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Reading Modality Shapes Reading Network in Proficient Blind Readers of Braille

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Abstract

The neural basis of reading is highly consistent across a wide range of languages and scripts. Are there alternative neural routes to reading? How does the sensory modality of symbols (tactile vs. visual) influence their neural representations? We examined these questions by comparing reading of visual print by sighted people (n=15) and reading of tactile Braille by people born blind (n=19). Blind and sighted proficient readers were presented with written and spoken stimuli that varied in word-likeness. Written stimuli consisted of real words, consonant strings and non-letter shapes. Auditory stimuli consisted of words and backward speech sounds. Consistent with prior work, vOTC was active during Braille and visual reading. A posterior/anterior vOTC word-form gradient was observed only in sighted readers with more anterior regions preferring larger orthographic units (words). No such gradient was observed in blind readers of Braille. Consistent with connectivity predictions, in blind Braille readers, posterior parietal cortices (PPC) and parieto-occipital areas were recruited to a greater degree and PPC contained word-preferring patches. Lateralization of Braille in blind readers was predicted by laterality of spoken language, as well as by reading hand. These results suggested that the neural basis of reading is influenced by symbol modality and support connectivity-based views of cortical function.

Significance Statement

Is there a universal neural basis for reading among different language and writing systems? The study of tactile Braille reading offers a unique insight into this question. Unlike visual reading, tactile information in Braille reading enters the brain from the somatosensory-motor cortex rather than the visual cortex. Our study found that tactile Braille reading does not show the posterior-to-anterior functional word-form gradient in the ventral occipito-temporal cortex that is observed in sighted readers of visual print. Importantly, we found posterior parietal cortices contain a word-preferring patches, and its lateralization was predicted by laterality of spoken language, suggesting the PPC was recruited to a greater degree in Braille reading. These results provide the first evidence that the neural basis of reading is influenced by symbol modality.

Main Text

Introduction

Written language is among the most impressive human cultural achievements. The capacity to record and transmit information over space and time has enabled the accumulation of scientific, technological, and historical knowledge across generations and continents. How does the human brain accommodate this cultural invention, which emerged only approximately 5,000 years ago?

Despite being a recent cultural invention, the neural basis of reading is highly consistent across a variety of languages and visual scripts, including alphabetic, logographic (e.g., Chinese), and syllabic writing systems (e.g., Japanese Kana) (1–6). All of these reading systems engage regions within the left lateral ventral occipitotemporal cortex (vOTC). A region in the left lateral vOTC has been termed the 'visual word form area' (VWFA) because of its preferential response to written words and letter combinations over other visual stimuli (7–10). The VWFA is situated within a posterior/anterior processing gradient. During reading, visual symbols are first processed by early visual cortices and posterior portions of vOTC, which represent simple visual features (e.g., line junctions) (11, 12). By contrast, the middle and anterior potions of lateral vOTC are specialized for progressively larger orthographic units, from written letters, letter combinations/bigrams, and finally whole words (11, 13, 14).

An open question is whether the vOTC posterior/anterior processing stream is the only way for the brain to implement reading and, relatedly, why the neural basis of reading takes this particular form. Comparing tactile Braille reading among congenitally blind individuals to print reading in sighted people offers unique insights into the causal mechanisms that determine the neural basis of reading. Braille is read by passing the fingers along raised dot patterns, with each Braille character a three-rows-by-two-columns dot matrix (15). This distinctive reading system provides insight into whether and how the sensory modality of symbols influences their neural representations.

A prominent view holds that, past the initial sensory entry points in V1 (print) and S1 (Braille), reading depends on the same vOTC mechanisms for Braille and visual print alike (16–19). In support of this view, several studies report that reading tactile Braille elicits activation in the anatomical location of the 'VWFA' (16, 18–21). In sighted adults who are trained to recognize Braille words, transcranial magnetic stimulation (TMS) to the VWFA disrupts reading accuracy (21, 22).

At the same time, the neural basis of Braille and visual print reading may differ in important ways. Unlike visual print, Braille does not enter the vOTC from V1 and posterior vOTC regions, but rather originates in primary somatosensory cortex (S1). This different entry point is likely to influence the neural processing stream. Previous studies also find that 'visual' cortices, including vOTC, V1 and lateral occipital cortices show enhanced responses to spoken language in people who are born blind and become sensitive to semantic and grammatical information in this population (23–27). Since the neural basis of spoken language influences that of written language, the neural basis of Braille could be affected by this plasticity in the spoken language system (28–30).

The first goal of the current study was to test whether sighted print and blind Braille readers recruit a similar posterior/anterior orthographic gradient within vOTC. To answer this question, we compared responses during Braille (blind) and visual print (sighted) reading of analogous written stimuli of different orthographic richness (words, consonant strings, and unfamiliar shapes (control)). The same participants were also presented with spoken words and backwards speech control stimuli, to enable comparison of written and spoken language processing.

The complementary second goal of the current study was to ask whether Braille uniquely recruits regions outside of the vOTC, closer to somatosensory cortices. In sighted readers, the vOTC is

the culmination of the visual object recognition stream (31). Arguably, an analogous position to the vOTC in blind readers of Braille is occupied by posterior parietal cortices (PPC). The PPC lie adjacent and posterior to early somatosensory cortex (SMC) on the one hand and are connected to language and working memory systems on the other (32–36). The PPC plays a key role in tactile shape and texture perception and higher order tactile processing (37, 38). For example, stronger PPC activity is observed during tactile pattern discrimination compared to vibrotactile detection (38). Whether the PPC of proficient blind Braille readers contains Braille specialization, akin to specialization for visual letters and words found in vOTC of sighted readers, is not known. We tested whether regions in PPC show preferential responses to Braille over non-linguistic but perceptually similar tactile stimuli on the one hand and preferential responses to Braille over spoken language on the other. Moreover, we hypothesized that analogous to the vOTC gradient, word-preferring portions of PPC would likely be found further, and consequently posterior to, primary somatosensory cortices.

Several previous neuroimaging studies have documented PPC activity during Braille reading tasks but have not explored whether these responses are Braille-specific (20, 21, 39–41). Previous studies find that early somatosensory cortices (SMC) show expanded finger representations in proficient Braille readers, but preferences for Braille over matched non-Braille tactile stimuli have not been found in SMC (25, 39, 41–44). We used sensitive, individual subject region of interest (ROI) analyses and winner-take-all gradient maps to probe and compare responses of SMC, PPC as well as the vOTC. Such analysis approaches are particularly relevant in the context of understanding the neural basis of reading, since previous studies find that in sighted readers preferential responses to print in vOTC are ‘islands’ among swaths of cortex that respond to complex visual shapes (45–47).

Finally, we used lateralization patterns to test the hypothesis that neural localization of spoken language influences the localization of Braille, analogous to what is observed in sighted readers of print. In sighted readers, strong connectivity to spoken language networks predicts the localization of reading networks within vOTC and the lateralization of written language follows that of spoken language (28, 30, 48). Reading, like spoken language, is on average strongly left-lateralized in sighted people but those sighted readers whose spoken language responses are localized to the right hemisphere also show right-lateralized written language (49–53). Unlike the strong left-lateralization of spoken language in sighted people, lateralization of spoken language is highly variable across congenitally blind individuals and on average only weakly left-lateralized (26, 54, 55). We predicted that lateralization of Braille would follow that of spoken language across blind individuals. We also tested the effect of reading hand on lateralization and predicted that cortical areas situated at earlier stages of Braille recognition (i.e., S1) would show stronger effects of reading hand, whereas the effect of spoken language laterality would emerge in orthographic and higher-order language regions (PPC, vOTC and inferior frontal cortex).

Results

Behavioral Results

Sighted and blind readers alike were more accurate at remembering more word-like stimuli in both the reading and listening tasks (reading: main effect of lexicality (words and consonant strings > control): $F_{(2, 54)} = 13.963$, $p < 0.001$; listening (words > control): $F_{(1, 29)} = 50.944$, $p < 0.001$). Participants were also faster at responding to word-like stimuli across reading (words and consonant strings < control; $F_{(2, 54)} = 8.09$, $p < 0.001$) and listening tasks (words < control; $F_{(1, 29)} = 50.944$, $p < 0.001$). No other effects were significant (see SI results for details; also see Figure S1).

fMRI Results

Visual (sighted) but not tactile Braille reading (blind) elicits a posterior-to-anterior functional gradient in left vOTC and shows left-lateralization

We divided the left and right vOTC into posterior, middle, and anterior subregions (ROIs) and observed different posterior-to-anterior and lateralization patterns across visual and Braille reading (Figure 1). A four-way hemisphere (left, right) by posterior/anterior subregion (posterior, middle, anterior) by lexicality (words, consonant strings, control) by group (sighted, blind) ANOVA on the reading task revealed a four-way interaction (F (4, 128) = 3.028, p < 0.05), indicating that lexicality, hemisphere, and posterior/anterior subregion interacts with group (see SI for a complete summary of all effects).

As predicted, the sighted group showed the previously documented posterior-to-anterior functional gradient in left but not right vOTC: larger responses to words in anterior vOTC, to consonant strings in middle vOTC and no differences between visual conditions in posterior vOTC (three-way interaction between hemisphere (left, right), posterior/anterior subregion (posterior, middle, anterior) and lexicality (words, consonant strings, control): $F_{(4, 56)} = 4.287$, $p < 0.01$; in left vOTC two-way interaction between lexicality (words, consonant strings, control) and posterior/anterior subregion (posterior, middle, anterior): $F_{(4, 56)} = 9.69$, $p < 0.001$) (see SI for pairwise comparisons within each subregion).

By contrast, no gradient or laterality differences were observed in the blind group. Rather, all subregions of bilateral vOTC responded most to words, followed by consonant strings followed by control shapes (Figure 1) (three-way hemisphere (left, right) by posterior/anterior subregion (posterior, middle, anterior) by lexicality (words, consonant strings, control) ANOVA interaction: $F_{(4, 56)} = 0.877$, $p = 0.482$) (see SI for pairwise comparisons and listening task results). Since prior studies have also identified responses to Braille in V1 of blind readers (57,59), we also examined this region and found a similar functional profile to that observed in vOTC (See SI for details).

The group differences identified by ROI analyses (above) were confirmed by a data-driven topographical preferences winner-take-all map (Figure 1B). In the sighted group, a clear posterior-to-anterior gradient in the left vOTC was observed. The most anterior portion of vOTC showed a preference for words, medial portions of vOTC preferred consonant strings and the most posterior section shows a preference for control (false font) stimuli. Right vOTC of the sighted group showed strongest responses to false fonts throughout. This pattern contrasts starkly with the blind vOTC map, which shows a clear, bilateral preference for words relative to consonant strings and tactile shapes throughout the entire extent of vOTC.

The posterior parietal cortex (PPC) but not S1 of blind readers shows a preference for written Braille words and consonant strings

The PPC response profile differed significantly across blind Braille and sighted print readers (two-way lexicality (words, consonant strings, control) by group (sighted, blind) ANOVA in the reading task, group by lexicality interaction: $F_{(2, 64)} = 5.123$, $p < 0.01$; main effect of lexicality: $F_{(2, 64)} = 13.206$, $p < 0.001$; main effect of group: $F_{(1, 32)} = 1.452$, $p = 0.237$).

In blind readers, regions within PPC responded more to Braille words and Braille consonant strings than control tactile shapes (Bonferroni-corrected paired t-tests, words vs. consonant strings: $t_{(18)} = 1.571$, $p = 0.298$; consonant strings vs. control: $t_{(18)} = 3.028$, $p < 0.01$; words vs. control: $t_{(18)} = 3.165$, $p < 0.01$) (Figure S4). In the sighted group, consonant strings elicited higher responses than words and control stimuli (Bonferroni-corrected paired t-tests, words vs. consonant strings: $t_{(14)} = -3.805$, $p < 0.01$; consonant strings vs. control: $t_{(14)} = 6.922$, $p < 0.001$; words vs. control: $t_{(14)} = 1.406$, $p > 0.99$).

The PPC also showed larger responses to tactile than auditory stimuli in the blind group (two-way modality (tactile, auditory) by lexicality (word, control) ANOVA, main effect of modality: $F_{(1, 18)} = 14.556$, $p < 0.001$; main effect of lexicality: $F_{(1, 18)} = 12.442$, $p < 0.01$; modality by lexicality interaction: $F_{(1, 18)} = 5.529$, $p < 0.05$). Responses to visual and auditory stimuli in the sighted were not different (two-way modality (visual, auditory) by lexicality (word, control) ANOVA, main effect of modality: $F_{(1, 14)} = 3.948$, $p = 0.067$; main effect of lexicality: $F_{(1, 14)} = 3.515$, $p = 0.082$; modality by lexicality interaction: $F_{(1, 14)} = 0.029$, $p = 0.867$). There was a larger response to auditory words than auditory control stimuli in both groups (two-way lexicality (audio words, audio control) by group (sighted, blind) ANOVA**,** main effect of lexicality: words > control, $F_{(1, 32)} = 11.112$, $p < 0.01$; main effect of group: $F_{(1, 32)} = 3.275$, $p = 0.08$; group by lexicality interaction: $F_{(1, 32)} = 2.372$, $p = 0.133$, Figure S4).

In all, the PPC of blind readers preferred tactile over auditory stimuli and among tactile stimuli it preferred Braille words and consonant strings over tactile control stimuli. This pattern is consistent with the hypothesis of Braille specialization in PPC of congenitally blind readers.

A data-driven topographic winner-take-all map revealed that preferential responses to Braille words were concentrated in the most posterior portion of PPC and extended into parieto-occipital and dorsal occipital regions (Figure 2). A small middle region in left and right PPC showed highest responses to consonant strings. The most anterior portions of PPC, immediately adjacent to S1, showed preferential responses to tactile shapes. This pattern is suggestive of an anterior-to-posterior decoding gradient in PPC analogous to the posterior-to-anterior gradient observed in vOTC of sighted print readers.

By contrast to the PPC, early somatosensory cortices (SMC hand region, Figure S4) did not show a preferential response to Braille words and showed the same functional profile across blind and sighted readers (two-way lexicality (words, consonant strings, control) by group (sighted, blind) ANOVA, main effect of lexicality: $F_{(2, 64)} = 7.265$, $p < 0.001$; main effect of group: $F_{(1, 32)} = 0.604$, $p = 0.443$; group by condition interaction: $F_{(2, 64)} = 1.501$, $p = 0.231$). (See SI for details of listening task results.) Likewise, the left IFC, a high-level language region, showed a similarly preferential response to linguistic stimuli (i.e., words) across groups and tasks (reading task, two-way lexicality (words, consonant strings, control) by group (sighted, blind) ANOVA, main effect of lexicality: $F_{(2, 64)} = 46.313$, $p < 0.001$; main effect of group: $F_{(1, 32)} = 0.004$, $p = 0.947$; lexicality by group interaction: $F_{(2, 64)} = 1.017$, $p = 0.367$) (see SI for details). In sum, the PPC and adjacent parieto-occipital cortices showed differential recruitment for Braille reading in people born blind as compared to reading of visual print in sighted people.

Lateralization of Braille correlates with spoken language lateralization and Braille-reading hand

Lateralization index (LI) analysis revealed left-lateralized responses to written and spoken words in vOTC and IFC of sighted readers, consistent with prior studies (one-sample *t* tests of LI = 0, visual print words > rest: vOTC: $t_{(14)} = 5.31$, $p < 0.001$; IFC: $t_{(13)} = 5.776$, $p < 0.001$; spoken words > rest: vOTC: $t_{(14)} = 3.42$, $p < 0.01$; IFC: $t_{(13)} = 3.767$, $p < 0.01$; see SI for other ROIs). By contrast, the blind group did not show systematic left-lateralization in any regions (one-sample *t* tests of LI = 0, Braille words > rest: vOTC: $t_{(18)} = 0.799$, $p = 0.435$; IFC: $t_{(18)} = -0.054$, $p = 0.958$; spoken words > rest: vOTC: $t_{(18)} = 0.322$, $p = 0.751$; IFC: $t_{(18)} = -1.135$, $p = 0.271$; see SI for other regions). There was substantial variability in lateralization of spoken and written language among blind participants, with some participants showing strong left and others strong right lateralization (54) (Figure 3).

Individual difference analysis revealed a strong relationship between the lateralization of spoken and written language in the blind group in all regions except early somatosensory cortex (SMC), including IFC, vOTC and PPC (multiple regression with the LI of spoken words in IFC and dominant reading hand entered as the regressors in each region, for the regressor LI of spoken words, IFC: $t_{(18)} = 6.247$, $p < 0.001$; vOTC: $t_{(18)} = 4.338$, $p < 0.001$; PPC: IFC: $t_{(18)} = 5.376$, $p <$

0.001; SMC: $t_{(18)}$ = 0.146, p = 0.261). Conversely, relative to other regions, the SMC showed a strong effect of reading hand on lateralization (multiple regression, for the regressor dominant reading hand: $t_{(18)}$ = 6.759, $p < 0.001$). The effect of reading hand was also observed in PPC and vOTC but not in the IFC (multiple regression, for the regressor dominant reading hand: PPC $t_{(18)}$ = 5.88, $p < 0.001$; vOTC $t_{(18)}$ = 3.668, $p < 0.01$; IFC $t_{(18)}$ = -0.948, p = 0.359, see SI for details.) Correlations between spoken and written language lateralization were weaker in the sighted group and only reached significance in IFC and PPC (IFC: r = 0.732, $p < 0.01$; PPC: r = 0.55, $p <$ 0.05). This is likely due to low variability of laterality scores in the current sighted sample (i.e., uniformly strong left-lateralization, see SI for details).

Whole cortex analyses

Reading-related activity (relative to rest) was left-lateralized in the sighted and bilateral in the blind group. For reading as compared to rest, both sighted (visual words) and blind (Braille words) readers activated the bilateral vOTC (blind peak: -41, -57, -13; sighted peak: -41, -58, -12), including the location of the classic VWFA (peak: -46, -53, -20), as well as early visual cortices, specifically the foveal confluence (V1/V2/V3) (Figure 4). vOTC responses in the blind group extended medially and anteriorly, as well as into lateral occipito-temporal cortex. Both groups also activated prefrontal cortices (inferior frontal gyrus and middle frontal gyrus). (See Table S2 for complete list of foci.)

Reading Braille in the blind group (relative to rest) extensively activated posterior parietal cortices (superior parietal lobule, supramarginal gyrus (SMG)), posterior to early sensory-motor hand representations. This activity extended into parieto-occipital and dorsal occipital regions in the blind group. The sighted group activated a small cluster within PPC. A lateral temporal region was active in the sighted but not blind group.

Like responses to Braille, responses to spoken words were left-lateralized in the sighted group and bilateral in the blind group. Listening to words (audio words > rest) activated bilateral vOTC (peak: -42, -44, -16), including the location of the classic VWFA, and early 'visual' cortices, in the blind group only. Both groups activated classic fronto-temporal language regions in inferior and prefrontal as well as lateral temporal cortices (Figure 4).

When reading and listening to words was compared directly, for the sighted group, reading induced greater activation in bilateral vOTC, including the typical location of the VWFA and regions posterior to it, as well as bilateral early visual cortices. The blind group also activated a region in left vOTC (fusiform; peak: -27, -61, -14), but this activation was medial to the typical VWFA location. A cluster of activity was also observed lateral to the typical VWFA location in the blind group, in the inferior temporal/lateral occipital cortex (peak: -45 -67 -6) as well as in left foveal early 'visual' cortices.

The blind but not sighted group showed extensive activation for Braille words > spoken words in PPC, including the SMG and superior parietal lobule, extending into dorsal occipital/parieto-occipital cortices.

In sum, although both groups activated vOTC during reading, the peak location, distribution and functional profile of responses in vOTC were distinct across groups. The blind group activated more extensive posterior parietal, parieto-occipital, and dorsal occipital areas during reading (Braille).

Discussion

vOTC of sighted but not blind readers contains a hierarchical word form gradient

Consistent with past research, we observed a posterior-to-anterior functional gradient, with highest responses to words anteriorly, in left vOTC of sighted readers (7, 56–58). By contrast, in the vOTC of blind readers we found no evidence for left-lateralization, no evidence for a posterior-

to-anterior functional gradient, or posterior/anterior change in modality preference. The entire posterior/anterior extent of bilateral vOTC, as well as V1, showed a preference for words (23, 25, 59). There was also no change in preference for written as opposed to spoken words along the posterior/anterior extent of vOTC in blind readers. There thus appears to be no orthographic gradient in vOTC of blind Braille readers.

Whole-cortex analysis also revealed partially different reading responses in vOTC across blind and sighted people. When Braille and spoken words were each compared to rest, a peak of activation was observed in the classic VWFA location. However, when reading words was compared to hearing words, activity peaked medial to the VWFA in the blind but not sighted group (peak: -27, -61, -14). A similar medial vOTC region was recently found to be functionally connected with dorsal parietal cortices in sighted people (57, 60–63). Previous studies have also found that in people who are blind, the classic lateral VWFA location is sensitive to syntactic complexity of spoken sentences, shows enhanced responses to spoken language and enhanced connectivity with fronto-temporal language networks (20, 64–67). An intriguing possibility to be tested in future work, is that medial vOTC is responsive to Braille-specific input from PPC, whereas the classic, more later VWFA location, is driven by linguistic information from fronto-temporal networks.

Parieto-occipital decoding stream in blind readers of Braille

We observed more extensive and different involvement of posterior parietal/parieto-occipital cortices in Braille as opposed to visual print reading. In blind readers, posterior PPC and parieto-occipital areas responded preferentially to Braille words relative to both tactile shapes and spoken words. In contrast, anterior regions of PPC, adjacent to S1, responded most to unfamiliar tactile shapes comprised of Braille dots. The hand regions of S1 itself did not show robust or preferential responses to Braille (25, 39). Based on this response profile, we hypothesize that PPC and adjacent parieto-occipital areas contain a Braille reading processing stream, with anterior regions supporting recognition of tactile patterns that constitute Braille and posterior regions performing Braille-specific, orthographic processing.

Further work is needed to uncover the precise contribution of PPC and parieto-occipital cortices to Braille reading. In sighted readers, the PPC shows sensitivity to phonological rather than orthographic information, during visual reading, and is involved in effortful letter-by-letter reading (e.g., when words are degraded) (61, 62, 68–76). Future work should closely compare the contributions of posterior PPC to visual print and Braille reading and determine the degree to which PPC of blind readers responds to orthographic information.

Lateralization of Braille reading: effects of spoken language lateralization and reading hand

Laterality of responses to written words throughout the entire reading network were predicted by the laterality of spoken language across blind individuals. In other words, those blind individuals who show right-lateralized responses to spoken words also show right-lateralized responses to written words. The only region which did not show this pattern was early somatosensory cortex, where laterality was predicted only by reading hand. Previous studies with sighted readers with right hemisphere spoken language responses have likewise observed co-lateralization of spoken and written language (49, 53). All sighted readers in the current study had strongly left-lateralized responses to spoken language and we did not observe a strong relationship between laterality of spoken and written language, likely due to reduced variability. Together with prior evidence, our data suggest that written and spoken language co-lateralize regardless of reading modality. This observation is consistent with the hypothesis that strong connectivity and proximity to spoken language networks is one of the determining factors of which regions become ‘recycled’ for reading (28, 30, 45).

In contrast to the effect of spoken language on laterality, the effect of reading hand was strongest at early stages of processing (in the primary somatosensory cortex), weaker at intermediate stages (in PPC and vOTC), and absent in a high-level language region (IFC). These laterality effects support the view that PPC and vOTC participate in reading related processes in blindness, rather than solely sensory recognition or high-level language processing.

An analogous connectivity principle appears to govern lateralization of reading in sighted and blind readers: lateralization depends jointly on connectivity to sensory input regions (unilateral S1/ bilateral V1) and language networks.

General conclusions

The neural basis of tactile Braille and visual print reading is governed by analogous principles but has distinct anatomical profiles. While visual print reading recruits a posterior/anterior vOTC gradient, no such gradient is observed in the vOTC of blind readers of Braille. Blind readers of Braille recruit posterior parietal cortices to a greater degree and in a different way compared to visual print reading in sighted people. Only blind readers show preferential responses to written words in PPC and parieto-occipital cortex. We observed suggestive evidence for an anterior-to-posterior stream of processing in the parietal cortex of blind Braille readers, with anterior parietal areas responsive to non-Braille tactile patterns and more posterior parietal, parieto-occipital and dorsal occipital regions responsive to Braille words. In blind and sighted readers alike, lateralization of spoken language predicts lateralization of written language, although Braille is not strongly left-lateralized in people born blind and reading hand also affects lateralization.

The present results suggest that the neural basis of reading is influenced by the sensory modality of reading symbols and the neural basis of spoken language. The findings are thus consistent with connectivity-based theories of cortical specialization, where the neural basis of a cognitive domain (e.g., reading) is determined in part by the neural basis of the input and output systems with which it communicates.

Method

Participants

Nineteen congenitally blind (12 females, mean age = 40.36 years, SD = 14.82) and 15 sighted controls (9 females, mean age = 23 years, SD = 6) participated (Table S1). The data from 10 blind and 15 sighted participants have been reported previously (66). All participants were native English speakers, and none had suffered from any known cognitive or neurological disabilities (screened through self-report). Blind participants had at most minimal light perception from birth. Blindness was caused by pathology anterior to the optic chiasm (i.e., not due to brain damage). All blind participants were fluent, frequent Braille readers who began learning Braille at an average age of 4.6 years (SD = 1.49) and rated their reading ability as proficient to expert (mean = 4.57, SD =0.69 on a scale of 1 to 5). We obtained information on Braille-reading hand dominance through a post-experimental survey conducted over the telephone with 17 of the 19 blind adult participants (Table S1). All participants gave informed consent according to procedures approved by the Johns Hopkins Institutional Review Board.

Stimuli and experimental procedures

The fMRI task included three reading conditions: words, consonant strings, and non-letter shapes (Figure 1) and two listening conditions: words, backwards speech. Reading stimuli were visual for sighted participants and tactile for blind participants. Braille words were written in Grade-II contracted English Braille, which is the most common form of Braille in the United States. The visual words were matched to the Braille words on average character length. Each consonant string stimulus consisted of 4 visual/Braille consonants. The tactile control stimuli consisted of 24 unique strings of 4 non-letter shapes made of raised Braille dots. To prevent participants from processing the shapes as Braille letters, the shapes varied in size and pin number within arrays

ranging in size from 4 × 5 to 7 × 7. The visual control stimuli were 24 unique strings, each comprised of 4 characters, which were false fonts. The auditory words were recorded by a female native English speaker. The average word length was 5 letters long (SD = 1.4 letters) and the average playtime was 0.41 s (SD = 0.3 s). The control auditory stimuli comprised backward speech sounds created by playing each audio word in reverse.

On each trial, participants were presented with 6 stimuli from a single condition (e.g., Braille words) followed by a memory probe. Participants judged whether that probe had appeared among the previous 6 stimuli. The experiment had a total of 5 runs, each with 20 trials. The blind participants were asked to read with their dominant hand and responded with the other hand. Each condition was repeated 4 times per run, and the order of conditions was counterbalanced across runs. There were 6 rest periods (16 s) throughout each run. One sighted participant and two blind participants were excluded from behavioral analysis due to failure to record their responses (see SI for details)(66).

fMRI data acquisition

Functional and structural images were acquired using a 3T Phillips scanner at the F. M. Kirby Research Center. T1-weighted images were collected using a magnetization-prepared rapid gradient-echo (MP-RAGE) in 150 axial slices with 1 mm isotropic voxels. Functional BOLD scans were collected T1-weighted structural images were collected in 150 axial slices with 1 mm isotropic voxels. Functional BOLD scans were collected in 36 sequential ascending axial slices. TR = 2 s, TE = 30 ms, flip angle = 70°, voxel size = 2.4 × 2.4 × 2.5 mm, inter-slice gap = 0.5 mm, field of view (FOV) = 192 × 172.8 × 107.5.

fMRI data analysis

Preprocessing and whole-cortex analysis

Analyses were performed using FSL (version 5.0.9), FreeSurfer (version 5.3.0), the Human Connectome Project workbench (version 1.2.0), and custom in-house software. The cortical surface was created for each participant using the standard FreeSurfer pipeline (77–79). For task data, preprocessing of functional data included motion-correction, high-pass filtering (128 s cut-off), and resampling to the cortical surface. Cerebellar and subcortical structures were excluded. On the surface, the task data were smoothed with a 6 mm FWHM Gaussian kernel.

Three conditions of the reading task and two conditions of the listening task were included in a general linear model. Analysis focused on the time-period during the initial six stimuli of each trial. Probe stimulus and response periods were modeled separately and are not reported. White matter signal, CSF signal, as well as motion spikes, were included as the covariates of no interest.

Whole-cortex random-effects analysis were run using mixed-effects and thresholded at $p < 0.01$ vertex-wise, and $p < 0.05$ cluster-wise, Family Wise Error corrected for multiple comparisons across the cortex.

fMRI ROI analysis

We examined five regions of interest: vOTC, V1, inferior frontal cortex (IFC), and posterior parietal cortex (PPC), and the hand region of the left primary somatosensory-motor cortex (SMC) (see SI for the search space construction details). Individual-subject functional ROIs were defined within each of the above search spaces using a leave-one-run-out cross-validation procedure to avoid double-dipping. Each individual subject's ROI was defined as the top 5% of vertices activated for tactile/visual consonant strings > tactile/visual shapes. Consonant string contrasts were used for the primary analysis to focus on orthographic as opposed to semantic responses. Words > control contrasts are reported in the supplementary materials (Figure S3 and Figure S5).

Repeated-measured ANOVAs were used to analyze the ROI data, and two-tailed paired *t*-tests were used for pairwise comparisons. All *p* values were Bonferroni-corrected (see SI for details).

Topographical preference map

To examine topographic gradients in a data-driven way, we used a winner-take-all approach. Within bilateral vOTC and PPC masks, each vertex was color-coded according to which stimulus condition showed highest activity. We also divided the PPC mask into 13 segments centered along an equal distanced spline and plotted average activity for three tactile conditions in each segment (see SI for details).

Laterality index analysis

LI was calculated separately for the reading and listening tasks for each participant in the SMC, PPC, vOTC, and IFC. For the reading task, LI was determined based on the tactile/visual words > rest contrast. For the listening task, LI was determined using the audio words > rest contrast. The LI was calculated using the standard formula: (L - R) / (L + R), where L and R refer to the sums of the *z* statistics from the relevant contrast within the left and right hemispheres, respectively. LI ranges from -1 to 1, with a score of 1 indicating strong left lateralization and -1 strong right lateralization. The bootstrap/histogram method was used to ensure that LIs were not overly influenced by arbitrary threshold choice or outlier voxels. Participants were excluded from the LI analysis if they did not have suprathreshold activation in both hemispheres (see SI for details).

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Figures and Tables

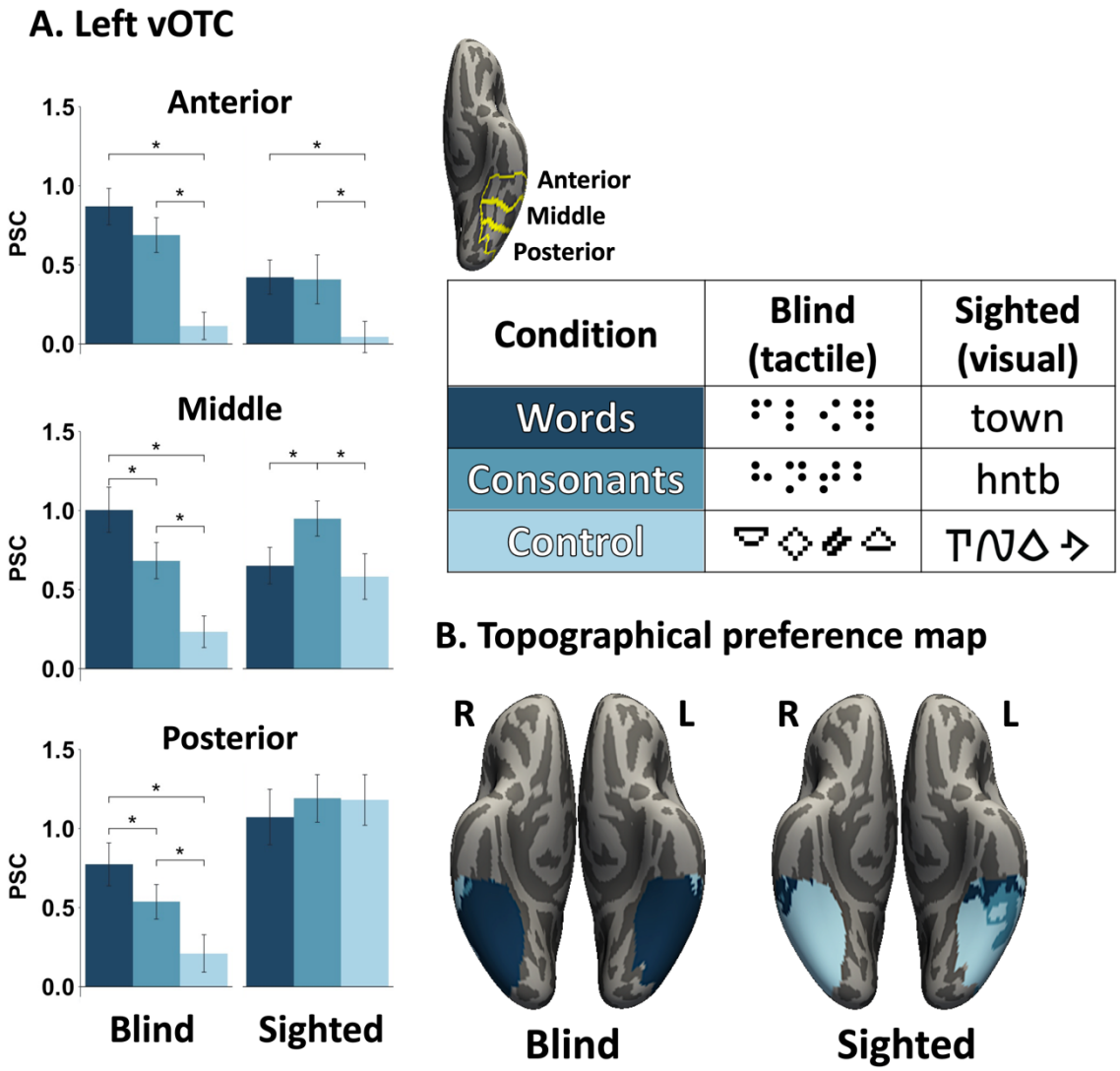

Figure 1. (A) Responses in left vOTC across the posterior, middle, and anterior subregions for blind and sighted groups during the reading tasks. Bars show results from consonant string > control leave-one-run out individual subject ROI analysis. Error bars denote standard errors +/- the mean. Asterisks (*) denote significant Bonferroni-corrected pairwise comparisons ($p < 0.05$). (B) Topographical preference maps of vOTC during the reading task: words, consonant strings, control stimuli.

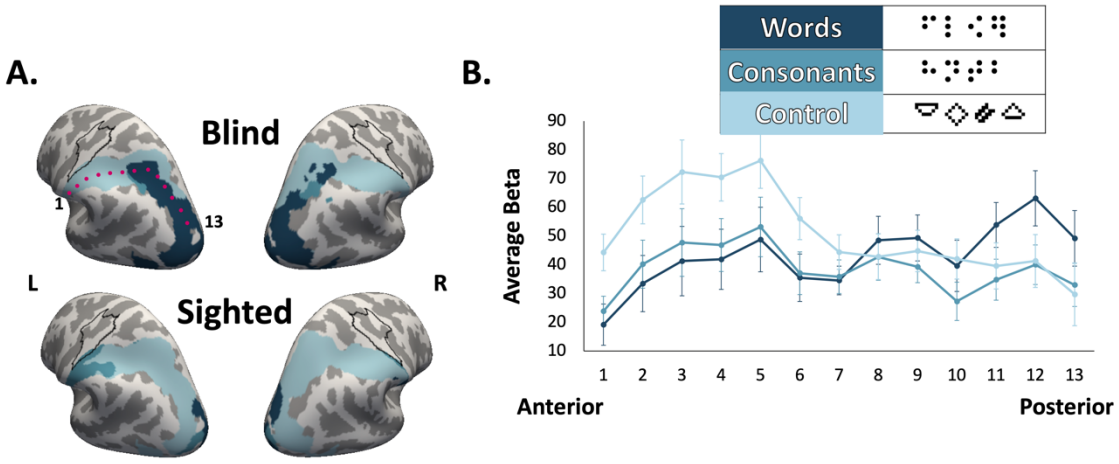

Figure 2. (A) Posterior parietal cortex (PPC) winner-take-all map during the reading task: words, consonant strings, and control stimuli. Black outline indicates hand region of the primary sensory-motor cortex (Neurosynth). (B) Mean response to each reading condition along left anterior/posterior PPC extent in blind group (13 segments). Segment centers are marked by red dots in panel A (see SI for details, also see Figure S6 for right PPC).

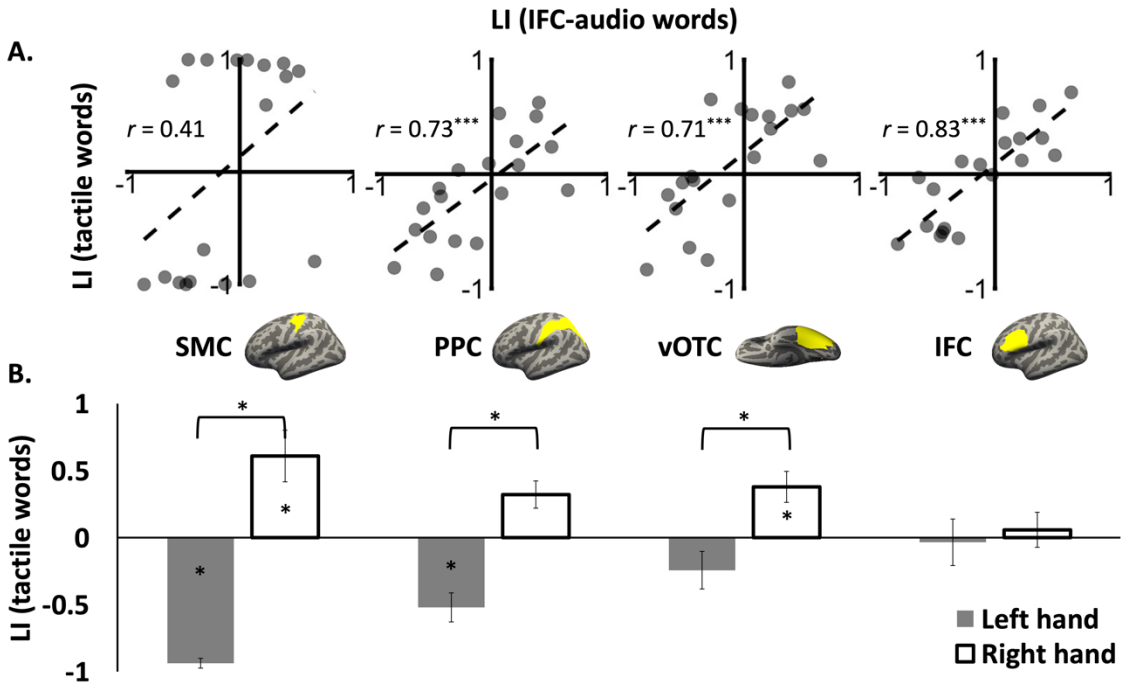

Figure 3. (A) Correlations between the Laterality Index (LI) of audio words in IFC and the LI of tactile words in SMC, PPC, vOTC in blind Braille readers. Data points represent individual participants. LI 1 score indicates strong left lateralization and -1 indicates strong right lateralization. (B) LI of Braille reading with left (grey) and right (white) hand separately. Asterisks (*) on the bar denotes significant difference from 0; asterisks (*) between two bars denote significant difference between the LI of left- vs. right-hand reading (p <0.05).

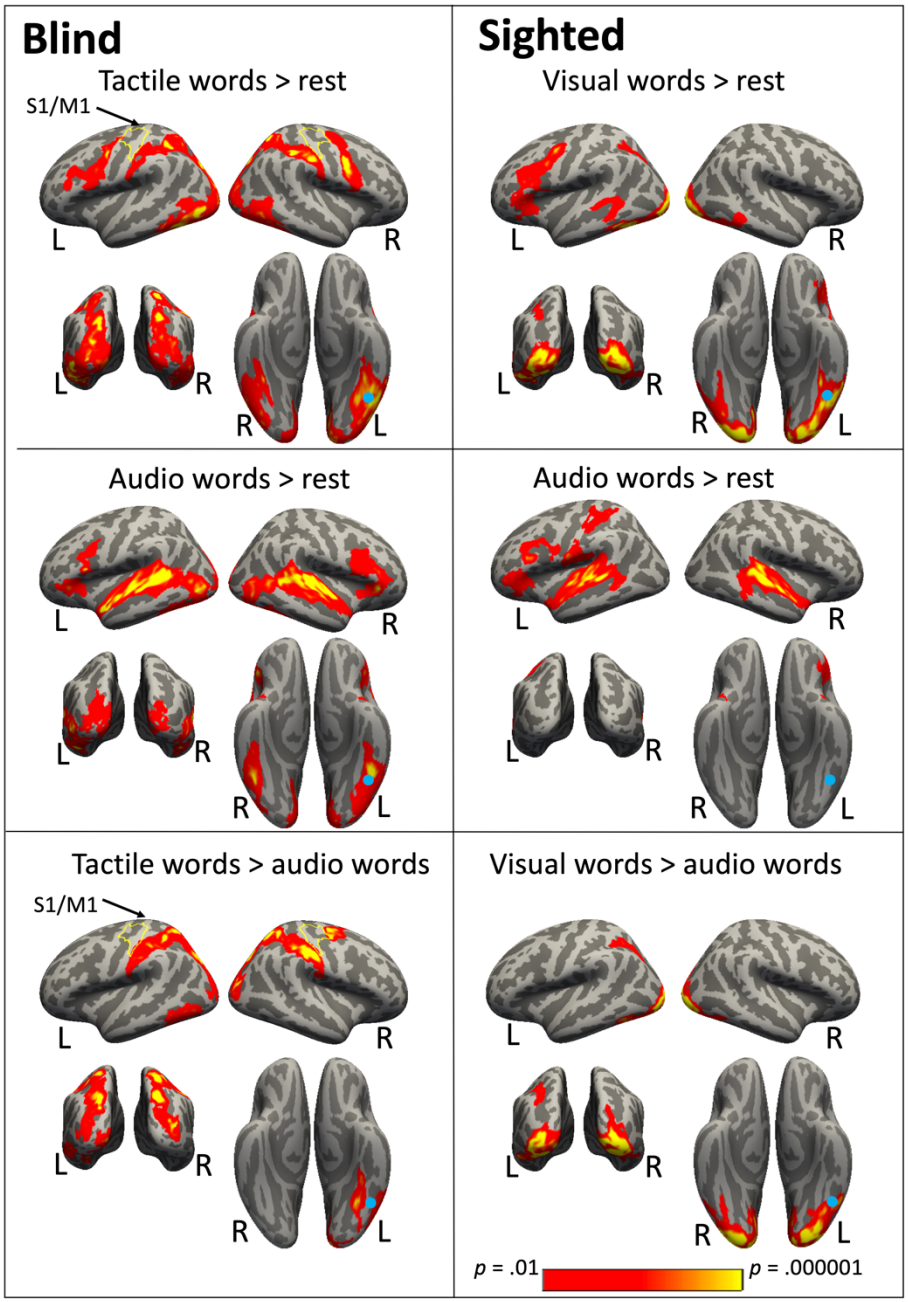

Figure 4. Whole-cortex results for blind (left column) and sighted (right column) $p < 0.05$ cluster-corrected. Blue circles mark previously reported location of VWFA (MNI coordinate: -46, -53, -20) (9). The yellow outline marks the hand S1/M1 region.