. Distinct cortical areas are able to process information in a supramodal fashion, that is, independently from the sensory modality that carries that information to the brain. These observations strongly support the hypothesis of a modality-independent, i.e. more abstract, cortical organization, and may contribute to explain how congenitally blind individuals may interact efficiently with an external world that they have never seen.

Keywords: Blindness, supramodality, cross-modal plasticity, brain imaging, brain functional architecture, mental representation

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Introduction

The information that we acquire through our eyes plays a central role in shaping the manner in which we represent and interact with the world around us. The ancient Greek term for the verb 'to know' was the past tense of the verb 'to see', indicating that knowledge was subordinated to prior visual experience (I saw and thus I know).

Though lack of visual experience may often delay childhood physiological development in blind individuals,[1–3] modulate their cognitive strategies[4–7] or affect to some extent their social functioning,[1,2] congenitally blind individuals overall show perceptual, cognitive and social skills comparable to those of sighted individuals – see for instance, Cattaneo *et al.*,[5] Pasqualotto *et al.*,[7–9] Ricciardi *et al.*,[10–13] Klinge *et al.*,[14] Bedny *et al.*[15] and Proulx *et al.*,[16] among many other behavioural observations.

The fact that congenitally blind individuals show comparable-to-sighted performances, in spite of the relevance of the visual modality for human and non-human primates, raises some fundamental questions, including in the first place to what extent is vision truly necessary for the human brain to develop and function, and which fate visual brain areas undergo in blind individuals.

While historically the latter question has been widely investigated both in humans as well as in animal models with congenital or acquired blindness, more recently researchers from distinct labs across the world, including our own, have developed innovative lines of research finalized understand how much vision is a mandatory prerequisite for the brain morphological and functional development to occur.

Here we discuss general findings from brain structural and functional studies in congenitally blind individuals that have contributed to understand not only the cross-modal plastic modifications that do occur in the 'visual' regions as a consequence of the lack of visual input, but mainly the role of (lack of) visual experience on the development of the brain morphological and functional architecture in humans. Novel hypotheses, open questions and ill-defined aspects regarding the 'blind brain' are reviewed.[a]

How does the brain reorganize when vision lacks since birth?

The structural and functional characterization of the brain in people who lack vision since birth and report no visual experience represents an unprecedented tool for understanding how cross-modal plasticity reorganizes sensory-deprived brain areas.[12,13,17–19] Because sight has always been considered as the most important sense for humans to acquire knowledge of the surrounding world, researchers have been constantly interested in defining the fate of unisensory 'visual' brain areas in blind individuals.

Notably, a functional recruitment of 'visual' occipital areas in the 'blind brain' has been described both at rest (that is, in the absence of any sensory stimulation) and during various non-visual tasks since the earliest studies.[20–22] Over the last 15 years the neural modifications subserving the processes through which 'visual' brain regions undergo a plastic cross-modal reorganization in sight-deprived individuals have been characterized to a greater detail. Nonetheless, several questions still remain to be addressed.

For instance, the functional specificity of these cross-modal adaptations within occipital areas is still under debate. As a matter of fact, occipital activations in blind individuals appear to play a fundamental role in sensory processing across a wide gamut of experimental tasks (e.g. lexical, verbal and phonological processing, object discrimination, selective attention, verbal and episodic memory, sound localization).[19,23–26] In addition, their recruitment relates to the individual behavioural outcome and is transitorily disrupted by transcranial magnetic stimulation (TMS).[19,27] However, the lack of a precise anatomical and functional characterization of these cross-modal responses leaves still open the question whether occipital regions in blind individuals reorganize in a task-specific and performance-correlated manner, or whether this sensory-deprived cortex may just respond to non-visual inputs irrespectively from their perceptual content.[28–32]

This issue tightly relates to another still-open key question regarding the 'blind brain': how does non-visual information reach 'visual' occipital cortical regions? After sensory deprivation, the human visual cortex rewires and accommodates non-visual sensory inputs.[18,33] The loss of a specific sense allows the deprived cortical area to be invaded by inputs originating from other primary cortical regions, as early sensory areas physiologically show direct, heteromodal connections.[34,35] In addition, two other anatomical pathways should be taken into account. First, non-visual information reaches the occipital cortex through cortico-cortical connections. In particular, the parieto-occipital pathway[18,19] becomes stronger after vision loss[18,33,36–38] and conveys information from somatosensory and multisensory parietal areas to the reorganized occipital cortex.[39–42] Second, a concomitant reorganization of thalamic-cortical connections occurring after vision loss in early life may contribute to reorganize sense-specific links among distinct sensory cortical areas,[43,44] including afferences to the occipital cortex. Nevertheless, it is yet to be fully understood how these different pathways convey the information to the occipital cortex in blind individuals.

A possible modality-specific, but task-independent localization of cross-modal responses in different portions of the occipital cortex in blind individuals has been recently proposed.[b] Using a meta-analytic approach, an enhanced recruitment of the dorsal occipital and parietal cortex was found specifically across tactile-prompted tasks in blind as compared to sighted individuals. This tactile-induced recruitment in blind subjects suggests that tactile information may be primarily conveyed from sensorimotor areas to parietal-occipital regions through a potentiation of the existing cortico-cortical connections.[39–42] On the contrary, an enhanced recruitment of more medial and ventral occipital and inferior temporal areas was found specifically across auditory-prompted tasks in blind. Consequently, auditory information may be directly brought to occipito-temporal areas via direct heteromodal or subcortical connections.[35,45] As the different modalities, such hearing and touch, convey sensory inputs with peculiar spatio-temporal and organizational features (e.g. global *vs*. analytic; simultaneous *vs*. sequential) and distinctively link to the occipital clusters,[46] the cross-modal adaptation in blind people is likely to be affected by the sensory channel variable[a].[47]

A final consideration relative to neural adjustments occurring after sensory deprivation regards the modulation of cross-modal phenomena due to the age of blindness onset or the cause of sensory loss. The examination of different subpopulations of sensory-deprived individuals is actually offering novel and surprising suggestions in the comprehension of cross-modal plasticity in blindness.

For instance, the degree of plastic compensatory changes is influenced by the age at which sight loss occurs, and is reflected by the extent of cross-modal phenomena in 'visual' occipital areas. Typically, late blind individuals show a limited activation in occipital areas and a reduced connectivity between occipital and stimulus-processing areas.[40,42] Nonetheless, late blind individuals provide a fundamental comparison to fully characterize the behavioural and neural changes that occur in people who have had no visual experience, and thus exploit the potentiality of sensory-substitution or prosthetic devices in sighted individuals who lost vision later in life.[48]

Similarly, anophthalmic and monocular patients represent unique models to study the effects of sensory deprivation, as compared to other causes of blindness. In anophthalmia, retinal input to the visual system is absent due to the congenital lack of eye development, and therefore it is possible to investigate the structural and functional cerebral reorganization that results from truly absolute peripheral blindness with no central nervous system involvement.[49–51] On the other hand, the study of monocular individuals is useful to understand behavioural and neural compensatory processes associated with receiving images through one eye only.[5]

How does the brain organize independently from visual experience?

As previously discussed, most of the research in blind individuals typically has focused on the compensatory plastic rearrangements that follow sensory deprivation. However, the loss of sight represents a powerful tool also to understand to what extent the brain morphological and functional architecture is programmed to develop independently from any visual experience.

Vision is indeed considered crucial to provide the main sensory inputs to explore the world around us. Visual stimuli are received and hierarchically processed in the human brain along segregated, though integrated, pathways that process distinct, simpler elements into more complex, unified percepts.[52] As a matter of fact, from a neuroanatomical perspective, the 'visual brain' is parcellated into distinct, hierarchical connected functional areas that extends from striate and peristriate occipital regions, to temporal, parietal and even frontal cortex.[53]

While we know that early visual-processing areas in occipital cortex undergo adaptative cross-modal modifications, the question is what takes place in the other areas of the ''visual'' brain in congenitally blind individuals. As a matter of fact, most of the functional elements along the visual pathways have been shown to be able to process external information regardless of the sensory modality through which such an information has been acquired.

Behavioural protocols have shown that several perceptual, cognitive and social skills are substantially comparable between congenitally blind and sighted individuals.[12,54] More recently, brain functional studies have demonstrated that during perceptual tasks congenitally blind people rely on patterns of neural response that overlap to those in sighted individuals.[12] For instance, in both sighted and blind individuals, visual and non-visual recognition of object form activates the inferior temporal and ventral occipital cortex,[55–58] visual, tactile and auditory motion discrimination activates the middle temporal areas,[59,60] and spatial representation, either processed through vision, tactile exploration or sound localization, relies on parietal networks.[29,61,62] If a given 'visual' area is recruited for visual and non-visual tasks in sighted individuals, as well as in congenitally blind individuals for non-visual tasks, then this activation indicates a more abstract, supramodal representation of a specific content of information, and cannot be simply ascribed to a plastic rearrangement due to the lack of vision.[12,13,33] Thus, a supramodal brain region shares a specific, more abstract representation of the perceived stimuli, which does not depend uniquely on the input from a specific sensory modality.

For the most part, the supramodal nature of neural representation of sensory stimuli has been primarily assessed within the well-known functional organization of the visual system. As briefly stated above, highly specialized regions subserving object form recognition (lateral occipital clusters), motion processing (middle temporal complex), spatial layout coding (parahippocampal cortex) and spatial localization (dorsal occipito-parietal pathway) have been the most explored 'visual' brain areas through visual and non-visual stimulation paradigms, in both sighted and congenitally blind individuals (e.g. Pietrini *et al.*,[57] Ricciardi *et al.*,[60] Bonino *et al.*,[61] Weeks *et al.*,[62] De Volder *et al.*,[63] Peelen *et al.*[64] and Kupers *et al.*[65]). These initial studies not only assessed the overlapping patterns of neural responses in both sighted and blind individuals, but also determined that supramodal brain areas share overlapping connectivity maps in sighted and blind individuals,[40,41] yield to task-specific, modality-independent behavioural impairments when functionally-inhibited via TMS,[66,67] and even respond when a specific information is conveyed by visual-to-auditory or visual-to-tactile sensory substitution devices.[48,68] Altogether, these observations from imaging studies indicate that the brain functional organization of 'visual' pathways is able to process information in a supramodal fashion, does not strictly depend on the contribution of a specific sensory modality to function and is to a large extent independent from visual experience, or from visually-based mental imagery, to form and to develop.

More recently, as reported in details by Ricciardi *et al.*, the description of supramodal responses rapidly moved from the 'simpler' perceptual contents within the visual pathways to more complex semantic representations – such as tool use or action recognition,[11,69] – and in the direction of affective functioning – such as representations of others' emotions and mental states.[15,70] The concept of supramodality appears to be not limited to functionally specialized cortical clusters but rather extends to distributed brain networks. Thus, at different levels of stimulus processing, the human brain may rely on a broader 'supramodal mechanism', which advances sensory information towards a more abstract, possibly 'conceptual', representation. While this mechanism may result clearer when dealing with semantic knowledge, it remains to be defined at which processing level the information content of stimuli separates from sensory input features and becomes supramodal.[12,13,71]

This theoretical framework tightly relates to still uncertain aspects of supramodality. Do the overlapping activations in a particular brain region elicited by distinct sensory modalities reflect an identical recruitment of individual supramodal neurons, or rather a selective recruitment of distinct unimodal subpopulations within the same cortical areas? In other words, at which level (e.g. single neuron, cluster or cortical network) does the supramodal representation of information occur? Are similarities in the functional patterns between sighted and blind individuals limited to the topographic localization of the recruited cortical areas (i.e. simple overlapping of brain activations), or conversely involve the content of the neural responses (i.e., rely on the same neural representation)?

While several protocols have been developed in animals for investigating cross-modal plasticity (recently reviewed by Kupers *et al.*[18] and Kupers and Ptito[54]), very few studies have been conducted to assess the neuronal correlates of supramodality. For instance, in monkeys, more abstract representations of grating orientation have been found in occipital area V4,[72] and in neurons in the ventral premotor cortex for specific finalized motor acts.[73] Interestingly, these studies suggest that supramodal properties may be

restricted to only a part of the whole neuronal populations within the different brain areas, whereas the majority of neurons show unimodal responses, and concern representations of different perceptual complexity (e.g. stimulus orientations *vs.* action goals).

Recent brain functional studies in humans have used pattern-classification algorithms and multivariate analysis to decode the information that is represented in a spatially distributed pattern of neural activity, and to identify those brain regions that may contribute significantly to the discrimination of different mental states.[74–76] Consequently, pattern recognition approaches may be employed to describe overlapping neural responses across experimental samples (e.g. congenitally blind and sighted) and/or sensory modalities. As compared to the 'more classical' univariate approach in imaging studies, the homologies in the functional representation obtained with multivariate approaches are not limited only to a mere overlap in the topographical localization of neural activations, but do involve the intrinsic content of the neural responses.

Multi-voxel pattern analyses have revealed a more abstract representation in congenitally blind and sighted individuals across visual and/or non-visual presentation of motion direction in middle temporal areas,[77] and for hand-made actions in the bilateral, though left-prevalent, action–observation network.[78] Similarly to what has been reported in animal studies and in line with early imaging studies in humans, pattern recognition approaches have shown that supramodal properties are restricted to only a part of the whole neuronal populations within the different brain areas – suffice to mention the LOtv cluster within the broader lateral occipital cortex,[55,57] the anterior portion of human middle temporal complex,[59,60] or the more limited ventral premotor and inferior parietal clusters within the more extended action observation network (see Figure 3 of Ricciardi *et al.*[78]) – and concerned representations of different perceptual complexity (e.g. motion discrimination *vs.* action goals).

The comprehension of how unisensory information is processed and integrated into a supramodal representation represents a major challenge for research in the neuroscience of the 'blind brain'. To date, interesting hints have been prompted from recent studies that investigate the relationship between sensory modality and conceptual knowledge.

Theories on the organization of conceptual knowledge proposed two types of neural representation models in relation to perceptual processing: modality-specificity and domain-specificity.[79] The modality-specificity theories postulate that conceptual knowledge is organized by the sensory modality (e.g. visual, motor, tactile) enrolled during the acquisition or the processing of concepts, while according to the domain-specificity theories this organization is based on a more abstract, semantic categorization regardless of the sensory modality that conveys the information to the brain.[80] On this topic, neuropsychological evidence appears to support a domain-specific organization in the human brain. Specifically, selected patients with brain lesions may develop category-specific and category-selective semantic deficits (i.e. for animals or fruit/vegetables), that are usually not associated with impairments in perception (for a review by Gainotti[81]). Conversely, impairments within sensory modalities are not inevitably associated with category specific semantic deficits: for instance, neuropsychological observations showed that perception of colour is represented autonomously from object colour knowledge.[82]

The entangle between sensory modality and conceptual knowledge can be also evaluated from a linguistic point of view. Even if they acquire conceptual knowledge through auditory or haptic inputs, congenitally blind individuals show globally a high similarity in language properties as compared to sighted ones, including when processing knowledge directly related to visual experience (i.e. colour terms, verbs of vision).[83] Moreover, even when restricting to semantic categorial features in language production, only few differences are found between blind and sighted individuals, especially in categories in which vision is salient (i.e. fruits and vegetables).[84,85]

The neuropsychological and linguistic approaches did not fully clarify to which extent conceptual knowledge is grounded into the sensory modalities. Novel approaches in functional neuroimaging studies are indicating that 'concepts' are characterized by a more complicated and distributed organization within the human brain.[58,86] Further studies should look for potential functional similarities between congenitally blind and sighted individuals and assess whether these are dependent on sensory modalities and sensory experiences, particularly when dealing with conceptual knowledge across several semantic categories.

Final considerations

Over the last two decades, functional brain studies in blind individuals have offered a unique opportunity to examine the role of visual experience in forming a representation of the external world, as well as to understand to what extent visual experience is a mandatory prerequisite for the human brain to develop and function. Individuals who lack sight since birth have provided inspiring ideas on many questions regarding both the cross-modal plastic rearrangements that take place when vision is absent, and the development of the morphological and functional organization of the sighted brain itself. The demonstration of the modality independent, more abstract nature of the functional cortical organization, and consequently of information representation, may contribute to explain how congenitally blind individuals are able to acquire knowledge and interact with an external world that they have never seen. This proficient mental representation would not only explain the perceptual, cognitive and social performances comparable to those in sighted individuals,[5,12,18,19] but mainly indicate that the blind brain is not 'disable', but rather 'differentially abled'.[12,13,33,87]

Nevertheless, blind individuals certainly experience important sensorial limitations, including the inability to perceive features that are strictly 'visual' (e.g. colours, perspective, shadows, etc.), and to have immediate simultaneous synoptic representation (as touch and hearing only allow for a sequential processing of information). These

differences may result in the adoption of distinct mental strategies to perform a given task, as well as in impaired behavioural responses, as in the case of spatial representations that involve complex mental abilities, including angle discrimination or three-dimensional spatial imagery tasks (e.g. Noordzij *et al*.,[4] Cattaneo *et al*.,[5] Pasqualotto *et al*.,[7] Pasqualotto and Proulx[88] and Gori *et al*.[89]).

Interestingly, from a neurofunctional perspective, the demonstration of a similar supramodal brain organization in normally sighted people and in individuals deprived of sight since birth indicates that visual experience is not necessary for the brain to develop its morphological and functional architecture. Thus, this supramodal cortical functional development appears to be to some extent hard-wired in our genetic code,[12] though vision and the other unimodal sensory inputs certainly play an important role in the shaping of the perceptual processing system.

Of note, recent exceptional reports in congenitally blind individuals, who recovered sight in their adulthood after eye surgery, indicate that these subjects do not exhibit an immediate transfer of their tactile knowledge to the visual domain during an object form detection task.[90,91] Nonetheless, these abilities were acquired after a very short time, thus suggesting a rapid learning process for establishing relationships across sensory modalities.[90,91] This observation may induce to hypothesize that the rapidity of the cross-modal mapping may be facilitated by a shared, supramodal representation of object form. The newly acquired sensory experience, however, appears to require some extra time to gain access to such a representation, suggesting that some functional reorganization may anyway be needed.

In conclusion, the blind brain is a fascinating model to investigate the molecular and neurobiological underpinnings of how the brain develops its marvellous morphological and functional architecture. We believe that step forwards in the comprehension of both cross-modal adaptative plastic responses and supramodal functional cortical organization will expand our understanding of the nature *versus* nurture role in the shaping of the human brain and will improve our ability to significantly develop novel educational/rehabilitative programs and sensory-substitution devices for sensory-deprived individuals.[48]

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NOTES

a. Researchers who work on the effects of blindness on the brain by using neuroimaging and molecular methodologies, recently gathered together to discuss the state-of-the-art and future perspectives on what we can learn from studying the blind brain ('The Blind Brain Workshop: How Blindness Can Open Our Eyes', San Giuliano Terme, Pisa, Italy, 16–18 October 2013, http://www.theblindworkshop.com). Cortical development, cross-modal plasticity, supramodal organization, multisensory integration and sensory-substitution devices were the major topics discussed in the two-day workshop.

b. Ricciardi E, Tozzi L, Leo A, Pietrini P. Modality dependent cross-modal functional reorganization following congenital visual deprivation within occipital areas: a meta-analysis of tactile and auditory studies. Submitted for publication.

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