

Reduced Left Lateralization of Language in Congenitally Blind Individuals

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Abstract

■ Language processing depends on a left-lateralized network of frontotemporal cortical regions. This network is remarkably consistent across individuals and cultures. However, there is also evidence that developmental factors, such as delayed exposure to language, can modify this network. Recently, it has been found that, in congenitally blind individuals, the typical frontotemporal language network expands to include parts of “visual” cortices. Here, we report that blindness is also associated with reduced left lateralization in frontotemporal language areas. We analyzed fMRI data from two samples of congenitally blind adults ($n = 19$ and $n = 13$) and one sample of congenitally blind children ($n = 20$). Laterality indices were computed for sentence comprehension relative to three different control conditions: solving math equations (Experiment 1), a memory task with nonwords (Exper-

iment 2), and a “does this come next?” task with music (Experiment 3). Across experiments and participant samples, the frontotemporal language network was less left-lateralized in congenitally blind than in sighted individuals. Reduction in left lateralization was not related to Braille reading ability or amount of occipital plasticity. Notably, we observed a positive correlation between the lateralization of frontotemporal cortex and that of language-responsive occipital areas in blind individuals. Blind individuals with right-lateralized language responses in frontotemporal cortices also had right-lateralized occipital responses to language. Together, these results reveal a modified neurobiology of language in blindness. Our findings suggest that, despite its usual consistency across people, the neurobiology of language can be modified by nonlinguistic experiences. ■

INTRODUCTION

In the mid 19th century, neuropsychologists discovered two neuroanatomical features that characterize the neurobiology of language. First, language processing depends on the left hemisphere more than the right hemisphere. Second, within the left hemisphere, inferior frontal and posterior lateral temporal areas are key nodes (Wernicke, 1874; Broca, 1861, 1865; Dax, 1865). We now know that the language network includes areas outside the left perisylvian cortices (Dronkers, Wilkins, Van Valin, Redfern, & Jaeger, 2004; Hickok & Poeppel, 2000). For example, frontotemporal regions in the right hemisphere contribute to prosodic and pitch processing (Zatorre, Evans, Meyer, & Gjedde, 1992; Ross & Mesulam, 1979). Nevertheless, the basic tenets of these early discoveries have held up over the past 150 years. Studies using the Wada technique with patients with epilepsy and neuroimaging with healthy participants confirmed that left-hemisphere language dominance is present in 96% of right-handed participants (Pujol, Deus, Losilla, & Capdevila, 1999; Rasmussen & Milner, 1977). With regard to localization within hemispheres, inferior frontal and posterior lateral temporal areas are active during a wide range of language

comprehension and production tasks (Binder, Desai, Graves, & Conant, 2009; Vigneau et al., 2006; Friederici, 2002). Damage to these frontotemporal areas causes profound deficits in language processing (Dronkers et al., 2004).

The neurobiological phenotype of language is stable across individuals and is preserved over a range of experiential differences. A similar network of left-lateralized frontotemporal areas is involved in processing English, Mandarin Chinese, and various sign languages (e.g., Newman, Supalla, Fernandez, Newport, & Bavelier, 2014; Chee et al., 1999; Neville et al., 1997). Moreover, the seeds of typical language processing appear to be present early on in the developing brain. Infants as young as 2 months old activate lateral temporal and prefrontal regions while listening to speech (Dehaene-Lambertz, Dehaene, & Hertz-Pannier, 2002). There is also some evidence that, within the first months of life, responses to spoken language in the lateral temporal cortex are left-lateralized and specific to speech as opposed to other sounds (Dehaene-Lambertz et al., 2010).

However, there is also evidence that both laterality and within-hemisphere localization of language can be modified during development. Evidence that the right hemisphere can independently support language processing comes from studies with children who experience early brain injuries. Children with early left-hemisphere damage

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to frontotemporal cortices go on to develop language abilities within the normal range (Thal et al., 1991; Vargha-Khadem, O’Gorman, & Watters, 1985; Woods & Teuber, 1978). Neuroimaging studies show that, in these individuals, language processing depends on right-hemisphere homologues of left-hemisphere language areas (Liégeois et al., 2004; Rasmussen & Milner, 1977).

Recent evidence also suggests that the localization of language within a hemisphere can be modified. In individuals who are blind from birth, classic frontotemporal language areas are supplemented with “visual” cortices. Congenitally blind individuals activate “visual” areas during Braille reading, verb generation, and sentence comprehension (Burton, Snyder, Diamond, & Raichle, 2002; Röder, Stock, Bien, Neville, & Rösler, 2002; Sadato et al., 1996). Responses in these “visual” areas are larger for more linguistically rich stimuli. Greater responses are observed for sentences than unconnected lists of words, which in turn elicit more activity than meaningless strings of non-words (Bedny, Pascual-Leone, Dodell-Feder, Fedorenko, & Saxe, 2011). “Visual” cortex language areas are sensitive to manipulations of grammatical complexity. Visual cortices of blind individuals respond more to sentences with syntactic movement than to matched sentences without syntactic movement (Lane, Kanjlia, Omaki, & Bedny, 2015; Röder, Stock, Bien, et al., 2002). There is also some evidence that occipital activity during language tasks is relevant to behavior. TMS to the occipital pole impairs blind individuals’ ability to read Braille and produce semantically appropriate verbs to heard nouns (Amedi, Floel, Knecht, Zohary, & Cohen, 2004; Cohen et al., 1997). Thus, studies of blindness suggest that regions outside the typical frontotemporal circuit can be incorporated into the language network.

Until now, the dominant view has been that in blindness, occipital areas are added to an otherwise unchanged frontotemporal language system. Consistent with this view, several studies have shown that blind individuals activate frontotemporal language areas during reading, spoken sentence processing, and word generation (Bedny, Richardson, & Saxe, 2015; Bedny et al., 2011; Burton, Snyder, Conturo, et al., 2002; Burton, Snyder, Diamond, et al., 2002; Röder, Stock, Bien, et al., 2002). Furthermore, the response profile of frontotemporal regions across conditions is similar between blind and sighted individuals. For example, in both groups, frontotemporal areas show greater responses to sentences that are grammatically complex (Lane et al., 2015; Röder, Stock, Bien, et al., 2002). Blind and sighted individuals also activate a similar middle temporal gyrus region during verb processing (Bedny et al., 2011). These studies suggest that frontotemporal language circuits develop similarly in blind and sighted individuals.

There is one way in which the frontotemporal language network may differ in blindness. Some studies suggest that, in blindness, the laterality of classic language areas is reduced. Blind adults show a reduced right ear advantage

compared with sighted adults during a dichotic listening task with spoken digits (Karavatos, Kaprinis, & Tzavaras, 1984; but see Marcotte, O’Brien, Holbby, & LaBarba, 1992, for conflicting results). One neuroimaging study and one ERP study found less left-lateralized responses to language in blind individuals (Röder, Stock, Bien, et al., 2002; Röder, Rösler, & Neville, 2000), although neither study directly compared laterality between blind and sighted groups. On the other hand, a number of neuroimaging studies with blind adults report left-lateralized activation in blind individuals during language tasks (Bedny et al., 2011; Amedi, Raz, Pianka, Malach, & Zohary, 2003; Burton, Snyder, Diamond, et al., 2002). Because none of these previous experiments formally compared language laterality between blind and sighted individuals, it remains uncertain whether blindness is associated with reduced language laterality. The goal of this study was to determine whether classic frontotemporal language areas are less left-lateralized in congenitally blind individuals.

We tested the reduced lateralization hypothesis in three separate sentence comprehension experiments designed to engage high-level linguistic processes, such as lexical retrieval, sentence level syntax, and compositional semantics. In all three experiments, participants listened to sentences and performed a comprehension task. As a control, participants solved spoken math equations in Experiment 1, performed a memory task with nonword sequences in Experiment 2, and performed a “does this come next” task with music in Experiment 3. Laterality indices (LIs) were calculated for contrasts comparing each sentence comprehension task with its control task. These contrasts enabled us to compare the laterality of lexical and sentence level linguistic processes between blind individuals and sighted controls.

Across the three experiments, we obtained fMRI data from two different samples of congenitally blind adults and one sample of congenitally blind children between 4 and 17 years old. We compared the lateralization of frontotemporal language responses between blind individuals and sighted age- and education-matched controls. To foreshadow, we observed reduced left lateralization of language responses in blind individuals across the three different sentence comprehension tasks. Next, we examined possible mechanisms for reduced lateralization in blindness.

One possibility is that the addition of occipital areas to the language network causes reduced lateralization in frontotemporal language areas. If occipital language regions lack the intrinsic left lateralization of the frontotemporal language network, this could lead to a more bilateral language system as a whole. We tested this hypothesis in the current study by asking whether blind individuals with larger occipital responses to language also have less left-lateralized language responses in frontotemporal cortices. Relatedly, we asked whether occipital and frontotemporal language responses are co-lateralized. If so, this would provide further evidence that, in blindness, occipital areas are incorporated into the language processing network.

An alternative proposal is that learning to read Braille causes reduced lateralization of spoken language in blindness (Röder, Stock, Bien, et al., 2002; Karavatos et al., 1984; Hermelin & O'Connor, 1971). According to one view, Braille perception is spatial and therefore depends on the right hemisphere, which in turn leads to a broader right-hemisphere involvement in spoken language processing (Hermelin & O'Connor, 1971). An alternative possibility is that reading Braille with the left hand causes Braille processing to rely on the right hemisphere. On either of these views, the Braille hypothesis posits that the neurobiology of written language influences the laterality of spoken language. We tested the Braille hypothesis by measuring language lateralization in blind children and adolescents who varied in Braille reading ability. The 4-year-old children in our sample were not yet able to read Braille. By contrast, the 17-year-old participant in this sample was an adult level Braille reader. This variation allowed us to ask whether the left lateralization of language is inversely related to a blind individual's ability to read Braille.

A final possibility is that vision loss per se changes the lateralization of the language network. Blindness is known to alter the timing of language acquisition. Blind children are slightly delayed in producing their first words and multiword utterances (Landau & Gleitman, 1985; Norris, 1957). These delays are mild and short-lived. Nonetheless, it is possible that the different maturational phase of cortex at the time of language acquisition affects the lateralization of language (Bishop, 2013; Mayberry, Chen, Witcher, & Klein, 2011; Bates et al., 1997; Locke, 1997; Corballis & Morgan, 1978). Alternatively, blindness could affect language laterality indirectly by altering the development of nonlinguistic cognitive systems, such as spatial cognition or motor control. It has been shown that the laterality of language and nonlinguistic functions are systematically and, in some cases, inversely related across individuals (Cai, Van der Haegen, & Brysbaert, 2013; Vingerhoets et al., 2013). Irrespective of the precise mechanism, if blindness influences language lateralization, it would suggest that experience can modify the neurobiology of language, without changing language input.

METHODS

Participants

Thirty-two blind adults and 20 blind children and adolescents took part in the experiments (Tables 1 and 2). All blind participants were totally blind with at most minimal light perception. All but one of the blind participants were blind from birth or became blind within the first months of life. One blind child became totally blind between the age of 2 and 5 years. Blindness was due to an abnormality at or anterior to the optic chiasm and not due to brain damage. Common causes of vision loss included retinopathy of prematurity, Leber's congenital amaurosis, and

microphthalmia. None of the participants had any known cognitive or neurological disabilities. In all three experiments, sighted participants were blindfolded for the duration of the study.

Nineteen congenitally blind adults (13 women) and 21 sighted adults (10 women) participated in Experiments 1 and 2 (Table 1). Three additional blind participants were scanned but excluded from the imaging analyses because of poor performance (sentence comprehension accuracy below the 75th percentile of binomial "chance" distribution). Participants were between 21 and 75 years old. Blind participants and sighted controls were matched on age ($t(38) = 0.68, p = .5$), years of education ($t(38) = 0.79, p = .44$), and dominant hand preference ($\chi^2(1) = 0.03, p = .86$).

Experiment 3 included 13 congenitally blind adults (six women) and 16 sighted adults (seven women) (Table 2). All adult participants were between 18 and 64 years old. Blind and sighted participants were matched on age ($t(27) = -0.04, p = .97$), years of education ($t(25) = -0.1, p = .92$), and dominant hand preference ($\chi^2(1) = 2.01, p = .16$). Educational history was unavailable for two blind adults.

Experiment 3 also included 20 blind children (nine girls, age range = 4–17 years) and 19 sighted children (13 girls, age range = 4–16 years; Table 2). Blind and sighted children were matched on age ($t(37) = -0.14, p = .89$), years of education ($t(37) = -0.38, p = .71$), and dominant hand preference ($\chi^2(1) = 0, p = 1.0$). Detailed demographic information about blind children is reported in Bedny et al. (2015). Child participants in the current study were identical to those reported in Bedny et al. (2015), except that one additional blind child is included in the current sample. Seven additional children took part in the study but were excluded from analyses because of excessive motion in the scanner (one blind child and one sighted child), autism spectrum disorder diagnosis and inability to do the experimental task (one blind child), inability to remain in the scanner (two sighted children and one blind child), and abnormal neuroanatomy (one sighted child). Of the 39 children included in the laterality analysis, 30 contributed behavioral data. For four sighted children, behavioral data were not collected because of a technical error. In addition, we excluded from behavioral analyses participants who responded on fewer than half of the trials. This resulted in dropping one sighted child and four blind children, all of whom were 5 years old or younger. One additional blind child was excluded from response time analyses after failing to answer correctly on any of the music trials.

Behavioral Procedure

In Experiment 1, adult participants heard pairs of sentences. The task was to decide whether the two sentences had the same meaning. One of the sentences in each pair was in active voice; and the other, in passive voice. On

Table 1. Participant Demographic Information for Blind and Sighted Adults in Experiments 1 and 2

<i>Group</i>	<i>Participant No.</i>	<i>Age (years)</i>	<i>Sex</i>	<i>Cause of Vision Loss</i>	<i>Handedness</i>	<i>Reading Hand</i>	<i>Reading Frequency (hr)</i>
BA	1	22	M	LCA	Right	Bi-R	21
BA	2	32	F	ROP	Right	L	14
BA	3	70	F	ROP	Right	R	7
BA	4	43	M	Unknown eye condition	Amb.	L	2
BA	5	67	M	ROP	Right	Bi-R	7
BA	6	67	F	ROP	Right	Bi-R	7
BA	7	26	F	ROP	Right	Bi-R	56
BA	8	64	F	ROP	Left	L	63
BA	9	35	F	LCA	Right	Bi-L	14
BA	10	47	M	LCA	Right	Bi-R	7
BA	11	39	F	ROP	Right	L	14
BA	12	49	F	LCA	Left	R	11
BA	13	25	F	LCA	Amb.	Bi-R	49
BA	14	62	F	ROP	Right	–	–
BA	15	36	M	Glaucoma and cataracts	Right	Bi-L	70
BA	16	62	M	ROP	Right	Bi-R	18
BA	17	60	F	ROP	Right	L	18
BA	18	46	F	ROP	Right	–	–
BA	19	61	F	ROP	Left	Bi-L	7
SA	<i>n</i> = 21	45	10 F	–	2 left, 2 amb.	–	–

Group labels include blind adults (BA) and sighted adults (SA). Participant numbers for blind participants correspond to figure labels in Figure 2. Abbreviated causes of blindness include Leber’s congenital amaurosis (LCA) and retinopathy of prematurity (ROP). Reading handedness categories are right-hand only (R), right-hand dominant bimanual (Bi-R), left-hand dominant bimanual (Bi-L), and left-hand only (L). Reading frequency is in hours per week. F= female; M = male; Amb. = ambidextrous.

“same” trials, the thematic roles and relations were maintained across both sentences (e.g., Sentence 1: “The child that chased the babysitter ate the apple.”; Sentence 2: “The apple was eaten by the child that chased the babysitter.”). On “different” trials, the roles of the people in the sentences were reversed in the second sentence (e.g., Sentence 1: “The boy that insulted the girl started the fight.”; Sentence 2: “The fight was started by the girl that insulted the boy.”).

As a control, participants performed a symbolic math task. Participants heard pairs of spoken subtraction equations involving two numbers and a variable *X*. The task was to decide whether the value of *X* was the same in both equations. There were 48 sentence trials and 96 math trials in the experiment, divided evenly among six runs and counterbalanced with respect to condition across runs using a Latin-square design. Each trial was 14 sec long. Trials began with a beep (0.25 sec) followed by a pair of sentences or spoken math equations (3.5 sec per sentence/equation, separated by a 2.75-sec pause). Participants had 4 sec to make their response.

In Experiment 2, adult participants listened to sentences and answered yes/no comprehension questions about them (e.g., sentence: “The paramedic that the exhausted surgeon at the trauma center criticized gave the patient too much painkiller.”; question: “Was it that the paramedic criticized the surgeon?”). The questions required participants to attend to the thematic relations in the sentence (i.e., who did what to whom). Half of the sentences contained a syntactic movement dependency, making them more syntactically complex (Lane et al., 2015). The syntactic complexity manipulation is not analyzed here.

As a control, participants performed a memory task with sequences of nonwords. Participants heard a sequence of nonwords (the target) followed by a shorter sequence (the probe). The probes were made up of some of the nonwords from the target, either in their original order or shuffled. The participants’ task was to decide whether the items in the probe were in their original order.

Experiment 2 contained 108 sentence trials and 54 nonword sequence trials divided evenly among six runs and counterbalanced with respect to condition within each

Table 2. Participant Demographic Information for Blind and Sighted Adults and Children in Experiment 3

<i>Group</i>	<i>Participant No.</i>	<i>Age (years)</i>	<i>Sex</i>	<i>Cause of Vision Loss</i>	<i>Handedness</i>	<i>WJII Reading Score (%)</i>
BC	20	15	M	Anophthalmia	Right	–
BC	21	8	M	ROP	Left	30
BC	22	5	M	Microphthalmia	Amb.	12
BC	23	4	F	ROP	Right	0
BC	24	17	F	Optic nerve hypoplasia	Right	99
BC	25	7	F	Uveitis	Right	34
BC	26	9	F	Microphthalmia	Left	31
BC	27	9	F	FEV	Right	75
BC	28	14	M	Detached retinas	Amb.	70
BC	29	8	M	LCA	Right	54
BC	30	9	M	LCA	Right	94
BC	31	7	F	LCA	Right	57
BC	32	4	M	LCA	Right	15
BC	33	11	F	LCA	Left	91
BC	34	5	M	Microphthalmia	Right	–
BC	35	5	F	LCA	Right	7
BC	36	6	M	LCA	Right	20
BC	37	7	M	LCA	Right	37
BC	38	5	F	Microphthalmia	Right	12
BC	39	9	M	LCA	Right	51
BA	40	58	M	ROP	Right	–
BA	41	41	M	Detached optic nerve	Left	–
BA	42	41	M	Retinoblastoma	Right	–
BA	43	25	F	Detached optic nerve	Right	–
BA	44	64	F	Malformed optic nerve	Right	–
BA	45	30	M	Retinitis pigmentosa	Left	–
BA	46	32	M	ROP	Left	–
BA	47	62	F	ROP	Right	–
BA	48	57	F	ROP	Right	–
BA	49	62	F	ROP	Right	–
BA	50	25	F	ROP	Right	–
BA	51	24	M	Anophthalmia	Right	–
BA	52	38	M	LCA	Right	–
SC	<i>n</i> = 19	9	13 F	–	5 left, 0 amb.	–
SA	<i>n</i> = 16	44	7 F	–	0 left, 0 amb.	–

Group labels include blind children (BC), blind adults (BA), sighted children (SC), and sighted adults (SA). Abbreviated causes of blindness include Leber's congenital amaurosis (LCA), familial exudative vitreoretinopathy (FEV), and retinopathy of prematurity (ROP). Reading scores on the Woodcock-Johnson III Test of Achievement are reported for 18 of the 20 blind children.

run. The sentences and nonword sequences were matched in number of words/nonwords (sentence = 17.9, nonword = 17.8; $p > .3$), number of syllables per word (sentence = 1.61, nonword = 1.59; $p > .3$), and mean bigram frequency per word (sentence = 2342, nonword = 2348; $p > .3$; Duyck, Desmet, Verbeke, & Brysbaert, 2004). Each trial was 16 sec long. Trials began with a beep (1 sec) followed by a sentence or nonword sequence (6.7 sec). Participants then heard a spoken question or nonword probe (2.9 sec on average) and had until the end of the trial to respond. (See Kanjlia, Lane, Feigenson, & Bedny, 2016, and Lane et al., 2015, for details on Experiments 1 and 2.)

In Experiment 3, participants (children and adults) performed a “Does this come next?” task. Each trial began with a target clip in one of three conditions: an English story, a story in a foreign language (Hebrew, Korean, or Russian), or instrumental music (20 sec). Participants then heard the question, “Does this come next?”, followed by a probe (story, foreign speech, or music; 4.5 sec). Participants then had 6.5 sec to judge whether the probe was the correct continuation of the initial story or the continuation of a different story (story condition), the same foreign language or a different foreign language (foreign speech condition), or the same melody by the same instrument or instead a different melody by a different instrument (music condition).

Experiment 3 contained 24 story trials, eight foreign speech trials, and eight music trials, divided evenly into four runs. Trial order was counterbalanced with respect to the condition across runs using a Latin-square design. All analyses in the current article focus on the comparison of the story and music conditions.

After the scanning session in Experiment 3, the blind children completed a subset of the Woodcock Johnson III Test of Achievement in Braille (Woodcock, McGrew, & Mather, 2001) to assess their Braille reading and cognitive abilities (Table 2). (See Bedny et al., 2015, for details on Experiment 3.)

We obtained Braille-reading hand dominance and reading frequency information through a post-experimental survey conducted over the telephone with 17 of the 19 blind adult participants from Experiments 1 and 2. Participants reported their dominant reading hand, whether they read bimanually, as well as how many hours they read per week (Table 1).

MRI Data Acquisition and Analysis

MRI structural and functional data from Experiments 1 and 2 were collected on a 3-T Phillips scanner at the F.M. Kirby Research Center for Functional Brain Imaging affiliated with the Johns Hopkins University. T1-weighted structural images were collected in 150 axial slices with 1-mm isotropic voxels. Functional BOLD images were collected in 36 axial slices with $2.4 \times 2.4 \times 3$ mm voxels (repetition time = 2 sec). Data for Experiment 3 were collected on a

3-T Siemens (Erlangen, Germany) scanner at the Martinos Imaging Center at the Massachusetts Institute of Technology. T1-weighted structural images were collected in 128 axial slices with 1.33-mm isotropic voxels. Functional data were acquired in $3 \times 3 \times 4$ mm voxels in 30 near-axial slices (repetition time = 2 sec).

All data analyses were performed using FSL, FreeSurfer, the Human Connectome Project workbench, and custom software (Glasser et al., 2013; Smith et al., 2004; Dale, Fischl, & Sereno, 1999). Cortical surface models were created for each participant using the standard FreeSurfer pipeline. During preprocessing, functional data were motion corrected, high-pass filtered with a 128-sec cutoff, and resampled to the cortical surface. Once on the surface, the data were smoothed with a 10-mm FWHM Gaussian kernel. Note that smoothing on the surface is more accurate than smoothing in the volume, because the smoothing kernel is restricted to gray matter and cannot cross through sulci/gyri (Hagler, Saygin, & Sereno, 2006).

A general linear model was used to analyze BOLD activity as a function of condition for each participant. In all three experiments, the stimulus portion of each trial was modeled using a boxcar regressor convolved with a standard double-gamma hemodynamic response function. In Experiments 2 and 3, the response periods were modeled separately from the stimulus presentations. Temporal derivatives for each covariate were also included to account for differences in hemodynamic response function onset across voxels. The data were not prewhitened before the statistical analysis. Fixed effects analyses were used to combine runs within participants. Covariates of no interest were included to remove the effect of mean white matter and CSF signal as well as motion spikes (frame-wise displacement relative to previous time point > 1.5 mm). One run of data was discarded from a sighted child because of excessive motion (more than half of the data points categorized as motion spikes).

Laterality Analysis

Language laterality was assessed based on the sentences $>$ math equations contrast in Experiment 1, the sentences $>$ nonword sequences contrast in Experiment 2, and the stories $>$ music contrast in Experiment 3. All three of these contrasts compare spoken language processing with auditory control conditions. Sentence $>$ control contrasts from Experiments 1 and 2 focus on lexical and sentence level linguistic processes, controlling for early auditory and phonological processes. Both contrasts have been used in previous studies and are known to elicit canonical perisylvian responses (e.g., Monti, Parsons, & Osherson, 2012; Fedorenko, Hsieh, Nieto-Castañón, Whitfield-Gabrieli, & Kanwisher, 2010; Humphries, Binder, Medler, & Liebenthal, 2006; Röder, Stock, Neville, Bien, & Rösler, 2002; Friederici, Meyer, & von Cramon, 2000; Hagoort et al., 1999). The control conditions in Experiments 1 and 2 were high in working memory load so as to distinguish linguistic

Table 3. Summary of Behavioral Performance

	Accuracy (SD), %		RT (SD), sec	
	Language	Control	Language	Control
<i>Experiment 1</i>				
Blind adults	83 (12)	81 (16)	2.65 (0.57)	2.8 (0.68)
Sighted adults	83 (10)	88 (13)	2.83 (0.64)	2.82 (0.59)
<i>Experiment 2</i>				
Blind adults	86 (10)	66 (12)	2.62 (0.48)	2.82 (0.39)
Sighted adults	80 (8)	66 (6)	2.58 (0.36)	2.65 (0.32)
<i>Experiment 3</i>				
Blind adults	99 (2)	100 (0)	3.48 (0.94)	2.28 (1.02)
Sighted adults	98 (3)	99 (3)	2.94 (0.7)	2.2 (0.78)
Blind children	76 (25)	83 (27)	4.34 (0.83)	4.03 (0.69)
Sighted children	90 (14)	96 (11)	4.59 (0.81)	3.69 (0.9)

“Language” columns correspond to the sentence conditions in Experiments 1 and 2 and the story condition in Experiment 3. “Control” columns correspond to the math equation condition in Experiment 1, the nonword sequence condition in Experiment 2, and the music condition in Experiment 3. RT measurements include correct trials only.

processes from general working memory and task difficulty effects (Lane et al., 2015). The stories > music contrast in Experiment 3 includes phonological as well as lexical and sentence level processes.

We calculated LIs based on sentence > control contrasts for each participant. LIs range from -1 , indicating strong right lateralization, to $+1$, indicating strong left lateralization. LIs were calculated using the combined bootstrap/histogram method (Wilke & Schmithorst, 2006). The bootstrap/histogram method ensures that LIs are not unduly influenced by the choice of activation threshold or by outlier voxels.

Bootstrapped LIs were computed across 20 evenly spaced thresholds ranging from $z = 1.28$ to $z = 4.26$ (corresponding to one-sided $p = .1$ to $p = .00001$, uncorrected). To compute the LI for a specific threshold, the participant’s sentence > control z statistic map was first masked, and all subthreshold voxels were discarded. Next, we sampled the suprathreshold voxels (with replacement) 100 times in each hemisphere at a sampling ratio of $k = 1.0$. LIs were then calculated for every pair of left and right hemisphere samples, yielding a histogram of 10,000 threshold-specific LIs. LIs were calculated using the standard formula: $(L - R) / (L + R)$, where L and R refer to the sums of left and right hemisphere z statistics, respectively. A single summary LI for the threshold was computed from the histogram by taking the average after excluding the upper and lower 25% of values. Finally, we computed the average of the threshold-specific LIs, weighted by the thresholds, to give the participant’s final bootstrapped LI.

LIs were computed for a network of five frontotemporal language areas: (1) orbital and (2) triangular inferior frontal

gyrus as well as (3) anterior, (4) middle, and (5) posterior lateral temporal cortex. These five regions were selected from a publicly available set of language ROIs because they show the most reliable responses during sentence comprehension across participants (Fedorenko, Behr, & Kanwisher, 2011; Fedorenko et al., 2010; web.mit.edu/evelina9/www/funcloc.html). The five ROIs were combined into a single frontotemporal network mask, except where noted otherwise. In addition, we calculated LIs for the occipital lobe (Van Essen, 2005). Before computing LIs, all occipital voxels were removed from the mask of the frontotemporal language network.

Occipital Extent Analysis

The amount of occipital activation for each blind participant was calculated as the sum of z statistics above a $z = 3.09$ (one-sided $p < .001$) threshold in the occipital lobe, across both hemispheres. This measure combines anatomical extent across voxels as well as the degree of activation of each individual voxel.

RESULTS

Behavioral Performance

Behavioral data are summarized in Table 3. Across Experiments 1–3, there were no consistent differences, between blind and sighted participants in sentence comprehension performance. Behavioral performance in Experiments 1 and 2 has been described previously (Lane et al., 2015). In Experiment 3, all adult participants performed at ceiling (mean accuracy > 98% for both blind and sighted adults,

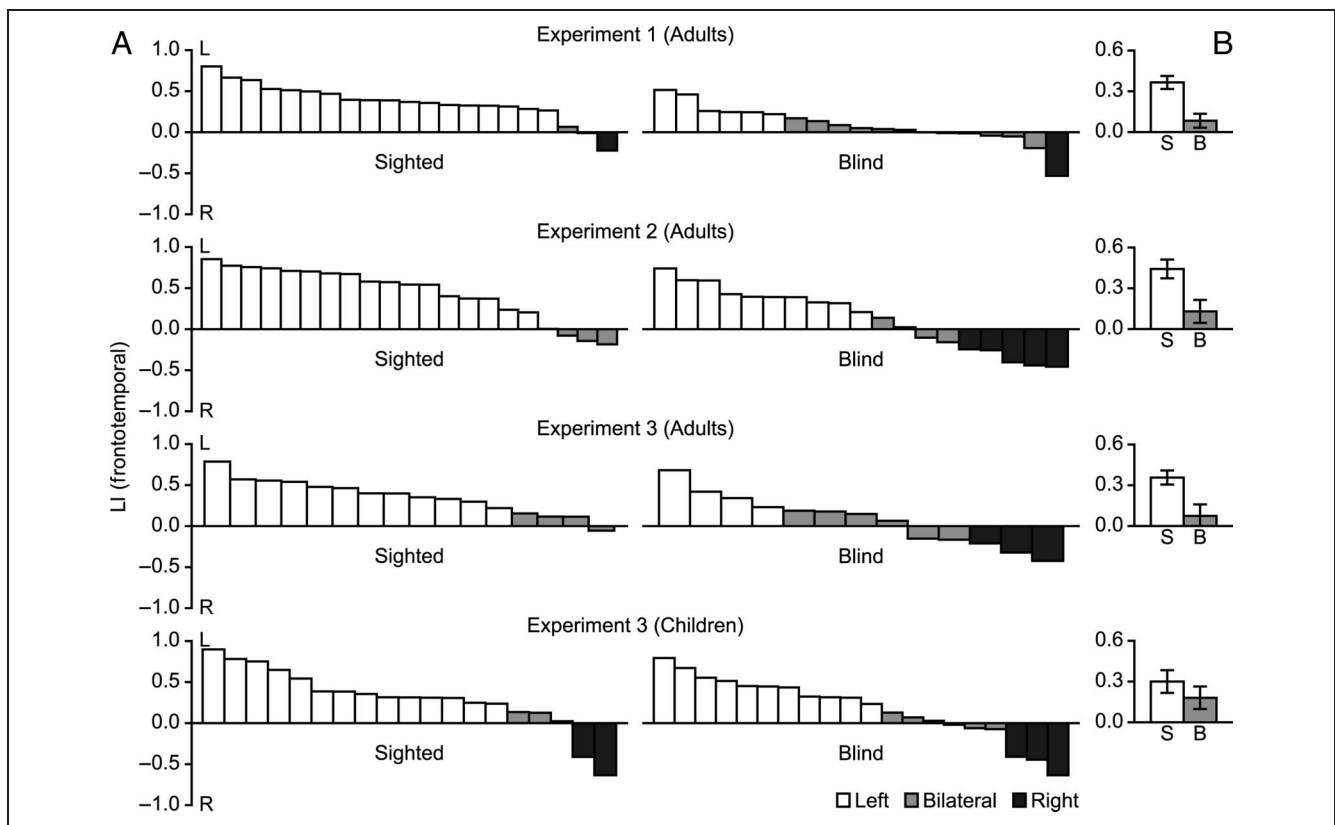


Figure 1. Frontotemporal LIs in blind and sighted individuals. (A) Sorted LIs for blind and sighted individuals across experiments. Bars represent individual participants. LIs range from +1, indicating strong left lateralization, to -1, indicating strong right lateralization. Lateralization category is indicated by shading (threshold for bilateral LIs = ± 0.2). (B) Group-averaged LIs for sighted and blind individuals. Error bars represent SEM. All LIs were calculated within the frontotemporal language network. LIs were based on the sentence > math equation contrast (Experiment 1), the sentence > nonword sequence contrast (Experiment 2), and the story > music contrast (Experiment 3). Experiment 3 includes a new sample of blind and sighted adults and children.

in sentence and music conditions). Blind and sighted adults were faster on music than sentence trials, but this effect was somewhat larger in the blind group (response time ANOVA including correct trials only; main effect of Music vs. Language: $F(1, 27) = 83.6, p < .001$; main effect of Group: $F(1, 27) = 1.06, p = .312$; Group \times Condition interaction: $F(1, 27) = 4.88, p = .036$). Blind and sighted children were both more accurate and faster on music than sentence trials, with a slightly larger RT effect in the blind children (accuracy: main effect of Condition, $F(1, 28) = 4.7, p = .04$; main effect of Group, $F(1, 28) = 3.79, p = .061$, Group \times Condition interaction, $F(1, 27) = 0.04, p = .839$; RT, including correct trials only: main effect of Condition, $F(1, 27) = 35.27, p < .001$; main effect of Group, $F(1, 27) = 0.04, p = .843$; Group \times Condition interaction, $F(1, 27) = 7.2, p = .012$).

Frontotemporal Language Network Is Less Left Lateralized in Congenitally Blind Individuals

Consistent with prior work, sighted participants had strongly left-lateralized activation during sentence comprehension in the frontotemporal language network (one-sample t tests of LI = 0, Experiment 1, sentences >

math: LI = 0.36, $t(20) = 7.38, p < .001$; Experiment 2, sentences > nonwords: LI = 0.44, $t(20) = 6.29, p < .001$). By contrast, blind participants' activation during sentence comprehension was not systematically lateralized in either experiment (Experiment 1, sentences > math: LI = 0.08, $t(18) = 1.58, p = .132$; Experiment 2, sentences > nonwords: LI = 0.13, $t(18) = 1.5, p = .152$; Figures 1 and 2). LIs were lower in the blind group than in the sighted group (between-group t tests, Experiment 1: $t(38) = -3.88, p < .001$; Experiment 2: $t(38) = -2.82, p = .008$). LIs were moderately correlated between the two experiments across participants (correlations in the sighted group: $R^2 = .4, p = .002$; blind group: $R^2 = .38, p = .005$).

The pattern of reduced lateralization in blind adults was consistent across the language network. In both experiments, we found a main effect of group and no Group \times ROI interaction (Group \times ROI ANOVA, main effect of Group, Experiment 1: $p < .001$, Experiment 2: $p = .006$; main effects of ROI: $ps < .001$; Group \times ROI interaction: $ps > .3$; Figure 3).

We found a similar pattern of reduced lateralization in our second sample of blind adults and in blind children in Experiment 3 (Figure 1). Responses to stories > music in Experiment 3 were strongly left-lateralized in sighted

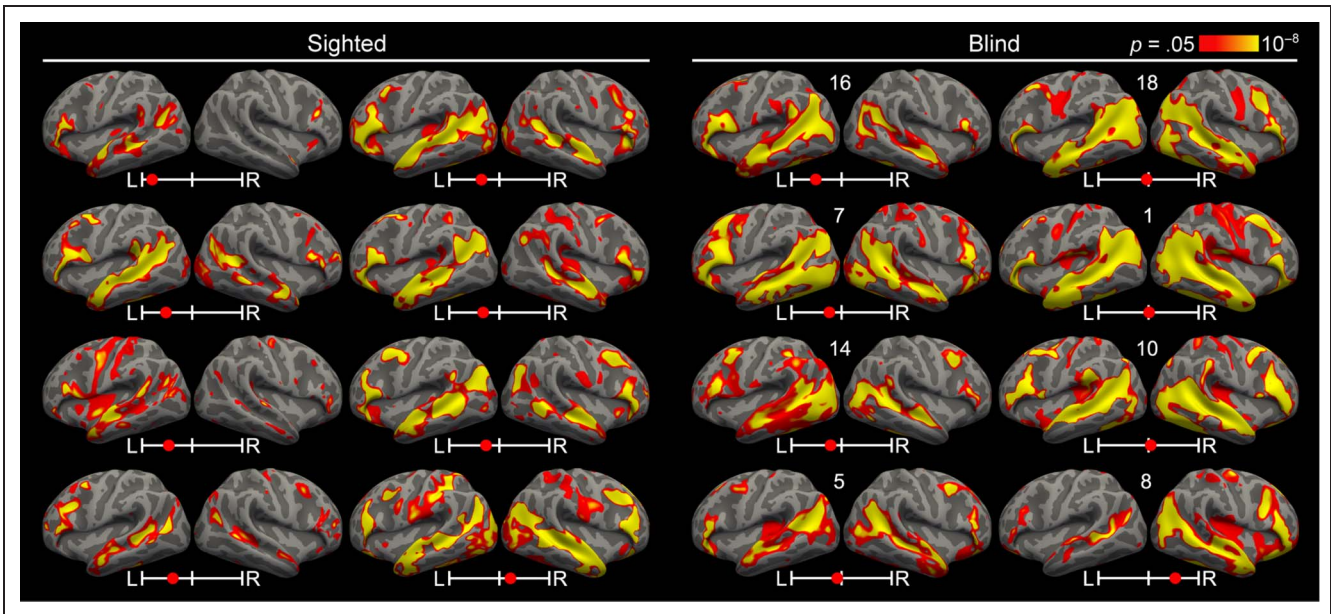


Figure 2. Individual participant activation maps for the sentence > math equation contrast in Experiment 1. Eight representative participants spanning the observed range of LIs were selected for both sighted and blind groups. Each participant's LI for the frontotemporal language network is plotted on a number line below his or her activation maps. Individual participant labels corresponding to Table 1 are included for blind participants. Activation maps are thresholded at $p = .05$, false discovery rate corrected.

adults and children (one-sample t test with age as a covariate: $LI = 0.32$, $t(33) = 6.15$, $p < .001$; effect of Age: $t(33) = 0.45$, $p = .659$) but were only weakly left lateralized in blind adults and children ($LI = 0.14$, $t(31) = 2.19$, $p = .036$; effect of Age: $t(33) = -0.42$, $p = .677$). The

left lateralization of language was lower in the blind group than in the sighted group, and neither the effect of Age nor the Group \times Age interaction was significant (Group \times Age ANOVA, main effect of Group: $F(1, 64) = 5.25$, $p = .025$; effect of Age: $F(1, 64) = 0.0$, $p = .981$; Group \times Age interaction: $F(1, 64) = 0.37$, $p = .543$).

Similar results were obtained when ambidextrous and left-handed individuals were excluded from analyses. As before, lateralization was significantly reduced in blind compared with sighted right-handed adults (between-group t tests, Experiment 1: $t(29) = -4.4$, $p < .001$; Experiment 2: $t(29) = -3.02$, $p = .005$). In Experiment 3, the left lateralization of language was also lower in blind right-handers compared with sighted right-handers, irrespective of age (Group \times Age ANOVA, main effect of Group: $F(1, 51) = 6.77$, $p = .012$; effect of Age: $F(1, 51) = 0.57$, $p = .45$; Group \times Age interaction: $F(1, 51) = 0.00$, $p = .997$).

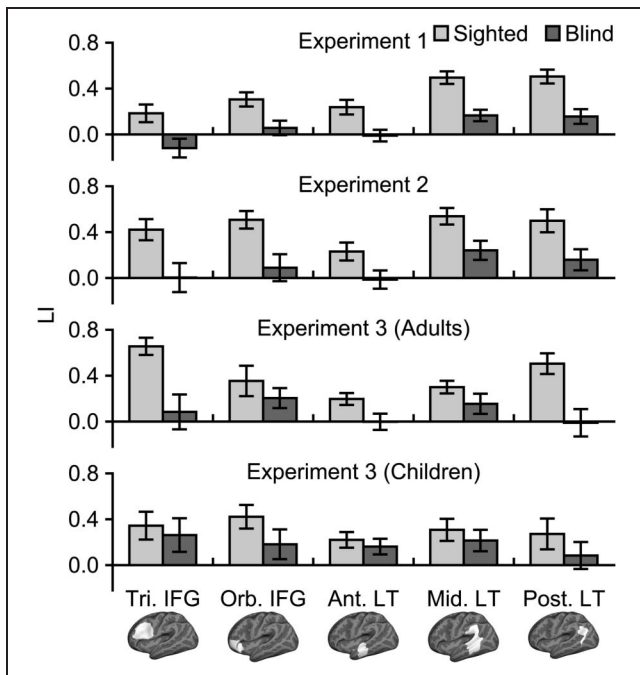


Figure 3. LIs for sighted and blind individuals, across five subregions of the frontotemporal language network. ROIs include triangular (Tri.) and orbital (Orb.) inferior frontal gyrus (IFG) as well as anterior (Ant.), middle (Mid.), and posterior (Post.) lateral temporal cortex (LT). Error bars represent SEM.

Relationship of Language Laterality, Etiology, and Performance

One possibility is that the etiology of blindness and not blindness itself influences language laterality. Sixty-three percent of blind adults in Experiments 1 and 2 and 46% of blind adults in Experiment 3 were blind due to prematurity. We therefore asked whether prematurity itself, as opposed to blindness per se, causes reduced lateralization. The blind children in Experiment 3 did not contribute to this analysis because only 2 of the 20 participants were born prematurely. We did not find any differences in laterality between premature and nonpremature participants in any of the three experiments (group t tests in frontotemporal language network, $p > .26$ in all three experiments).

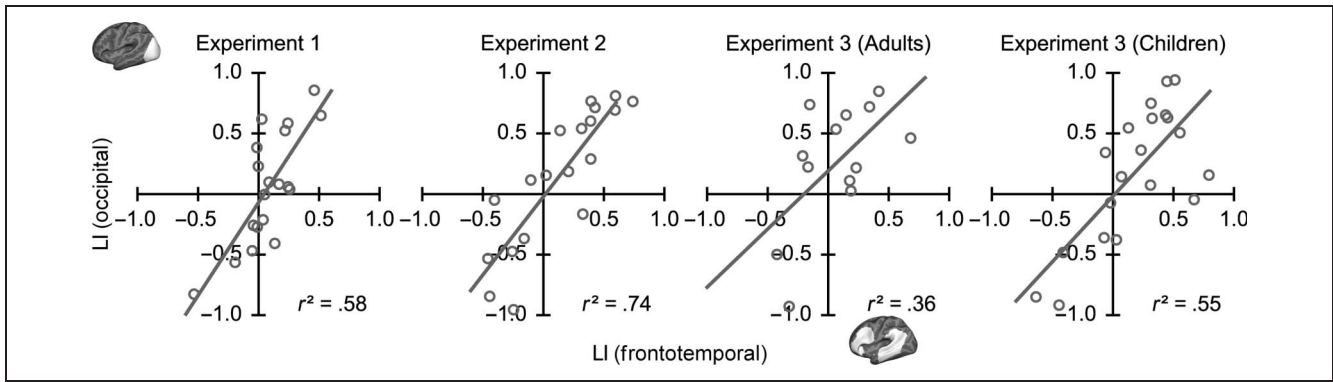


Figure 4. Occipital LIs correlated with frontotemporal LIs in blind individuals. Data points represent individual participants.

These results suggest that vision loss and not prematurity is predictive of reduced lateralization in our sample.

Reduced lateralization of function was not systematically related to performance on comprehension tasks. We did not observe a correlation between performance and lateralization in Experiment 1 ($R^2 = .09$, $p = .21$). In Experiment 2, blind adults with reduced left lateralization were marginally worse at answering comprehension questions about the syntactically complex sentences (LIs correlated with performance on complex sentences, $R^2 = .2$, $p = .058$). In Experiment 3, performance in the story task was at ceiling across blind and sighted adults. Among blind children, there was no relationship between language lateralization and performance on the story task or on a standardized test of linguistic abilities (LIs correlated with story comprehension performance: $R^2 < .01$, $p = .92$; LIs correlated with Woodcock–Johnson verbal performance: $R^2 = .04$, $p = .45$).

Relationship of Occipital Plasticity and Frontotemporal Laterality

Another possible cause for the laterality shift in blindness is the emergence of occipital responses to language. Contrary to this idea, we found no relationship between the amount of occipital activation during sentence comprehension and the degree of language lateralization in the frontotemporal language network (LIs correlated with the amount of occipital activation, $R^2 < .02$, $p > .5$, across Experiments 1–3).

Nonetheless, we found that responses to spoken language in occipital and frontotemporal cortices were lateralized to similar degrees in blind adults (paired t tests of LIs between frontotemporal language network and the occipital lobe, $p > .29$). Furthermore, occipital and frontotemporal LIs were strongly correlated across blind individuals (Experiment 1: $R^2 = .58$, $p < .001$; Experiment 2: $R^2 = .74$, $p < .001$; Experiment 3: $R^2 = .45$, $p < .001$; Figure 4). Blind individuals with right-lateralized responses to language in front-temporal cortices also tended to have right-lateralized responses to language in occipital cortices.

Braille Reading Ability and Left Lateralization of Spoken Language

We asked whether learning to read Braille affects frontotemporal laterality in the group of blind children in Experiment 3. In the sample of children, Braille reading ability varied from none to adult level. We did not observe a correlation between Braille reading ability and language lateralization either when Braille reading ability was modeled alone ($R^2 = .06$, $p = .31$) or when age and Braille ability were both included as covariates (effect of Age: $t(15) = -1.44$, $p = .17$; effect of Braille ability: $t(15) = 0.63$, $p = .54$; Figure 5). Note that all of the blind adults in our sample were proficient Braille readers (see Table 1 for details). Thus, we could not ask whether Braille literacy in our adult sample was related to language lateralization.

Another possibility is that Braille-reading handedness, and not reading proficiency, affects language lateralization. For example, reading Braille primarily with the left hand might cause neural responses to spoken language to become right-lateralized. Five of the 19 blind adult participants in Experiments 1 and 2 reported reading Braille with the left hand only; 3 of 19, bimanually but left-hand dominant; 7 of 19, bimanually but right-hand dominant; and 2 of 19, with the right hand only (Table 1). Two blind participants did not complete the post-experimental

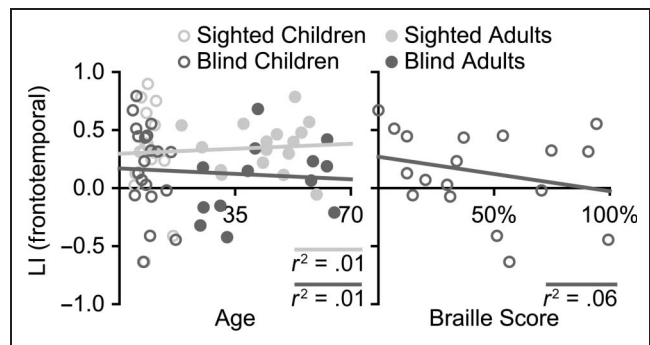


Figure 5. Frontotemporal LIs correlated with age (left) and Braille reading ability (right) in sighted and blind individuals. LIs were calculated based on Experiment 3, story > music contrast. Data points represent individual participants.

survey. Interestingly, although only 3 of the 19 participants in our sample were left-handed, approximately half self-reported as left-hand dominant for reading Braille. However, we found no effect of Braille-reading hand dominance (coded as a single-ordered factor, with four levels of increasing left dominance) on language laterality (one-way ANOVA with an ordered factor, testing for a polynomial relationship between reading hand and laterality, Experiment 1: $F(3, 13) = 1.11, p = .38$; Experiment 2: $F(3, 13) = 0.17, p = .92$).

DISCUSSION

Across the three experiments, we observed a higher incidence of bilateral and right-lateralized cortical activation during sentence processing in blind individuals. Reduced laterality was observed throughout frontotemporal language areas as well as in occipital cortices recruited for language processing. The present results add to the existing literature on the neurobiology of language in blind individuals. Previous studies show that individuals who are blind from birth recruit visual cortices during language production and comprehension tasks. The current findings suggest that the frontotemporal language network is also modified in blindness in that it is less left lateralized.

One possibility is that these two changes to the language network of blind individuals—occipital plasticity and reduced left lateralization—are causally related. Several pieces of evidence from the current study suggest that this is not the case. First, the amount of occipital activation during sentence comprehension did not predict reduced lateralization in frontotemporal cortices across participants. Second, occipital plasticity and reduced lateralization do not have a similar relationship with linguistic behavior. Whereas occipital responses to language are associated with better performance on a sentence comprehension task among blind individuals (Lane et al., 2015), reduced left lateralization of language has, if anything, a weak negative relationship. These observations suggest that occipital plasticity and reduced lateralization likely occur via different mechanisms.

On the other hand, we found a strong relationship between the lateralization of occipital and frontotemporal cortices. Blind individuals with right-lateralized responses to language in frontotemporal regions also tended to have right-lateralized responses in occipital cortices. This observation provides further evidence that regions within occipital cortices are integrated into the frontotemporal language network in blindness.

In our sample, there was no relationship between reduced left lateralization of spoken language and Braille reading ability. Child participants in Experiment 3 varied widely in age and Braille reading ability, yet neither age nor Braille reading proficiency predicted lateralization. Our sample of blind adults consisted only of proficient Braille readers. The confluence of congenital blindness

and Braille illiteracy is fortunately rare in the United States. Thus, we cannot rule out a relationship between Braille reading ability and spoken language lateralization in blind adults. In blind adults, Braille reading hand dominance did not predict spoken language lateralization. Blind adults who reported reading Braille with their left hand were no more likely to have right-lateralized responses to spoken language. It remains possible that we failed to find a subtle relationship between laterality and Braille reading because of insufficient power. At the very least, it appears that Braille reading ability does not fully explain the reduced lateralization of spoken language in blindness.

There are reasons to believe that the laterality of spoken language is relatively impervious to changes in literacy. In sighted children, the left lateralization of responses to spoken language is well established by 4 years old, before literacy (Holland et al., 2007; Szaflarski, Holland, Schmithorst, & Byars, 2006). Although print reading is arguably both bilateral and spatial, like Braille, learning to read print does not reduce left lateralization of language responses (Dehaene et al., 2010; Holland et al., 2007). Instead, experience with print leads to the development of reading-specific visual areas in the ventral occipitotemporal cortices (e.g., Rothlein & Rapp, 2014; Ben-Shachar, Dougherty, Deutsch, & Wandell, 2011; McCandliss, Cohen, & Dehaene, 2003; Cohen et al., 2000). The laterality of these responses to written letter and word forms follows the laterality of the previously established system for the processing of spoken language (Seghier & Price, 2011; Cai, Paulignan, Brysbaert, Ibarrola, & Nazir, 2010; Cai, Lavidor, Brysbaert, Paulignan, & Nazir, 2008). We hypothesize that, similarly, the laterality of Braille reading follows the laterality of spoken language.

One possibility is that blindness reduces language lateralization by changing the lateralization of other cognitive functions. It has been proposed that language is “forced out” of the right hemisphere by right-lateralized visuospatial functions (Kosslyn, 1987; Levy, 1969). Consistent with this idea, individuals who have visuospatial functions lateralized to the left hemisphere show right-lateralized activity during language production (Cai et al., 2013). Other functions such as tool use are co-lateralized with language (Vingerhoets et al., 2013). Changes in the laterality of any of these functions could indirectly modify the laterality of language.

Alternatively, blindness could reduce the left lateralization of language by delaying the timing of language acquisition. Blind children are slightly delayed in producing their first words and their first two-word utterances (Landau & Gleitman, 1985; Norris, 1957). These delays are believed to result from reduced access to the extralinguistic context that supports language learning. The left lateralization of language may have a sensitive period akin to the sensitive period for language acquisition (Johnson & Newport, 1989). According to this hypothesis, any extrinsic factor that delays language acquisition reduces left lateralization (Bishop, 2013; Locke, 1997). Evidence for this idea

comes from populations with reduced access to language in early development. Children from families with low socioeconomic status receive reduced linguistic stimulation and show reduced left lateralization in Broca's area during a rhyming task (Raizada, Richards, Meltzoff, & Kuhl, 2008). Deaf children who have little access to sign language early in life show a reduced right hemifield advantage for understanding signs, as compared with early signing deaf children (Leybaert & D'Hondt, 2003). Deaf adults who acquire their first language late because of lack of access to sign language show reduced activation of left prefrontal areas during language processing relative to deaf adults who acquire sign language early (Mayberry et al., 2011). These data are consistent with the possibility that delays in language acquisition reduce left lateralization. There are, however, important differences between these prior examples and blindness. First, the language acquisition delays in blindness are subtle and short-lived (Landau & Gleitman, 1985). Furthermore, unlike the examples above, blindness delays language acquisition without altering the language input itself. Interpreted in this light, the present results suggest that the maturational state of the brain at the time of acquisition, and not just the language input, affects lateralization. More broadly, the present results suggest that nonlinguistic experience, in this case, the absence of visual experience, can modify the neurobiological development of language.

In summary, we find that frontotemporal language areas are less left-lateralized in blindness. Previous work has also shown that blind individuals recruit occipital cortices during language processing. We find that occipital and frontotemporal responses to language are colateralized across individuals, providing further evidence that occipital areas are incorporated into the language network. The present findings are consistent with the proposal that the adult neurobiological system that supports language emerges from complex interactions between innate predispositions of frontotemporal cortices, the innate predispositions of other neurocognitive systems, and the time course of brain development and experience. The present results further suggest that the lateralization of function in the human brain is affected by lifetime experiences.

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