EVIDENCE FOR EXTREME CORTICAL FLEXIBILITY: HIGHER COGNITIVE FUNCTIONS IN "VISUAL" CORTICES OF BLIND INDIVIDUALS

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Abstract

Are structure and function inextricably linked in the brain? In the early 19th century, phrenologists endeavored to localize cognition to areas of the brain. Though neuroscientists have updated the methodology and the notion of what constitutes a mental process, the goal remains the same: to map functions to locations. But how flexible are these structure-to-function mappings? Studying adaptations of the “visual” cortex to blindness offers insight on the extent to which brain structures can carry out functions for which they did not evolve.

In this dissertation, I ask how flexible visual cortices are in the absence of expected visual information. I examine the ability of blind individuals’ occipital cortices to take on functions that are higher cognitive and, therefore, radically different from vision. First, Chapter 2 explores the extent of higher cognitive takeover of “visual” cortices in blindness. Using naturalistic stimuli, I find that “visual” cortices of blind individuals synchronize to a shared interpretive, rather than a shared perceptual, experience. This suggests systematic and widespread repurposing of “visual” cortices for higher-cognitive functions. Next, Chapter 3 asks whether “visual” cortices of blind individuals are repurposed for higher cognitive functions other than language, and executive functions in particular. I find evidence for executive functions in primarily right-lateralized “visual” cortices using both a non-verbal response-inhibition task and by examining functional connectivity at rest. Finally, Chapter 4 examines the functional relevance of previously observed language and executive function responses in the “visual” cortices of blind individuals. I find that blind individuals are better than matched sighted controls at comprehending syntactically complex sentences and at inhibiting prepotent button pressing. This suggests that repurposed "visual" cortices may confer a behavioral advantage.

Taken together, this dissertation demonstrates that "visual" cortices of blind individuals are meaningfully repurposed for higher cognitive functions. Though brain structures may seem particularly suited to implement a particular function, such structure-to-function mappings are not evidence of functional rigidity. In contrast, evidence from blindness suggests that human cortex is highly flexible at birth.

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Chapter 1

Introduction

1.1 Blindness as a model for understanding cortical flexibility

The brain appears to be governed by a tight mapping between its structures and the functions that they implement. Across individuals, specific cognitive functions are implemented in consistent cortical locations. At the macroscopic level, for example, language processing is supported by a left-lateralized fronto-temporal network, and visual information is processed in the posterior cortex along the calcarine fissure. At the microscopic level, neurons in the calcarine fissure are organized according to a retinotopic map such that adjacent cortical regions represent adjacent regions in the visual field. These structure-to-function mappings are believed to arise because the intrinsic anatomy of each network in the brain determines its cognitive role. Each cortical location has a distinctive cyto-architecture and profile of inter-regional connectivity. Such a systematic relationship between structure and function seems to suggest that intrinsic physiology tightly constrains each cortical region to implement particular cognitive operations.

Since individuals each have unique experiences, the brain needs some functional flexibility. For example, symbolic math is specific to a subset of cultures. The Piraha are an Amazonian tribe whose language has no words for representing exact quantities (e.g. "seven" fish; Gordon 2004; Frank et al. 2008). Similarly, not all people learn to read. The relatively recent emergence, and rapid proliferation, of reading suggests that brain structures that support reading have not evolved specifically for such functionality. In both of these cases, brain regions exhibit adaptations for the unexpected experiences. Symbolic math comes to be represented in brain regions that support approximate number representations (Dehaene et al. 2004; Cantlon et al. 2006; Nieder and Dehaene 2009; Piazza:2007il Prado et al. 2011). Orthography takes over a portion of the left fusiform gyrus that previously supported visual discrimination of faces (Dehaene et al. 2015). These brain regions are said to be "recycled" to support the functions required as a result of cultural learning (Dehaene and Cohen 2007). For example, in the fusiform gyrus, cortical tissue that supports facial feature recognition becomes repurposed for grapheme recognition. These examples demonstrate that brain structures allow for some leniency in the environmental input that drives functional specialization. However, in both of these cases, the evolutionarily predisposed operation of the brain region (i.e. visual contour discrimination in the fusiform gyrus) are plausibly at least partially preserved (Dehaene and Cohen 2011).

How does the brain reorganize when the changes to experience are more substantial? Though individuals encounter different types of visual information throughout their lifetimes, exposure to visual information is a ubiquitous experience. However, not in cases of congenital blindness. Studies of sensory loss, such as in blindness and in deafness, provide a rare opportunity to test just how tightly brain structures constrain cognitive functions. These studies suggest that more dramatic changes in experience lead to correspondingly more dramatic functional reorganization of the brain.

Across most people, neurons posterior to the lateral occipital gyrus process visual information and neurons in the transverse gyrus process auditory information. Across mammals, homologous brain regions perform auditory and visual functions similar to those performed in humans and thus suggestive of an evolved structure-to-function mapping. In fact, the occipital cortices and the transverse temporal gyrus are so functionally invariant that they are colloquially referred to by their function—i.e., as the visual and auditory cortices, respectively. Notably, "visual" cortices of blind individuals and "auditory" cortices of deaf individuals change their response properties. In blindness, retinotopic "visual" cortices respond to auditory and tactile stimuli (Wanet-Defalque et al. 1988; Uhl et al. 1991; Sadato et al. 1996). In deafness, "auditory" cortices respond to visual and tactile stimuli (Levänen et al. 1998; Finney et al. 2001). These brain structures can, therefore, effectively adapt to the absence of expected sensory experience.

A key outstanding question is, what functions do these repurposed areas perform and how similar are they to the typical sensory function? The goal of this dissertation is to investigate the mechanism of occipital cortex reorganization in blindness as a window into how human cortical areas acquire their functions.

In the rest of this chapter (Chapter 1), I review previous evidence for "visual" cortex plasticity in blindness. This evidence raises questions about the mechanisms of functional reorganization of visual cortex in blindness and the extent to which deafferented sensory cortices truly change their function even in cases of sensory loss (Bavelier and Neville

2002; Amedi et al. 2017; Bedny 2017). A prominent hypothesis is that “visual” cortices continue to perform vision-like functions, even in cases of cross-modal plasticity, but instead over input from audition and touch. Alternatively, functional repurposing of “visual” cortices may be much more extreme. This dissertation will test the hypothesis that “visual” cortices of blind individuals are repurposed for higher-cognitive functions. In Chapter 2 I use naturalistic stimuli to determine the extent to which “visual” cortices of blind individuals exhibit systematic repurposing. Because naturalistic stimuli contain both sensory and higher cognitive information, they also allow one to broadly distinguish sensory and higher cognitive functions in the “visual” cortices. In Chapter 3, I test for the presence of a non-verbal higher cognitive function, specifically executive functions, in “visual” cortices. Finally, in Chapter 4, I ask whether the extra “visual” cortex representation of higher cognitive functions confers a behavioral benefit to blind individuals. I compare performance of blind and age- and education matched sighted controls on sentence comprehension, working memory, and an executive function task.

1.2 Meta-modal brain structures: sensory functions in “visual” cortices

Early studies in sensory deprivation suggested takeover of available cortices by remaining sensory modalities. “Visual” cortices of visually deprived animals come to respond to auditory information, while “auditory” cortices of auditory deprived animals come to respond to visual and somatosensory information (Rebillard et al. 1977; Heil et al.

1991; Yaka et al. 2000; Meredith and Lomber 2011). With the advent of neuroimaging, researchers could examine such “cross-modal” plasticity in humans. Similar to non-human animals, “visual” cortices of blind individuals are active during tactile and auditory tasks, while “auditory” cortices of deaf individuals were observed active during visual and tactile tasks (Wanet-Defalque et al. 1988; Uhl et al. 1991; Sadato et al. 1996). In blindness, “visual” cortices respond during echolocation (Thaler et al. 2011), tactile vibrations (Burton et al. 2004; 2010), tactile space discrimination (Sadato et al. 1996; Merabet et al. 2004; Amedi et al. 2007; Stilla et al. 2008), auditory localization (Wanet-Defalque et al. 1988; Kujala et al. 1992; Weeks et al. 2000; Collignon et al. 2011), and both auditory and tactile motion perception (Poirier et al. 2006; Ricciardi et al. 2007; Wolbers et al. 2011). For example, “the “visual” cortices of blind individuals are active when they are asked to touch a raised dot display with their index finger and determine whether the central dot is right or left offset (Stilla et al. 2008).

One interpretation of these findings is that, in instances of plasticity, sensory cortices preserve their underlying cognitive operation but change the sensory modality over which they operate. For example, in blind individuals, retinotopic areas typically involved in fine-grained spatial discriminations for visual information respond to fine-grained spatial discriminations for tactile information (Sadato et al. 1996; Merabet et al. 2004; Sathian and Stilla 2010). Analogously, in deaf individuals, auditory areas that typically discern auditory rhythm become responsive to rhythmic sequences of light (Bola et al. 2017). Cortical structures are, therefore, “meta-modal” (Pascual-Leone and Hamilton 2001). Though this hypothesis suggested greater functional pliancy to brain structures than had previously been considered, it preserved the notion that each brain region is constrained to implement a specific cognitive function.

Support for the meta-modal hypothesis came from numerous studies in blindness demonstrating cross-modal responses in “visual” cortices. Because visual cortices of sighted individuals contain distinct sub-regions of functional specialization, the meta-modal hypothesis predicted that these loci of functional specialization would be maintained in in blindness. In sighted individuals, the middle temporal area (MT) processes visual motion. In blind individuals, MT is active when participants are asked to discern the direction of a moving sound or a moving tactile dot pattern (Poirier et al. 2006; Ricciardi et al. 2007). Similarly, in blind individuals, dorsal occipital areas that typically localize visual information respond to tasks of auditory localization (Wanet-Defalque et al. 1988; Kujala et al. 1992; Weeks et al. 2000), and more so than they respond to non-spatial auditory tasks such as pitch discrimination (Collignon et al. 2011).

While motion and location representations in “visual” cortices suggest preservation of the dorsal “where” pathway in blindness, representations of identity in “visual” cortices suggest a preserved ventral "what” pathway (Mishkin et al. 1983). In blind individuals, “visual” cortices activate for both tactile and auditory-encoded letters, peaking precisely in the area that shows sensitivity for visual word forms in sighted individuals (i.e., the VWFA) (Uhl et al. 1991; Sadato et al. 1996; Reich et al. 2011; Striem-Amit et al. 2012). Similarly, an area that typically processes visual number form in sighted individuals (i.e., the VNFA) is preferentially active when blind individuals are asked to discern a sound-encoded roman numeral (i.e. V = 5), rather than when they are asked to discern the sound-encoded letter (i.e. “v”) or sound-encoded color of the exact same stimulus. In blind individuals, ventro-temporal regions that are selective for either visual faces, body parts, scenes, or objects in sighted individuals (Kanwisher 2010) show preserved selectivity for such category knowledge conveyed through audition or touch (Pietrini et al. 2004; Mahon et al. 2009; He et al. 2013; van den Hurk et al. 2017). For example, in blindness, the fusiform face area (FFA), a region typically sensitive to visual facial features, is more active to sounds of a person laughing or whistling (face) than to sounds of crashing waves (scenes), fans (objects), or footsteps (body parts) (van den Hurk et al. 2017).

Consistent with the meta-modal hypothesis, these findings suggest that “visual” cortices of blind individuals continue to perform vision-like functions, but over input from audition and touch. Brain structures are, therefore, built for particular cognitive functions but adaptive for the modality of information. Accordingly, repurposed cortices preserve intra- regional connectivity patterns (Striem-Amit et al. 2015; 2016), but inter-regional connections must change to route auditory and tactile information to “visual” cortices. This can occur via increased afferent connections to “visual” cortices from the thalamus, from poly-modal association cortices, or directly from other primary sensory cortices (i.e. A1) (Bavelier and Neville 2002). In blind mole rats, the inferior colliculus, a midbrain structure that primarily relays auditory information to auditory cortices, increases its projections to the visual system (Doron and Wollberg 1994). However, in blind humans there is no evidence of additional anatomical tracts to “visual” cortices and thalamic tracts to “visual” cortices are, if anything, atrophied (Shimony et al. 2005; Shu, Li, et al. 2009; Shu, Liu, et al. 2009).

1.3 Pluripotent brain structures: higher cognitive functions in "visual" cortices

A growing body of evidence suggests that some of the functional repurposing of visual cortex is far more extreme. In blindness, retinotopic regions of "visual" cortex come to respond to language (Burton et al. 2002; Bedny et al. 2011). In blind, but not sighted, participants "visual" areas show sensitivity to semantic and syntactic information, respond more to words than meaningless sounds, more to sentences than unconnected lists of words, and more to grammatically complex than grammatically simple sentences (Röder et al. 2002; Burton et al. 2003; Bedny et al. 2011; Lane et al. 2015). Repurposing from vision to language is striking in light of the cognitive differences between these domains. Since language and vision are cognitively and evolutionarily distinct, these observations challenge the idea that cortical areas have fixed functions, even meta-modal ones.

Further evidence comes from higher cognitive domains other than language. Dorsal retinotopic "visual" areas are active when congenitally blind individuals solve spoken math equations (e.g. 17-4=X), more so than when blind participants listen to non-mathematical sentences, and the amount of activity scales with equation difficulty (Kanjlia et al. 2016). These math-responsive "visual" regions are differentially localized from sentence-responsive regions within occipital cortices. "Visual" cortices of blind individuals are also active during verbal memory tasks, such as retrieving previously encoded words from long-term memory or retrieving an associated verb from an auditory presented noun (Amedi et al. 2003; Raz et al. 2005). Importantly, one such verbal memory task elicited “visual” cortex activity in the absence of any auditory or tactile stimuli, as participants were asked to covertly recall previously learned words (Amedi et al. 2003). Analogously, in deaf individuals, “auditory” cortices respond to visuo-spatial working memory demands (Ding et al. 2015)

Evidence from functional connectivity analyses also suggests higher cognitive takeover of “visual” cortices. In the absence of an explicit task, synchrony between occipital cortices and frontal-parietal cortices is increased in blindness (Liu et al. 2007; Bedny et al. 2010; 2011; Wang et al. 2013; Burton et al. 2014; Deen et al. 2015; Liu et al. 2017). Moreover, resting-state synchrony between occipital cortices and primary sensory and motor cortices (i.e. A1, S1, and M1) is reduced in blind, relative to sighted, individuals (Liu et al. 2007; Yu et al. 2008; Wang et al. 2013; Burton et al. 2014).

These findings suggest that rather than being “meta-modal” the human cortex is pluripotent— i.e. capable of taking on a wide range of functions (Bedny 2017). According to the pluripotency hypothesis, the microcircuitry of a given cortical area does not limit it to performing a particular cognitive operation. Rather, a brain area’s cognitive function is heavily influenced by the information that it receives during development. This information, in turn, is jointly determined by long-range anatomical connectivity and experience.

In the case of the “visual” cortex of blind individuals, the top two sources of anatomical projection come from the visual (lateral geniculate) nucleus of the thalamus and from top-down higher cognitive systems (Tong 2003). Tracer studies in non-human primates provide evidence for frontal, parietal, and temporal afferents to visual cortices (Maunsell and Van Essen 1983; Selemon and Goldman-Rakic 1988; Felleman and Van Essen 1991; Ungerleider et al. 1998; Falchier et al. 2002; Rockland and Ojima 2003; Beer et al. 2011; Ungerleider et al. 2008; Martino et al. 2010; Anderson et al. 2011; Yeterian et al. 2012). The visual cortices receive comparatively fewer projections from non-visual thalamic nuclei or from other primary sensory systems— e.g. auditory and somatosensory (Falchier et al. 2002). As a result, when input from the lateral geniculate nucleus is removed in blindness, "visual" cortices are colonized by higher cognitive rather than lower-level sensory areas.

In summary, the pluripotency hypothesis suggests that early in development, cortical areas are capable of differentiating into structures that support diverse types of functional specialization. In particular, it predicts that "visual" cortices of blind individuals, will perform higher cognitive functions as a result of colonization by extensive fronto-parietal anatomical projections.

1.4 Overview of Chapter 2: Widespread systematic repurposing of "visual" cortices for higher cognitive functions

Despite, or perhaps because of, the plethora of evidence for visual cortex plasticity, central questions remain. While it seems clear that "visual" cortices of blind individuals do not lay fallow, the functions for which they are colonized remain disputed. One possibility is that the diverse functional findings represent variability in repurposing of "visual" cortices across unique cases of blindness. Alternatively, “visual” cortices may be systematically repurposed for similar functions across individuals. Evidence for different functional signatures may exist because unique sub-regions of “visual” cortices are repurposed for different functions. If so, can these functions be broadly characterized according to either the meta-modal or pluripotency hypotheses?

These questions are difficult to answer with a typical fMRI design which tests for the presence of one or two specific cognitive processes. Therefore, Chapter 2 takes a different tack to studying functional plasticity in blindness. Blind and sighted participants listened to auditory movies and a comedy routine while undergoing fMRI. Naturalistic stimuli are a model-free method to assess the functional profile of cortical areas. Richly engaging stimuli allow brain responses to fluctuate according to many simultaneous, but independently, varying features. Rather than correlate brains to a model of a particular cognitive process, brain responses were assessed by correlating the timecourse of each brain area in one individual to the timecourse of the same brain area in all other individuals. This allowed me to determine the extent of systematic repurposing of “visual” cortices across unique cases of blindness. Moreover, because synchronization across individuals only occurs if the stimulus contains content that is meaningful to that brain area, I varied the level of higher cognitive content to determine the extent to which higher-cognitive, as opposed to sensory auditory, functions are present in the blind “visual” cortices. I find that “visual” cortices of blind individuals synchronize for higher, but not lower, cognitive content. This suggests systematic repurposing of “visual” cortices for higher cognitive functions.

1.5 Overview of Chapter 3: Executive function responses in “visual” cortices

An interesting finding from Chapter 2 is extensive bilateral synchronization of “visual” cortices for higher cognitive functions. Thus far, language, which is predominantly left-lateralized in both fronto-temporal and “visual” cortices, is the most reliably found higher cognitive function in “visual” cortices. An open question is, therefore, whether there exist cognitive functions in “visual” cortices that are not verbally mediated.

In Chapter 2, the bilateral synchronization of “visual” cortices is mirrored by bilateral synchronization of fronto-temporal cortices. This synchronization symmetry provides a possible hint. If left “visual” cortices are colonized by left fronto-temporal cortices, the same may be true of right “visual” cortices. This suggestion is consistent with the pluripotency hypothesis that “visual” cortices take on higher-cognitive functions because of intrinsic functional flexibility of local visual cortex circuits and top-down fronto-parietal afferents. If the pluripotency hypothesis is correct, I would expect that aside from language, other non-verbal higher-cognitive functions that typically depend on fronto-parietal networks also invade the “visual” cortices in blindness. Moreover, because anatomical connectivity is stronger within a hemisphere than across hemispheres, I would expect higher cognitive takeover in “visual” cortices to occur from the fronto-parietal network specific to each hemisphere—i.e. such that left hemisphere fronto-parietal networks colonize left “visual” cortices and right hemisphere fronto-parietal networks colonize right “visual” cortices.

Chapter Two tests the hypothesis that non-verbal higher-cognitive functions invade the visual system. Congenitally blind and sighted participants performed an auditory go/no-go task, with non-verbal sounds, while undergoing fMRI. I also collected resting state data. In the go/no-go task, participants either made a quick button press (for “go” sounds, 75%) or withheld a button press (for “no-go” sounds, 25%). Go trials included two sub-types: frequent (50%) and infrequent (25%). Right-hemisphere fronto-parietal cortices of both groups responded most to no-go trials, followed by infrequent-go, and finally by frequent-go. Sensorimotor cortices of both groups responded most to go trials.

Crucially, I find that right-lateralized occipital cortices of blind, but not sighted, individuals mirror the executive-function pattern observed in fronto-parietal systems. In resting state data, these executive function-responsive occipital cortices also increase in functional connectivity to prefrontal executive function areas and decrease in functional connectivity to sensorimotor areas in blind, relative to sighted, individuals.

These data provide evidence that language is not the only higher-cognitive function assumed by “visual” cortices in blindness and, therefore, cannot be a special case of meta-modality. Executive function responses in “visual” cortices of blind individuals support the fronto-parietal takeover hypothesis of plasticity in blindness.

1.6 Overview of Chapter 4: Behavioral relevance of higher cognitive functions in “visual” cortices

If human cortices are highly adaptable to experience, one would predict that repurposed cortices are functionally relevant to behavior. However, up until now, no studies have tested the impact of “visual” cortex plasticity on high-level linguistic performance (e.g. sentence processing) or response-inhibition. It is an open question whether responses to language processing and response-inhibition in the “visual” cortices are functionally relevant and, if so, whether they confer any behavioral benefit.

In Chapter 4, I test the hypothesis that “visual” cortex plasticity for language and executive function improves sentence comprehension and response-inhibition, respectively, in blindness. Age and education-matched blind and sighted participants answered yes/no comprehension questions on spoken sentences that varied in syntactic complexity. Syntactic complexity was manipulated in two independent ways, by introducing syntactic movement and creating garden paths. Congenitally blind individuals are more accurate and faster than the sighted controls. This advantage is more pronounced for syntactically complex garden-path sentences. Using the same go/no-go task from Chapter 3, I also find evidence that blind individuals outperform sighted individuals on measures of response-inhibition.

Additionally, I assessed the relationship between each of the higher cognitive tasks. Sentence comprehension ability was not predicted by individual differences in working memory or response-inhibition. Verbal working memory span was weakly predictive of response inhibition in the blind group only.

These data provide evidence that congenital blindness confers a specific advantage to sentence processing and response-inhibition, and that these advantages are distinct. Though these findings cannot directly attribute “visual” cortex repurposing to the observed behavioral advantage, they suggest that “visual” cortices of blind individuals may be deftly integrated into pre-existing brain networks to provide extra processing power to the individual.

1.7 Summary

Blindness is a model for understanding functional specialization within the human brain. The dramatically different experience of blind individuals provide insight into the malleability of normally observed structure-to-function mappings in the brain. This dissertation tests for maximal pliancy, i.e. higher cognitive functions in the “visual” cortices of blind individuals. In Chapter 2, I ask whether “visual” cortices of blind individuals are extensively and systematically repurposed for higher cognitive functions. In Chapter 3, I ask whether “visual” cortices are also repurposed for non-verbal higher cognitive functions, specifically executive function. In Chapter 4, I ask whether observed higher cognitive responses in “visual” cortices confer a behavioral advantage to blind individuals. In the work presented here, I find evidence for large-scale verbal and non-verbal higher cognitive repurposing of “visual” cortices in blindness. Blind individuals also outperform sighted individuals at the higher cognitive tasks for which “visual” cortices are repurposed. This dissertation shows that the intrinsic physiology of brain structures does not result in functional rigidity. Rather, intrinsic physiology provides an advantageous mechanism whereby brain structures are radically flexible to take on novel functions as needed by the individual.

Chapter 2

Widespread systematic repurposing of “visual” cortices for higher cognitive functions

2.1 Introduction

Can brain structures meaningfully adapt to carry out functions for which they did not evolve? Studying the “visual” cortices in cases of congenital blindness offers unique insight into this question. In blindness, typically “visual” cortices activate in response to non-visual stimuli (Wanet-Defalque et al. 1988; Sadato et al. 1996; Bavelier and Neville 2002). “Visual” cortices of blind individuals respond during auditory and tactile tasks such as motion detection, shape discrimination, sound localization, and echolocation (Uhl et al. 1991; Weeks et al. 2000; Merabet et al. 2004; Gougoux et al. 2005; Poirier et al. 2006; Stilla et al. 2008; Collignon et al. 2011; Thaler et al. 2011; Wolbers et al. 2011). “Visual” cortices are also active during higher cognitive tasks with auditory and tactile stimuli, including Braille reading, auditory sentence comprehension, and solving auditorily presented equations (Sadato et al. 1996; Bedny et al. 2011; Kanjlia et al. 2016). Non-visual responses in “visual” cortices demonstrate that a sensory brain region can adapt the modality over which it operates.

Important questions remain, however, regarding the mechanism and extent of functional repurposing in “visual” cortices of blind individuals. First, what should one make of the extensive range of cognitive tasks that have been associated with “visual” cortex responses in blindness? One possibility is that, when a cortical area is not able to perform its evolutionarily predisposed function, cognitive specialization is haphazard across individuals. As such, the cognitive function assumed by a given part of “visual” cortices will vary widely across blind individuals. Alternatively, a given “visual” cortical area may assume a similar function across blind individuals but different parts of the visual system assume different functions. Second, how topographically extensive is “visual” cortex repurposing in blindness? Because reported activation is typically circumscribed to particular sub-regions within the “visual” cortices, the spatial extent of the repurposing is unknown. Third, are “visual” cortices of blind individuals deployed during everyday cognitive operations in naturalistic contexts? Experimental paradigms use stimuli that are unlike what is encountered in daily life. Often they are more cognitively taxing. For example, a study that found language responses in “visual” cortices used sentences with syntactic movement over long dependencies—e.g. “The actress that the creator of the gritty HBO crime series admires often improvises her lines” (Lane et al. 2015). Such complex sentences are rarely encountered in conversation and are made even more difficult to parse due to removal of prosodic cues. Indeed, there is evidence that natural language tends to minimize dependency length (Gildea and Temperley 2010). Therefore, “visual” cortices may come online only during unusually demanding cognitive tasks, i.e. as an “overflow” processor.

The goal of the current study was to use naturalistic stimuli to inform these questions, as they overcome some of the limitations of traditional experimental designs. Movies and narrated stories offer a kind of “kitchen sink” of cognitive processes that vary simultaneously, and to some extent independently, from one another. Rather than correlating a participant’s voxel timecourse to a hypothesized model of every possible cognitive process, functional activity is assessed by comparing timecourses across participants. The participant’s voxel timecourse is correlated to that same voxel timecourse in other individuals (Hasson, Nir et al., 2004). Therefore, inter-subject correlations driven by rich stimuli allow one to test broadly, and without pre-specification, for shared functionality across individuals. We can assess how much of the “visual” cortices respond similarly across blind individuals. Moreover, because this functionality is observed under naturalistic conditions, it can inform the extent to which neural circuits are recruited during everyday tasks. In prior work, naturalistic stimuli have been used to show shared brain responses across people (Hasson, Nir et al., 2004; Hasson et al. 2010).

Inter-subject synchronization also provides a different angle on an important puzzle within the plasticity literature: what types of cognitive functions are assumed by the “visual” cortices? While high inter-subject synchronization suggests shared functionality, the level of content required to drive such synchronization can give some clue as to which function is shared. Synchronization of a particular brain area across individuals occurs only if the stimulus contains content that is meaningful to that area (Hasson, Nir et al., 2004; Hasson et al. 2008). For example, pre-frontal language areas synchronize to naturalistic speech and movies but not to meaningless sounds (e.g. backward speech) or distorted versions of the same naturalistic speech (Lerner et al. 2011; Naci et al. 2016). In contrast, primary auditory cortices synchronize comparably to all auditory stimuli (Lerner et al. 2011; Naci et al. 2016). Analogously, for visually presented stimuli in sighted individuals, V1 and other low-level visual areas synchronize equally well by intact movies and movies that have been cut into short segments and scrambled in time (Hasson et al. 2008; Naci et al. 2016). Based on this observation, it has been proposed that cortical areas can be described as having a particular place within a hierarchy based on the temporal structure of the stimuli by which they are synchronized. Higher-order cognitive, but not low-level sensory areas, require structure over long segments of time to be synchronized (Hasson et al. 2008).

It is an open question whether the place of “visual” cortex within this temporal hierarchy is related to its genetically prespecified cytoarchitecture or whether it is instead malleable by experience. Do “visual” cortices preserve their place in the cortical hierarchy across blind and sighted individuals? Alternatively, do “visual” cortices move up in the cortical hierarchy, behaving more like amodal higher-cognitive areas?

To shed light on these questions, the current study presented naturalistic auditory stimuli to congenitally blind participants and sighted controls while undergoing fMRI. Congenitally blind and blindfolded sighted individuals listened to four intact naturalistic stimuli: three movies (visuals removed) and one stand-up comedy routine. Participants also listened to two stimuli non-intact stimuli: the same comedic routine played backward, i.e., with no discernible language, and a shuffled version of the comedic routine that preserved sentences but lacked a coherent plotline. This designed enabled me to determine the degree and spatial extent to which “visual” cortices assume a similar temporal profile across different blind individuals, whether “visual” cortices are deployed under naturalistic conditions, and how such synchronization compares to synchrony during auditory stimuli that are meaningless or have reduced or absent structure over long timescales (e.g. shuffled lists of sentences or backwards speech).

2.2 Materials and Methods

Participants.

18 congenitally blind (6 male; 13 right-handed, 2 ambidextrous; age: mean=41.87 SD=16.41; years of education: mean =16.72, SD=2.52) and 18 sighted controls (3 male; 16 right-handed; age: mean=41.23, SD=13.19; years of education: mean =18.39, SD=4.26) contributed data to the current experiment. Blind and sighted participants were matched on average age and education level (age: t(34)=0.13, p>0.5; education: t(34)=1.43, p=0.16). All blind participants self-reported minimal-to-no light perception since birth, i.e. never able to distinguish colors, shapes, or motion. Participants had no known neurological disorders, head injuries, or brain damage. For all blind participants, the causes of blindness excluded pathology posterior to the optic chiasm (see Table 1 for details). All participants gave written consent under a protocol approved by the Institutional Review Board of Johns Hopkins University. 5 additional sighted and 3 additional blind individuals participated in the experiment but were dropped from analyses due to performance (see below). 1 additional blind participant was dropped from analyses because of subsequently reported

temporary vision during childhood. Reported statistics refer only to participants included in analyses.

Blindness Etiology	**N**	**N LP**
Leber Congenital Amaurosis	7	6
Retinopathy of Prematurity	5	2
Optic Nerve Hypoplasia	3	1
Retinitis Pigmentosa	1	1
Unknown	2	1

Table 1. Blindness Etiology for Chapter 2 Participants

Per cause of blindness, total N(umber) of participants and N(umber) with light perception (LP).

Stimuli and procedure.

Participants listened to 4 intact and 2 scrambled entertainment clips while blindfolded and undergoing functional magnetic resonance imaging. Intact stimuli were excerpted from movies (Brian De Palma’s Blow Out, Pierre Morel’s Taken, and James Wan’s The Conjuring) and a comedic narration (Jim O’Grady’s Pie-Man). To enable a shared interpretive experience across participants, I chose intact clips to be suspenseful, entertaining, and easy to follow. Non-intact stimuli were generated from the intact Pie-Man stimulus. Backward was time-reversed to lack intelligible speech; sentence-shuffle was spliced from intact, permuted sentences to lack a coherent plotline. To construct the sentence-shuffle stimulus, individual sentences were clipped to make the shortest possible stand-alone sentence. Compound sentences were divided into each of its standalone components, sometimes beginning with the word “and.” This resulted in 96 sentences (length: mean= 4.37 s, SD=3.43 s) that were randomly reordered such that newly adjoining sentences had an original distance of at least 4 sentences between them. I also collected a rest run in which no stimulus was presented and participants were told to relax but not to fall asleep.

Before each auditory clip (and scan), participants were read a 2-3 sentence contextualizing prologue to facilitate interpretation of the clip. After the entire scan-session, participants were given an expected multiple-choice comprehension test for each intact clip. There were five questions per clip and the questions probed detailed information, e.g. names of characters, locations of events, and critical plot points. All stimulus data was excluded from participants who did not correctly answer at least 3 out of 5 questions for at least 3 (out of 4) intact runs. Additionally, for each intact clip, participant data was excluded if the participant failed the comprehension assessment for that particular clip or if the participant reported having previously seen the movie from which that particular clip was taken. Analyses thus included 15-18 participants per stimulus, per vision group. (See Supplementary Table 1 for total number of participants, age, and education information for each stimulus.) For each stimulus, blind and sighted participants were statistically equivalent with respect to age and years of education.

Each auditory clip was preceded by 5 s of rest and followed by 20-22 seconds of rest. I subsequently discarded the first 20 seconds and last 18 seconds of each functional scan to remove scans with rest and the auditory stimulus onset (accounting for the hemodynamic lag). The duration of each stimulus, not counting the rest periods before and after the clip, were as follows: Rest (7.4 min.), Backward, Sentence-Shuffle, and Pie-Man

(6.8 min.), The Conjuring (5.1 min), Taken (5 min.), and Blow Out (6.5 min.). Presentation order of the six stimuli were counterbalanced across participants, with blind and sighted participants yoked to receive the same orderings. In addition to the comprehension questions, I also asked 3 questions to probe participants' subjective experience. Each participant rated each intact clip on suspense, entertainment, and following ease according to a 5-point Likert scale. (Mean rating for each movie, by vision group, is also available in Supplementary Table 2.)

Auditory stimuli were presented over Sensimetrics MRI-compatible earphones at the maximum comfortable volume for each participant. To ensure that participants could hear the lower sounds in the auditory clips over the scanner noise, a relatively low sound was played to participants during acquisition of the anatomical image; all participants indicated hearing the sound via button press.

MRI data acquisition and cortical surface analysis.

MRI structural and functional data of the whole brain were collected on a 3 Tesla Phillips scanner. T1-weighted structural images were collected in 150 axial slices with 1 mm isotropic voxels using a magnetisation-prepared rapid gradient-echo (MP RAGE). T2*-weighted functional images were collected in 36 axial slices with 2.4 x 2.4 x 3 mm voxels and 2 s TR. Data analyses were performed using FSL, Freesurfer, the HCP workbench, and custom software (Dale et al., 1999; Smith et al., 2004; Glasser et al., 2013).

Preprocessing.

Functional data were motion corrected, slice-time corrected, and registered to the participant’s anatomical image using FSL’s FEAT. Nuisance covariates were regressed out of the timeseries of all gray matter voxels. For ISC analysis, this consisted of a linear trend and any motion spikes (i.e., timepoints with a root mean squared framewise-displacement greater than 1.75 mm). As a result, motion spikes were set to the run-mean (number per run: sighted: mean=0.23, SD=0.58; blind: mean=0.64, SD=0.88; t(34)=1.65, p=0.11). Resulting time-series residuals were high pass filtered with a 128 s cutoff, resampled to a common cortical surface (discarding subcortical structures and the cerebellum), and dilated and eroded by 2.5 mm to fill small holes. Data was smoothed with a 12 mm FWHM Gaussian kernel for whole-brain analyses. Analysis used a mix of HCP Workbench and Freesurfer tools. For auditory stimuli, timepoints before and after stimulus presentation were trimmed (as explained above). Finally, timecourse values were divided by the global grey-matter mean and multiplied by 10,000.

Inter-subject whole-cortex correlation (ISC).

I first asked whether comparable anatomical locations perform a consistent function across different individuals. For each vertex in the brain, I assessed the extent of stimulus-driven synchronization (i.e. correlation) to that same vertex in other people’s brains. Synchrony of brain activity was determined within and across vision groups— i.e., each congenitally blinds individual’s brains to the mean of all other congenitally blind individuals, each sighted individual to the mean of all other sighted individuals, congenitally blind individuals to the sighted mean, and sighted individuals to the congenitally blind mean. For each run, I calculated vertex-wise synchrony as the average pearson product-moment correlation coefficient (r) between each subject's timecourse and the average of the reference group (Hasson, Nir et al., 2004; Lerner et al. 2011). For example, the blind group's ISC value at vertex 99 was calculated by correlating the timecourse of blind participant 1's vertex 99 to the mean timecourse in the blind group (without participant 1) of vertex 99, repeating for all blind participants, and then averaging ISC values across blind participants. For the "across vision group" ISC, I correlated each blind subject to the average of all sighted subjects and each sighted subject to the average of all blind subjects, and then averaged all the individual subject maps. For all three groups comparisons (i.e. blind to blind, sighted to sighted, across vision group), averaged r-value ISC maps were transformed to Fisher's z-values (i.e. arctanh(r)) to enable comparisons of correlations across different stimuli/groups. Differences in synchronization between stimuli and/or between groups were compared by subtracting the relevant z-maps (i.e. blind > sighted = blind – sighted). A mean "movie" synchronization map was created by averaging z-maps of the 3 intact movie stimuli—i.e., conjuring, taken, blow out. Resulting z-maps were subsequently back-transformed to r-maps (i.e. tanhz(r)).

Because ISC maps violate several assumptions of parametric hypothesis testing, I performed a non-parametric, permutation analysis to assess the statistical significance of the inter-subject correlations. First, within group ISC maps (i.e. blind-to-blind) are not independent because each participants is present in all other participant's correlation maps—i.e., in a hypothetical 2 participant blind group, participant 1 is correlated to the leave-one-out blind group (i.e. participant 2) and participant 2 is correlated to the leave-one-out blind group (i.e. participant 1), resulting in the same ISC value for both participants. Therefore, the sample standard deviation is uninformative and all ISC results do not make use of standard error calculations. Secondly, timecourse datapoints are not independent from each other (usually dealt with by pre-whitening in a standard fMRI GLM analysis).

Therefore, to assess statistical significance of the ISC maps, I generated a null distribution via permutation of the original data. Preprocessed timecourse-values were phase-randomized to generate null correlations amongst participants. Timecourses were shuffled independently for all participants. Importantly, each timecourse preserved its original power spectrum in order to mirror empirical dependence between timepoints (Lerner et al. 2011; Regev et al. 2013). ISC values, for all stimuli and comparisons, were calculated on these permuted timecourses, as in the regular analysis. A null distribution, for each stimulus and comparison, was obtained by repeating the procedure 1000 times.

To correct for multiple comparisons across the cortex, only the largest ISC value across all brain vertices, in each of the 1000 permutations, contributed to the null distribution. I rejected the null hypothesis for a particular comparison if the real data’s ISC value was in the upper 5% of all 1,000 values in each null distribution. The statistical test is, therefore, one tailed. R-value criteria for examined contrasts varied from 0.10 – 0.20. Differences in criteria reflect different variances for each of the null sampling distributions, likely due to differences in degrees of freedom amongst the stimuli (e.g., number of timepoints) and between groups (e.g., number of participants), as well as the computation performed (e.g. the "movies > backward" comparison subtracts movie ISC values from backward ISC values and, therefore, sums the variances of both the movies and backward distributions). Since the sighted group's ISC criteria were a bit higher than the blind group's ISC criteria, I thresholded all sighted ISC figures with the blind group's criteria to more conservatively test our hypothesis that the sighted group's visual cortices will not synchronize for any stimuli. Results were qualitatively the same as those obtained by using the sighted group's own criteria.

The correction for multiple comparisons was very conservative, as there is a 5% probability of rejecting one or more true nulls in each 64,000 vertex family of statistical tests. Therefore, for contrasts between groups (i.e. blind ISC > sighted ISC for the backward stimulus) and for contrasts between conditions that are likely to be more similar (i.e. pie-man > sentence-shuffle), I used a cluster correction. Rather than form a null-distribution from the highest vertex-wise ISC value in each permutation, I first generated an uncorrected criterion (of $p < 0.001$) by taking the r-value higher than 99.9% of all the vertices and averaging this value across all permutations. Phase-randomized ISC maps were thresholded at this criterion, and assessed for maximum cluster size. For each of the 1000 permutations, a maximum whole-cortex cluster was obtained (for each stimulus and comparison). The size of the maximum ISC clusters thus from a null distribution of cluster size. Cluster-correction criteria at $p < 0.001$ were, likewise, set as the cluster-size larger than 99.9% of all other clusters. Real-data ISC maps were cluster-corrected by first thresholding each vertex at the uncorrected $p < 0.001$ criterion and then thresholding clusters at the cluster threshold of $p < 0.001$. Criteria for reported contrasts ranged from 9.92 -16.64 mm.

Inter-subject correlation (ISC) ROI analysis.

I interrogated inter-subject correlation (ISC) values in select ROIs of interest. I used a primary visual cortex (V1) ROI from a previously published anatomical surface-based atlas (PALS-B12 visuotopic; (Van Essen 2005)). I defined an early auditory cortex ROI as the transverse temporal portion of a gyral based atlas (Morosan et al. 2001; Desikan et al. 2006). For brevity, the early auditory cortex ROI will be abbreviated to A1, although it may not be strictly limited to primary auditory cortices. A higher-cognitive bilateral superior temporal gyrus (STG) ROI was taken from parcels that have previously been observed to be responsive to high-level linguistic content in sighted subjects (Fedorenko et al. 2010).

ROI analyses were performed on unsmoothed functional data. For each participant, a timecourse was obtained for each ROI by averaging across all vertices present in the bilateral ROI. From here, ISC analysis proceeded as in the whole brain analysis. For each ROI, each participant’s ROI timecourse was correlated to the average ROI timecourse of all participants in the leave-one-out group (for within vision group analysis) or to the whole group (for across vision group analysis).

All statistics for factor comparisons (i.e. ROI, group, and/or conditions) were obtained by subtraction of the relevant z-transform-r ISC values. For example, within A1 sighted group: backward ISC vs. rest ISC = A1 sighted backward z-transformed-r ISC -

A1 sighted rest z-transformed-r ISC. Fisher's z-transformed-r ISC values were subsequently transformed back to r (correlation coefficient) values.

Statistical significance of ROIs was assessed as in the whole-brain analysis. Timecourse data was permuted 1,000 times to generate a null distribution. Critically, for ROI analysis, I permuted the ROI timecourse after aggregating across vertices. This generates a realistic timecourse signal that accounts for the lack of independence amongst spatially proximal vertices. Using these null ROI timecourses, analysis proceeded as in the empirical ROI ISC analysis. As in the empirical ROI analysis, statistics for all factor comparisons were generated by subtracting the relevant ISC-ROI values from the permuted timecourse. Doing so over all permutations resulted in a null distribution for each statistic. Reported probabilities were calculated relative to that statistic's null distribution (formed by performing the relevant subtractions over null distribution values for each component). Probabilities reflect the proportion of null values whose magnitude is greater than, or equal to, the empirically observed value. ROI tests for statistical significance are thus two-tailed. Empirical values are considered significantly different from the null hypothesis if $p < 0.05$.

2.3 Results

High inter-subject correlation in the "visual" cortices of blind individuals for cognitively complex stimuli

I first used whole-cortex inter-subject correlation analysis to compare synchrony across blind and sighted groups, and across intact and shuffled stimuli. Among both sighted and blind groups, significant inter-subject synchronizations for the auditory backward stimulus were observed only in the transverse temporal gyrus (Figure 1, $p < 0.05$ vertex-wise corrected). By contrast, auditory movies evoked significant additional inter-subject synchronization across the superior temporal gyrus/sulcus, angular gyrus, precuneus, inferior frontal gyrus/sulcus, and the middle frontal junction (Figure 1, $p < 0.05$ vertex-wise corrected). For both blind and sighted groups, a direct comparison of the movies and backward stimuli revealed significantly more synchronization for movies along the superior temporal gyrus/sulcus and precuneus (Figure 1, $p < 0.05$, vertex-wise corrected). Similar but weaker results were obtained for pie-man compared to backwards (Supplementary Figure 2, $p < 0.001$, cluster-corrected). The sentence-shuffle condition produced an intermediate pattern between movies/pie-man and backwards speech (Supplementary Figure 2).

Within the blind, but not the sighted group, there was significant inter-subject synchronization in the occipital cortices for the movie stimuli, bilaterally on medial, lateral, and ventral occipital cortices and absent only on the posterior occipital cortices (Figure 1, $p < 0.05$ vertex-wise corrected). By contrast, the backwards stimulus did not significantly drive synchronization within the occipital cortices of blind individuals (Figure 1, $p < 0.05$ vertex-wise corrected). A direct comparison revealed higher inter-subject synchronization for movies than for the backward stimulus within the primary visual cortices of the blind group (Figure 1, $p < 0.05$ vertex-wise corrected). Overall, 65.04% of occipital cortices (PALS-B12 Lobes parcel; Van Essen 2005) were significantly synchronized across blind participants during movie listening. Across each of the 4 intact stimuli, blind participants reliably synchronized the same sub-regions of their “visual” cortices (see Supplementary Figure 1).

Directly comparing synchronization within the blind group to synchronization within the sighted group, I observed a small cluster within the right lateral occipital surface to the backward stimulus (Figure 1, $p < 0.001$ cluster-corrected). By comparison, the movie stimuli drove higher synchronization in the blind group, than in the sighted group, extensively across the occipital cortices (Figure 1; $p < 0.001$ cluster-corrected). An interaction contrast (blind > sighted x movies > backward) revealed areas along the lateral, medial, and ventral occipital cortices in which a greater increase in synchronization for movies, compared to the backward stimulus, was observed within the blind group, than within the sighted group (Figure 1, $p < 0.001$ cluster-corrected; for pie-man and sentence-shuffle results see Supplementary Figure 2.)

For completeness, I also correlated brain activity between blind and sighted groups directly. Non-occipital cortices were synchronized similarly across groups as they were within groups (Supplementary Figure 3; $p < 0.05$ vertex-wise corrected). Additionally, I observed synchronization across vision groups bilaterally along the calcarine sulcus. The degree of synchrony in V1 was lower across vision groups than within the blind group.

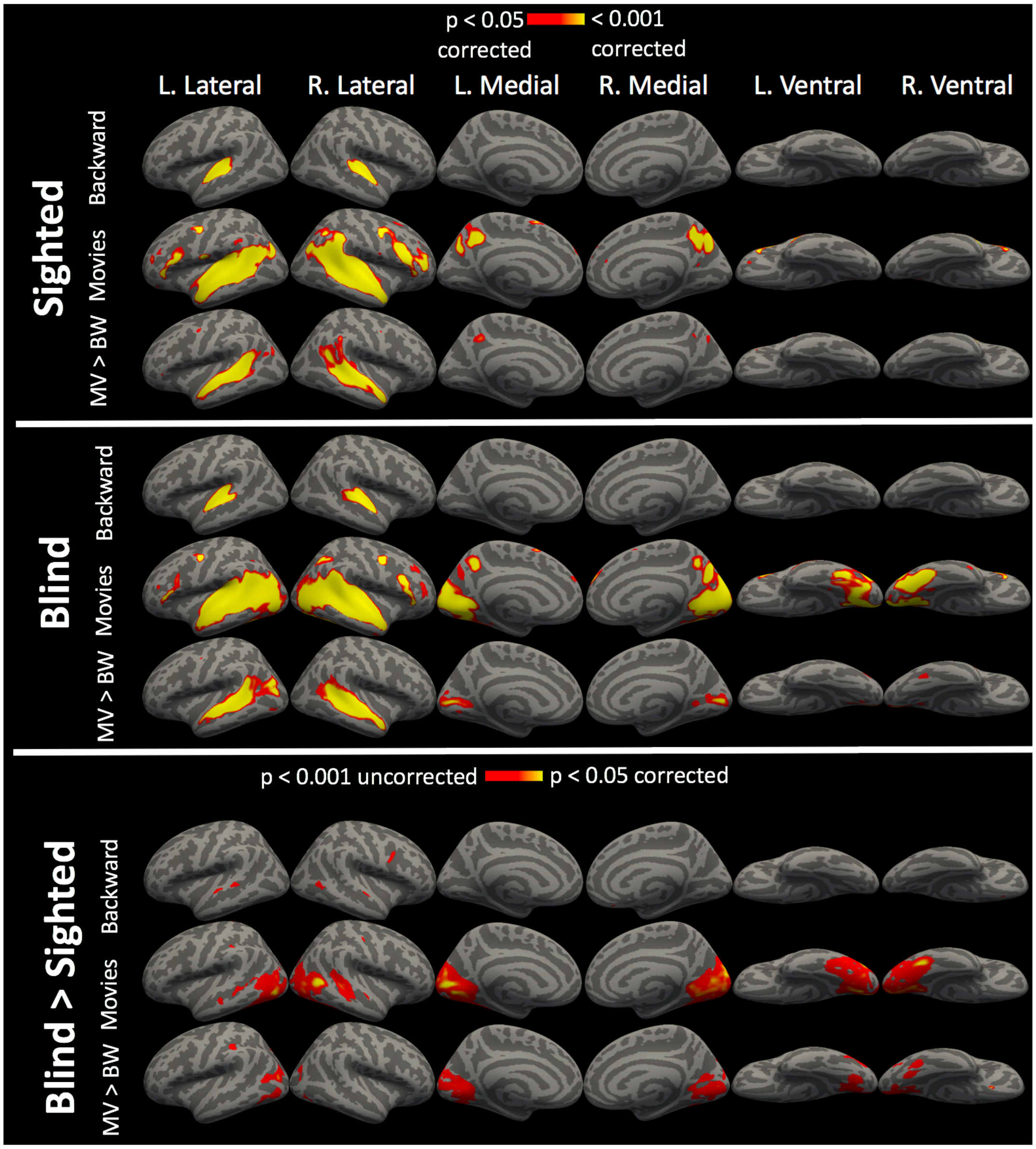


Figure 1. Inter-Subject Correlations

Inter-subject correlations (ISC) for the backward stimulus, all movie stimuli, and for the comparison of movie greater than backward (MV > BW). Synchronization is shown within the sighted group and within the blind group, vertex-wise corrected for multiple comparison. A comparison of blind group synchronization greater than sighted group synchronization (Blind > Sighted) is also shown, cluster-corrected for multiple comparison (at $p < 0.001$).

Across stimulus types, the inter-subject correlation profile of V1 in blindness resembles that of higher-cognitive but not early auditory networks.

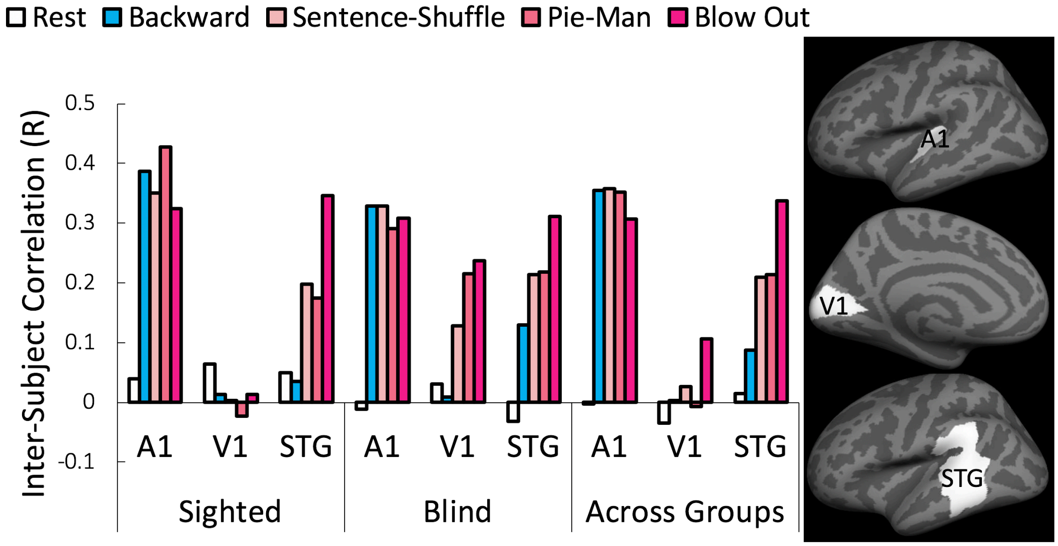


Figure 2. Inter-Subject Correlations within Regions of Interest

Inter-subject correlations (ISCs) of the sighted group, blind group, and across vision groups. ISCs are shown for select conditions within early auditory cortices, primary visual cortices, and the superior temporal gyrus. ROIs are displayed in the left hemisphere, but inter-subject correlations are assessed bilaterally.

I conducted a region of interest analysis to more closely compare the inter-subject synchronization profile of primary visual cortex (V1) to that of a low-level auditory area, early auditory cortex (A1), and to a higher-cognitive area, the superior temporal gyrus (STG). I compared synchronization of these ROIs across stimulus types and vision groups (Figure 2).

In early auditory cortex of the sighted group, all stimuli—including movies, pie-man, sentence-shuffle, and backwards speech—drove high inter-subject synchronization

(Figure 2 and Supplementary Figure 4; sighted A1: backward vs. rest, r=0.35, p<0.001; sentence-shuffle vs. rest, r=0.31, p<0.001; pie-man vs. rest, r=0.39, p<0.001, movies vs. rest, r=0.47, p<0.001). By contrast, the STG of the sighted showed high levels of synchrony only for the cognitively complex stimuli, and not for backwards speech (Figure 2, sighted STG: backward vs. rest, r=0.01, p>0.5; pie-man + blow vs. rest, r=0.22, p<0.001; pie-man + blow out vs. backward, r=0.23, p<0.001).

A similar pattern was observed in A1 and STG of the blind group. First, I asked whether A1 of the blind group, like A1 of the sighted group, showed levels of synchrony for backwards speech comparable to that of the cognitively complex stimuli—i.e., pie-man and blow out. This was indeed the case (Figure 2, blind A1: pie-man + blow out vs. backward, r=0.03, p=0.36). The STG of the blind group did synchronize to the backward stimulus, but, consistent with the STG of the sighted group, synchronized most for the cognitively complex stimuli (Figure 2, blind STG: backward vs. rest, r=0.16, p=0.001; pie-man + blow out vs. rest, r=0.29, p<0.001; pie-man + blow out vs. backward, r=0.14, p<0.001; group (sighted vs. blind) x condition (pie-man + blow out vs. backward) interaction, r=0.09, p=0.09).

Notably, among the movie stimuli, two (i.e., taken and conjuring) were observed to have higher inter-subject correlations than backwards speech even in A1. This difference in A1 synchronization between the stimuli is possibly due to greater variation in low level auditory features such as frequency and amplitude (Supplementary Figure 4; sighted A1: taken vs. backwards, r=0.18, p<0.001; conjuring vs. backwards, r=0.31, p<0.001). In STG, these two movies also had higher inter-subject correlations than the other two intact stimuli (pie-man and conjuring), suggesting that they may have also contained greater variation in cognitively complex features (Supplementary Figure 4; sighted STG: taken vs. pie-man, r=0.30, p<0.001; taken vs. blow out, r=0.13, p=0.03; conjuring vs. pie-man, r=0.30, p<0.001; conjuring vs. blow out, r=0.13, p=0.02). However, in order to ensure that differences across stimuli (movies vs. scrambled and backwards) were driven by higher-cognitive rather than low-level auditory differences, I focused analyses of V1 on the cognitively complex stimuli that showed comparable levels of synchrony to backward speech in early auditory cortex (A1) of sighted individuals, i.e. the pie-man and blowout movie (Figure 2; sighted A1: pie-man vs. backward, r=0.05, p=0.2; blow out vs. backward, r=0.07, p>0.5; pie-man + blow out vs backward, r=0.01, p>0.5). ROI ISC data for all of the stimuli are presented in Supplementary Figure 4).

Within the sighted group, V1 failed to synchronize for both backward or intact stimuli (Figure 2, sighted V1: backward vs. rest, r=0.05, p=0.31; pie-man + blow out vs. rest, r=0.07, p=0.1; pie-man + blow out vs. backward, r=0.02, p>0.5). By contrast, within the blind group, V1 synchronized for intact stimuli (blind V1: pie-man + blow out vs. rest, r=0.20, p<0.001;). V1 of the blind group did not synchronize for the backward speech stimulus, and direct comparison of the two types of stimuli showed significantly higher synchronization for the intact stimuli than for the backward stimulus (Figure 2, blind V1: backward vs. rest, r=0.02, p>0.5; pie-man + blow out vs. backward, r=0.22, p<0.001). Comparing synchrony of V1 to the other ROIs across stimuli in the blind group, I found that the inter-subject synchronization profile of V1 was similar to STG and different from A1 (blind: condition (pie-man + blow out vs. backward) x ROI (V1 vs. STG) interaction, r=0.08, p=0.17; condition (pie-man + blow out vs backward) x ROI (V1 vs. A1) interaction: r=0.25, p<0.001).

Next I directly compared V1 synchrony within the blind group to V1 synchrony within the sighted group. V1 of the blind group demonstrated significantly higher synchronization than V1 of the sighted group, but only for the intact stimuli (Figure 2, V1 blind vs. sighted: backward, r = 0.00, p>0.5; pie-man + blow out, r = 0.23, p<0.001). Moreover, the blind, but not the sighted, group showed a significant effect of cognitive complexity on synchronization (Figure 2, V1: group (blind vs. sighted) x condition (pie-man + blow out vs. backward) interaction r=0.24, p<0.001).

Finally, as in the whole brain analysis, I assessed common functionality across vision groups by directly correlated sighted individuals to the blind groups, and vice-versa. I found similar levels of synchrony in A1 and STG across, as within, groups (Figure 2 and Supplementary Figure 4; across group A1: backward vs. rest, r=0.36, p<0.001; sentence-shuffle vs. rest, r=0.36, p<0.001; pie-man vs. rest, r=0.35, p<0.001, movies vs. rest, r=0.47, p<0.001; STG: backward vs. rest, r=0.07, p=0.02; sentence-shuffle vs. rest, r=0.19, p<0.001; pie-man vs. rest, r=0.20, p<0.001, movies vs. rest, r=0.41, p<0.001; A1 movies: across group vs. blind group, r =0.03, p=0.19; across group vs. sighted group: r=0.04, p=0.13; STG movies: across group vs. blind group, r =0.004, p>0.5; across group vs. sighted group: r=0.002, p>0.5). In V1 I observed low but significant levels of correlation between the blind and sighted subjects for the 3 movies, but not for the other intact stimulus, pie-man (Figure 2 and Supplementary Figure 4; across group V1: backward vs. rest, r=0.04, p=0.27; sentence-shuffle vs. rest, r=0.06, p=0.07; pie-man vs. rest, r=0.03, p=0.4, movies > rest, r=0.17, p<0.001). Overall, synchrony in V1 for the movie stimuli was lower across vision groups than within the blind group (Supplementary Figure 4, across group vs. blind group: movies, r =0.16, p <0.001) and higher than within the sighted group (Supplementary Figure 4, across group vs. sighted group: movies, r =0.06, p =0.03). Unlike V1 synchronization within the blind group, V1 synchronization across vision groups did not systematically increase with increasing cognitive complexity of the stimuli (Figure 2; across group V1: pie-man + blow-out vs. backward, r=0.05, p=0.10). The effect of cognitive complexity on V1 synchronization was significantly smaller in the across group correlation than in the blind group and no different from that within the sighted group (V1: group (blind vs. across group) x condition (pie-man + blow out vs. backward) interaction r=0.17, p=0.001; group (sighted vs. across group) x condition (pie-man + blow out vs. backward) interaction r=0.07, p=0.2).

2.4 Discussion

“Visual” cortices of blind individuals synchronize to each other during naturalistic listening to movies and a comedic routine. Auditory movies drove collective responding in 65% of the “visual” cortices, by surface area. This was in contrast to the lack of synchrony observed in the visual cortices of the sighted group. In the blind group, synchronization of “visual” cortices was observed bilaterally, and spanned both retinotopic and higher order areas on the lateral, medial, and ventral surfaces of the occipital lobe. This is a lower, rather than an upper, bound to the topographical extent of “visual” cortex repurposing since failure to synchronize could occur because the naturalistic stimuli used in the current study did not contain relevant cognitive content for some subset of "visual" cortices. The current findings are consistent with the idea that in blindness, most of the available cortical tissue undergoes systematic adaptation and appears to be used during everyday tasks.

A key observation is that naturalistic stimuli (with a temporally extended plot) synchronize "visual" cortices of blind individuals more than stimuli that lack a plot. Like fronto-temporal cortices, but unlike early auditory cortices, synchronization of "visual" cortices increased parametrically with the cognitive complexity of the driving audio clip. In other words, like fronto-temporal cortices and unlike early auditory cortices, "visual" cortices did not synchronize while blind individuals listened to a nonsense backward auditory stream. For shuffled sentences, I observed an intermediate, but much lower, level of synchronization than for movies. This was similar to the intermediate, but much lower, level of synchrony for scrambled sentences in fronto-temporal cortices of both blind and sighted groups. In contrast, synchronization of early auditory cortices was similar for higher cognitive and low level auditory content. In sum, "visual" cortices of blind individuals, like fronto-temporal cortices of both groups, synchronized to a shared higher cognitive experience, rather than to a shared sensory experience.

Previous work has used the observations of varying levels of synchrony across stimuli of different cognitive complexity to characterize the "temporal response window" of different cortical networks (Hasson et al. 2008; Lerner et al. 2011). According to this framework, cortical networks differ according to the length of the temporal window over which the integrate information. Higher cognitive areas integrate information over longer time windows and therefore synchronize only for stimuli that have structure at this long timescale. By contrast, low-level sensory areas, including early visual cortices, integrate information only over short time windows. As a result, structure at longer time scales has no effect on the levels of synchrony in these early sensory areas (Hasson et al. 2008). Here I find that, in blind individuals, "visual" cortices exhibit a long temporal response window that is comparable to that of higher-order cognitive areas; longer even than a single sentence. These results demonstrate that the temporal response window of a cortical area is not related to its intrinsic physiology, but rather to the type of information over which it operates.

This observation that repurposed "visual" cortices assume a role that is higher in the cognitive hierarchy is consistent with the pluripotency hypothesis (Bedny 2017). Previous studies have found that "visual" cortices of blind individuals activate in response to language (Bedny, Pascual-Leone et al., 2011; Lane, Kanjlia, et al., 2015; Röder, Stock, et al., 2002) and to memory recall (Amedi et al. 2003; Raz et al. 2005). For example, the "visual" cortices of blind individuals respond more to sentences than to lists of unrelated words and more to sentences with complex syntax than sentences with simple syntax (Röder et al. 2002; Bedny et al. 2011; Lane et al. 2015). "Visual" cortices are also active when blind individuals are asked to generate an associated verb to a presented noun, when naming words from a previously memorized list, and when manipulating items in short term memory (Amedi et al. 2003; Park et al. 2011). I hypothesize that the present naturalistic stimuli engaged some of these cognitive processes. Following a plot-line engages such cognitive processes as language comprehension, recall of past information, and selective attention and inhibition. The "visual" cortices of blind individuals may, similarly, participate in such processes. The present results add to the existing literature of higher cognitive processes in “visual” cortices of blind individuals. They suggest that take-over by higher-cognitive fronto-parietal networks is extensive and robust.

I also observed some hints of non-visual information reaching visual cortices even in the sighted group. When blind and sighted data were directly correlated with each other, I observed synchrony between foveal V1 of the sighted group and foveal V1 of the blind group. The degree of this synchrony was low, relative to what was observed among individuals who are blind and the levels of synchronization did not vary across stimuli according to any discernible type of content. For example, across-group synchronization was highest for conjuring and taken, but very low for pie-man.

What drove such synchrony among the sighted and blind in the current study? One possibility is that the sighted group shows a smaller version of the pattern observed in the blind group. In other words, foveal V1 of sighted individuals may also receive strong top-down input from higher-cognitive systems, but to a lesser and more restricted extent than in the blind group. However, as noted above, synchrony among blind and sighted individuals was not consistent across stimulus types. Previous findings of non-visual responses in the “visual” cortices of sighted individuals also suggest that they occur under partially different conditions than those observed in people who are blind (e.g. only for some tactile tasks or only after short periods of blindfolding; Sathian et al. 1997; Zangaladze et al. 1999; Facchini and Aglioti 2003; Sathian 2005; Merabet et al. 2008; Voss et al. 2016).

An alternative possibility is that V1 synchrony across groups is driven by different features of the stimuli in the sighted and the blind. This could occur because low-level and higher-cognitive content is partially confounded in naturalistic stimuli. For example, suspenseful and important plot points are often cued by loud noises. It is therefore possible that V1 of the sighted group has marginal synchronization for low-level auditory content, and synchronization between groups is a consequence of confounded auditory and higher cognitive content in the driving stimuli. In future studies it will be important to understand what type of non-visual information reaches visual cortices in the sighted and in what ways it is similar to what occurs in people who are blind.

Irrespective of the source of such between-group synchrony, its existence nevertheless suggests that non-visual information is reaching occipital cortices even in the sighted, albeit to a lesser degree. This observation is consistent with a number of previous findings showing activity in visual cortex of sighted subjects during non-visual tasks. For example, visual cortex activity has been observed in sighted subjects during vivid visual imagery (Sathian et al. 1997; Zangaladze et al. 1999; James et al. 2002; Merabet et al. 2004; 2008). These results support the idea that there are pathways for non-visual information to reach occipital cortices in both sighted and blind individuals. However, blindness modifies the function of these pathways and what “visual” cortex does with this incoming information.

A key open question to be resolved concerns the behavioral relevance of “visual” cortices to cognition in blindness. Prior studies show that transiently disrupting “visual” cortex function with transcranial magnetic stimulation (TMS) can disrupt performance. For example, TMS to the occipital pole causes subjects to make semantic errors when generating verbs nouns heard nouns and to misread Braille letters (Cohen et al. 1997; Amedi et al. 2004). Such evidence suggests that activity in the “visual” cortices of blind individuals is relevant to behavior. However, the behavioral relevance of “visual” cortices to other higher-cognitive functions (e.g. sentence comprehension) and to everyday naturalistic tasks remains an open question.

2.5 Summary

In Chapter 2, I used naturalistic stimuli to ask whether the “visual” cortices are repurposed systematically across congenitally blind individuals and, if so, for what kinds of functions. Richly engaging stimuli allow brain responses to fluctuate according to many simultaneous, but independently, varying features. Here, I harnessed this free-form complexity to test broadly for both higher cognitive and lower sensory responses. I found that, across blind individuals, naturalistic movie listening drove similar activity in "visual" cortices. Because synchronization of "visual" cortices varied according to stimulus complexity, "visual" cortices behaved more like higher-cognitive, rather than primary sensory, areas. Overall, Chapter 2 finds evidence that “visual” cortices undergo widespread and systematic repurposing for higher cognitive functions. In congenital blindness, repurposed “visual” cortices do not just come “online” during unusually demanding tasks, but are engaged on an everyday basis. These data suggest that a major mechanism of plasticity in blindness is take-over of “visual” cortices by higher-cognitive fronto-parietal networks. Human cortex is thus highly functionally flexible early in life.

2.6 Supplementary Materials

Supplementary Table 1. Demographic Information for Chapter 2 Participants

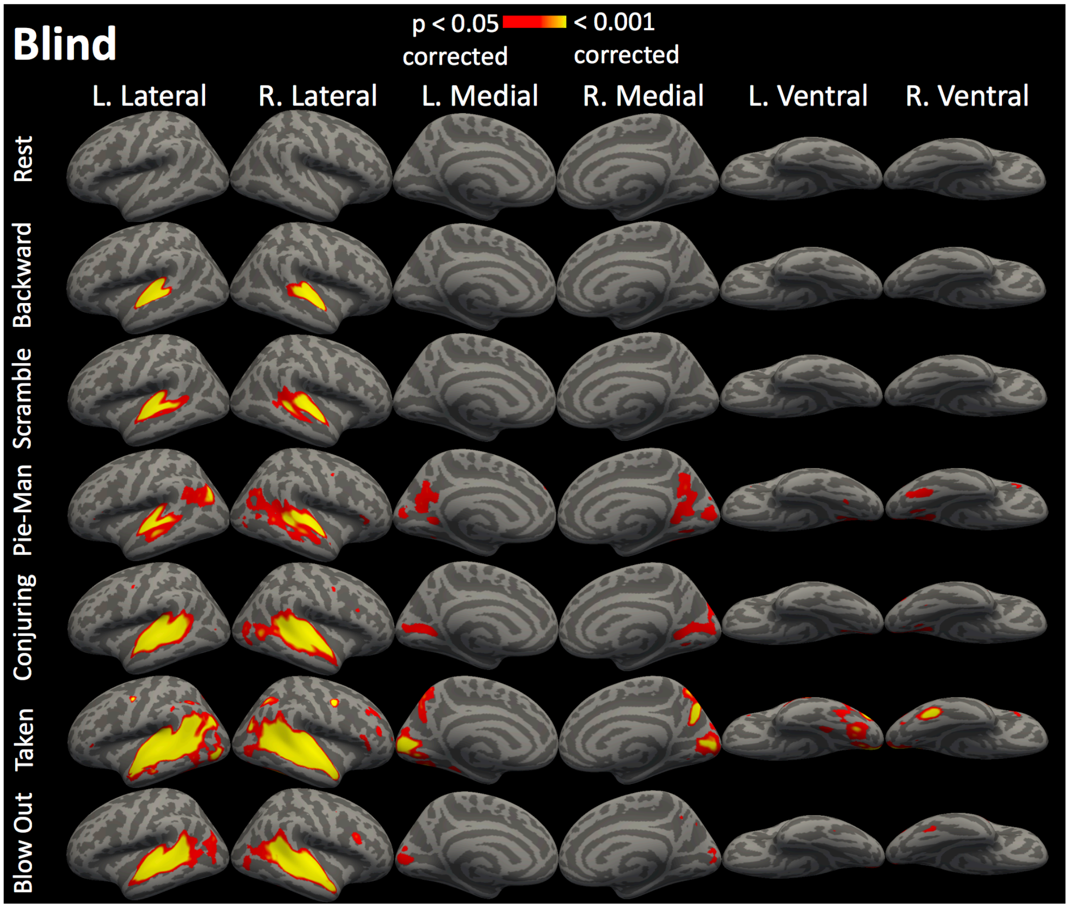
Participant demographic information—i.e., N(umber) and N(umber) of males, age, and years of education—by stimulus and vision group –i.e., S(ighted) and B(lind). Age and Education report mean and standard deviation, as well as a test statistic of the difference between sighted and blind groups.

	N (N Male)	Age	Education
Rest	S: 17 (3) B: 18 (6)	S: $\bar{x} = 42.1, SD = 13.1$ B: $\bar{x} = 41.9, SD = 16.4$ t(33) = 0.04, p > 0.5	S: $\bar{x} = 18.5, SD = 4.4$ B: $\bar{x} = 16.7, SD = 2.5$ t(33) = 1.52, p = 0.14
Backward / Sentence-Shuffle (all participants)	S: 18 (3) B: 18 (6)	S: $\bar{x} = 41.2, SD = 13.2$ B: $\bar{x} = 41.9, SD = 16.4$ t(34) = 0.13, p > 0.5	S: $\bar{x} = 18.4, SD = 4.3$ B: $\bar{x} = 16.7, SD = 2.5$ t(34) = 1.43, p = 0.16
Pie-Man	S: 17 (3) B: 17 (5)	S: $\bar{x} = 40.9, SD = 13.5$ B: $\bar{x} = 41.6, SD = 16.9$ t(32) = 0.12, p > 0.5	S: $\bar{x} = 18.3, SD = 4.4$ B: $\bar{x} = 16.7, SD = 2.6$ t(32) = 1.29, p = 0.21
The Conjuring	S: 18 (3) B: 15 (5)	S: $\bar{x} = 41.2, SD = 13.2$ B: $\bar{x} = 40.7, SD = 16.7$ t(31) = 0.11, p > 0.5	S: $\bar{x} = 18.4, SD = 4.3$ B: $\bar{x} = 16.9, SD = 2.7$ t(31) = 1.19, p = 0.24
Taken	S: 16 (3) B: 17 (6)	S: $\bar{x} = 41.4; SD = 12.8$ B: $\bar{x} = 40.0; SD = 14.9$ t(31) = 0.28; p > 0.5	S: $\bar{x} = 18.8, SD = 4.3$ B: $\bar{x} = 16.9, SD = 2.4$ t(31) = 1.5, p = 0.14
Blow Out	S: 17 (2) B: 17 (5)	S: $\bar{x} = 41.4, SD = 13.6$ B: $\bar{x} = 43.2, SD = 15.8$ t(32) = 0.37, p > 0.5	S: $\bar{x} = 18.4, SD = 4.4$ B: $\bar{x} = 16.9, SD = 2.4$ t(32) = 1.21, p = 0.23

Supplementary Table 2. Subjective Ratings of Naturalistic Stimuli

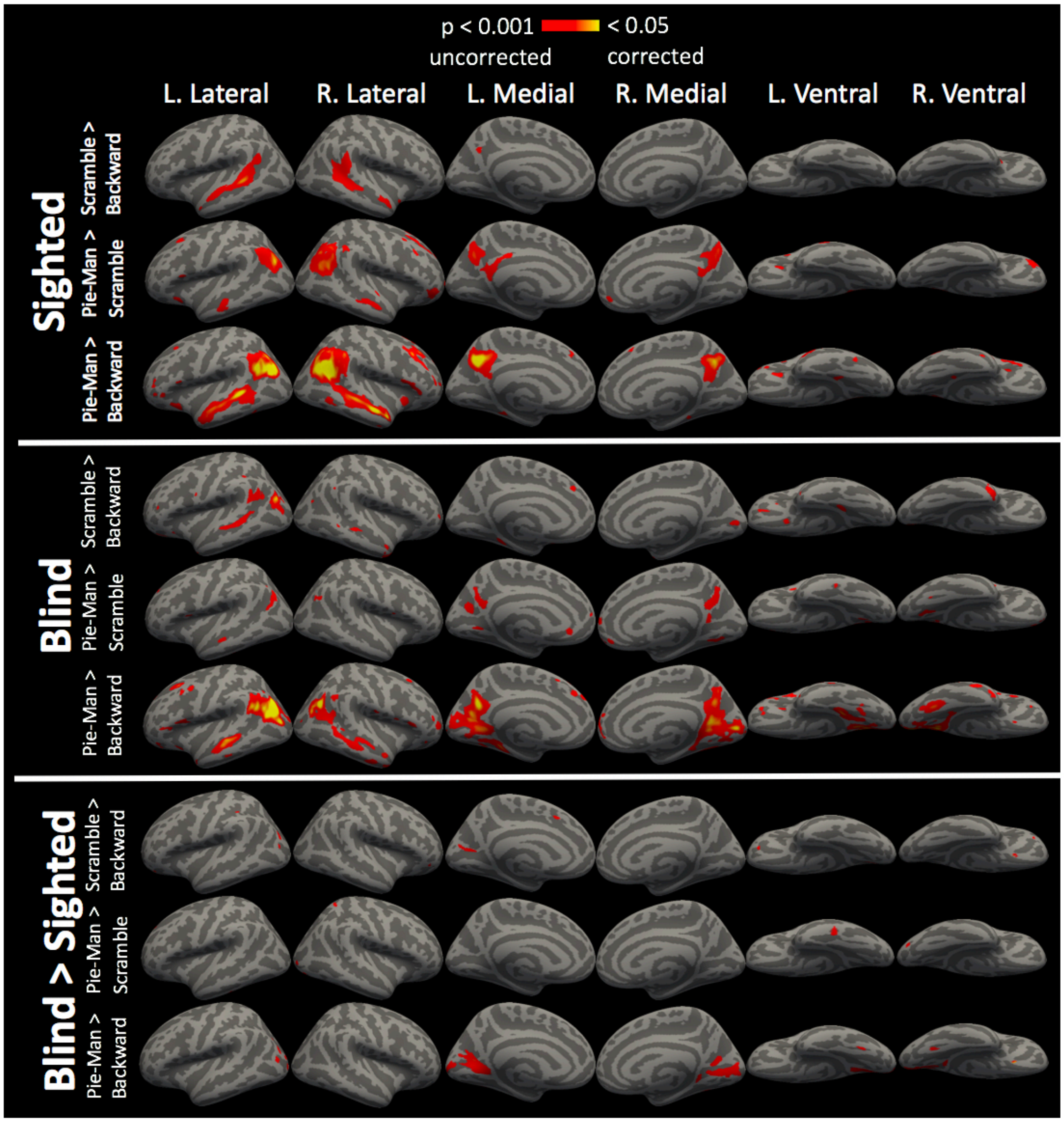
Average Likert Scale Rating (1=Not at all, 5=Extremely) for entertainment, suspense, and following ease.

	Entertaining	Suspenseful	Easy to Follow
Pie-Man	S: $\bar{x} = 3.24$, $SD = 1.15$ B: $\bar{x} = 3.29$, $SD = 1.31$ t(32) = 0.14, p > 0.5	S: $\bar{x} = 2.06$, $SD = 0.97$ B: $\bar{x} = 1.94$, $SD = 1.14$ t(32) = 0.32, p > 0.5	S: $\bar{x} = 4.65$, $SD = 0.86$ B: $\bar{x} = 4.53$, $SD = 0.72$ t(32) = 0.43, p > 0.5
The Conjuring	S: $\bar{x} = 3.00$, $SD = 1.33$ B: $\bar{x} = 3.27$, $SD = 1.53$ t(31) = 0.54, p > 0.5	S: $\bar{x} = 3.89$, $SD = 0.96$ B: $\bar{x} = 4.07$, $SD = 1.03$ t(31) = 0.51, p > 0.5	S: $\bar{x} = 3.67$, $SD = 0.91$ B: $\bar{x} = 3.33$, $SD = 0.98$ t(31) = 1.0.2, p = 0.32
Taken	S: $\bar{x} = 3.84$, $SD = 0.93$ B: $\bar{x} = 3.88$, $SD = 1.36$ t(31) = 0.09, p > 0.5	S: $\bar{x} = 3.88$, $SD = 1.02$ B: $\bar{x} = 4.41$, $SD = 0.71$ t(31) = 1.76, p = 0.09	S: $\bar{x} = 4.00$, $SD = 0.97$ B: $\bar{x} = 4.18$, $SD = 1.01$ t(31) = 0.51, p > 0.5
Blow Out	S: $\bar{x} = 3.18$, $SD = 1.01$ B: $\bar{x} = 3.41$, $SD = 1.12$ t(32) = 0.64, p > 0.5	S: $\bar{x} = 2.94$, $SD = 1.20$ B: $\bar{x} = 4.00$, $SD = 0.94$ t(32) = 2.87, p = 0.01	S: $\bar{x} = 3.35$, $SD = 1.11$ B: $\bar{x} = 3.47$, $SD = 1.28$ t(32) = 0.29, p > 0.5



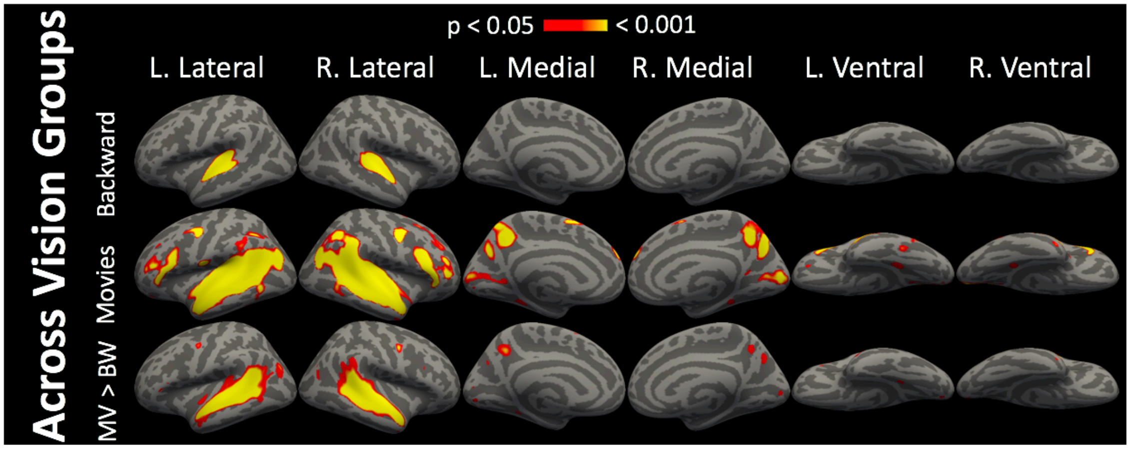
Supplementary Figure 1. Inter-Subject Correlations in the Blind Group for All Stimuli

Inter-subject correlations (ISC) for each stimulus within the blind group, vertex-wise corrected for multiple comparison.



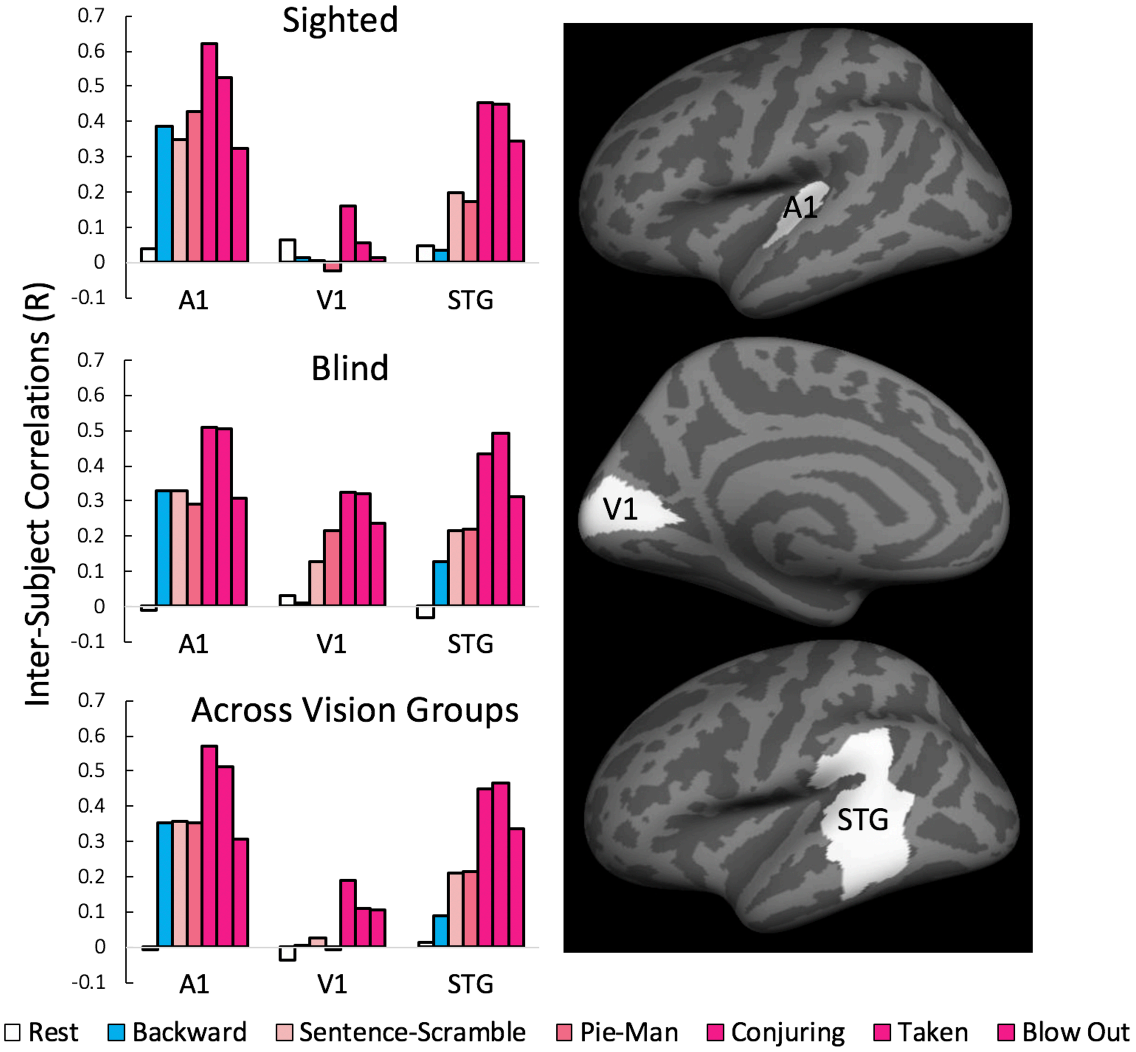
Supplementary Figure 2. Inter-Subject Correlations, Comparisons of Cognitive Complexity

Comparisons of inter-subject correlations (ISC) for sentence-shuffle > backward, pie-man > sentence-shuffle, and pie-man > backward. Synchronization is shown within the sighted group and within the blind group. A comparison of blind group synchronization greater than sighted group synchronization (Blind > Sighted) is also shown. All figures are cluster-corrected for multiple comparison (at $p < 0.001$).



Supplementary Figure 3. Inter-Subject Correlations Across Vision Groups

Inter-subject correlations between vision groups (i.e. sighted to blind and blind to sighted), shown for the backward stimulus, the movie stimuli, and for movie > backward (i.e. MV > BW).



Supplementary Figure 4. Region of Interest Inter-Subject Correlations for all Movies

Inter-subject correlations (ISC) by stimulus, within bilateral early auditory (A1), primary visual cortices (V1), the superior temporal gyrus (STG), and the prefrontal cortex (PFC). ISCs are shown within the sighted group, within the blind group, and across vision groups (i.e. blind to sighted and vice-versa). Movies appear in the order listed.

Chapter 3

Executive function responses in “visual” cortices

3.1 Introduction

In Chapter 2, I found evidence of widespread takeover for higher cognitive functions in “visual” cortices of blind individuals. This is consistent with the pluripotency hypothesis of “visual” cortex takeover by higher cognitive functions. The naturalistic experimental design used in Chapter 2, however, could not provide insight into which specific higher cognitive functions are implemented in “visual” cortices of blind individuals. Therefore, this next chapter will delve more deeply into assessing whether a specific higher cognitive process, executive function, is present in “visual” cortices.

A reliable body of literature suggests that “visual” cortices become responsive to language. In blindness, retinotopic “visual” areas, including V1, become sensitive to meaning and grammar. In blind, but not sighted, individuals, occipital cortices respond more to words than meaningless sounds, more to sentences than unconnected lists of words, and more to grammatically complex than grammatically simple sentences (Röder et al. 2002; Bedny et al. 2011; Lane et al. 2015). Furthermore, language-responsive “visual” cortices become correlated at rest with prefrontal language regions (Bedny et al. 2011).

Since language and vision are cognitively and evolutionarily distinct, these observations challenge the idea that cortical areas have fixed functions, even meta-modal ones.

There are, however, ways to reconcile findings of language repurposing in “visual” cortices of blind individuals with the idea that cortical areas have fixed functions. One possibility is that the occipital cortices are specifically predisposed for both vision and language. For example, visual scene perception and sentence processing could share an underlying cognitive operation, such as hierarchical structure building. Another possibility is that Braille bootstraps the “visual” cortices into language processing (Bavelier and Neville 2002). Braille recognition is similar to vision in that both involve fine-grained spatial discrimination; language processing could invade the visual cortices as a secondary consequence of Braille learning. Therefore, findings from language could be reconciled with the idea that visual areas preserve their underlying functions in blindness.

A key open question, therefore, is whether language is the only higher-cognitive function assumed by “visual” cortices in blindness. If so, language encroachment into the “visual” system may be a special case of meta-modality. If not, language encroachment into the visual system is part of a broader phenomenon of pluripotency, whereby the functional specialization of deafferented “visual” cortices is driven by top-down anatomical inputs from prefrontal, parietal, and temporal networks (Bedny 2017).

Preliminary evidence for the higher-cognitive takeover hypothesis comes from a recent study of mathematical processing in blindness. Dorsal retinotopic “visual” areas are active when congenitally blind individuals solve spoken math equations (e.g. 17-4=X), more so than when blind participants listen to non-mathematical sentences, and the amount of activity scales with equation difficulty (Kanjlia et al. 2016). These math-responsive “visual” regions are differentially localized within occipital cortices from sentence-responsive regions and show a distinctive functional connectivity profile with the fronto-parietal number network (Kanjlia et al. 2016). Furthermore, even at rest, their activity is correlated with fronto-parietal regions in blind individuals (Kanjlia et al. 2016).

These results provide tentative support for the idea that language is not the only higher-cognitive function found in deafferented visual cortices. However, spoken math equations arguably share important properties with language: they include spoken words, they are symbolic, they involve hierarchical structure, and they can also be written in Braille. Additionally, all intact naturalistic stimuli used in Chapter 2 contained language. An outstanding question is whether “visual” cortices of blind individuals are also involved in entirely non-verbal higher-cognitive functions.

Findings from Chapter 2 suggest that higher cognitive functions in “visual” cortices of blind individuals may not be limited to language (or math). Language responses in “visual,” as well as fronto-temporal, cortices are predominantly left-lateralized. Math responses have been observed bilaterally along the posterior cortex. In contrast, synchronization of “visual” cortices to rich auditory vignettes was observed bilaterally along the ventral, lateral, and medial surfaces. Findings from Chapter 2, therefore, raise the possibility that the non-posterior, right “visual” cortices are repurposed for higher cognitive functions other than language or math.

Fronto-parietal executive functions offer a natural test case for answering this question. Executive functions regulate behavior towards task-relevant goals through processes such as selective attention and response selection (Miyake 2000; Banich 2009; Diamond 2013). In sighted individuals, fronto-parietal executive systems modulate activity in visual cortices during visual perception tasks (Moran and Desimone 1985; Desimone and Duncan 1995; Miller and Cohen 2001). This is accomplished via known anatomical projections (in primates) to the visual system from polymodal parietal and, to a lesser degree, frontal cortices (Maunsell and Van Essen 1983; Selemon and Goldman-Rakic 1988; Ungerleider et al. 1998; Rockland and Ojima 2003; Ungerleider et al. 2008; Martino et al. 2010; Anderson et al. 2011; Yeterian et al. 2012). Executive systems are, therefore, likely to constitute a robust input to deafferented “visual” cortices in blindness. The higher-cognitive takeover hypothesis predicts that “visual” cortices of blind individuals take on domain-general executive operations, apart from language processes.

A handful of previous studies are broadly consistent with the idea that “visual” cortices take on non-verbal executive functions in blindness. For example, Park et al. (Park et al. 2011) reported greater “visual” cortex activity during a 2-back than a 0-back control task with tones. Electrophysiological and fMRI studies find that “visual” cortices of blind individuals respond to deviant presentations of tones and tactile stimuli. These responses are thought to reflect attentional, rather than automatic sensory, processes because they occur later and only for attended stimuli (Kujala, Alho, et al. 1995; Kujala, Huotilainen, et al. 1995; Kujala et al. 1997; Liotti et al. 1998; Kujala et al. 2005; Weaver and Stevens 2007). Another study observed elevated responses in “visual” cortices of blind individuals during the response portion of working memory task, when participants were making a button press (Bedny et al. 2012). These studies provide some evidence that “visual” cortices are sensitive to the higher-cognitive demands of non-verbal tasks. However, the precise cognitive processes performed by “visual” cortices during these tasks remain uncertain and alternative explanations in terms of sensory stimulation have not been ruled out (e.g. (Burton et al. 2004; 2010)).

Therefore, the goal of the current study was to test the prediction that regions within the “visual” cortices of blind individuals are incorporated into non-verbal executive function networks. Specifically, I predicted that in blindness a subset of visual cortex would be sensitive to response selection demands in a non-verbal go/no-go task when other factors, such as somatosensory stimulation, are controlled. To test these predictions, congenitally blind and sighted-blindfolded participants performed an auditory go/no-go task with complex non-verbal sounds.

During the go-no/go task, participants made button-presses to some sounds (go trials) and withheld responses to other sounds (no-go trials). Go trials were much more frequent than no-go trials (25% vs. 75%) and participants had to respond quickly (within 900 MS). As a result, the button press becomes pre-potent and must inhibited on no-go trials (Garavan et al. 1999; Aron et al. 2014). The increased executive demands of no-go relative to go trials are evidenced both behaviorally and neurally. Participants make more errors of commission (going on no-go trials) than errors of omission (not going on go-trials). Neurally, no-go trials produce elevated activity in right-lateralized fronto-parietal executive function networks among sighted individuals (Konishi et al. 1998; Garavan et al. 1999; Liddle et al. 2001; Menon et al. 2001; Garavan et al. 2002; Mostofsky et al. 2003; Chikazoe et al. 2008; Barber et al. 2013). I predicted that “visual” cortices of blind individuals would respond more to no-go than to go trials, indicating recruitment for non-verbal executive functions and in particular of response selection demands.

Importantly, the current design enables one to distinguish “visual” cortex responses to executive demands from other potentially confounded processes. First, since the current task does not involve language stimuli, “visual” cortex responses are unlikely to be related to language processing. I further predicted that unlike previously observed responses to language in the “visual” cortices, responses to domain-general executive demands would be right-lateralized, similar to responses to executive demands in the fronto-parietal cortices (Aron et al. 2004; Wager et al. 2005; Aron 2006). Second, the current task was not spatial; therefore, observed effects are unlikely to reflect vision-like processing. Finally, the design pitted executive demands against low-level sensorimotor demands. If “visual” cortices of blind individuals respond to executive demands, they should be more active during no-go trials. By contrast, if the “visual” cortices respond to sensorimotor demands, they should be more active during go trials, since only the go trials contain a button press and associated tactile feedback. Indeed, previous studies have shown that unlike executive function networks, sensorimotor cortices respond more to go trials than no-go trials (Garavan et al. 1999; Liddle et al. 2001; Mostofsky et al. 2003). Thus, in the current experiment I predicted a double dissociation between activity in sensorimotor cortices and activity in the “visual” cortices of blind individuals.

In the current version of the go/no-go task I also included an intermediate executive demand condition, the infrequent-go. The infrequent-go condition was associated with a distinct sound; it occurred only 25% of the time (like the no-go condition) and required a button press response (unlike the no-go condition). All together there were thus three types of trials: frequent-go (50%), infrequent-go (25%), and no-go (25%). A previous study using a similar design observed an intermediate level of activity for the infrequent-go condition (less activity than no-go but more activity than frequent-go) in prefrontal executive function areas of sighted individuals (Chikazoe et al. 2008). We, therefore, predicted that “visual” cortices of blind individuals would respond most to no-go trials, followed by infrequent-go trials, and least to frequent-go trials.

A second prediction of the current study was that executive-load responsive “visual” areas would become functionally connected at rest with fronto-parietal executive function systems in blindness. To test this prediction, I collected resting state data from a large sample of congenitally blind (n=25) and sighted (n=25) participants. I then asked whether the connectivity of executive-function responsive “visual” cortex is stronger with fronto-parietal executive function networks than with either non-visual sensory-motor areas (early auditory and somatosensory cortices) or language responsive prefrontal cortices. Such a result would support the hypothesis that these “visual” cortex regions are incorporated into the executive system.

In sum, I make four predictions: (1) that the occipital cortices of the blind, but not sighted, group will respond to executive function demands, i.e. most to no-go trials and least to frequent-go trials; (2) that the sensorimotor cortices will display the opposite ordering of responses to the conditions, i.e. most activity for go and least activity for no-go trials, thereby diverging from the executive function profile observed in the blind group’s “visual” cortices; (3) that “visual” cortex responses to executive function demands will be right-lateralized and, thereby, both neuroanatomically dissociable from “visual” cortex responses to language and co-lateralized with fronto-parietal responses to executive function; and (4) that, at rest, executive-function responsive “visual” cortices of blind individuals will show increased functional connectivity to fronto-parietal executive function regions, specifically.

3.2 Materials and Methods

Participants.

19 congenitally blind and 19 sighted controls (blind: 13 females; 12 right-handed, 3 ambidextrous; age: mean=45.3, SD=17.43; years of education: mean=17.00, SD=2.73; sighted: 14 females; 18 right-handed; age: mean=41.71, SD=14.74; years of education: mean=17.97, SD=3.68) contributed task-based data. Blind and sighted participants were matched on average age (t(36)=0.50, p=0.69) and education level (t(36)=0.36, p=0.93).

All but one sighted participant from the task-based go/no-go experiment contributed resting state data. Resting state data from an additional 6 blind and 7 sighted participants were included, resulting in the following group-wise demographics (blind: N=25; 18 females; age: mean = 46.63, SD=16.9; sighted: N=25; 15 females; age: mean = 43.16, SD=12.26; blind vs. sighted age, t(48)=0.83, p=0.41). During the resting state scan, participants were instructed to relax but remain awake.

All blind participants self-reported minimal-to-no light perception since birth, i.e. having never been able to distinguish colors, shapes, or motion. (One blind participant was born with no light perception, but reported some functional vision in one eye between 5 and 11 years of age, following several corrective surgeries. This participant's data was no different from the remaining blind group and is included in the sample.) Blind and sighted participants had no known neurological disorders, head injuries, or brain damage. For all blind participants, the causes of blindness excluded pathology posterior to the optic chiasm (see Table 2 for details). All participants gave written consent under a protocol approved by the Institutional Review Board of Johns Hopkins University. All participants wore light exclusion blindfolds for the duration of the scan to equate light conditions across participants.

Blindness Etiology	**No.**	**LP No.**
Leber Congenital Amaurosis	5 (+2)	4 (+2)
Retinopathy of Prematurity	8 (+4)	4
Optic Nerve Hypoplasia	2	0
Retinitis Pigmentosa	1	1
Glaucoma	1	0
Unknown	2	1

Table 2. Blindness Etiology for Chapter 3 Participants

Per cause of blindness, total number of participants (No.) and number with light perception (LP No.). Amounts outside of parentheses are for participants in task-based go/no-go experiment. Amounts within parentheses are for additional participants included in resting-state analyses.

fMRI data acquisition.

MRI structural and functional data of the whole brain were collected on a 3 Tesla Phillips scanner. T1-weighted structural images were collected in 150 axial slices with 1 mm isotropic voxels using a magnetisation-prepared rapid gradient-echo (MP-RAGE). T2*-weighted functional images were collected in 36 axial slices with 2.4 x 2.4 x 3 mm voxels and a 2 second TR. I acquired 3 runs of task-based fMRI data per subject and between 1 and 4 runs of resting state data (mean number of runs: sighted = 1.28, blind =2.08; $t(48) = 3.78$, $p < 0.001$). Acquisition parameters were identical for resting and task-based data.

Behavioral task.

Participants heard complex non-verbal sounds (450 MS with 450 MS ISI), each representing 1 of 3 conditions: frequent-go (50% trials), no-go (25%), and infrequent-go (25%) and were asked to make speeded button presses in response to the go sounds and to withhold responding to the no-go sounds. Each run was comprised of 400 trials and 4 20-second rest periods, spaced equidistantly, for a total time of 7.67 minutes per run. The full experiment consisted of three runs. Presentation order was constrained so that each infrequent condition – i.e. infrequent-go and frequent-go – could not occur on more than 3 consecutive trials. Feedback on performance accuracy was given after every run. To avoid making participants explicitly aware of the frequency manipulation, the frequent-go and infrequent-go conditions were referred to as “go 1” and “go 2,” respectively. Prior to taking part in the main experiment, participants performed 400 practice trials (100 inside the scanner) with auditory feedback after each trial.

The 3 stimulus sounds were chosen to be easily and immediately discerned from each other. All 3 sounds differed from each other at the sound onset and remained relatively homogenous throughout the sound duration. To discourage chunking of sounds across conditions, sounds were selected to be equally dissimilar (Amazon Mechanical Turk pre-experiment pilot testing revealed no one sound as the “odd one out”; chi-sqd(2)=1.66, N=49; $p > 0.5$). Assignment of sounds to conditions was counterbalanced across participants and matched across blind and sighted groups.

Auditory stimuli were presented over Sensimetrics MRI-compatible earphones (http://www.sens.com/products/model-s14/) at the maximum comfortable volume for each participant. The volume was adjusted for all stimuli or selectively for a specific stimulus (2 sighted, 2 blind) according to participant’s request. Adjustments did not affect the analyzed data, as they were implemented prior to the first functional run. Participants were free to make responses with their preferred hand (right hand for all but 1 sighted and 4 blind participants).

fMRI task-based data analysis.

Data analyses were performed using FSL, Freesurfer, the HCP workbench, and custom software (Dale et al. 1999; Smith et al. 2004; Glasser et al. 2013). Functional data were motion corrected, slice-time corrected, high pass filtered with a 128 s cutoff, pre-whitened, and resampled to the cortical surface (discarding subcortical structures and the cerebellum). The data were smoothed with a 12 mm FWHM Gaussian kernel on the surface, which affords better spatial accuracy than comparable smoothing in the volume (Hagler et al. 2006; Jo et al. 2007; Anticevic et al. 2008; Tucholka et al. 2012).

For each subject, I defined a GLM to predict BOLD activity according to the following event types, each convolved with the hemodynamic response function: successful frequent-go, successful infrequent-go, successful no-go, failed frequent-go, failed infrequent-go, failed no-go, false starts, and extra button presses. Results report only successful trials. All trial events began at the onset of the auditory stimulus and ended at the offset of the auditory stimulus or the participant's button press (whichever sensory event ended last).

A covariate of no interest was included to account for motion. Timepoints with framewise-displacement (relative movement) greater than 1.5 mm were excluded by modeling each timepoint as an individual regressor with a value of 1 at the time point and 0 everywhere else (drops per run: blind mean=0.30, SD=0.80; sighted mean=0.12, SD=0.25; difference between groups t(36)=0.91, p=0.37).

Fixed-effects analyses were used to combine runs within each subject, which were then submitted to a group analyses with subject represented as a random-effect. To control for vertex-wise multiple comparisons, I performed a cluster-wise permutation analysis (Nichols and Hayasaka 2003; Hagler et al. 2006). Whole-brain maps are first thresholded, and resulting cluster-sizes are then tested against a cluster-size null distribution generated from 5,000 permutations. This approach corrects for multiple comparisons because the each permutation's null value is determined by the highest cluster size, across the whole brain. Reported whole-brain contrasts were run as one-sided tests, thresholded at $p < 0.01$ vertexwise, and $p < 0.05$ cluster-corrected. Because this can eliminate small clusters, I also performed a multiple comparison correction using a false discovery rate (FDR) of 5%, per hemisphere, on one-tailed p-values (Genovese et al. 2002).

fMRI task-based ROI analysis.

I performed individual-subject functional regions of interest (ROIs) by defining three (ROIs) in each participant: 1) a prefrontal (PFC) executive function ROI, 2) a sensory-motor (SMC) ROI and 3) a medial visual cortex (VC). ROIs were defined by selecting responsive vertices for each participant within a group-wise search space using a leave-one run out procedure.

Search spaces were defined as follows. For the executive function PFC ROI and the sensorimotor cortex (SMC) ROI I defined a search based on previous studies that observed response-inhibition and hand-movement activity, respectively, using neurosynth.org (Yarkoni et al. 2011). Both volumetric search-spaces were projected to the surface, thresholded at $z > 1.65$, dilated and eroded at 12 mm (to fill small holes), and restricted to the anatomical area of interest. For the PFC, I confined the functionally derived search space to right lateral prefrontal lobe, anterior to the pre-central gyrus. For the SMC, I confined the functionally derived search space to the left central sulcus and pre- and post-central gyri, as defined by a surface-based atlas (Destrieux et al. 2010). The visual cortex (VC) search space was defined by combining V1, V2, dorsal V3, and ventral V3 (VP) parcels from the PALS-B12 visuotopic surface-based atlas (Van Essen 2005). All search spaces were created in the right hemisphere and mirrored to the left hemisphere.

Within each search space, I used a leave-one-run out procedure to define and test subject-specific functional ROIs. The PFC ROI was defined based on the no-go > frequent-go contrast. In the SMC ROI, I selected hypothesized somatosensory and motor responsive vertices using the frequent-go + infrequent-go > no-go contrast. I searched for both PFC-type and SMC-type responses in the VC by defining ROIs based on both contrasts. For all ROIs, I selected the top 20% of vertices that most strongly responded to the contrast of interest in all but one run and extracted signal from the left-out run. Beta-values, for each condition, were obtained by averaging whole-brain GLM Betas across the selected ROI vertices. This procedure was repeated iteratively, leaving out one run at a time, and the resulting Betas were averaged across run iterations, for each subject. ROIs vertices were defined according to a subset of runs and those vertices were assessed on non-overlapping subset of runs. Because ROIs were selected and tested orthogonally for the contrast of interest, participant’s ROIs will only show the contrast of interest if preferential activity replicates across runs (i.e., if not driven by noise).

Resting state functional connectivity analysis.

I used the CONN Toolbox (Whitfield-Gabrieli and Nieto-Castanon 2012) to compare visual cortex functional connectivity during rest. BOLD data were first smoothed 23 diffusion steps on the surface and registered to MNI-152 standard space. To control for temporal confounds, white matter and cerebrospinal fluid BOLD signals were regressed out and the residual was bandpass filtered (0.008-0.1). Time-courses were first averaged within ROIs and then either correlated to each other (ROI-to-ROI) or to the time-course of each and every vertex (ROI-to-whole-brain).

I defined 1 visual and 4 non-visual cortex group-wise regions of interest. An OC-EF ROI was defined as the largest cluster within the entire occipital cortex that responded more to go than no-go in blind, relative to sighted, participants in the cluster-corrected map. A prefrontal executive-function (PFC-EF) ROI was defined as the area with the largest contiguous all-subject activation for no-go > frequent-go ($p < 0.05$ FDR-corrected), constrained to the PFC search space. Similarly, a sensorimotor (S1/M1) ROI was selected as the largest contiguous all-subject activation for go > no-go ($p < 0.05$ FDR-corrected), constrained to the SMC search space. A prefrontal language (PFC-LG) ROI was taken from parcels that have previously been observed to be responsive to linguistic content in sighted subjects (Fedorenko et al. 2010). Finally, I selected a primary auditory cortex (A1) ROI as the transverse temporal portion of a gyral based atlas (Morosan et al. 2001; Desikan et al. 2006). All ROI analyses were conducted in the right hemisphere so as to match the hemisphere of the visual cortex OC-EF region. Two ROIs that were originally defined in the left hemisphere (i.e. S1/M1 and PFC-LG) were mirrored to the right-hemisphere. This procedure ensures that any functional connectivity differences amongst ROIs are not driven by differences in connectivity across hemispheres.

3.3 Results

Behavioral performance.

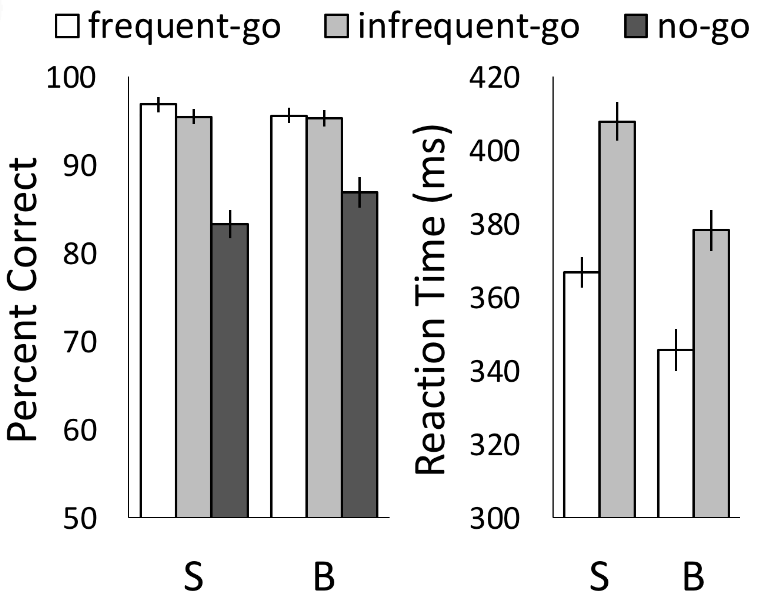


Figure 3. Behavioral Performance on Go/No-Go Task

Behavioral performance. Percent correct and response times for sighted (S) and blind (B) participants. Error bars indicate the within-subjects standard error of the mean.

In both go conditions, participants responded quickly (Figure 3, RT: sighted frequent-go mean=366.77 MS, SD=52.80 MS; sighted infrequent-go mean=407.87 MS, SD=51.94 MS; blind frequent-go mean=345.70 MS, SD=67.92 MS; blind infrequent-go mean=378.26 MS, SD=60.74 MS) and made few errors of omission (Figure 3, % correct: sighted frequent-go mean=96.88, SD=4.35; sighted infrequent-go mean=95.47, SD=4.49; blind frequent-go mean=95.61, SD=8.14; blind infrequent-go mean=95.30, SD=9.22).

Both blind and sighted participants made some errors of commission on no-go trials (Figure 3, % correct: sighted mean=83.28, SD=11.17; blind mean=86.88, SD=11.82).

Participants in both groups made more errors on no-go than frequent-go or infrequent-go trials (frequent-go vs. no-go sighted t(18)=5.54, p<0.001, blind t(18)=3.40, p=0.003; infrequent-go vs. no-go: sighted t(18)=5.00, p<0.001, blind t(18)=3.16, p=0.005), with no difference between groups (group x condition ANOVA: main effect of condition: F(2,72)=35.08, p<0.001; main effect of group: F(1,36)=0.10, p>0.05, group x condition interaction: F(2,72)=1.48, p=0.235). Frequent and infrequent-go accuracy were different in the sighted, but not the blind, group (sighted t(18)=2.10, p=0.05, blind t(18)=0.63, p>0.5). Differences between the two go conditions were evidenced in response times for both groups: blind and sighted groups were slower to respond on infrequent-go than frequent-go trials (sighted t(18)=7.67, p<0.001, blind t(18)=6.19, p<0.001; group x condition ANOVA: main effect of condition F(1,36)=96.27, p<0.001, main effect of group F(1,36)=1.84, p=0.18, group-by-condition interaction F(1,36)=1.30, p=0.26).

fMRI Results.

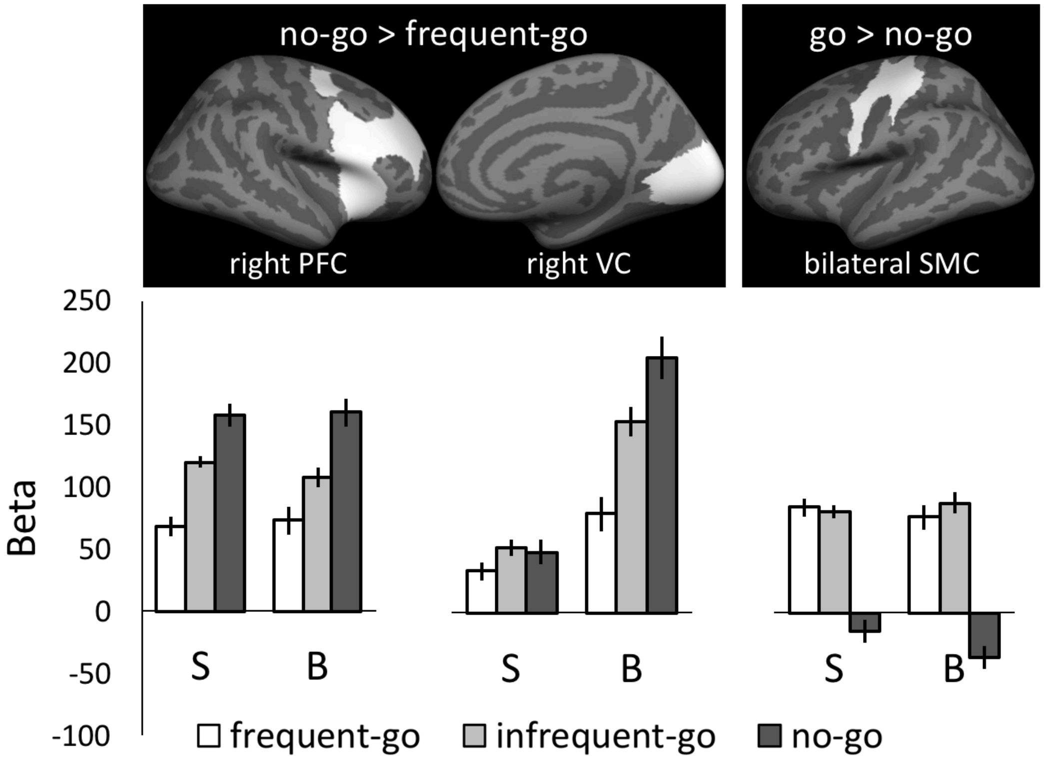


Figure 4. Region of Interest Analysis for Go/No-Go Task

Beta values for task conditions within sighted (S) and congenitally blind (B) participants’ prefrontal cortex (PFC), medial visual cortex (VC), and sensorimotor cortex (SMC). Error bars indicate the within-subjects SEM.

Right-lateralized “visual” cortices of blind individuals responds to executive function, similar to right-lateralized prefrontal cortices (individual subject functional ROI analysis)

In both the sighted and the blind groups, areas of the right prefrontal cortex (PFC) responded more to the no-go than the infrequent- or frequent- go conditions (Figure 4;

sighted: no-go vs. frequent-go t(18)=5.58, p<0.001; no-go vs infrequent-go t(18)=3.15, p=0.006; blind: no-go vs. frequent-go t(18)=4.28, p<0.001; no-go vs infrequent-go t(18)=3.44, p=0.003). I also observed higher responses to the infrequent-go than the frequent-go condition in the rPFC (sighted: t(18)=5.82, p<0.001; blind t(18)=2.15, p=0.045). Responses in the rPFC did not differ between groups (group x condition ANOVA: main effect of condition F(2,72)=33.91, p<0.001; main effect of group F(1,36)=0.01, p>0.5; group x condition interaction F(2,72)=0.39, p>0.5).

In blind individuals, the right retinotopic visual cortex (VC; i.e. V1-V3) showed a functional profile consistent with the executive function pattern observed in the right PFC: greater response to no-go than frequent-go, a greater response to the infrequent-go than the frequent-go, and a (trending) greater response to no-go than infrequent-go (Figure 4; no-go vs frequent-go t(18)=4.33, p<0.001; infrequent-go vs. frequent-go t(18)=3.75, p=0.001; no-go vs infrequent-go t(18)=1.99, p=0.06). By contrast, I did not observe this profile of response in the visual cortices of sighted blindfolded controls (Figure 4; no-go vs frequent-go t(18)=0.96, p = 0.35; no-go vs infrequent-go t(18)=0.24, p>0.5; infrequent-go vs. frequent-go t(18)=1.77, p=0.09; condition x group ANOVA: main effect of condition F(2,72)=12.30, p < 0.001, main effect of group F(1,36)=7.01, p=0.01, group x condition interaction F(2,72)=7.31, p=0.001).

Within the congenitally blind group’s “visual” cortices, the executive function profile was more pronounced in the right hemisphere than left hemisphere (hemi x condition ANOVA: main effect of condition, F(2,36)=9.37, p = 0.001; main effect of hemi F(1,18)=2.34, p=0.14, hemi x condition interaction F(2,36)=3.59, p = 0.04). Likewise, a hemispheric difference with respect to condition was also present in the PFC (blind group only, hemi x condition ANOVA: main effect of condition, F(2,36)=12.57, p<0.001; main effect of hemi F(1,18)=4.97, p = 0.04, hemi x condition interaction F(2,36)=4.75, p=0.015). Within the blind group, prefrontal and “visual” cortices behaved similarly. There was no difference between the PFC and the VC with respect to condition and/or hemisphere (ROI x hemi x condition ANOVA: main effect of ROI F(1,18)=2.66, p=0.12; ROI x condition interaction F(2,36)=2.53, p=0.09; ROI x hemi interaction F(1,18)=0.50, p=0.49; ROI x hemi x condition F(2,36)=0.09, p>0.5).

Primary sensory-motor, but not “visual” cortices, of blind individuals respond to sensorimotor demands (individual-subject functional ROI analysis)

In the bilateral sensory-motor cortices (SMC), I observed higher activity for both of the go conditions than the no-go in both the sighted (Figure 4; frequent-go vs no-go t(18)=6.20, p<0.001; infrequent-go vs no-go t(18)=7.47, p<0.001; frequent-go vs. infrequent-go t(18)=0.42, p=0.68) and the blind group (frequent-go vs no-go t(18)=6.61, p < 0.001; infrequent-go vs. no-go t(18)=8.29, p<0.001; frequent-go vs. infrequent-go t(18)=0.68, p=0.51). This response profile is consistent with SMC involvement in execution of the button press and associated tactile feedback. There was no difference between go conditions in the SMC for either group (sighted: t(18)= 0.42, p > 0.5; blind t(18)=0.68, p>0.5). The SMC profile was similar in blind and sighted individuals (group x condition ANOVA: main effect of condition F(2,72)=73.64, p<0.001; main effect of group F(1,36)=0.05, p>0.5; group x condition interaction F(2,72)=0.87, p=0.42).

In contrast to the SMC, I failed to observe a sensorimotor related effect in the right visual cortices of blind individuals even when I searched specifically for vertices that preferred trials with a button press (frequent and infrequent go) to no-go trials (Supplementary Figure 5, frequent-go vs no-go t(18)=-0.96, p=0.35; infrequent-go vs no-go t(18)=1.40, p=0.18; frequent-go vs. infrequent-go t(18)=2.33 p=0.03). Interestingly, in the sighted group there was a trend towards higher responses to the two button press conditions (Supplementary Figure 5, frequent-go vs no-go t(18)=2.07, p=0.053; infrequent-go vs no-go t(18)=2.03, p=0.057; frequent-go vs. infrequent-go t(18)=0.13 p>0.5).

Whole-brain analysis.

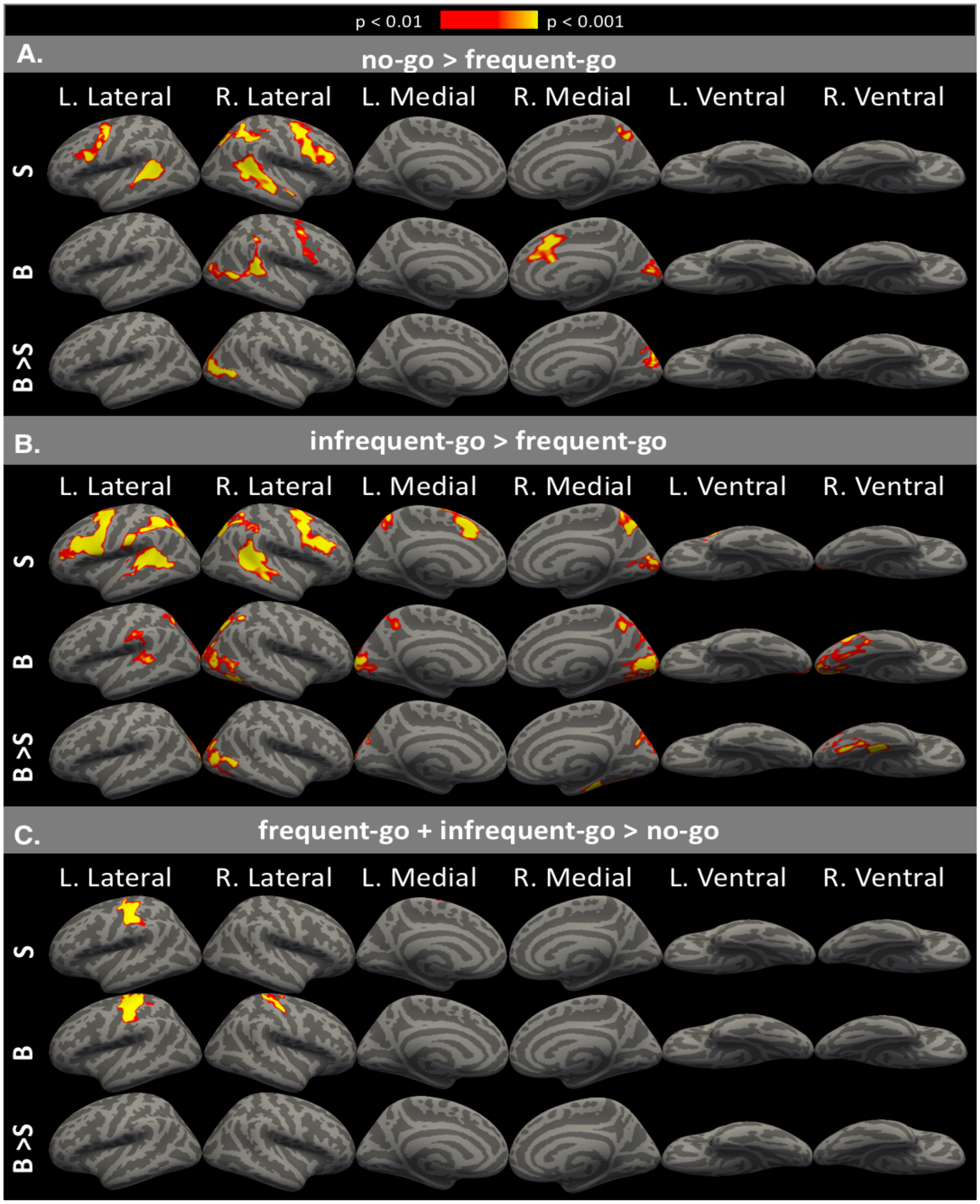


Figure 5. Go/No-Go Activations

Whole brain contrasts for sighted (S), blind (B), and blind > sighted (B > S). Areas shown are $p < 0.05$ cluster-corrected p-values, with intensity representing uncorrected vertex-wise probability.

Consistent with the ROI analysis and with previous findings, the no-go > frequent-go contrast revealed robust responses in right-lateralized, prefrontal and parietal executive function networks of both blind and sighted groups (Figure 5A). Greater activity for no-go than frequent-go was observed along the precentral sulcus, inferior frontal sulcus, inferior frontal junction (IFJ), and intraparietal sulcus (IPS), as well as the superior temporal sulcus and gyrus (STG/STS; Figure 5A & Supplementary Table 3). Additionally, I observed greater activity for the no-go condition in the supplementary motor area/anterior cingulate cortex (SMA/ACC) of the blind group and in the posterior precuneus of the sighted group. In the blind and sighted groups, responses to no-go > frequent-go, were observed bilaterally but were stronger on the right (Figure S2).

Similar to no-go, infrequent-go also elicited greater activity in executive function regions, relative to frequent-go in both the sighted and blind groups (Figure 5B & Supplementary Table 3). In the sighted group, the same fronto-parietal and temporal areas that responded more to no-go than frequent-go also responded more to infrequent-go than frequent-go. Notably, fronto-parietal networks were recruited more bilaterally for infrequent-go than for no-go. In the blind group, infrequent-go > frequent-go activity was observed in parts of the IPS, STS, and posterior precuneus. Fronto-parietal responses to executive demands were somewhat less extensive in the blind relative to the sighted group.

In the blind but not sighted group, retinotopic "visual" cortices responded more to the no-go than to the frequent-go condition (Figure 5A & Supplementary Table 3). Activity in the occipital cortices of the blind group mirrored that of fronto-parietal cortices in right-hemisphere dominance. Occipital cortex activity, in the blind group, peaked in the cuneus and the lateral middle occipital gyrus. Comparing blind and sighted groups directly, I observed greater activity in the congenitally blind group, for no-go relative to frequent-go, on the lateral and medial surface of the right occipital cortex (Figure 5A & Supplementary Table 3).

The infrequent > frequent go contrast also revealed activity in occipital cortices, but this time in both the blind and sighted groups. In the blind group, the anatomical distribution of the infrequent > frequent go response overlapped with the “no-go” response in the cuneus and lateral medial occipital gyrus but also extended into the right fusiform gyrus and the calcarine sulcus bilaterally. As in prefrontal cortices, occipital cortices exhibited reduced right-lateralization for the infrequent-go > frequent-go contrast, relative to the no-go > frequent-go contrast. In the sighted group, infrequent > frequent go activity was anatomically constrained to the posterior calcarine sulcus—i.e. the functional location of foveal V1—and bilateral (Figure S2). When blind and sighted groups were compared to each other directly, there was greater activity in the blind group in lateral occipital cortices as well as the medial fusiform (Figure 5B, Supplementary Table 3).

Primary sensory and motor cortices, but not occipital cortices, responded to sensorimotor demands of frequent-go and infrequent-go. For both blind and sighted groups, left-hemisphere primary sensory and primary motor cortices were more active for both go conditions than for the no-go condition (Figure 5C & Supplementary Table 3). For the blind group, greater activity for the go conditions was also observed in the right primary sensory and primary motor cortices, consistent with fact that more blind individuals using their left hand to respond (see Methods). Consistent with the ROI analysis, no “visual” cortex activity was observed in the blind group for frequent- and infrequent-go conditions relative to the no-go condition. Moreover, a direct comparison between blind and sighted groups revealed no interaction of group by condition.

Resting state functional connectivity

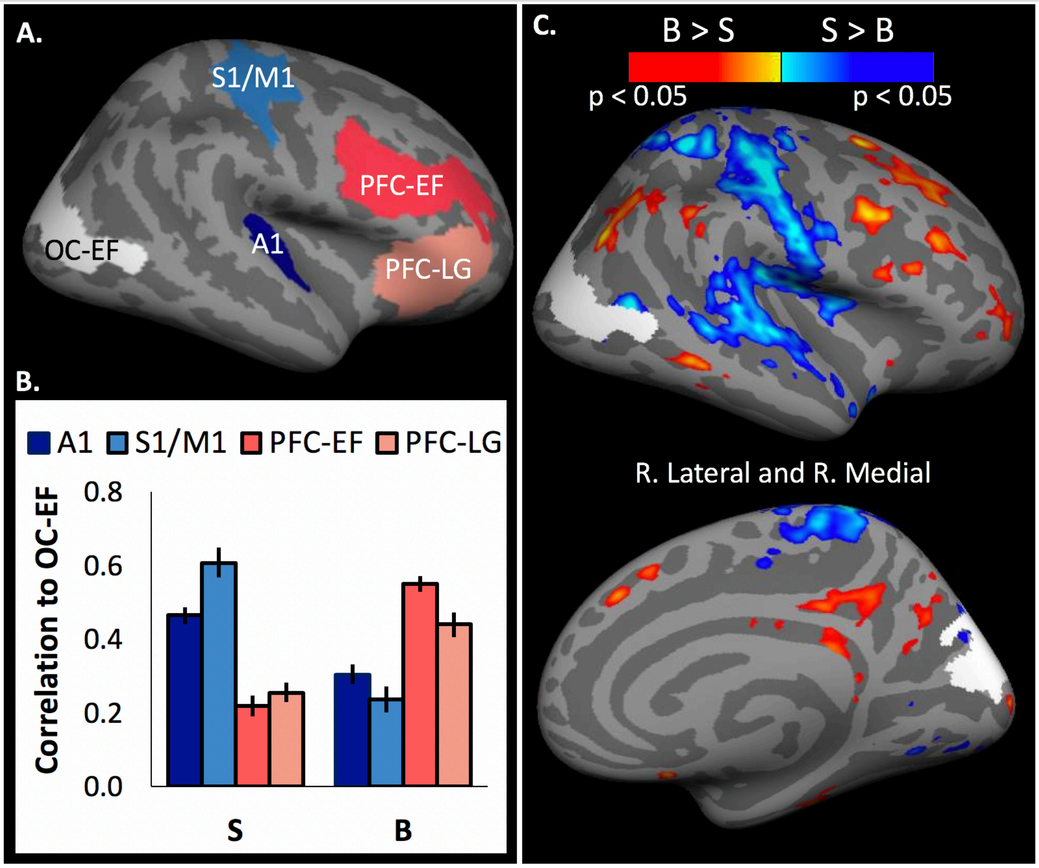


Figure 6. Resting-State Functional Connectivity with Go/No-Go Responsive Seed

Functional connectivity of executive-function responsive occipital cortex (OC-EF) to sensory/motor and prefrontal regions in sighted and blind.

A. Regions of interest for resting state analyses: OC-EF, primary auditory cortex (A1), primary sensorimotor cortices (S1/M1), executive-function responsive (PFC-EF), and language responsive (PFC-LG).

B. Fisher-transformed correlation coefficients between OC-EF and non-visual ROIs. Error bars indicate the within-subjects SEM.

C. Between-group differences in connectivity to executive-function responsive occipital cortex (OC-EF, in white). FDR-corrected contrasts for blind > sighted (in red) and sighted > blind (in blue).

I used resting state data to examine functional connectivity of executive-load responsive "visual" cortex among blind individuals. An executive-function responsive visual ROI (OC-EF) was defined based on the blind > sighted x no-go > frequent-go contrast (see Methods for details). For both blind and sighted participants, I assessed OC-EF connectivity to two primary sensory regions—A1 and S1/M1— and to two prefrontal regions—one responsive to executive-function, PFC-EF, and one responsive to language, PFC-LG (Figure 6A).

An ANOVA comparing the connectivity of executive-function responsive visual cortex (OC-EF) to executive-function responsive prefrontal, language-responsive prefrontal, sensory-motor and primary auditory ROIs across groups revealed a significant group by ROI interaction (ROI (PFC-EF, PFC-LG, A1, S1/M1) x group ANOVA: main effect of ROI $F(3,144)=1.48$, $p=0.22$; main effect of group $F(1,48)=0.01$, $p>0.5$; group x ROI interaction $F(3,144)=41.63$, $p<0.001$). An ANOVA within sighted individuals revealed that the executive function responsive visual cortex (OC-EF) was more correlated to non-visual primary sensory areas (A1 and M1/S1) than to either of the executive function or language-responsive prefrontal ROIs (mean of PC-EF and PC-LG < mean of A1 and M1/S1: $F(1,24)=42.98$, $p<0.001$). Conversely, in blind individuals, OC-EF was more correlated to prefrontal than to primary sensory regions (mean of PC-EF and PC-LG > mean of A1 and M1/S1: $F(1,24)=21.99$, $p<0.001$). Finally, among the prefrontal cortex ROIs, OC-EF of blind but not sighted individuals was preferentially correlated to executive function-responsive prefrontal cortex than language-responsive prefrontal cortex (blind

PC-EF vs. PC-LG t(24)=3.47, p=0.002, sighted PC-EF vs. PC-LG t(24)=-1.17, p=0.25; group x ROI (PFC-EF vs. PFC-LG) interaction F(1,48)=10.86, p=0.002).

Next, I compared OC-EF functional connectivity between groups throughout the whole-brain. Relative to sighted individuals, blind individuals had increased OC-EF connectivity to fronto-parietal regions and decreased OC-EF connectivity to primary sensory areas (Figure 6C). Moreover, for blind individuals, the set of regions that preferentially increased their correlation to OC-EF at rest was equivalent to the set of regions that exhibited an executive-function response profile during the go/no-go task. Areas that were more functionally connected to the OC-EF for blind individuals included the precentral sulcus, superior and inferior frontal sulcus, inferior frontal junction (IFJ), intraparietal sulcus (IPS), middle temporal gyrus (MTG), precuneus, and the anterior and posterior cingulate cortex (ACC and PCC). In contrast, the pre-to-post central gyrus, transverse temporal gyrus, and ventral superior temporal gyrus (STG) were more functionally connected to the OC-EF in sighted, than in blind, individuals.

3.4 Discussion

Two key findings support the hypothesis that a right-lateralized subset of “visual” cortex is incorporated into a right-lateralized fronto-parietal non-verbal executive function network in congenital blindness. First, in blind individuals, a right-lateralized sub-network within “visual” cortices is sensitive to executive demands during a non-verbal, non-spatial, go/no-go task. The occipital cortices of congenitally blind (but not sighted) adults were most active during no-go trials, i.e. when withholding a button press. Amongst the go trials, responses in the “visual” cortices of the blind group were larger for the infrequent-go condition than for the frequent-go condition. This response-profile (no-go > infrequent-go > frequent-go) mirrored that observed in the fronto-parietal executive function network of both blind and sighted groups. Second, in blindness executive-function responsive “visual” cortex becomes functionally coupled with prefrontal executive function areas, even at rest.

Visual cortices of congenitally blind individuals are sensitive to executive demands in a non-verbal and non-spatial task

I find that in blindness, regions of the “visual” cortices are sensitive to non-verbal executive demands. These responses are functionally and anatomically distinct from several previously documented cross-modal effects. As noted in the introduction, “visual” cortices of blind individuals show sensitivity to linguistic information and to mathematical difficulty (Röder et al. 2002; Bedny et al. 2011; Lane et al. 2015; Kanjlia et al. 2016). However, the present stimuli were not linguistic or mathematical. Furthermore, previously observed “visual” cortex responses to language are on-average left-lateralized and responses to math were observed bilaterally (Bedny et al. 2011; Lane et al. 2015; Kanjlia et al. 2016). In contrast, executive-function responses observed in the current study are lateralized to the right-hemisphere. Furthermore, while mathematical responses were limited to the posterior “visual” cortices, executive function responses were observed laterally and medially, as well as posteriorly. Different cortical locations for executive function responses, compared to language or math responses, suggests functionally distinct repurposing in the “visual” cortices. Future work should test for functionally-selective sub-regions within the “visual” cortices of blind individuals, rather than at the group level.

Low-level sensorimotor demands are also unlikely to explain executive function responses in the “visual” cortices observed in the current study. First, the condition that elicited the most activity (i.e. no-go) had the highest executive demand but the lowest tactile feedback and motor planning demand. Second, I failed to find a response profile within the “visual” cortices of blind individuals akin to the response of sensorimotor cortices. Previous studies with blind participants have also failed to find “visual” cortex activity during low-level sensorimotor tasks, such as passive vibro-tactile stimulation, tactile sweeping of non-sense Braille without discrimination, and finger tapping, despite task recruitment of sensorimotor cortices (Sadato et al. 1996; Gizewski et al. 2003). Similarly, passively presented visual and tactile stimuli failed to elicit “auditory” cortex activity in a congenitally deaf participant, despite recruitment of primary visual and sensorimotor cortices, respectively (Hickok et al. 1997). Together with these prior results, our findings suggest that “visual” cortices are not likely to be repurposed for primary sensory-motor functions in blindness.

Finally, responses to executive demands observed in the current study are unlikely to be related to spatial processing. As noted in the introduction, previous studies have observed “visual” cortex responses during tasks that require localization— e.g. localization of sounds in space and discrimination of tactile patterns (Wanet-Defalque et al. 1988; Sadato et al. 1996; Merabet et al. 2004; Gougoux et al. 2005; Sathian and Stilla 2010; Collignon et al. 2011). By contrast, in the current experiment, auditory stimuli were not situated in space and the task did not require localization nor did the task involve fine-grained tactile discrimination. The present findings thus demonstrate that executive-demands influence visual cortex activity independent of spatial processing. I hypothesize that, in blindness, spatial processing engages different subsets of “visual” cortices as compared to executive, linguistic, and numerical processes.

In future work, it will be important to determine the precise nature of the executive operations that drive activity in deafferented “visual” cortices. Executive processes include a diverse set of operations, such as response selection, response inhibition, shifting attention, and saliency orienting. According to some views, these subtypes of executive control are dissociable within fronto-parietal cortices (Nagahama et al. 2001; Corbetta and Shulman 2002; Mostofsky et al. 2003; Rubia et al. 2003; Aron et al. 2004; Brass et al. 2005; Nee et al. 2007; Chikazoe et al. 2008; Goghari and MacDonald 2009; Chikazoe 2010; Levy and Wagner 2011; Xu et al. 2017). In the current study, “visual” cortices responded to both stimulus infrequency (infrequent-go and no-go) and response infrequency/inhibition (no-go). One possibility is that “visual” cortices are specifically sensitive to response inhibition, and that intermediate activity for the infrequent-go is reflective of participants “tapping the brakes” on their go response (as in a “continue” trial; (Aron et al. 2014)). Alternatively, the observed executive functions responses may reflect a response selection process that scales according to novelty of the stimulus-response mapping (i.e. frequent-go has both a habitual stimulus and a habitual response, infrequent-go has a novel stimulus but a habitual response, and no-go has both a novel stimulus and a novel response; (Chikazoe et al. 2008)). Whether the “visual” cortex contain dissociable response selection and response inhibition processes and whether it is sensitive to other types of executive processes are interesting avenues for future research.

Interestingly, in the current study I also observed responses to non-visual stimuli in the visual cortices of blindfolded, sighted adults. Importantly, these responses were functionally and anatomically distinct from those observed in the “visual” cortices of blind individuals. While the “visual” cortices of the blind group showed a graded executive demand response (with the highest response to no-go and the lowest response to frequent-go), the visual cortices of the sighted group showed selective high responses to the infrequent-go condition. Moreover, while “visual” cortex responses in the blind group were predominantly right-lateralized and extended along the medial, lateral, and ventral surface, visual cortex responses in the sighted group were bilateral and strictly localized to the calcarine sulcus (V1).

The cognitive role of visual cortex responses to non-visual stimuli in sighted individuals is not known. Some prior studies have also observed responses to non-visual stimuli in visual cortex of sighted subjects, for example, in participants who are trained to associate a visual flash with an auditory noise, visual cortex activity is observed during subsequent presentation of the noise alone (Sathian et al. 1997; Zangaladze et al. 1999; Macaluso et al. 2000; James et al. 2002; Merabet et al. 2004; Driver and Noesselt 2008; Merabet et al. 2008; Zangenehpour and Zatorre 2010). One possibility is that the visual cortex responses in sighted subjects observed in the current study reflect automatic orienting. It has been hypothesized that unexpected auditory stimuli elicit a “reflexive overt orienting response” towards the location of visual space where the stimulus is most likely to occur (Azevedo et al. 2015). According to this account, in the absence of further spatial information, there is automatic orienting to the center of the visual field and pre-activation of foveal V1 specifically in cases of planning a motor action and when the stimulus response mapping is not highly overlearned (i.e., as in infrequent-go). At present these interpretations are speculative and will require testing in future research. However, such effects are consistent with the idea that there are routes for non-visual information to reach “visual” cortex in blind and sighted alike and these routes are modified by absence or lack of visual experience.

Insights into the relationship of connectivity and function from “visual” cortex plasticity in blindness

Further support for the idea that, in blindness, parts of right “visual” cortices are incorporated into fronto-parietal executive function networks comes from resting state data. The executive-function responsive “visual” cortex of blind individuals was coupled with executive-load responsive prefrontal cortices. Specifically, blind and sighted groups displayed different profiles of functional connectivity for the occipital cortex area in which executive-function responses were observed in blindness. In the sighted group, executive-function responsive visual cortex was more correlated with non-visual sensory-motor areas (A1 and M1/S1) than with prefrontal cortices. Conversely, in the blind group, executive-function responsive “visual” cortex was more correlated with prefrontal cortices than with non-visual sensory-motor areas. This change in connectivity was driven both by a reduction in resting state correlations with A1 and S1/M1 as well as an increase in correlations with prefrontal cortices in blindness. This result is consistent with prior studies, which have also found reduced connectivity of “visual” cortices, in blindness, to A1 and to sensory-motor cortices (Liu et al. 2007; Yu et al. 2008; Wang et al. 2013; Burton et al. 2014; Bedny et al. 2011). By contrast, resting-state synchrony between “visual” cortices and frontal-parietal cortices is increased in blindness (Liu et al. 2007; Bedny et al. 2010; 2011; Wang et al. 2013; Burton et al. 2014; Deen et al. 2015; Liu et al. 2017).

Importantly, among prefrontal regions, executive-load responsive “visual” cortex was more correlated with executive-function responsive prefrontal cortex, than with language responsive prefrontal cortex, and this effect was specific to the blind group. This result supports the hypothesis that the executive load responsive “visual” areas identified in the present study are functionally distinct from previously identified language-responsive visual areas. Analogously, previous studies have found that prefrontal language areas are more synchronized to the parts of “visual” cortices that respond to language than to the parts of “visual” cortices that respond to math (Kanjlia et al. 2016). These results demonstrate that resting-state connectivity and functional specialization within “visual” cortex go hand in hand in blindness.

3.5 Summary

In Chapter 3, I used a non-verbal auditory go/no-go task to ask whether visual cortices of congenitally blind individuals are recruited for higher-cognitive executive functions in the absence of language. In congenitally blind individuals, right-lateralized “visual” cortices responded to executive-function demands. These right-lateralized occipital cortices of blind, but not sighted, individuals mirrored the executive-function pattern observed in fronto-parietal systems. In blindness, the same “visual” cortex area, at rest, also increased its synchronization with prefrontal executive control regions and decreased its synchronization with auditory and sensorimotor cortices. Executive function represents a previously undiscovered higher cognitive function in “visual” cortices of blind individuals. Together with Chapter 2, Chapter 3 supports the pluripotency hypothesis of top-down fronto-parietal takeover of “visual” cortices, and suggests that human cortex is highly flexible at birth.

3.6 Supplementary Materials

Supplementary Results.

I also looked for a sensorimotor response in the bilateral medial visual cortex (in case effects were lateralized, as in the sensorimotor cortices). Results were similar to those obtained in the right visual cortex. No sensorimotor effect was found in the bilateral “visual” cortices of blind participants (Supplementary Figure 5; frequent-go vs no-go $t(18)=0.36$, $p>0.5$; infrequent-go vs no-go $t(18)=2.09$, $p=0.051$; frequent-go vs. infrequent-go $t(18)=2.26$ $p=0.03$). In the sighted group, the visual cortices responded more to the two button press conditions (Supplementary Figure 5, frequent-go vs no-go $t(18)=2.20$, $p=0.04$; infrequent-go vs no-go $t(18)=2.27$, $p=0.04$; frequent-go vs. infrequent-go $t(18)=0.06$ $p>0.5$).

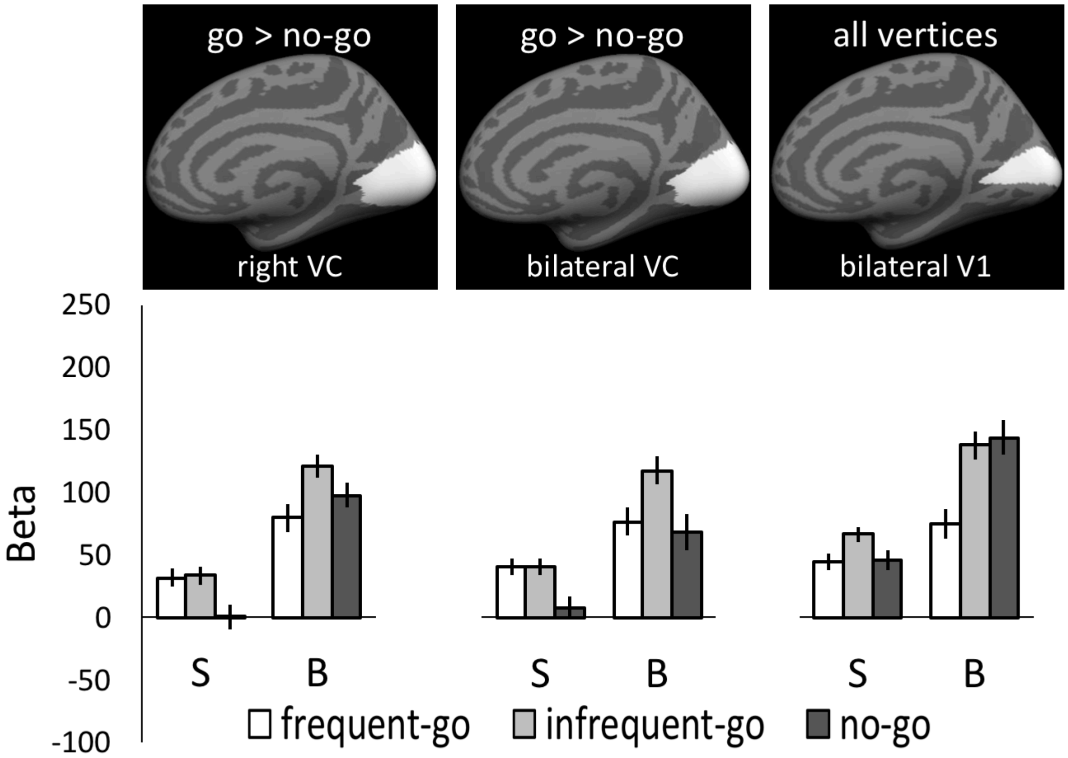
In bilateral V1 (across all vertices), I observed preferential activity for the infrequent-go condition within the sighted group (Supplementary Figure 5; infrequent-go vs frequent-go $t(18)=2.45$, $p=0.03$; infrequent-go vs no-go $t(18)=1.73$, $p=0.10$; no-go vs. frequent-go $t(18)=0.08$ $p>0.5$). In contrast, bilateral V1 of the blind group responded preferentially to both infrequent conditions (Supplementary Figure 5; infrequent-go vs frequent-go $t(18)=3.42$, $p=0.003$; no-go vs. frequent-go $t(18)=2.89$ $p=0.01$; infrequent-go vs no-go $t(18)=0.26$, $p>0.5$).

Supplementary Table 3. Cortical Locations of Activation for Go/No Task

Brain regions differentially active across conditions, from cluster-corrected whole-brain analysis. Rows represent extrema, each characterized by a Destrieux Atlas gyral/sulcal name, an X- Y- and Z- MNI coordinate, and a t-stat(istic). Extrema are part of clusters, each of a mm^2 size and a cluster-wise permutation probability. Extrema without listed cluster information are part of the preceding characterized cluster.

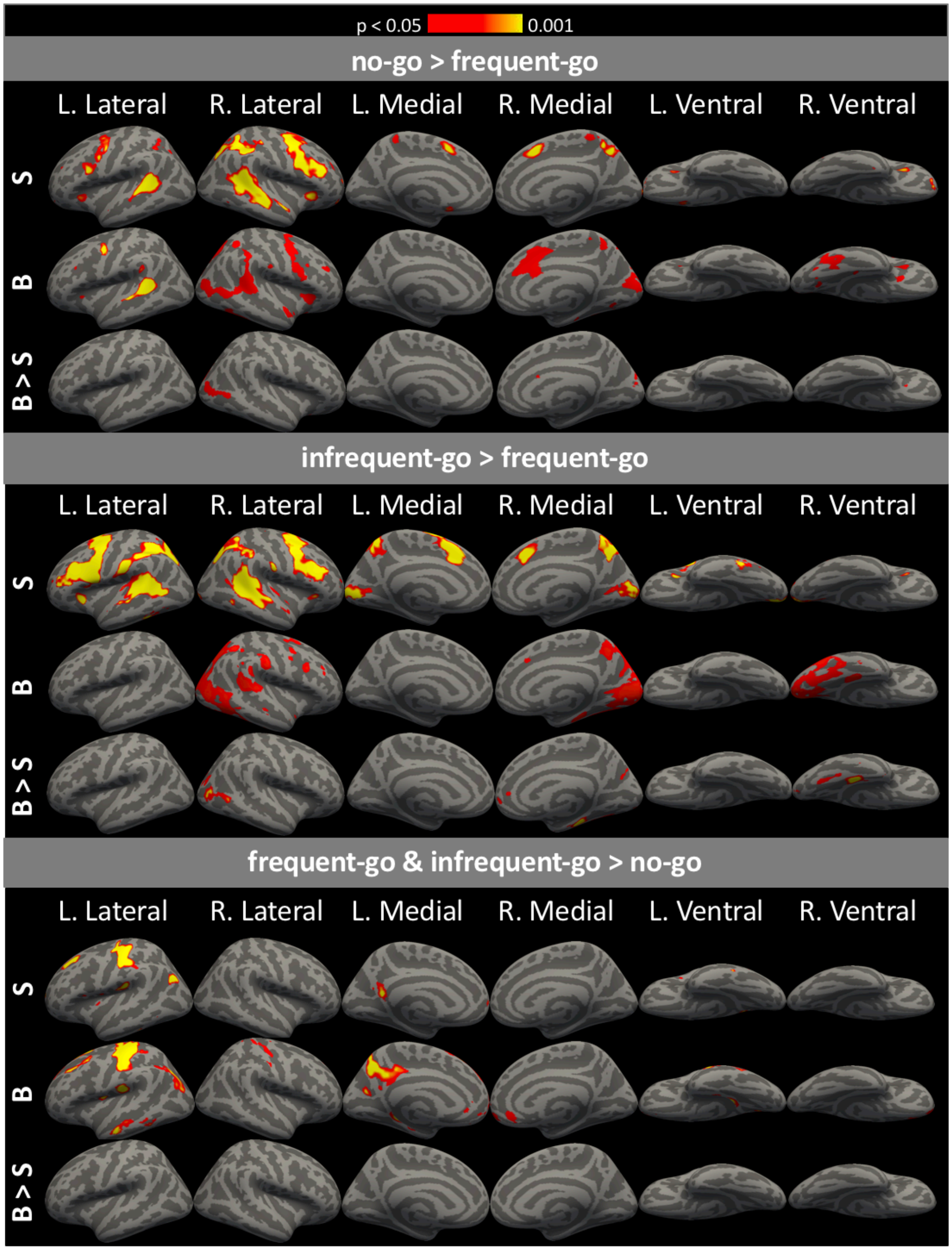
Brain region	X	Y	Z	t-stat	mm^2	cwp
no-go > frequent-go						
Sighted						
L. Inferior frontal sulcus	-39	9	24	5.26	1569	0.017
L. Superior precentral sulcus	-27	-4	46	4.44		
L. Superior temporal gyrus	-64	-41	7	7.93	1195	0.036
R. Superior precentral sulcus	40	-2	45	6.39	2807	0.003
R. Inferior precentral sulcus	40	4	27	5.86		
R. Middle frontal gyrus	48	29	25	5.08		
R. Sulcus intermedius primus (of Jensen)	44	-45	37	6.20	2459	0.004
R. Superior parietal lobule	34	-52	62	5.46		
R. Precuneus	5	-51	54	4.37		
R. Postcentral gyrus	47	-27	53	3.89		
R. Superior temporal sulcus	58	-41	13	5.68	2414	0.004
R. Lateral superior temporal gyrus	56	-1	-14	4.97		
Blind						
R. Superior temporal sulcus	56	-39	9	5.24	1975	0.010
R. Middle temporal gyrus	51	-61	3	4.82		
R. Supramarginal gyrus	52	-41	44	4.41		
R. Middle occipital sulcus	33	-81	9	4.12		
R. Superior precentral sulcus	41	-1	47	4.26	1539	0.013
R. Inferior precentral sulcus	49	6	25	3.63		
R. Superior frontal sulcus	24	1	58	3.48		
R. Middle-anterior cingulate gyrus/sulcus	10	15	42	4.80	1164	0.030
R. Cuneus	4	-75	12	4.07	1135	0.030
Blind > Sighted						
R. Inferior temporal sulcus	49	-61	3	5.19	2630	0.006
R. Middle occipital sulcus	33	-81	9	4.81		
R. Superior occipital sulcus	21	-91	20	4.25		
R. Cuneus	6	-82	16	3.81		
infrequent-go > frequent-go						
Sighted						
L. Inferior precentral sulcus	-47	-1	34	8.29	4691	< 0.001
L. Middle-anterior cingulate gyrus/sulcus	-9	15	50	8.16		
L. Inferior frontal sulcus	-38	22	22	7.22		
L. Superior frontal gyrus	-17	3	69	6.55		
L. Intraparietal sulcus	-35	-49	49	6.96	3088	0.002
L. Supramarginal gyrus	-58	-24	27	6.44		
L. Intraparietal sulcus	-27	-66	39	6.41		
L. Precuneus	-10	-58	55	4.52		

L. Planum temporale	-64	-36	13	8.22	2182	0.007
R. Superior frontal sulcus	25	1	48	7.16	2756	< 0.001
R. Inferior precentral sulcus	41	3	41	6.92		
R. Inferior frontal sulcus	40	21	27	6.49		
R. Precuneus	5	-62	40	5.85	2578	0.001
R. Superior occipital sulcus	28	-66	28	5.80		
R. Superior parietal lobule	33	-53	61	4.59		
R. Supramarginal gyrus	57	-39	45	4.01		
R. Superior temporal sulcus	54	-44	4	8.23	2254	0.003
R. Planum temporale	63	-31	12	6.82		
R. Cuneus	7	-88	6	4.83	1036	0.036
Blind						
L. Cuneus	-7	-98	11	5.37	2438	0.004
L. Superior occipital gyrus	-20	-85	37	3.54		
L. Superior temporal gyrus	-65	-39	7	3.96	1254	0.026
L. Supramarginal gyrus	-58	-27	31	3.83		
L. Intraparietal sulcus	-23	-64	50	4.19	977	0.044
L. Precuneus	-8	-51	45	3.77		
R. Inferior temporal gyrus	57	-58	-14	5.32	8336	< 0.001
R. Calcarine sulcus	15	-78	10	5.13		
R. Superior parietal lobule	15	-69	55	4.98		
R. Superior occipital gyrus (O1)	17	-88	25	4.38		
R. Precuneus	8	-57	43	4.34		
R. Lateral fusiform gyrus	29	-61	-15	3.73		
Blind > Sighted						
L. Middle occipital gyrus	-27	-96	12	4.07	1377	0.024
L. Superior occipital gyrus	-20	-87	36	3.85		
R. Middle occipital gyrus	48	-78	9	4.69	2483	0.004
R. Middle temporal gyrus	52	-58	1	4.46		
R. Superior occipital sulcus	34	-80	18	4.24		
R. Parieto-occipital sulcus	19	-73	23	3.98		
R. Superior occipital sulcus	19	-87	24	3.95		
R. Medial collateral and lingual sulcus	34	-25	-22	5.95	1423	0.017
R. Lateral fusiform gyrus	28	-63	-14	3.95		
frequent-go + infrequent-go > no-go						
Sighted						
L. Postcentral gyrus	-53	-17	52	9.78	2136	0.004
Blind						
L. Postcentral gyrus	-38	-33	66	11.81	3063	0.004
R. Postcentral gyrus	27	-32	71	6.12	1537	0.014
R. Central sulcus	34	-21	43	5.14		
R. Precentral gyrus	26	-19	71	3.89		
Blind > Sighted						
N/A						



Supplementary Figure 5. Region of Interest Analysis for Go/No-Go Task, Additional Contrasts

Beta values for task conditions within sighted (S) and congenitally blind (B) participants’ medial visual cortex (VC) and primary visual cortex (V1). Error bars indicate the within-subjects SEM. Right and bilateral VC values are reported from a leave-one out analysis where vertices were chosen based on the contrast frequent-go + infrequent-go > no-go (similar to those reported in the bilateral SMC). Bilateral V1 values were chosen from the entire V1 search-space.



Supplementary Figure 6. Go/No-Go Activations II

FDR-corrected whole brain contrasts for sighted (S), blind (B), and blind > sighted (B > S). p-values are FDR-adjusted.

Chapter 4

Behavioral relevance of higher cognitive responses in “visual” cortices

4.1 Introduction

In Chapter 2, I find evidence of widespread higher cognitive functions across “visual” cortices of blind individuals. In Chapter 3, I find evidence that, in addition to math and language, “visual” cortices are recruited for executive-function. A key open question, therefore, is whether this extra “visual” cortex territory confers a behavioral advantage to the higher-order cognitive functions that it implements.

A large body of evidence suggests sensory behavioral advantages associated with blindness. For example, blind individuals are more accurate than sighted controls at judging whether an auditory pitch is falling or rising, and blind individuals outperform sighted individuals at detecting orientations of tactually-presented gratings (Van Boven et al. 2000; Goldreich and Kanics 2003; Gougoux et al. 2004; Rokem and Ahissar 2009; Wan et al. 2010; Wong et al. 2011). These improvements are not ubiquitous, but specific to a subset of perceptual tasks (Lewald 2002; Alary et al. 2009). For instance, blind individuals are more accurate than sighted individuals at localizing sounds in peripheral, but not central, space. Blind individuals also have improved tactile acuity on the Braille-reading finger, but not on the lips (Roder et al. 1999; Wong et al. 2011). Critically, some of the tasks on which blind individuals outperform the sighted – e.g. auditory localization and fine-grained tactile discrimination – are also associated with “visual” cortex plasticity (Kujala et al. 1992; Roder et al. 1999; Weeks et al. 2000; Gougoux et al. 2005; Collignon et al. 2008; Voss et al. 2008; Collignon et al. 2011). One possibility, therefore, is that recruitment of “visual” cortices for non-visual tasks enhances performance. If so, the same might be true of observed higher cognitive function in “visual” cortices of blind individuals. However, it is also possible that sensory loss in one modality selectively improves abilities to extract information from other modalities on account of practice induced changes to non-visual sensory cortices.

Nevertheless, temporary-lesion studies of “visual” cortices suggest that “visual” cortices are functionally relevant. Transiently disrupting “visual” cortex function with transcranial magnetic stimulation (TMS) can impair performance. For example, TMS to the occipital pole causes subjects to make semantic errors when generating verbs nouns heard nouns (i.e. “kick” for “ball”) and to misread Braille letters (Cohen et al. 1997; Amedi et al. 2004). Deaf cats perform better than normal cats at localization of peripheral visual stimuli, and there is some evidence that this benefit is mediated by repurposing of “auditory” cortices (Lomber et al. 2010; Meredith et al. 2011). However, the functional relevance of such cortical tissue for higher cognitive functions has yet to be determined. Moreover, even if “visual” cortices are meaningfully incorporated into behavior, the extra cortical tissues need not confer any advantage. For higher cognitive functions, specifically, amount of cortical tissue may not meaningfully impact processing competence.

Notably, evidence from another higher cognitive domain – memory – suggests that extra “visual” cortex tissue may indeed improve performance. Blind individuals activate “visual” cortex during higher cognitive verbal memory tasks, such as retrieving previously encoded words from long-term memory, and the amount of visual cortex activity predicts memory performance (Amedi et al. 2003; Raz et al. 2005). Importantly, blind children and adults outperform sighted individuals on memory tasks, recalling larger numbers of words, letters and digits over both short and long delays and more accurately reproducing the serial order of encoded words (Tillman and Bashaw 1968; Hull and Mason 1995; Roder et al. 2001; Amedi et al. 2003; Raz et al. 2007; Rokem and Ahissar 2009; Swanson and Luxenberg 2009; Pasqualotto et al. 2013; Withagen et al. 2013; Dormal et al. 2016). Moreover, there is some evidence to suggest that, amongst blind individuals, greater “visual” cortex activity during recall is associated with better performance on memory tasks (Amedi et al. 2003; Raz et al. 2005).

“Visual” cortex plasticity data suggests that blind individuals may also show superior high-level linguistic abilities that are critical for computing complex syntactic structures (Lane et al. 2015), as well as improved response inhibition (Chapter 3). “Visual” cortices are active during spoken sentence processing tasks and the amount of activity varies as a function of meaning and syntactic structure: “visual” cortices respond more to sentences than lists of unconnected words, more to sentences than Jabberwocky, and more to Jabberwocky than to lists of non-words (e.g., glorf, blig, marp, …) (Röder et al. 2002;

Burton et al. 2003; Bedny et al. 2011). Furthermore, larger “visual” cortex responses are observed for grammatically complex sentences with a syntactic long-distance dependency (e.g., “The girl, that the boy admires, is vacationing in Spain”) (Röder et al. 2002; Lane et al. 2015). Finally, blind participants who show larger “visual” cortex responses to sentences also show superior performance at answering comprehension questions about complex sentences (Lane et al. 2015). Analogously, Chapter 3 finds evidence of executive function responses in the “visual” cortices of blind individuals.

Critically, language and executive function responses in “visual” cortices appear to be integrated into pre-existing language and executive-function networks, respectively. Language-responsive parts of “visual” cortex show synchronized activity with fronto-temporal language areas, even in the absence of a task (Bedny et al. 2011; Deen et al. 2015). Additionally, “visual” cortex responses to language are co-lateralized with fronto-temporal language areas, suggesting incorporation of “visual” cortices into language networks (Lane et al. 2017). Similarly, executive-function responsive parts of “visual” cortex show synchronized activity with fronto-parietal executive-function networks, and executive function responses in “visual” cortices are also co-lateralized with executive-function responses in fronto-parietal cortices (Chapter 3). This suggests that executive-function responsive “visual” cortices may also be incorporated into executive-function networks. More broadly, integration into pre-existing brain networks suggests that visual cortex plasticity may be relevant to behavior.

It is currently unknown whether language responses in “visual” cortices of blind individuals improve linguistic processing. Previous studies of blind people’s linguistic behavior have focused on whether blind individuals have superior speech perception and word recognition abilities but have not examined higher-order aspects of language (i.e. syntax and semantics). Indeed, blind adults are better than the sighted at identifying syllables in a task of dichotic listening (Hugdahl et al. 2004) and at identifying words under high-noise conditions (Muchnik et al. 1991). Two studies also suggest faster lexical access among individuals who are blind. One study found faster lexical decision times for spoken words and non-words among blind individuals (Röder et al. 2003). Blind individuals also show a faster onset of the N400 event-related potential component upon encountering an incongruent word at the termination of a sentence—e.g. “Tomorrow Bobby will be ten years hill” (Roder et al. 2000). All of these results have been interpreted as evidence for more efficient perceptual speech processing.

Similarly, it is currently unknown whether visual cortex plasticity confers a benefit to response inhibition. In the go/no-go task tested, the blind group were faster and more accurate, on average, than the sighted group, but this difference did not reach significance. One possibility is that blind participants failed to outperform sighted participants because vision groups were not accurately matched on age. Although average ages of blind and sighted groups were equivalent, the blind group had more older participants. Because response-inhibition performance declines with age (Sebastian et al. 2013), the larger age variability of the blind group may have masked any possible “visual” cortex benefit. Another possibility is that blind individuals need a more demanding version of the response-inhibition task to demonstrate performance improvements.

Although no one has of yet found response inhibition improvements in blindness, there is some evidence that blind individuals outperform sighted individuals in a related task of bi-modal divided attention (Collignon et al. 2006). Blind participants are faster than sighted participants when asked to selectively detect the combination of a right-sided sound and a left-sided pulse. However, evidence for such attentional benefits is scarce and the neural mechanisms for response inhibition may be distinct from those for other cognitive control processes such as divided attention (Aron et al. 2004; 2015). Therefore, it is currently unknown whether any benefit is conferred from recruitment of “visual” cortices during tasks of response inhibition.

The goal of the current study was to directly test the hypothesis that blind individuals develop superior abilities in two higher-cognitive domains that are known to recruit the “visual” cortices: sentence processing and response inhibition. I measured accuracy and reaction time while blind individuals answered yes/no comprehension questions based on spoken sentences that varied in syntactic complexity. Syntactic complexity was manipulated in two independent ways, by introducing syntactic movement and creating garden paths. Sentences with syntactic movement displace referents from related information—e.g. “The actress that the creator of the gritty HBO crime series admires often improvises her lines.” Garden path sentences exploit semantic associations and ambiguous verb phrases to mislead the listener to form an erroneous syntactic parse. For example, in the garden-path sentence “While the little girl dressed the doll that she was playing with sat on the floor of her bedroom,” the little girl is dressing herself, rather than the doll. Performance on syntactically complex sentences was compared to matched control sentences. I hypothesized that blind individuals would show superior sentence-comprehension ability relative to the sighted and that this advantage would be most pronounced for syntactically complex sentences.

I measured executive function via a non-verbal go/no-go task. Participants heard non-verbal complex sounds that required either a quick button press (“go” response, within 900 MS) or no button press (“no go” response). Go trials were much more frequent (75%) than no-go trials (25%). Since go trials are more frequent and fast, go-ing becomes pre-potent and no-go trials require inhibition. Previous studies have shown that on no-go trials participants make errors of commission, erroneously going, and activate executive control networks during (Garavan et al. 1999; Aron et al. 2014). The task was intentionally designed to tap into non-language related aspects of executive function, unlike language-related executive tasks such as the STROOP or ambiguous word comprehension (Bedny et al. 2008; January et al. 2009). The goal was to determine whether, blind individuals show independent enhancements on non-verbal executive function and language.

Finally, I measured short term memory for spoken letters, in blind and sighted participants. The goal was to replicate the previous finding that blind participants show enhancements in verbal working memory and to determine whether these enhancements are related to improvements in language or non-verbal executive control (Hull and Mason 1995; Amedi et al. 2003).

Importantly, different higher-cognitive functions, such as language, math, and response inhibition activate different parts of the “visual” cortex (Lane et al. 2015; Kanjlia et al. 2016), and Chapter 3). Furthermore, these different “visual” areas show enhanced functional connectivity to the specific fronto-parietal network with which they share functionality (Kanjlia et al. 2016 and Chapter 3). Therefore, in addition to testing for improvements in language and response inhibition, I was also interested in assessing the behavioral relationship between these cognitive functions. Distinct neural responses for language and executive function within the “visual” cortices of blind individuals suggest that any behavioral improvements conferred by this extra cortical tissue will be unrelated.

Blind and sighted participants were also tested on a series of control tasks, including a symbolic math task and verbal portions of the Woodcock-Johnson III, which test skills such as vocabulary and reading ability. These tasks enabled me to test the specificity of higher-cognitive enhancements. I predicted that sentence-processing advantages and working memory advantages in blind individuals would persist, even when blind and sighted groups are matched on other cognitive abilities.

4.2 Materials and Methods

Participants.

25 congenitally blind individuals (15 female) and 52 sighted age and educated matched controls (36 female) contributed data on the sentence processing tasks (age: blind mean=32.64, SD=9.86; sighted mean=33.31, SD=11.51; blind vs. sighted t(75)=-0.25, p=0.80; years of education: blind mean=16.68, SD=2.61, sighted mean=16.59, SD=2.20; blind vs. sighted t(75)=0.15, p=0.88). Almost all of these participants also contributed working memory, arithmetic, and WJIII data (missing data are marked on Table 3). Only

10 blind (7 female) and 19 (14 female) sighted participants took part in the go/no-go task (age: blind mean=28.90, SD=8.96; sighted mean=34.37, SD=10.75; blind vs. sighted t(27)=1.37, p=0.18; years of education: blind mean=16.10, SD=3.31, sighted mean=16.89, SD=2.71, blind vs. sighted t(27)=0.70, p=0.49).

Task Category	Task	CB (N)	S (N)
WJ-III	Word Letter ID	25	52
	Word Attack	25	52
	Synonyms	25	52
	Antonyms	25	52
	Analogies	24	52
Arithmetic	Subtraction	25	52
	Division	24	52
Working Memory	Forward Span	25	51
	Backward Span	25	51
Language	Sentences	25	52
Executive Function	Go/No-Go	10	19

Table 3. Number of Participants per Behavioral Task for Chapter 4

N(umber) of Congenitally Blind (CB) and Sighted (S) participants per task

2 blind and 2 sighted participants were excluded for poor performance on the Woodcock-Johnson III (outliers on any individual measure, defined according to Rosner’s extreme studentized deviate test for multiple outliers, two-sided, $p < 0.05$, maximal 10 (Rosner 1975)). Reported numbers of blind and sighted participants do not include these excluded participants.

All participants were native or near-native English speakers, with 1 (of 25) blind and 3 (of 52) sighted having learned English between 3 and 4 years of age. Data was collected from blind participants at two separate conventions of the National Federation for the Blind (2014 and 2016). Sighted participants were tested at Johns Hopkins University. Blind participants had minimal-to-no light perception since birth, due to pathologies in or anterior to the optic chiasm (see Table 4). All participants reported no cognitive or neurological disabilities. Since premature birth is sometimes associated with cognitive disabilities (Dann et al. 1964), participants who were blind due to retinopathy of prematurity (ROP) were not included in the study.

All participants were native or near-native English speakers, with 1 (of 25) blind and 3 (of 52) sighted having learned English between 3 and 4 years of age, which is considered to be well within the critical period for language acquisition (Johnson and Newport 1989).

To match visual conditions across groups, sighted participants were blindfolded for all tasks except for the participant-read portions of the Woodcock Johnson-III (WJ-III). Participants listened to all auditory tasks via headphones. Volume was adjusted for each participant, according to their own comfortable listening volume. All experiments were run using either PsychoPy or Matlab’s Psychtoolbox (Brainard 1997; Peirce 2007).

Blindness Etiology	**N**	**N LP**
Leber Congenital Amaurosis	9	5
Glaucoma	3	1
Optic Nerve Hypoplasia	6	1
Anopthalmia	3	0
Micropthalmia	2	0
Retinal Blastoma	1	1
Septo-optic dysplasia	1	0

Table 4. Blindness Etiology for Chapter 4 Participants

Per cause of blindness, total N(umber) of participants and N(umber) with light perception (LP).

Sentence processing task: materials and procedure.

Participants listened to sentences (n=180) and answered a yes/no comprehension question for each sentence (see Table 5). Participants had 6 seconds from the onset of the question to make a button press. I removed all trials in which a participant either failed to respond or false started (i.e. responded in < 150 MS). On average, blind and sighted participants missed fewer than 1 question per each condition (overall misses: mean blind 1.48 items; mean sighted 1.92 items; n.s. difference between groups $t(75)=0.92$, $p=0.36$). Sighted participants had more missed responses than blind participants, but this difference was not significant (move: $t(75)=0.66$, $p>0.5$; non-move: $t(75)=1.25$, $p=0.21$; garden-path: $t(75)=1.75$, $p=0.08$; non-garden path: $t(75)=0.61$, $p>0.5$).

The dependent measure was accuracy (binary success or failure on each trial) and speed (reaction-time, from question onset, for correct trials only). The syntactic complexity of sentences was manipulated in two ways: by introducing a long-distance dependency or a garden path syntactic ambiguity. Each of these two conditions was paired to a matched, control condition that lacked the critical syntactic manipulation—i.e. no-move and non-garden path sentences (see Table 5). In addition to the critical sentences, I included filler sentences. In order to avoid syntactic priming, fillers varied in their grammatical constructions and did not contain either long-distance dependencies or garden paths. Overall there were: 60 move, 60 no-move, 10 garden path, 10 non-garden path, and 40 filler trials. A subset of initial participants (5 blind and 13 sighted; proportion of total approximately matched across groups) received a longer version of the paradigm with 248 total questions, consisting of 84 move, 84 no-move, 10 garden path, 10 non-garden path, and 60 filler trials. The experiment was subsequently shortened to reduce testing time. To control for item effects, only the items that appeared in the short-form were analyzed—i.e., 60 of 84 move and 60 of 84 non-move— for the participants who received the longer version of the paradigm.

Move	The actress that the creator of the gritty HBO crime series admires often improvises her lines.
No-Move	The creator of the gritty HBO crime series admires that the actress often improvises her lines.
Garden-Path	While the little girl dressed the doll that she was playing with sat on the floor of her bedroom.
No Garden-Path	While the nanny dressed the baby that was small and cute the baby's mother was in the kitchen preparing dinner.
Filler	The precocious child thought that that the rude waitress's purple cotton dress and orange shoes clashed horribly.

Table 5. Sample Sentence Comprehension Items

Sentences with syntactic movement contain words or phrases that are displaced, or "moved," with respect to their modifying phrases. Syntactic movement was achieved via object-extracted relative clauses, where the "actress," as the object of the verb "admires," is extracted from its normal position after the transitive verb and moved to the head of the relative clause. The non-movement counterpart used a sentential complement clause structure, which was similar in meaning to the relative clause version and contained nearly identical words but did not include a long-distance movement dependency. Matched movement and non-movement sentences were counterbalanced across two lists, such that each participant heard only one version of the sentence. Comprehension questions required participants to attend to thematic relations of words in the sentence (i.e., who did what to whom), and could not be answered based on recognition of individual words. Half of the move and half of the non-move stimuli had comprehension questions in which “yes” was the correct response. The stimuli were a subset of those used in a previously published study in our lab (Lane et al. 2015).

The second type of syntactic complexity manipulation was garden path sentences with temporary syntactic ambiguities. The listener is led down a “garden-path” in which an initially favored sentence parse turns out to be irreconcilable with subsequent words in the sentence. “Dressed” can be transitive with “the doll” as the direct object (i.e. the little girl dressed the doll) or reflexive (i.e. the little girl dressed *herself*). While the former interpretation is usually favored due to its higher subcategorization frequency, the subsequent verb “sat” requires “the doll” to be its subject, and hence disambiguates the two alternatives in favor of the reflexive form. I added a relative clause modifier to the critical, ambiguous noun phrase in order to amplify the garden-path effect (Ferreira and Henderson 1991; Christianson et al. 2001). All garden path sentences were of the following form: While [Noun Phrase 1] [Reflexive Verb] [Noun Phrase 2] [Verb Phrase]. Non-garden path control sentences were formatted as follows: While [Noun Phrase 1] [Transitive Verb] [Noun Phrase 2] [Noun Phrase 3] [Verb Phrase]. The additional [Noun Phrase 3] requires the ambiguous verb to be transitive, consistent with the listener’s initial parse. Unlike the control sentences for the movement manipulation, the non-garden path sentences were not lexically matched across individual garden path conditions. Sentences across the 2 conditions contained different words and had distinct meanings, but followed the same structure templates, with the exception of the additional Noun Phrase in non-garden path sentences. All questions tested correct comprehension of the verb, in the format: Did [Noun Phrase 1] [Reflexive/Transitive Verb] [Noun Phrase 2]? For example, “Did the little girl/nanny dress the doll/baby?” Therefore, the correct response for garden path and non-garden path control questions was always “no” and “yes,” respectively. Sentences were adapted from a published set of stimuli (Christianson et al. 2001).

Condition ordering, across trials, was pseudo-randomized such that each condition could not appear in more than 2 contiguous trials, and the conditions were evenly dispersed across each 1/8th block of the experiment. For half of the trials the correct response was “yes.” Before starting, all participants performed a set of 10 practice trials with feedback. Sentences were pre-recorded and spoken by a male voice in a flat intonation, in order to minimize cues to correct syntactic parsing.

Working-memory tasks.

Forward and Backward Letter Span tasks were adapted from the Forward and Backward Digit Span components of the Wechsler Adult Intelligence Scale (WAIS) by mapping the digits 1-9 to the letters A-I. For both letter span tasks, participants listened to a recording of a female speaking a series of letters. After the last presented letter, participants were asked to repeat all letters back to the experimenter in either the exact order (Forward) or the exact opposite order (Backward). Trials were presented according to span-length, starting with a length of 2 and going up to 9 (for Forward) and 8 (for Backward), with 2 trials for each span length. Failure to get both trials of a given span length correct terminated the task. Accuracy was calculated as a percentage correct out of all possible trials, with incorrect recall assumed for un-tested spans. All participants did the Forward Letter Span followed immediately by the Backward Letter Span.

Executive-function task.

Participants heard complex non-verbal sounds (450 MS with 450 MS ISI; 400 trials), each representing 1 of 3 conditions: frequent-go (50% trials), no-go (25%), and infrequent-go (25%). Participants were instructed to make speeded button presses in response to go sounds and to withhold responses to no-go sounds. The high proportion of go sounds and fast pace induced a pre-potent button-press response that had to be inhibited during the no-go condition. Prior to the task, participants received 7.5 minutes of practice with auditory feedback on accuracy. Assignment of sounds to conditions was counterbalanced across blind participants. The majority of sighted participants received 1 sound ordering.

In keeping with Woodard et al. (2016), I used “no-go cost” as our measure of executive function. No-Go cost was calculated as the difference between omissions on frequent-go trials and successful inhibition on no-go trials. Therefore, a low “no-go cost” (i.e. better performance) is associated with smaller numbers (i.e. higher magnitude negative values). Because infrequent-go may be intermediate in executive demands, I chose to exclude infrequent-go performance in our baseline measure of “going” performance.

I also computed d’ as a composite measure of going discrimination defined—i.e., the difference between the standard score for the proportion of going on frequent-go sounds and the standard score for the proportion of going on no-go sounds (Green and Swets 1966).

Woodcock-Johnson III (control).

I collected control measures to ensure that blind and sighted groups did not differ on general cognitive abilities. Participants were tested on 5 sections of the Woodcock-Johnson III (WJ-III). Blind participants completed the WJIII in printed Braille. The following sections were tested: Letter-Word Identification in which the participant are asked to read and correctly pronounce 60 English words (e.g. “bouquet”); Word Attack in which the participant read and correctly pronounce 33 nonsense words (e.g. “paraphonity”); Oral Vocabulary-Synonyms in which the participant read each of 12 words and generate a synonym (e.g. “wild” → “untamed”); Oral Vocabulary-Antonym in which the participant read each of 13 words and generate an antonym (e.g. “authentic” → “fake”); and Oral Vocabulary-Analogies in which participants read each of 12 incomplete analogies and generate a word analogous to the unpaired word according to the relationship established by the first word pair (e.g. “Wrist is to shoulder, as ankle is to …” → “hip”). Participants were allowed to skip any items they could not complete but were not allowed to go back. Responses were considered correct if they matched one of the words designated by the WJ-III. Accuracy for each section was scored as percentage correct of all trials. All participants performed the WJ-III sections in the order listed above.

Arithmetic (control).

Participants were tested on speeded arithmetic calculations in 2 separate tasks:

subtraction and division. All problems contained 2 operands, with the following digit lengths: minuends and subtrahends (2), divisors (1), and dividends (2-3). For each task, participants were given 4 minutes to accurately complete as many problems as possible. (Participants were allowed to complete any problems begun before the 4 minutes had expired.) Problems were pre-recorded to minimize differences in presentation between participants. Participants pressed a button to initiate auditory presentation of each problem and had to state their answer to the researcher. Participants could choose to skip problems and to repeat auditory presentation of the current problem but were not allowed to go back to skipped problems. Participants were not allowed to use writing devices to solve the problems. The subtraction and division sections contained 30 and 33 problems, respectively. Accuracy was scored as percentage correct of all trials, regardless of whether they were attempted. All participants performed the subtraction task immediately before the division task. Problems were taken from the Kit of Factor-Referenced Cognitive Tests (Ekstrom et al. 1976).

4.3 Results

WJ-III and arithmetic (control).

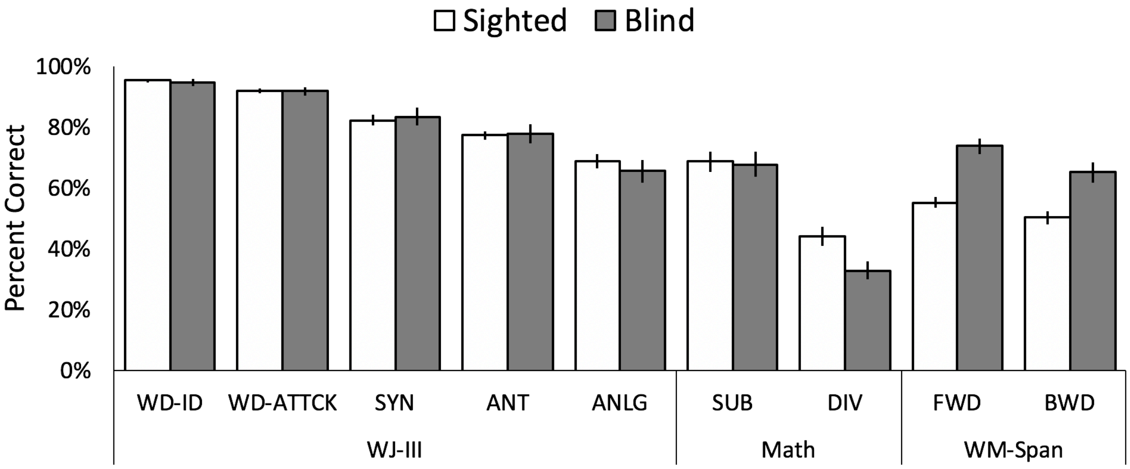


Figure 7. Performance on Woodcock-Johnson III, Arithmetic, and Working-Memory Tasks

Mean accuracy for the sentence comprehension subset of sighted and blind participants in Woodcock-Johnson III measures—Word Letter Identification (WD-ID), Word Attack (WD-ATTCK), Synonyms (SYN), Antonyms (ANT), and Analogies (ANT), arithmetic—subtraction (SUB) and division (DIV), and working memory span—forward (FWD) and backward (BWD). Error bars reflect SEM.

Blind and sighted participants performed equivalently on the WJ-III subsections (Figure 7, group x WJ-III measure ANOVA, main effect of group not significant, F(1,74)=0.05, p>0.5; group x measure interaction not significant, F(4,296)=0.49, p>0.5). For the math tasks, a group by operation (division vs. subtraction) ANOVA revealed a main effect of math operation with division more difficult than subtraction (Figure 7, F(1,74)=185.81, $p < 0.001$). Overall, blind and sighted participants did not differ in their math performance (Figure 7, main effect of group not significant, F(1,74)=1.29, p=0.26). However, there was a significant interaction between group and math-operation with blind participants differentially worse at division (F(1,74)=7.05, p=0.01).

The subset of blind and sighted participants who performed the executive function task also performed equivalently on the WJ-III subsections (Figure 7, group x WJ-III measure ANOVA, main effect of group n.s., F(1,27)=0.30, $p>0.5$; group x measure interaction n.s., F(4,108)=1.15, p=0.34). For the math tasks, a group by operation (division vs. subtraction) ANOVA revealed a main effect of math operation with division more difficult than subtraction, F(1,26)=92.12, $p<0.001$). Overall, blind and sighted participants did not differ in their math performance (n.s. main effect of group, F(1,26)=0.12, $p>0.5$; n.s. group x operation interaction, F(1,26)=2.24, p=0.15).

Sentence comprehension.

I compared performance across groups for the movement and garden path manipulations. For all accuracy analyses, I used a mixed-effect generalized-linear (logit) model with participant and item included as random effects (Clark 1973; Baayen et al. 2008; Jaeger 2008). For all reaction time analyses, I used a mixed-effect general linear model with participant and item included as random effects. I analyzed responses to movement and garden-path sentences separately.

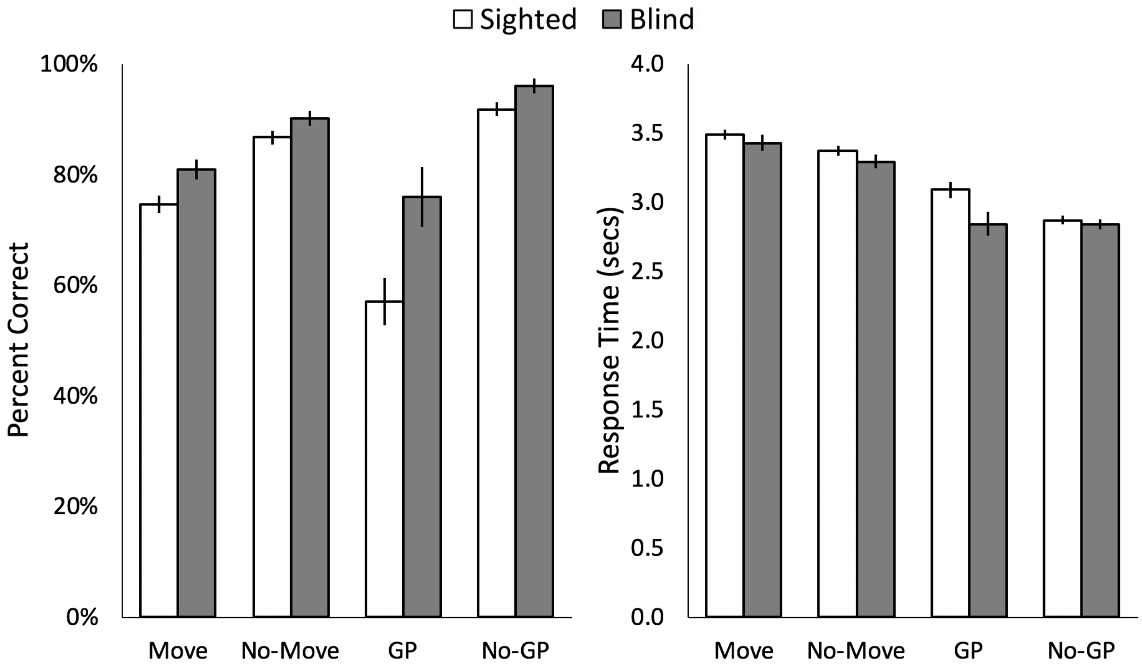


Figure 8. Sentence Comprehension Performance

Mean accuracy and response times for sighted and blind participants in syntactic movement (Move), matched non-movement (No-Move), garden path (GP) and matched non-garden path (No-GP) sentences. Error bars reflect SEM.

Blind participants were overall more accurate for both move and non-move control sentence types (Figure 8, sighted non-move mean=86.61%, SD=8.74%; sighted move mean=74.53%, SD=11.63%; blind non-move mean=90.16%, SD=6.69%; blind move mean=80.91%, SD=8.91%; group x complexity ANOVA, main effect of group, log-odds coefficient B=0.39 (SE=0.16), p=0.014; corresponding odds coefficient e^B=1.48). For both blind and sighted participants, accuracy was worse for move sentences than for non-move sentences (Figure 8, main effect of complexity, log-odds coefficient B=0.90 (SE=0.12), p<0.001; corresponding odds coefficient e^B=2.46, n.s. group x complexity interaction, log-odds coefficient B=-0.06 (SE=0.13), $p>0.5$; corresponding odds coefficient $e^B=0.94$).

Better accuracy of the blind group for move and non-move sentences was not driven by a speed-accuracy tradeoff. On the contrary, blind participants were slightly, but not significantly, faster at responding than sighted participants (Figure 8, sighted non-move mean=3.37 s, SD=0.27 s; sighted move mean=3.48 s, SD=0.26 s; blind non-move mean=3.29 s, SD=0.26 s; blind move mean=3.42 s, SD=0.30 s; group x complexity ANOVA: n.s. main effect of group, B=-0.07 (SE=0.06), p=0.28, n.s. group x complexity interaction, B=0.1 (SE=0.03), $p>0.5$). Both groups responded to move sentences more slowly than to non-move sentences (main effect of sentence-type, B=-0.12 (SE=0.03), p=0.001).

Blind participants were overall more accurate across garden-path (Figure 8, blind mean=76.00%, SD=27.08%; sighted mean=56.99%, SD=30.18%) and control sentences (blind mean=96.00%, SD=7.07%; sighted mean=91.80%, SD=8.43%; group x complexity ANOVA: main effect of group, log-odds coefficient B=1.03 (SE=0.39), p=0.008, corresponding odds coefficient $e^B=2.79$). Although the group difference was numerically more pronounced for the garden-path sentences, the group-by-sentence type interaction did not reach significance (group x complexity interaction, log-odds coefficient B=-0.28 (SE=0.43), $p>0.5$; corresponding odds coefficient $e^B=0.75$). Accuracy was worse for garden path than non-garden path control sentences for both groups (main effect of complexity, log-odds coefficient B=2.74 (SE=0.47), $p<0.001$; corresponding odds coefficient $e^B=15.49$).

A group-by-condition interaction was observed in the reaction time data for the garden path and garden-path control sentences. While sighted participants were slower to respond to garden-path than non-garden path sentences, blind participants responded with equal speed to both sentence types (Figure 8, sighted non-garden path mean=2.87 s, SD=0.22 s; sighted garden path mean=3.09 s, SD=0.42 s; blind non-garden path mean=2.84 s, SD=0.20 s; blind garden path mean=2.84 s, SD=0.44 s; group x complexity ANOVA, main effect of group, B=-0.14 (SE=0.06), p=0.03, group x complexity interaction, B=0.22 (SE=0.06), p=0.001; n.s. main effect of sentence-type, B=-0.07 (SE=0.14), p> 0.5). The lack of a slowdown for more complex sentences was not due to overall slower performance of the blind group. In contrast, blind participants were overall faster to respond to the complex garden-path sentences than sighted participants were to respond to the simple non-garden path sentences, though this difference was not significant (t(75)=0.36, p>0.5).

Since all garden-path sentences required a “no” response, I checked if group differences in response-bias might have driven the observed difference in performance. I measured bias to respond “no” for difficult questions as the percentage of “no” responses on incorrect move, non-move, and filler items. Blind participants were not more biased to respond “no” (n.s. difference between groups: t(75)=1.01, p=0.31)

Working-memory span.

A group x direction (forward vs. backward) ANOVA, revealed a main effect of span direction, with forward span significantly easier than backward span (Figure 8, F(1,74)=13.70, p<0.001). Overall, blind participants had better working memory than sighted participants (Figure 8, main effect of group, F(1,74)=33.21, p<0.001; n.s. group x direction interaction, F(1,74)=0.94, p=0.34).

Relationship between working memory span and sentence comprehension.

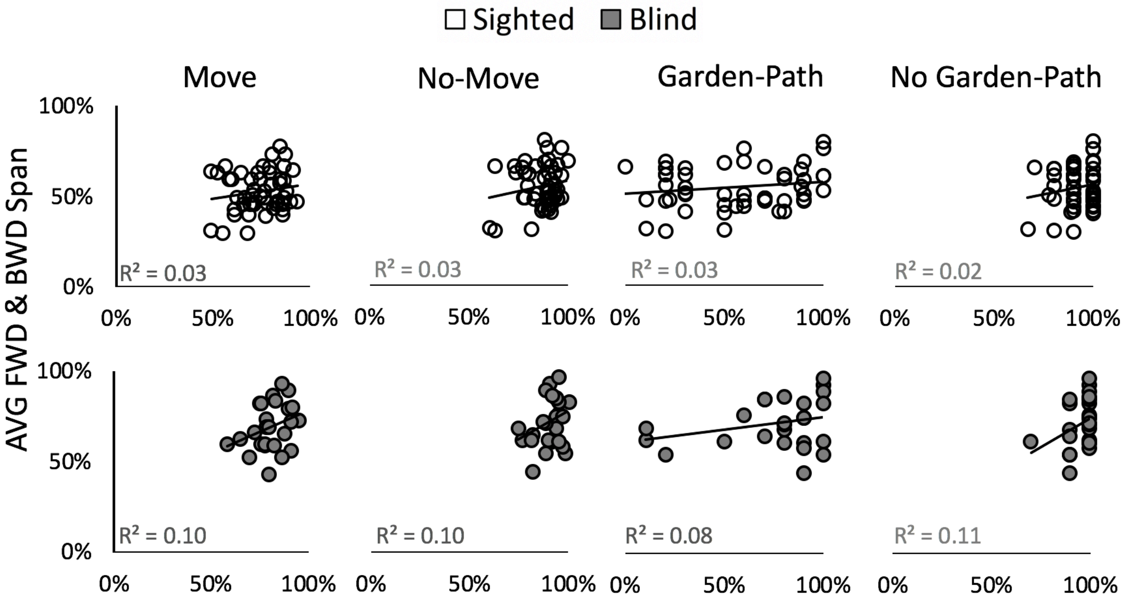


Figure 9. Relationship between Working Memory Span and Sentence Comprehension

Participants’ mean forward and backward letter span accuracy correlated with their accuracy in each sentence condition (move, no move, garden path, no garden path). Top row is within the sighted group, and bottom row is within the blind group.

Working memory span did not significantly predict sentence comprehension performance in either the blind or the sighted groups for any sentence types (Figure 9, correlation with average forward & backward span: blind accuracy: move: r=0.31, p=0.13, non-move: r=0.31, p=0.12, garden path: r=0.28, p=0.17, non-garden path: r=0.33, p=0.10; sighted accuracy: move: r=0.17, p=0.23, non-move: r=0.17, p=0.23, garden path: r=0.17, p=0.24, non-garden path: r=0.16, p=0.28).

Working memory span also did not significantly predict sentence comprehension response times in either the blind or the sighted group for any sentence types (Figure 9, correlation with average forward & backward span: blind RT: move: r=-0.23, p=0.27, non-move: r=-0.20, p=0.35, garden path: r=-0.18, p=0.38, non-garden path: r=-0.04, p>0.5; sighted RT: move: r=-0.09, p>0.5, non-move: r=-0.26, p=0.07, garden path: r=0.11, p=0.45, non-garden path: r=0.02, p>0.5).

Executive function.

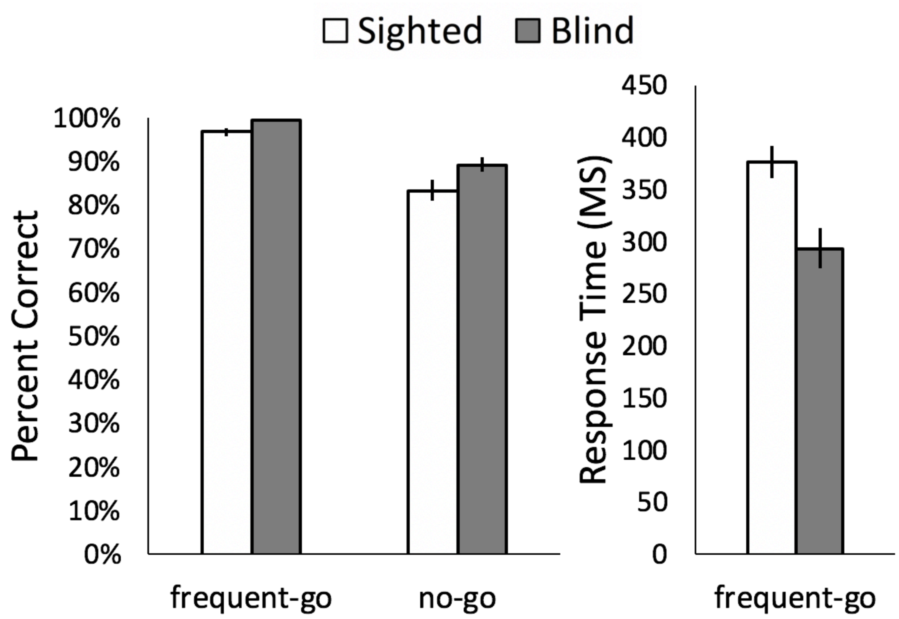


Figure 10. Go/No-Go Performance for Chapter 4 Participants

Sighted and blind participants’ mean accuracy and RT on the executive function task. Error bars reflect SEM.

Blind participants made fewer errors of omission to frequent-go sounds than sighted participants (frequent-go % correct: blind mean=99.55%, SD=0.50%; sighted mean=96.79%, SD=4.09%; blind vs. sighted, t(27)=2.90, p=0.01). Blind participants also made fewer errors of commission to no-go sounds, but this difference was not significant (no-go % correct: blind mean=89.30%, SD=5.21%; sighted mean=83.37%, SD=10.42%; blind vs. sighted, t(27)=1.68, p=0.10). The composite measures, which simultaneously accounted for going and withholding accuracy, were both significantly better in the blind group (*d’:* blind mean=3.9, SD=0.37; sighted mean=3.17, SD=0.89; blind vs. sighted, t(27)=3.10, p=0.005; no-go cost*:* blind mean=-0.89, SD=0.05 MS; sighted mean=-0.81, SD=0.13; blind vs. sighted, t(27)=-2.57, p=0.02). Composite measures were, expectedly, highly correlated (blind r=-0.79, p=0.006; sighted r=-0.91, p<0.001).

Blind participants also responded faster than sighted participants to the go sounds (frequent-go RT: blind mean=293.8 MS, SD=60.13 MS; sighted mean=376.3 MS, SD=66.00 MS; blind vs. sighted, t(27)=-3.29, p=0.003).

Relationship between executive function and sentence comprehension.

No-go cost did not significantly predict sentence comprehension performance in either the blind or the sighted groups for any sentence types (correlation with no-go cost: blind accuracy: move: r=0.12, p>0.5, non-move: r=-0.28, p=0.44, garden path: r=0.09, p>0.5, non-garden path: r=-0.23, p>0.5; sighted accuracy: move: r=-0.41, p=0.09, non-move: r=-0.32, p=0.18, garden path: r=-0.10, p>0.5, non-garden path: r=0.13, p>0.5). Similarly, going discrimination d’ did not significantly predict sentence comprehension performance in either group for any sentence type (correlation with going d’: blind accuracy: move: r=-0.01, p>0.5, non-move: r=0.49, p=0.15, garden path: r=0.16, p>0.5, non-garden path: r=0.17, p>0.5; sighted accuracy: move: r=0.41, p=0.08, non-move: r=0.28, p=0.25, garden path: r=0.14, p>0.5, non-garden path: r=0.01, p>0.5).

Similarly, no-go cost did not significantly predict sentence comprehension response times in either the blind or the sighted groups for any sentence types (correlation with no-go cost: blind RT: move: r=-0.15, p>0.5, non-move: r=-0.09, p>0.5, garden path: r=0.07, p>0.5, non-garden path: r=-0.07, p>0.5; sighted RT: move: r=-0.13, p>0.5, non-move: r=-0.11, p>0.5, garden path: r=0.14, p>0.5, non-garden path: r=-0.29, p=0.24). Similarly, going discrimination d’ did not significantly predict sentence comprehension performance in either group for any sentence type (correlation with going d’: blind RT: move: r=-0.06, p>0.5, non-move: r=-0.15, p>0.5, garden path: r=-0.33, p=0.36, non-garden path: r=-0.15, p>0.5; sighted RT: move: r=0.13, p>0.5, non-move: r=0.05, p>0.5, garden path: r=-0.06, p>0.5, non-garden path: r=0.23, p=0.35).

Relationship between executive function and working memory.

Examining the relationship between verbal working memory and non-verbal response inhibition revealed a significant correlation, only in the blind group, between average letter span and go/no-go d’ (but not no-go cost) (correlation with average forward & backward span: blind no-go cost: r=-0.38, p=0.28; sighted no-go cost: r=-0.21, p=0.40; blind going *d’*: r=0.67, p=0.03; sighted going *d’*: r=0.23, p=0.34).

4.4 Discussion

I find that early and total blindness improves performance on working memory maintenance, response-inhibition in a non-verbal go/no-go task, and grammatically complex sentence comprehension. These improvements were observed among blind individuals who were matched to sighted participants on age, education and crucially performance on a range of cognitive measures such as vocabulary, reading ability, and basic algebra proficiency. Although previous studies have identified improved performance among blind individuals on some auditory perception tasks, I think such improvements are unlikely to account for the effects of the current study since blind individuals typically outperform the sighted only under demanding (i.e. noisy or ambiguous) conditions (Niemeyer and Starlinger 1981; Muchnik et al. 1991; Hugdahl et al. 2004; Stevens and Weaver 2005). In contrast, the current experiment took place in a noise-controlled setting, utilized pre-recorded audio played through noise-blocking headphones, and allowed the participants to adjust volume. The present findings thus suggest that blindness confers benefits on higher-cognitive functions that are analogous but different from benefits to sensory processes in preserved modalities.

Furthermore, although blind individuals showed improvements in three different higher-cognitive tasks, individual differences in response inhibition and working memory did not predict individual differences on the sentence comprehension performance, either in the sighted or in the blind. These results suggest that congenital blindness confers independent advantages to different higher cognitive systems. This finding is consistent with evidence that, in blindness, different sub-networks within “visual” cortices are recruited for different higher-cognitive domains, including response inhibition, memory and sentence comprehension. Behavioral compensation may be partially enabled by such “visual” cortex plasticity. However, the behavioral enhancements are also likely related to the compensatory use of alternative cognitive mechanisms to solve everyday tasks for which the sighted (visually encumbered) use vision. Thus, improvement in higher-order cognitive domains may be a pervasive compensation mechanism in sensory loss, parallel to the enhanced use of other sensory modalities.

Blindness confers an advantage to sentence processing, how and why?

I find that congenitally blind individuals are more accurate than matched, sighted controls at answering who-did-what-to-whom questions about sentences. This advantage is particularly pronounced for sentences that are syntactically complex. Unlike sighted adults, blind individuals respond as quickly to questions about garden-path sentences as they do to matched, non-garden-path control sentences, showing no garden path cost in reaction time. This advantage in sentence processing cannot be explained by differences in general cognitive abilities across groups: blind participants performed no better than sighted participants on control tasks assessing reading and phonetics, vocabulary, analogies, and arithmetic. Furthermore, though blind participants outperformed sighted participants on forward and backward letter span tasks, as well as on a non-verbal go/no-go task, these improvements did not predict sentence comprehension performance.

As noted in the introduction, unlike sighted adults, blind individuals recruit “visual” cortices during sentence processing tasks and more so for syntactically complex sentences (Röder et al. 2002; Bedny et al. 2011; Lane et al. 2015). Furthermore, blind individuals with larger “visual” cortex responses to grammatically complex sentences also tend to show better performance when answering sentence-comprehension questions about those sentences (Lane et al. 2015). More direct evidence for the idea that “visual” cortices are behaviorally relevant to verbal tasks comes from studies using transcranial magnetic stimulation. Transcranial magnetic stimulation to the occipital pole caused blind individuals to make semantic errors during a verb-generation task and induced Braille reading errors (Amedi et al. 2004; Cohen et al., 1997). The available evidence is thus consistent with the hypothesis that extra “visual” cortex plasticity confers a behavioral advantage to blind individuals in language processing and in sentence processing in particular. However, it is worth noting that whether “visual” cortex is functionally relevant to sentence-processing remains to be directly tested using techniques such as TMS.

The availability of “visual” cortex territory is only one of several non-mutually exclusive reasons for why blindness might improve sentence processing ability. Vision and language often provide analogous information about our environment. For the sighted, vision provides high fidelity information about the identity of objects and agents and about who did what to whom, precisely the type of information that language refers to. There is extensive evidence that sighted individuals rapidly integrate linguistic and visual information during online comprehension to build situation models. According to constraint-based theories of sentence processing, comprehension occurs by integrating various sources of information, including not only syntactic and lexical information, but also extra-linguistic cues such as what objects are present in the environment (Tyler and Marslen-Wilson 1977; MacDonald et al. 1994; Nagel et al. 1994; Trueswell et al. 1994; Tanenhaus et al. 1995; Bader 1998; McRae et al. 1998; Tanenhaus et al. 2000; Chambers et al. 2002; Bailey and Ferreira 2003; Trueswell and Gleitman 2004). Sighted listeners use visual cues to disambiguate garden-path sentences similar to those used in the current study. When participants hear “put the frog on the towel in the box” they are more likely to quickly arrive at the correct parse (i.e. put the frog into the box, not onto the towel) if they see two frogs, one on a towel and one not on a napkin (Tanenhaus et al. 1995; Spivey et al. 2002; Chambers et al. 2004; Farmer et al. 2007). Studies of online eye- and hand-tracking behavior among sighted participants suggest that visual cues are integrated rapidly with lexical and syntactic information during comprehension (Huettig et al. 2011).

Unlike such vision-supported comprehension, in the current experiment, participants heard sentences in the absence of visual cues. In this respect, the task may more closely resemble the language comprehension environment encountered by blind than sighted individuals in their everyday lives. Although audition and touch also contain relevant contextual information, there are reasons to believe that vision is a particularly efficient source of information about the types of things that language refers to: object and agent identity, their location, and the events in which they participate. Since blind individuals have no access to such visual cues, they may develop better abilities to use language-internal information during sentence parsing. Such an improvement in sentence-processing abilities would be analogous to improved auditory and tactile perception among blind individuals, where absence of visual cues leads to better attention to, and extraction of, information from non-visual cues.

This construal of the findings relates studies of blindness to research on cue combination. Humans efficiently combine sensory information from different modalities during perception. For example, when judging the height of a raised edge visual and tactile information is combined optimally and even brief experiences can change how different cues are weighed (Atkins et al. 2001; Ernst and Banks 2002). Analogously, combination of cues has been suggested to play a role during sentence processing (Martin 2016). In blindness, habitual reliance on language alone may change cue weighting and optimize the system to function in the absence of language external visual constraints.

It is worth noting that the practice-based argument articulated above is not inconsistent with the hypothesis that “visual” cortex plasticity enables behavioral improvements. The availability of extra language wetware in the “visual” cortex could make behavioral improvements possible in the presence of pressure from the environment to acquire them. Conversely, reliance on language as a source of information could increase pressure for language (as opposed to other cognitive functions) to colonize available territory in the “visual” cortex.

An interesting question is whether other types of experiential change, apart from blindness, could put similar pressure on the language processing system to improve its function and, if so, whether behavioral improvements would result even in the absence of extra available “wetware.” For example, would training sighted speakers to parse sentences in the absence of visual cues improve sentence comprehension performance? Naturalistic experiences that might deliver such “training” could include extensive reading or listening to books on tape. Efforts to train sighted speaker to become better at parsing complex sentences in the laboratory have met with mixed success. Though one study reported that successful training on a demanding N-back task improved performance on syntactically ambiguous sentences, the longevity of such effects is not known (Novick et al. 2012). Some studies suggest that experience with particular types of grammatical constructions enhances performance with those constructions (Roth 1984; Long and Prat

2008; Wells et al. 2009; Fine et al. 2013). However, even those studies that do observe benefits, find relatively subtle and narrow effects, i.e. specific to trained sentence constructions. The effects manifest themselves in faster reaction times and are not long lasting (Roth 1984; Long and Prat 2008; Wells et al. 2009). Blindness-related improvements in sentence-processing may be more robust, either because blindness causes more extensive and varied “training” or perhaps because of the availability of a distinct neural mechanisms in blind as opposed to sighted speakers.

Improvement in executive function and working memory and their relationship to improvements in sentence processing.

As noted above, apart from improvements on sentence processing I also find that blind participants perform better than the sighted on working memory tasks (Tillman and Bashaw 1968; Hull and Mason 1995; Amedi et al., 2003; Raz et al. 2007; Rokem and Ahissar 2009; Withagen et al. 2013) and on a non-verbal, go/no-go task of response inhibition. Like language, these tasks also activate the “visual” cortices of blind individuals. However, non-verbal executive control activates distinct “visual” regions from language (Chapter 3). Although I did observe a correlation between go/no go and working memory performance among individuals who are blind, enhancements on sentence processing appear to be independent from enhancements on go/no-go and working memory tasks. Blind individuals that show improved sentence processing abilities are not the same as those that show maximal improvements in working memory or executive function. This observation is consistent with evidence that language and non-verbal response inhibition recruit different parts of “visual” cortices, as well as fronto-parietal and fronto-temporal cortices, in blind individuals (Chapter 3).

Although improvements in sentence comprehension are independent from improvements in memory and executive function, improvements may occur for similar reasons. One possibility is that sentence processing improves because blind individuals become better at maintaining linguistic information in working memory during sentence parsing. It has been suggested that sentence parsing relies on a dedicated working memory system that is separate but analogous to the verbal working memory system that maintains arbitrary verbal lists (Caplan and Waters 1999). As a sentence unfolds in time, listeners keep previously heard information active in working memory and blind listeners may maintain more of this information, with higher fidelity and perhaps for a longer amount of time. In the case of garden path sentences, blind individuals may maintain the initially dis-preferred sentence parse in working memory (Just and Carpenter 1992; Hickok 1993; MacDonald et al. 1994; Gibson 1998; McRae et al. 1998; Stevenson 1998) to a greater extent than sighted participants. When this dis-preferred parse turns out to be the correct one, blind individuals show a reduced performance cost. Analogously, for sentences with a movement dependency, blind individuals may be better able to maintain information before it can be integrated into the sentence structure. For example, maintaining the matrix subject in memory across the intervening clause until the associated relative clause verb is encountered. One prediction of this account is that blind individuals will perform better on those language tasks for which it would be advantageous to keep linguistically relevant information active in working memory.

An alternative possibility, is that blindness improves executive function mechanisms that are involved in selection of the preferred sentence interpretation in the context of syntactic ambiguity (Novick et al. 2005; 2012; Woodard et al. 2016). This would be consistent with the fact that in the current study, blindness-related improvements were most pronounced for garden-path sentences. Again, as in the case of verbal working memory for lists, I find that there is no relationship between go/no go performance and sentence processing performance among blind (or sighted) participants. Therefore, blind individuals appear to independently improve their sentence-processing and non-verbal executive control performance. However, improvements in sentence processing could occur by an analogous mechanism to the improvements observed in non-verbal executive function. Ambiguity resolution is a key need within language processing and there is some evidence for language-specific ambiguity resolution mechanisms (Thompson-Schill et al. 2005; January et al. 2009; Novick et al. 2010). One hypothesis is that, in blindness, working memory and ambiguity resolution mechanisms both within and outside of language improve for related reasons: the need to maintain and select information more efficiently in the absence of visual cues.

In future work it will be important to test blind participants on a larger battery of linguistic and higher-cognitive tasks to delineate the precise mechanism of blindness-mediated improvements in language processing, working memory, and non-verbal executive control. For example, if blindness enhances selection mechanisms that are involved in sentence comprehension, I would predict that blind individuals would show superior performance at other tasks involving ambiguity resolution (e.g. tasks with homonymous words). In contrast, if the enhancements are mediated by sentence-specific working memory mechanisms I would not expect advantages in lexical tasks, whether they involve ambiguity or not. It would also be interesting to ask whether blindness enhances other aspects of linguistic processing, apart from those involved in sentence structure building (e.g. morphological processes).

4.5 Summary

In Chapter 4 I asked whether the higher cognitive functions observed in Chapters 2 and 3, as well as in previous work, confer any behavioral advantage. Most of the findings of performance improvements in blindness have focused on the idea that in the absence of one sense, there are improvements in the other senses—i.e. better visual localization in deafness (Neville and Lawson 1987) and better sound localization in blindness (Lessard et al. 1998; Roder et al. 1999; Voss et al. 2004; Fieger et al. 2006; Rice 2017). In this chapter, I find evidence that sensory loss also leads to behavioral adaptation in higher-cognitive domains. Blind individuals are better at recalling information from long term memory (Raz et al. 2007), maintaining information in working memory, inhibiting a prepotent motor response on a go/no go task, and comprehending syntactically complex sentences. These results illustrate how changes in one dimension of early experience reverberate to affect cognitive abilities that are unrelated but can nevertheless be used to achieve similar behavioral goals. Moreover, they suggest that, in blindness, “visual” cortices are deftly repurposed for meaningful impact on cognitive domains that differ radically from vision.

Chapter 5

General conclusions

Are brain structures and functions inextricably linked? Across individuals, different cognitive functions are implemented in consistent cortical locations, each of which has a distinctive cyto-architecture and inter-regional connectivity profile. This systematic relationship between structure and function suggests that intrinsic physiology tightly constrains each cortical region to implement particular cognitive operations. Contrary to this idea, studies of sensory loss, such as in blindness and deafness, demonstrate that experience can modify this structure to function mapping. In blind individuals, retinotopic "visual" cortices respond to auditory and tactile stimuli (Wanet-Defalque et al. 1988; Sadato et al. 1996), and in deaf individuals, auditory cortices respond to visual and tactile stimuli (Levänen et al. 1998; Finney et al. 2001).

One view is that sensory cortices preserve their original cognitive operation, even in cases of cross-modal plasticity (Pascual-Leone and Hamilton 2001; Renier et al. 2010; Meredith et al. 2011; Striem-Amit et al. 2011; Renier et al. 2014; Cecchetti et al. 2016; Amedi et al. 2017). According to the meta-modal hypothesis, in blindness, "visual" cortices continue to perform vision-like functions, but over input from audition and touch. Consistent with this idea, dorsal occipital areas that are part of the visual "where" pathway in sighted individuals become active during sound localization in blind individuals (Wanet-Defalque et al. 1988; Gougoux et al. 2005; Collignon et al. 2011). Analogously, it has been suggested that retinotopic areas typically involved in fine-grained visuospatial discrimination become involved in fine-grained somatosensory discriminations, such as texture perception, in blindness (Sadato et al. 1996; Merabet et al. 2004; Sathian and Stilla 2010). In these instances of cross-modal plasticity, sensory cortices appear to preserve their underlying cognitive operation, even when the sensory modality to which they respond changes. One interpretation of these findings is that while the preferred sensory modality is malleable, the cognitive operation itself (e.g. spatial localization) is specified by intrinsic physiology (Pascual-Leone and Hamilton 2001).

An alternative possibility is that cortices are capable of drastically altering their function based on early experience (Bedny 2017). Evidence for this idea comes from studies of blindness which demonstrate that “visual” cortices become responsive to language. In blindness, retinotopic “visual” areas, including V1, become sensitive to meaning and grammar. In blind, but not sighted, individuals, occipital cortices respond more to words than meaningless sounds, more to sentences than unconnected lists of words, and more to grammatically complex than grammatically simple sentences (Röder et al. 2002; Bedny et al. 2011; Lane et al. 2015). Furthermore, language-responsive “visual” cortices become correlated at rest with prefrontal language regions (Bedny et al. 2011). Since language and vision are cognitively and evolutionarily distinct, these observations challenge the idea that cortical areas have fixed functions, even meta-modal ones.

This dissertation assesses the extent to which cortical regions truly change their function in cross-modal plasticity. I find that, consistent with the pluripotency hypothesis, human cortical areas can take on a dramatically different cognitive functions depending on early experience, and that this plasticity likely influences behavior.

First, Chapter 2 shows that repurposing of "visual" cortices is systematic across individual cases of blindness. "Visual" cortices synchronize to each other when blind individuals listen to rich, entertaining vignettes. This synchronization of "visual" cortices occurs during naturalistic listening conditions, suggesting that "visual" cortices are not just recruited as an "overflow" processor for uncommon psychological tasks, but are utilized during everyday life. Moreover, Chapter 2 provides a broad brush answer to the debate over which kinds of functions take over "visual" cortices—i.e., lower sensory or higher cognitive. I find that "visual" cortex synchronization varies parametrically with the amount of higher cognitive content in the stimulus to which participants are exposed. This pattern of synchronization mirrors that of fronto-temporal cortices and breaks from that of non-visual sensory cortices. Chapter 2 cannot inform which higher cognitive content drives synchronization between "visual" cortices of blind individuals. However, it does provide a lower bound (of 65%) on the topographic extent to which higher cognitive functions take over "visual" cortices. Moreover, because synchronization to higher cognitive content was observed bilaterally in "visual" cortices, and language responses are typically lateralized, findings from Chapter 2 provide a hint that higher cognitive functions in "visual" cortices are not limited to language.

Chapter 3, therefore, directly tests for the presence of a non-verbal higher-cognitive function in “visual” cortices of blind individuals. Using a go/no-go task of response inhibition, I find evidence for executive function in right-lateralized “visual” cortices. Like fronto-parietal cortices, and unlike sensory-motor cortices, of both blind and sighted groups, “visual” cortices of blind individuals respond to executive load. Moreover, a functional connectivity analysis of brain activity at rest provides independent evidence that regions of “visual” cortices are incorporated into fronto-parietal executive-function networks in blindness. Executive-function responsive “visual” cortices increase their synchronization with prefrontal executive control regions and decrease their synchronization with auditory and sensory-motor areas. Executive function responses in “visual” cortices represent, possibly, the first finding of non-verbal higher cognitive function in “visual” cortices of blind individuals. Importantly, executive-function responsive “visual” cortices demonstrate that language functions in “visual” cortices are not a solitary anomaly to the hypothesis of meta-modality. Thus, Chapter 3 compliments Chapter 2 in providing strong evidence for fronto-parietal higher cognitive takeover of “visual” cortices in blindness.

Finally, in Chapter 4, I find evidence for a behavioral benefit in the very higher cognitive functions for which “visual” cortices are repurposed. Blind individuals outperform sighted individuals in tests of sentence comprehension and in a task of response inhibition. Importantly, in blind and in sighted groups, individual differences in response inhibition and working memory do not predict individual differences on sentence comprehension performance. This suggests distinct neural mechanisms mediating sentence comprehension and executive function. This finding is consistent with the observation that observed responses for language and executive function are spatially distinct within "visual" cortices of blind individuals. Findings from Chapter 4 cannot rule out the possibility that non-"visual" cortices are responsible for the behavioral advantage. However, Chapter 4 suggests that, if such "visual" cortex responses are functionally relevant, they may mediate the behavioral benefit observed.

Together with prior findings of language and math responses in "visual" cortices of blind individuals (Bedny et al. 2011; Kanjlia et al. 2016), this dissertation provides evidence that typically sensory visual cortices undergo extensive repurposing for higher cognitive functions in cases of blindness. In three independent instances— 2 stimulus driven and 1 in the absence of a stimulus— I observed that "visual" cortices of blind individuals concord with higher cognitive fronto-tempero-parietal cortices and dissociate from primary auditory, somatosensory, and motor cortices (Chapter 2 & Chapter 3). More broadly, the work presented here suggests that human cortices are radically amenable to fulfilling functional roles for which they did not evolve. Adapted cortical tissues may be deftly incorporated into pre-existing networks to provide a behavioral benefit.

An open question is whether different functions take up larger or smaller amounts of cortical real estate in different cases of blindness. Evidence of behavioral benefits from "visual" cortex plasticity suggest an intriguing possibility that behavioral necessity may mediate the extensiveness of "visual" cortex takeover by each fronto-parietal network. According to this hypothesis, "visual" cortices of each blind individual would show distinct sub-regions for language, math, and executive function, but the relative amount of each area of functional specialization would reflect which higher cognitive functions are of most benefit to that particular individual.

Interestingly, in the work presented here, I also observed two independent instances of responses to non-visual stimuli in the visual cortices of blindfolded, sighted adults (Chapter 2 & Chapter 3). The cognitive role of visual cortex responses to non-visual stimuli in sighted individuals is not known. In both cases, however, visual cortex responses in the sighted group differed qualitatively from "visual" cortex responses in the blind group. One possibility is that, under conditions of visual deprivation, visual cortices of sighted individuals receive the same input as "visual" cortices of blind individuals but responses are dissimilar because the occipital cortices have not undergone the same developmental changes to local circuitry. Another possibility is that visual cortices of blindfolded sighted individuals receive predominantly different input. This latter possibility is consistent with my finding that, in blindfolded sighted individuals, functional connectivity is stronger between visual cortices and sensory/motor cortices than between visual cortices and fronto-parietal cortices (Chapter 3). The occipital cortices of sighted, but not blind, individuals may thus show hints of meta-modality.

Together, the available resting-state and task-based findings from blindness support the hypothesis that anatomical connectivity plays a major role in driving cortical function. The finding that occipital cortices of blind individuals take on fronto-parietal functions is consistent with the observation that, in sighted and blind individuals alike, fronto-parietal networks constitute a main source of anatomical afferent connections to the visual system (Bressler et al. 2008; Gilbert and Li 2013). Since there is no evidence of large-scale additional anatomical tracts in blind relative to sighted individuals, these functional changes are likely to result from long-range connectivity between fronto-parietal networks and visual cortices that are present in both blind and sighted groups (Shimony et al. 2005; Shu, Li, et al. 2009; Shu, Liu, et al. 2009). I hypothesize that the functional reorganization observed in blindness is mediated by local synaptic changes that alter the efficacy of top-down anatomical inputs from higher-cognitive regions.

Further support for the idea that long-range anatomical connectivity directs the function of cortex comes from the localization of different functions within the "visual" cortices of blind individuals. Across multiple examples of plasticity, "visual" cortex functions in blind individuals are co-lateralized with the non-visual cortices that classically implement such functions. Executive function activity is right lateralized in both fronto-parietal and "visual" cortices (Chapter 3). By contrast, language responses in the "visual" cortices are on average more pronounced in the left hemisphere, in keeping with left lateralization of language in frontotemporal cortices (Röder et al. 2002; Bedny et al. 2011; Lane et al. 2015). Moreover, in blind individuals with right-lateralized language processing in fronto-temporal cortices, language responses in "visual" cortices are also right-lateralized (Lane et al. 2017). Because anatomical connectivity is stronger within, than across, hemispheres, co-lateralization of blind "visual" cortices is consistent with the hypothesis that plasticity is constrained by pre-existing anatomical connections to the occipital cortices.

Support for anatomical connectivity-based directives to functional specialization also comes from studies outside of blindness (O'Leary 1989; Johnson 2000; Dehaene and

Cohen 2007; Mahon and Caramazza 2011). For example, anatomical connectivity predicts which region of the ventral object-recognition stream will become the "visual word form area" (VWFA) (Saygin et al. 2016). Relative to other parts of the ventral stream, this cortical location has strong reciprocal anatomical connectivity with fronto-temporal language networks, even prior to onset of literacy (Dehaene et al. 2015). Such results are consistent with findings from studies of blindness. Together, these studies support the view that anatomical connectivity plays a major role in shaping cortical function. However, the functional repurposing that occurs in blindness is far more extensive than in the case of reading. In cases of neuronal recycling, cortical tissues undergo slight adaptations to accommodate cultural inventions—e.g., reading and math. Importantly, the new functions assumed share something with the original functions putatively prescribed by evolution. In cases of blindness, input from fronto-parietal cortices dramatically changes the functional profile of "visual" cortices. Studies of blindness, therefore, uniquely inform the extent to which cortical structures can flexibly take on novel functions. Studies of congenital blindness also tease apart the contribution of intrinsic constraints and experience. In contrast, cultural domains, such as reading and number, build on the effects of previous experiences that occurred early in life.

In this dissertation, I observed large-scale functional flexibility of "visual" cortices in blindness. The same anatomical connectivity pattern that mediates communication between vision and higher-order cognition in those who are sighted enables the incorporation of occipital cortices into higher cognitive networks in blindness. Individual experiences drastically alter biases in anatomical connectivity. Anatomical afferents, in turn, differentiate cortical areas by regulating a cortical area's input. Differences in functional specialization thus result from differences in anatomical connectivity directives. At birth, human cortices are radically flexible to take on area-novel functional roles.

Summary

Blindness is a window into understanding cortical specialization. This dissertation provides evidence that the human brain is much more pliant than previously thought. Though blind and sighted occipital cortices contain similar long-range connectivity, different connections become primary as a result of experience. In blindness top-down input from fronto-parietal and temporal networks comes to dominate the "visual" system. In this way, studies in blindness inform not just the functional plasticity of the brain but also uncover how anatomy directs functional specialization. Rather than having predetermined functions, brain structures appear to functionally differentiate in accord with each individual's unique experience and intrinsic anatomical connectivity biases. Therefore, radical plasticity does not implicate a complete break between structure and function, but rather a break between structure and anatomical location. A brain structure's function is determined not by its location but by what it is connected to. This extreme flexibility of the human brain suggests that evolution doesn't just provide for what is expected. Rather, it goes so far as to provide a safeguard for the unexpected.

References

Alary F, Duquette M, Goldstein R, Elaine Chapman C, Voss P, La Buissonnière-Ariza V, Lepore F. 2009. Tactile acuity in the blind: A closer look reveals superiority over the sighted in some but not all cutaneous tasks. Neuropsychologia. 47:2037–2043.

Amedi A, Floel A, Knecht S, Zohary E, Cohen LG. 2004. Transcranial magnetic stimulation of the occipital pole interferes with verbal processing in blind subjects. Nature Neuroscience. 7:1266–1270.

Amedi A, Hofstetter S, Maidenbaum S, Heimler B. 2017. Task Selectivity as a Comprehensive Principle for Brain Organization. Trends in Cognitive Sciences. 1–3.

Amedi A, Raz N, Pianka P, Malach R, Zohary E. 2003. Early “visual” cortex activation correlates with superior verbal memory performance in the blind. Nature Neuroscience. 6:758–766.

Amedi A, Stern WM, Camprodon JA, Bermpohl F, Merabet L, Rotman S, Hemond C, Meijer P, Pascual-Leone A. 2007. Shape conveyed by visual-to-auditory sensory substitution activates the lateral occipital complex. Nature Neuroscience. 10:687–689.

Anderson JC, Kennedy H, Martin KAC. 2011. Pathways of Attention: Synaptic Relationships of Frontal Eye Field to V4, Lateral Intraparietal Cortex, and Area 46 in Macaque Monkey. Journal of Neuroscience Methods. 31:10872–10881.

Anticevic A, Dierker DL, Gillespie SK, Repovs G, Csernansky JG, Van Essen DC, Barch DM. 2008. Comparing surface-based and volume-based analyses of functional neuroimaging data in patients with schizophrenia. NeuroImage. 41:835–848.

Aron AR. 2006. Cortical and Subcortical Contributions to Stop Signal Response Inhibition: Role of the Subthalamic Nucleus. Journal of Neuroscience Methods. 26:2424–2433.

Aron AR, Cai W, Badre D, Robbins TW. 2015. Evidence Supports Specific Braking Function for Inferior PFC. Trends in Cognitive Sciences. 1–2.

Aron AR, Robbins TW, Poldrack RA. 2004. Inhibition and the right inferior frontal cortex. Trends in Cognitive Sciences. 8:170–177.

Aron AR, Robbins TW, Poldrack RA. 2014. Inhibition and the right inferior frontal cortex: one decade on. Trends in Cognitive Sciences. 18:177–185.

Atkins JE, Fiser J, Jacobs RA. 2001. Experience-dependent visual cue integration based on consistencies between visual and haptic percepts. Vision Res. 41:449–461.

Azevedo FAC, Ortiz-Rios M, Li Q, Logothetis NK, Keliris GA. 2015. A Potential Role of Auditory Induced Modulations in Primary Visual Cortex. Multisensory Research. 28:331–349.

Baayen RH, Davidson DJ, Bates DM. 2008. Mixed-effects modeling with crossed random effects for subjects and items. Journal of Memory and Language. 59:390–412.

Bader M. 1998. Prosodic Influences on Reading Syntactically Ambiguous Sentences. In: Reanalysis in Sentence Processing. Studies in Theoretical Psycholinguistics. Dordrecht: Springer, Dordrecht. p. 1–46.

Bailey K, Ferreira F. 2003. Disfluencies affect the parsing of garden-path sentences. Journal of Memory and Language. 49:183–200.

Banich MT. 2009. Executive function: The search for an integrated account. Current Directions in Psychological Science. 18:89–94.

Barber AD, Caffo BS, Pekar JJ, Mostofsky SH. 2013. Effects of Working Memory Demand on Neural Mechanisms of Motor Response Selection and Control. Cognitive Neuroscience, Journal of. 25:1235–1248.

Bavelier D, Neville HJ. 2002. Cross-modal plasticity: where and how? Nature Reviews: Neuroscience.

Bedny M. 2017. Evidence from Blindness for a Cognitively Pluripotent Cortex. Trends in Cognitive Sciences. 21:637–648.

Bedny M, Konkle T, Pelphrey K, Saxe R, Pascual-Leone A. 2010. Sensitive Period for a Multimodal Response in Human Visual Motion Area MT/MST. Current Biology. 20:1900–1906.

Bedny M, McGill M, Thompson-Schill SL. 2008. Semantic Adaptation and Competition during Word Comprehension. Cerebral Cortex. 18:2574–2585.

Bedny M, Pascual-Leone A, Dodell-Feder D, Fedorenko E, Saxe R. 2011. Language processing in the occipital cortex of congenitally blind adults. Proc Natl Acad Sci USA. 108:4429–4434.

Bedny M, Pascual-Leone A, Dravida S, Saxe R. 2012. A sensitive period for language in the visual cortex: distinct patterns of plasticity in congenitally versus late blind adults. Brain Lang. 122:162–170.

Beer AL, Plank T, Greenlee MW. 2011. Diffusion tensor imaging shows white matter tracts between human auditory and visual cortex. Exp Brain Res. 213:299–308.

Bola Ł, Zimmermann M, Mostowski P, Jednoróg K, Marchewka A, Rutkowski P, Szwed M. 2017. Task-specific reorganization of the auditory cortex in deaf humans. Proc Natl Acad Sci USA. 114:E600–E609.

Brainard DH. 1997. The Psychophysics Toolbox. Spat Vis. 10:433–436.

Brass M, Derrfuss J, Forstmann B, Cramon von DY. 2005. The role of the inferior frontal junction area in cognitive control. Trends in Cognitive Sciences. 9:314–316.

Bressler SL, Tang W, Sylvester CM, Shulman GL, Corbetta M. 2008. Top-Down Control of Human Visual Cortex by Frontal and Parietal Cortex in Anticipatory Visual Spatial Attention. Journal of Neuroscience Methods. 28:10056–10061.

Burton H, Diamond JB, McDermott KB. 2003. Dissociating cortical regions activated by semantic and phonological tasks: a FMRI study in blind and sighted people. Journal of Neurophysiology.

Burton H, Sinclair RJ, Dixit S. 2010. Working memory for vibrotactile frequencies: Comparison of cortical activity in blind and sighted individuals. Hum Brain Mapp.

Burton H, Sinclair RJ, McLaren DG. 2004. Cortical activity to vibrotactile stimulation: An fMRI study in blind and sighted individuals. Hum Brain Mapp. 23:210–228.

Burton H, Snyder AZ, Diamond JB, Raichle ME. 2002. Adaptive changes in early and late blind: a FMRI study of verb generation to heard nouns. Journal of Neurophysiology.

Burton H, Snyder AZ, Raichle ME. 2014. Resting state functional connectivity in early blind humans. Front Syst Neurosci.

Cantlon JF, Brannon EM, Carter EJ, Pelphrey KA. 2006. Functional Imaging of Numerical Processing in Adults and 4-y-Old Children. PLoS Biol. 4:e125–11.

Caplan D, Waters GS. 1999. Verbal working memory and sentence comprehension. Behav Brain Sci. 22:77–94.

Cecchetti L, Kupers R, Ptito M, Pietrini P, Ricciardi E. 2016. Are Supramodality and Cross-Modal Plasticity the Yin and Yang of Brain Development? From Blindness to Rehabilitation. Front Syst Neurosci. 10:247–248.

Chambers CG, Tanenhaus MK, Eberhard KM, Filip H, Carlson GN. 2002. Circumscribing Referential Domains during Real-Time Language Comprehension. Journal of Memory and Language. 47:30–49.

Chambers CG, Tanenhaus MK, Magnuson JS. 2004. Actions and Affordances in Syntactic Ambiguity Resolution. Journal of Experimental Psychology: Learning, Memory, and Cognition. 30:687–696.

Chikazoe J. 2010. Localizing performance of go/no-go tasks to prefrontal cortical subregions. Current Opinion in Psychiatry. 23:267–272.

Chikazoe J, Jimura K, Asari T, Yamashita KI, Morimoto H, Hirose S, Miyashita Y, Konishi S. 2008. Functional Dissociation in Right Inferior Frontal Cortex during Performance of Go/No-Go Task. Cerebral Cortex. 19:146–152.

Christianson K, Hollingworth A, Halliwell JF, Ferreira F. 2001. Thematic Roles Assigned along the Garden Path Linger. Cogn Psychol. 42:368–407.

Clark HH. 1973. The language-as-fixed-effect fallacy: A critique of language statistics in psychological research. Journal of Verbal Learning and Verbal Behavior. 12:335–359.

Cohen LG, Celnik P, Pascual-Leone A, Corwell B. 1997. Functional relevance of cross-modal plasticity in blind humans. Nature.

Collignon O, Renier L, Bruyer R, Tranduy D, Veraart C. 2006. Improved selective and divided spatial attention in early blind subjects. Brain Research. 1075:175–182.

Collignon O, Vandewalle G, Voss P. 2011. Functional specialization for auditory–spatial processing in the occipital cortex of congenitally blind humans. In:. Presented at the Proceedings of the National Academy of Sciences.

Collignon O, Voss P, Lassonde M, Lepore F. 2008. Cross-modal plasticity for the spatial processing of sounds in visually deprived subjects. Exp Brain Res. 192:343–358.

Corbetta M, Shulman GL. 2002. Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews: Neuroscience. 3:201–215.

Dale AM, Fischl B, Sereno MI. 1999. Cortical Surface-Based Analysis: Segmentation and Surface Reconstruction. NeuroImage. 1–16.

Dann M, Levine SZ, New EV. 1964. A long term follow-up study of small premature infants. Pediatrics. 33:945–955.

Deen B, Saxe R, Bedny M. 2015. Occipital Cortex of Blind Individuals Is Functionally Coupled with Executive Control Areas of Frontal Cortex. Cognitive Neuroscience, Journal of. 87:1–15.

Dehaene S, Cohen L. 2007. Cultural Recycling of Cortical Maps. Neuron. 56:384–398.

Dehaene S, Cohen L. 2011. The unique role of the visual word form area in reading. Trends in Cognitive Sciences. 15:254–262.

Dehaene S, Cohen L, Morais J, Kolinsky R. 2015. Illiterate to literate: behavioural and cerebral changes induced by reading acquisition. Nature Publishing Group. 16:234–244.

Dehaene S, Molko N, Cohen L, Wilson AJ. 2004. Arithmetic and the brain. Current Opinion in Neurobiology. 14:218–224.

Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, Buckner RL, Dale AM, Maguire RP, Hyman BT, Albert MS, Killiany RJ. 2006. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. NeuroImage. 31:968–980.

Desimone R, Duncan J. 1995. Neural mechanisms of selective visual attention. Annu Rev Neurosci. 18:193–222.

Destrieux C, Fischl B, Dale A, Halgren E. 2010. Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. NeuroImage. 53:1–15.

Diamond A. 2013. Executive Functions. Annu Rev Psychol. 64:135–168.

Ding H, Qin W, Liang M, Ming D, Wan B, Li Q, Yu C. 2015. Cross-modal activation of auditory regions during visuo-spatial working memory in early deafness. Brain. 138:2750–2765.

Dormal V, Crollen V, Baumans C, Lepore F, Collignon O. 2016. Early but not late blindness leads to enhanced arithmetic and working memory abilities. Cortex. 83:212–221.

Doron N, Wollberg Z. 1994. Cross-Modal Neuroplasticity in the Blind Mole-Rat Spalax-Ehrenbergi - a WGA-HRP Tracing Study. Neuroreport. 5:2697–2701.

Driver J, Noesselt T. 2008. Multisensory Interplay Reveals Crossmodal Influences on “Sensory-Specific” Brain Regions, Neural Responses, and Judgments. Neuron Review. 57:11–23.

Ekstrom RB, French J, Harman HH, Dermen D. 1976. Manual for kit of factor-referenced cognitive tests.

Ernst MO, Banks MS. 2002. Humans integrate visual and haptic information in a statistically optimal fashion. Nature. 415:429–433.

Facchini S, Aglioti SM. 2003. Short term light deprivation increases tactile spatial acuity in humans. Neurology. 60:1998–1999.

Falchier A, Clavagnier S, Barone P, Kennedy H. 2002. Anatomical evidence of multimodal integration in primate striate cortex. J Neurosci. 22:5749–5759.

Farmer TA, Anderson SE, Spivey MJ. 2007. Gradiency and visual context in syntactic garden-paths. Journal of Memory and Language. 57:570–595.

Fedorenko E, Hsieh P-J, Nieto-Castanon A, Whitfield-Gabrieli S, Kanwisher N. 2010. New Method for fMRI Investigations of Language: Defining ROIs Functionally in Individual Subjects. Journal of Neurophysiology. 104:1177–1194.

Felleman DJ, Van Essen DC. 1991. Distributed hierarchical processing in the primate cerebral cortex. Cerebral Cortex. 1:1–47.

Ferreira F, Henderson JM. 1991. Recovery from misanalyses of garden-path sentences. Journal of Memory and Language. 30:725–745.

Fieger A, Röder B, Teder-Sälejärvi W, Hillyard SA, Neville HJ. 2006. Auditory spatial tuning in late-onset blindness in humans. J Cogn Neurosci. 18:149–157.

Fine AB, Jaeger TF, Farmer TA, Qian T. 2013. Rapid Expectation Adaptation during Syntactic Comprehension. PLoS ONE. 8:e77661.

Finney EM, Fine I, Dobkins KR. 2001. Visual stimuli activate auditory cortex in the deaf. Nature Neuroscience. 4:1171–1173.

Frank MC, Everett DL, Fedorenko E, Gibson E. 2008. Number as a cognitive technology: Evidence from Pirahã language and cognition. Cognition. 108:819–824.

Garavan H, Ross TJ, Murphy K, Roche R, Stein EA. 2002. Dissociable executive functions in the dynamic control of behavior: inhibition, error detection, and correction. NeuroImage.

Garavan H, Ross TJ, Stein EA. 1999. Right hemispheric dominance of inhibitory control: an event-related functional MRI study. Proc Natl Acad Sci USA. 96:8301–8306.

Genovese CR, Lazar NA, Nichols T. 2002. Thresholding of Statistical Maps in Functional Neuroimaging Using the False Discovery Rate. NeuroImage. 15:870–878.

Gibson E. 1998. Linguistic complexity: locality of syntactic dependencies. Cognition. 68:1–76.

Gilbert CD, Li W. 2013. Top-down influences on visual processing. Nature Reviews: Neuroscience. 14:350–363.

Gildea D, Temperley D. 2010. Do Grammars Minimize Dependency Length? Cognitive Science. 34:286–310.

Gizewski ER, Gasser T, de Greiff A, Boehm A, Forsting M. 2003. Cross-modal plasticity for sensory and motor activation patterns in blind subjects. NeuroImage. 19:968–975.

Glasser MF, Sotiropoulos SN, Wilson JA, Coalson TS, Fischl B, Andersson JL, Xu J, Jbabdi S, Webster M, Polimeni JR, Van Essen DC, Jenkinson M, Consortium FTW-MH. 2013. The minimal preprocessing pipelines for the Human Connectome Project. NeuroImage. 80:105–124.

Goghari VM, MacDonald AW. 2009. The neural basis of cognitive control: Response selection and inhibition. Brain Cogn. 71:72–83.

Goldreich D, Kanics IM. 2003. Tactile Acuity is Enhanced in Blindness. Journal of Neuroscience Methods. 23:3439–3445.

Gordon P. 2004. Numerical Cognition without Words: Evidence from Amazonia. Science. 306:496–499.

Gougoux F, Lepore F, Lassonde M, Voss P, Zatorre RJ. 2004. Pitch discrimination in the early blind: People blinded in infancy have sharper listening skills than those who lost their sight later. Nature.

Gougoux F, Zatorre RJ, Lassonde M, Voss P, Lepore F. 2005. A Functional Neuroimaging Study of Sound Localization: Visual Cortex Activity Predicts Performance in Early-Blind Individuals. PLoS Biol. 3:e27–10.

Green D, Swets J. 1966. Signal detection theory and psychophysics.

Hagler DJ, Saygin AP, Sereno MI. 2006. Smoothing and cluster thresholding for cortical surface-based group analysis of fMRI data. NeuroImage. 33:1093–1103.

Hasson U, Malach R, Heeger DJ. 2010. Reliability of cortical activity during natural stimulation. Trends in Cognitive Sciences. 14:40–48.

Hasson U, Nir Y, Levy I, Fuhrmann G, Malach R. 2004. Intersubject Synchronization of Cortical Activity during Natural Vision. Science. 303:1634–1640.

Hasson U, Yang E, Vallines I, Heeger DJ, Rubin N. 2008. A hierarchy of temporal receptive windows in human cortex. J Neurosci. 28:2539–2550.

He C, Peelen MV, Han Z, Lin N, Caramazza A, Bi Y. 2013. Selectivity for large nonmanipulable objects in scene-selective visual cortex does not require visual experience. NeuroImage. 79:1–9.

Heil P, Bronchti G, Wollberg Z, Neuroreport HS, 1991. Invasion of visual cortex by the auditory system in the naturally blind mole rat. Neuroreport.

Hickok G. 1993. Parallel parsing: Evidence from reactivation in garden-path sentences. J Psycholinguist Res. 22:239–250.

Hickok G, Poeppel D, Clark K, Buxton RB, Rowley HA, Roberts T. 1997. Sensory mapping in a congenitally deaf subject: MEG and fMRI studies of cross-modal non-plasticity. Hum Brain Mapp. 5:437–444.

Huettig F, Rommers J, Meyer AS. 2011. Using the visual world paradigm to study language processing: A review and critical evaluation. Acta Psychologica. 137:151–171.

Hugdahl K, Ek M, Takio F, Rintee T, Tuomainen J, Haarala C, Hämäläinen H. 2004. Blind individuals show enhanced perceptual and attentional sensitivity for identification of speech sounds. Cognitive Brain Research. 19:28–32.

Hull T, Mason H. 1995. Performance of blind children on digit-span tests. Journal of Visual Impairment Blindness.

Jaeger TF. 2008. Categorical data analysis: Away from ANOVAs (transformation or not) and towards logit mixed models. Journal of Memory and Language. 59:434–446.

James TW, Humphrey GK, Gati JS, Servos P, Menon RS, Goodale MA. 2002. Haptic study of three-dimensional objects activates extrastriate visual areas. Neuropsychologia. 40:1706–1714.

January D, Trueswell JC, Thompson-Schill SL. 2009. Co-localization of stroop and syntactic ambiguity resolution in Broca's area: implications for the neural basis of sentence processing. Cognitive Neuroscience, Journal of. 21:2434–2444.

Jo HJ, Lee J-M, Kim J-H, Shin Y-W, Kim I-Y, Kwon JS, Kim SI. 2007. Spatial accuracy of fMRI activation influenced by volume- and surface-based spatial smoothing techniques. NeuroImage. 34:550–564.

Johnson JS, Newport EL. 1989. Critical period effects in second language learning: the influence of maturational state on the acquisition of English as a second language. Cogn Psychol. 21:60–99.

Johnson MH. 2000. Functional brain development in infants: elements of an interactive specialization framework. Child Dev. 71:75–81.

Just MA, Carpenter PA. 1992. A capacity theory of comprehension: individual differences in working memory. Psychological Review. 99:122–149.

Kanjlia S, Lane C, Feigenson L, Bedny M. 2016. Absence of visual experience modifies the neural basis of numerical thinking. Proc Natl Acad Sci USA. 113:11172–11177.

Kanwisher N. 2010. Functional specificity in the human brain: a window into the functional architecture of the mind. Proceedings of the National Academy of Sciences

Konishi S, Nakajima K, Uchida I, Sekihara K, Miyashita Y. 1998. No-go dominant brain activity in human inferior prefrontal cortex revealed by functional magnetic resonance imaging. European Journal of Neuroscience. 10:1209–1213.

Kujala T, Alho K, Huotilainen M, Ilmoniemi RJ, Lehtokoski A, Leinonen A, Rinne T, Salonen O, Sinkkonen J, Standertskjöld-Nordenstam CG, Näätänen R. 1997. Electrophysiological evidence for cross-modal plasticity in humans with early- and late-onset blindness. Psychophysiology. 34:213–216.

Kujala T, Alho K, Kekoni J, Hämäläinen H, Reinikainen K, Salonen O, Standertskjöld-Nordenstam CG, Näätänen R. 1995. Auditory and somatosensory event-related brain potentials in early blind humans. Exp Brain Res. 104:519–526.

Kujala T, Alho K, Paavilainen P, Summala H, Näätänen R. 1992. Neural plasticity in processing of sound location by the early blind: an event-related potential study.

Electroencephalography and Clinical Neurophysiology/ Evoked Potentials. 84:469–472.

Kujala T, Huotilainen M, Sinkkonen J, Ahonen AI, Alho K, Hämäläinen MS, Ilmoniemi RJ, Kajola M, Knuutila JE, Lavikainen J. 1995. Visual cortex activation in blind humans during sound discrimination. Neuroscience Letters. 183:143–146.

Kujala T, Palva MJ, Salonen O, Alku P, Huotilainen M, Järvinen A, Näätänen R. 2005. The role of blind humans' visual cortex in auditory change detection. Neuroscience Letters. 379:127–131.

Lane C, Kanjlia S, Omaki A, Bedny M. 2015. "Visual" Cortex of Congenitally Blind Adults Responds to Syntactic Movement. Journal of Neuroscience Methods. 35:12859–12868.

Lane C, Kanjlia S, Richardson H, Fulton A, Omaki A, Bedny M. 2017. Reduced Left Lateralization of Language in Congenitally Blind Individuals. Cognitive Neuroscience, Journal of. 29:65–78.

Lerner Y, Honey CJ, Silbert LJ, Hasson U. 2011. Topographic Mapping of a Hierarchy of Temporal Receptive Windows Using a Narrated Story. Journal of Neuroscience Methods. 31:2906–2915.

Lessard N, Pare M, Lepore F, Lassonde M. 1998. Early-blind human subjects localize sound sources better than sighted subjects. Nature. 395:278–280.

Levänen S, Jousmäki V, Hari R. 1998. Vibration-induced auditory-cortex activation in a congenitally deaf adult. Current Biology. 8:869–872.

Levy BJ, Wagner AD. 2011. Cognitive control and right ventrolateral prefrontal cortex: reflexive reorienting, motor inhibition, and action updating. Annals of the New York Academy of Sciences. 1224:40–62.

Lewald J. 2002. Vertical sound localization in blind humans. Neuropsychologia. 40:1868–1872.

Liddle PF, Kiehl KA, Smith AM. 2001. Event-related fMRI study of response inhibition. Hum Brain Mapp. 12:100–109.

Liotti M, Ryder K, Woldorff MG. 1998. Auditory attention in the congenitally blind: where, when and what gets reorganized? Neuroreport. 9:1007–1012.

Liu L, Yuan C, Ding H, Xu Y, Long M, Li Y, Liu Y, Jiang T, Qin W, Shen W, Yu C. 2017. Visual deprivation selectively reshapes the intrinsic functional architecture of the anterior insula subregions. Nature Publishing Group. 1–11.

Liu Y, Yu C, Liang M, Li J, Tian L, Zhou Y, Qin W, Li K, Jiang T. 2007. Whole brain functional connectivity in the early blind. Brain. 130:2085–2096.

Lomber SG, Meredith MA, Kral A. 2010. Cross-modal plasticity in specific auditory cortices underlies visual compensations in the deaf. Nature Neuroscience. 13:1421–1427.

Long DL, Prat CS. 2008. Individual differences in syntactic ambiguity resolution: Readers vary in their use of plausibility information. Memory & Cognition. 36:375–391.

Macaluso E, Frith CD, Driver J. 2000. Modulation of Human Visual Cortex by Crossmodal Spatial Attention. Science (New York, NY). 289:1206–1208.

MacDonald MC, Pearlmutter NJ, Seidenberg MS. 1994. The Lexical Nature of Syntactic Ambiguity Resolution. Psychological Review. 102:245–245.

Mahon BZ, Anzellotti S, Schwarzbach J, Zampini M, Caramazza A. 2009. Category-Specific Organization in the Human Brain Does Not Require Visual Experience. Neuron. 63:397–405.

Mahon BZ, Caramazza A. 2011. What drives the organization of object knowledge in the brain? Trends in Cognitive Sciences. 15:97–103.

Martin AE. 2016. Language Processing as Cue Integration: Grounding the Psychology of Language in Perception and Neurophysiology. Front Psychol. 7:247–17.

Martino J, Brogna C, Robles SG, Vergani F, Duffau H. 2010. Anatomic dissection of the inferior fronto-occipital fasciculus revisited in the lights of brain stimulation data. Cortex. 46:691–699.

Maunsell JH, Van Essen DC. 1983. The connections of the middle temporal visual area (MT) and their relationship to a cortical hierarchy in the macaque monkey. Journal of Neuroscience Methods. 3:2563–2586.

McRae K, Spivey-Knowlton MJ, Tanenhaus MK. 1998. Modeling the influence of thematic fit (and other constraints) in on-line sentence comprehension. Journal of Memory and Language. 38:283–312.

Menon V, Adleman NE, White CD, Glover GH, Reiss AL. 2001. Error-related brain activation during a Go/NoGo response inhibition task. Hum Brain Mapp. 12:131–143.

Merabet L, Thut G, Murray B, Andrews J, Hsiao S, Pascual-Leone A. 2004. Feeling by sight or seeing by touch? Neuron. 42:173–179.

Merabet LB, Hamilton R, Schlaug G, Swisher JD, Kiriakopoulos ET, Pitskel NB, Kauffman T, Pascual-Leone A. 2008. Rapid and Reversible Recruitment of Early Visual Cortex for Touch. PLoS ONE. 3:e3046–12.

Meredith MA, Kryklywy J, McMillan AJ, Malhotra S, Lum-Tai R, Lomber SG. 2011. Crossmodal reorganization in the early deaf switches sensory, but not behavioral roles of auditory cortex. Proc Natl Acad Sci USA. 108:8856–8861.

Meredith MA, Lomber SG. 2011. Somatosensory and visual crossmodal plasticity in the anterior auditory field of early-deaf cats. Hearing Research. 280:38–47.

Miller EK, Cohen JD. 2001. An integrative theory of prefrontal cortex function. Annu Rev Neurosci. 24:167–202.

Mishkin M, Ungerleider LG, Macko KA. 1983. Object vision and spatial vision: two cortical pathways. Trends in Neurosciences. 6:414–417.

Miyake A. 2000. The Unity and Diversity of Executive Functions and Their Contributions to Complex “Frontal Lobe” Tasks: A Latent Variable Analysis. Cogn Psychol. 41:49–100.

Moran J, Desimone R. 1985. Selective Attention Gates Visual Processing in the Extrastriate Cortex. Science. 229:782–784.

Morosan P, Rademacher J, Schleicher A, Amunts K, Schormann T, Zilles K. 2001. Human Primary Auditory Cortex: Cytoarchitectonic Subdivisions and Mapping into a Spatial Reference System. NeuroImage. 13:684–701.

Mostofsky SH, Schafer JGB, Abrams MT, Goldberg MC, Flower AA, Boyce A, Courtney SM, Calhoun VD, Kraut MA, Denckla MB, Pekar JJ. 2003. fMRI evidence that the neural basis of response inhibition is task-dependent. Cognitive Brain Research. 17:419–430.

Muchnik C, Efrati M, Nemeth E, Malin M, Hildesheimer M. 1991. Central Auditory Skills in Blind and Sighted Subjects. Scandinavian Audiology. 20:19–23.

Naci L, Sinai L, Owen AM. 2016. Detecting and interpreting conscious experiences in behaviorally non-responsive patients. NeuroImage. 1–10.

Nagahama Y, Okada T, Katsumi Y, Hayashi T, Yamauchi H, Oyanagi C, Konishi J, Fukuyama H, Shibasaki H. 2001. Dissociable mechanisms of attentional control within the human prefrontal cortex. Cerebral Cortex. 11:85–92.

Nagel HN, Shapiro LP, Nawy R. 1994. Prosody and the processing of filler-gap sentences. J Psycholinguist Res. 23:473–485.

Nee DE, Wager TD, Jonides J. 2007. Interference resolution: insights from a meta-analysis of neuroimaging tasks. Cogn Affect Behav Neurosci. 7:1–17.

Neville HJ, Lawson D. 1987. Attention to central and peripheral visual space in a movement detection task: an event-related potential and behavioral study. II. Congenitally deaf adults. Brain Research. 405:268–283.

Nichols T, Hayasaka S. 2003. Controlling the familywise error rate in functional neuroimaging: a comparative review. Psychological Reports.

Nieder A, Dehaene S. 2009. Representation of Number in the Brain. Annu Rev Neurosci. 32:185–208.

Niemeyer W, Starlinger I. 1981. Do the Blind Hear Better? Investigations on Auditory Processing in Congenital or Early Acquired Blindness II. Central Functions. Int J Audiol. 20:510–515.

Novick JM, Hussey E, Teubner-Rhodes S, Harbison JI, Bunting MF. 2012. Clearing the garden-path: improving sentence processing through cognitive control training. Language, Cognition and Neuroscience. 29:186–217.

Novick JM, Trueswell JC, Thompson-Schill SL. 2005. Cognitive control and parsing: Reexamining the role of Broca's area in sentence comprehension. Cogn Affect Behav Neurosci. 5:263–281.

Novick JM, Trueswell JC, Thompson-Schill SL. 2010. Broca's Area and Language Processing: Evidence for the Cognitive Control Connection. Language Ling Compass. 4:906–924.

O'Leary DDM. 1989. Do Cortical Areas Emerge From a Protocortex. Trends in Neurosciences. 12:400–406.

Park H-J, Chun J-W, Park B, Park H, Kim JI, Lee JD, Kim J-J. 2011. Activation of the Occipital Cortex and Deactivation of the Default Mode Network During Working Memory in the Early Blind. J Int Neuropsychol Soc. 17:407–422.

Pascual-Leone A, Hamilton R. 2001. The metamodal organization of the brain. Prog Brain Res. 134:427–445.

Pasqualotto A, Lam JSY, Proulx MJ. 2013. Congenital blindness improves semantic and episodic memory. Behavioural Brain Research. 244:162–165.

Peirce JW. 2007. PsychoPy—Psychophysics software in Python. Journal of Neuroscience Methods. 162:8–13.

Pietrini P, Furey ML, Ricciardi E, Gobbini MI, Wu W-HC, Cohen L, Guazzelli M, Haxby JV. 2004. Beyond sensory images: Object-based representation in the human ventral pathway. Proc Natl Acad Sci USA. 101:5658–5663.

Poirier C, Collignon O, Scheiber C, Renier L, Vanlierde A, Tranduy D, Veraart C, De Volder AG. 2006. Auditory motion perception activates visual motion areas in early blind subjects. NeuroImage. 31:279–285.

Prado J, Mutreja R, Zhang H, Mehta R, Desroches AS, Minas JE, Booth JR. 2011. Distinct representations of subtraction and multiplication in the neural systems for numerosity and language. Hum Brain Mapp. 32:1932–1947.

Raz N, Amedi A, Zohary E. 2005. V1 activation in congenitally blind humans is associated with episodic retrieval. Cerebral Cortex. 15:1459–1468.

Raz N, Striem E, Pundak G, Orlov T, Zohary E. 2007. Superior Serial Memory in the Blind: A Case of Cognitive Compensatory Adjustment. Current Biology. 17:1129–1133.

Rebillard G, Carlier E, Rebillard M, R. Pujol. 1977. Enhancement of visual responses on the primary auditory cortex of the cat after an early destruction of cochlear receptors. Brain Research

Regev M, Honey CJ, Simony E, Hasson U. 2013. Selective and Invariant Neural Responses to Spoken and Written Narratives. Journal of Neuroscience Methods. 33:15978–15988.

Reich L, Szwed M, Cohen L, Amedi A. 2011. A ventral visual stream reading center independent of visual experience. Curr Biol. 21:363–368.

Renier L, De Volder AG, Rauschecker JP. 2014. Cortical plasticity and preserved function in early blindness. Neuroscience & Biobehavioral Reviews. 41:53–63.

Renier LA, Anurova I, De Volder AG, Carlson S, VanMeter J, Rauschecker JP. 2010. Preserved Functional Specialization for Spatial Processing in the Middle Occipital Gyrus of the Early Blind. Neuron. 68:138–148.

Ricciardi E, Vanello N, Sani L, Gentili C, Scilingo EP, Landini L, Guazzelli M, Bicchi A, Haxby JV, Pietrini P. 2007. The Effect of Visual Experience on the Development of Functional Architecture in hMT. Cerebral Cortex. 17:2933–2939.

Rice CE. 2017. Perceptual Enhancement in the Early Blind? Psychol Rec. 19:1–14.

Rockland KS, Ojima H. 2003. Multisensory convergence in calcarine visual areas in macaque monkey. International Journal of Psychophysiology. 50:19–26.

Roder B, Rösler F, Neville HJ. 2000. Event-related potentials during auditory language processing in congenitally blind and sighted people. Neuropsychologia. 38:1482–1502.

Roder B, Rösler F, Neville HJ. 2001. Auditory memory in congenitally blind adults: a behavioral-electrophysiological investigation. Brain Res Cogn Brain Res. 11:289–303.

Roder B, Teder-Sälejärvi W, Sterr A, Rösler F. 1999. Improved auditory spatial tuning in blind humans. Nature.

Rokem A, Ahissar M. 2009. Interactions of cognitive and auditory abilities in congenitally blind individuals. Neuropsychologia. 47:843–848.

Rosner B. 1975. On the Detection of Many Outliers. Technometrics. 17:221–227.

Roth FP. 1984. Accelerating language learning in young children. Journal of Child Language. 11:89–107.

Röder B, Demuth L, Streb J, Rösler F. 2003. Semantic and morpho-syntactic priming in auditory word recognition in congenitally blind adults. Language and Cognitive Processes. 18:1–20.

Röder B, Stock O, Bien S, Neville H, Rösler F. 2002. Speech processing activates visual cortex in congenitally blind humans. European Journal of Neuroscience. 16:930–936.

Rubia K, Smith AB, Brammer MJ, Taylor E. 2003. Right inferior prefrontal cortex mediates response inhibition while mesial prefrontal cortex is responsible for error detection. NeuroImage. 20:351–358.

Sadato N, Pascual-Leone A, Grafman J, Ibañez V, Deiber MP, Dold G, Hallett M. 1996. Activation of the primary visual cortex by Braille reading in blind subjects. Nature. 380:526–528.

Sathian K. 2005. Visual cortical activity during tactile perception in the sighted and the visually deprived. Dev Psychobiol. 46:279–286.

Sathian K, Stilla R. 2010. Cross-modal plasticity of tactile perception in blindness. Restor Neurol Neurosci. 28:271–281.

Sathian K, Zangaladze A, Hoffman JM, Grafton ST. 1997. Feeling with the mind's eye. Neuroreport. 8:3877–3881.

Saygin ZM, Osher DE, Norton ES, Youssoufian DA, Beach SD, Feather J, Gaab N, Gabrieli JDE, Kanwisher N. 2016. Connectivity precedes function in the development of the visual word form area. Nature Neuroscience. 19:1250–1255.

Sebastian A, Baldermann C, Feige B, Katzev M, Scheller E, Hellwig B, Lieb K, Weiller C, Tüscher O, Klöppel S. 2013. Differential effects of age on subcomponents of response inhibition. Neurobiol Aging. 34:2183–2193.

Selemon LD, Goldman-Rakic PS. 1988. Common Cortical and Subcortical Targets of the Dorsolateral Prefrontal and Posterior Parietal Cortices in the Rhesus-Monkey - Evidence for a Distributed Neural Network Subserving Spatially Guided Behavior. Journal of Neuroscience Methods. 8:4049–4068.

Shimony JS, Burton H, Epstein AA, McLaren DG, Sun SW, Snyder AZ. 2005. Diffusion Tensor Imaging Reveals White Matter Reorganization in Early Blind Humans. Cerebral Cortex. 16:1653–1661.

Shu N, Li J, Li K, Yu C, Jiang T. 2009. Abnormal diffusion of cerebral white matter in early blindness. Hum Brain Mapp. 30:220–227.

Shu N, Liu Y, Li J, Li Y, Yu C, Jiang T. 2009. Altered Anatomical Network in Early Blindness Revealed by Diffusion Tensor Tractography. PLoS ONE. 4:e7228–13.

Smith SM, Jenkinson M, Woolrich MW, Beckmann CF, Behrens TEJ, Johansen-Berg H, Bannister PR, De Luca M, Drobnjak I, Flitney DE, Niazy RK, Saunders J, Vickers J, Zhang Y, De Stefano N, Brady JM, Matthews PM. 2004. Advances in functional and structural MR image analysis and implementation as FSL. NeuroImage. 23:S208–S219.

Spivey MJ, Tanenhaus MK, Eberhard KM, Sedivy JC. 2002. Eye movements and spoken language comprehension: Effects of visual context on syntactic ambiguity resolution. Cogn Psychol. 45:447–481.

Stevens AA, Weaver K. 2005. Auditory perceptual consolidation in early-onset blindness. Neuropsychologia. 43:1901–1910.

Stevenson S. 1998. Parsing as Incremental Restructuring. In: Reanalysis in Sentence Processing. Studies in Theoretical Psycholinguistics. Dordrecht: Springer, Dordrecht. p. 327–363.

Stilla R, Hanna R, Hu X, Mariola E, Deshpande G, Sathian K. 2008. Neural processing underlying tactile microspatial discrimination in the blind: A functional magnetic resonance imaging study. J Vis. 8:13–13.

Striem-Amit E, Almeida J, Belledonne M, Chen Q, Fang Y, Han Z, Caramazza A, Bi Y. 2016. Topographical functional connectivity patterns exist in the congenitally, prelingually deaf. Nature Publishing Group. 6:1–13.

Striem-Amit E, Cohen L, Dehaene S, Amedi A. 2012. Reading with Sounds: Sensory Substitution Selectively Activates the Visual Word Form Area in the Blind. Neuron. 76:640–652.

Striem-Amit E, Dakwar O, Reich L, Amedi A. 2011. The large-Scale Organization of “Visual” Streams Emerges Without Visual Experience. Cerebral Cortex. 22:1698–1709.

Striem-Amit E, Ovadia-Caro S, Caramazza A, Margulies DS, Villringer A, Amedi A. 2015. Functional connectivity of visual cortex in the blind follows retinotopic organization principles. Brain. 138:1679–1695.

Swanson HL, Luxenberg D. 2009. Short-Term Memory and Working Memory in Children with Blindness: Support for a Domain General or Domain Specific System? Child Neuropsychology. 15:280–294.

Tanenhaus MK, Magnuson JS, Dahan D, Chambers C. 2000. Eye movements and lexical access in spoken-language comprehension: evaluating a linking hypothesis between fixations and linguistic processing. J Psycholinguist Res. 29:557–580.

Tanenhaus MK, Spivey-Knowlton MJ, Eberhard KM, Sedivy JC. 1995. Integration of visual and linguistic information in spoken language comprehension. Science. 268:1632–1634.

Thaler L, Arnott SR, Goodale MA. 2011. Neural Correlates of Natural Human Echolocation in Early and Late Blind Echolocation Experts. PLoS ONE. 6:e20162–16.

Thompson-Schill SL, Bedny M, Goldberg RF. 2005. The frontal lobes and the regulation of mental activity. Curr Opin Neurobiol. 15:219–224.

Tillman MH, Bashaw WL. 1968. Multivariate analysis of the WISC scales for blind and sighted children. Psychological Reports. 23:523–526.

Tong F. 2003. Cognitive neuroscience: Primary visual cortex and visual awareness. Nature Reviews: Neuroscience. 4:219–229.

Trueswell JC, Gleitman L. 2004. Children's Eye Movements during Listening: Developmental Evidence for a Constraint-Based Theory of Sentence Processing. Interface of Vision, Language and Action. 1–28.

Trueswell JC, Tanenhaus MK, Garnsey SM. 1994. Semantic Influences On Parsing: Use of Thematic Role Information in Syntactic Ambiguity Resolution. Journal of Memory and Language. 33:285–318.

Tucholka A, Fritsch V, Poline J-B, Thirion B. 2012. An empirical comparison of surface-based and volume-based group studies in neuroimaging. NeuroImage. 63:1443–1453.

Tyler LK, Marslen-Wilson WD. 1977. The on-line effects of semantic context on syntactic processing. Journal of Verbal Learning and Verbal Behavior. 16:683–692.

Uhl F, Franzen P, Lindinger G, Lang W, DEECKE L. 1991. On the Functionality of the Visually Deprived Occipital Cortex in Early Blind Persons. Neuroscience Letters. 124:256–259.

Ungerleider LG, Courtney SM, Haxby JV. 1998. A Neural System for Human Visual Working Memory. Proc Natl Acad Sci USA. 95:883–890.

Ungerleider LG, Galkin TW, Desimone R, Gattass R. 2008. Cortical Connections of Area V4 in the Macaque. Cerebral Cortex. 18:477–499.

Van Boven RW, Hamilton RH, Kauffman T, Keenan JP, Leone AP. 2000. Tactile spatial resolution in blind Braille readers. Neurology. 54:2230–2236.

van den Hurk J, Van Baelen M, Op de Beeck HP. 2017. Development of visual category selectivity in ventral visual cortex does not require visual experience. Proc Natl Acad Sci USA. 114:E4501–E4510.

Van Essen DC. 2005. A Population-Average, Landmark- and Surface-based (PALS) atlas of human cerebral cortex. NeuroImage. 28:635–662.

Voss P, Alary F, Lazzouni L, Chapman CE, Goldstein R, Bourgoin P, Lepore F. 2016. Crossmodal Processing of Haptic Inputs in Sighted and Blind Individuals. Front Syst Neurosci. 10:2037–11.

Voss P, Gougoux F, Zatorre RJ, Lassonde M, Lepore F. 2008. Differential occipital responses in early- and late-blind individuals during a sound-source discrimination task. NeuroImage. 40:746–758.

Voss P, Lassonde M, Gougoux F, Fortin M, Guillemot J-P, Lepore F. 2004. Early- and Late-Onset Blind Individuals Show Supra-Normal Auditory Abilities in Far-Space. Current Biology. 14:1734–1738.

Wager TD, Sylvester C-YC, Lacey SC, Nee DE, Franklin M, Jonides J. 2005. Common and unique components of response inhibition revealed by fMRI. NeuroImage. 27:323–340.

Wan CY, Wood AG, Reutens DC, Wilson SJ. 2010. Early but not late-blindness leads to enhanced auditory perception. Neuropsychologia. 48:344–348.

Wanet-Defalque MC, Veraart C, De Volder A, Metz R, Michel C, Dooms G, Goffinet A. 1988. High metabolic activity in the visual cortex of early blind human subjects. Brain Research. 446:369–373.

Wang D, Qin W, Liu Y, Zhang Y, Jiang T, Yu C. 2013. Altered resting-state network connectivity in congenital blind. Hum Brain Mapp. 35:2573–2581.

Weaver KE, Stevens AA. 2007. Attention and sensory interactions within the occipital cortex in the early blind: an fMRI study. Cognitive Neuroscience, Journal of. 19:315–330.

Weeks R, Horwitz B, Aziz-Sultan A, Tian B, Wessinger CM, Cohen LG, Hallett M, Rauschecker JP. 2000. A Positron Emission Tomographic Study of Auditory Localization in the Congenitally Blind. Journal of Neuroscience Methods. 20:2664–2672.

Wells JB, Christiansen MH, Race DS, Acheson DJ, MacDonald MC. 2009. Experience and sentence processing: Statistical learning and relative clause comprehension. Cogn Psychol. 58:250–271.

Whitfield-Gabrieli S, Nieto-Castanon A. 2012. Conn: A Functional Connectivity Toolbox for Correlated and Anticorrelated Brain Networks. Brain Connect. 2:125–141.

Withagen A, Kappers AML, Vervloed MPJ, Knoors H, Verhoeven L. 2013. Research in Developmental Disabilities Short term memory and working memory in blind versus sighted children. Research in Developmental Disabilities. 34:2161–2172.

Wolbers T, Zahorik P, Giudice NA. 2011. Decoding the direction of auditory motion in blind humans. NeuroImage. 56:681–687.

Wong M, Gnanakumaran V, Goldreich D. 2011. Tactile spatial acuity enhancement in blindness: evidence for experience-dependent mechanisms. J Neurosci. 31:7028–7037.

Woodard K, Pozzan L, Trueswell JC. 2016. Taking your own path: Individual differences in executive function and language processing skills in child learners. J Exp Child Psychol. 141:187–209.

Xu KZ, Anderson BA, Emeric EE, Sali AW, Stuphorn V, Yantis S, Courtney SM. 2017. Neural Basis of Cognitive Control over Movement Inhibition: Human fMRI and Primate Electrophysiology Evidence. Neuron. 1–30.

Yaka R, Yinon U, Rosner M, Wollberg Z. 2000. Pathological and experimentally induced blindness induces auditory activity in the cat primary visual cortex. Exp Brain Res. 132:416–416.

Yarkoni T, Poldrack RA, Nichols TE, Van Essen DC, Wager TD. 2011. Large-scale automated synthesis of human functional neuroimaging data. Nat Methods. 8:665–670.

Yeterian EH, Pandya DN, Tomaiuolo F, Petrides M. 2012. The cortical connectivity of the prefrontal cortex in the monkey brain. Cortex. 48:58–81.

Yu C, Liu Y, Li J, Zhou Y, Wang K, Tian L, Qin W, Jiang T, Li K. 2008. Altered functional connectivity of primary visual cortex in early blindness. Hum Brain Mapp. 29:533–543.

Zangaladze A, Epstein CM, Grafton ST, Sathian K. 1999. Involvement of visual cortex in tactile discrimination of orientation. Nature. 401:587–590.

Zangenehpour S, Zatorre RJ. 2010. Crossmodal recruitment of primary visual cortex following brief exposure to bimodal audiovisual stimuli. Neuropsychologia. 48:591–600.

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