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Opinion

Evidence from Blindness for a Cognitively Pluripotent Cortex

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Cognitive neuroscience seeks to discover how cognitive functions are implemented in neural circuits. Studies of plasticity in blindness suggest that this mind–brain mapping is highly flexible during development. In blindness, 'visual' cortices take on higher-cognitive functions, including language and mathematics, becoming sensitive to the grammatical structure of spoken sentences and the difficulty of math equations. Visual cortex activity at rest becomes synchronized with higher-cognitive networks. Such repurposing is striking in light of the cognitive and evolutionary differences between vision, language, and mathematics. We propose that human cortices are cognitively pluripotent, that is, capable of assuming a wide range of cognitive functions. Specialization is driven by input during development, which is itself constrained by connectivity and experience.

'The child who methodically adds two numbers from right to left, carrying a digit when necessary, may be using the same algorithm that is implemented by the wires and transistors of the cash register in the neighborhood supermarket . . . '
Vision, 1982, David Marr

Blindness As a Window into Cortical Specialization

David Marr famously pointed out that the same cognitive task can be implemented by different neural and non-neural hardware. The brain of a 6-year-old and a cash register both implement arithmetic [1]. The flip side of this question remains a fundamental puzzle: What are the limits of functional flexibility in the human brain? Can the same tissue implement radically different cognitive functions? Alternatively, is the function of cortical areas specified by intrinsic physiology from birth? Blindness and deafness offer unique insights into these questions because they represent a change in 'species typical experience'. In a seminal article, Greenough *et al*. (1987) [2] distinguished between two ways in which information from the environment causes neural change. One is the familiar sort of learning that humans undergo throughout their lifetime, such as learning how to drive a car, acquiring new words, or learning to recognize new faces. Such learning varies widely across species members (i.e., any two people know different subsets of faces). The other is experience that is nearly ubiquitous across individuals, such as binocular vision from two eyes, exposure to faces in general, the presence of sound in the environment, and for humans, exposure to language and social interactions. Such experiences form the very fabric of our early lives and are a potent and yet at times invisible force in organizing the developing mind and brain. Sensory loss early in life is a large-scale, yet selective change to such species' typical experience. As such, it provides insights into how experience contributes to functional specialization of cortex during development.

Studies of blindness have long been an impetus in expanding thinking about cortical flexibility. Early investigations with dark reared animals and blind humans showed that visual cortices can become more responsive to auditory and tactile stimulation, demonstrating for the first time that

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In blindness, visual cortices are recruited during processing of written and spoken language. Activity is modulated by semantic and grammatical properties of language stimuli and is relevant to higher-cognitive behavior.

In blindness, visual cortices participate in multiple distinct higher-cognitive functions, including numerical processing and memory. Different subregions of visual cortices are specialized for distinct higher-cognitive functions.

Blindness leads to increased connectivity between different subnetworks within visual cortices and distinct higher-cognitive frontoparietal networks. 'Visual' regions that participate in language processing are correlated with frontoparietal language networks, whereas those active during number tasks are correlated with the frontoparietal number network.

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experience can change the sensory modality that drives a cortical region [3–5]. In the present article, I argue that another surprising phenomenon in blindness motivates revising models of human brain development and plasticity: in blindness, visual cortices come to participate in higher-cognitive functions, such as language and symbolic numerical processing [6–12]. We hypothesize that in the absence of bottom–up visual input from the lateral geniculate nucleus, input from higher-cognitive networks dominates activity in the developing visual cortex and causes it to take on higher-cognitive functions (Figure 1; see Box 1 for white matter pathways to visual cortex that could carry higher-cognitive information).

Recruitment of visual cortices for language and mathematical reasoning is striking in light of the cognitive and evolutionary differences between vision and these higher-cognitive domains. Whereas vision is analogical, language relies on discrete symbols. Unlike vision, language is uniquely human. Also unlike vision, math depends on cultural learning. Mathematical sophistication varies widely across individuals and depends on language as well as explicit teaching. Such drastic functional repurposing motivates us to rethink the idea that intrinsic physiology slates cortical areas for a particular cognitive function or even a range of similar cognitive functions. Blindness reveals the potent role of experience in determining the functional consequences of anatomical predispositions. Experience can do more than modifying the sensory modality that drives a cortical area: it can drastically change its cognitive role.

Based on these findings we propose that at birth, human cortical areas are cognitively pluripotent: capable of assuming a broad range of unrelated cognitive functions. The cognitive content represented and processed by a cortical area is determined by the information it receives during development. In this framework, the intrinsic physiology of a region (including its microcircuitry and long-range connectivity) creates computational predispositions, but does not specify a coherent cognitive role, just as the hardware specifications of a computer do not
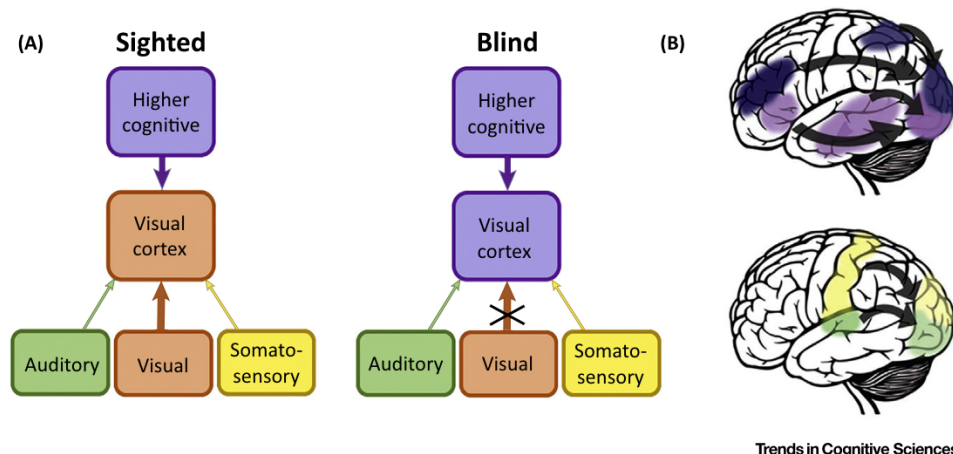
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Figure 1. Mechanisms of Plasticity in Blind Visual Cortex. (A) Schema of competition between visual, sensory, and higher-cognitive information in 'visual' cortices of blind individuals. Arrow thickness represents input efficacy to visual cortex, which is determined in part by strength of anatomical connectivity but is also influenced by timing and coordination of activity. Visual input comes from the lateral geniculate nucleus (LGN), auditory from A1 (or auditory thalamus), and somatosensory from S1 or somatosensory thalamus. Note that these are the logically possible source of input. The presence of S1 input to visual cortex has not been established nor have inputs from the auditory or somatosensory thalamic nuclei (Box 1). (B) Right panel depicts two different types of information [higher-cognitive (top) and sensory (bottom)] that could reach visual cortices in blindness and how this information is segregated within visual cortices. Bottom schematic shows sensory information input from primary auditory (green) and primary somatosensory (yellow) cortices. The top panel depicts higher-cognitive input from language networks (light purple) and number network (dark purple). Recent evidence suggests that information within visual cortices is segregated along higher-cognitive dimensions (i.e., language vs. number). Whether segregation exists along sensory lines is not known.

Box 1. Long-Range Connectivity of Visual Cortex and Its Relationship to Plasticity

Even in sighted humans, nonvisual information reaches the visual system as evidenced by the fact that visual processing in occipital cortices is influenced by tactile and auditory stimuli as well as task goals and attention [88]. This implies existence of anatomical tracts that carry nonvisual information to visual cortices in sighted and blind humans alike. In principle, information could come from nonvisual thalamic sensory nuclei (e.g., auditory medial geniculate nucleus), other sensory cortices (A1, S1), or amodal/polymodal systems [20]. Current understanding of anatomical tracts that carry information into the human visual cortex is incomplete as a result of methodological limitations on measuring connectivity [89]. Nevertheless, to the best of our knowledge there are more connections between the visual cortices and amodal/polymodal systems than direct connections between visual cortices and other sensory systems. At present, there is no evidence of projections from nonvisual sensory thalamic nuclei to visual cortices in primates, nor evidence of direct projections from early somatosensory cortices [90]. There are direct projections from A1 to V1 and V2 in the macaques. However, these are outnumbered by projections from amodal/polymodal areas [67,91]. Polymodal regions of the parietal, temporal and, to a lesser degree, frontal cortices project to various levels of the visual hierarchy [67,92–94]. For example, in macaques MT and V2 receive projections from parietal cortex, V4 from anterior portions of the inferior temporal lobe and the frontal eye fields, and V1 from polymodal superior temporal cortices [66,92,95–98].

We hypothesize that in blindness numerical and spatial information reaches the visual system from the parietal cortex. Dorsal stream visual areas (e.g., MT) are thus more likely to receive such information because they have stronger parietal connectivity [72,99]. Linguistic information could reach visual cortices either via temporal or frontal areas. For example, the VWFA in the occipitotemporal cortex has strong anatomical connectivity to retinotopic visual cortices on the one hand and frontotemporal language networks on the other, even prior to literacy [100]. In blindness, the VWFA could serve as a gateway for linguistic information to enter the visual system. In addition, superior temporal cortices could send linguistic information directly to retinotopic visual cortices [34,35]. Finally, prefrontal cortex is connected with occipital cortices by the fronto-occipital fasciculus in humans [101]. Furthermore, the arcuate fasciculus, which connects prefrontal and temporal language regions, reaches into posterior aspects of the temporal lobe in humans [102]. Failure to prune posterior branches of the arcuate in blindness could facilitate transfer of linguistic information to secondary 'visual' areas.

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uniquely determine the content of its software. Long-range connectivity plays a particularly important role in constraining function because it determines the range of networks that send information to a cortical circuit [13]. But ultimately, it is the information transmitted and not the wires themselves that cause specialization. As a result, it is possible for the occipital cortices to support visual perception in those who grow up with vision, and higher-order cognitive functions in those who grow up without sight. In the following sections, I begin by describing previous theories of cortical specialization that were motivated by studies of cross-modal plasticity. I then lay out evidence for the pluripotency hypothesis and end with some predictions.

Evidence for Functional Modification of Cortex from Cross-Modal Plasticity

The human brain has a characteristic structure to function mapping that is highly consistent across individuals. Cytoarchitecture and connectivity change across the cortical sheet in a systematic way across individuals and so does function [13]. Distinct networks support functions such as auditory pitch perception, visual localization, and linguistic processing. We can describe the function of any given cortical region in terms of its preferred sensory modality (e.g., visual, auditory, tactile, no preference) and its preferred cognitive domain (e.g., motion, shape, location, numerosity, language). A natural assumption based on the typically high consistency of this structure to function mapping is that structure and function are inextricably linked. Early investigations of blindness and deafness showed, however, that the preferred sensory modality that drives cortex can be changed by experience [3]. In blind, but not sighted participants multiple 'visual' areas, including V1, are highly active during Braille reading, less active during active touch with nonmeaningful tactile patterns and least during passive touch [4], and are active during sound localization [14].

These early studies of cross-modal plasticity loosened the link between structure and function but they did not break it. Since cross-modal plasticity was first discovered, the prevailing view has been that in blindness visual cortices take on sensory functions that are akin to vision, such as fine-grained tactile discrimination and auditory localization [4,14]. According to this view,

blindness changes the source of sensory input to visual cortices (from vision to touch and audition), but the cognitive function (e.g., shape recognition) performed by a given 'visual' area is preserved [15–19]. Blindness is said to unmask or strengthen input to visual cortices from nonvisual sensory thalamic nuclei (e.g., auditory medial geniculate nucleus), primary sensory cortices (e.g., A1), or top–down regions that convey sensory information (parietal cortex conveys somatosensory input to visual areas) [20,21]. The visual cortices then compute similar operations over this input as they would have done over input from the visual lateral geniculate nucleus. An influential formulation of this idea is the metamodal hypothesis according to which cortical regions have intrinsic modality-independent functions (e.g., shape processing, spatial localization) [17]. For example, the ventral occipitotemporal cortex is thought to be intrinsically predisposed to process shape and can do so based on input from vision (sighted), touch (blind), and even from sound through sensory substitution [16], so long as shape information is conveyed. While no specific anatomical mechanism is postulated, the metamodal account assumes that cognitive functions are 'built into' cortical areas, whereas modality preference is a product of input.

The metamodal hypothesis generated a stream of fruitful inquiry because it makes testable predictions: The cognitive functions assumed by visual cortices in blindness should be analogous to visual functions in the sighted and the functional specialization within visual cortices of blind individuals should follow that of the sighted. For example, visual regions that process shape in the sighted will continue to process shape in blindness, whereas those specialized for motion will continue to process motion. This prediction follows directly from the claim that areas have intrinsic cognitive roles but flexible modality preferences. A considerable number of studies are consistent with these predictions. Visual cortices of blind individuals are active during various vision-related tasks including tactile discrimination, auditory localization, and motion perception, and functional specialization resembles that of sighted adults [22–27]. Perhaps the most well-documented example is the middle temporal motion complex (MT). In sighted primates MT plays a key role in visual motion processing [28–30]. In blindness, MT responds preferentially to moving auditory and tactile stimuli [24,31,32]. Other examples of preservation include activation of the visual 'where' pathway when blind participants localize sounds, recruitment of the 'visual word form area' (VWFA) for Braille reading, and recognition of letters presented through auditory sensory substitution as well as activation of medial ventrolateral occipitotemporal cortex (i.e., the parahippocampal place area) when blind individuals hear names of places [23,27,33–37]. These studies are consistent with the idea that cortical areas have an intrinsic, albeit modality independent, cognitive function, which is preserved in cross-modal plasticity.

Evidence for Pluripotency: Higher-Cognitive Functions in Visual Cortices

An ever-growing body of evidence suggests, however, that much of the functional reorganization in the visual cortices of blind individuals does not preserve their underlying function. Retinotopic visual cortices of congenitally blind individuals are active during various language tasks. As noted above, visual cortices are involved in Braille reading, including reading words and sentences [3,4,11,12,38]. This could be because visual cortex is involved in fine-grained tactile discrimination of Braille dots [22]. However, visual cortices also respond to spoken language. Visual cortices are active when congenitally blind participants make semantic or phonological decisions about single words, generate semantically relevant verbs to heard nouns, and listen to spoken sentences [8,9,11,39,40]. Responses to spoken language are present in visual cortices of blind children by 4 years of age and are unrelated to Braille literacy [41]. Activity is observed within the pericalcarine cortex (the anatomical location of V1), as well as throughout the visual hierarchy, including in the lateral and ventral occipitotemporal cortices and medial extrastriate areas [7,8,42] (Figure 2). Although visual cortex responses to spoken language could be related to low-level auditory processing of speech, there is ample evidence

MT | LO | V3a | V3 | V2 | V1 | V4v | V8 | S > NW
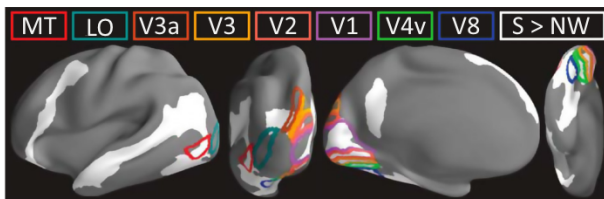
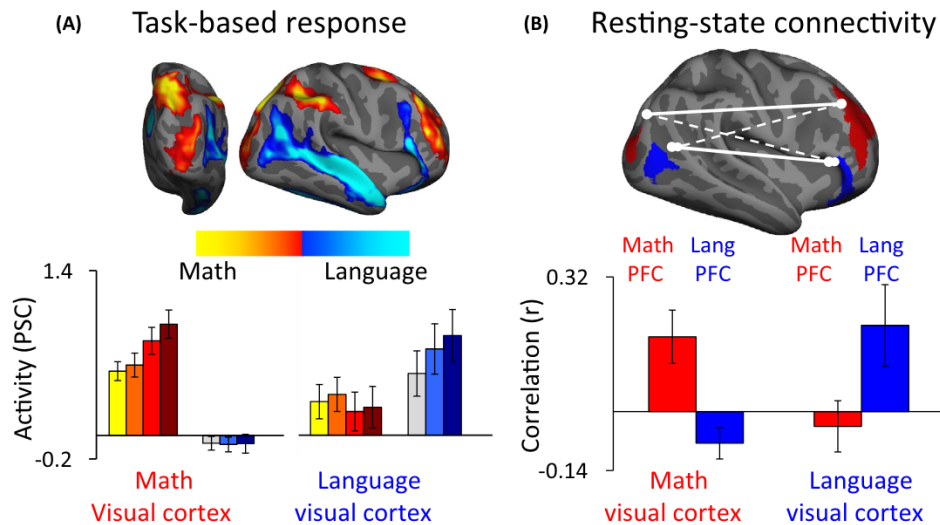**Trends in Cognitive Sciences**

Figure 2. Visual Cortex Activation during Auditory Sentence Comprehension in Blind Participants Relative to Functional Subdivision of Visual Cortex in the Sighted. Activity for sentences greater than working memory task with nonwords shown in white. Visuotopic maps displayed as outlines of different color [117]. Reprinted from [44].

that this is not the case. Visual cortices are active even when blind participants recall words from long-term memory, in the absence of any overt stimulation [43]. Crucially, responses to spoken language in visual cortices are modulated by the grammatical and semantic properties of linguistic stimuli. Activity is greater for stimuli that have meaning (i.e., larger for lists of words than for lists of nonwords) and grammatical structure (larger for sentences and Jabberwocky than for lists of words or nonwords) [7,8]. In this regard, the functional profile of visual areas mirrors the responses of classic language regions in frontotemporal cortices. Perhaps most remarkably, visual cortices are sensitive to subtle manipulations of grammatical structure. For two sentences with nearly identical meanings and words, the sentence that is more grammatically complex (i.e., has a syntactic movement dependency) produces larger responses [8,44]. This finding suggests, among other things, that visual cortex responses to language are not related to imagery, since the grammatically complex sentences are no more imageable. Among blind participants, those who show the largest visual cortex responses to grammatical complexity (complex > simple) also show superior performance at answering comprehension questions about the complex sentences [44]. None of the aforementioned effects are observed in visual cortices of blindfolded sighted controls. These findings demonstrate that information processed by visual cortex during language tasks is symbolic and abstract, rather than spatial or sensory.

One possibility is that language invades visual cortex because of some previously unrecognized functional homology between language and vision. Contrary to this idea, there is evidence that language is not the only higher-cognitive function that colonizes the visual cortices of blind individuals. Visual cortices are involved in memory tasks and the amount of activity is predictive of performance outside the scanner [43,45–47]. Furthermore, a subset of visual cortices is recruited for numerical processing [6]. Visual cortices of blind but not sighted individuals are active while solving auditory math equations and activity increases parametrically as the equations become more difficult. Crucially, visual cortex responses to number are anatomically separate from responses to language. Number-responsive regions are sensitive to math equation difficulty, but not to the grammatical complexity of sentences and the opposite pattern is observed in language-responsive regions (Figure 3A) [6,48]. These studies demonstrate that in blindness, multiple different higher-cognitive functions colonize visual cortices and there is regionalization within visual cortex along higher-cognitive dimensions (Figure 3).

Additional support for the idea that visual cortices are involved in higher-cognition comes from studies that measure spontaneous correlations of BOLD signal at rest. Many physiological factors affect such correlations, including vascular oscillations [49,50]. However, brain areas with strong anatomical connections and similar functions, such as the right and left motor cortices, have strongly correlated activity and these correlations can be used to carve the brain into functional networks [50]. In visual cortex, regions that are closer in retinotopic space have stronger resting-state correlations with each other, even in blindness [51–53]. However, in blind individuals visual cortices become functionally coupled with frontoparietal networks that are involved in language, executive control, and numerical processing, that is, correlations are higher than in sighted blindfolded controls [7,10,51,52,54–57]. By contrast, resting-state correlations between auditory cortex and visual cortex are actually reduced in blindness,

Figure 3. Higher-Cognitive Takeover of 'Visual' Cortices in Congenitally Blind Individuals. (A) Depiction of task-based activation in visual cortices in response to language and number tasks. Figure at the top left depicts a contrast map with larger responses during an auditory math task than an auditory sentence task in red and the reverse contrast in blue (thresholded at $P < 0.05$). Bottom left panel shows dissociation in selectivity of math and language-responsive regions of visual cortex in blind individuals. Progressively darker bars depict more complex stimuli in math (red colors) and language (blue colors) tasks. The math stimuli consisted of auditory-presented math equations that varied according to four levels of complexity, with the most complex equations having larger numbers and having the variable 'X' in the wrong location (e.g., $8-3 = X$ vs. $X - 22 = 14$). In the language experiment, sentences that were more grammatically complex contained a syntactic movement dependency (dark blue). The gray bar depicts activity for lists of meaningless nonwords. (B) Depiction of dissociations in functional connectivity among different regions of visual cortices. Math-responsive regions of visual cortex are preferentially correlated with math-responsive regions of prefrontal cortex, whereas language-responsive regions of visual cortex are preferentially correlated with inferior frontal language regions. Modified from [6]. Abbreviation: PFC, prefrontal cortex.

although engaging in auditory tasks induces coupling between auditory and visual networks [23,56,58]. Notably, studies using diffusion tensor imaging have failed to find any increase in 'anatomical' connectivity between visual cortex and the rest of the brain in blindness, finding reduced connectivity both among visual areas and between visual areas and the rest of the brain instead [59–62]. Thus, repurposing of visual cortex likely occurs primarily through change to the function of existing connections, rather than large-scale increases in long-range fibers. Recent evidence further suggests that functional specialization within visual cortex is related to functional connectivity. Activity of 'visual' number-responsive areas is correlated at rest with frontoparietal number areas, in blind but not sighted individuals. By contrast, language-responsive regions of visual cortex are correlated with prefrontal language regions [6,50]. In sum, resting-state studies suggest that visual cortices of blind individuals become coupled with multiple distinct higher-cognitive networks of frontoparietal cortices, including networks that support language, numerical cognition, and executive control.

There is also some evidence that visual cortices are functionally relevant to higher-cognitive behavior. Disrupting visual cortex activity with transcranial magnetic stimulation to the occipital pole interferes with blind individuals' ability to generate semantically appropriate verbs to heard nouns and participants make semantic rather than phonological errors [9]. Transcranial magnetic stimulation to visual cortex also interferes with Braille reading and abolishes repetition priming during Braille reading tasks [12,63]. Further work is clearly needed to fully understand the functional relevance of visual cortices to tasks such as sentence processing and solving math equations. However, the available evidence shows that in blindness visual cortices are functionally relevant to higher-cognitive behavior.

In sum, in blindness, cortical circuits that are thought to have evolved for visual perception come to participate in abstract and symbolic higher-cognitive functions, including language processing. Such plasticity is inconsistent with the idea that cortical areas have intrinsically set functions. Instead, this evidence suggests that during development a given cortical area is pluripotent: capable of assuming a heterogeneous range of cognitive roles, from low-level vision to sentence processing and mathematics. As Marr argued long ago, neural hardware and cognitive software are only loosely linked.

One could attempt to account for the fact that the same cortex can support what appear to be very different cognitive functions by appealing to cognitive similarity explanations. For example, by claiming that visual cortex participates in both sentence processing and vision because both syntax and visual scenes are hierarchical. However, an increasingly long list of such explanations is required to account for the various higher-cognitive functions found in visual cortices (e.g., number, memory). It is also difficult for such explanations to be general enough to capture the similarity between vision and syntax and yet specific enough to generate useful predictions about cortical function. A more parsimonious account of the findings appeals to the informational input received by the visual cortices during development. Visual cortices have abundant anatomical connectivity with higher-cognitive networks of frontal, parietal, and temporal cortices [64,65] (Box 1). Such connections outnumber direct projections from other sensory systems, such as primary auditory and somatosensory cortices [66,67]. In sighted individuals, these connections modulate visual processing based on attention, task goals, and conceptual information [68–70]. We hypothesize that in blindness, informational input from these higher-cognitive networks causes the visual cortices to take on higher-cognitive functions.

The hypothesis that function is determined by input naturally accounts not only for evidence of higher-cognitive plasticity in blindness but also for apparent preservation of function in visual cortices of blind individuals. Within this framework, elements of 'visual' function are preserved in plasticity when nonvisual input is from the same cognitive domain, as the visual input would have been. For example, MT retains its motion selectivity in blindness, not because it is hardwired to compute motion, but because it receives motion-relevant information in both sighted and blind individuals [71]. Whereas in sighted individuals this information comes from V1 and other retinotopic visual areas as well as from parietal circuits, in blind individuals the information comes from parietal cortex alone.

Predictions from Pluripotency Hypothesis

In addition to accounting for existing evidence, the input-based hypothesis makes concrete predictions about plasticity, in both blindness and other forms of experiential change. In the case of blindness, newly acquired functions of visual cortex should be predicted by patterns of connectivity. For example, dorsal parts of the visual stream, such as MT, are more likely to assume spatial and numerical functions associated with the parietal cortices because they receive large amounts of input from parietal areas involved in these functions [23,72,73]. Crucially, the pluripotency account predicts that even in cases where the functional signature of the 'plastic' region shares some features with the original visual function, the cognitive operations could be different across blind and sighted individuals, if the nature of the informational input during development is itself different. For example, in the sighted, MT receives low-level sensory input from primary visual cortices, whereas by hypothesis MT of blind individuals receives highly processed motion-related information from parietal cortices. If so, the contribution of MT to motion perception in blind individuals would be more higher order. The current account further predicts that other frontoparietally-mediated higher-cognitive functions, such as working memory or cognitive control, will also invade the visual system as a result of top–down connectivity from frontoparietal cortices to the visual system. In general, the current framework suggests that cognitive similarity to the 'canonical' function is the wrong metric for

predicting the new cognitive function of a cortical area in cases of plasticity. Rather, the relevant variable is the informational input.

The outlined framework also makes predictions regarding experience-based plasticity outside of human blindness. First, we hypothesize that takeover by higher-cognitive networks is a major form of reorganization in all forms of human sensory loss, including deafness, because in humans, early sensory regions have stronger anatomical connectivity with higher-cognitive networks than with other early sensory areas or sensory thalamic nuclei. Some recent studies of deafness are consistent with the idea of higher-cognitive takeover [74–76]. This does not rule out the possibility that some low-level sensory information reaches deprived sensory cortices and contributes to processing. The degree to which this is the case will depend on the precise connectivity pattern of that particular deprived area. However, according to the current framework, true cross-modal takeover, of one sensory area by another sensory function, comprises a small fraction of functional repurposing in human sensory loss. By contrast, in lower mammals, direct invasion of one sensory system by another should be more common because input to deprived regions is more likely to be sensory: there is less cortical territory devoted to higher-cognitive functions, sensory cortices are anatomically more proximal to each other, and altricial birth gives more opportunity for sensory experience to influence basic anatomical architecture [77,78].

Box 2. Relating Plasticity in Blindness to Cultural Learning and Training

Evidence from sensory loss provides complementary insights to evidence from studies of cultural learning and training. Learning to read causes the development of a letter and word-selective region within the ventral stream, known as the VWFA [103]. Across individuals, the VWFA is situated in a consistent location within the left fusiform gyrus, in the same general location as regions involved in visual object recognition, such as the fusiform face area [104]. Analogously, training juvenile monkeys to recognize different sets of shapes (i.e., written symbols, tetris shapes, and cartoon faces) results in patches of selectivity for the different shape types in consistent cortical locations across animals, independent of training order [105]. Studies of blindness and visual training are thus consistent in finding that anatomy constrains localization of function across individuals, even in plasticity [6,48]. Furthermore, evidence from blindness is consistent with theories of cultural learning that emphasize the role of connectivity and competing inputs in driving functional specialization [106]. For example, connectivity to frontotemporal language network in a subset of the ventral stream, prior to literacy, predicts the localization of the VWFA after learning [100]. According to one hypothesis, informational input from early visual cortices on the one hand and language networks on the other hand cause the VWFA to become involved in reading [106].

At the same time, studies of blindness reveal that the potential for functional change is broader than what one might have concluded based on studies of cultural learning and training alone. Learning to recognize visual characters and words is itself a subtype of visual object recognition, whereas blindness is a more dramatic experiential change. When the change in experience is more dramatic, as in the case of blindness, so too is the change in cortical function.

An influential metaphor for how culture repurposes previously evolved cortical regions for culturally constructed behaviors such as reading and formal mathematics is recycling [107]. Evidence from blindness suggests some important qualifications to this metaphor. Recycling presupposes that a cortical circuit has a function; one can recycle a milk carton into a birdfeeder but it is less clear what it would mean to recycle a rock or a flower, since they never had an intended function to begin with. The argument proposed in this article is that cortical areas do not have intrinsic functions, and therefore cannot be recycled. A key point to consider here is that the neural substrates of cultural behaviors, such as reading, are shaped not only by innate constraints but also by the preceding species' typical experiences. Unlike congenital blindness, learning to read takes place after children have substantial experience with visual object recognition and have acquired their native language. Plasticity in cultural learning is therefore a product not only of intrinsic predispositions of cortex and cultural experience but also the species typical experience that precedes the cultural experiences. Thus, to the extent that culture is recycling neural mechanisms, it is recycling not only the product of evolution but also the product of preceding species typical experiences. If we want to apply the recycling metaphor specifically to the products of evolution, it is the cognitive adaptations that are recycled, rather than cortical regions, since any given cognitive function, cultural or otherwise, is supported by a network of diverse areas. Reading can thus be said to recycle the cognitive mechanisms of visual object recognition and language. In neural terms, reading is recycling the putative adaptations that were instantiated in the human brain by evolution to support these functions.

The hypothesis that informational input determines the cognitive function of cortical regions implies that the function of any given cortical area will depend in part on the information processing capacities of the rest of the brain and on other, nondeprivation-related aspects of experience. Said differently, language invades the visual cortices in humans, not only because of connectivity, but also because language is behaviorally central to the species and thus has a lot of non-occipital cortical territory devoted to it. We might therefore predict that the sensory systems of visually or auditory deprived non-human primates assume functions that are ecologically relevant to that particular species. Furthermore, we would predict that in humans, other aspects of experience − unrelated to the sensory loss itself − would influence cortical repurposing. For example, in deaf-blind individuals the degree to which visual cortices assume language functions could depend on the degree to which that individual had access to manual sign language early in life. Culture and training (e.g., Braille) could also influence functional repurposing, but only if training-related input to the deprived region is stronger than other source of information (Box 2).

Finally, the pluripotency hypothesis predicts that takeover by competing cognitive functions is a pervasive phenomenon in human cortical development. Evidence from blindness illustrates how cognitive specialization of cortical areas during development results from a self-organizing process, where different inputs of information compete for cortical real estate, just as the left and right eyes compete for cells in V1 [79,80]. We therefore predict that in cases of social or linguistic deprivation in early life, networks that typically participate in social and linguistic processes are colonized by other cognitive functions, potentially impacting future behavioral capacity for social cognition and language.

Concluding Remarks

Having argued for the flexibility of cortex, it is worth ending by pointing out how the current proposal differs from historic ideas about equipotentiality. First, the degree to which cortical areas play drastically different cognitive roles within the same adult brain across contexts remains an important avenue of future inquiry. Indeed, studies of adult-onset blindness suggest

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Box 3. Cognitive Flexibility of Cortex in the Adult Brain

The current article focuses on cortical specialization during development and therefore all of the reported data in the main text are from individuals who are blind from birth. Can cortical circuits change their function even in adulthood (e.g., in adult-onset blindness)? If so, is it furthermore possible for a single cortical area to perform substantially different cognitive functions within the same individual, in different contexts (e.g., eyes open vs. blindfolded)? At present, the answer to this question remains uncertain. Even in sighted individuals visual cortices are engaged during tasks where no visual stimulus is present, such as imagery or deciding whether a school bus is more similar in color to butter or egg yolk [108]. What is less clear is whether visual cortices of late blind or blindfolded sighted individuals perform cognitive functions that are qualitatively different from vision. In support of this idea, responses to nonvisual information in visual cortices are observed in late blindness and even after 5 days of blindfolding [38,42,109–111], including during some linguistic tasks [38,42,112]. A recent study found increased functional connectivity between Broca's area and visual cortex in retinitis pigmentosa, a degenerative retinal disease that typically progresses to total blindness in adulthood [55].

At the same time, there is evidence that the functional potential of cortex is qualitatively different in adulthood. Functional connectivity changes in visual cortices differ among the late and congenitally blind ([52,113], but see [55]). Cross-modal responses are smaller and differentially localized in late blind as compared with congenitally blind adults [38,42,81,111,114]. Perhaps most relevantly, the cognitive role of cross-modal activation in late blindness also appears to be different (e.g., [82,113]). Visual cortices are functionally relevant to Braille reading in those who are congenitally but not late blind [115]. One study found that in late blind, but not congenitally blind individuals, activity in visual cortex is equally high during auditory sentence comprehension and a working memory task with noise. Furthermore, only in the late blind group activity peaks during the response portion of the trial [83]. These studies suggest that the cognitive role of visual cortices is different in congenitally and late blind individuals. At present, there is therefore little evidence for the idea that visual cortices take on higher-cognitive computations in adulthood. Nevertheless, only a handful of studies have examined this question and the full cognitive potential of adult cortex remains to be tested. Even if drastic cognitive repurposing occurs only during childhood, it is possible that pharmacological and brain stimulation techniques could be used to reopen critical periods and enable cognitive repurposing in the adult brain in cases of damage or disease [116].

Outstanding Questions

Can we predict the function of a cortical area based on connectivity and experience? Language and numerical processing are likely only a small subset of the functional profiles present in blind visual cortex. What are the other functions? One hypothesis is that due to frontoparietal connectivity with visual cortex, functions that are typically supported by frontoparietal networks, such as executive control and working memory, are also found in the visual system.

What information is represented in visual cortices of blind individuals and what is the spatial code of such representations? Although a large number of studies demonstrate activity in visual cortices during nonvisual tasks, comparatively few have used multivariate approaches to characterize the informational content of the representations. Within the general domains of language and number, what information is represented in visual cortices? A further interesting question is whether the spatial code for higher-cognitive information in visual cortices is different or more variable across people than the spatial code in the more typical frontoparietal and temporal lobe systems.

Do visual cortices of blind individuals have a unique computational role relative to other cortical circuits? Many previous studies show that subsets of visual cortex mirror activity in other networks, such as those involved in spatial localization and language. Do subsets of visual cortices also assume unique functional profiles that are not observed elsewhere in the brain? This could occur because of interaction between the intrinsic physiology of visual cortex and the information that it processes.

that the cognitive range of cortex becomes narrower in adulthood (Box 3) ([38,42], for review see [81–84]). Even when we restrict ourselves to development, the computational capacity of a cortical circuit is constrained by evolutionary predispositions. It is useful here to distinguish between the actual function that a cortical area assumes, as reflected in its selectivity profile, and the cortical area's computational capacity. The claim here is that the function a cortical area assumes depends on the informational input it receives during the self-organizing process of development and this function is therefore in a sense independent of what was 'intended' for the cortical circuit by evolution, except to the extent that evolution has constrained the informational input itself by modifying connectivity. The evolutionary influence on input can even be severed artificially by rewiring [85,86]. By contrast, a cortical region's cognitive computational capacity, that is, how well it performs the cognitive function it acquired during development and therefore its contribution to behavior, is influenced in part by variation in intrinsic physiology across the cortical sheet, including both long-range connectivity and microcircuitry [13]. The fact that visual cortices are behaviorally relevant to higher-cognitive functions suggests that even this computational capacity is cognitively heterogeneous and broad – perhaps because cortical areas are not generated *de novo* but are evolutionary modifications of other cortical regions [87]. Nevertheless, we do not expect computational capacity of cortex to be infinite (i.e., equipotential). Future studies of plasticity in blindness and deafness could uncover computational limitations of specific cortical areas and shed light on how physiology relates to function (see Outstanding Questions).

The pluripotency hypothesis is thus not inconsistent with the possibility that evolution modified the human brain specifically to enable abilities such as motion perception and language. But it did not do so by creating a collection of areas that by their very nature perform specific cognitive functions. The cognitive capacity of cortical areas at birth does not constitute a natural kind at the cognitive level of analysis. Cognitive functions such as language and motion perception are the software that is acquired by a given subset of wetware as a result of multiple intrinsic and extrinsic factors including microcircuitry, connectivity, the function of other neural networks, the history of activation before birth, and crucially developmental experience.

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