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Research report

Decoding letter position in word reading

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ABSTRACT

A fundamental computation underlying visual word recognition is the ability to transform a set of letters into a visual word form. Neuropsychological data suggest that letter position within a word may be independently affected by brain damage, resulting in a dissociable subtype of peripheral dyslexia. Here we used functional magnetic resonance imaging and supervised machine learning techniques to classify letter position based on activation patterns evoked during reading Hebrew words. Across the entire brain, activity patterns in the left intraparietal sulcus provided the best classification accuracy (80%) with respect to letter position. Importantly, the same set of voxels that showed highest classification performance of letter position using one letter-of-interest also showed highest classification performance using a different letter-of-interest. A functional connectivity analysis revealed that activity in these voxels co-varied with activity in the Visual Word Form Area, confirming cross-talk between these regions during covert reading. The results converge with reports of patients with acquired letter position dyslexia, who suffer from left occipito-parietal lesions. These findings provide direct and novel evidence for the role of left IPS within the reading network in processing relative letter positions.

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1. Introduction

The ability of the human visual system to conduct efficient and successful orthographic analysis of written words is a fundamental step in reading. Despite comprehensive research, the functional and structural properties of the neural mechanisms underlying successful visual word recognition are not yet fully elucidated. During the last two decades, advances in neuroimaging measurements provided consistent evidence that visual word processing relies on both ventral and dorsal visual networks. Within the ventral pathway, a series of regions including the Visual Word Form Area (VWFA, located in the posterior occipitotemporal sulcus), were found to respond robustly and consistently to written word stimuli (Cohen et al., 2002; Price & Devlin, 2011; Wandell,

Abbreviations: LPD, letter position dyslexia; fMRI, functional magnetic resonance imaging; VWFA, visual word form area; IPS, intraparietal sulcus; MVPA, multivariate pattern analysis; GLM, general linear model; PPI, psychophysiological interaction; SVM, support vector machine; FDR, false discovery rate; BOLD, blood oxygenation level dependent.

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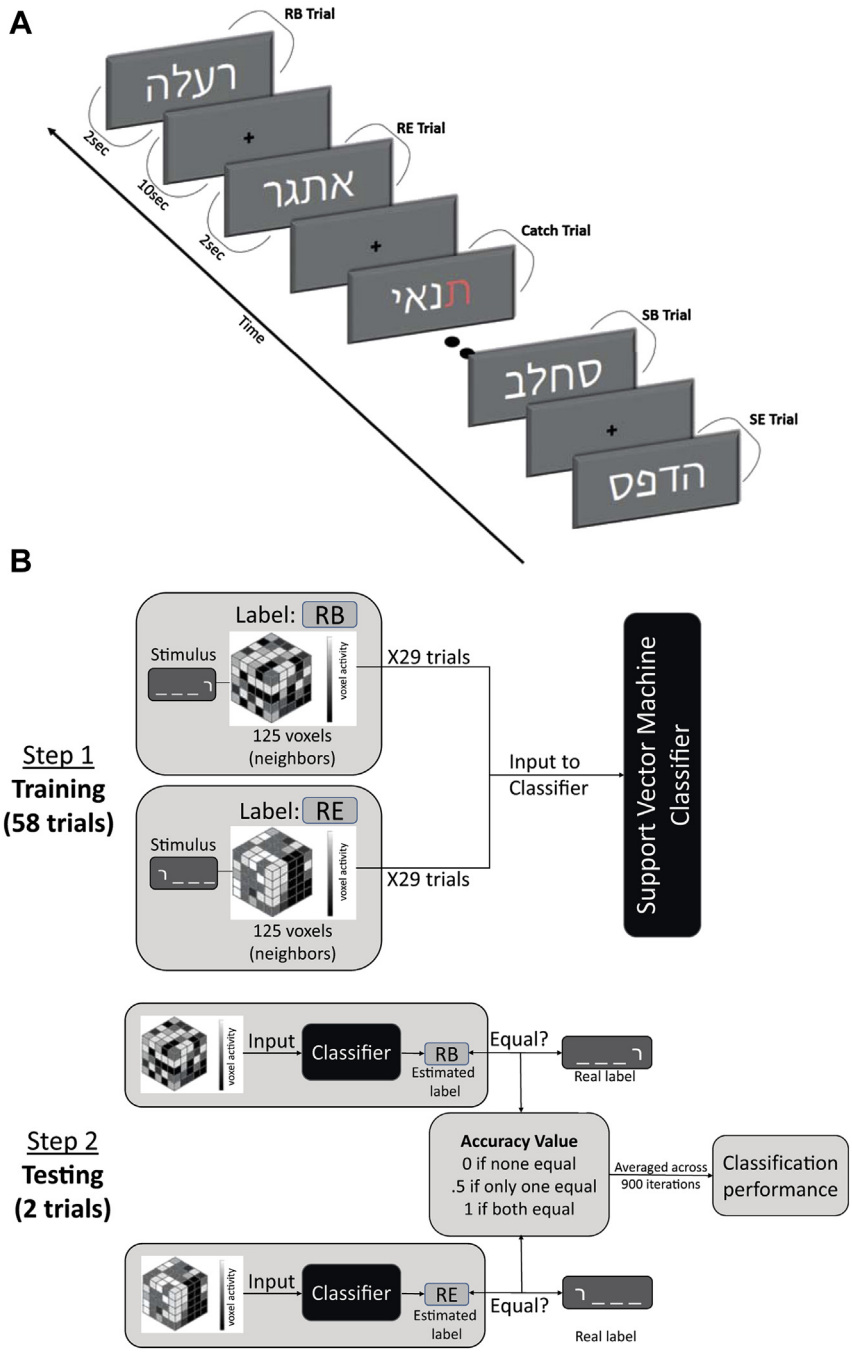

Fig. 1 – (A) Experimental design: Four-letter words were presented in a pseudo-random manner. The figure shows example stimuli from each of the 5 conditions (left to right: RB, RE, catch trial, SB, SE). (B) Classification analysis: For each voxel, we used data from 125 neighboring voxels (5 voxels in each dimension) across 58 trials to train the classifier (Step 1). Next, we used the remaining two trials to test the classifier's performance (Step 2) ('leave-one-trial-out').

2011). Within the dorsal pathway, regions in the left and right posterior intraparietal sulcus (IPS) and the adjacent temporoparietal junction were found to be engaged during reading tasks (Cohen, Dehaene, Vinckier, Jobert, & Montavont, 2008; Gabrieli, 2009; Reilhac, Peyrin, Démonet, & Valdois, 2012).

Computational modeling (Gomez, Ratcliff, & Perea, 2008; McClelland & Rumelhart, 1981), cognitive and neuropsychological studies (Coltheart, 1981; Ellis, Flude, & Young, 1987; Friedmann & Gvion, 2001; Rastle, 2007) argue that encoding of letter position within words may be selectively impaired. Other computational models, supported by neuropsychological studies showing non selective letter-order deficits, suggest that orthographic analysis units do not contain precise information about letter position (Grainger & Van Heuven, 2003; Katz & Sevush, 1989; Whitney, 2001).

Several studies have established a causal role for the VWFA in orthographic processing (Cohen et al., 2003; Dehaene, 2009; Gaillard et al., 2006; Rauschecker et al., 2011, Rauschecker, Bowen, Parvizi, & Wandell, 2012). The VWFA is argued to respond to words as holistic constructs (Glezer, Jiang, & Riesenhuber, 2009) suggesting that encoding of letter position might be performed elsewhere. On the other hand, the VWFA could be indirectly involved in encoding letter positions, as part of a ventral cascade of areas that are sensitive to larger and larger letter combinations (Dehaene, Cohen, Sigman, & Vinckier, 2005; Thesen et al. 2012; Vinckier et al., 2007). We hypothesized that dorsal parietal areas are natural candidates for encoding letter positions. This hypothesis builds on their well-documented involvement in spatial attention (Shafritz, Gore, & Marois, 2002; Xu, 2007), as well as their known involvement in visual word processing, particularly of spatially distorted words (Cohen et al., 2008; Vinckier et al., 2006). Further support for this hypothesis is provided by evidence from two documented patients who sustained left occipital-parietal lesions, displaying acquired letter position dyslexia (LPD) – a selective impairment in encoding letter positions (Friedmann & Gvion, 2001).

Here, we used fMRI measurements and multi-voxel pattern analysis (MVPA) techniques in a searchlight strategy to examine which cortical regions provide the most information about the position of a letter-of-interest within visually presented words. Using this data driven approach across the entire brain, we show that the left intraparietal sulcus (L-IPS) provides the best classification with respect to letter position, regardless of letter identity. These findings provide clear support for the hypothesis that letter position encoding in word reading can be supported by activity patterns of neuronal populations in the left parietal cortex.

2. Materials and methods

2.1. Subjects

Twelve healthy subjects (4 females, mean age: 27.8, range: 20–34 years) participated in this study after providing informed consent. Subjects were native Hebrew speakers, with normal or corrected-to-normal vision and no reported cognitive deficits or structural brain abnormality. The protocol was approved by the Ethics Committee of Tel-Aviv University and the Helsinki committee at the Tel-Aviv Sourasky Medical Center. Subjects were compensated for their time.

2.2. Stimuli and task

Subjects covertly read four-letter Hebrew words. The words included one of two possible letters-of-interest (Resh: 'ר' or Samech: 'ס'), located at one of two positions (beginning or end; Fig. 1A). We used 20 different nouns separated to 4 conditions of five words, according to the letter-of-interest included in the word and its position within the word: Resh Beginning (RB) – words that begin with the Hebrew letter Resh, 'ר' (i.e., 'ר' is the rightmost letter of the words, see Fig. 1A); Resh End (RE) – words that end with 'ר'; Samech Beginning (SB) – words that begin with 'ס'; Samech End (SE) – words that end with 'ס'. The word frequencies were balanced across letter position (RB: mean = 27.2, range = 7–55; RE: mean = 27.6, range = 12–43; SB: mean = 93.4, range = 58–159; SE: mean = 96.4, range = 43–151; See Table 1 for all word exemplars). The letter-of-interest was the only shared letter across the five words from the same condition and it did not appear more than once within a single word. Subjects were not told of the existence or identity of letters-of-interest. Words were rendered in white font "Gisha" (36 pt) within a gray rectangular frame and centered such that 2 letters were placed on each side of the fixation cross (viewing angle of 4.13°). In each trial, a single word was presented for 2 sec followed by 10 sec of fixation cross (Fig. 1A). Each word was presented 6 times throughout the experiment, with repetitions separated by at least 5 trials.

To keep subjects attentive, we also presented 20 different four-letter words each incorporating one colored letter as "catch trials", to which subjects were instructed to respond by pressing a button. These stimuli did not necessarily include the letters of interest. Responses were collected using an MRI-compatible response box and data from these trials were discarded from further analysis.

All stimuli were presented using the COGENT toolbox implemented in MATLAB 7.0.4 software (http://www.vislab.ucl.ac.uk/cogent_2000.php). Stimuli were projected on a tangent screen mounted in front of the subject's eyes in the scanner and viewed through a tilted mirror. The experiment included two consecutive runs, each consisting of 70 trials composed of words from all conditions (15 trials for each condition RB, RE, SB, SE and 10 catch trials) presented in pseudo-random order. Each run started and ended with a 20 sec blank screen and lasted a total of 870 sec.

2.3. fMRI data acquisition

Blood oxygenation level dependent (BOLD) contrast was obtained on a 3T General Electric scanner with an 8 channel head coil located at the Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel. An echo-planar imaging sequence was used to obtain the functional data (26 contiguous ascending axial slices, 4 mm thickness, slice gaps = 0; TR = 2000 msec; flip angle = 90°; TE = 30 msec; in-plane resolution = 1.72 × 1.72 mm; matrix size = 128 × 128). In addition, anatomical reference was obtained by T1-weighted scan (voxel size = 1 × 1 × 1 mm) for each subject.

Table 1 – Word exemplars used in the main experiment.

RB	RE	SB	SE
רקטה	קלמר	סרגל	הדפס
רכבת	אתגר	סנטר	תירס
רעלה	הפקר	סבתא	פנקס
רציף	חזיר	סעיף	טניס
רמאי	מעצר	סחלב	אטלס

List of words for each one of the conditions RB (Resh 'ר' in the beginning of the word), RE (Resh in the end), SB (Samech 'ס' in the beginning of the word) and SE (Samech in the end). Each word was presented 6 times throughout the experiment, with repetitions separated by at least 5 trials. The letter-of-interest was the only common letter across all five words from the same condition and it did not appear more than once within a single word.

2.4. Preprocessing

All fMRI data were processed using the BrainVoyager QX software (version 2.6, Brain Innovation, Maastricht, Netherlands; http://www.brainvoyager.com). Prior to statistical analysis, a preprocessing procedure was performed on all functional images and included cubic spline slice-time correction, trilinear 3D motion correction, and high-pass filtering (above .006 Hz). Furthermore, we assessed head movements and excluded scans with head movement exceeding 2 mm. The 2D functional images were co-registered to the anatomical images and the complete dataset was transformed into the Talairach coordinate system for multi-subject comparisons (Talairach et al., 1988).

2.5. Classification analysis

We checked whether there are brain regions with activity patterns across voxels that are sensitive to the location of the letter-of-interest within a word (e.g., regions in which the fMRI signal can be used to determine whether, for example, 'ר' is located at the beginning or the end of the Hebrew word 'רחוב'). To that end, we used two different approaches. First, we used the general linear model (GLM; Frith et al., 1995). In this approach, the time course of each voxel is modeled using linear regressors that correspond to the presentation timing of each letter position within the experimental run. Since GLM relies on activation of single voxels, it is unable to account for information that is encoded by spatial patterns of activity. Therefore, we also employed multivariate decoding methods in a whole brain searchlight strategy to discriminate evoked spatial activation patterns of fMRI signal across multiple voxels in the different experimental conditions (Hoeft et al., 2011; Tong & Pratte, 2012). For each letter-of-interest, we constructed a linear classifier to decode letter position. The classifier was provided with labeled stimuli and corresponding response patterns according to the position of the letter-of-interest (beginning or end) collapsed across all 5 word exemplars and 6 repetitions (total of 30 trials per position of a given letter of interest; Fig. 1B).

We used a Matlab implementation of a support vector machine (SVM) classifier (Chang & Lin, 2011; http://www.csie.ntu.edu.tw/~cjlin/libsvm) to classify the position of the letter of interest (beginning or end) for the two letters separately ('ר' or 'ס'; i.e., discrimination of RB *vs* RE or SB *vs* SE respectively). As input to the classifier, we took the signal amplitude at the time point corresponding to 6 sec following word presentations (3rd TR). Signal amplitude was expressed as percent signal change relative to baseline – defined as the average signal at time points −4 sec to 0 sec relative to stimulus onset. Thus, for each letter-of-interest, the time-course of each voxel was reduced to two 1 × M vectors (one vector for each letter position, containing data from M trials).

For each voxel in the brain, the following classification procedure was implemented: First, data from this center-voxel and 125 of its neighbors (defined by minimum Euclidean distance) were extracted – resulting in a 125 × M matrix of values for each condition. Next, we randomly chose data from one trial from each condition to be used as test set and the classifier was trained on the remaining two datasets of M-1 trials. Following training, classification performance was assessed on the test set ('leave-one-trial-out'). The average performance level across all 900 possible permutations (30 trials per condition) was assigned to the center voxel. The entire procedure described above was then repeated choosing a different center voxel in an exhaustive manner for all voxels in the brain.

To verify the training and testing datasets are entirely independent, we also split the data to 4 independent datasets and performed 4-fold cross validation estimation similar to the analysis described above. In this analysis a single set was retained for testing, and the remaining 3 were used for training. This was repeated 4 times where each of the datasets was used once as the test set. Each dataset was analyzed and preprocessed independently.

Additionally, to examine generalization across words, we trained the classifier using only 4 exemplars from each condition and tested it on the remaining word. This 'leave-one-exemplar-out' classification verifies that the classifier is not able to learn any property of the tested exemplar which might otherwise appear in the training set. This was performed for each letter-of-interest and classification performance was averaged across all possible exemplar permutations.

In order to assess statistical significance of classification performance level, we first generated single-subject classification maps using shuffled labels as input to the classifier. This was performed by randomly splitting the pool of 10 words of a given letter-of-interest into two conditions (beginning or end). The exemplars in each shuffled condition (5 words × 6 trials = 30 data points for a certain letter position) were used as the new dataset for classification. The total number of permutations for each letter is thus 125:

$$\sum_{Permutations} = \left[\sum_{one_word_switch}\right] + \left[\sum_{two_word_switch}\right] = \left[5\cdot 5\right] + \left[\left(5\cdot 4/2\right)\cdot\left(5\cdot 4/2\right)\right] = 125$$

Where $\sum_{one_word_switch}$ indicates the number of options to choose 1 word from each condition and switch. $\sum_{two_word_switch}$ indicates the number of options to choose 2 words from each condition and switch. Since picking one set of five out of ten is equivalent to picking its complement, the equation needs to be divided by two. The threshold for statistical significance in each subject for a particular letter-of-interest was assessed by taking the highest classification level obtained in a single voxel across the entire brain across all 125 shuffled classification maps. The number of shuffle-labeled maps sets a bound on our significance level at $p = 1/125 < .01$. Voxels with classification performance higher than the classification threshold were declared significant for that particular letter-of-interest. In other words, the probability of obtaining a voxel or a cluster of voxels with higher classification level in maps created using shuffle-labeled data is less than .01.

2.6. Localizing cortical regions in the reading network

In order to map the network of brain regions involved in reading, all subjects underwent an additional separate

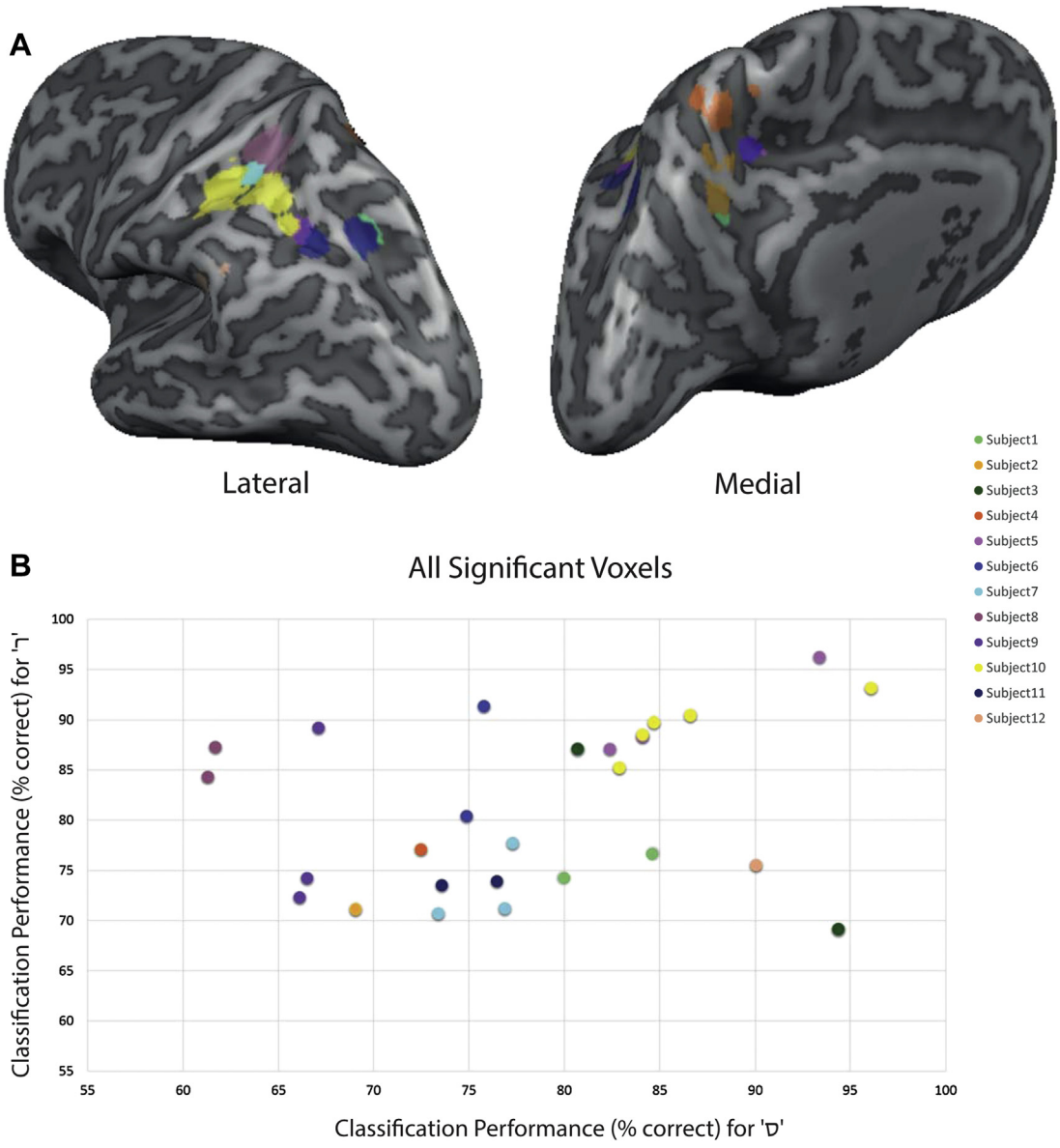

Fig. 2 – (A) Significant set of classifying voxels: Significant classifying voxels ($p < .01$) projected on the left hemisphere of subject 10 in Talairach space. Each color denotes all significant classifying center-voxels from the entire brain of each subject (along with its 125 neighbors that were used as input to the algorithm). (B) Performance results: Accuracy levels of the classifiers for each letter-of-interest ('ר' and 'ס') in all significant voxels found in A. Overall, average classification performance (RB/RE or SB/SE) across all 12 subjects and both letters, 'ר' and 'ס', was 80.87% (STD = 4.63).

localizer run. We used 36 four-letter Hebrew nouns that were rendered similarly to the main experiment. As a visual baseline, we created a phase-scrambled stimulus for each one of the words by computing 2-dimensional Fourier transform of the word image, similar to Ben-Shachar, Dougherty, Deutsch, & Wandell, 2007. The amount of noise (S) was set to .82 where 1 is full noise (Fig. 3A). This level of noise does not allow for word recognition, but maintains the same spatial frequency content of the original stimuli.

The word stimuli were presented in a block design with two conditions – Word or Scrambled. Each block lasted 12 sec in which six different stimuli were presented (2 sec each). Experimental conditions were followed by fixation blocks of the same length (gray background with + sign, Gisha font size 36 pt, bold). Block types were ordered randomly with maximum 3 consecutive blocks of the same type. Subjects were engaged in passive reading.

Reading areas were defined for individual subjects using a GLM, contrasting the Word condition against the Scrambled condition. The resulting maps were corrected by controlling the False Discovery Rate (FDR; Benjamini & Hochberg, 1995) and thresholded at q(FDR) < .05, with a minimum cluster size of 40 voxels. We also examined the average BOLD signal change of each one of these clusters to verify that 6 sec is the optimal time point for classifier input (i.e., timing of peak signal amplitude).

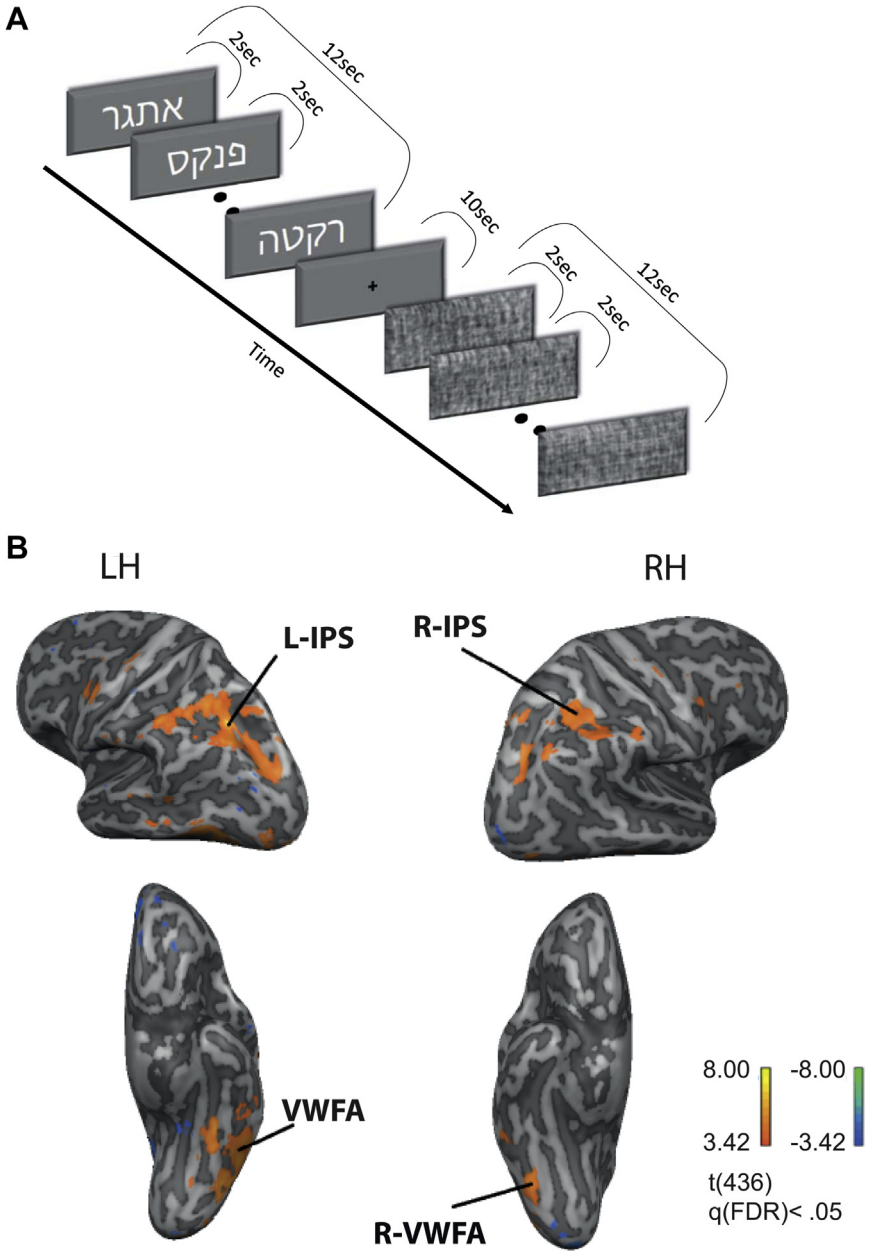

Fig. 3 – (A) Localizer experiment: Two types of stimuli – regular Hebrew words and phase-scrambled words, were presented in a standard block design, interleaved with fixation blocks. (B) Localizer activation map: Random effect multi-subject activation map ($N = 12$; q(FDR) < .05) for the localizer experiment presented on a lateral and ventral view (LH = left hemisphere, RH = right hemisphere). The map presents reading-related areas obtained by contrasting words > phase-scrambled words. Main activation clusters are found in R-IPS, L-IPS, left inferior frontal gyrus, left VWFA, and right VWFA (R-VWFA).

2.7. *Functional connectivity analysis*

To further investigate the role of the letter localization region in the reading process, we conducted a psychophysiological interaction analysis (PPI; Friston et al., 1997) using the significant classifying voxels in L-IPS of each subject as seed regions. The resulting PPI design matrix represents the correlation between activity in this seed region and all other voxels, allowing a whole-brain search for voxels that exhibit a context-dependent correlation with this seed region. We calculated PPI regressors for each subject as the dot product of the z-normalized time course in the seed region of interest (during the experimental run) and the z-normalized design matrix convolved with the two gamma hemodynamic response function. The resulting four PPI regressors (corresponding to the experimental conditions) were compared with rest to reveal areas that are functionally correlated with the activity pattern in the seed region during reading. To investigate the consistency of PPI patterns across subjects, we calculated a probabilistic

Table 2 – Talairach coordinates of significant classifying center-voxels.

Subject	Coordinates (x, y, z)
1	[−15, −59, 34]; [−21; −59; 33]
2	[−14, −55, 35]
3	[−32, −38, 36]; [−36, −30, 41]
4	[−14, −52, 54]
5	[−23, −35, 38]; [−26, −37, 37]; [−30, −34, 37]
6	[−26, −42, 40]; [−31, −47, 41]
7	[−22, −38, 39]; [−26, −36, 41]; [-28, −38, 35]
8	[−29, −41, 46]
9	[−26, −50, 30]; [−34, −50, 27]; [−27, −49, 27]
10	[−30, −43, 32]; [−33, −47, 30]; [−35, −43, 28]; [−35, −41, 47]; [−40, −37, 20]
11	[−21; −58; 32]; [−36; −61; 25]
12	[−44, −42, 27]

Talairach locations of each subject's significant classifying center-voxels ($p < .01$, Fig. 2B).

functional map from PPI-based correlation maps of individual subjects.

3. Results

Subjects responded to the colored letters in catch trials with 94% accuracy showing they were attentive to the task.

We employed a whole brain searchlight strategy using MVPA classifiers to search for activity patterns of multiple voxels that significantly classify the position of a letter-of-interest within words. For each letter-of-interest, we constructed a linear classifier that was provided with labeled stimuli and corresponding response patterns according to the position of the letter-of-interest (beginning or end) collapsed across all words per position (Fig. 1B; see Materials and methods). Our decoding analysis was performed at multiple levels – 'leave-one-trial-out', 'leave-one-exemplar-out' and 'leave-one-dataset-out' (See Methods and materials). Interestingly, the set of significant voxels in each subject (defined using the 'leave-one-trial-out' strategy) classifying letter position for one letter-of-interest (e.g., RB/RE) was identical to the set of significant voxels classifying letter position for the other letter-of-interest (e.g., SB/SE). As can be seen in Fig. 2A, in all subjects the significant set of voxels is located in the Parietal cortex within the vicinity of the L-IPS (range: 1–5 significant voxels per subject; for Talairach coordinates of center voxels see Table 2). The average classification threshold across subjects required for statistical significance (as calculated from shuffle-labeled data; see Methods and materials) was 67.2% (range across subjects: 65.3%–70.1%) for the letter 'ר', and 69.5% (range across subjects: 68%–71.2%) for the letter 'ס'. Based on data from the significant voxels, the algorithm classified letter position for the letter 'ר' with mean accuracy across subjects 78.8% (STD = 2.9) and for the letter 'ס' with mean accuracy 80.06% (STD = 1.9; See Fig. 2B for subject's accuracy levels for each letter-of-interest).

In the 'leave one exemplar out' classification (see Methods and materials), we found the same set of significant voxels in the L-IPS, though the evaluated accuracy based on these voxels (69.2%; STD = 4.9 averaged across both letters-of-interest and 12 subjects), as well as the accuracy based on shuffled data (51.7%; range across subjects: 49.7%–56.7%) was lower. Finally, in the 4-fold cross validation analysis, we again found the same set of significant voxels and similar mean classification accuracy as in the leave-one-trial-out – 79.63% (STD = 3.5) for the letter 'ס' and 82.11% (STD = 3.47) for 'ר', whereas accuracy in the shuffled condition was 65.29% (range across subjects: 63.3%–68.1%) for 'ס', and 66.7% (range across subjects: 62.7%–71.1%) for 'ר'.

We note that performing a direct comparison of letter position (i.e., RB *vs* RE or SB *vs* SE) using the standard GLM method at the single subject level yielded anatomically inconsistent and scattered voxels in 2 subjects, and empty maps for the others. Indeed, at the group level, GLM analysis yielded an empty statistical parametric map. Similarly, collapsing across letters-of-interest, and contrasting letter position (i.e., RB + SB *vs* RE + SE) yielded empty maps at the individual subject level highlighting the advantage of using advanced multivariate methods.

Next, we examined the relationship of the set of significant voxels defined using our searchlight strategy with the network of reading-related regions as defined by traditional GLM localizer mapping (Fig. 3A; see Materials and methods). Fig. 3B displays the multi-subject GLM activation map using the contrast of Word > Scrambled ($N = 12$). Importantly, in all 12 subjects, all the voxels that showed significant classification performance across the entire brain (Fig. 2A), were located inside the L-IPS activation cluster as defined independently by the functional GLM localizer in each individual subject. Fig. 4A displays this overlap in one subject. Using the independent localizer data we also examined whether our choice of time window used for classification in the main experiment could somehow introduce a bias in favor of the L-IPS. We found no difference between parietal and temporal regions with respect to the time it took the BOLD signal to reach peak amplitude (6 sec following trial onset in both). This validates our choice of input to the MVPA classifier, and goes against different temporal characteristics of the BOLD signal across regions as an alternative explanation to the differences in classification levels.

Finally, we performed a functional connectivity analysis using the significant classifying voxels in L-IPS of each subject as seed regions. We found significant functional connectivity with clusters in VWFA and right IPS (see Fig. 4B for a probabilistic functional map across all subjects). This finding confirms cross-talk between L-IPS and other key regions within the reading network, as defined from the localizer experiment (over 75% of the voxels defined by the localizer overlapped with voxels defined by the PPI analysis across all four regions and subjects).

4. Discussion

The current study investigated cortical sensitivity to letter position within Hebrew written words using advanced whole

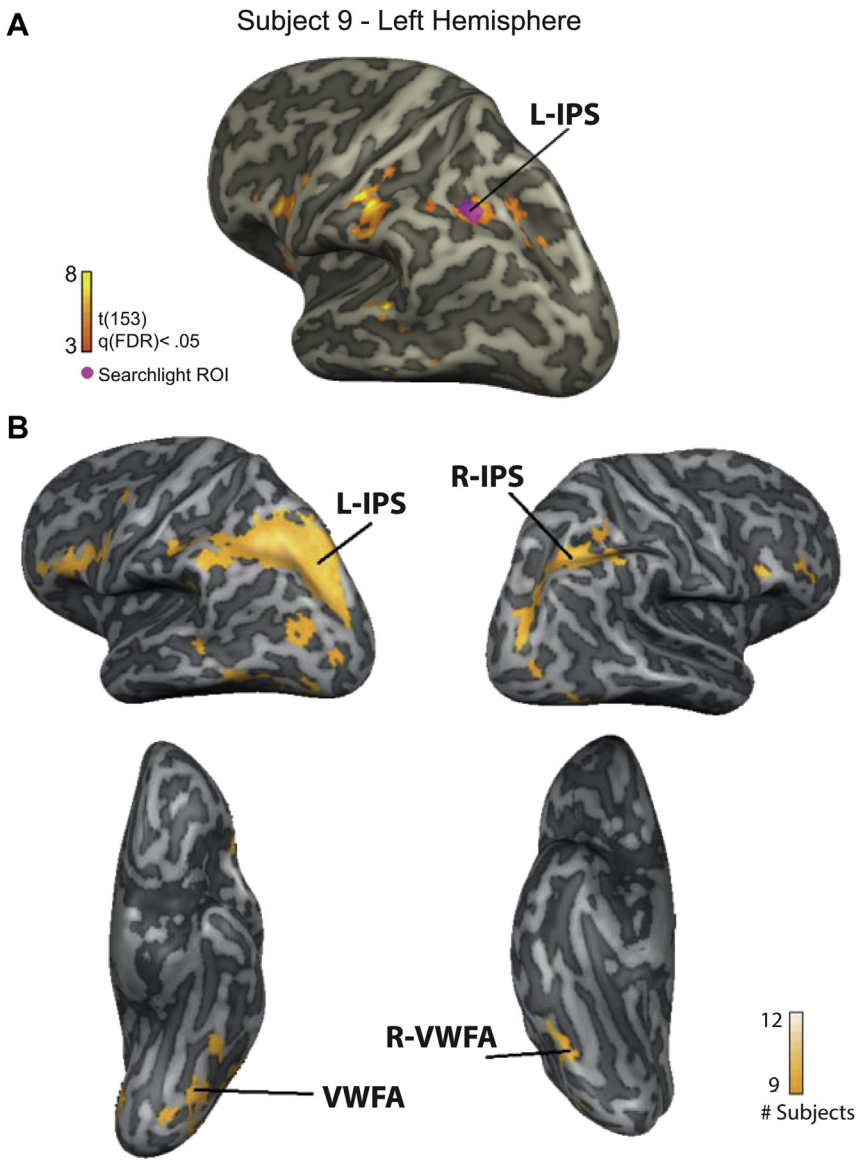

Fig. 4 – (A) Significant classifying voxels and the reading network: Voxels that were found to be significant classifiers of letter position in the whole brain searchlight analysis were also found to fall within the L-IPS cluster, as defined by the functional localizer using standard GLM in each of the 12 subjects. Panel A shows the significant voxels (purple patch) and localizer data (orange) of Subject 9. (B) Functional connectivity map: Multi-subject overlap probability map presented on a lateral and ventral view (N = 12; each subject's random effect functional connectivity map was corrected using q(FDR) < .05 and all maps were used to generate a probability map; LH = left hemisphere, RH = right hemisphere). Using the significant voxels in L-IPS as seed regions (shown in Fig. 2A), the same reading related areas detected by the functional localizer (Fig. 3B) showed the strongest functional connectivity.

brain classification methods. This strategy allowed us to identify the underlying relationship between patterns of brain activity across several voxels, without making any prior assumption regarding anatomical ROIs. We found that activation patterns in the left IPS carry information that is sufficient to discriminate between two letter positions of two different Hebrew letters, at nearly 80% accuracy. This was true even though the letters do not share visual features. Interestingly, classification levels based on activity patterns in other regions within the reading network, including VWFA, R-VWFA and R-IPS, did not reach significance levels. However, we did find functional correlations between significant decoding voxels in L-IPS and these other regions, suggesting that the information about letter position could be inherited from this region to the rest of the reading network.

These results provide strong evidence for a specialized neural subsystem located in left parietal cortex for encoding letter positions in Hebrew words. These findings agree with previous neuropsychological findings in two patients with acquired LPD, reported to suffer from left occipital-parietal lesions (Friedmann & Gvion, 2001). Further, the current results imply that parietal regions which were found to be engaged in

spatial aspects of word recognition (Cohen et al., 2008; Vinckier et al., 2006) and in visual feature binding (Shafritz et al., 2002; Xu, 2007) are also recruited in binding letters to relative position when reading Hebrew words.

Although the VWFA has been found to be involved in reading words in this study and many previous ones (Dehaene, 2009), we did not find significant classification accuracy in this region with respect to letter position. A previous study using machine learning has reported that fMRI activity in VWFA allows significant classification of word position in visual space and that classification levels increase when adding information from the rVWFA (Rauscheker, Bowen, Parvizi, & Wandell, 2012). These results suggest that these regions encode spatial information at the whole word level. Our results suggest that relative to L-IPS, the VWFA is less suited for encoding relative letter positions within a word, in agreement with previous claims about its holistic nature (Glezer et al., 2009). Our functional connectivity results support the idea of a 'cross-talk' between the dorsal and ventral streams regarding letter position. These results are consistent with a recent study by Vogel, Miezin, Petersen, and Schlaggar (2012) demonstrating functional connections between VWFA and left IPS, and other studies providing evidence for structural connectivity between the two areas (Ben-Shachar, Dougherty, & Wandell, 2007; Yeatman, Rauschecker, & Wandell, 2013).

Reading Hebrew words places an unusual burden on letter position encoding since transposing two adjacent letters in a written Hebrew word is very likely to produce a different real word. This means that binding letters to their relative positions within a word is critical for correct recognition, unlike the situation in many non-semitic orthographies. Future studies will be necessary to assess whether the left parietal involvement in letter position encoding generalizes to other orthographies.

Our results shed new light on the neural mechanism underlying LPD. LPD is a reading impairment in which patients mistake the word 'board' for 'broad' or the word 'trial' for 'trail'. Friedmann and Gvion (2001) reported two Hebrew-speaking patients with acquired LPD who suffered a left Occipito-Parietal lesion. This dyslexia was also reported in its developmental form (Friedmann & Rahamim, 2007; Reilhac, Jucla, Iannuzzi, Valdois, & Démonet, 2013), yet there is no study that has isolated the neural substrate underlying LPD. Our study is the first to show brain imaging data in healthy subjects supporting a left parietal mechanism for letter position encoding. If indeed left parietal abnormality correlates with an LPD diagnosis, it raises the exciting possibility of using fMRI pattern analysis for diagnostic purposes.

Finally, it is an open question whether successful letter position encoding in the L-IPS will generalize to other positions, e.g., internal letter positions that are known to be less sensitive to transpositions, at least in Indo-European languages (Perea & Lupker, 2003; But see Frost, 2012). Furthermore, based on neuropsychological data, we expect this encoding to be neurally dissociated from similar processes applied to other stimuli such as digits or musical notes (Dotan & Friedmann, 2007). Future neurophysiological studies could exploit the current strategy to explore the role of L-IPS in processing relative position under broader conditions including different letters, lexical status or orthographies.

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