Supporting Information

Kanjlia et al. 10.1073/pnas.1524982113

SI Experimental Procedures

Definition of ROI for Task-Based Analyses. IPS and visual cortex (rMOG) ROIs were defined in individual subjects using the math > sentence contrast (orthogonal to the differences between math conditions). ROIs were defined in each participant as the top 5% of voxels with the highest math > sentences *z* value. Individual-subject ROIs were defined within search spaces created based on group data. Search space definition was orthogonal to the contrast of interest (differences between math conditions) and orthogonal to subject (see below).

The left and right IPS search spaces were defined using the sighted and congenitally blind groups' average responses for the math > sentences contrast within the anatomical location of the IPS ($P < 0.01$, uncorrected) (57).

rMOG search spaces were defined using a leave-one-subject-out analysis (on 10 mm smoothed data). We iteratively excluded one subject and defined the rMOG search space, based on the remaining subjects, as the cluster within visual cortex that showed an interaction between the math > sentences contrast and blind > sighted contrast ($P < 0.001$, uncorrected). This procedure ensures that search space definition is orthogonal to subject—that is, a given subject did not contribute to the definition of his or her own search space. Before data extraction, the resulting search spaces of all sighted and blind participants were manually trimmed to ensure that they did not extend into the IPS and to avoid irregularly shaped search spaces.

Definition of ROIs for Resting-State Correlation Analyses. We correlated activity in left and right IPS with the rest of the cortex in blind and sighted participants. Anatomically defined left and right IPS ROIs were used as seeds in the resting-state analyses (57). Time series were averaged over voxels in left and right IPS seeds and then correlated with voxels across the whole cortex. Results are reported for the left and right IPS seeds separately (Fig. 1, *Lower* and Fig. S6).

Five group ROIs were defined for the ROI-to-ROI resting-state correlation analyses in the right hemisphere: three math-responsive ROIs [rMOG (visual), rIPS (parietal), rPFC (frontal)] and two language-responsive ROIs [rVOT (visual) and rIFC (frontal)]. The IPS ROI was identical the IPS search spaces used in the functional ROI analysis (described above). A right math-responsive PFC ROI was defined for the blind and sighted group, separately, by taking a cluster in the right prefrontal cortex that responded to the math > language contrast in each group (blind threshold: $P < 0.01$, uncorrected; sighted threshold: $P < 0.1$, uncorrected). In visual cortex, the rMOG seed was defined by taking a cluster that responded to the math > language in all blind > sighted ($P < 0.001$, uncorrected; manually trimmed; see above). The language-responsive IFC seed was defined as a cluster within literature-defined language-responsive inferior frontal cortex that responded to language > math in the blind and sighted groups, separately (blind: $P < 0.01$, uncorrected; sighted $P < 0.1$, uncorrected). The rVOT seed was defined by taking a cluster in ventral occipitotemporal cortex that responded to the language > math contrast in all blind > sighted ($P < 0.001$, uncorrected; manually trimmed; see above).

A similar seed-to-seed resting-state analysis was performed in the left hemisphere using analogously defined seeds. In blind individuals, we find a dissociation in the functional connectivity patterns of left math and language visual areas with left math-responsive IPS and left language-responsive IFC. However, we did not find this same dissociation between left math and language visual areas and left math and language prefrontal areas.

SI Results

Behavioral Results. Accuracy (percentage correct) and response time data were analyzed using a 2 × 2 × 2 repeated-measures ANOVA with group (blind vs. sighted) as a between-subjects factor and digit–number (single vs. double-digit) and algebraic complexity (algebraically simple vs. complex) as within-subject factors. Two-way interactions and main effects are reported in the main text. There were no three-way interactions among group, digit–number, and algebraic complexity [accuracy: group × digit–number × algebraic complexity interaction: $F(1, 34) = 1.82$, $P = 0.19$; response time: $F(1, 34) = 1.11$, $P = 0.30$].

Preserved Frontoparietal Responses to Number in Congenital Blindness. Within-group (blind and sighted separately) results from the IPS ROI analysis were analyzed using a 2 × 2 × 2 repeated-measures ANOVA with digit–number (single vs. double-digit), algebraic complexity (algebraically simple vs. complex), and hemisphere (left vs. right) as within-subject factors. The left and right IPS of congenitally blind adults responded more to trials with double-digit math equations than single-digit math equations [$F(1, 16) = 36.70$, $P < 0.001$; digit–number × hemisphere interaction: $F(1, 16) = 0.02$, $P = 0.9$] and more to algebraically complex equations than algebraically simpler equations [$F(1, 16) = 8.13$, $P = 0.01$; algebraic complexity × hemisphere interaction: $F(1, 16) = 1.74$, $P = 0.21$] (Fig. 2 and Fig. S3). A similar pattern was observed in the sighted group [main effect of digit–number: $F(1, 18) = 13.85$, $P = 0.002$; main effect of algebraic complexity: $F(1, 18) = 11.05$, $P = 0.004$] (Fig. 2 and Fig. S3).

Between-group results from the IPS ROI analysis were analyzed using a 2 × 2 × 2 × 2 repeated-measures ANOVA with group (blind vs. sighted) as a between-subjects factor and digit–number (single vs. double-digit), algebraic complexity (algebraically simple vs. complex), and hemisphere (left vs. right) as within-subject factors. Two-way interactions and main effects are reported in the main text. There was no digit–number × algebraic complexity interaction [$F(1, 34) = 1.92$, $P = 0.18$]. There was no three-way interaction among group, digit–number, and algebraic complexity [$F(1, 34) = 0.00$, $P = 1.0$].

Responses to Number in Visual Cortex of Blind Adults. Within-group (blind and sighted separately) results from the rMOG ROI analysis were analyzed using a 2 × 2 repeated-measures ANOVA with digit–number (single vs. double-digit) and algebraic complexity (algebraically simple vs. complex) as within-subject factors. The rMOG of congenitally blind individuals was sensitive to algebraic complexity [marginal effect of algebraic complexity: $F(1, 16) = 4.20$, $P = 0.06$; digit–number × algebraic complexity interaction: $F(1, 16) = 1.19$, $P = 0.30$] (Fig. 2). By contrast, the rMOG of sighted individuals was not sensitive to algebraic complexity [main effect of algebraic complexity: $F(1, 18) = 2.01$, $P = 0.17$; digit–number × algebraic complexity interaction: $F(1, 18) = 0.30$, $P = 0.59$]. Within group effects of digit–number are reported in the main text.

Between-group results from the rMOG ROI analysis were analyzed using a 2 × 2 × 2 repeated-measures ANOVA with group (blind vs. sighted) as a between-subjects factor and digit–number (single vs. double-digit) and algebraic complexity (algebraically simple vs. complex) as within-subject factors. Two-way interactions and main effects are reported in the main text. There was no digit–number × algebraic complexity interaction [$F(1, 34) = 1.0$, $P = 0.33$]. There was no three-way interaction among group, digit–number, and algebraic complexity [$F(1, 34) = 0.08$, $P = 0.78$].

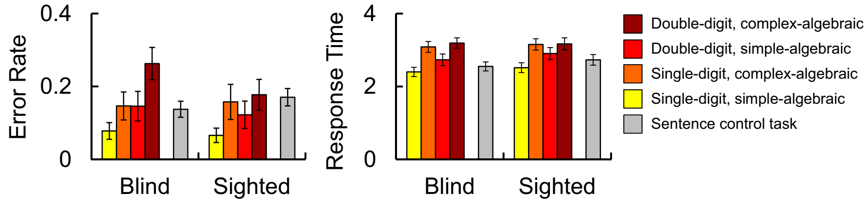

Fig. S1. Congenitally blind (n = 17) and sighted (n = 19) groups' error rates (*Left*) and response times (*Right*) for all conditions in math task and language control task.

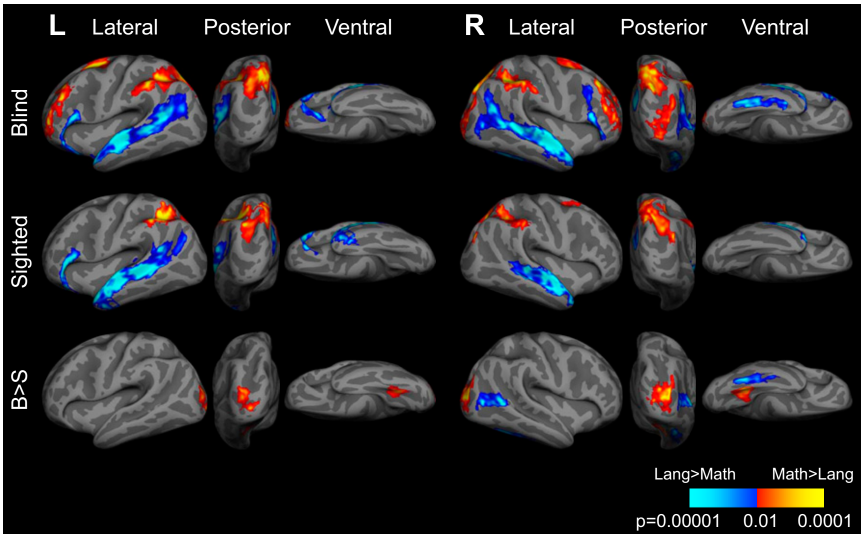

Fig. S2. Brain regions active during math task (red) and language task (blue) in blind (B; n = 19) and sighted (S; n = 17) individuals, and brain regions more active in blind individuals relative to sighted individuals (B > S) ($P < 0.05$, cluster corrected). Response times included as regressor in general linear model (GLM) at time of response.

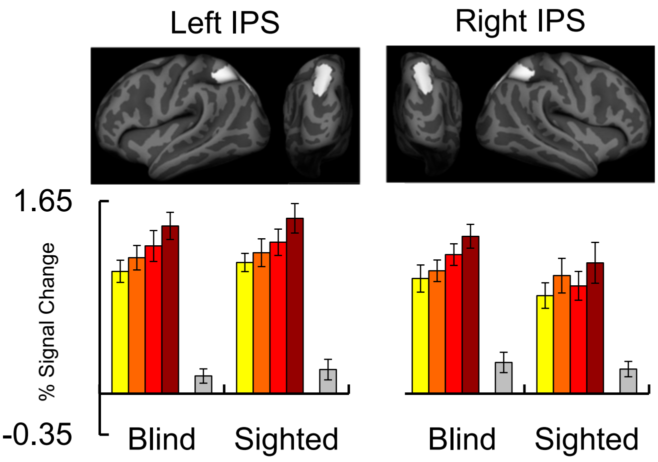

Fig. S3. Responses to math difficulty in left and right IPS ROIs in blind (n = 17) and sighted (n = 19) individuals (error bars represent SEM). Percentage of signal change relative to rest was extracted from individual subject ROIs (*Lower*) defined within left and right IPS search spaces (*Upper*).

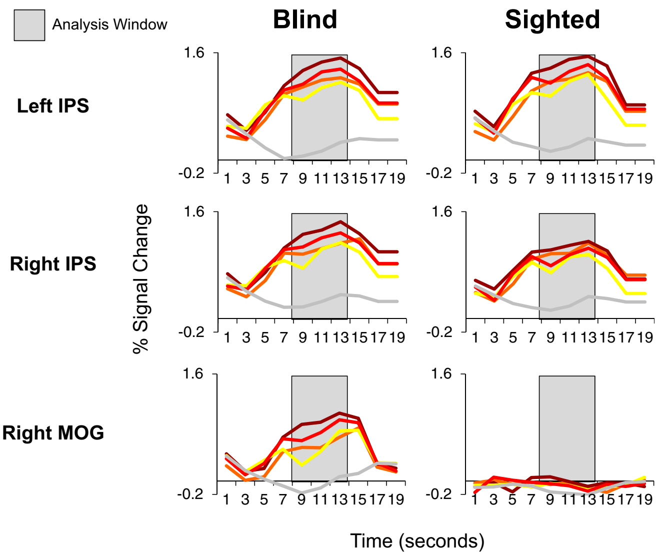

Fig. S4. Percentage of signal change relative to rest over time in left and right IPS and right MOG in blind (*Left*; *n* = 17) and sighted (*Right*; *n* = 19) individuals.

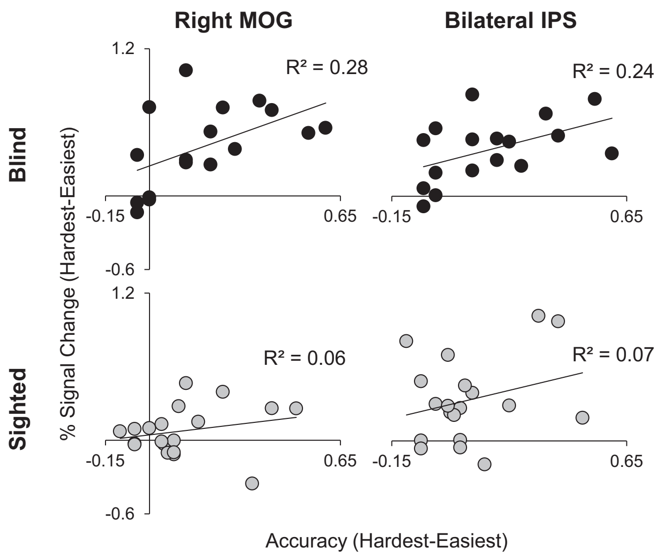

Fig. S5. Percentage of signal change difference between hardest and easiest math trials in rMOG (*Left*), bilateral IPS (*Right*) correlated with difference in accuracy between hardest and easiest math trials [black: correlations for blind group (*n* = 17); gray: correlations for sighted group (*n* = 19)].

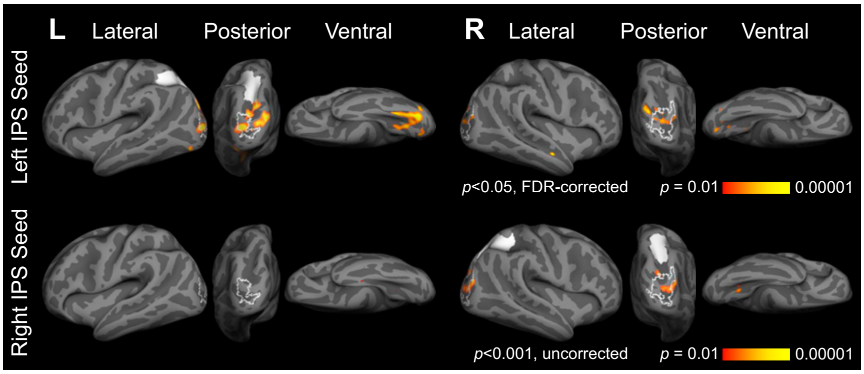

Fig. S6. Brain regions more correlated with left and right IPS seeds (shown in white) at rest in blind group (n = 13) relative to sighted group (n = 9). Functional activation for blind > sighted, math > sentences contrast (P < 0.05, cluster corrected) shown in white outline.

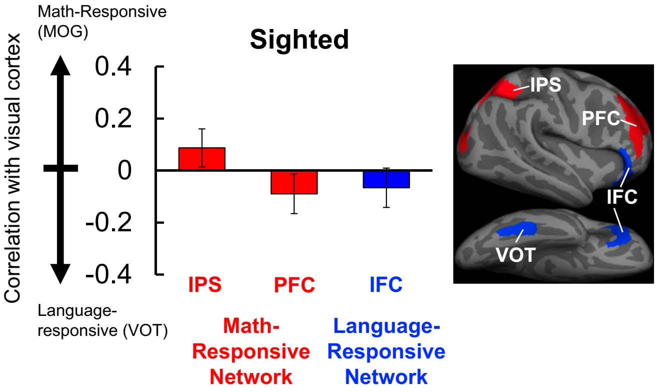

Fig. S7. Resting-state correlations between visual and frontoparietal areas in the sighted group (n = 9). On the y axis is the difference between correlations across number- and language-responsive regions of visual cortex (defined math > language, blind > sighted). Positive scores (red) indicate stronger correlation with number-responsive visual cortex (MOG), and negative scores (blue) indicate stronger correlation with language-responsive visual cortex (VOT) (error bars represent SEM).

Table S1. Participant demographic information

Participant	Gender	Age, y	Cause of blindness	Light perception	Education
B1	M	23	LCA	Minimal	Some college
B2	F	33	ROP	Minimal	BA
B3	F	70	ROP	Minimal	High School
B4*	M	44	Unknown	None	JD
B5	F	68	ROP	None	MA
B6*	F	27	ROP	Minimal	MA
B7*	F	65	ROP	None	MA
B8*	F	35	LCA	Minimal	MA
B9*	M	48	LCA	None	JD
B10*	F	40	ROP	None	MA
B11*	F	50	LCA	Minimal	MA
B12*	F	25	LCA	Minimal	MA
B13*	F	63	ROP	None	MA
B14*	M	37	CG/Cat	None	MA
B15*	M	63	ROP	None	BA
B16*	F	61	ROP	None	JD
B17*	F	47	ROP	None	BA
Average					
Blind	12 F	47	–	–	BA
Sighted	9 F	45	–	–	BA

*Indicates that participant contributed resting-state data. –, Indicates that column feature was either not applicable for the group or incalculable for the group.

BA, bachelor of arts; Cat, cataracts; CG, congenital glaucoma; JD, juris doctor; LCA, Leber's congenital amaurosis; MA, master of arts; ROP, retinopathy of prematurity.

Table S2. Brain regions more active for math than sentences

Brain region	x	y	z	Peak t	mm^2	$P_{cluster}$
Blind						
Left superior parietal lobule	−17	−70	45	8.25	3,268.82	0.0002
Left precuneus	−6	−72	50	7.95		
Left supramarginal gyrus	−54	−39	47	6.82		
Left postcentral sulcus	−35	−44	42	6.36		
Left intraparietal sulcus	−28	−64	43	5.87		
Left superior parietal lobule	−15	−58	60	5.47		
Left middle frontal gyrus	−39	50	9	7.71	1,376.01	0.008
Left transverse frontopolar gyri and sulci	−21	59	−3	6.78		
Left middle frontal gyrus	−45	31	29	6.56		
Left superior frontal sulcus	−22	3	50	7.96	932.94	0.0172
Left superior precentral sulcus	−34	−8	46	4.1		
Left pericallosal sulcus	−2	−30	27	6.47	792.97	0.021
Left marginal branch of cingulate sulcus	−11	−41	45	5.93		
Left middle-anterior cingulate gyrus and sulcus	−8	5	48	5.9	487.78	0.0426
Left superior frontal gyrus	−7	31	31	5.58		
Right intraparietal sulcus	24	−60	50	7.89	1,585.75	0.0084
Right precuneus	5	−61	56	7.82		
Right superior occipital gyrus	23	−75	44	7.09		
Right superior parietal lobule	24	−59	61	5.87		
Right middle occipital sulcus	33	−82	9	6.4	1,206.92	0.012
Right middle occipital gyrus	40	−83	22	5.76		
Right occipital pole	24	−98	8	5.52		
Right superior occipital sulcus	26	−83	16	5.29		
Right inferior frontal sulcus	43	33	20	7.27	1,124.94	0.0128
Right middle frontal gyrus	38	27	39	7.12		
Right superior frontal sulcus	26	34	34	5.25		
Right supramarginal gyrus	59	−25	36	4.79		
Right middle frontal sulcus	27	49	3	4.57		
Right middle frontal gyrus	35	4	55	8.39	829.84	0.018
Right superior frontal gyrus	23	3	66	5.45		
Right posterior cingulate gyrus and sulcus	3	3	34	8.35	517.48	0.0316
Right pericallosal sulcus	5	−15	30	4.04		
Right marginal branch of cingulate sulcus	7	−41	44	6.89	439.95	0.0418
Right medial occipitotemporal sulcus	32	−43	−15	5.84	393.22	0.0488
Sighted						
Left intraparietal sulcus	−34	−46	42	7.9	2,574.59	0.0016
Left angular gyrus	−29	−69	41	7.62		
Left superior parietal lobule	−13	−61	61	5.99		
Left marginal branch of cingulate sulcus	−16	−37	41	10.86	1,014.38	0.0086
Left posterior-dorsal cingulate gyrus	−3	−25	33	4.75		
Left pericallosal sulcus	−2	−28	27	4.11		
Right marginal branch of cingulate sulcus	13	−28	38	7.48	2,090.13	0.0014
Right superior parietal lobule	16	−75	45	5.99		
Right middle occipital gyrus	40	−80	30	5.98		
Right superior parietal lobule	17	−63	63	5.93		
Right precuneus	8	−54	59	5.23		
Right intraparietal sulcus	36	−46	36	5.96	907.48	0.008
Right supramarginal gyrus	58	−36	44	4.96		
Right superior precentral sulcus	31	−4	46	4.92	432.29	0.0402
Right superior frontal gyrus	18	14	62	4.61		
Blind > sighted						
Left middle occipital sulcus	−25	−95	1	5.08	508.99	0.0282
Left medial occipitotemporal sulcus	−29	−55	−12	4.84	399.62	0.0474
Right middle occipital sulcus	33	−82	9	6.38	962.39	0.0064
Right superior occipital sulcus	27	−84	15	5.19		
Right occipital pole	24	−98	8	5.08		
Right medial occipitotemporal sulcus	32	−45	−14	5.56	574.51	0.0194

Peaks of brain regions active more for math than language ($P < 0.05$, cluster corrected; $P < 0.01$ cluster-forming threshold; 10 mm minimum distance between peaks). Coordinates reported in MNI space. Peak t: t values corresponding to local maxima; mm^2: area occupied by cluster on cortical surface; $P_{cluster}$: P value for entire cluster.

Table S3. Brain regions correlated with left and right IPS at rest

Brain region	*x*	*y*	*z*	Peak *t*	Peak P_{FDR}
Correlation with left IPS in blind > sighted					
Left posterior transverse collateral sulcus	−30	−78	−11	5.99	0.01476
Left middle occipital sulcus	−30	−87	6	5.91	0.01476
Left superior occipital gyrus	−11	−95	13	5.83	0.01476
Left fusiform gyrus	−30	−54	−18	5.17	0.01476
Left superior occipital sulcus	−24	−84	22	5.13	0.01476
Left medial occipitotemporal sulcus	−23	−59	−10	4.89	0.01476
Left lingual gyrus	−10	−83	−12	4.63	0.01478
Left middle frontal sulcus	−30	46	19	3.83	0.02811
Right superior temporal sulcus	50	−11	−20	5.53	0.12521
Right superior occipital gyrus	15	−90	20	5.03	0.12521
Right occipital pole	20	−82	−14	4.76	0.12521
Right middle occipital gyrus	31	−89	15	4.47	0.12521
Right medial occipitotemporal sulcus	24	−65	−5	4.12	0.12521
Right lingual gyrus	20	−45	−11	3.97	0.12521
Right inferior occipital gyrus and sulcus	38	−76	−15	3.94	0.12521
Right middle occipital sulcus	34	−82	2	3.94	0.12521
Right postcentral sulcus	32	−35	44	3.8	0.12521
Correlation with right IPS in blind > sighted					
Right middle occipital gyrus	42	−79	15	4.85	0.17848
Right superior occipital sulcus	27	−78	20	4.47	0.17848
Right medial occipitotemporal sulcus	28	−53	−7	4.23	0.17848
Right cuneus	7	−82	9	3.56	0.24553

Peaks of brain regions correlated with left and right IPS during rest (10 mm minimum distance between peaks). Coordinates reported in MNI space. Peak *t*: *t* values corresponding to local maxima; peak P_{FDR}: FDR-corrected *P* value corresponding to significance of peak.