

Reading Without Speech Sounds: VWFA and its Connectivity in the Congenitally Deaf

Xiaosha Wang^{1,2}, Alfonso Caramazza^{3,4}, Marius V. Peelen⁴, Zaizhu Han^{1,2} and Yanchao Bi^{1,2}

¹State Key Laboratory of Cognitive Neuroscience and Learning & IDG/McGovern Institute for Brain Research, ²Center for Collaboration and Innovation in Brain and Learning Sciences, Beijing Normal University, Beijing 100875, China, ³Department of Psychology, Harvard University, Cambridge, MA 02138, USA and ⁴Center for Mind/Brain Sciences, University of Trento, 38068 Rovereto, Italy

Address correspondence to Yanchao Bi, State Key Laboratory of Cognitive Neuroscience and Learning & IDG/McGovern Institute for Brain Research, Center for Collaboration and Innovation in Brain and Learning Sciences, Beijing Normal University, Beijing 100875, China.
Email: ybi@bnu.edu.cn

The placement and development of the visual word form area (VWFA) have commonly been assumed to depend, in part, on its connections with language regions. In this study, we specifically examined the effects of auditory speech experience deprivation in shaping the VWFA by investigating its location distribution, activation strength, and functional connectivity pattern in congenitally deaf participants. We found that the location and activation strength of the VWFA in congenitally deaf participants were highly comparable with those of hearing controls. Furthermore, while the congenitally deaf group showed reduced resting-state functional connectivity between the VWFA and the auditory speech area in the left anterior superior temporal gyrus, its intrinsic functional connectivity pattern between the VWFA and a fronto-parietal network was similar to that of hearing controls. Taken together, these results suggest that auditory speech experience has consequences for aspects of the word form-speech sound correspondence network, but that such experience does not significantly modulate the VWFA's placement or response strength. This is consistent with the view that the role of the VWFA might be to provide a representation that is suitable for mapping visual word forms onto language-specific gestures without the need to construct an aural representation.

Keywords: auditory speech experience, congenitally deaf, functional connectivity, resting state, visual word form area

Introduction

Reading is assumed to involve multiple routes of processes, including one that maps parts of the visually computed letter/character representations onto phonological representations and one that can access word meanings and whole-word phonological representations directly (e.g., Coltheart et al. 2001). One fundamental step in these processes is the computation of the visual word representation that serves as input for subsequent language processes.

A brain region that is commonly hypothesized to be crucial for computing the visual word representation lies in the left ventral occipitotemporal cortex (vOTC; McCandliss et al. 2003; Dehaene et al. 2010; Dehaene and Cohen 2011). This region has been shown to be consistently activated by written words with remarkable anatomical reproducibility across individuals (Cohen et al. 2002) and writing systems (Bolger et al. 2005; Liu et al. 2008; Nakamura et al. 2012), and is often dubbed the visual word form area (VWFA; Cohen et al. 2000; Dehaene and Cohen 2011).

A major debate about the origin of the VWFA is the role of higher-order language regions (Dehaene and Cohen 2011;

Price and Devlin 2011). One notion is that connections with language regions are necessary for VWFA selectivity, which might arise from the synthesis of bottom-up input with top-down predictions from language regions (Price and Devlin 2011). An alternative view posits that connections with the language system contribute only during reading acquisition, such that the anatomical localization of the VWFA might be influenced by projections to higher-order language regions, but that once the VWFA neurons have been tuned to the shape properties of scripts (i.e., words learned), the top-down feedback becomes optional (Dehaene and Cohen 2011; Szwed et al. 2012). Several recent studies have shed new light on this debate. Notably, Grainger et al. (2012) showed that baboons can be successfully trained to distinguish real words from nonwords, suggesting that the distinct properties of visual words may be appreciated without prior linguistic experience. Furthermore, symbol learning in nonhuman primates has been associated with neural changes in the vOTC (Srihasam et al. 2012). On the other hand, congenitally blind readers show VWFA activity that is highly similar to that of the sighted, with both tactile input (Braille reading) (Buchel et al. 1998; Reich et al. 2011) and auditory input (sounds produced by a sensory substitution device) (Striem-Amit et al. 2012), indicating that the VWFA may be sensitive to abstract properties of word forms that could be accessed through nonvisual modalities.

Despite these differences, both accounts assume some kind of contribution of the connections of the VWFA to the language system in shaping its functions. Several recent studies have empirically examined the connectivity pattern of the VWFA. Vogel et al. (2012) showed that, in the resting state, the VWFA is functionally synchronized with bilateral intraparietal sulci and frontal regions. Additionally, structural connections have been observed between VWFA and regions of the anterior temporal lobe, frontal lobe, and lateral occipital-parietal cortex via the inferior longitudinal fasciculus, the inferior frontal occipital fasciculus, and the vertical occipital fasciculus, respectively (Yeatman et al. 2013). While these findings are largely consistent with the hypothesis that VWFA is structurally and functionally connected with language networks in frontal and parietal regions, it is critical to test the functions of these connections by examining how the connectivity patterns are related to various types of experience.

Congenitally deaf individuals provide a unique opportunity to examine the effects of auditory speech experience—a fundamental component in language development—in shaping the regional and connectivity profile of the VWFA. Spoken language far precedes written language at both the species and

individual levels. Learning to read critically involves the mapping between visual and (input and/or output) spoken word forms, which come to influence one another interactively following extensive training (Seidenberg and McClelland 1989). Therefore, speech sounds have been the primary candidate among many language components assumed to provide top-down constraints to the VWFA (Dehaene and Cohen 2011; Price and Devlin 2011; Mano et al. 2013). Theoretically, examining the effects of auditory speech experience deprivation on the VWFA allows testing a major question regarding the origin of the region, that is, whether or not the VWFA can be shaped without normal auditory exposure to spoken language. Previous studies have reported the activation of the left vOTC by visual word stimuli in congenitally deaf subjects (Aparicio et al. 2007; Waters et al. 2007; Emmorey et al. 2013). However, these studies did not systematically compare the location distribution, activation strength, and functional connectivity of VWFA in deaf and hearing participants.

The current study examined whether the lack of auditory speech experience leads to noticeable differences in the VWFA either in terms of activation or placement, and whether any potential difference is coupled with changes in the VWFA's functional connectivity pattern with other language areas.

Materials and Methods

Participants

Fifteen congenitally deaf signers (2 males) and 16 hearing subjects (2 males) participated in the study. All subjects were right-handed, except for one deaf subject who was ambidextrous, and all had normal or corrected-to-normal vision. For the task-based functional magnetic resonance imaging (fMRI) data analysis, one deaf and two hearing subjects were excluded due to excessive head movement (>3 mm or 3°), leaving 14 deaf and 14 hearing subjects. For the resting-state fMRI scan, 1 deaf and 2 hearing subjects were discarded due to excessive head motion and 1 deaf participant due to failure in normalization, leaving 13 deaf and 14 hearing subjects. Deaf subjects (mean age = 20.43 years; range: 17–22 years) were undergraduate students studying at the Special Education College of Beijing Union University. They were given a questionnaire about their hearing loss and language (sign and speech articulation) use. All reported that they were born profoundly deaf with a hearing loss of >90 dB. All attended specialized schools for the deaf at around age 6–8. In school, they communicated with each other primarily by sign language and at home with their parents by writing and/or signing. Their speech articulation ability was at floor—they could at most speak simple words with poor intelligibility. Three had deaf, signing parents. Hearing subjects (mean age = 20.07 years; range: 18–22 years), all native Chinese speakers, were undergraduate students from Beijing Normal University. Congenitally deaf and hearing subjects were matched on age ($t_{27} = 0.73$, $P = 0.48$). The experiments were approved by the Institutional Review Board of the State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University. All subjects gave their informed consent and were paid for their participation.

Eleven of the deaf subjects and 10 of the hearing subjects also participated in a series of behavioral tasks, including 1 numeric and 7 written-language judgment tests that assess skills involved in processing orthographic, phonological, semantic, and grammatical aspects of written words. Table 1 summarizes the performance (accuracy) of the 2 groups in each task. While there was no significant difference between the 2 subject groups in the number judgment test ($t_{19} = 1.25$, $P = 0.23$), deaf subjects showed significantly poorer performance in most of the language tests ($P_s < 0.028$), except for character-level lexical decision and phoneme detection. These results indicate that the deaf subjects in our study exhibited a lower reading level than hearing subjects.

Table 1

Group comparison of hearing and deaf readers for accuracies in a series of behavioral tests (mean \pm SD)^a

Task (item number)	Hearing	Congenitally deaf	T-value	P-value
Character lexical decision ($N = 120$)	0.94 \pm 0.03	0.91 \pm 0.05	1.27	0.218
Phoneme detection ($N = 60$)	0.97 \pm 0.03	0.96 \pm 0.05	0.59	0.563
Rhyme judgment ($N = 60$)	0.95 \pm 0.02	0.85 \pm 0.10	2.92	0.009
Word lexical decision ($N = 70$)	0.95 \pm 0.04	0.88 \pm 0.08	2.63	0.017
Word semantic associative matching ($N = 147$)	0.93 \pm 0.03	0.87 \pm 0.07	2.37	0.028
Sentence acceptability judgment ($N = 100$)	0.93 \pm 0.09	0.81 \pm 0.09	3.83	0.001
Sentence synonymy judgment ($N = 52$)	0.88 \pm 0.04	0.76 \pm 0.12	2.83	0.011
Sentence-picture matching ($N = 76$)	0.95 \pm 0.03	0.89 \pm 0.07	2.67	0.015
Number judgment ($N = 50$)	0.95 \pm 0.03	0.93 \pm 0.05	1.25	0.226

^aBased on data from 11 deaf and 10 hearing participants.

Stimuli and Experimental Protocol

A reading task was used to functionally localize the VWFA in hearing and congenitally deaf subjects. Word stimuli consisted of 40 two-character nouns denoting 4 semantic categories: common places, tools, face parts, and body parts. These words covered a wide range of word frequency (1–241 per 1.8 million, mean log word frequency = 0.89) (Sun et al. 1997) and visual complexity (6–26 strokes and 3–10 logogramemes per word). They were presented with font SONG and subtended approximately $6.18^\circ \times 2.57^\circ$ of visual angle. Participants were asked to perform a one-back object size judgment task, that is, to press a button with their right index finger when the object denoted by the current word was larger than the previous one. Each trial consisted of a 1200-ms fixation period followed by the word stimulus presented for 800 ms. Subjects received 2 fMRI sequences, each comprising sixteen 20-s experimental blocks (4 per category). A 20-s fixation block followed every 4 experimental blocks. The order of categories was counterbalanced within and across runs.

Imaging Data Acquisition

Images were acquired using a Siemens TRIO 3-T scanner at the Imaging Center for Brain Research, Beijing Normal University. The participants lay supine with their heads snugly fixed with straps and foam pads to minimize head movement. Acquired before task sessions, the resting-state functional imaging data were comprised of 200 continuous echo-planar imaging (EPI) whole-brain functional volumes [32 axial slices; 4 mm thickness; repetition time (TR) = 2000 ms; echo time (TE) = 33 ms; flip angle (FA) = 73° ; matrix size = 64×64 ; field of view (FOV) = 200×200 mm; voxel size = $3.125 \times 3.125 \times 4$ mm]. During resting-state fMRI scanning, participants were instructed to close their eyes, keep still, and not think about anything systematically or fall asleep. Functional images for the task fMRI experiment were obtained using an EPI sequence with the following parameters: 33 axial slices; 4 mm thickness; TR = 2000 ms; TE = 30 ms; FA = 90° ; matrix size = 64×64 ; FOV = 200×200 mm; voxel size = $3.125 \times 3.125 \times 4$ mm. In addition, a high-resolution, T_1 -weighted sagittal three-dimensional magnetization-prepared rapid gradient-echo sequence was acquired: 144 slices; 1.33 mm thickness; TR = 2530 ms; TE = 3.39 ms; inversion time = 1100 ms; FA = 7° ; FOV = 256×256 mm; voxel size = $1.0 \times 1.0 \times 1.33$ mm; matrix size = 256×256 .

Task fMRI Data Preprocessing and Analysis

Task fMRI data preprocessing and analyses were performed with the SPM8 software (Wellcome Department of Cognitive Neurology, London, UK). The first 5 volumes were discarded to eliminate the nonequilibrium effects of magnetization. Functional scans were corrected for head motion, normalized to the Montreal Neurological Institute (MNI) space using T_1 image unified segmentation (the resampling voxel size was $3 \times 3 \times 3$ mm), and smoothed with a 6-mm full-width at half maximum Gaussian kernel.

For the first-level analysis, 2 general linear models (GLMs) were built separately, with the first focusing on word activation and the

second on the effects of semantic category. Functional images were modeled with 1 regressor, words, in the first GLM and 4 regressors, one for each category, in the second GLM, convolved with the canonical SPM hemodynamic response function. The high-pass filter was set at 128 s. After model estimation, individual beta-weight images were produced for the contrasts of all written words or words of each category versus baseline for subsequent analyses.

For word activation, one-sample *t*-tests were performed on individual beta-weight images within hearing and congenitally deaf groups, respectively. Activation maps were thresholded at voxelwise $P < 10^{-5}$, cluster-level $P < 0.05$, family-wise error (FWE) corrected across the brain volume. Clusters with a minimum cluster size of 10 voxels (270 mm³) were reported to further eliminate too small clusters. Significant clusters were referred to as “word-responsive” regions hereafter. We also directly compared activation maps in the 2 subject groups to further explore possible group differences. The group contrast was performed within areas showing greater activation for words in either group. The resulting contrast map was thresholded at voxelwise $P < 0.001$, FWE-corrected cluster-level $P < 0.05$. This threshold was used for all following analyses, unless otherwise indicated.

The peak coordinate in the left vOTC identified in each group was taken as the VWFA. The activation strength in the VWFA of each group was compared between the 2 subject groups. Mean beta values were extracted from a sphere of 6 mm radius centering on the VWFA coordinate of each group for the word versus baseline contrast and then compared using a two-sample *t*-test.

Moreover, semantic category effects were evaluated in the VWFA to demonstrate whether word-evoked responses in this area were driven by any specific categories. Mean beta values for the contrasts of words in each category versus baseline were extracted and compared using analysis of variance (ANOVA) with Category as the within-subject factor and Group as the between-subject factor.

The anatomical consistency of word-evoked activations in the left vOTC in hearing and congenitally deaf groups was evaluated on both group and individual-subject levels. First, individual statistical parametric maps for the word versus baseline contrast obtained from the first-level analysis were thresholded at voxelwise $P < 10^{-5}$, FWE-corrected cluster-level $P < 0.05$, cluster size ≥ 10 voxels. For the group analysis, these individual maps were binarized and overlaid for each group. This created a map illustrating for each voxel the overlap across subjects for visual word activation. For the individual analysis, we created a mask encompassing left inferior occipital gyrus, left fusiform gyrus, and left inferior temporal gyrus based on the Automated Anatomical Labeling template (Tzourio-Mazoyer et al. 2002). Within this mask, the word versus baseline contrast typically resulted in multiple subpeaks, at least 4 mm apart, ranging from posterior occipital regions to anterior vOTC. We followed the conventional approach of defining individual VWFA (Cohen et al. 2004; Glezer et al. 2009; Reich et al. 2011) by selecting for each subject the subpeak closest to the VWFA coordinate of each group. In ambiguous cases, where 2 or more subpeaks had the same distance, the one with the highest *t*-score was reported. We then computed, for a given individual VWFA, its Euclidean distances to the averaged VWFA coordinates of its own group (within-group distance, e.g., deaf–deaf) and the other group (between-group distance, e.g., deaf–hearing). To avoid circularity, the given individual participant was not included in the within-group average VWFA coordinate computation. These distances were compared using ANOVA with Distance as the within-subject factor and Group as the between-subject factor. The same analysis was also performed on the distance for each axis (*x*, *y*, *z*) separately.

Comparing VWFA Localization Contrasts

The VWFA has been localized using various types of contrasts in the literature, and it has been shown that lenient contrasts produce virtually identical locations as more stringent contrasts [e.g., contrasting words to fixation and to checkerboard (see Cohen et al. 2003); contrasting words to checkerboard and to phase-scrambled words (see Rauschecker et al. 2011)]. In an additional fMRI experiment, involving an independent group of hearing subjects (10 females; mean age = 20.7 years; range: 18–24 years, right-handed), we confirmed this to be the case (see Results). This group was tested with a more stringent

contrast, that is, contrasting real Chinese characters versus phase-scrambled ones. Ninety-six single Chinese character nouns (SONG font, visual angle: 3.57°) that have high frequency (no less than 100 per 1.8 million) and 7–15 strokes were used as real characters. Fully phase-scrambled characters were then created from this set of characters. Participants were asked to passively view all the stimuli. Two fMRI sequences were given, each comprising sixteen 12-s experimental blocks of characters or phase-scrambled characters alternated with 6-s blocks of fixation. Each block comprised 24 unique trials, consisting of a 200-ms presentation of real or phase-scrambled characters followed by a 300-ms fixation period. The order of stimuli within the real-character blocks was pseudorandomized such that consecutive trials were not orthographically or phonologically similar. Scanning parameters and data preprocessing procedures were the same as the main experiment.

Resting-State fMRI Data Preprocessing and Analysis

The resting-state functional connectivity (RSFC) analysis was performed using the Resting-State fMRI Data Analysis Toolkit (Song et al. 2011). Resting-state functional images were preprocessed using the same procedure as those used for the task-based fMRI data except for the following: (1) The first 10 volumes were discarded; (2) slice-timing correction was performed before head motion correction; (3) after spatial smoothing, the linear trend of the time courses was removed and a band-pass filter (0.01–0.1 Hz) was applied to reduce low-frequency drift and high-frequency noise; and (4) 9 nuisance covariates were regressed out to control for physiological effects and head motion (6 head motion parameters and 3 regressors corresponding to the whole brain, white matter, and cerebrospinal fluid signal).

The mean VWFA coordinate defined by averaging the individual VWFA coordinates from 2 groups (MNI *x*, *y*, *z*: –46, –53, –12) was used as the seed for the RSFC analysis. A spherical region of interest was created centering on this coordinate with a radius of 6 mm. To obtain the whole-brain seed-to-voxel RSFC patterns of the VWFA, we computed the mean time series of the seed region by averaging the time series of all the voxels in it, and then correlated this against the time series of every other voxel in the brain so as to produce an RSFC *r*-map for each subject. These *r*-maps were then converted into *z*-maps using Fisher's *r*-to-*z* transformation. A one-sample *t*-test was computed on individual RSFC *z*-maps to generate VWFA RSFC maps for each group separately. We only presented and discussed the positive RSFCs, given that negative correlations could result from the removal of global signal and their implications remain controversial (Fox et al. 2009; Murphy et al. 2009).

We also carried out the VWFA RSFC analyses without regressing out the global signal. To further quantify the reproducibility of VWFA RSFC patterns, for each group we generated the group-averaged VWFA RSFC maps with or without removing global signal. We then calculated Pearson correlation of these maps, within a mask containing voxels showing significantly positive RSFC with VWFA when global signal was removed. A high correlation would indicate that the VWFA RSFC patterns were not significantly influenced by the global signal removal procedure.

Finally, we compared the VWFA RSFC patterns between hearing and congenitally deaf subjects. First, a union mask including significant voxels surviving the FWE correction in either hearing or congenitally deaf groups was created. Note that recent studies have suggested that, for the analysis of between-group RSFC comparison, the head motion effects need to be further scrutinized beyond the application of standard realignment and motion regression analysis strategies (Power et al. 2012; Van Dijk et al. 2012). We thus calculated the mean frame-by-frame displacement (FD) during the resting-state scan for each subject, which was defined as the mean absolute displacement of each brain volume compared with the previous volume in translation and rotation in the *x*, *y*, and *z* directions. We used mean FD in translation (derived from the following formula) as the measure of head motion, given that FD in translation and rotation have been shown to be strongly correlated (Van Dijk et al. 2012):

$$\text{mean FD} = \frac{\sum_i^n \sqrt{(\Delta d_{ix})^2 + (\Delta d_{iy})^2 + (\Delta d_{iz})^2}}{(n - 1)},$$

where $\Delta d_{ix} = d_{ix} - d_{(i-1)x}$ ($i = 2 \dots n$, i refers to the i th frame of the resting scan; n is the total number of frames) and similarly for the other parameters Δd_{iy} and Δd_{iz} . With mean FD as the covariate, we conducted a two-sample t -test based on individual RSFC z -maps within the union mask to compare the VWFA RSFC patterns of hearing and congenitally deaf groups.

Results

Comparable Localization and Activation of VWFA in Hearing and Congenitally Deaf Subjects

Group VWFA Results

Word-sensitive regions were localized by contrasting fMRI activity to words versus baseline, following previous work (Dehaene et al. 2002; Cohen et al. 2003; Duncan et al. 2009; Dehaene et al. 2010; Twomey et al. 2011). As shown in Figure 1A, in hearing subjects, this contrast produced robust activation in the left vOTC [x, y, z : $-45, -57, -15$, Brodmann Area (BA) 37, peak $t = 9.00$, 85 voxels]. A control study involving a separate group of hearing participants (see Materials and Methods) showed that a visually more controlled contrast, between real characters and phase-scrambled characters, gave virtually identical peak coordinates in the left vOTC (x, y, z : $-45, -60, -18$, BA 37, peak $t = 9.23$), confirming previous reports (Cohen et al. 2003; Rauschecker et al. 2011). In congenitally deaf subjects, similar effects were identified, with a word-sensitive peak in the left vOTC (x, y, z : $-48, -51, -9$, BA 37, peak $t = 11.95$) that was part of a larger cluster that including more posterior visual regions (Fig. 1A). However, the vOTC cluster can be separated from the posterior visual regions at a more stringent threshold, with a separate cluster of 89 voxels at voxelwise $P < 10^{-6}$. The peak coordinates for both groups are consistent with the VWFA coordinates reported previously with various contrasts and scripts (e.g., Cohen et al. 2000: $-45, -57, -12$; Bolger et al. 2005: $-52, -56, -9$; Liu et al. 2008: $-47, -55, -16$) [VWFA locations in these studies are reported in Talairach coordinates as follows: Cohen et al. (2000): $-43, -54, -12$; Bolger et al. (2005): $-49, -53, -10$; Liu et al. (2008): $-44, -51, -16$. We converted these Talairach coordinates into MNI coordinates (Eickhoff et al. 2009)]. These results demonstrate the presence of the VWFA in both hearing and congenitally deaf groups, and that the VWFA locations are comparable as well. In the network of word-responsive regions, the direct contrast of hearing and deaf subjects showed that deaf subjects had significantly stronger activation in the right vOTC (24 voxels, peak x, y, z : $51, -54, -12$, peak $t = 4.68$) and right inferior frontal gyrus (IFG; 52 voxels, peak x, y, z : $33, 24, 6$, peak $t = 5.14$) (Fig. 1B). This analysis identified no regions showing stronger activation in hearing than in deaf subjects.

The strength of the VWFA activation did not differ between the 2 groups (beta value_{hearing} = 1.91 ± 0.21 , beta value_{deaf} = 1.90 ± 0.18 ; $t_{26} = 0.04$, $P = 0.96$). The ANOVA test comparing activation to the 4 semantic categories of words included in the study found no significant main effect of Group or Category, and no Group \times Category interaction ($F_s < 1.58$, $P_s > 0.22$), indicating that the word-sensitive effects in this region are homogeneous across semantic categories. Furthermore, the VWFA coordinate did not overlap with the classical regions showing selectivity for specific object categories [e.g., tools in the left occipitotemporal cortex, peak MNI x, y, z : $-54, 60, 0$, see (Peelen et al. 2013)] and thus, the VWFA activity identified

here is not likely to be driven by processing of particular semantic categories.

Individual VWFA Results

To confirm that the localization of the VWFA is reproducible across subjects in each group, we created a map showing the overlap of binarized statistical parametric maps of all the subjects within each group for the word versus baseline contrast (voxelwise $P < 10^{-5}$, FWE-corrected cluster-level $P < 0.05$, cluster size ≥ 10 voxels). As shown in Figure 1C, for both groups, almost all participants overlapped in the left vOTC (13 of 14 in the hearing group and 12 of 14 in the deaf group). Note that 11 of 14 deaf subjects also showed overlap in the right vOTC, whereas only 5 of 14 hearing subjects overlapped in this region. This observation, consistent with the above-mentioned whole-brain group comparison results, indicates stronger involvement of the right vOTC in reading circuits in deaf readers.

We identified the VWFA in each subject using a frequently used approach (e.g., Cohen et al. 2004; Reich et al. 2011): selecting the location of the subpeak closest to the group analysis peak for the word versus baseline contrast (see Materials and Methods). Individual VWFA regions could be localized in 13 of 14 subjects in both hearing and deaf groups [Fig. 1D; mean VWFA coordinates (SD) across individuals for the hearing group: -44.54 (2.70), -53.77 (3.77), -12.92 (4.96); for the deaf group: -46.85 (3.98), -52.15 (4.98), -10.85 (2.88)]. The distance variations in terms of individual VWFAs were comparable in the 2 groups, with approximately 5 mm standard deviation in the x, y , and z axes for both groups.

To test whether the anatomical locations of VWFA differed systematically between hearing and deaf groups, we computed, for a given individual VWFA, its Euclidean distances to the averaged VWFA coordinates of its own group (within-group distance, e.g., deaf–deaf) and the other group (between-group distance, e.g., deaf–hearing). An ANOVA test with Distance as the within-subject factor and Group the between-subject factor showed that there was no main effect of Distance or Group, and no Distance \times Group interaction ($F_s < 1$). These results indicate that the anatomical location of the VWFA in a given subject is equally distant to the average VWFA location of its own group as to that of the other group [hearing–hearing (6.63 ± 2.54) mm vs. hearing–deaf (6.84 ± 2.93) mm; deaf–deaf (6.62 ± 3.16) mm vs. deaf–hearing (6.62 ± 3.84) mm; data are expressed as mean \pm SD]. The same distance analysis was performed for each of the 3 axes (x, y , and z) separately. No significant effects were found in any axes ($F_s < 1$).

RSFC Patterns of the VWFA in Hearing and Congenitally Deaf Subjects

The RSFC maps of the VWFA revealed a distributed connectivity pattern, with considerable overlap between hearing and congenitally deaf groups (Fig. 2A, left column; Table 2). In both groups, the VWFA exhibited positive RSFC with right vOTC, bilateral middle occipital gyri (MOG) extending anteriorly into intraparietal sulcus (IPS) and supramarginal gyrus (SMG), left precentral gyrus extending into the pars opercularis of the left IFG.

We compared the RSFC maps of the VWFA of the 2 subject groups within the mask containing clusters significantly and positively correlated with the VWFA in either group (Fig. 2B, left column). Note that the 2 subject groups differed significantly

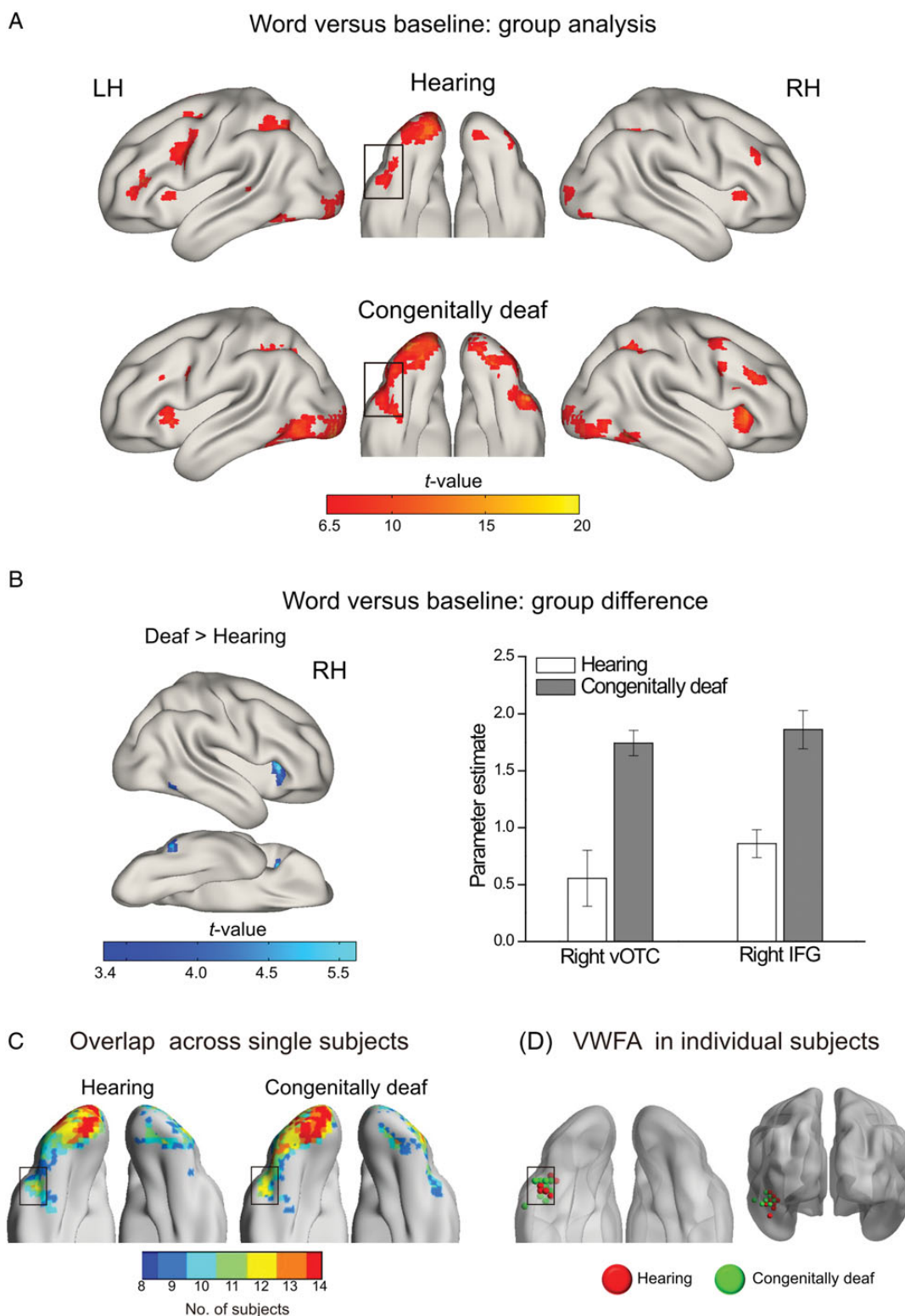


Figure 1. (A) Word-responsive regions activated for the word versus baseline contrast, including left vOTC cluster (VVFA) highlighted within the black square, in hearing and congenitally deaf individuals (voxelwise $P < 10^{-5}$, FWE-corrected cluster-level $P < 0.05$, cluster size ≥ 10 voxels). (B) The direct group comparison shows stronger activation in deaf than in hearing subjects in the right vOTC and right IFG (voxelwise $P < 0.001$, cluster-level $P < 0.05$, FWE-corrected within the mask of the word-responsive regions in either group). The bar chart shows mean beta values (word vs. baseline), for the 2 groups, in the right vOTC and right IFG. Error bars indicate SEM. (C) In each group, the overlap of individual binarized statistical parametric maps is shown for the word versus baseline contrast (voxelwise $P < 10^{-5}$, FWE-corrected cluster-level $P < 0.05$, cluster size ≥ 10 voxels). (D) The VVFA is shown for each individual subject in the hearing (red color-coded) and deaf group (green color-coded). In each subject, VVFA was defined as the subpeak closest to the VVFA peak of each group. LH, left hemisphere; RH, right hemisphere. The results were mapped on cortical surfaces using the BrainNet viewer (Xia et al. 2013).

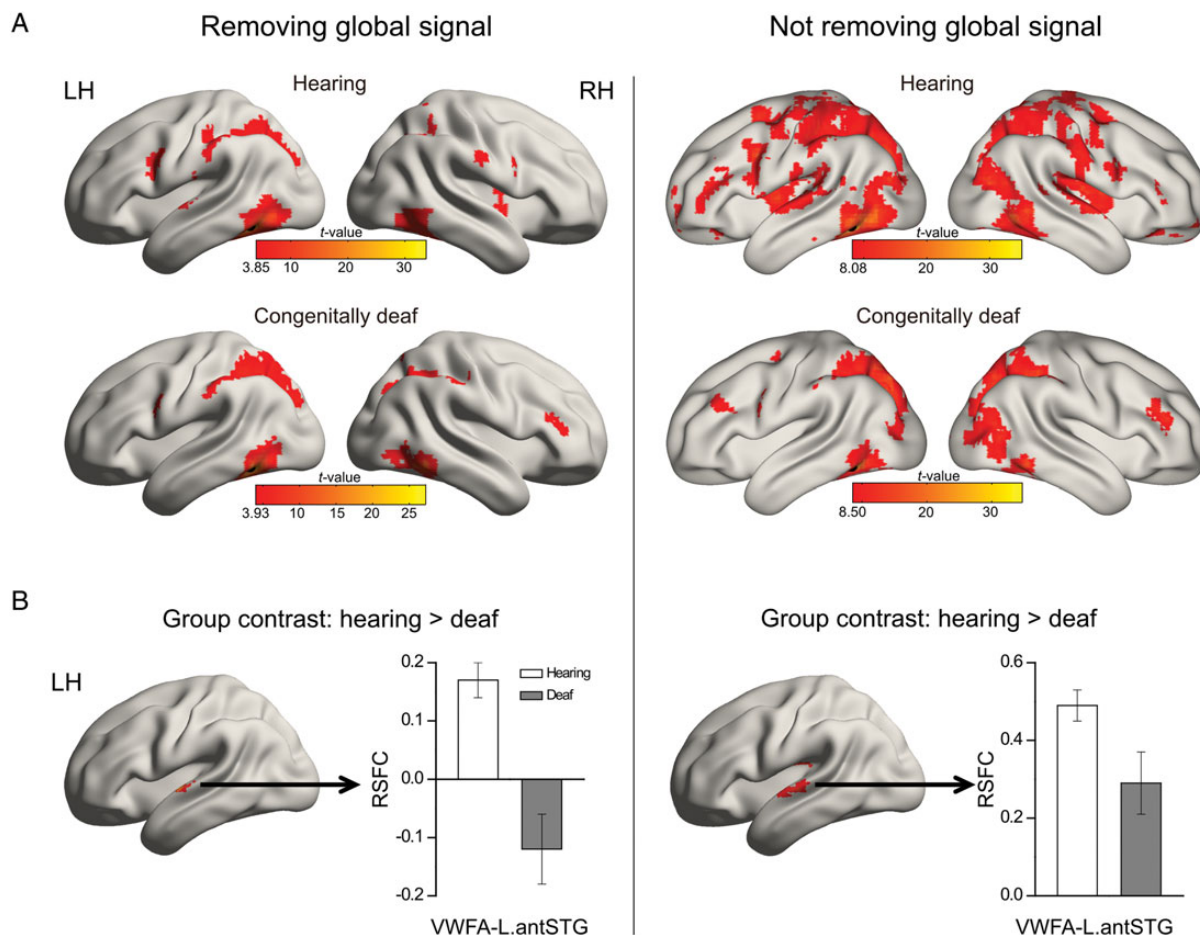


Figure 2. RSFC patterns of the VWFA. (A) Maps show voxels having significantly positive RSFC with the VWFA in hearing subjects (upper panel) and congenitally deaf subjects (lower panel). When global signal was removed, the threshold was set at voxelwise $P < 0.001$, FWE-corrected cluster-level $P < 0.05$; when global signal was not removed, the threshold was set at voxelwise $P < 10^{-6}$, FWE-corrected cluster-level corrected $P < 0.05$, cluster size ≥ 10 voxels. The seed region for the RSFC analysis was a sphere with a radius of 6 mm centering on the average of the individual VWFA coordinates across the 2 groups (x, y, z : $-46, -53, -12$, labeled by the black dot). (B) Group differences in the RSFC maps of the VWFA. The threshold for the analyses with global signal removed was voxelwise $P < 0.001$, FWE-corrected cluster-level $P < 0.05$; for the ones without global signal removal was voxelwise $P < 0.001$, FWE-corrected cluster-level $P < 0.1$. The FWE correction was performed within a mask containing clusters significantly and positively correlated with the VWFA in either group. The bar chart shows the mean RSFC strength (mean Fisher z -transformed Pearson correlation coefficient \pm SEM) of the VWFA–L.antSTG connection in hearing and deaf subjects, respectively. LH, left hemisphere; RH, right hemisphere.

in the mean FD index [hearing (0.05 ± 0.03) mm vs. deaf (0.09 ± 0.05) mm, $t_{25} = 2.19$, $P = 0.038$], indicating that the deaf tended to move more than the hearing during the scan. We controlled for this head motion difference in the group RSFC comparison by including mean FD as a covariate. Results showed that the connection between the VWFA and the antero-lateral region of the left superior temporal gyrus (L.antSTG, 29 voxels, peak x, y, z : $-54, -9, 0$; peak $t = 5.13$) was significantly reduced in deaf subjects relative to controls. This analysis did not reveal any regions showing stronger RSFC in deaf than in hearing subjects.

We also calculated the task-state connectivity patterns of VWFA in both groups of subjects to test whether the above-mentioned resting-state findings hold during the word comprehension task state. A similar data preprocessing protocol was adopted for task-state BOLD series as the resting state except for the following modifications: (1) Slice timing was not performed for task data series; (2) after preprocessing, task-state BOLD series were segmented into word blocks with hemodynamic delay accounted for (Liang et al. 2013) and functional connectivity of the VWFA was computed within each block

and then averaged across 8 blocks to obtain individual VWFA connectivity maps. Direct group comparisons again revealed a cluster in the left STG exhibiting reduced coupling with VWFA in deaf participants (peak x, y, z : $-60, -30, 12$, peak $t = 3.42$, 18 voxels at voxelwise $P < 0.005$), although it did not survive multiple comparison correction.

Furthermore, given the current controversy on global signal removal in RSFC (Fox et al. 2009; Murphy et al. 2009), we also performed the above-mentioned analyses without regressing out the global signal. The reduced VWFA–L.antSTG connection in deaf subjects relative to controls was reproducible when global signal was not removed (Fig. 2B, right column). The deaf group showed reduced RSFC between the VWFA and L. antSTG (35 voxels, peak x, y, z : $-57, -12, 0$; peak $t = 4.01$) and left insula (41 voxels, peak x, y, z : $-39, -15, 24$; peak $t = 5.20$) that was marginally significant at the cluster level for FWE correction (voxelwise $P < 0.001$, FWE-corrected cluster-level $P < 0.1$). No stronger RSFC was identified in deaf than in hearing individuals. The overall RSFC patterns associated with VWFA of the 2 groups were also largely stable (Fig. 2A, right column), as indicated by the high correlation of VWFA RSFC

Table 2
Regions showing significantly positive RSFC with VWFA (x, y, z : -46, -53, -12) in hearing and congenitally deaf groups, when global signal was removed (voxelwise $P < 0.001$, FWE-corrected cluster-level $P < 0.05$)

Approximate location	Hearing					Congenitally deaf				
	x	y	z	T	Volume (voxel)	x	y	z	T	Volume (voxel)
L vOTC	-45	-51	-15	33.59	843	-48	-54	-12	27.19	488
L MOG/SOG/IPS/SMG	-27	-78	30	6.79	515	-27	-87	30	8.34	758
L STG/postcentral gyrus	-63	-18	12	6.52	57					
L anterior medial temporal cortex	-24	-3	-24	8.36	170					
L precentral gyrus/IFG (pars opercularis)	-42	-3	27	9.98	176	-33	3	24	5.85	60
R vOTC	51	-63	-6	9.79	476	54	-51	-12	14.03	291
R MOG/IPS/SMG/AG/postcentral gyrus	66	-9	30	8.43	312	30	-66	39	8.56	571
R insula/precentral gyrus/IFG (pars opercularis)	33	0	15	8.70	107					
R IFG (pars triangularis)						48	36	15	6.17	57
R cerebellum	21	-75	-48	5.85	50					

Coordinates are the peak of the clusters.

L, left; R, Right; vOTC, ventral occipitotemporal cortex; MOG, middle occipital gyrus; SOG, superior occipital gyrus; IPS, intraparietal sulcus; SMG, supramarginal gyrus; STG, superior temporal gyrus; IFG, inferior frontal gyrus; AG, angular gyrus.

maps with or without removing global signal (hearing $R = 0.937$, deaf $R = 0.940$; see Materials and Methods).

Given that we observed group differences in terms of the intrinsic connectivity between VWFA and L.antSTG, it is important to understand whether the overall connectivity pattern of L.antSTG is altered in general or the alteration is specifically related to other functionally related regions. Previous anatomical studies have demonstrated white matter reductions in STG for deaf compared with hearing individuals, suggesting that early-life auditory deprivation may lead to degeneration of fibers projecting to and from auditory cortices (Emmorey et al. 2003; Shibata 2007). To examine whether the reduced functional connection between VWFA and L.antSTG may result from the isolated nature of STG with other cortical regions due to general white matter loss, or may be specifically related with hypoplasia of speech-related tracts, we compared the RSFC patterns of L.antSTG in hearing and deaf subjects. While the 2 groups showed overlapping RSFC of L.antSTG in bilateral superior temporal gyri, insula, and middle cingulate cortex (see Fig. 3A), there were also significant group differences. Relative to controls, deaf subjects showed stronger connections between L.antSTG and left putamen (35 voxels, peak x, y, z : -21, -3, 9; peak $t = 4.58$) and reduced connections with bilateral visual regions, including bilateral inferior occipital gyri and bilateral vOTC (see Fig. 3B). Intriguingly, among all the regions that exhibited reduced functional connectivity with STG in deaf individuals, bilateral vOTC showed the greatest extent of reduction (left vOTC, 29 voxels, peak x, y, z : -45, -54, -18; peak $t = 5.97$; right vOTC, 44 voxels, peak x, y, z : 54, -48, -15; peak $t = 7.44$). This suggests that the reduced VWFA–L.antSTG connectivity in deaf subjects may reflect a specific reduction of visual–auditory word form mapping, instead of an overall RSFC reduction of STG.

Discussion

We tested whether auditory speech experience is crucial in the development of the VWFA by examining its location and functional connectivity patterns in congenitally deaf individuals. We observed a highly similar pattern of VWFA regional activities for congenitally deaf and hearing individuals: (1) Both groups had a region showing strong activation to visual words in the left vOTC, a finding consistent with previous studies

(Aparicio et al. 2007; Waters et al. 2007; Emmorey et al. 2013); (2) the 2 groups' VWFA anatomical locations were indistinguishable at both group and individual levels, and both were close to the location reported in the literature with various contrasts and scripts (hearing individuals), and tactile and auditory inputs (congenitally blind individuals); (3) the VWFA activation strength was comparable between the 2 groups. These findings indicate that the VWFA appears to develop normally even without auditory exposure to spoken language.

Importantly, we found that the RSFC pattern of the VWFA in deaf subjects had reduced connections with the speech perception area, that is, left antSTG, relative to hearing controls. The VWFA–RSFC patterns of the 2 groups also showed important similarities: in both groups, the VWFA seed region showed positive RSFC with left IFG and bilateral MOG extending into the IPS and SMG. Taken together, these results suggest that auditory speech experience has direct consequences for aspects of the network that computes visual word form to speech sound correspondence, but that such experience does not appear to affect the location or strength of the VWFA.

We also observed that deaf individuals showed greater activation in the right homolog of VWFA than hearing controls, both at the group and individual levels. One possible explanation is that use of sign language may enhance the involvement of the right hemisphere in language processing (Neville et al. 1998), which could further modulate the function of right VWFA in a top-down manner (Van der Haegen et al. 2012).

Auditory Speech Experience Is not Necessary in the Development of the VWFA

By testing congenitally deaf participants, we were able to examine the specific role of auditory speech experience in shaping local activity and connectivity patterns of the VWFA. We found that congenitally deaf individuals showed comparable VWFA locations and activation magnitude to hearing controls. Furthermore, we observed that the lack of auditory speech experience significantly affected the VWFA's intrinsic connection to the language network, specifically in relation to auditory perception regions: While the VWFA in hearing individuals had positive intrinsic connectivity with L.antSTG, this connectivity was negative in deaf individuals. A further comparison of the RSFC patterns of L.antSTG identified bilateral vOTC as regions showing the greatest extent of reduction in

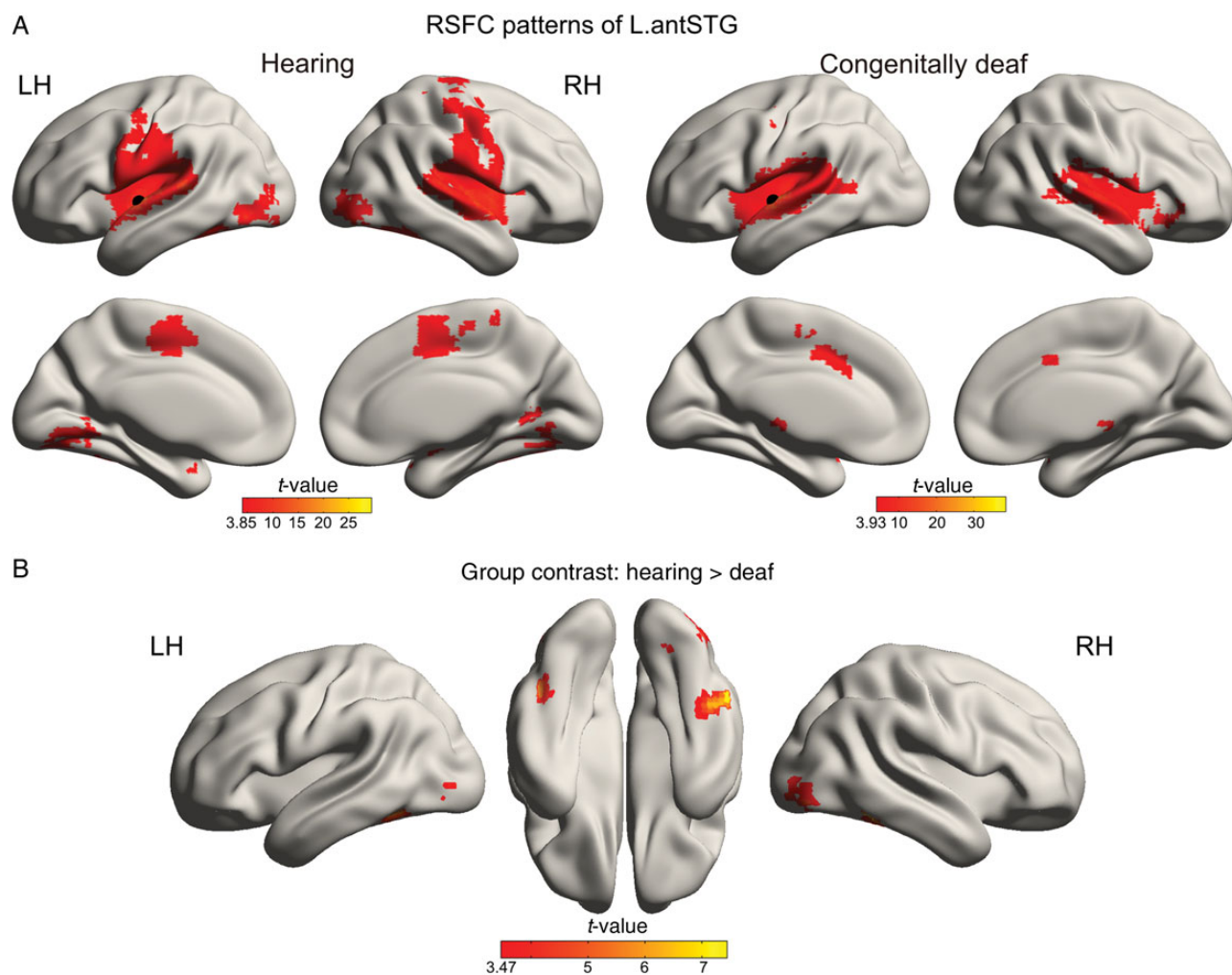


Figure 3. RSFC patterns of the L.antSTG. (A) Maps show voxels having significantly positive RSFC with L.antSTG (voxelwise $P < 0.001$, FWE-corrected cluster-level $P < 0.05$) in hearing subjects (left panel) and congenitally deaf subjects (right panel). The seed region for the RSFC analysis was a sphere with a radius of 6 mm centering on the peak coordinate of L. antSTG (x, y, z : $-54, -9, 0$; labeled by the black dot). (B) Regions showing reduced RSFC with L.antSTG in the group of deaf relative to hearing subjects (voxelwise $P < 0.001$, cluster-level $P < 0.05$, FWE-corrected within a mask containing clusters significantly and positively correlated with L.antSTG in either group). Note that the group contrast also revealed stronger RSFC between L.antSTG and left putamen in deaf relative to hearing subjects (see Results), which is not shown here. LH, left hemisphere; RH, right hemisphere.

deaf relative to hearing subjects (see Fig. 3B), indicating that the reduced connectivity between L.antSTG and vOTC did not reflect an overall connectivity reduction of L.antSTG.

A similar trend of reduced VWFA–L.antSTG connectivity in deaf individuals was observed in the task-state connectivity analysis, though with a weaker effect size. The interpretation of task-state functional connectivity is not straightforward, however, considering that such connectivity is modulated by the nature of specific task demands (Craddock et al. 2013). Since our task did not require participants to explicitly map visual word forms onto phonological codes, it is difficult to assess the extent to which the VWFA–STG connection may have a functional role in hearing and deaf subjects. In comparison, resting-state connectivity serves as a useful tool to reveal the intrinsic neuronal activity in the brain (Zhang and Raichle 2010), which can be shaped by experiences associating various modalities of language during development. More specifically, probably as a result of deprivation of auditory speech experience since birth, the reduced VWFA–L.antSTG connection we found in deaf subjects may reflect alterations in intrinsic brain activity and hence is more likely to be

uncovered using resting-state connectivity analyses. Future studies investigating connectivity patterns under different task states that probe directly into orthographic–phonological correspondence are warranted to more comprehensively unravel the dynamics across different cognitive states.

The left antSTG identified in our study corresponds well with the human voice area (Vigneau et al. 2006; coordinates in our study: $-54, -9, 0$ vs. $-56, -12, -3$ in Vigneau et al. 2006) and is also in close proximity to the auditory word form area identified in a recent meta-analysis (DeWitt and Rauschecker 2012). Critically, while auditory speech experience modulated functional connectivity of the VWFA to speech sound areas, such modulation is not coupled with changes in terms of location or strength of the VWFA.

Our results provide a useful context for interpreting studies that have highlighted the role of the speech system in VWFA activation. For instance, training studies in which novel scripts were associated with native or nonnative speech sounds found increased VWFA activity, but no such increase was observed when scripts were associated with nonspeech sounds (Hashimoto and Sakai 2004; Xue et al. 2006). Such results have been

interpreted as support for the view that the VWFA's primary function is to provide a suitable representation for mapping visual word forms onto speech sounds/phonological representations (Mano et al. 2013). In these studies, it is generally difficult to separate the effects of 2 kinds of vision-to-sound mapping—visual form to auditory speech and visual form to articulatory speech (Hickok and Poeppel 2007), or the effects of other language components such as semantic or syntactic properties (see below). The results of our study allow us to narrow the hypothesis space of the factors that determine the development of the VWFA: Experience in the script-to-sound mapping (especially aural representations) may not be necessary for the development of the VWFA both in terms of its location and activation strength for visually presented words. Finally, we contend that, in hearing individuals, auditory speech experience may still partly drive VWFA selectivity, but our results emphasize that such experience is not necessary for the establishment of the VWFA, and in the absence of auditory input other types of linguistic computations might function similarly.

Role of Connections with Other Language Components in the Origin of VWFA

While our results indicate that auditory speech experience is not necessary for VWFA development, they are consistent with a potentially important role of other language regions that are shared by congenitally deaf and hearing populations. In both groups, the VWFA seed region was functionally connected with pars opercularis of left IFG, and bilateral MOG extending into the IPS and SMG, consistent with previous studies of the connectivity patterns of the VWFA during the resting state (Koyama et al. 2010; Zhao et al. 2011; Vogel et al. 2012) or when performing a phonological lexical decision task (van der Mark et al. 2011) in hearing populations. Interestingly, children with dyslexia showed significant disruption of the task-based functional connectivity between VWFA and these 2 regions (van der Mark et al. 2011), suggesting the relevance of these connections for reading skills. These functional connections also have a structural basis in that the inferior frontal occipital fasciculus and the vertical occipital fasciculus pass within close proximity to the VWFA and project to inferior frontal and parietal regions, respectively (Wandell et al. 2012; Yeatman et al. 2013).

Below we discuss several potential mechanisms for higher-order language effects in the light of the RSFC results: Mapping of visual form with articulatory speech programs, mapping with more general “multimodal” motor programs (articulatory speech and signing), and mapping with other language properties such as semantic/syntactic functions. Note that while fingerspelling used by British sign language users manually encodes alphabetic writing systems and conveys dynamic information about the orthography of the language (Waters et al. 2007), it is rarely used by Chinese signers, and thus the effects of this type of experience is not considered here.

The left IFG (BA 44/45, Broca's area) and SMG have consistently been implicated in tasks involving speech production, including phonological and articulatory encoding in hearing participants (Hickok and Poeppel 2007), and sign language processing in deaf participants (Petitto et al. 2000; MacSweeney et al. 2008; Hu et al. 2011). Nonetheless, in our deaf subjects, any role of the visual word form-to-articulatory speech mapping in shaping the VWFA was very likely highly limited given that the speech articulation skills of our deaf subjects

were at floor. In the questionnaire on the speech articulation ability, all subjects but one denied receiving any systematic training in speech articulation and rarely practiced or applied this skill for daily communication. To further quantify the effects of speech articulation, we administered a test that required our deaf subjects to read aloud 30 words. Two naive raters judged the intelligibility on a 5-point scale (5 being most clear), with high inter-rater reliability (Spearman's $\rho = 0.89$). The mean rating was 0.7 (range: 0–2.8, SD: 0.7). The 2 extreme cases on the articulation ability continuum—the one whose articulation was the clearest and the one who could not articulate any sound at all—did not differ in VWFA activation or location from other participants. While not directly tested here, a candidate factor in shaping the functional connections between the VWFA and other brain regions is the mapping between visual (or multimodal, in case of the blind reading Braille) word forms and language production sequences: either speech, in hearing people, or hand gesture programs (signing), in deaf people. An interesting note is that it is tempting to assume such mapping to be segmental in nature, that is, mapping between perceptual segments (e.g., graphemes in alphabetic languages) and production segments (e.g., phonemes). However, while Chinese character forms and sounds can be segmented, the mapping is whole-character-syllable based (so-called “addressed phonology,” see Tan et al. 2005). The cross-linguistic universality in the VWFA-related findings thus invites further investigation to uncover the exact mechanisms of such mappings.

The role of bilateral IPS in the VWFA–RSFC network is less straightforward. The IPS has been reported to mediate visuospatial processing, or to direct attention to the related spatial configuration (Corbetta and Shulman 2002). Given that the VWFA is also a visual region responsive to object contours, the VWFA–IPS connection may be a nonreading-specific visual pathway for general visuospatial analysis of visual stimuli (Vogel et al. 2012). This is consistent with the finding that the IPS is functionally connected with frontal language regions in both language and nonlanguage tasks (Lohmann et al. 2010). Alternatively, bilateral IPS may be involved in phonological processing. These regions were activated in both hearing and deaf subjects when they performed syllable counting tasks on written words, with deaf subjects showing greater activation than hearing subjects, suggesting increased phonological processing efforts in the deaf (Emmorey et al. 2013).

Finally, the regions showing RSFC with VWFA in our study did not overlap with regions typically associated with semantic processing (Binder et al. 2009), consistent with Vogel et al.'s (2012) suggestion that the semantic system might not be part of the intrinsic network that drives the VWFA's specialization for reading.

Comparing Congenitally Deaf and Dyslexic Individuals

Deaf participants generally have poorer reading ability than matched hearing controls (Goldin-Meadow and Mayberry 2001), not unlike dyslexic individuals (MacSweeney et al. 2009). It is compelling, therefore, that the VWFA activity of the deaf was more similar to hearing controls than to dyslexics, who showed hypoactivation in the VWFA (Richlan et al. 2009). While literacy may modulate the strength of VWFA activity during normal development (Ben-Shachar et al. 2011), the VWFA selectivity to word forms is established in ex-illiterates with variable informal education during adulthood (Dehaene et al. 2010) and

in participants receiving short training sessions with novel scripts (Hashimoto and Sakai 2004; Brem et al. 2010), indicating that the presence of the VWFA can well be formed even without optimal reading efficiency. Taken together, these results suggest that the VWFA hypoactivation in dyslexic participants may not be the consequence of deficits in processing speech sounds *per se*, since the deaf are not able to process such sounds at all and yet showed normal VWFA activation, but may relate instead to potential impairments in linking patterned visual forms to articulated (patterned) gestures or other high-level language components. Consistent with this hypothesis, a recent study showed that even in a task that probes rapid visual print processing under minimized phonological demands, adolescent dyslexic readers, unlike matched controls, did not exhibit letter selectivity in the left vOTC (Kronshabel et al. 2013).

To conclude, in congenitally deaf individuals, the location and activation pattern of the VWFA were indistinguishable from hearing controls, even though the VWFA's intrinsic functional connectivity strength with speech-related regions in the left anterior superior temporal gyrus was reduced in the deaf group. The pattern of VWFA's functional connectivity with left inferior frontal and occipitoparietal regions was similar in the deaf and hearing groups, suggesting that these functional connections are sufficient in shaping VWFA's selectivity for reading. Extending recent findings that the VWFA's selectivity to scripts is independent of input modalities through which reading is acquired (Reich et al. 2011; Striem-Amit et al. 2012), the results reported here demonstrate that the top-down modulation of the VWFA may arise from higher-order linguistic properties that are common to all natural language systems, that is, modality-independent.

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