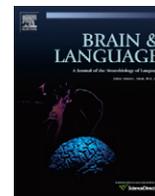


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A sensitive period for language in the visual cortex: Distinct patterns of plasticity in congenitally versus late blind adults

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ABSTRACT

Recent evidence suggests that blindness enables visual circuits to contribute to language processing. We examined whether this dramatic functional plasticity has a sensitive period. BOLD fMRI signal was measured in congenitally blind, late blind (blindness onset 9-years-old or later) and sighted participants while they performed a sentence comprehension task. In a control condition, participants listened to backwards speech and made match/non-match to sample judgments. In both congenitally and late blind participants BOLD signal increased in bilateral foveal-pericalcarine cortex during response preparation, irrespective of whether the stimulus was a sentence or backwards speech. However, left occipital areas (pericalcarine, extrastriate, fusiform and lateral) responded more to sentences than backwards speech only in congenitally blind people. We conclude that age of blindness onset constrains the non-visual functions of occipital cortex: while plasticity is present in both congenitally and late blind individuals, recruitment of visual circuits for language depends on blindness during childhood.

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1. Introduction

Humans are believed to have specific neural adaptations that enable them, and no other species, to acquire language (Pinker, 1994). Consistent with this possibility, the neural basis of language is highly stable across languages and cultures. Languages as varied as Mandarin Chinese, English, and various sign languages, are supported by a common left-lateralized network of brain areas (Chee et al., 1999; MacSweeney, Capek, Campbell, & Woll, 2008). This network includes regions within the frontal, temporal and parietal lobes such as Broca's area and Wernicke's area. The capacity for language is commonly assumed to depend on intrinsic properties of these brain areas. However, recent research with blind individuals suggests that under some circumstances, brain regions thought to have evolved for vision can participate in language processing.

Blind individuals engage occipital regions during a variety of verbal tasks including Braille reading, verb generation (in response to heard nouns), covert retrieval of words from long-term memory and sentence comprehension (Amedi, Floel, Knecht, Zohary, &

Cohen, 2004; Amedi, Raz, Pianka, Malach, & Zohary, 2003; Burton, Diamond, & McDermott, 2003; Burton, Snyder, Diamond, & Raichle, 2002; Sadato et al., 1996; Uhl, Franzen, Lindinger, Lang, & Deecke, 1991). Occipital activity is observed in various visual areas including the pericalcarine cortex (the anatomical location of V1 and the first stage of cortical visual processing in humans) as well as in secondary visual regions on the lateral and ventral surface of the occipital lobe.

In congenitally blind adults, occipital areas show a response profile that is similar to classic language areas: During sentence comprehension, occipital regions are sensitive to high-level linguistic information such as the meanings of words and compositional sentence structure (Bedny, Pascual-Leone, Dodell-Feder, Fedorenko, & Saxe, 2011; Burton et al., 2003; Roder, Rosler, & Neville, 2000; Roder, Stock, Bien, Neville, & Rosler, 2002). Like classic language areas, occipital regions respond most to sentences, less to lists of words and to Jaberwocky (non-word sentences), and still less to lists of nonsense words and backwards speech (Bedny, Konkle, Pelphrey, Saxe, & Pascual-Leone, 2011; Bedny, Pascual-Leone et al., 2011; Pallier, Devauchelle, & Dehaene, 2011). There is also some evidence that occipital activation is functionally relevant to language processing: rTMS to the occipital pole leads to verb-generation errors and impairs Braille reading in congenitally blind individuals (Amedi et al., 2004; Cohen et al., 1997; Kupers et al., 2007).

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These data suggest that blindness enables occipital areas to participate in language processing. A key open question is whether this remarkable plasticity results from blindness early in life, or can be caused by long periods of blindness at any age.

Early and late blindness could cause qualitatively different forms of plasticity for at least two reasons. First, there may be a sensitive period in the functional development of human visual circuits. Absence of vision early in life has distinctive effects on the neurophysiology and function of the mammalian visual system (Fagiolini, Jensen, & Champagne, 2009; Hensch, 2004; Hensch, 2005; Hubel & Wiesel, 1970; Morishita & Hensch, 2008; Smirnakis et al., 2005). In animals, dark rearing impairs the development of the direction and orientation selectivity and enlarges receptive field size of cells in primary visual cortex (Crair, Gillespie, & Stryker, 1998; Fagiolini, Pizzorusso, Berardi, Domenici, & Maffei, 1994; Li, Fitzpatrick, & White, 2006; Li, Van Hooser, Mazurek, White, & Fitzpatrick, 2008; Wang, Sarnaik, & Cang, 2010). Visual deprivation in adulthood does not result in similar deficits (Fagiolini et al., 2009; Hensch, 2004; Hensch, 2005; Morishita & Hensch, 2008; Smirnakis et al., 2005). These animal studies suggest that early blindness could have more dramatic effects on the function of the human visual system.

Second, there may be a sensitive period in the plasticity of the language system itself. Once established, the neural architecture of language may not be as flexible. There is considerable evidence that the language system is more flexible during development than later in life. For example, damage to classic left hemisphere language regions during development has much less pronounced effects on language abilities than damage to the same brain regions in adulthood (Bates, 1999). Similarly, language acquisition early in life is more facile than in adulthood (Johnson & Newport, 1989). Occipital areas may only get incorporated into the language system during this key developmental period.

To assess whether early and late blindness differentially effect the visual system's capacity to take on language functions, we compared the response of occipital cortex to language in congenitally blind and late blind individuals. If occipital responses to language emerge specifically as a result of early blindness, congenitally blind but not late blind individuals should show this language response.

Existing studies are ambiguous as to whether there is a sensitive period for language-related plasticity in occipital cortex. On the one hand, there is clear evidence of functional plasticity in occipital cortex for both congenitally and late blind adults (Sadato, Okada, Honda, & Yonekura, 2002) and occipital areas are active during verbal tasks in both populations (Buchel, Price, Frackowiak, & Friston, 1998; Burton, 2003; Burton & McLaren, 2006; Burton, Snyder, Conturo et al., 2002). On the other hand, it is not clear whether occipital activity in congenitally and late blind people reflects similar cognitive processes. In congenitally blind people, occipital cortex responds more during verbal than non-verbal tasks, even when the non-verbal tasks are more difficult and when no overt responses are required (Amedi et al., 2003; Amedi et al., 2004; Bedny, Pascual-Leone et al., 2011; Roder et al., 2002). Such data suggest that occipital areas respond specifically to linguistic content. By contrast, in late blind people, verbal tasks have been compared to passive or less difficult non-verbal tasks (for example, verb generation compared to passive listening to non-verbal stimuli) (Burton, Snyder, Diamond et al., 2002). These results leave open the possibility that occipital activity in late blind people is driven by non-verbal components of the task, such as response preparation.

Several existing pieces of evidence suggest that occipital activity might be related to different cognitive processes in congenitally blind and late blind people. First, occipital activity is much less pronounced in late blind as compared to congenitally blind participants (Burton, Snyder, Diamond et al., 2002; Burton, Snyder,

Conturo et al., 2002; Burton, 2003). Second, there is some evidence that responses occur in different parts of occipital cortex in these two populations. For example, during verb generation occipital activity is left-lateralized in congenitally blind participants, but bilateral or right-lateralized in late blind individuals (Buchel et al., 1998; Burton, 2003; Burton, Snyder, Diamond et al., 2002; Burton, Snyder, Conturo et al., 2002). There is also some evidence that occipital activity has different functional relevance in these populations. One study found that rTMS to the occipital pole impairs Braille reading in congenitally blind and early onset blind participants, but not in late blind individuals (Cohen et al., 1999). On the other hand, in late blind participants rTMS to occipital cortex does impair performance on non-verbal tasks (Merabet et al., 2009).

In light of prior data, the goal of the present study was to examine whether occipital plasticity in congenitally blind and late blind individuals is qualitatively similar. In particular, we wished to establish whether occipital areas respond to language in late blind individuals as they do in congenitally blind participants.

To explore this question, we presented late blind, congenitally blind and sighted participants with a sentence comprehension task. Participants heard short passages and answered true/false questions about them. In a control condition, participants heard the same sentences played backwards and performed a match to sample task. Backwards speech is unintelligible and lacks linguistic information, such as sentence structure, meanings of words or phonology. On the other hand, both the language and the backwards speech tasks required encoding and maintenance of information in working memory, and the auditory matching task was more difficult than the true/false task with sentences so that if we observed a larger response to sentences this could not be explained by the difficulty of the task itself. We reasoned that (1) a language-sensitive response should be higher for sentences than for backwards speech, and (2) a language-sensitive response should be present during the story portion of the trial, when no response preparation is required.

Our primary analyses examined the response of left pericalcarine cortex. In sighted people, pericalcarine cortex is anatomically the location of the primary visual cortex, V1, which is the earliest cortical recipient of visual information in primates (Lamme, Super, & Spekreijse, 1998). V1 is believed to have evolved for visual perception and has well described anatomical properties such as an enlarged layer IV which receives inputs from the lateral geniculate nucleus (Gennari, 1782). Therefore, an important question is whether plasticity in this early visual area occurs in the same way during and after early childhood. We focused our analyses on left, as opposed to right, pericalcarine cortex because prior studies have found left-lateralized pericalcarine responses to language in congenitally blind people (e.g. Amedi et al., 2003; Bedny, Konkle et al., 2011; Bedny, Pascual-Leone et al., 2011; Roder et al., 2002). We asked whether similar responses are present in people who become blind later in life.

There is some evidence that late blind and congenitally blind participants manifest plasticity in partially distinct areas of pericalcarine cortex along the caudal/rostral axis. In late blind people, pericalcarine activity appears to be relatively restricted to the foveal/parafoveal region (Burton, 2003). To formally test this hypothesis, we measured percent signal change (PSC) in the in foveal/parafoveal (caudal) and peripheral (rostral) pericalcarine cortex separately.

2. Materials and methods

2.1. Participants

Twenty-two sighted (12 females, mean age 41 years, SD 19), 11 congenitally blind (6 females, mean age 49 years, SD 9), and 9 late

blind (3 females, mean age 48, SD 9) participants took part in the study. Groups did not differ in age ($P > .2$). Blind participants had lost their vision due to pathology anterior to or in the optic chiasm, and had at most minimal residual light perception. None of the blind participants could see colors, shapes, or motion. Congenitally blind participants had at most minimal light perception from birth. Late blind participants lost their vision in late childhood or later (range: 9–29 years-of-age). The present definition of late blindness is consistent with a number of prior studies (Burton, Snyder, Diamond et al., 2002; Burton, Snyder, Conturo et al., 2002), but differs from some, which consider late blind only those participants who lost their vision after age 16 (Sadato et al., 2002). Detailed demographic information, including gender, age, age of blindness onset, cause of blindness, presence of residual light perception, and highest level of education is summarized in Table 1. None of the participants had any known neurological disorders or had ever sustained a head injury. The study was approved by the institutional review board and all participants gave written informed consent.

2.2. Behavioral procedures

Participants heard brief verbal passages (<12 s) and answered true or false questions about them (<6 s) in a blocked design (each block containing a single trial). Passages consisted of two to three sentences (Mean 2.43, SD .62, Mean words per sentences 13.35, SD 2.74). Words in the sentences had on average 1.40 syllables (SD .17), a Celex log frequency of 2.12 (SD .25) and an average concreteness of 445 (SD 44). True/false questions always consisted of a single declarative sentence (Number of words 9.76 (SD 2.45), syllables per word 1.42 (SD .21), Freq 2.20 (SD .38), concreteness 440 (SD 112)).

In the control condition, participants performed an auditory match to sample task with backwards speech. Backwards speech is unintelligible and lacks information about sentence structure, word meanings and English phonology. Participants first heard a long segment of backwards speech (<12 s) followed by a short segment of backwards speech (<6 s). They were asked to determine whether the short string of backward speech was a piece of the long string or a new string. On match trials, the short string was spliced from the long backwards speech string. Every trial was followed by 12 s of resting baseline.

Stimuli were digitally recorded by a female native English speaker at a sampling rate of 44,100 Hz to produce 32-bit digital sound files. The stories were on average 9.81 s long, (SD 1.27), –20 RMS amplitude, and the questions were on average 3.02 s long (SD .78), –19 RMS. Long segments of backwards-speech were created by playing the stories backwards, and short segments were created by playing the questions backwards, for non-matched trials. Long segments of backwards speech were 9.74 s long (SD 1.27) and –20 RMS in amplitude. Short segments were 3.96 s long (SD 1.13), –21 RMS. Stories and long backwards speech segments were not different in either duration or amplitude ($P > .3$). The short segments of backwards speech were longer and louder than the questions ($P < .005$).

The task was performed in 6 runs with 12 items per run (8 stories and 4 backward-speech). Each run was 6 min and 12 s long. There were a total of 48 stories and 24 unique segments of backwards speech; each stimulus was heard once during the experiment. Stimuli were presented in different pseudorandom orders across participants. Order of conditions was counterbalanced across participants and runs.

2.3. fMRI Data Acquisition and Analysis

MRI structural and functional data of the whole brain were collected on a 3 Tesla Siemens scanner. T1-weighted structural images were collected in 128-axial slices with 1.33 mm isotropic voxels (TR = 2 ms, TE = 3.39 ms). Functional, blood-oxygenation-level-dependent (BOLD) data were acquired in $3 \times 3 \times 4$ mm voxels (TR = 2 s, TE = 30 ms), in 30 near-axial slices. The first four seconds of each run were excluded to allow for steady-state magnetization. Data analyses were performed using SPM2 (SPM2 <http://www.fil.ion.ucl.ac.uk/>) and Matlab-based in-house software. Prior to modeling, data were realigned to the first image of the first run to correct for head motion, smoothed with a 5 mm smoothing kernel, and normalized to a standard template in Montreal Neurological Institute (MNI) space.

Left and right pericalcarine ROIs were drawn by tracing the calcarine sulcus in each congenitally blind and late blind participant using their individual normalized structural scan. Foveal/parafoveal and peripheral ROIs covered the posterior and anterior portions of the sulcus respectively. In sighted people, foveal/parafoveal pericalcarine cortex represents the foveal/parafoveal

Table 1

Demographic table describing participants. Abbreviations: Retrolental Fibroplasia (RLF), years (y), education (Ed), Masters Degree (MA), Bachelors Degree (BA), Congenitally Blind (CB), Late Blind (LB), Female (F), Male (M).

ID	Gender	Age (y)	Age totally blind (y)	Cause of blindness	Residual LP	Highest level Ed (y)
CB1	F	47	Birth	Premature birth/RLF	No	3 years of college
CB2	F	61	Birth	Optic chiasm malformation	Left Eye	Multiple MAs (22)
CB3	M	46	Birth	Retinoblastoma	No	MA (18)
CB4	M	54	Birth	Premature birth/RLF	No	MA (18)
CB5	F	43	Birth	Premature birth/RLF	No	BA (16)
CB7	M	44	Birth	Congenital Rubella Syndrome	No	BA (16)
CA8	F	57	Birth	Premature birth/RLF	No	MA (18)
CA10	F	53	Birth	Premature birth/RLF	Yes	MA (18)
CB11	M	39	Birth	Premature birth/RLF	Yes	MA (18)
CB12	M	36	Birth	Premature birth/RLF	No	MA (18)
CB14	F	61	Birth	Premature birth/RLF	No	BA (16)
LB1	M	47	29	Retinitis pigmentosa	Yes	3y Post-grad (19)
LB2	M	50	Adult	Retinitis pigmentosa	Yes	High school (12)
LB3	M	54	9	Retinoblastoma (enucleated)	No	MA (18)
LB4	F	50	25	Glaucoma	No	MA (18)
LB5	M	53	16	Glaucoma	No	MA (18)
LB6	M	51	11	Accident with chemicals	No	BA (16)
LB7	F	57	15	Retinoblastoma	No	MA (18)
LB8	F	26	20	Marfan syndrome	Yes	BA (16)
LB9	M	40	9	Congenital Cataracts	No	High school
Sighted	12F	41(19)	–	–	–	–

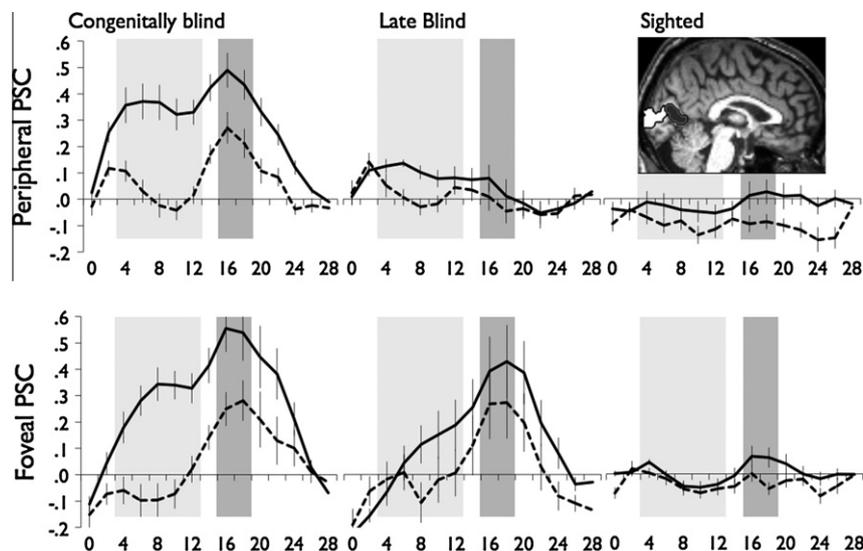


Fig. 1. Light gray: story portion of the trial, dark gray: question portion of the trial. Solid line: sentences, dotted line: backwards speech. Time is on the X-axis in seconds, percent signal change (PSC) is on the Y-axis. Inset displays an example foveal and peripheral pericalcarine ROI from a blind participant. Foveal region is shown in white, peripheral region in dark gray.

portions of the retina and the center of the visual field, whereas the peripheral pericalcarine cortex represents the peripheral portion of the retina and visual field. The peripheral ROI extended from the rostral end of the calcarine sulcus to the middle of the calcarine sulcus, whereas the foveal/parafoveal ROI extended from the mid-line to the edge of the occipital pole (in the rostral/caudal direction). The dorsal and ventral edges of the peripheral ROI were approximately 5 mm above and below the calcarine sulcus respectively. Because the pericalcarine cortex has a larger representation of the fovea, we drew the rostral edge of the foveal/parafoveal ROI 5 mm away from the calcarine sulcus and the caudal edge 12 mm from the calcarine sulcus. In the medial/lateral plane, we traced the calcarine sulcus starting at the most medial slice and moved laterally until the calcarine could not be identified (see Fig. 1 for example ROIs). ROIs were also created for a subset ($N = 10$) of the sighted participants. ROI analyses were performed on percent signal change (PSC) from rest, extracted from each ROI. We calculated PSC for every time point after the onset of the trial for each condition and then separately averaged PSC from all the time-points of the story (4 s to 16 s) and question (18 s to 22 s) [(raw signal during condition – raw signal during resting baseline)/raw signal during resting baseline]. PSC was first calculated in each voxel and then averaged over all the voxels in the ROI.

In whole-brain analyses, a general-linear model was used to analyze BOLD activity of each subject as a function of condition (sentences and backwards speech). We modeled each block of task as an 18 s event. Covariates of interest were convolved with a standard hemodynamic response function. Nuisance covariates included run effects, an intercept term, and global signal and data were high-pass filtered (1 cycle/128 s). BOLD signal differences between conditions and groups were evaluated through second level, random-effects analysis thresholded at $\alpha < .05$ (corrected) by performing Monte-Carlo permutation tests on the data (cluster size threshold of 3) using snPM (Hayasaka & Nichols, 2004; Nichols & Holmes, 2002).

3. Results

3.1. Behavioral results

Participants were more accurate on the language task (Accuracy: Language 84%, SD = 12, Backwards Speech 54%, SD = 12, main

effect of condition $F(1,37) = 86.79$, $P < .0001$, group-by-condition interaction $F(2,37) = .56$, $P = .58$). Although performance was poor on the backwards speech task, participants were marginally above chance ($t(38) = 1.93$, $P = .06$). Responses were slightly slower for the language task (Reaction Time (RT) Language 4354 ms, SD = 373; backwards speech 4416 ms, SD = 431, main effect of condition $F(2,36) = 4.61$, $P = .04$, group-by-condition interaction $F(2,36) = .33$, $P = .72$). Congenitally blind, late blind and sighted groups did not differ either in accuracy or reaction time (main effect of group Accuracy $F(2,37) = .02$, $P = .98$; RT $F(2,36) = 2.26$, $P = .11$). Behavioral data are summarized in Table 2.

3.2. Response in left pericalcarine cortex

We first examined the response of left pericalcarine cortex in congenitally blind, late blind and sighted individuals. To ask whether occipital areas contribute to language comprehension, we examined BOLD signal during the story portion of the trial (Fig. 1). In this time-window, the congenitally blind group had a larger response to sentences than backwards speech (Effect of Condition $F(1,30) = 38.9$, $P < .0001$) and a larger response in the peripheral than foveal ROI (Effect of ROI $F(1,30) = 4.8$, $P < .05$). By contrast, sentences did not lead to a larger response than backwards speech in either the sighted or late blind groups, nor was there a difference in the response of the foveal/parafoveal versus peripheral ROIs in either of these groups (sighted effect of condition $F(1,28) = .85$, $P = .37$, effect of ROI ($F(1,28) = 1.5$, $P = .23$; late

Table 2

Average accuracy and reaction time data from neuroimaging experiment. Standard deviations of the mean are presented in parentheses.

	Accuracy (%)	Reaction time (ms)
<i>Congenitally blind</i>		
Backwards speech	55 (11)	4441 (248)
Language	84 (14)	4372 (261)
<i>Late blind</i>		
Backwards speech	56 (11)	4259 (415)
Language	82 (10)	4330 (257)
<i>Sighted</i>		
Backwards speech	52 (13)	4413 (332)
Language	85 (12)	4257 (279)

blind effect of condition $F(1,25) = 1.76$, $P = .20$, effect of ROI $F(1,25) = 2.47$, $P = .13$).

When the groups were compared directly to each other, the congenitally blind group showed a larger effect of condition (sentences > backwards speech) than the late blind group (group by condition interaction, $F(1,54) = 11.1$, $P < .005$). This group difference remained significant after duration of blindness was added as a predictor in a multiple regression (group by condition interaction $F(1,53) = 4.90$, $P = .03$, duration-of-blindness by condition interaction $F(1,53) = .06$, $P = .81$). The effect of condition was not different in the late blind and sighted groups ($F(1,51) = .3$, $P = .58$). These data suggest that 1) congenitally blind, but not late blind individuals show a language-sensitive response in pericalcarine cortex and 2) the difference between congenitally and late blind people is not accounted for by differences in duration of blindness.

During the question portion of the trial, congenitally blind participants still had a higher BOLD signal for sentences than backwards speech in both parts of pericalcarine cortex (condition $F(1,30) = 20.0$, $P < .0001$, effect of ROI $P = .60$, and interaction $P = .68$). By contrast, in the late blind participants the effect of condition was again not reliable ($F(1,24) = 1.45$, $P = .24$). However, there was a large response during the question portion of the trial both for sentences and for backwards speech in the foveal/parafoveal, but not peripheral ROI (main effect of ROI, $F(1,24) = 10.2$, $P < .005$). These data suggest that a part of pericalcarine cortex is recruited during task performance in late blind participants, but this effect is not specific to language stimuli.

We then directly compared congenitally blind and late blind participants to each other in a group by condition by ROI ANOVA (during the question portion of the trial). The difference between BOLD signal in the foveal/parafoveal ROI versus the peripheral ROI was larger in the late blind group than the congenitally blind group (group by ROI interaction, ($F(1,54) = 5.6$, $P < .05$). This analysis suggests that in late blind but not congenitally blind individuals, pericalcarine activity during the question portion of the trial is confined to the foveal/parafoveal region.

The analyses above suggest that late blind participants have a distinct response profile during the story and question portions of the trial. To directly test this hypothesis, we analyzed PSC in the pericalcarine ROI as a function of time in late blind participants. In this group, BOLD signal was higher during the question portion of the trial than during the story portion (main effect of time, $F(1,57) = 5.9$, $P < .05$). The effect of time was more pronounced in the foveal/parafoveal ROI than in the peripheral ROI (time by ROI interaction, $F(1,57) = 10.5$, $P < .005$). Furthermore, the effect of time and time by ROI interaction were more

pronounced in the late blind than in the congenitally blind group (time by group interaction, $F(1,165) = 8.7$, $P < .001$; time by group by ROI interaction, $F(2,165) = 7.0$, $P = .001$). That is, congenitally blind participants showed activity over the whole pericalcarine region, sustained over the whole trial, but specific to linguistic stimuli; by contrast, late blind participants showed activity relatively restricted to the foveal/parafoveal region and restricted to the later phase of the trial, which generalized to both linguistic and non-linguistic stimuli.

3.3. Laterality of pericalcarine response to language

Our initial analyses revealed that in congenitally blind participants left pericalcarine cortex responds more to language than backwards speech during the story portion of the trial. We then examined whether this response to language was left-lateralized by comparing PSC in left and right pericalcarine areas. In congenitally blind participants, the sentences > backwards speech difference was larger in left pericalcarine cortex than in right pericalcarine cortex; there was no effect of laterality in the other groups (sentence PSC-backwards speech PSC outcome measure, 2-by-2 ANOVA foveal/parafoveal versus peripheral by Left versus Right, effect of hemisphere: congenitally blind $F(1,33) = 7.13$, $P = .01$, late blind $F(1,24) = 2.69$, $P = .14$, sighted $F(1,27) = 2.04$, $P = .16$, Fig. S1). There was no difference between foveal and parafoveal cortex in this analysis ($P > .3$). The laterality of the language effect was larger in congenitally blind than sighted people (group by hemisphere interaction $F(1,60) = 8.09$, $P = .006$), but did not differ between the congenitally and late blind groups ($F(1,57) = .68$, $P = .41$). We also found that the overall response of pericalcarine cortex (collapsing across conditions), was more left-lateralized in congenitally as compared to late blind participants (group by hemisphere interaction ($F(1,19) = 5.39$, $P = .03$).

3.4. Whole-brain analysis

The analyses above suggest that occipital cortex of congenitally blind but not late blind individuals responds specifically to linguistic information. To further test this hypothesis, we used whole-brain analyses to compare the response to sentences and backwards speech in congenitally blind, late blind, and sighted individuals.

We first compared the congenitally blind and late blind groups each to sighted participants. For sentences (relative to backwards speech) congenitally blind individuals had greater recruitment of a left lateralized group of occipital areas including pericalcarine cortex, lateral occipital and fusiform areas, than sighted participants

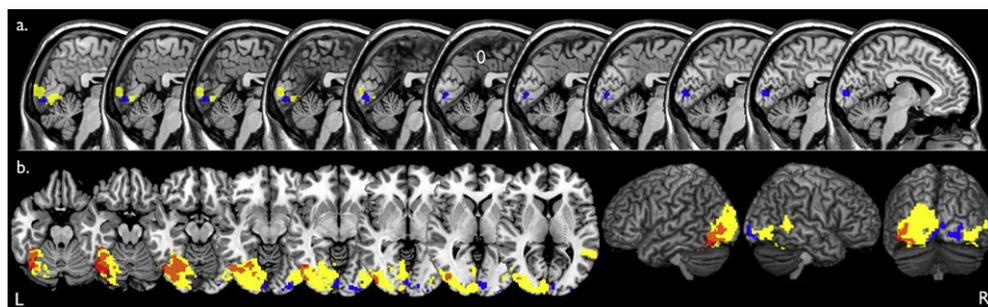


Fig. 2. Group-by-condition interaction results: Congenitally blind > sighted, sentences > backwards speech (yellow), Congenitally blind > late blind, sentences > backwards speech (red), Late blind > sighted, backwards speech > rest (blue). (a) The pericalcarine region shown in sagittal slices from $X = -5$ to $X = 5$ in MNI coordinates. (b) Axial slices $Z = -22$ to $Z = 6$. Note that consistent with the ROI analyses, the response to sentences in congenitally blind participants is left-lateralized within the pericalcarine cortex and extended from the foveal/parafoveal region into peripheral pericalcarine cortex. By contrast, the response to backwards speech in late blind participants was right lateralized and only present in the foveal/parafoveal region of pericalcarine cortex.

Table 3
Peak activations observed in whole-brain analyses ($^*P < .05$, corrected, $^\dagger P < .10$, corrected). Data are shown in Fig. 3.

Contrast Group	Voxel			Peak <i>t</i>	<i>x</i>	<i>y</i>	<i>z</i>	Brain area (Brodmann area)
	<i>k</i>	<i>w</i>	<i>P_{combo}</i>					
<i>Sentences > backwards speech</i>								
Congenitally blind > sighted	4680	9.52	0.000*	7.98	−38	−74	−12	Left inferior occipital gyrus (19)
	772	6.57	0.006*	7.54	−30	−60	−14	Left cerebellum declive
	332	4.40	0.047*	7.21	−44	−84	−2	Left middle occipital gyrus (19)
				6.26	34	−90	−6	Right middle occipital gyrus (18)
				4.91	44	−54	−20	Right fusiform gyrus (37)
				5.49	48	−48	4	Right superior temporal gyrus (22)
			4.25	56	−48	−2	Right middle temporal gyrus (22)	
<i>Late blind > sighted</i>								
	–	–	–	–	–	–	–	–
Congenitally Blind > Late Blind	1006	5.24	0.022*	6.14	−36	−54	−20	Left fusiform/middle occipital gyri (37/19)
				5.16	−34	−64	−14	Left cerebellum/fusiform gyrus
				4.90	−46	−72	−16	Left fusiform/inferior occipital gyrus (37/19/18)
<i>Backwards speech > rest</i>								
Congenitally blind > sighted	728	5.39	0.019*	5.05	0	−80	14	Right cuneus (18)
				4.97	10	−68	6	Right lingual gyrus (18)
				4.93	2	−86	24	Right cuneus (18)
Late Blind > Sighted	350	4.04	0.066 [†]	4.85	6	−94	6	Right cuneus (18/17)
				4.49	0	−88	0	Right lingual gyrus (18/19)
				4.27	−4	−92	−8	Right lingual gyrus (18/19)
Congenitally blind > late blind	–	–	–	–	–	–	–	–

(Fig. 2 yellow; Table 3). By contrast, late blind participants did not show any elevated activity compared to the sighted group for sentences (relative to backwards speech). We then compared congenitally and late blind participants directly to each other and found a significantly larger response in congenitally blind participants for sentences in secondary visual areas: left posterior fusiform and left lateral occipital cortex (Fig. 2 red, Table 3) Inspection of the time-course in these secondary visual regions revealed that as in pericalcarine cortex, PSC was higher for sentences than backwards speech both during the story and question portions of the trial in congenitally blind participants (Fig. S2). Despite increased language-selectivity in occipital cortex of congenitally blind people relative to sighted and late blind participants, we found no evidence of decreased language selectivity in classic frontotemporal language areas in this group (see Supplementary material for details).

While late blind participants did not have a language-sensitive response, they did have an elevated response for backwards speech relative to rest, compared to sighted participants (Fig. 2 blue, peak coordinates: [6, −94, 6]; [0, −88, 0]; [−4, −92, −8]). Neuroanatomically, this effect was distinct from the language-sensitive effect observed in congenitally blind participants: it was more pronounced in the right hemisphere and was confined to the foveal/parafoveal region of pericalcarine cortex and the occipital pole (BA17/18). Congenitally and late blind individuals did not differ in the magnitude of occipital response to backwards speech, relative to rest. This analysis suggests that the response-related effect that is common to language and backwards speech is of similar magnitude irrespective of age of blindness onset.

4. Discussion

Although both congenitally- and late- blind adults show plasticity in occipital cortex, we find that plasticity for language is present only in congenitally blind people. In congenitally blind adults, left occipital cortex is active while listening to speech without making a response, and is more active while listening to speech than while listening to non-language sounds. Language-related activity is left lateralized and occurs in high-level visual areas as well as left pericalcarine cortex (both foveal/parafoveal and peripheral regions). We find a different, non-language related effect, in both

congenitally and late blind participants. Right-lateralized occipital areas in the foveal/parafoveal region of pericalcarine cortex and the occipital pole are active when blind individuals make a response or decision, but not while simply listening to sounds. This occipital activity is of similar magnitude for linguistic and non-linguistic tasks and might reflect response preparation or attention.

Our findings of distinct occipital plasticity in late and congenitally blind individuals are consistent with several prior studies. As previously observed, we find that occipital activity during verbal tasks is more extensive and left-lateralized in congenitally blind people. In late blind participants, pericalcarine activity is right-lateralized and confined to the foveal/parafoveal region (Buchel et al., 1998; Burton, Snyder, Diamond et al., 2002; Burton, Snyder, Conturo et al., 2002; Burton et al., 2003; Cheung, Fang, He, & Legge, 2009). The present data extend and clarify prior findings by demonstrating that only in congenitally blind people a left-lateralized component of the occipital response is specific to language.

Based on the present data we speculate that previously observed occipital activity in late blind people during verbal tasks might reflect response preparation or attention. For example, during verb-generation (as compared to passive listening or Braille reading), occipital activity might be related to generating a verbal response (Burton, Snyder, Diamond et al., 2002; Burton, Snyder, Conturo et al., 2002). Similarly, one study found right pericalcarine activity when late blind participants generated semantically related words, but not when they generated rhyming words, in response to lists of heard nouns. We hypothesize that this occipital activity reflected the greater response preparation or attentional demands of the semantic task. Consistent with this possibility, sighted and blind participants alike manifested higher responses in premotor and prefrontal cortex during the semantic task (Burton et al., 2003). Like the response-associated activity found in the present study, occipital activity of late blind people was right-lateralized and concentrated in the foveal/parafoveal region of pericalcarine cortex.

Together, the available data suggest that occipital plasticity for language occurs only in people who are blind during childhood. This might explain why occipital activity has distinct functional significance in congenitally and late blind populations (Cohen et al., 1999).

4.1. How does experience enable occipital areas to participate in language processing?

The present findings suggest that blindness during development is necessary for occipital circuits to get engaged in language. In this regard, our data are consistent with a large body of animal work showing qualitatively different effects of developmental and lifelong experience on the mammalian brain (Berardi, Pizzorusso, & Maffei, 2000). Our findings are also consistent with prior research showing distinct behavioral and neural changes in late and congenitally blind individuals (Bedny, Konkle et al., 2011; Buchel et al., 1998; Cohen et al., 1997).

We argue here that the difference between the occipital response of congenitally blind and late blind individuals results from different ages of blindness onset. However, it is important to point out that there are other differences between congenitally blind and late blind populations that could in principle contribute to distinct plasticity patterns. Late blind adults generally have more residual vision than congenitally blind adults. In the present study, it is unlikely that differences in residual vision could explain the observed differences between groups since most of the late and congenitally blind participants had no residual light perception (See Table 1 for details). Late blind participants are also blind for less time than congenitally blind participants. However, in the present study, 8 of the 9 late blind participants were totally blind for 17 years or more (the one remaining participant lost her vision 6 years prior to the study). The average blindness duration, for the late blind adults, was 17 years. It seems unlikely that blindness for even longer than 17 years would qualitatively change the occipital response to language. Furthermore, congenital versus late blindness, but not duration of blindness predicted the selectivity of left pericalcarine cortex for language in the present study. For these reasons, in the present study the most likely explanation for group differences between late and congenitally blind participants is age of blindness onset.

Our data suggest that in adulthood blindness during childhood is necessary for a language-sensitive response in occipital cortex, since people who were blind from birth had a language-sensitive response in occipital areas whereas people who became blind later did not. However, the present data do not allow us to precisely delineate the time-window of this 'sensitive period' during childhood. Among the late blind participants in our study, the youngest to go blind was 9 years old. In future work it would be very interesting to further explore the timing of the 'sensitive period' for the linguistic response in occipital cortex. Does blindness from birth, blindness during early childhood (e.g. 5 years), or blindness during language acquisition, produce a linguistic response? A better understanding of the time-window of this plasticity would help

determine whether recruitment of occipital areas for language is limited by plasticity of visual brain regions or by plasticity of the language system itself.

Another factor that might influence occipital reorganization is etiology of blindness (Bridge, Cowey, Ragge, & Watkins, 2009), which varies among late and congenitally blind groups (as well as between individuals within each group). For example, some late blind individuals lose their sight gradually (as in the case of Retinitis pigmentosa), while others have sudden vision loss (e.g. due to an accident). Within the congenitally blind group, etiology of blindness might effect not only postnatal but also prenatal input to the visual cortex. The presence of an intact retina and optic nerve during (specific stages of) fetal development might alter the function of occipital regions (Catalano & Shatz, 1998; Stellwagen & Shatz, 2002). Among late blind participants, disorders of the retina versus optic nerve might have different effects on occipital reorganization. These are important topics for future research.

4.2. How does linguistic information reach occipital circuits of congenitally blind participants?

A key question for understanding occipital language responses in blind individuals is how the connectivity of the brain allows linguistic information to reach occipital areas. It seems unlikely that linguistic information comes to occipital circuits from primary auditory cortex (A1) or the middle geniculate nucleus (MGN) because these auditory regions do not have specific linguistic responses. Furthermore, a recent study found language-related occipital activity in a deaf-blind individual. This participant was born deaf and became blind at age 6 due to a chemical accident. In this individual, activity was observed in a left-lateralized network of occipital areas, while he "listened" to haptic ASL (Obretenova, Halko, Plow, Pascual-Leone, & Merabet, 2010). These data suggest that in adulthood occipital recruitment for language does not depend on input from auditory brain regions. Because this individual was deaf at the time of language acquisition, the results also suggest that the occipital response to language does not originate developmentally from early auditory areas.

Instead, linguistic information may reach occipital areas from language regions in the temporal lobe, prefrontal cortex or language-relevant nuclei of the thalamus (Munte & Kutas, 2008; Radanovic, Azambuja, Mansur, Porto, & Scaff, 2003; Wahl et al., 2008). Consistent with this idea, a number of studies have found enhanced resting-state correlations between left prefrontal language areas and occipital cortex in congenitally blind people (Bedny, Konkle et al., 2011; Bedny, Pascual-Leone et al., 2011; Liu et al., 2007). One possibility suggested by the present data is that secondary visual areas in the lateral and ventral temporal cortex

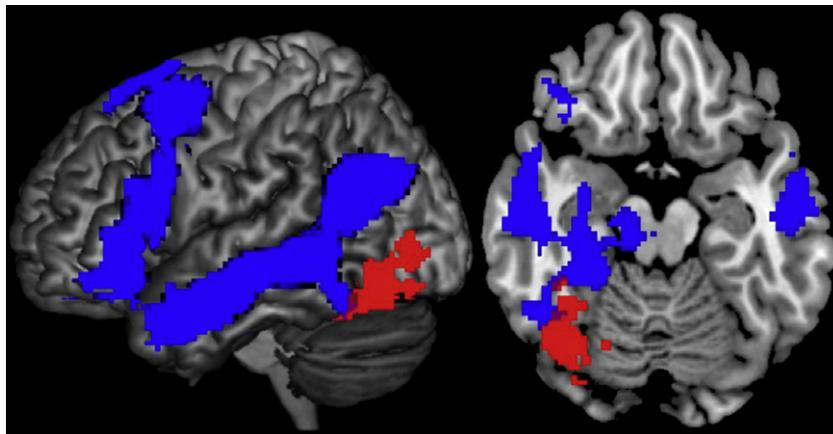


Fig. 3. Sighted: sentences > backwards speech (blue), congenitally blind > late blind, sentences > backwards speech (red).

are a gateway that carries linguistic information to occipital circuits. Secondary visual areas, such as the lateral occipital complex (LO) and the visual word form area (VWFA) are relatively close to language regions of sighted individuals (Fig. 3) (Dehaene & Cohen, 2011; Malach et al., 1995). The inputs that carry language-relevant information to language areas could also carry linguistic information to the nearby secondary visual areas. Such connections might exist in all children and be typically pruned away or modified as a result of visual experience. In blind children, these connections may remain intact. Alternatively, nearby temporal-lobe language areas could themselves relay linguistic information to secondary visual regions of the fusiform and lateral occipital cortex. Linguistic information might subsequently reach primary visual areas, including the pericalcarine cortex, via these secondary visual areas.

There may also be a more direct route to pericalcarine cortex from language areas in the cortex or the thalamus (Wahl et al., 2008). For example, in non-human primates there are a small number of direct projections from polysensory areas of the lateral temporal lobe to primary visual cortex (Clavagnier, Falchier, & Kennedy, 2004; Falchier, Clavagnier, Barone, & Kennedy, 2002). Further work is needed to clarify the cortical and subcortical circuits that carry linguistic information to occipital areas.

4.3. Distinct cognitive processes supported by occipital areas of congenitally and late blind adults

A key finding of the present study is that occipital areas support partially distinct cognitive processes in congenitally and late blind adults. In congenitally blind participants a left-lateralized component of occipital activity is related to language processing. Like prior studies, we find that this response to language is not related to general working memory demands (i.e. non-language specific working memory) (Burton, Sinclair, & Dixit, 2010). In the present study, both the language task and the control task (backwards speech) required encoding and maintenance of auditory information, but occipital activity was much higher during the language task in congenitally blind participants. Left-lateralized occipital areas could contribute to a range of language related processes, such as encoding and maintenance of linguistic information, building of sentence structures, and/or retrieving word-meanings from long term memory (see also Bedny, Konkle et al., 2011; Bedny, Pascual-Leone et al., 2011; Amedi et al., 2003; Burton, Snyder, Diamond et al., 2002; Burton, Snyder, Conturo et al., 2002; Roder et al., 2002).

In contrast to congenitally blind people, we did not observe language-related activity in occipital cortex of late blind people. However, a different, non-language related response is present both in congenitally and late blind adults. Occipital activity increased when participants prepared to answer a question. Unlike the occipital responses to language, this activity was right-lateralized and restricted to foveal/parafoveal area of pericalcarine cortex. The magnitude of this response was similar for language and backwards speech. This activity might reflect response preparation, execution or attention. Factors such as task structure, attentional demands, and reward have been shown to influence activity in early visual areas of sighted and blind people (Garg, Schwartz, & Stevens, 2007; Jack, Shulman, Snyder, McAvoy, & Corbetta, 2006; Roder, Rosler, & Hennighausen, 1997; Serences, 2008). In blind people such effects might be enhanced due to absence of bottom up visual input. For example, in blind but not sighted people right occipital activity rises with increased auditory attention (Stevens, Snodgrass, Schwartz, & Weaver, 2007).

Together with prior evidence, the response-related activity observed in late blind adults illustrates that cross-modal functional change can occur in adulthood (Buchel et al., 1998; Burton, 2003; Burton, Snyder, Diamond et al., 2002; Burton, Snyder, Conturo

et al., 2002; Burton et al., 2003). Indeed, some such changes might occur very quickly – in a matter of days (Merabet et al., 2008), hours or even immediately with the changing state of the organism (Anderson, 2011).

5. Conclusions

We find a sensitive period in the responsiveness of occipital areas to language: the left occipital cortex responds to linguistic information in congenitally but not late blind people. Along with prior evidence, these data suggest that blindness early in life enables left occipital circuits to participate in language processing. In addition, we also observed a neuroanatomically distinct response-related effect in occipital cortex of congenitally and late blind people. Unlike the language-sensitive effect, this response-related occipital activity does not appear to have a sensitive period. In summary, we find that during verbal tasks occipital areas make distinct functional contributions in congenitally and late blind people.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bandl.2011.10.005.

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