Selective visual representation of letters and words in the left ventral occipito-temporal cortex with intracerebral recordings

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We report a comprehensive cartography of selective responses to visual letters and words in the human ventral occipito-temporal cortex (VOTC) with direct neural recordings, clarifying key aspects of the neural basis of reading. Intracerebral recordings were performed in a large group of patients ($n = 37$) presented with visual words inserted periodically in rapid sequences of pseudofonts, nonwords, or pseudowords, enabling classification of responses at three levels of word processing: letter, prelexical, and lexical. While letter-selective responses are found in much of the VOTC, with a higher proportion in left posterior regions, prelexical/lexical responses are confined to the middle and anterior sections of the left fusiform gyrus. This region overlaps with and extends more anteriorly than the visual word form area typically identified with functional magnetic resonance imaging. In this region, prelexical responses provide evidence for populations of neurons sensitive to the statistical regularity of letter combinations independently of lexical responses to familiar words. Despite extensive sampling in anterior ventral temporal regions, there is no hierarchical organization between prelexical and lexical responses in the left fusiform gyrus. Overall, distinct word processing levels depend on neural populations that are spatially intermingled rather than organized according to a strict postero-anterior hierarchy in the left VOTC.

word reading | lexical representation | intracerebral recordings | SEEG | fusiform gyrus

The ability to read relies on the rapid mapping of perceived visual letters and their combinations (i.e., visual word forms) to phonology and meaning. The central role of the left ventral occipito-temporal cortex (VOTC) in processing letter strings, initially suggested by pure alexia in lesion studies (1–3), is now widely accepted (4–6). However, within this region, the precise organization for processing letters and their combination remains largely unknown. Here, we report a comprehensive functional mapping of the VOTC for selective responses to visual letter strings and words with intracerebral recordings in a large population of individual human brains. Objective identification and quantification of VOTC activity during rapid discrimination of words from pseudofonts, nonwords, or pseudowords (Fig. 1) shed light on key issues regarding the neural basis of visual letter and word processing.

A first outstanding issue is whether there is a hierarchy of increasingly complex linguistic processes along the postero-anterior axis in VOTC (7). According to this view, bilateral early visual cortices, V1 to V4, or even MT (8), extract oriented bars, local letter features, and case-specific letter shapes (9), which are then recombined into increasingly abstract letter string representations up to the middle section of the left lateral fusiform gyrus [the visual word form area (VWFA)] (3, 7). This view is supported by functional magnetic resonance imaging (fMRI) evidence: in posterior VOTC, the fMRI signal does not differ for various categories of wordlike stimuli (pseudofonts, consonant strings, pseudowords), while in the (more anterior) VWFA, the fMRI signal is larger for words and pseudowords than for less wordlike stimuli (10). However, opposite results have been reported, with larger fMRI activity for less wordlike stimuli in the VWFA (11, 12). Moreover, the location of the brain region showing greater selectivity for letter strings as opposed to nonletters varies from the VWFA site ($y \simeq -54$ in Talairach coordinates) to more anterior VOTC regions ($y \simeq -42$) (13, 14) (for a recent metaanalysis, see ref. 15), depending on the contrasted material (checkerboards, pseudofonts, or symbols), the task, as well as the stimulus presentation time.

In general, whether the functional organization of the VOTC obeys a hierarchy of increasingly complex representations from individual letters to words (10), and if so up to which region, has proved difficult to resolve not only due to methodological differences between studies but moreover because the fMRI signal-to-noise ratio (SNR) is not equivalent across the VOTC, with large magnetic susceptibility artifacts in its anterior portion (4). In this context, a complementary approach to increase understanding of the function of the VOTC in reading, which is not affected by such artifacts, is to record electrical field potentials in awake patients implanted with intracranial electrodes. While

Significance

The left ventral occipito-temporal cortex (VOTC) is a critical part of the reading circuitry. We made measurements with intracerebral electrodes in 37 participants to understand whether this region contains functionally separated brain loci for processing letters and words. Letter-selective responses are found in much of VOTC. Responses to word forms are absent in posterior VOTC but are present and intermingled with letter-specific responses in left anterior VOTC. The results are inconsistent with a hierarchical model in which posterior regions uniquely perform letter identification functions and increasingly anterior regions perform increasingly complex linguistic functions.

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Data deposition: The raw electrophysiological data used for analyses in this paper, along with the xyz coordinates for the position of the electrodes, and the stimuli used have been deposited in the Dryad Digital Repository (doi:10.5061/dryad.6s39h64).

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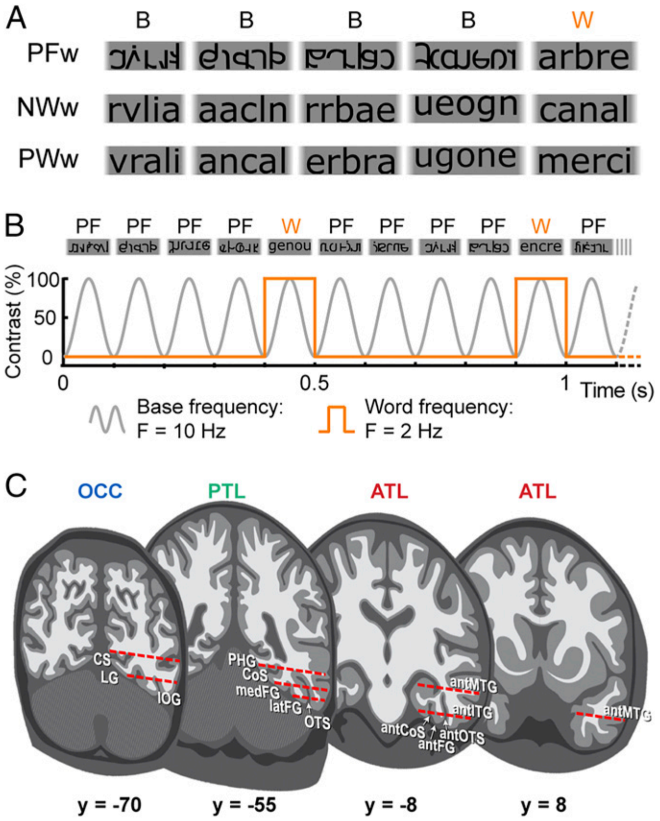

Fig. 1. Fast periodic visual stimulation (FPVS) and SEEG methods. (*A*) Experimental conditions and example stimuli. Words (w) are inserted within three different types of base stimuli (B), that is, in three conditions: words in pseudofonts (PFw), in nonwords (NWw), and in pseudowords (PWw). (*B*) FPVS paradigm. Sequences of PW, NW, and PF are presented at a rate of 10 Hz through sinusoidal contrast modulation with words inserted every fifth item, at 2 Hz, that is, 10 Hz/5 (the PFw condition is represented here). (*C*) Schematic coronal representation of the typical trajectories of depth electrodes implanted in the VOTC. Electrodes consist of 8–15 contiguous recording contacts (red rectangles) spread along the electrode length, along the mediolateral axis. Acronyms: ant, anterior; ATL, anterior temporal lobe; CoS, collateral sulcus; CS, calcarine sulcus; FG, fusiform gyrus; IOG, inferior occipital gyrus; ITG, inferior temporal gyrus; lat, lateral; LG, lingual gyrus; med, medial; MTG, middle temporal gyrus; OCC, occipital lobe; OTS, occipito-temporal sulcus; PHG, parahippocampal gyrus; PTL, posterior temporal lobe.

fMRI measurements typically reflect a general elevation of neural activity only partly due to stimulus-locked responses, intracranial recordings may isolate stimulus-locked responses (16). A seminal study using subdural grids of electrodes [electrocorticography (ECoG)] reported that various letter strings (words, pseudowords, or nonwords) generate an equivalent intracranial response (N200) over the posterior fusiform gyrus, while selectivity to words interpreted in terms of semantic processing was found only in more anterior sections of the VOTC (17). More recently, letter-selective responses (consonant strings > pseudofonts) were found in a more posterior region of the left fusiform gyrus than word-selective responses (words > consonant strings) (18). These observations support a hierarchy of word form processing in the VOTC. However, these recent recordings were performed in targeted VOTC subregions, such that a comprehensive mapping and quantification across the whole VOTC for selective responses to letter strings and words aiming at thoroughly evaluating its hierarchical organization, is currently lacking. Moreover, in these studies, the use of ECoG, which is restricted to the gyral surface, may have underestimated responses arising from sulci. The success of a comprehensive mapping for letter and word processing may thus be enhanced by evenly measuring responses from both gyri and sulci with depth intracerebral electrodes, and by a relatively large recording sample (see ref. 19).

A second outstanding issue regarding the neural basis of letter and word processing is whether the VOTC, in particular the VWFA, is sensitive to whole-word form (i.e., lexical) representations of written strings or is only tuned to prelexical factors characterizing letter strings (e.g., orthographic structure, such as frequently co-occurring letters in a given orthography). This issue is usually operationalized by testing for differential representation of visual real words (lexical items) and pseudowords (orthographically and phonologically plausible sequences of letters) in the VWFA. Here again, previous studies yielded conflicting findings. On the one hand, most fMRI studies did not report differential responses to words vs. pseudowords in this region (10, 20, 21), supporting a prelexical representation level in the VWFA (3, 7, 22). On the other hand, larger responses have been found in this region for pseudowords vs. words (23–26), and for nonfrequent vs. frequent words (27); these observations being interpreted in terms of neural sensitivity to whole-word forms, thus lexical representation. fMR-adaptation paradigms have also shown that the decrease of the response due to pseudoword repetition depends on the number of repeated letters, with a single letter identity change in words resulting in full release from adaptation (24, 25), hence supporting whole-word form coding. Finally, recent intracranial electrophysiology findings suggest that words and pseudowords recruit identical populations of neurons in the VWFA but at different timescales (28). However, the stimuli compared in that study differed only by prelexical factors (number of common letters or bigram frequency). Moreover, since depth recording in three individual brains was limited to the left VWFA only, whether differential responses to words and pseudowords extend to other VOTC regions remains unknown.

Here, we clarify these issues by providing a comprehensive functional mapping of the VOTC for selective responses to visual letter strings at the level of letter recognition, prelexical, or lexical processing. We report data of 37 patients (60 hemispheres) implanted in the VOTC with multiple intracerebral electrodes, each comprising 8–15 recording contacts (2,172 recording contacts in the gray matter) during stereoencephalography (SEEG) (Fig. 1*C*). In our paradigm, validated in scalp EEG studies (29, 30), visual words appear periodically among different stimuli presented at 10 Hz and varying in wordlikeness (Fig. 1 *A* and *B*): (*i*) pseudofonts (PF; Movie S1), (*ii*) letter strings that form orthographically implausible words [nonwords (NW; Movie S2)], or (*iii*) letter strings that form orthographically plausible words [pseudowords (PW; Movie S3)].

We classified each intracerebral recording contact based on the pattern of present (+) or absent (−) significant responses in these three conditions. Three response patterns have a clear theoretical interpretation, reflecting increasingly complex linguistic processing levels. First, contacts with a significant response only to words among PF but not among NW or PW (+PFw, −NWw, −PWw) reflect a letter-selective neural response. Second, discrimination of words from PF and NW but not from PW (+PFw, +NWw, −PWw) reflects a prelexical level of processing. Finally, discrimination of words in all three conditions (+PFw, +NWw, +PWw) reflects a lexical processing level. We focus on these three response patterns and refer to these responses as "word discrimination responses" in the manuscript. Importantly, wordlike stimuli (PF, NW, PW) are presented at a rapid rate of 10 Hz in different 70-s streams, with words inserted every five items (i.e., every 500 ms or 2 Hz; Fig. 1 *A* and *B*; Movies S1–S3). In these conditions, briefly presented words (100-ms stimulus onset asynchrony) are forward- and backward-masked by wordlike stimuli, and word discrimination neural responses can be objectively identified and quantified in the intracerebral EEG spectrum at 2 Hz and harmonics (see refs. 19 and 31 for this frequency-tagging approach in intracerebral SEEG mapping). Moreover, the rapid presentation rates and low attentional-demand tasks reduce the involvement of higher level (semantic) processes (10).

A strict hierarchical view of letter string representation in the VOTC predicts a posterior-to-anterior hierarchy of responsive contacts following the three levels of word discrimination tested. Moreover, if the VWFA responds only to statistical mappings of recurring letters and not to whole-word forms (3, 10), words should not be discriminated from PW in this region but rather in the ventral anterior temporal lobe, extensively sampled here. However, if the VWFA is tuned to whole-word forms (25), contacts reflecting lexical discrimination should be found in this region, with a potential intraregion hierarchical organization (i.e., prelexical posterior to lexical anterior contacts).

Results

Despite the brief recording time (two to six sequences of 70 s per condition), high SNR word discrimination responses were identified in the VOTC exactly at the word presentation frequency (2 Hz) and its harmonics following fast Fourier transform (FFT) (Fig. 2*A*) of SEEG data. Significant word discrimination responses were determined based on a combination of the first four harmonics (i.e., 2, 4, 6, and 8 Hz; Fig. 2*B*) and a *z*-score transform ($z > 3.1$, $P < 0.001$; Fig. 2*C*).

Broad Distribution of Word Discrimination Responses Along the Left VOTC. Across the VOTC, we found 212 significant word discrimination contacts in 27 participants, that is, 9.8% of all recorded contacts. Note that word discrimination contacts can be letter selective (+PF, −NW, −PW), prelexical (+PF, +NW, −PW), or lexical (+PF, +NW, +PW). Every word discrimination contact was labeled according to the individual anatomy (Table 1 and Fig. 3*A*), using a topographic parcellation of the VOTC (*SI Appendix*, Fig. S1; see ref. 32). Word discrimination contacts were distributed broadly across the VOTC with two prominent features: (*i*) these contacts were much more numerous in the left hemisphere; and (*ii*) their density was highest around the left fusiform region (Fig. 3*A* and *SI Appendix*, Fig. S1). In addition, anterior temporal lobe (ATL) word discrimination contacts were mostly restricted to its posterior part, close to the junction with the posterior temporal lobe (PTL) (Fig. 3*A*).

Overall, the proportion of word discrimination contacts relative to all recorded contacts (i.e., responsive and unresponsive) was much higher in the left than in the right hemisphere (left: 169/1,326, 12.7%; right: 43/846, 5.1%; two-tailed permutation test, $p < 0.0001$). To estimate and visualize the prominence of word discrimination contacts at a more local level over the group of participants, we computed maps of the proportion of word discrimination contacts relative to all recorded contacts (Fig. 3*B*). In the left hemisphere, the proportion of word discrimination contacts was significantly above zero ($P < 0.01$) in the ventro-medial occipital cortex (VMO) and all along the left fusiform gyrus and adjacent sulci (from the posterior fusiform gyrus close to the occipital lobe to the anterior fusiform gyrus). We found a similar pattern of results when considering the local proportions of individual brains showing word discrimination contacts (*SI Appendix*, Fig. S2). In the right hemisphere, the proportion of contacts was also significantly above zero along the fusiform gyrus with a maximum in the posterior lateral fusiform gyrus (latFG) (Fig. 3*B*). Nevertheless, the proportion of word discrimination contacts was significantly higher in the left hemisphere in part of the VMO and along the fusiform gyrus (Fig. 3*C*).

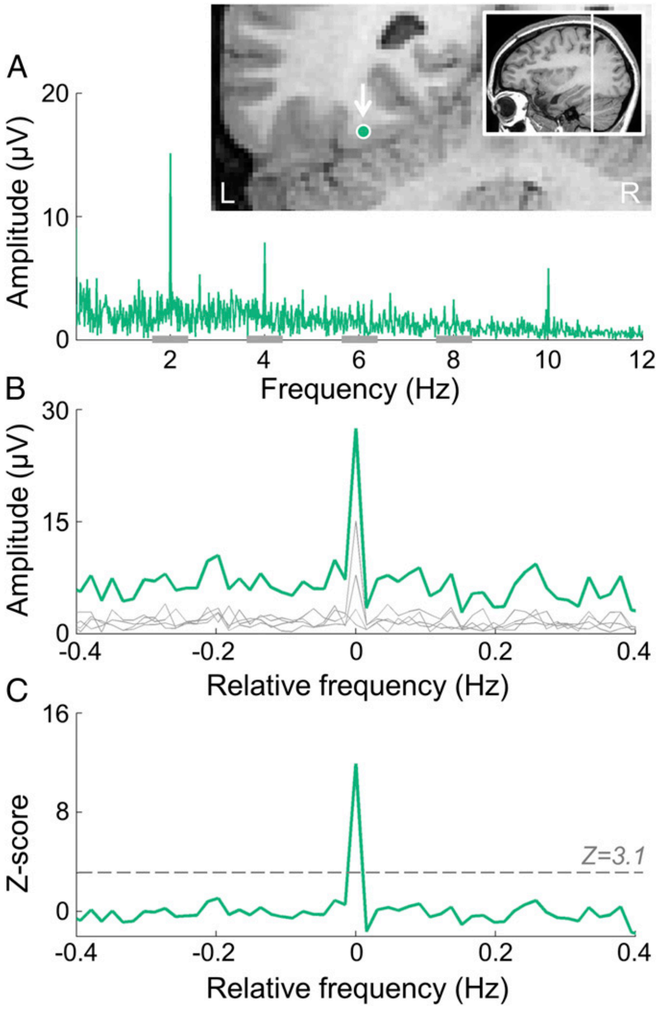

Fig. 2. Objective and high-SNR intracerebral word discrimination responses recorded in the VOTC. (*A*) SEEG frequency-domain responses recorded at an individual recording contact in the PFw condition. The displayed contact was the 10th best of this type, with an average response amplitude of 21 μV, while the best contact had a response amplitude of 86.8 μV. The anatomical location of the contact (in the left latFG, white arrow) is shown in a coronal MRI slice. Word discrimination responses are observed at the exact word stimulation frequency and harmonics (mainly at 2 and 4 Hz). (*B*) Significant word discrimination responses were determined by first segmenting the FFT spectrum into four segments centered at the frequency of word stimulation and its harmonics up to 8 Hz (i.e., 2, 4, 6, and 8 Hz). Individual FFT segments are shown in gray (see horizontal gray bars on the *X* axis in *A*, representing the length of each FFT segment). The four segments, containing both the signal and the surrounding noise, were then summed (green line). The 0 mark corresponds to the word stimulation frequency. (*C*) *Z*-score transformation of the summed FFT spectrum for statistical purpose. The *Z* score at the word stimulation frequency exceeds 3.1 ($P < 0.001$), indicating that this contact shows a significant word discrimination response.

Spatial Dissociation Between Letter and Word Processing Levels. Fig. 4 illustrates the classification of letter-selective (+PFw, −NWw, −PWw), prelexical (+PFw, +NWw, −PWw), and lexical (+PFw, +NWw, +PWw) word discrimination contacts with the data of a few individual participants (*SI Appendix*, Fig. S3). The respective number of contacts at each level of discrimination is shown in Table 2. The other classes of response patterns, that is, significant responses in at least one condition but without an unambiguous a priori theoretical interpretation (e.g., −PFw, +NWw, +PWw, exhibiting a discrimination response for words presented among the most but not the least wordlike conditions; *SI Appendix*, Table S1), were not considered in the main analysis. This led to the exclusion of 16.2% of the contacts. Although interpretation of these responses is not straightforward, these contacts may reflect subtle lexical and prelexical processes (*Discussion*). Therefore, we performed the same analyses as presented here, including these contacts, yielding virtually identical findings (*SI Appendix*, Fig. S4).

The spatial organization of the three types of word discrimination contacts across all individual brains is displayed in Fig. 5*A*. Letter-selective contacts were the most frequent and were widely distributed across all individually defined anatomical VOTC regions [VMO, inferior occipital gyrus (IOG), medial fusiform

Table 1. Number of contacts and corresponding number of participants (in parentheses) showing word discrimination responses in each anatomical region

Regions	Left	Right	Both hemispheres
VMO	21 (4)	1 (1)	22 (4)
IOG	13 (4)	6 (2)	19 (6)
Total OCC	34 (5)	7 (3)	41 (9)
MedFG	21 (12)	2 (1)	23 (13)
LatFG	34 (10)	8 (3)	42 (12)
MTG/ITG	19 (7)	1 (1)	20 (8)
Total PTL	74 (14)	11 (4)	85 (17)
AntCOS	23 (12)	8 (4)	31 (13)
AntFG	10 (6)	2 (2)	12 (8)
AntOTS	25 (11)	7 (3)	32 (14)
AntMTG/ITG	3 (1)	8 (4)	11 (5)
Total ATL	61 (17)	25 (8)	86 (20)
Total VOTC	169 (17)	43 (11)	212 (27)

gyrus (medFG), latFG, middle temporal gyrus and inferior temporal gyrus (MTG/ITG), anterior collateral sulcus (antCoS), anterior fusiform gyrus (antFG), anterior occipito-temporal sulcus (antOTS), antMTG/ITG, bilaterally]. Despite this wide distribution, the proportion of letter-selective contacts was maximal in posterior regions (occipital lobe and posterior part of the fusiform gyrus; Fig. 6*A*) and progressively decreased along the anterior axis of the VOTC (Fig. 6*B*).

We found fewer contacts supporting the existence of prelexical (+PFw, +NWw, −PWw) and lexical (+PFw, +NWw, +PWw) visual word representations in the VOTC. Strikingly, these contacts were almost all located along the left fusiform gyrus and adjacent sulci (medFG, latFG, antCoS, antFG, and antOTS; Fig. 5*A* for group visualization). Hence, the proportion of prelexical and lexical contacts was above zero in a restricted middle and anterior area of the left fusiform gyrus and adjacent sulci, defined as midFG (Fig. 6*A*). This proportion was maximal at a postero-anterior location where the proportion of letter contacts was reduced by half compared with its maximum in the posterior region (Fig. 6*B*). The same observation was made considering the proportion of participants showing word discrimination contacts (*SI Appendix*, Fig. S2).

The spatial distribution of the different types of contacts therefore reveals a spatial dissociation between letter-selective and prelexical/lexical processing levels (Fig. 5*A*) in the left hemisphere: while letter-selective contacts are distributed from posterior to anterior VOTC, with a peak in posterior VOTC, prelexical and lexical contacts are confined to the middle and anterior left fusiform gyrus. This observation is also valid in individual participants (Fig. 5*B*) and does not depend on statistical thresholds used to classify word discrimination contacts (*SI Appendix*, Fig. S5).

Lexical Responses in the Left Fusiform Gyrus. A major finding here is the recording of lexical responses in the VOTC, that is, words discriminated even from the most wordlike stimuli, that is, PW (see Fig. 4 and *SI Appendix*, Fig. S3 for individual participants' lexical responses). In total, we found 18 left hemisphere lexical contacts in nine participants, specifically located along the fusiform

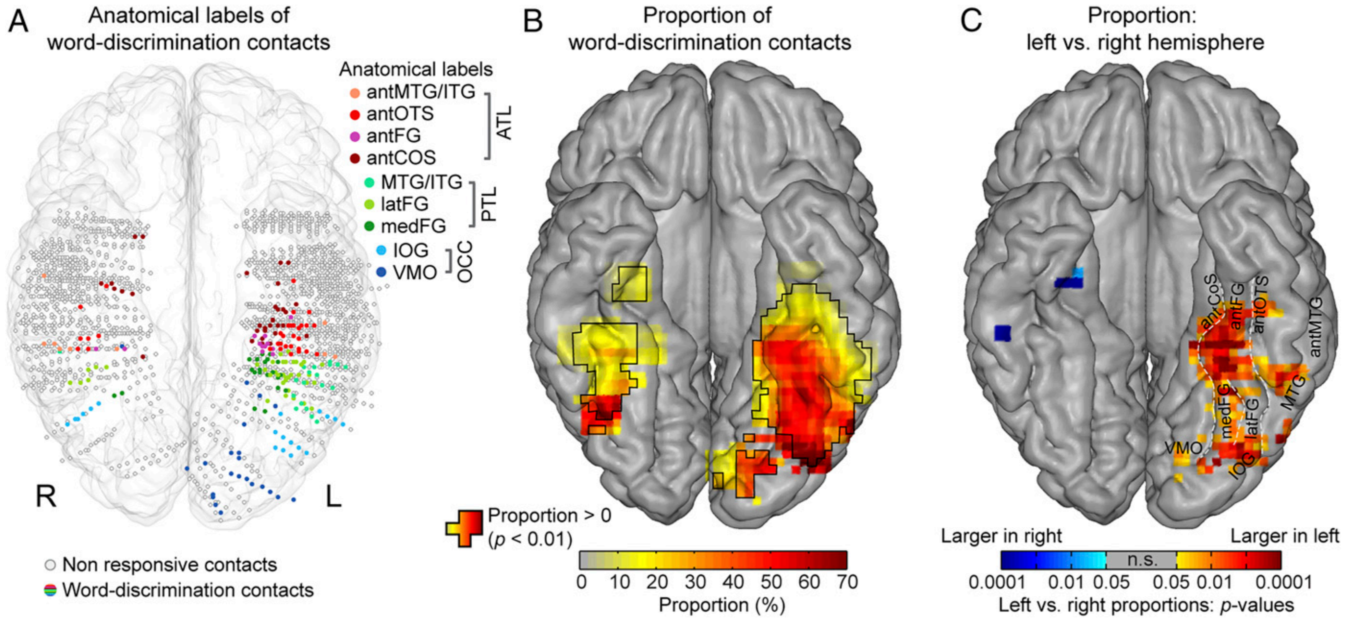

Fig. 3. Spatial distribution of word discrimination contacts in the MNI space (ventral view). (*A*) Map of all 2,156 VOTC recording contacts across the 37 individual brains displayed in the MNI space using a transparent reconstructed cortical surface of the Colin27 brain. Each circle represents a single contact. Color-filled circles correspond to word discrimination contacts colored according to their anatomical location in the original individual anatomy. White-filled circles correspond to contacts on which no word discrimination responses were recorded. For visualization purposes, individual contacts are displayed larger than their actual size (2 mm in length). Acronyms: antCoS, anterior collateral sulcus; antFG, anterior fusiform gyrus (located between the antCoS and the antOTS); antMTG/ITG, anterior middle and inferior temporal gyri; antOTS, anterior occipito-temporal sulcus; ATL, ventral anterior temporal lobe; IOG, inferior occipital gyrus; latFG, lateral fusiform gyrus and occipito-temporal sulcus; medFG, medial fusiform gyrus and collateral sulcus; MTG/ITG, the inferior and middle temporal gyri; OCC, occipital lobe; PTL, posterior temporal lobe; VMO, ventro-medial occipital cortex. (*B*) Map of the local proportion of word discrimination contacts relative to recorded contacts across VOTC, displayed on the cortical surface. Local proportions were computed in 15 × 15 voxels (for X and Y dimensions, respectively) using contacts collapsed over the Z dimension (superior–inferior) for better visualization. For the sake of replicability, only voxels containing significant responses from at least two individual brains were considered. Black contours outline proportions significantly above zero. (*C*) Statistical comparison of local proportions of word discrimination contacts across hemispheres. Proportions (as displayed in *B*) at corresponding voxels in the left and right hemisphere were statistically compared using permutation tests. P values associated with a significantly ($P < 0.05$) larger proportion in the left/right hemisphere are displayed using warm/cool colors over the left/right hemisphere.

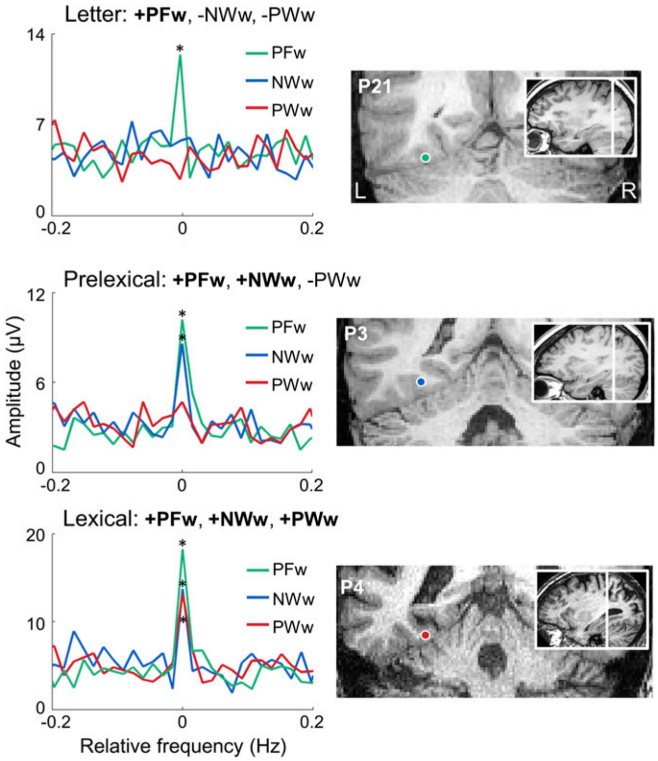

Fig. 4. Classification of word discrimination contacts in three processing levels: example in individual participants (P21, P3, and P4). Example of summed segmented FFT spectra for the three conditions recorded in three contacts (shown on coronal MRI slices). The three rows illustrate how hierarchical word processing levels are defined in each contact by the pattern of responses across conditions. Top row: a letter-selective contact significant only in the PFw condition; middle row: a prelexical contact significant in PFw and NWw conditions; bottom row: a lexical contact significant in all three conditions. The asterisk (*) indicates statistically significant responses ($Z > 3.1$, $P < 0.001$).

gyrus and adjacent sulci (i.e., left midFG), plus a single contact in the right hemisphere in a 10th participant (Table 2). In the left midFG, the proportion of participants with electrodes implanted in this region who showed lexical responses reached up to 50% (*SI Appendix*, Fig. S2). Fig. 7 displays SEEG frequency spectra averaged across the 18 left lexical contacts for each condition. High SNR word discrimination responses are visible in each condition, even in the most wordlike (PWw), in both original and summed-harmonic spectra.

Next, we tested whether lexical responses truly reflect a qualitatively unique level of word discrimination, or if SEEG responses at these contacts is generally larger. To test this, we quantified the response amplitude for each condition and each type of contact (Fig. 8*A*) and compared conditions across prelexical and lexical contacts types. If the difference between prelexical and lexical contacts reflects a general amplitude increase, there should be a significant difference in amplitude in all conditions between these types of contacts (note that the amplitude increase in the PWw condition between prelexical and lexical contacts is expected and noninformative, given that significance of response in this condition served to differentiate prelexical and lexical contacts). We found a highly significant interaction between Condition (PFw, NWw; i.e., excluding the PWw condition) and Contact Type [prelexical, lexical; two-way mixed-model ANOVA: $F_{(1,40)} = 8.14$, $P = 0.007$]. For the PFw condition, response amplitude was significantly larger in lexical (15.4 ± 8 µV) compared with prelexical (10.0 ± 4.3 µV) contacts ($P < 0.005$, permutation test), but this was not the case for NWw condition (lexical, 6.7 ± 2.8 µV; prelexical, 6.6 ± 3.1 µV; $P = 0.89$). Both the interaction and the lack of amplitude increase in the NWw condition indicate that the difference between prelexical and lexical contacts does not merely result from a general amplitude increase in all conditions. Rather, prelexical and lexical contacts appear to reflect functionally different word discrimination processes.

This conclusion is further supported by evaluating the relationship between the amplitudes in the PWw and the NWw conditions, separately for prelexical and lexical contacts (Fig. 8*B*). While there is a strong common source of variability in amplitude for both types of contacts (Pearson's $r = 0.52$; Fig. 8*B*), there is an additional source of variability separating lexical from prelexical contacts (i.e., the regression lines fitted to the two groups of contacts are separate and parallel). Hence, principal-component analysis reveals that lexical and prelexical contacts are significantly different along the second principal component ($P = 0.001$), which aligns well with the PWw axis of amplitude variation (i.e., roughly orthogonal to the regression lines in Fig. 8*B*).

Finally, given that NW and PW differ on a number of prelexical variables (bigram frequency, syllabic and consonant–vowel structure, etc.), the observation that in lexical contacts the response amplitude in the NWw condition is not significantly larger than in PWw (0.78-µV difference; 6.7 ± 2.8 vs. 5.9 ± 2.2 µV for NWw and PWw, respectively; $P < 0.07$, permutation test) implies that prelexical processes mostly do not contribute to the responses recorded in the PWw condition on lexical contacts.

No Hierarchical Organization Between Prelexical and Lexical Contacts. Prelexical and lexical responses appear intermingled in the same region in the left fusiform gyrus, at coordinates encompassing the VWFA as identified in fMRI, but also more anteriorly (up to $y = -25$; Fig. 6*B*). There was no statistical difference in the anterior–posterior axis of group average Talairach coordinates between prelexical and lexical contacts (mean ± SD: $y = -37.1 \pm 14.8$ vs. -40.8 ± 11.2; two-tailed permutation test: $P = 0.37$, uncorrected), going against a hierarchical organization at this level. Moreover, no differences were found in the other spatial dimensions ($x = -34.7 \pm 7$ vs. -31.9 ± 5.1, $P = 0.18$; $z = -13.7 \pm 5.5$ vs. -14.9 ± 5.5, $P = 0.45$). In an additional control analysis, we selected only participants who had both prelexical and lexical contacts in the left hemisphere ($n = 5$) and compared the mean coordinates of prelexical contacts to the mean coordinates of lexical contacts within participant. We found no significant difference along any dimensions (x: prelexical minus lexical $= -3.5 \pm 5.4$, $P = 0.25$; y: 11.2 ± 21.5, $P = 0.38$; z: -3.5 ± 8.6, $P = 0.94$). As in previous analyses, this spatial organization was independent of the exact definition of conditions (*SI Appendix*, Fig. S4) and statistical threshold (*SI Appendix*, Fig. S5).

Discussion

By coupling a fast periodic visual stimulation paradigm identifying selective responses objectively (i.e., at a predefined frequency) with intracerebral recordings in a large number of individual brains, our study provides original evidence regarding the functional organization of the human VOTC for reading. Word discrimination responses were measured between words (w) and three types of stimuli: (*i*) pseudofonts (PFw); (*ii*) letter strings that form implausible words, referred to as nonwords (NWw); and (*iii*) letter strings that are plausible words, referred to as pseudowords (PWw). We classified the response from each contact based on the presence (+) or absence (−) of a significant

Table 2. Number of contacts and corresponding number of participants (in parentheses) as a function of word discrimination level

Word discrimination level	Left	Right	Total
Letter	127 (20)	31 (10)	158 (24)
Prelexical	24 (12)	11 (4)	35 (16)
Lexical	18 (9)	1 (1)	19 (10)

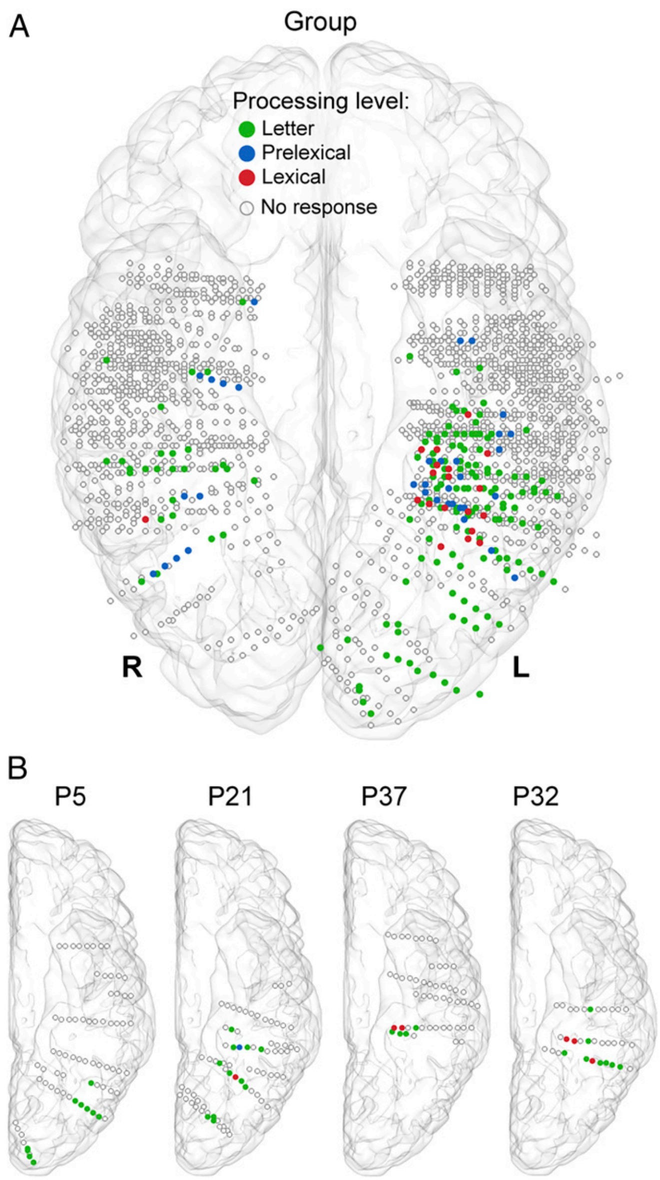

Fig. 5. Spatial organization across the three processing levels. (*A*) Map of all VOTC recording contacts across the 37 patients displayed in the MNI space. Each circle represents a single contact. White-filled circles correspond to contacts at which no word discrimination responses were recorded. Each color-filled circle corresponds to a word discrimination contact colored according to its level of processing. (*B*) Recorded contacts and word discrimination contacts in the left hemisphere of four example individual participants, displayed in MNI space over the Colin27 brain. For visualization purposes in both *A* and *B*, individual contacts are displayed larger than their actual size (2 mm in length).

response to these three types of contrasts: letter-selective (+PFw, −NWw, −PWw), prelexical (+PFw, +NWw, −PWw), and lexical (+PFw, +NWw, +PWw). We found a wide spatial distribution of letter-selective contacts over the VOTC in the left hemisphere. The left midFG, corresponding roughly to the VWFA, emerged from this analysis by the presence of intermingled significant prelexical and lexical contacts, which were found only in the anterior VOTC region. These findings have important implications for understanding the neural basis of reading.

Left Posterior Selectivity to Letters. The large coverage of the bilateral VOTC with intracerebral electrodes reveals widely distributed selective responses to letter strings in the left hemisphere (Figs. 3, 5, and 6). However, the proportion of letter-selective responses with respect to the number of recorded contacts clearly indicates the dominance of a left posterior region, the inferior occipital gyrus, in selective letter representation (Fig. 6). This finding contrasts with studies in which pseudofonts generate as much activation as letter strings in these posterior regions (e.g., ref. 10). In the RH, there were only few, scattered, responses in the midFG, with no response in posterior regions. Although sampling was limited in the right posterior cortex, these observations suggest an early (i.e., in terms of visual hierarchy) left-lateralized selective tuning to letters in the occipital cortex (18) rather than a posterior bilateral representation (7).

In the left hemisphere, there was a postero-anterior hierarchy between letter-selective and (pre)lexical responses. This is congruent with fMRI measures, in which posterior regions selective to letter shapes (i.e., words among pseudofonts) do not respond to words among alphabetic characters (7, 10). The maximal local proportion of letter-selective responses has been shown in the left IOG, in a region corresponding to a previously located "letter area" (18). In that study, participants had to perform a semantic task potentially triggering a shallower processing of nonmeaningful pseudofonts compared with letter strings. In contrast, in our study, there was no explicit reading task to extract the meaning of the presented strings. Hence, we provide original evidence that letter selectivity is triggered automatically in this left posterior region, even when letters appear for a brief time—less than 100 ms—among pseudofonts.

Our finding of a letter-selective brain region indicates that letters are processed specifically, independently of words, in the

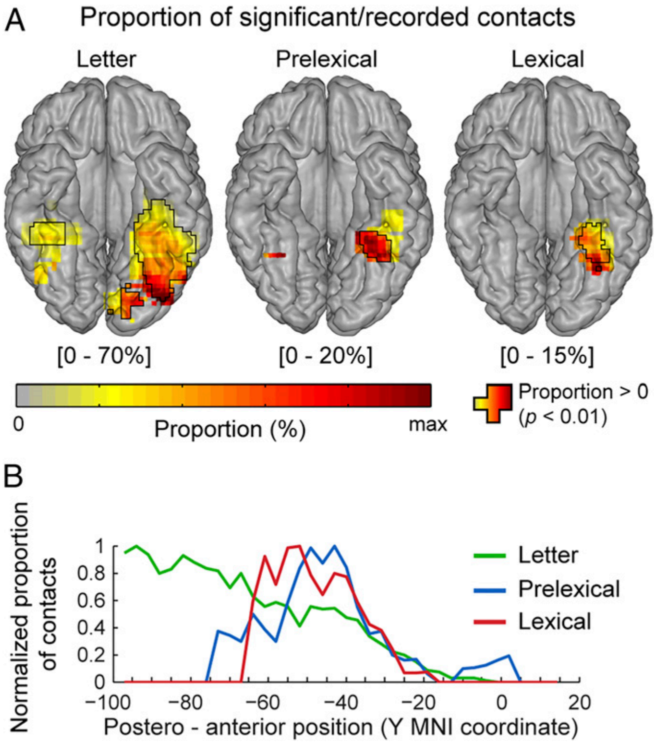

Fig. 6. Spatial dissociation between word processing levels. (*A*) VOTC maps of the local proportion of significant contacts over recorded contacts shown in MNI space for each word processing level. The color scale was adjusted for each map (see scaling values between brackets below each map). Black contours outline proportions significantly above zero. Note that, for letter contacts, the proportion is smaller in the midFG region than in posterior VOTC regions due to the far greater number of recorded (nonsignificant) contacts in the midFG. (*B*) The proportion of significant contacts relative to the number of recorded contacts (normalized between 0 and 1) is shown for each word processing level as a function of the position along the *Y* (posterior–anterior) dimension in the left hemisphere. See also *SI Appendix*, Fig. S2.

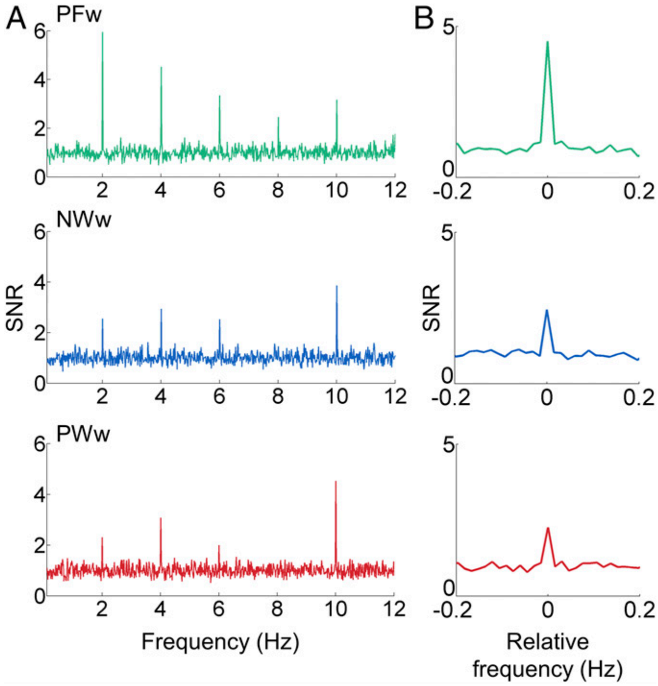

Fig. 7. SEEG lexical responses over the left hemisphere. (*A*) SNR frequency spectra recorded over the 18 lexical contacts in the left hemisphere for the PFw (top row), NWw (middle row), and PWw (bottom row) conditions. Raw FFT spectra were first averaged across the 18 lexical contacts separately for each condition and then transformed to SNR (as the ratio of the amplitude at the frequency bin of interest to the averaged amplitudes at neighboring bins). (*B*) Data from *A* replotted as summed-harmonic segmented FFT spectra (summed FFT spectra were averaged across the 18 lexical contacts separately for each condition and then transformed to SNR).

cortical hierarchy of reading. During reading acquisition, letters are first learned in isolation, that is, as single symbols representing specific phonemes, leading to an early left hemispheric lateralization in their cortical representation (30). Letters may be combined into syllables, morphemes, and words, and new combinations of letters may be encountered throughout the lifetime as new words. The independent representation of letters from words is supported by neuropsychological case studies of pure alexia, where patients cannot read words "at a glance" but can still recognize and name letters one by one (33, 34).

Another finding of the current study is that letter-selective responses were found up to the middle and even anterior FG, with a progressive decrease in proportion, not magnitude, of responses along the posterior–anterior axis (Fig. 6). This suggests that, while letters are selectively coded in the left posterior VOTC, this process extends in a distributed network of regions and overlaps with higher-level processes in anterior VOTC. This is consistent with the greater selectivity for words vs. pseudofonts even in anterior ventro-temporal regions in fMRI (e.g., refs. 10 and 13). Such larger responses to words (vs. pseudofonts) in these anterior regions have been interpreted as showing higher selectivity for increasingly large segments of letter strings (7, 10), or as reflecting phonological or semantic feedback (32, 35). Here, our data reveal letter selectivity even in anterior regions of the VOTC: on the very same contacts, words may not be distinguished from other alphabetic strings.

Identification of the Visual Word Form Area in Intracerebral Recordings. In our cartography of the VOTC, the left midFG showed the largest letter-selective response in amplitude across all significant contacts (*SI Appendix*, Table S2) and, most importantly, showed significant responses to words among other alphabetic strings (nonwords or pseudowords). This region corresponds relatively well to the VWFA as found in fMRI. While previous intracranial studies did not identify this region (17), or targeted directly and solely the midFG (28), it emerges here from our sampling of the whole VOTC with direct intracerebral recordings. While the range of coordinates of the region found here overlaps with the VWFA, the average coordinate is slightly anterior ($y \simeq -40$) to the VWFA as typically defined in fMRI (e.g., $y \simeq -54$ in ref. 3), with individual electrode contacts up to $y = -25$ here (Fig. 6*B*). As presented in the Introduction, this difference may be due to difficulties in recording the anterior section of the VOTC in fMRI due to large magnetic susceptibility artifacts (4). This observation further illustrates the additive value of human brain mapping with intracerebral recordings, in particular with a large sample of participants, a wide spatial coverage, and objective quantification of significant responses as afforded by EEG frequency tagging (31).

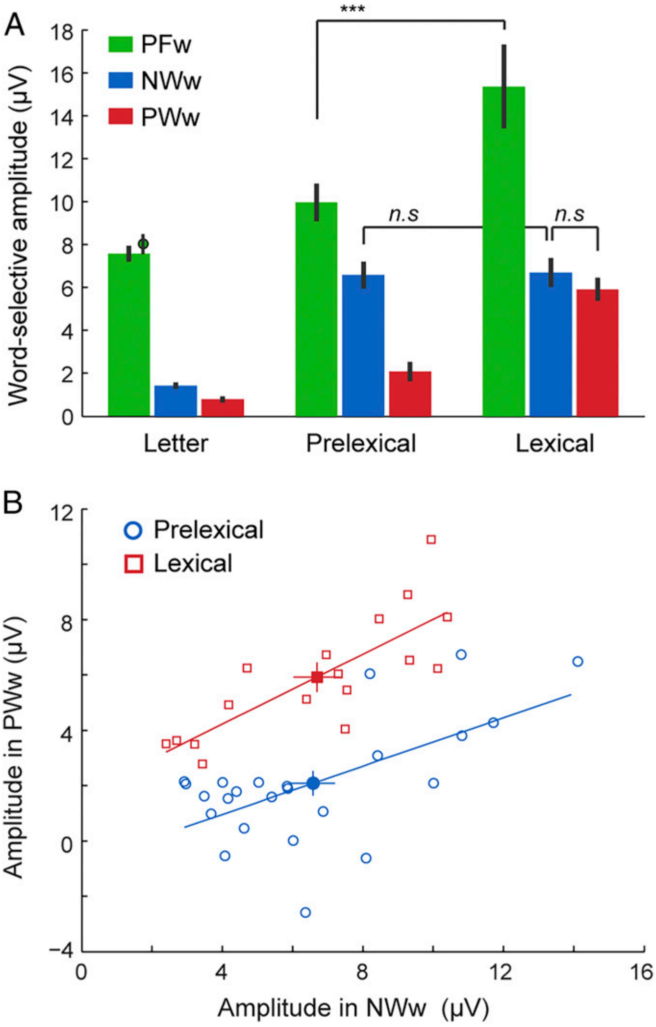

Fig. 8. Amplitude quantification across conditions and processing levels. (*A*) Response amplitudes were quantified as the average of the amplitudes across recording contacts, separately for each processing level (letter, prelexical, and lexical) and each condition (PFw, NWw, and PWw). The additional data point over the left-most column represents the averaged response amplitude over contacts located in the same anatomical regions as the prelexical and lexical contacts (latFG, medFG, antFG, antOTS, and antCoS). (*B*) Relationship between the amplitude in the PWw and the NWw conditions, separately for the prelexical and the lexical recording contacts. Each white-filled point is a single contact, and the mean across contacts is shown as filled markers. Lines represent the least-square linear fit computed separately for prelexical and lexical contacts. Error bars are the SEM.

An Objective Lexical Representation in the Left midFG. First, we found strong evidence for neuronal populations in the left midFG sensitive to familiar, known words, supporting visual lexical representations of written words. Whether the VWFA, and the VOTC in general, hold visual lexical representations is the matter of a long-standing debate in the scientific reading community. On the one hand, the VWFA is thought to compute abstract but prelexical representations (3, 7); on the other hand, it is thought to be tuned for whole-word forms and to discriminate words differing only by one letter (24, 25, 28). The present observations provide original and direct evidence supporting the latter view. Second, despite a wide sampling of the VOTC, including the most anterior ventral temporal regions, significant lexical responses were found almost exclusively in the left midFG (i.e., including the location of the VWFA), highlighting the fundamental role of this local region in reading. Note that this conclusion also holds even when lowering the statistic threshold (*SI Appendix*, Fig. S5) and when including response patterns that do not obey our strict criterion of significance for the three contrasts (*SI Appendix*, Fig. S4). Indeed, a number of additional contacts show responses to words only when presented among letter strings but not among pseudofonts (*SI Appendix*, Table S1). These contacts could potentially reflect more subtle processes, for example, selectivity to word forms only in the context of letters, that is, when a baseline level of activity is sufficiently high.

Both the large number of highly variable word and pseudoword stimuli used in the present study, and the strict control of stimuli in which pseudowords shared the same letters as words in a rearranged order (*Materials and Methods* and ref. 29) rule out an account of lexical responses in the midFG in terms of mere physical differences between words and pseudowords. This is supported by the lack of lexical responses in posterior visual regions sampled in this study. Moreover, although words and pseudowords differed in bigram frequency (*Materials and Methods*), and this factor can modulate VWFA activity in fMRI (36), lexical responses in this paradigm are unlikely to be related to this, for several reasons. First, in scalp EEG, the robust selective response over the left occipito-temporal cortex for words inserted in pseudowords is not reduced when bigram frequency is equated (29). Moreover, directly contrasting pseudowords differing significantly in bigram frequency does not lead to any EEG activity (29). Obviously, this does not completely rule out putative effects of bigram frequency inside the brain that would not be captured on the scalp. In this context, however, there is evidence that lexical contacts in the present intracerebral study do not show a modulation of the response according to bigram frequency. Specifically, while the difference in bigram frequency with words is much higher for NW (7,387 ± 3,291) than PW (2979 ± 4014), NWw responses are not significantly larger than PWw responses in lexical contacts (Fig. 8*A*). Finally, a complementary analysis (*SI Appendix*, Fig. S6) shows that the modulation of bigram frequency in different PWw sequences does not correlate with the response amplitude in these sequences.

Given the high stimulus presentation rate (10 Hz) as well as the forward and backward masking provided by the stimuli in the sequence (Fig. 1), we would like to argue that word selectivity effects found here likely reflect neural coding for visual word forms rather than integration of an abstract visual form with higher-order factors stemming from putative feedback from anterior language areas (32, 37). Supporting this view, we found no evidence of representations of letters and words anteriorly to the midFG in the left VOTC, contrary to intracranial findings with a slower stimulus presentation rate, revealing late semantic effects (17). Future studies could examine this issue further by defining the timing of lexical effects in the VOTC. This investigation is possible with the approach used here (e.g., see ref. 38) but requires inserting more stimuli between word items, reducing SNR as word repetition decreases in a given sequence length.

Interestingly, the contacts classified as lexical discriminate words from nonwords and pseudowords with a similar range of response amplitudes (Fig. 8). This result argues against additive processing stages (i.e., prelexical then lexical) at different time points, or parametrically modulated sensitivity to orthographic structure. Indeed, both of these modes of processing would have generated larger responses to words in the NWw than in the PWw condition in lexical contacts. Rather, in these left midFG populations of neurons classified as lexical, whole-word recognition is relatively independent of the letter strings' plausibility context.

Since responses to words among nonwords (NWw) are not larger in lexical than prelexical contacts, these contacts do not differ only quantitatively, that is, by a generally larger response in lexical contacts. However, the larger response to words among pseudofonts on these lexical contacts suggests that neuronal populations tuned to lexical representations could be less activated by nonletters. These representations could therefore reflect a recognition pattern within an orthographic memory system (26) or a storage of whole-word forms, that is, a lexicon (24, 25, 39). Such a unique visual coding of individual words, allowing fast recognition processes, is necessary for fluent reading. This is consistent with neuropsychological studies showing that lesions in the left midFG cause deficits in word reading, leading to slow and effortful letter-by-letter reading (2, 34, 40, 41).

Nonhierarchical Spatial Prelexical and Lexical Representations. Finally, a crucial finding of our intracerebral recording study is that different levels of word processing appear intermingled in the same region of the midFG: besides the lexical responses identified, some contacts responded to words among orthographically implausible nonwords (i.e., prelexical response) and not to words among pseudowords, without a clear spatial hierarchy between the two types of contacts (Fig. 5). This finding—which also holds when lowering the statistic threshold (*SI Appendix*, Fig. S5) and when including contacts that do not conform to the three strict combinations of conditions to define the three processing levels (*SI Appendix*, Fig. S4)—does not support the proposal of strict successive stages for the coding of letters, bigrams, and quadrigrams at specific positions along the *y* axis [$y = -64$, -56, and -48 respectively; LCD model (7)]. Indeed, according to this view, lexical contacts should have been located, on average, more anteriorly than prelexical contacts. Also, many contacts with the largest responses in the NWw condition did not discriminate words among pseudowords, ruling out a simple explanation in terms of magnitude of response (Fig. 8). Rather, responses to words at a prelexical level only may be considered as indirect evidence for responses to pseudowords: populations of neurons that are sensitive to the plausibility or statistical regularity of letter combinations rather than to letter strings previously encountered, that is, whole-word forms.

Both the spatial organization of prelexical and lexical contacts and the absence of additivity of responses in lexical contacts strongly suggest that prelexical processes and lexical processes are functionally separated (Fig. 8*B*) rather than constituting ordered additive, spatially hierarchical, stages in visual word recognition. Hence, within the midFG region, distinct neuronal populations compute different levels of representation of words: a letter-selective representation coding for abstract letters; a coarse word representation sensitive to visual characteristics such as plausibility of letter combinations; and a precise, fine-grained representation where neurons have become tuned to previously encountered words. This finding was afforded by our approach of intracerebral recordings where each electrode contact records electrophysiological responses from a limited neuronal population, compared with commonly used fMRI analyses where spatial smoothing and region-of-interest approach average responses originating potentially from different neuronal populations.

In summary, our large-scale intracerebral recording study with fast periodic visual stimulation clarifies the neural basis of reading by revealing (*i*) a spatial dissociation in the left VOTC between a posterior IOG/FG letter-selective representation, and a representation for words, at prelexical and lexical levels, confined to the middle and anterior section of the left fusiform gyrus; (*ii*) true lexical responses, that is, fine-tuning to real words, in a region extending more anteriorly than the visual word form area typically identified with fMRI; (*iii*) prelexical responses suggesting sensitivity to the statistical regularity of letter combinations only; and (*iv*) a lack of spatial organization between qualitatively distinct prelexical and lexical responses in the left fusiform gyrus.

Materials and Methods

Participants. The study included 37 native French-speaker participants (20 females; mean age, 33 ± 8.4 y; 35 right-handed) undergoing clinical intracerebral evaluation with depth electrodes (SEEG) (42) for refractory partial epilepsy, studied in the Epilepsy Unit of the University Hospital of Nancy between September 2013 and June 2016. Participants with at least one intracerebral electrode implanted in the VOTC were included in the study (Fig. 1*C*). They gave written consent to participate to the study, which was approved by the Ethics Committee of the University Hospital of Nancy.

Intracerebral Electrode Implantation and Recording. Intracerebral electrodes were stereotactically implanted within the participants' brains for clinical purposes, that is, to delineate their seizure onset zones (43). Each 0.8-mm diameter intracerebral electrode contains 8–15 independent recording contacts of 2 mm in length separated by 1.5 mm from edge to edge (for details about the electrode implantation procedure, see ref. 44). Intracerebral EEG was sampled at a 512 Hz and referenced to either a midline prefrontal scalp electrode (FPz, in 32 participants) or an intracerebral contact in the white matter (in five participants).

Fast Periodic Visual Stimulation Paradigm. The paradigm was previously validated in a scalp EEG study (29).

Stimuli. Stimuli were words, pseudowords, nonwords, and pseudofonts (30 of each type), all composed of five elements (letters or pseudofonts) (Fig. 1*A*). French words were selected from the Lexique 3.55 database (45) with the following criteria: they were frequent common nouns (84.99 per million) in singular form, with limited orthographic neighbors (average, 1.9; range from 0 to 4), no foreign language origin, and no accents. PW and NW were built on an item-by-item basis by rearranging the letters of the words [e.g., from the word "avril" ("April") were built the PW "vrali" and the NW "rvlia"]. PF items were also built on an item-by-item basis: letters from words were vertically flipped, segmented, and segments were rearranged into five pseudoletters with the same overall size as the original word. Each word thus had a corresponding PW, NW, and PF containing the exact same amount of black-on-white contrast, so that all conditions were similar in terms of lower-level visual properties. Bigram frequencies were calculated with Wordgen (46) and are reported as summated type bigram frequencies (from the French CELEX database). As in Lochy et al. (29), bigram frequencies differed between words (mean ± SD: 12,038 ± 3,715) and nonwords [4,650 ± 2,803; $t_{(29)} = 10.665$, $P < 0.0001$] as well as between words and pseudowords [9,059 ± 4,293; $t_{(29)} = 4.485$, $P < 0.0001$]. This was done intentionally to respect natural differences in bigram frequencies. Importantly, however, differences in bigram frequency alone do not contribute to selective responses to words recorded in this paradigm since (*i*) these responses are also found for words among pseudowords equated in bigram frequency and (*ii*) no response emerges when two sets of PWs differing in bigram frequency are contrasted [experiment 2; Lochy et al. (29)]. Stimuli were presented in Verdana font, with the size ranging from 4.8 to 7.7 (width) and 1.15 to 2 (height) degrees of visual angle.

Procedure. Participants viewed continuous sequences of visual stimuli (PW, NW, or PF) presented periodically at a rate of 10 Hz through sinusoidal contrast modulation (from 0 to 100% in 50 ms, then back to 0% in 50 ms) with words inserted as every fifth item, so that the word presentation frequency was 2 Hz (10 Hz/5) (Fig. 1*B* and Movies S1–S3). A sequence started by a fixation cross displayed for 2–5 s, followed by 70 s of visual stimulation: 66 s of stimulation at full contrast flanked by 2 s of fade-in and fade-out, wherein contrast gradually increased or decreased, respectively. Randomly selected words were inserted in three different sequences of base stimuli (PF, NW, or PW) resulting in three conditions (Fig. 1*A*): words embedded in PW (PWw; Movie S3), in NW (NWw; Movie S2), and in PF (PFw; Movie S1). Each condition was repeated two times, resulting in six sequences for a total of ∼10 min of testing time, including short breaks. The experiment was repeated a second time for 13 participants and a third time for 3 participants, depending on their availability. Participants were not informed about the periodicity of the words and were unaware of the objectives of the study. No participant had seizures in the 2 h preceding the recordings. During the sequences, participants were instructed to fixate a small blue cross (15 pix) presented continuously at the center of the stimuli, and to detect and respond to (by key press) brief (200-ms) nonperiodic color changes (blue to red, six times per sequence) of this fixation cross.

Intracerebral EEG Analysis. Intracerebral EEG analysis largely followed a procedure of a recently reported group study on the neural basis of selective face perception (31).

Frequency domain processing. Segments of SEEG corresponding to stimulation sequences were extracted, starting 2 s after the onset of the sequence (i.e., after the fade-in period) until ∼68 s (before stimulus fade-out) so as to contain an integer number of 2-Hz cycles (∼66 s). No artifact rejection was performed because intracerebral artifacts (mainly epileptic spikes, but also electro-oculographic and electro-myographic activity, since we used a prefrontal scalp electrode as reference electrode for most of the participants) are more broadly distributed across the frequency spectrum than the frequencies of interest (i.e., 2 Hz, 10 Hz, and their respective harmonics). Sequences were averaged in the time domain separately for each condition and each participant, and amplitude spectrum was computed for each contact using FFT.

Word discrimination responses. Word discrimination responses significantly above noise level at the word stimulation frequency (2 Hz) and its harmonics were determined in each condition as follows: (*i*) the FFT spectrum was cut into segments centered at the word response frequency and the four first harmonics, that is, 2, 4, 6, and 8 Hz (10 Hz corresponds to the base visual stimulation frequency and was not included in the analyses; no word discrimination responses were found above 10 Hz), and surrounded by 25 neighboring bins on each side (Fig. 2*A*); (*ii*) the amplitude values of these four FFT segments were summed (Fig. 2*B*); (*iii*) the summed FFT spectrum was transformed into a *Z* score (Fig. 2*C*). *Z* scores were computed as the difference between the amplitude at the word frequency bin and the mean amplitude of 48 surrounding bins (25 bins on each side, excluding the 2 bins directly adjacent to the bin of interest, i.e., 48 bins) divided by the SD of amplitudes in the corresponding 48 surrounding bins. A contact was considered as showing a word discrimination response in a given condition if the *Z* score at the frequency bin of word stimulation exceeded 3.1 (i.e., $P < 0.001$, one-tailed: signal > noise).

Levels of word discrimination contacts. Based on the pattern of word discrimination responses across the three conditions (i.e., significant or not), we labeled each contact according to three hierarchical levels of word discrimination: (*i*) contacts showing a significant word discrimination response only when presented among pseudofonts, that is, not in the NWw and PWw conditions, were defined as letter selective (+PFw, −NWw, and −PWw); (*ii*) contacts showing significant responses in the PFw and NWw conditions but not in the PWw condition were defined as prelexical (+PFw, +NWw, and −PWw); and (*iii*) contacts showing significant responses in the three conditions (PFw, NWw, and PWw) were defined as lexical (+PFw, +NWw, and +PWw). These three types of contacts are referred to as word discrimination contacts. Contacts that displayed a significant response in at least one condition but that did not conform to any of these three combinations of conditions (e.g., exhibiting a significant response in PWw and NWw conditions but not in more basic PFw condition) were excluded from the main analyses (*SI Appendix*, Fig. S4 and Table S1). Note that the three word processing levels result from combining an increasing number of significant conditions (1–3), resulting in a stricter statistical criterion (thus a different likelihood of false positives) across the three levels. Because these conditions are not statistically independent, one cannot solve this issue by simply adapting the statistical threshold according to the number of tests performed. This issue is not present when including all contacts responding to at least one condition and labeling these contacts according to a single test (*SI Appendix*, *Supplemental Analysis* and Fig. S4).

Quantification of response amplitude. Baseline-corrected amplitudes were computed as the difference between the amplitude at each frequency bin and the average of 48 surrounding bins (i.e., 50 bins, excluding the 2 bins directly adjacent to the bin of interest, i.e., 48 bins). Word discrimination responses were quantified as the sum of the baseline-subtracted amplitudes at the word frequency from the first until the fourth harmonic (2 Hz until 8 Hz) (38), and averaged for each condition and contact type. We removed a single outlier lexical contact in which the response amplitude in each condition was more than 3 SDs away from the mean. SNR spectra were also calculated as the ratio between the amplitude at each frequency bin and the average of the corresponding 48 surrounding bins for display purposes and comparison across studies.

Contact Localization in the Individual Anatomy. The exact position of each contact in the individual anatomy was determined by fusing the post-operative CT scan with a T1-weighted MRI. Contacts inside the gray matter were anatomically labeled in the individual anatomy using the same topographic VOTC parcellation as in ref. 32 (*SI Appendix*, Fig. S1), based on anatomical landmarks. Major VOTC sulci (collateral sulcus and occipito-temporal sulcus) served as medio-lateral divisions. Postero-anterior divisions were the anterior tip of the parieto-occipital sulcus for the border between occipital and temporal lobes, and the posterior tip of the hippocampus for the border between PTL and ATL.

Group Visualization and Proportion Analyses in MNI Space. In a separate analysis, anatomical MRIs were spatially normalized to determine Talairach and MNI coordinates of intracerebral contacts. MNI coordinates of the intracerebral contacts were used to perform group analyses and visualization. Using MNI transformed coordinates, we computed the local proportion of word discrimination intracerebral contacts across the VOTC. Local proportion of contacts was computed in volumes (i.e., "voxels") of size 15 × 15 × 100 mm (for the *X*, left–right; *Y*, posterior–anterior; and *Z*, inferior–superior dimensions, respectively) by steps of 3 × 3 × 100 mm over the whole VOTC. A large voxel size in the *Z* dimension was used as a way to collapse across contacts along the inferior–superior dimension.

For each voxel, we extracted the following information across all participants in our sample: (*i*) the number of recorded contacts located within the voxel; (*ii*) the number of contacts showing a significant response for each level of word discrimination; (*iii*) the number of participants having at least one contact recorded in the voxel; and (*iv*) the number of participants having at least one contact showing a significant word discrimination response. From these values, for each voxel and each level of word discrimination, we computed the proportion of significant contacts/participants over recorded contacts/participants (proportions are crucial here since sampling differs across regions). To ensure reliability and reproducibility, we only considered voxels in which at least two participants showed significant responses. Then, for each voxel, we determined whether the proportion of significant contacts was significantly above zero using a bootstrap procedure in the following way: (*i*) sampling contacts from the voxel (the same number as the number of recorded contacts in the voxel) with replacement; (*ii*) determining the proportion of significant contacts for this bootstrap sample and storing this value; (*iii*) repeating steps *i* and *ii* 5,000 times to generate a distribution of bootstrap proportions and to estimate the *P* value as the fraction of bootstrap proportions equal to zero. In addition, we also statistically compared proportions of word discrimination contacts across corresponding voxels of the left vs. right hemisphere using permutation tests with 20,000 permutations.

We also visualized the variations in the proportions of contacts in each word processing level as a function of the posterior–anterior axis (*Y* dimension) in the left hemisphere. Proportions were computed along the *Y* dimension (MNI coordinates) using a running average procedure (in segments of 15 mm by steps of 3 mm) by collapsing contacts across the *X* (lateral–medial) and *Z* (inferior–superior) dimensions. The resulting proportion profiles were normalized between 0 and 1.

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