Supporting Information

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SI Results

Hippocampal Activity in Blind Participants During Sentence Comprehension. We extracted PSC during sentence comprehension from bilateral hippocampal ROIs in the congenitally blind group. Hippocampal ROIs were created using a normalized template (Brain Imaging Toolbox, http://web.mit.edu/swg/software.htm). The hippocampus was not active above rest during the stimulus portion of the trail ($P > 0.3$), and the effect of condition on the hippocampal BOLD signal was not reliable [$F(4, 40) = 0.93$, $P > 0.3$].

Postscan Memory Test. Following the scan in experiment 2, participants performed a surprise memory test in which they heard 80 sentences and 80 jabberwocky sentences, half of which were from the fMRI experiment and half from sentences and jabberwocky sentences they had not yet heard. Participants were instructed to indicate whether they had heard the sentence/jabberwocky sentence during the fMRI experiment by pressing the corresponding button on a keyboard, and were told that approximately half of the stimuli would be from the actual experiment.

In a surprise postscan memory test of experiment 2, sentences were much better remembered than jabberwocky strings [d′ main effect of condition $F(1, 23) = 89.91$, $P < 0.0001$]. However, both groups were able to remember the jabberwocky and sentence stimuli above chance (*t* tests, $P < 0.05$). The effect of group and group × condition interaction was not reliable ($P > 0.2$, congenitally blind $d'_{sent} = 2.52$, $d'_{jabb} = 0.31$; sighted $d'_{sent} = 1.99$, $d'_{jabb} = 0.32$).

Sentences Greater than Backward Speech: Within-Group Analyses. Within the congenitally blind group, the BOLD signal was larger for sentences than backward speech in the left pericalcarine cortex. The peak of the sentences > backwards speech effect was in the posterior, or roughly foveal region. We also observed increased BOLD signal in a number of other early and secondary visual regions: the left and right fusiform gyri, the lateral middle occipital gyri BA18/19, and the left occipital pole (experiments 1 and 2). The neuroanatomical distribution of this language response was anatomically distinct from the response to sound per se. When comparing backward speech to rest, we observed right lateralized activity that was restricted to the medial wall of the occipital lobe with peaks in the pericalcarine cortex.

In both sighted and congenitally blind adults, classic language regions were also active during sentence comprehension. In both experiments and in both groups, listening to sentences relative to backward speech resulted in greater BOLD signal in the bilateral lateral-temporal cortices (middle, inferior, and superior temporal gyri), and the left angular gyrus. Sighted, but not congenitally blind, individuals also had increased BOLD signal in the precuneus and posterior cingulate regions as well as the left prefrontal cortex (left inferior and middle frontal gyri; $P < 0.05$, corrected). Left prefrontal activity (left inferior and middle frontal gyri) emerged in the blind group at an uncorrected threshold of $P < 0.001$, $k = 10$. No precuneus activity was observed in the blind group at this threshold.

These group differences in precuneus and prefrontal activity did not reach significance in the whole-brain analysis; there were no brain regions that were significantly more active in the sighted than the blind group.

Effect of Combinatorial Structure and Lexical Semantic Information in Classic Language ROIs (Defined Individually and in the Group). A 2 × 2 × 2 × 4 was used to compare the effect of compositional and lexical information on brain activity across groups (group × compositional × lexical × ROI). We first performed the analysis in individually defined ROIs and then in group ROIs (*SI Materials and Methods*).

In individually defined ROIs, we observed a main effect of compositional information [$F(1, 338) = 42.33$, $P < 0.0001$], a main effect of lexical information [$F(1, 338) = 39.37$, $P < 0.0001$], and a reliable compositional × lexical information interaction [$F(1, 338) = 4.15$, $P < 0.05$]. There was also a main effect of ROI [$F(1, 345) = 11.97$, $P < 0.0001$; the LMTG was more active than any other ROI] and a main effect of group [$F(1, 20) = 4.95$, $P < 0.05$; larger signal in the blind group].

A similar pattern was observed in group ROIs: main effect of compositional information [$F(1, 430) = 22.06$, $P < 0.0001$] and main effect of lexical information [$F(1, 430) = 17.74$, $P < 0.0005$]. The compositional × lexical information interaction did not reach significance [$F(1, 430) = 2.16$, $P = 0.14$]. There was also a main effect of ROI [$F(1, 430) = 62.07$, $P < 0.0001$; LMTG was overall more active than any other ROI]. No other main effects or interactions approached significance.

Effect of Combinatorial Structure and Lexical Semantic Information in Anatomically Defined Pericalcarine Cortex. In anatomically defined pericalcarine cortex, there was also an effect of sentence level combinatorial structure and lexical semantic information for congenitally blind, but not sighted, individuals [2 × 2 condition ANOVA: combinatorial $F(1, 30) = 6.41$, $P = 0.02$, lexical $F(1, 30) = 5.27$, $P = 0.03$, interaction $F(1, 30) = 0.004$, $P = 0.94$, and a two-way group × condition interaction 2 × 2 × 2 ANOVA: combinatorial × group $F(1, 59) = 6.59$, $P = 0.01$; lexical × group $F(1, 59) = 9.49$, $P = 0.003$]. Phonology did not affect pericalcarine activity differently in sighted and blind groups (interaction $P > 0.3$; Fig. S5).

SI Materials and Methods

fMRI Data Acquisition. T1-weighted structural images were collected in 128 axial slices with 1.33-mm isotropic voxels (TR = 2 ms, TE = 3.39 ms). Functional, BOLD data were acquired in 3 × 3 × 4 mm voxels (TR = 2 s, TE = 30 ms) in 30 near-axial slices. The first 4 s of each run were excluded to allow for steady-state magnetization.

fMRI Data Analysis: Definition of Individual-Subject Functional Language ROIs. Four language-responsive functional ROIs were manually defined by a trained observer, including LIFG, LMFG, LMTG, and LAng. These ROIs were chosen because they are most associated with language processing historically and across neuroimaging and neuropsychological studies. ROIs were defined using a combination of anatomical boundaries described below, and functional data from the sentences/backward speech contrast. Data were normalized and overlaid onto the individual subjects' normalized anatomical scan. This procedure allows for preserving the sulcul and gyral landmarks of the individual subject, which vary from person to person. For each region, we selected the most highly responsive voxel in the sentences/backward speech contrast. We then drew a 10-mm sphere around that voxel and included in the ROI all superthreshold voxels within the sphere. This procedure ensured that the ROIs preserved the shape of the activation as it was observed in that participant.

The anatomical boundaries of the ROIs were as follows: for the LIFG ROI, we chose the peak voxel within the LIFG. Across participants, the peak typically fell within BA 45/47. For the

LMFG ROI, we chose the peak voxel within the LMFG. The peak typically fell within BA 6/9/46. For the LMTG, we chose the peak voxel along the LMTG, not including the anterior temporal pole. This region typically fell in the middle portion of the LMTG (along the anterior/posterior axis) within BA 21/22. For the LAng ROI, we identified the peak voxel within the left temporoarietal junction, including the posterior aspect of the superior temporal gyrus (BA 22) and the adjacent parietal cortex including (BA 39/40).

fMRI Data Analysis: Definition of Group Functional ROIs. Group LIFG, MFG, MTG, and LAng language functional ROIs were defined based on the sentences/backward speech contrast from experiment 1. Data were thresholded at $P < 0.001$, $k = 10$. For group ROIs, spheres of 15 mm were drawn rather than spheres of 10 mm. We have found in previous studies that this larger radius is more optimal for group ROI definition, likely due to the variability of ROI location across participants. The same anatomical criteria that were used to define individual participant ROIs were used to define group ROIs.

Behavioral Procedures. In experiment 2, the passage and question were separated by a 0.25-s tone (without the tone, the question duration was 5.75 s). Passages were between two and four sentences (number of words: mean = 30, SD = 4). Questions were one sentence long (number of words: mean = 9, SD = 2). In the control condition, the same passages were presented backward (12 s), and subjects judged whether a brief segment of backward speech matched part of the first passage (6 s). Backward speech sounds were created by digitally reversing the stimuli, rendering them unintelligible, though similar in terms of low-level acoustic properties. The short strings of backward speech were made by playing the questions backward (for the "no" trials) or splicing out a piece of a backward story (for the "yes" trials). The task was performed in six runs with 12 items per run (eight speech, four backward speech). Each run was 6 min and 12 s long.

For both experiments, stimuli were digitally recorded by a female native-English speaker at a sampling rate of 44,100 to produce 32-bit digital sound files. The backward speech condition was created by digitally reversing the sentences and their probes. Audio files were normalized to each other in volume with respect to RMS amplitude such that all files (across conditions) had equal RMS (average RMS, 12.04 dB full scale).

Behavioral Analyses Methods. Because the probe durations were not matched across conditions, we corrected the reaction time data by probe duration. We calculated by how much the average probe duration for each condition differed from the mean probe duration across conditions. This duration was then added or subtracted from the average RT for that condition.

Procedures of Resting-State Study. Resting-state data were obtained from a separate experiment with 10 congenitally blind participants (six females; mean age 50 ± 8 y, mean years of education 17 ± 2). All participants had lost their vision at birth, had no measurable acuity, and had at most minimal light perception. Three of the participants had also taken part in experiment 2. During the resting-state study, participants heard pairs of words over headphones and indicated how related in meaning the words were on a scale of 1 to 4 by pressing buttons on a response pad. Five word-pairs made up a block. Blocks were 18 s long and were separated by 14 s of fixation. The experiment was broken up into five runs of 7.7 min each. In a control condition, participants heard pairs of backward speech sequences and performed an auditory similarity judgment on a scale of 1 to 4 (see ref. 55 for further details). Data from the rest periods in this study were used for the purposes of the resting-state connectivity analyses.

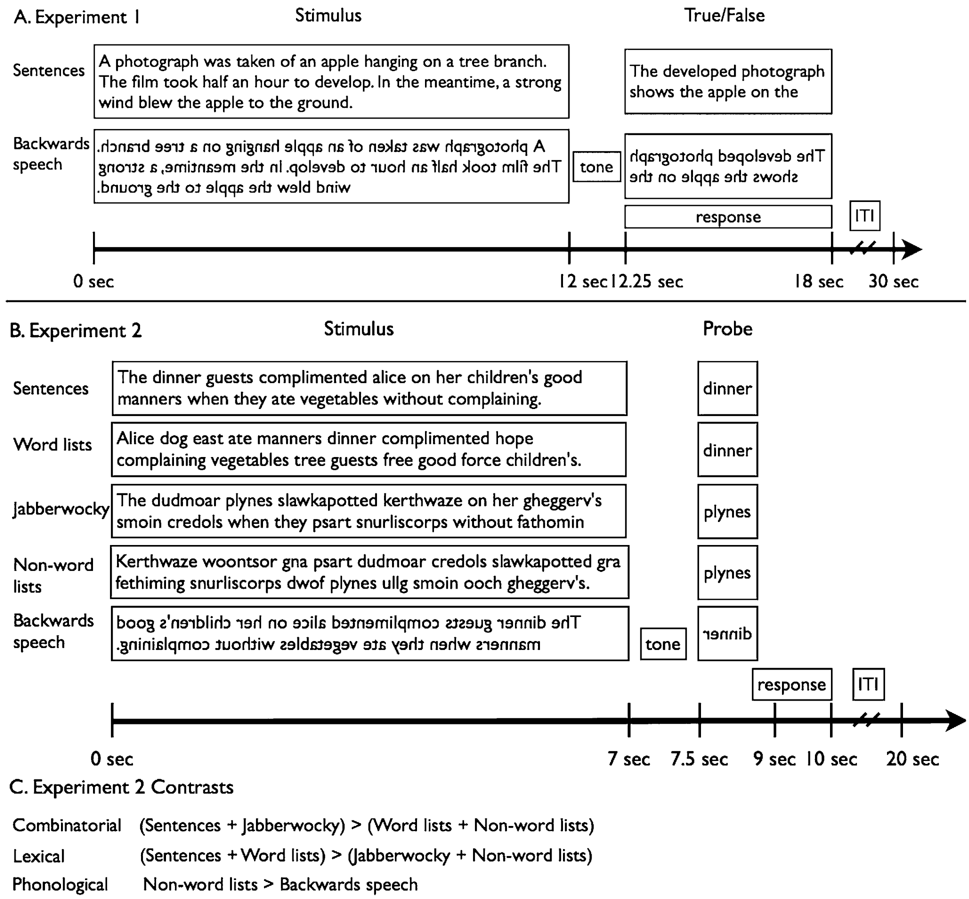

Fig. S1. (*A*) Experiment 1: Task and example stimuli. (*B*) Experiment 2: Task and example stimuli. (*C*) Experiment 2: Critical experimental contrasts.

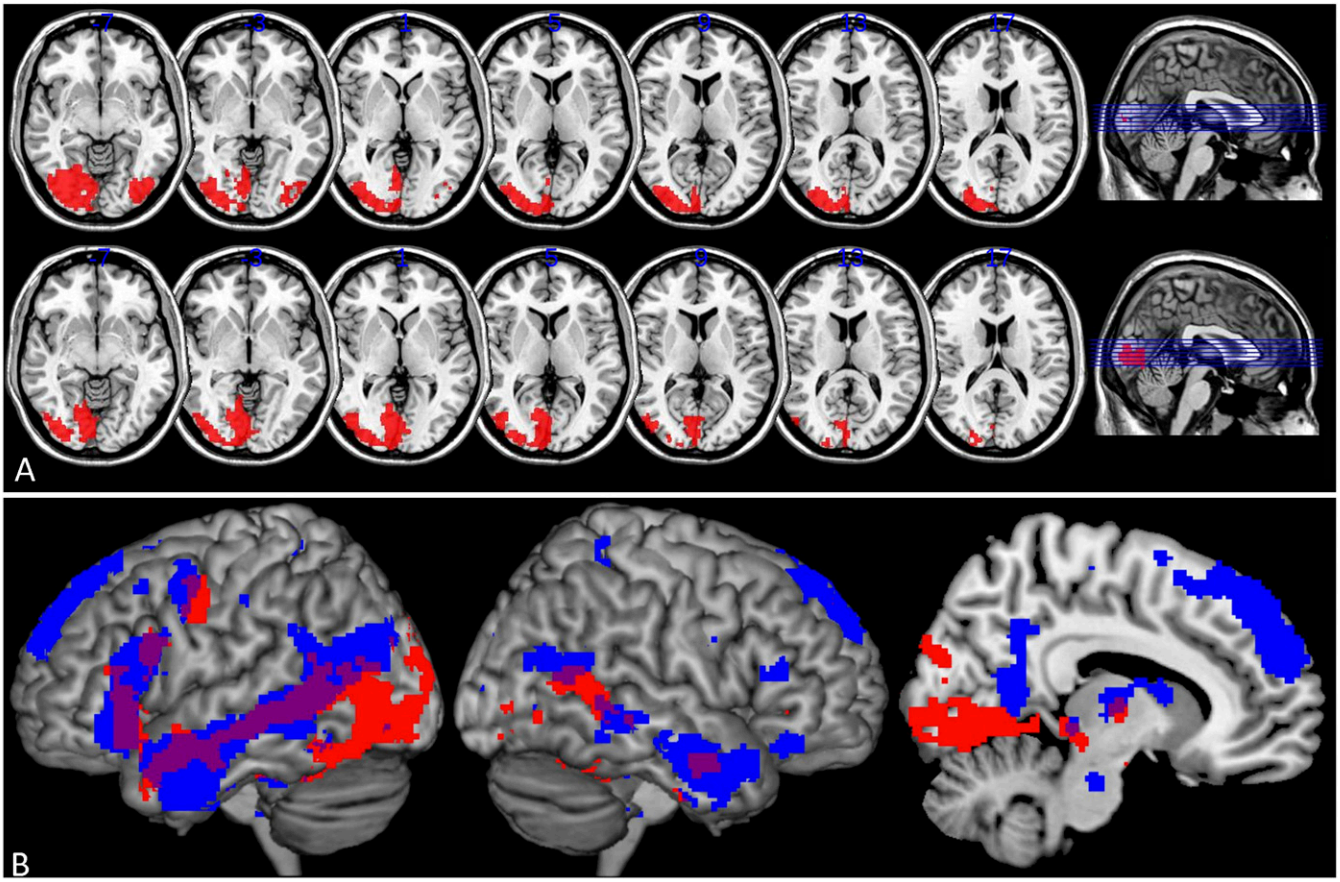

Fig. S2. (*A*) Group × condition interaction [congenitally blind > sighted (sentences > backward speech)]. (*Upper*) Experiment 1. (*Lower*) Experiment 2. For a list of brain regions, see Table S1. $P < 0.05$, corrected. (*B*) Within-group analysis of sentence/backward speech thresholded at $P < 0.005$, uncorrected to reveal full extent of activation.

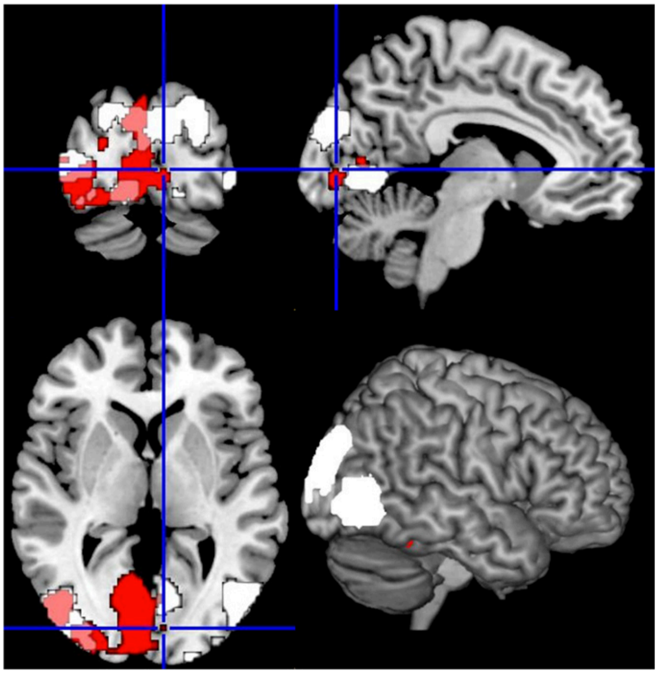

Fig. S3. Overlay of the occipital response to language (sentences > backward speech) as opposed to sound (backward speech > rest). Sentences > backward speech is shown in red, and backward speech > rest is shown in white ($P < 0.05$, corrected).

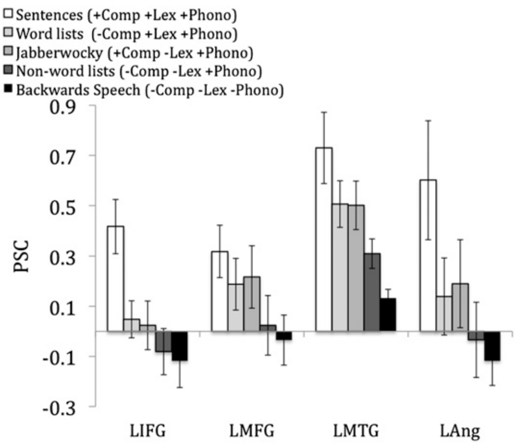

Fig. S4. Activity (PSC) in individual-subject, classic language ROIs of blind participants. Legend abbreviations indicating presence of a particular kind of linguistic information: Comp, compositional; Lex, lexical; Phono, phonological. Error bars represent SE of condition effect. Note that the *y* axis is expanded relative to the graph of the sighted group due to the higher overall signal of the LMTG in blind participants.

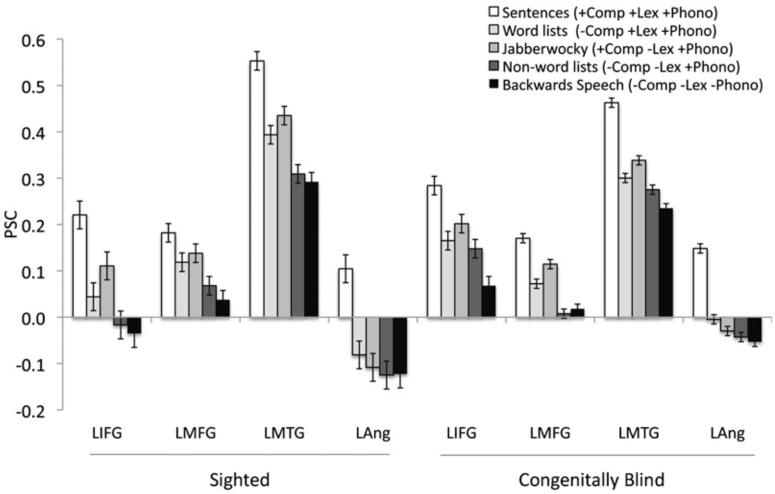

Fig. S5. Activity (PSC) in classic language ROIs of blind and sighted participants. ROIs were defined based on group data from experiment 1 and extracted from experiment 2. Legend abbreviations indicating presence of a particular kind of linguistic information: Comp, compositional; Lex, lexical; Phono, phonological. Error bars represent SE of condition effect.

Table S1. Brain regions more active for sentences than backward speech in congenitally blind adults relative to sighted adults

	Blind > sighted (sentences > backward speech)							
Region	BA	*x*	*y*	*z*	Peak *t*	W_{combo}	P_{combo}	mm^3
Experiment 1								
Left inf/mid occipital/fusiform gyri	18/19/37	−36	−74	−12	7.48	9.52	0.001	9,228
Left inf/occipital/lingual gyri	18	−36	−88	−4	6.85			
Right inf/occipital gyrus	18/17	32	−90	−6	6.87	8.82	0.001	1,458
Right inf/mid occipital/fusiform gyri	19/18	42	−78	−8	6.49			
Experiment 2								
Left fusiform gyrus	19	−4	−76	−4	6.78	7.91	0.001	8,406
Left lingual gyrus/cuneus	17/18/19	−40	−70	−18	5.93			
Left mid occipital/temporal gyri	19/37/39	−52	−74	6	5.77			

Regions that reached significance at $P < 0.05$, corrected using permutation analyses. Coordinates are reported in MNI space. Peak *t*, *t* value for the peak *t* statistic of the contiguous cluster; P_{combo} is the corrected *P* value using a combination of cluster size and voxel-wise *t* value; W_{combo} is the combined cluster and voxel test statistic; mm^3 is the size of the entire contiguous cluster in millimeters. BA, Broca's area.

Table S2. Brain activity in individually defined language ROIs of sighted and congenitally blind adults

Brain region	Lexical	Compositional	Compositional × lexical
LIFG	$F(1, 69) = 39.4$, $P < 0.0001$	$F(1, 69) = 41.6$, $P < 0.0001$	$F(1, 69) = 7.2$, $P < 0.01$
LMFG	$F(1, 63) = 27.0$, $P < 0.0001$	$F(1, 63) = 31.3$, $P < 0.0001$	$F(1, 63) = 0.4$, $P > 0.3$
LMTG	$F(1, 72) = 39.2$, $P < 0.0001$	$F(1, 72) = 40.0$, $P < 0.0001$	$F(1, 72) = 0.8$, $P > 0.3$
LAng	$F(1, 63) = 52.3$, $P < 0.0001$	$F(1, 63) = 57.5$, $P < 0.0001$	$F(1, 62) = 15.5$, $P < 0.001$
	Lexical × group	Compositional × group	Compositional × lexical × group
LIFG	$F(1, 69) = 0.9$, $P > 0.3$	$F(1, 69) = 0$, $P > 0.3$	$F(1, 69) = 0.9$, $P > 0.3$
LMFG	$F(1, 63) = 0.6$, $P > 0.3$	$F(1, 63) = 0$, $P > 0.3$	$F(1, 63) = 2.7$, $P = 0.11$
LMTG	$F(1, 72) = 0$, $P > 0.3$	$F(1, 72) = 0.9$, $P > 0.3$	$F(1, 72) = 0.2$, $P > 0.3$
LAng	$F(1, 63) = 2.4$, $P = 0.13$	$F(1, 63) = 7.5$, $P < 0.01$	$F(1, 63) = 0.1$, $P > 0.3$
	Group		
LIFG	$F(1, 23) = 0$, $P > 0.3$		
LMFG	$F(1, 21) = 0.2$, $P > 0.3$		
LMTG	$F(1, 24) = 5.3$, $P < 0.05$		
LAng	$F(1, 21) = 2.2$, $P = 0.15$		

We compared activity in individually defined language ROIs of sighted and congenitally blind adults in each ROI separately using 2 × 2 × 2 ANOVAs with group (blind or sighted), ±lexical, and ±compositional as factors. The only reliable group × condition interaction was observed in the LAng ROI, where congenitally blind participants showed a larger effect of compositional structure on BOLD signal. There was also more activity in the LMTG of blind participants across all conditions. There was also a trend toward a smaller lexical × compositional interaction in the blind participants in the LMFG. These group differences should be interpreted with caution because they were not predicted and are only weakly or marginally significant.

Table S3. Effects of lexical and compositional information on BOLD signal in sighted and congenitally blind groups (thresholded at $P < 0.05$, corrected)

Region	BA	*x*	*y*	*z*	Peak *t*	W_{combo}	P_{combo}	mm^3
Sentences + jabberwocky > word lists + nonword lists								
Sighted								
Right ant mid/inf temporal gyri	20/21	48	−12	−18	12.26	8.82	<0.001	5,994
Right parahippocampal gyrus	36	44	−20	−14	11.32			
Right post mid temporal gyrus	21/22	58	−40	−2	10.17			
Left sup/medial frontal gyrus	6/8	−4	14	58	9.92	8.82	<0.001	11,182
Right mid frontal gyrus	11/47	40	34	−14	7.72			
Left inf frontal gyrus	9/45	−56	18	24	9.32	9.52	<0.001	11,092
Left post mid temporal gyrus	22/21	−58	−48	2	8.73			
Left sup/mid temporal and angular gyri	22/42	−62	−34	6	8.57			
Left mid/precentral frontal gyri	6/8	−40	4	46	5.97	4.72	0.04	1,034
Left globus pallidus/VAN thalamus		−16	−6	10	5.86	4.92	0.03	1,594
Left caudate nucleus		−12	4	8	5.23			
Right caudate nucleus		8	8	14	4.72			
Blind								
Left ant mid/sup temporal gyri	21/22	−48	−26	−10	7.73	4.97	0.03	2,146
Left post mid/sup temporal	22/39	−42	−54	14	5.58			
Left cerebellum, culmen		−6	−64	−4	5.94	4.46	0.04	1,606
Left cuneus/lingual gyrus	17/18	−14	−94	2	5.15			
Left cuneus	19	−8	−86	26	4.92			
Right mid temporal gyrus	21/22	48	−34	−4	5.55	4.46	0.04	1,392
Right ant sup/mid temporal gyri	22/21	58	−2	−16	4.33			
Blind > sighted								
Left cerebellum/lingual/fusiform gyri	19/18	−14	−68	−12	6.30	6.63	0.01	5,562
Left lingual/fusiform gyri	19/18	−12	−60	−8	6.13			
Left lingual gyrus/cuneus	19/18/17	−8	−66	−4	5.54			
Sentences + word lists > jabberwocky + nonword lists								
Sighted								
Right post mid temporal gyrus	21/22	64	−42	2	9.61	8.13	0.001	3,206
Right ant mid/inf temporal gyri	21/20	50	−14	−18	8.12			
Left fusiform/mid/inf temporal gyri	20/21/37	−56	−4	−28	8.32	8.42	0.001	6,724
Left mid/sup temporal/angular gyri	22/21/	−58	−46	0	8.12			
Left mid/sup frontal gyri	8	−6	50	46	6.82	5.83	0.013	2,216
Left sup medial frontal gyri	8	−10	38	50	6.00			
Left precuneus/posterior cingulate	7/31	−10	−52	36	5.62	4.32	0.053	996
Left posterior cingulate/precuneus	30/23/31	−6	−52	20	4.91			
Blind								
Right cerebellum/fusiform gyrus	20	30	−42	−28	6.64	5.76	0.012	7,970
Left and right cuneus/lingual/occipital gyri	17/18	−8	−96	−8	6.28			
Right parahippocampal gyrus	36/35	22	−40	−16	6.24			
Left post sup/mid temporal gyri	22/39	−40	−56	16	6.51	4.77	0.031	2,724
Left ant mid/sup temporal gyri	21	−52	−22	−10	5.82			
Left mid occipital/temporal gyri	19	−44	−76	18	5.19			
Blind > sighted								
Left mid occipital gyrus	18/19	−30	−90	2	6.28	8.82	0.001	11,792
Left mid/inf occipital gyri	18	−24	−86	−10	6.06			
Left cerebellum/lingual/fusiform gyri and cuneus	19/18/17	−20	−68	−16	6.05			

Inf, inferior; sup, superior; mid, middle; post, posterior; ant, anterior; BA, Broca's area.

Table S4. Altered resting-state correlations between the left lateral occipital and the left medial occipital ROI and the rest of the brain in the congenitally blind relative to the sighted group

Brain area	BA	*x*	*y*	*z*	β	Peak *t*	*p*-FDR Voxel	*p*-FWE Cluster	mm^3
Source: Left lateral occipital area									
Increased correlations									
C1									
Left inf frontal gyrus	46	−40	38	4	0.08	7.04	<0.0001	<0.005	1,436
Left inf/mid frontal gyri	46/9/45	−42	20	26					
Left inf/mid frontal gyri	9/6	−42	8	34					
C2									
Left thalamus, VLN, and MDN		−10	−14	6	0.08	5.87	<0.0001	<0.005	1,304
Left thalamus, LPN		−14	−20	12					
Right thalamus, VLN, and MDN									
C3									
Left superior/medial frontal gyri	8/6/32	0	32	46	0.08	6.97	<0.0001	<0.005	1,136
Decreased correlations									
C1									
Right (and small left) cuneus/precuneus	18/19/31/17	18	−70	24	−0.15	−4.71	<0.0001	<0.005	15,170
Bilateral parahip/fusiform gyri	36/37	−28	−38	−10					
Right precuneus	19	20	−88	42					
C2									
Right postcent/precent	4/3	28	−28	66	−0.09	−5.79	<0.0001	<0.005	12,468
Left postcent/precent gyri	3/4	−12	−40	72					
Right postcent gyrus	43	52	−8	16					
C3									
Right hipp/parahipp gyrus	3/28	26	−16	−24	−0.07	−6.66	<0.005	<0.01	762
Right uncus	36	20	−2	−40					
Right parahip gyrus	35	24	−30	−28					
C4									
Parahip/rhinal cortex	36/28/35	−22	−4	−26	−0.07	−5.17	0.001	0.01	646
Source: Left medial occipital area									
Increased correlations									
C1									
Left thalamus, VLN, and MDN		−10	−14	4	0.10	5.79	<0.01	<0.0001	2,394
Decreased correlations									
C1									
Right parahip gyrus	35/36	32	−28	−30	−0.17	−4.74	<0.01	<0.0001	14,940
Right precuneus/cingulate/cuneus	19/18/7	12	−86	42					
Right parahip/lingual/fusiform gyri	30/27	16	−40	−4					
Middle occipital gyrus	19/37	50	−76	2					
C1									
Bilateral precent/postcent gyri	6/4/3	−58	−12	42	−0.10	−5.57	<0.01	<0.0001	14,094
Medial frontal gyrus	6	2	−26	62					

The correlation maps are thresholded at $P < 0.05$, false discovery rate (FDR) corrected at the voxel level, and $P < 0.05$, family-wise error (FWE), corrected at the cluster level. BA, Broca's area; postcent, postcentral; precent, precentral; inf, inferior; sup, superior; mid, middle; hipp, hippocampus; parahipp, parahippocampal; VLN, ventral lateral nucleus; MDN, medial dorsal nucleus; LPN, lateral posterior nucleus; *p*-FWE, FWE probability; *p*-FDR, FDR probability.

Table S5. Demographic information of participants

Participant	Gen	Age, y	Age of blindness	Cause of blindness	Residual light perception	Education (y)	Exp
EB1	F	47	Birth	Premature birth/RLF	None	Some college (15)	1
EB2	F	61	Birth	Optic chiasm atrophy	Minimal L	MAs (22)	1
EB3	M	46, 49	Birth	Retinoblastoma	None	MA (18)	1 and 2
EB4	F	54, 58	Birth	Premature birth/RLF	None	MA ongoing (17)	1 and 2
EB5	M	40, 44	Birth	Congenital cataracts	None	Some college (13)	1 and 2
EB6	F	43	Birth	Premature birth/RLF	None	BA (16)	1
EB7	M	55	2.5 y	Retinoblastoma	None	JD (19)	1
EB8	M	44	Birth	Congenital rubella	None	BA (16)	1
EB9	F	57	Birth	Premature birth/RLF	None	MA (18)	1
EB10	F	53	Birth	Premature birth/RLF	Minimal	MA (18)	1
EB11	M	39	Birth	Premature birth/RLF	Minimal	MA (18)	2
EB12	F	59	Birth	Premature birth/RLF	None	BA (16)	2
EB13	F	59	Birth	Premature birth/RLF	Minimal	MA (18)	2
EB14	M	29	Birth	Retinitis pigmentosa	None	High school (12)	2
EB15	F	21	Birth	LCA	Minimal	Some college (14)	2
EB16	M	35	Birth	Premature birth/RLF	None	MA (18)	2
EB17	M	37	Birth	Premature birth/RLF	None	BA (16)	2
EB18	M	57	Birth	Premature birth/RLF	Minimal	BA (16)	2

RLF, retrolental fibroplasia; LCA, lebers congenital amaurosis; Exp, experiment no.