

Word or Word-like? Dissociating Orthographic Typicality from Lexicality in the Left Occipito-temporal Cortex

Anna M. Woollams¹, Giorgia Silani², Kayoko Okada³,
Karalyn Patterson⁴, and Cathy J. Price³

Abstract

■ Prior lesion and functional imaging studies have highlighted the importance of the left ventral occipito-temporal (LvOT) cortex for visual word recognition. Within this area, there is a posterior–anterior hierarchy of subregions that are specialized for different stages of orthographic processing. The aim of the present fMRI study was to dissociate the effects of subword orthographic typicality (e.g., *cider* [high] vs. *cynic* [low]) from the effect of lexicality (e.g., *pollen* [word] vs. *pillen* [pseudoword]). We therefore orthogonally manipulated the orthographic typicality of written words and pseudowords (nonwords and pseudohomophones) in a visual lexical decision task. Consistent with previous studies, we identified greater activation for pseudowords than words (i.e., an effect of lexicality) in posterior LvOT cortex. In addition,

we revealed higher activation for atypical than typical strings, irrespective of lexicality, in a left inferior occipital region that is posterior to LvOT cortex. When lexical decisions were made more difficult in the context of pseudohomophone foils, left anterior temporal activation also increased for atypical relative to typical strings. The latter finding agrees with the behavior of patients with progressive anterior temporal lobe degeneration, who have particular difficulty recognizing words with atypical orthography. The most novel outcome of this study is that, within a distributed network of regions supporting orthographic processing, we have identified a left inferior occipital region that is particularly sensitive to the typicality of subword orthographic patterns. ■

INTRODUCTION

Like most “objects” in our visual world, written words have component parts: characters, which in alphabetic written languages correspond to letters. Even more than most other visual objects (e.g., faces), written words are composed of the same component parts occurring again and again in different, but sometimes highly similar, combinations (in English, e.g., *attitude*, *altitude*, *aptitude*). For reading to be a useful real-time activity, its practitioners need to acquire skill in rapid and accurate identification of written words without confusing one letter with another so that the correctly recognized letter sequence can quickly activate representations beyond orthography per se, especially those encoding phonological and semantic information. This article concerns the neural mechanisms that underpin the skill of visual word recognition with particular reference to characteristics of component parts.

The ease of recognizing a whole object is strongly affected by the frequency or familiarity of combinations of its components. This feature of written words is sometimes called orthographic typicality and is usually measured by the summed frequency of pairs or triplets of letters (bigrams or trigrams, respectively). As words are by definition more

familiar than pseudowords, the frequency of their components and hence their orthographic typicality will naturally tend to be higher (i.e., more wordlike). It is therefore important to manipulate orthographic typicality independently of lexicality (i.e., word or pseudoword). For example, in one of the tasks most often employed to assess word recognition, visual lexical decision, high orthographic typicality usually facilitates correct “yes” decisions to letter strings that are real words and slows correct “no” decisions to letter strings that are pseudowords (Holcomb, Grainger, & O’Rourke, 2002; Forster & Shen, 1996; Sears, Hino, & Lupker, 1995).

Apart from careful design of stimulus materials, one way to try to separate the impact of variables that are correlated in the natural world is functional brain imaging. Lexicality (is it a real word or not?) is a feature of a whole letter string whereas orthographic typicality can be considered a feature of subcomponents of the string (how frequent are the bigrams and trigrams?). One might therefore expect to observe the effects of these two features in different brain regions. Furthermore, one might expect typicality, relative to lexicality, to reveal its impact earlier in the sequence of processing stages, which in visual recognition means in a more posterior part of the ventral occipito-temporal stream.

The importance of the left ventral occipito-temporal (LvOT) cortex for fast parallel letter recognition was first identified in studies of patients with pure alexia after stroke,

¹University of Manchester, UK, ²University of Zurich, Switzerland,
³University College London, UK, ⁴University of Cambridge, UK

who have lesions in this region (or more typically in more medial OT areas that disconnect this region from visual input) and whose poststroke reading is slow, error prone, and strongly modulated by word length (Mycroft, Behrmann, & Kay, 2009; Leff, Spitsyna, Plant, & Wise, 2006; Cohen et al., 2003; Behrmann, Nelson, & Sekuler, 1998). Neuroimaging studies of healthy subjects have also consistently identified LvOT activation during visual word recognition, spatially localizing the effect to the vicinity of the left occipito-temporal sulcus, which lies between the fusiform gyrus and the lateral inferior temporal cortex. Within LvOT cortex, posterior activation ($y > -60$ mm in MNI space) has been associated with prelexical processing, whereas more anterior activation ($y = -45$ mm in MNI space) is thought to correspond to lexical or semantic processing (Seghier, Lee, Schofield, Ellis, & Price, 2008; Vinckier et al., 2007; Price & Mechelli, 2005; Dehaene et al., 2004). Other than this gross posterior–anterior anatomical distinction, however, the functional subdivisions in LvOT cortex remain unknown (Vinckier et al., 2007). In particular, there are debates as to which parts of the system are involved in prelexical versus lexical processing (Bruno, Zumberge, Manis, Lu, & Goldman, 2008; Kronbichler et al., 2004, 2007; Dehaene, Cohen, Sigman, & Vinckier, 2005; Dehaene et al., 2004). The aim of this study was to investigate the roles of different parts of LvOT cortex in orthographic processing. More specifically, we asked: Is there a region within LvOT cortex that is particularly sensitive to the typicality of orthographic patterns in written letter strings, irrespective of their lexicality?

Dehaene et al. (2005) have proposed a theoretical model of how the posterior-to-anterior gradient in the occipito-temporal pathway is progressively tuned to detect familiar letters, groups of letters, graphemes, syllables, morphemes, or even entire words, as processing moves anteriorly. Support for this local combination detector (LCD) model was provided by Vinckier et al. (2007): For passive viewing of stimuli with letter combinations that gradually increased in their approximation to familiar words, they reported a posterior-to-anterior progression of increasing selectivity to more word-like stimuli. Although there was more activation over the whole set of LvOT areas for frequent letters than infrequent letters and for frequent quadrigrams than frequent bigrams, there was no evidence for discrete regions that might reflect the demands on prelexical processing (i.e., more activated for processing of infrequent letter combinations).

The effect of orthographic familiarity has been investigated by assessing activation for familiar words relative to carefully matched sets of pronounceable pseudowords that either do or do not sound like words (e.g., *elboe* vs. *zebro*). In a task that required participants to decide if the pronunciation of the letter string sounded like a real word, two independent studies reported significantly higher activation for pseudohomophones and nonwords than for familiar words in LvOT cortex (at $[x = -48, y = -60, z = -18]$ in Kronbichler et al., 2007, and at $[x = -44, y = -53, z = -13]$ in Bruno et al., 2008). Both sets of authors argued

that, in this context, activation reflects word-specific orthographic processing that is higher when orthography is unfamiliar because of a longer search for missing representations. If this interpretation is correct, then the LCD model (Vinckier et al., 2007; Dehaene et al., 2005) would predict that prelexical orthographic processing should occur in LvOT areas that are posterior to lexical processing at $y = -60$.

In contrast to the interpretation of LvOT cortex as an orthographic lexicon (Kronbichler et al., 2007), Dehaene et al. (2004) have associated this region (also called the visual word form area) with prelexical letter processing, and Devlin, Jamison, Gonnerman, and Matthews (2006) with abstract visual form processing that is guided by top-down influences from other word recognition areas. Clearly then, there is by no means a unanimous assignment of function to the LvOT cortex. A further potential source of confusion is that activation in LvOT cortex is consistently associated with longer response times. For example, in the studies by Bruno et al. (2008) and Kronbichler et al. (2007), the longer response times for pseudohomophones and nonwords than familiar words might reflect more difficulty in translating unfamiliar orthographic patterns to phonology or, in Devlin et al. (2006), RT differences might indicate more successful top-down predictions of the visual form when the stimulus has familiar versus unfamiliar orthography. To summarize, the same LvOT region (at $y \approx -60$) has been associated with lexical (Bruno et al., 2008; Kronbichler et al., 2007), prelexical (Dehaene et al., 2004), and visual form processing (Devlin et al., 2006).

The principal manipulation in the current study was orthographic typicality as defined by the frequencies of letter bigrams. Because this variable concerns subword components, it can be used to probe prelexical orthographic processing within nonword letter strings. Binder, Medler, Westbury, Liebenthal, and Buchanan (2006) found increased LvOT activation (in the vicinity of $y = -60$) when participants detected visual features in letter strings with bigram frequencies that were high (e.g., *cemng*) relative to low (e.g., *zsvvb*). In contrast, using ERPs and a lexical decision task, Hauk et al. (2006) manipulated orthographic typicality and lexicality independently and demonstrated stronger LvOT activation (ERP, hence no precise coordinates) when participants made lexical decisions on words or pseudowords that had atypical (ghost/ghove) versus typical (grove/grost) orthographic patterns. The results reported by Binder et al. and Hauk et al. therefore confirm the relevance of LvOT cortex to orthographic processing but disagree in whether activation is greater for atypical or typical letter combinations. This discrepancy could be related to the use of different tasks and stimuli (visual feature detection on letter strings vs. lexical decision on words and pseudowords; predominantly unpronounceable letter strings vs. universally pronounceable nonwords and pseudohomophones). It is also important to note, however, that ERP studies do not have the spatial resolution to identify the exact source of the effect. We

therefore conducted a similar study to that of Hauk et al., using fMRI to localize the source of increased activation for atypical orthography.

The ERP study reported by Hauk et al. (2006) also suggested that top-down influences from the left anterior temporal cortex are particularly recruited in the recognition of words with atypical orthography. Atypical orthographic strings differentially activated LvOT cortex at 100 msec, followed by an interaction between typicality and lexicality with an estimated source in left anterior temporal cortex at 160 msec and then a main effect of lexicality (which is presumably the signal used to inform lexical decision) at 200 msec in LvOT cortex. Hence, it would seem that feedback from left anterior temporal cortex to LvOT cortex may differentially support the recognition of words with atypical versus typical orthography. This outcome is furthermore consistent with neuropsychological evidence: Patients with semantic dementia (Hodges, Patterson, Oxbury, & Funnell, 1992; Snowden, Goulding, & Neary, 1989), who have relatively selective atrophy of the anterior temporal lobes, perform well in two-alternative forced-choice visual lexical decision when the word choice is more orthographically typical than the nonword (e.g., *flute* vs. *fluit*) but poorly when the orthographic characteristics of the two choices are reversed (e.g., *fruit* vs. *frute*) (Patterson et al., 2006; Rogers, Lambon Ralph, Hodges, & Patterson, 2004).

The current fMRI study aimed to investigate further the effect of orthographic typicality on the visual word recognition processes that support lexical decision. On the basis of findings from Hauk et al. (2006) and Rogers et al. (2004), we expected increased activation for words with atypical versus typical orthography in posterior LvOT cortex and the left anterior temporal lobe. The higher spatial resolution of fMRI compared with ERP and lesion studies should allow us to determine the precise location of this orthographic typicality effect.

Our experimental design systematically manipulated the effect of atypical versus typical orthography in words and pseudowords under two different contexts where the foils were either pronounceable nonwords that did not sound like real words (e.g., *sprent*) or pseudohomophones that did sound like real words (e.g., *streek*). Lexical decision is more difficult in the context of pseudohomophones because the lexical status of the orthography is inconsistent with the lexical status of the phonology (Pexman & Lupker, 1999; Joordens & Becker, 1997; Borowsky & Masson, 1996; Shulman & Davidson, 1977). We therefore predicted that the pseudohomophone context would recruit other sources of information, particularly semantic (Plaut, 1997), in making lexical decisions.

METHODS

Participants

Fifteen healthy young adults with normal (or corrected-to-normal) vision participated in this study. All were right-

handed fluent English speakers, and none had any history of dyslexia. Subsequently, four participants were excluded as they made more than 30% errors in any given condition and/or more than 15% errors over all conditions. This accuracy inclusion criterion ensured that there were sufficient correct trials for each condition for each participant to compute reliable activation means for the imaging analyses. The remaining 11 participants had a mean age of 26 years; 6 participants were women.

Experimental Design

The design consisted of eight conditions that orthogonally manipulated lexicality (words vs. pseudowords) and orthographic typicality (atypical vs. typical), under two contexts: Pseudowords were either pseudohomophones that sounded like words or nonwords that did not sound like words. Participants were instructed to indicate, with a two choice keypress response, whether the stimulus was a word or not. The right index finger indicated “word” responses, and the right middle finger indicated “nonword” responses. We emphasized the importance of accuracy within the fixed 3-sec interstimulus onset interval.

Stimuli

There were 24 items per cell (a full listing of stimuli is available in Appendix I of the Supplementary Materials). Orthographic typicality was quantified in terms of type positional bigram frequency (PBF) as given by the McWord on-line database (Medler & Binder, 2005), which produces values based upon the CELEX lexical database (Baayen, Piepenbrock, & van Rijn, 1993). Typical strings had a type PBF of over 324, whereas atypical strings had a type PBF of below 106. Effectively, this means that the component letter pairs of the typical items occurred in the same position in more than 324 words in the database, whereas the component letter pairs of the atypical items occurred in the same position in fewer than 106 words in the database.

There were two sets of typical and atypical words, one matched to the typical and atypical nonwords (e.g., *breed* became *breeel*; *smirk* became *smirp*) and the other matched to the typical and atypical pseudohomophones (e.g., *rinse* became *rince*; *knife* became *knyfe*). This method of stimulus creation ensured that all eight conditions were matched perfectly in terms of number of syllables (mean = 1.82, $SD = 0.701$) and number letters (mean = 6.00, $SD = 0.834$). The values for each condition on a range of psycholinguistic variables are provided in Table 1. A between-items Typicality \times Context ANOVA showed that the four word conditions did not differ significantly on written frequency per million, $F_s(1, 92) < 2.19, p_s > .143$. A between-items Typicality \times Context ANOVA showed that the four nonword conditions did not vary in terms of the number of letters changed from the base word, $F_s(1, 92) < 0.62, p_s > .432$. Between-items Lexicality \times Typicality \times Context ANOVAs on type and token measures

Table 1. Mean (SD) Values for a Range of Psycholinguistic Variables for the Present Stimuli as a Function of Typicality, Lexicality, and Context

	Nonword Set			Pseudobomophone Set					
	Nonwords			Pseudobomophones			Words		
	Atypical	Typical	Words	Atypical	Typical	Words	Atypical	Typical	Words
Written frequency	NA	NA	8.04 (8.25)	11.64 (9.96)	NA	8.45 (9.70)	12.28 (16.82)		
Letters changed	1.17 (0.38)	1.21 (0.42)	NA	NA	1.21 (0.42)	NA	NA		
Type letter frequency	364.4 (134.6)	674.1 (234.9)	388.4 (149.1)	696.7 (233.6)	444.9 (169.2)	381.1 (148.4)	627.8 (218.4)		
Token letter frequency	4495.4 (1717.2)	8248.4 (2219.5)	4669.6 (1649.9)	8570.5 (2585.5)	5158.3 (1980.9)	4414.8 (1867.5)	7618 (2250.5)		
Type bigram frequency	20.5 (10)	88.3 (25.8)	22.1 (9.8)	97.7 (25.4)	22.7 (9.6)	22.3 (10.4)	86.8 (33.4)		
Token bigram frequency	197.7 (154.9)	1461 (826.6)	227.9 (159)	1605.6 (959.6)	233.7 (168.3)	216.7 (124.4)	1384.2 (574.4)		
Type trigram frequency	2.6 (2.4)	14.3 (6.4)	3.5 (2)	16.6 (7.2)	3 (2)	4 (2.4)	12.8 (6.4)		
Token trigram frequency	14.8 (14.1)	213.7 (137.7)	22.7 (17)	237.5 (121.5)	18.6 (25)	26.3 (20.7)	220.9 (135.3)		
Neighborhood size	1 (0.9)	2.3 (2.2)	0.5 (0.9)	2.2 (1.9)	1 (0.5)	0.5 (1)	2 (2.6)		
Neighborhood frequency	5.4 (10.7)	17.8 (30.8)	0.6 (1.3)	21 (32.7)	7.6 (9.9)	1.2 (3.5)	10.5 (18.1)		

of positional letter frequency revealed highly significant main effects of orthographic typicality, $F(1, 184) = 88.58, p < .0005$ and $F(1, 184) = 133.87, p < .0005$, with no other reliable main effects or interactions, $F_s(1, 184) < 2.57, ps > .110$ and $F_s(1, 184) < 1.96, ps > .163$. Analysis of type and token measures of PBF revealed only the desired highly significant main effects of orthographic typicality, $F(1, 184) = 288.83, p < .0005$ and $F(1, 184) = 245.08, p < .0005$, with no other reliable main effects or interactions, $F_s(1, 184) < 0.77, ps > .383$ and $F_s(1, 184) < 1.95, ps > .164$. Analysis of type and token measures of positional trigram frequency revealed highly significant main effects of orthographic typicality, $F(1, 184) = 210.28, p < .0005$ and $F(1, 184) = 198.96, p < .0005$. For the type measure of positional trigram frequency, there were marginally significant main effects of lexicality, $F(1, 184) = 3.10, p = .084$, and context, $F(1, 184) = 3.18, p = .076$, plus a significant interaction between typicality and context, $F(1, 184) = 5.83, p = .017$. There were no other reliable main effects or interactions, $F_s(1, 184) < 0.26, ps > .614$ and $F_s(1, 184) < 0.71, ps > .399$. Finally, analysis of type and token measures of orthographic neighborhood revealed highly significant main effects of typicality, $F(1, 184) = 198.96, p < .0005$ and $F(1, 184) = 198.96, p < .0005$. Borderline significant effects of lexicality were also observed, $F(1, 184) = 3.73, p = .055$ and $F(1, 184) = 3.99, p = .047$, which indicated that, in contrast to stimuli in the majority of visual lexical decision studies, the foils were slightly more word like than the words themselves in terms of the density of their neighborhoods. The token measure also revealed a marginally significant interaction between lexicality and context, $F(1, 184) = 3.10, p = .080$. There were no other reliable main effects or interactions, $F_s(1, 184) < 1.05, ps > .308$ and $F_s(1, 184) < 2.35, ps > .127$.

Procedure

All participants were presented with all items and an equal number of baseline trials, yielding 384 responses in total. Each of the eight conditions was randomly divided into eight sets of three items. Stimuli were presented in blocks of six trials, three of which required a “word” response and three of which required a “nonword” response. Within a block, the type of pseudoword (nonword or pseudohomophone) was held constant, and a pseudoword was never in the same block as its base word (i.e., *breel* and *breed* never occurred in the same block). Across blocks, typicality was fully counterbalanced in eight types of block (typical words with typical pseudowords, typical words with typical pseudohomophones, typical words with atypical pseudowords, atypical words with typical pseudowords, atypical words with typical pseudohomophones, atypical words with atypical pseudowords, and atypical words with atypical pseudohomophones). The order of these eight blocks was randomly determined for each participant, as was the order of items within each block. A further eight blocks of

baseline trials alternated with the eight experimental blocks described above. In the baseline blocks, the task (lexical decision) remained constant but the word stimuli were always displayed as “WORD” and nonword stimuli were always displayed as “XXXX.” Thus, the perceptual and linguistic demands of the task were minimized, but the task set and response were controlled.

All trials were presented in Helvetica 28-point font in white in the center of a black screen for 750 msec, with lexical decision trials appearing in lowercase and baseline trials appearing in uppercase. The fixed ISI was 2980 msec.

MRI Acquisition

Experiments were performed on a 1.5-T Siemens system (Siemens Medical Systems, Erlangen, Germany). Functional T2*-weighted echo-planar images with BOLD contrast comprised 34 axial slices of 2-mm thickness with 1-mm slice interval and 3×3 -mm in-plane resolution. Effective repetition time (TR) was 3.06 sec/volume, echo time = 50 msec, flip angle = 90° . TR and stimulus onset asynchrony did not match, allowing for distributed sampling of slice acquisition across the experiment (Veltman, Mechelli, Friston, & Price, 2002), which provides implicit “jittering.”

The EPI GRE sequence used here was optimized to minimize signal dropout by adjusting the slice tilt, the direction of the phase encoding, and the z-shim moment (for more details, see Weiskopf, Hutton, Josephs, & Deichmann, 2006). Functional scanning was always preceded by 18.36 sec of dummy scans to ensure tissue steady-state magnetization. To avoid ghost-EPI artifacts, image reconstruction was based on a generalized algorithm (i.e., trajectory-based reconstruction after calibrating a trajectory scan during a gel-phantom experiment).

For each participant, we also collected a structural T1-weighted image using a three-dimensional modified driven equilibrium Fourier transform sequence and 176 sagittal partitions with an image matrix of 256×224 and a final resolution of 1 mm^3 (TR/echo time/inversion time = 12.24/3.56/530 msec). This ensured that the participant was neurologically normal and facilitated spatial normalization.

fMRI Data Analysis

Data preprocessing and statistical analyses were conducted in Statistical Parametric Mapping SPM5 (Wellcome Trust Centre for Neuroimaging, London UK, <http://www.fil.ion.ucl.ac.uk/spm/>). All functional volumes were spatially realigned with unwarping (to correct for head motion), spatially normalized to the MNI 152 space (with conversion to 2-mm^3 voxels), and smoothed with an isotropic 6-mm FWHM Gaussian kernel.

First-level statistical analyses performed at an individual participant level were based on a least squares regression analysis using the general linear model in each voxel across the whole brain. Low-frequency noise and signal drift were removed from the time series in each voxel with high-pass

filtering (1/128 Hz cutoff). Residual temporal autocorrelations were approximated by an AR(1) model and removed. We used an event-related analysis for all trials without modeling epochs/block effects (for justification and details, see Mechelli, Henson, Price, & Friston, 2003). There were 13 regressors: 1–8 modeled trials with correct responses to each of the eight experimental conditions; 9–11 modeled incorrect responses to words, nonwords, and pseudo-homophones (irrespective of context); 12 modeled baseline trials with correct responses (summing over both WORD and XXXX trials); and 13 modeled incorrect baseline responses. Each stimulus onset was convolved with a canonical hemodynamic response function (with no dispersion or temporal derivatives).

For each subject, parameter estimates (i.e., beta images) were assessed with least squares regression analysis, and the contrast images (i.e., weighted beta images) were computed for each experimental condition (correct trials only) relative to baseline (correct trials only).

At the second level, we used an ANOVA with eight conditions per subject (each of the eight experimental conditions relative to baseline). This allowed us to look at the main effects of lexicality (pseudowords/words), orthographic typicality (atypical/typical), and context (nonwords/pseudo-homophones). Mean RTs for each subject in each condition were entered as covariates to allow condition-specific effects to be estimated.

Predictions and ROIs

On the basis of both ERP findings reported in a lexical decision study with normal participants (Hauk et al., 2006) and neuropsychological findings in lexical decision experiments with patients with semantic dementia (Patterson et al., 2006; Rogers et al., 2004), we expected activation to be higher for stimuli with atypical versus typical orthography in (a) the posterior LvOT cortex and (b) the left anterior temporal cortex. ERP and lesion studies, however, have low spatial resolution and do not specify the exact origin of the effects. Our threshold for significance was therefore corrected for multiple comparisons either across the whole brain or in four independent ROIs (8-mm radius) taken from Vinckier et al. (2007) in posterior LvOT cortex and from Noppeney et al. (2007) in the anterior temporal lobe. The posterior occipito-temporal coordinates from Vinckier et al. were $[x = -48, y = -56, z = -16]$, $[x = -46, y = -64, z = -14]$, and $[x = -36, y = -80, z = -12]$. These correspond to the areas that Dehaene et al. (2005) associated with bigram coding, letter coding, and early visual processing, respectively. The anterior temporal coordinates were $[x = -46, y = +5, z = -35]$, which correspond to the central location of a large contiguous mass of voxels identified as damaged in patients with semantic impairments (Noppeney et al., 2007). The central location of this mass was identified as the mean of the three peaks at $[x = -45, y = +15, z = -23]$, $[x = -44, y = -8, z = -44]$, and $[x = -51, y = +8, z = -39]$, reported in Noppeney et al.

RESULTS

Behavioral Data

The mean RTs and error rates in the various experimental conditions for the 11 participants included in the functional imaging analyses can be seen in Table 2. A repeated measures ANOVA on RTs with lexicality (pseudowords/words), orthographic typicality (atypical/typical), and context (nonwords/pseudohomophones) as factors revealed main effects of lexicality, $F(1, 10) = 15.83, p = .003$, and orthographic typicality, $F(1, 10) = 9.92, p = .010$, with a trend for longer RTs in the pseudohomophone context, $F(1, 10) = 3.20, p = .104$. There were no significant interactions between factors. The effect of lexicality reflected the usual finding of substantially longer response times to pseudowords (both for nonwords and for pseudohomophones) than to words. The effect of orthographic typicality reflected slightly longer response times to stimuli with typical orthography.

Parallel analyses of error rates identified a series of effects that were driven by high error rates for pseudohomophones. There was a marginal main effect of lexicality, $F(1, 10) = 4.61, p = .057$, a reliable main effect of context, $F(1, 10) = 14.92, p = .003$, and a significant interaction between lexicality and context, $F(1, 10) = 59.96, p < .0005$, because errors were greater for pseudohomophones than nonwords, $F(1, 14) = 57.41, p < .0005$, but there was no significant difference between error rates to words in the two different foil contexts. There was also a marginal three-way interaction with orthographic typicality, $F(1, 14) = 4.80, p = .053$, resulting from a greater effect of typicality

Table 2. Mean RTs and Error Rates (with *SD*) as a Function of Typicality, Lexicality, and Context

	<i>RT (msec)</i>	<i>Error Rate</i>
<i>Nonword Set</i>		
Nonwords		
Atypical	1007 (206)	6.06 (5.70)
Typical	1015 (213)	5.30 (2.69)
Words		
Atypical	844 (68)	7.58 (6.13)
Typical	899 (94)	8.71 (7.08)
<i>Pseudohomophone Set</i>		
Pseudohomophones		
Atypical	1025 (209)	16.29 (5.09)
Typical	1034 (173)	19.70 (6.99)
Words		
Atypical	885 (98)	7.95 (5.09)
Typical	916 (139)	6.82 (4.67)

on pseudohomophones than nonwords, $F(1, 14) = 5.71, p = .038$. This interaction was caused by a disadvantage for typical items emerging only for the pseudohomophones, although the effect itself did not reach significance ($t(14) = -1.70, p = .121$).

Imaging Data

Task

A main effect of lexical decision on words, nonwords, and pseudohomophones, relative to our baseline condition, identified activation in bilateral prefrontal, occipito-temporal, and parietal regions (see top row of Figure 1).

Lexicality

We also identified the expected effect of lexicality, with greater activation for nonwords than words in bilateral inferior frontal regions, left middle frontal cortex, left premotor cortex, left STS, and right angular gyrus (see second row of Figure 1, with MNI coordinates provided in Appendix II of the Supplementary Materials). In our four ROIs, the effect of lexicality (higher activation for nonwords and pseudohomophones than words) was significant only in posterior LvOT (at $[x = -46, y = -64, z = -12], Z = 3.5, p = .02$, after small volume correction centered on $[x = -46, y = -64, z = -14]$). As observed previously (Bruno et al., 2008; Kronbichler et al., 2007), there was also a nonsignificant trend for the effect of lexicality to be stronger in the pseudohomophone context than the nonword context (at $[x = -48, y = -68, z = -12], Z = 3.0, p = .10$; see top row of Figure 2).

Orthographic Typicality

A main effect of orthographic typicality (atypical > typical) was identified in the left inferior occipital ROI [at $x = -34, y = -86, z = -8$]. This was significant ($Z = 3.0, p < .05$) after a small volume correction in a spherical search volume (8-mm radius), centered on the coordinates $[x = -36, y = -80, z = -12]$ reported in Vinckier et al. (2007). This main effect of orthographic typicality was more than 2 cm posterior to the effect of lexicality in LvOT (see third and second rows of Figure 1, respectively). As can be seen in the middle row of Figure 2, activation in the left inferior occipital cortex indexed only the orthographic typicality of the letter strings, with no impact of lexicality or context.

There were no significant effects of orthographic typicality ($p > .05$ uncorrected) in the LvOT ROIs (centered on $[x = -48, y = -56, z = -16]$ and $[x = -46, y = -64, z = -14]$). There was, however, a significant typicality effect in the left anterior temporal ROI in the pseudoword context only (see bottom row of Figure 2) with a peak at $[x = -46, y = 0, z = -34]$ and a Z score of 4.1 ($p < .01$ after small volume correction). This was not observed in the nonword context ($p > .05$ uncorrected); therefore,

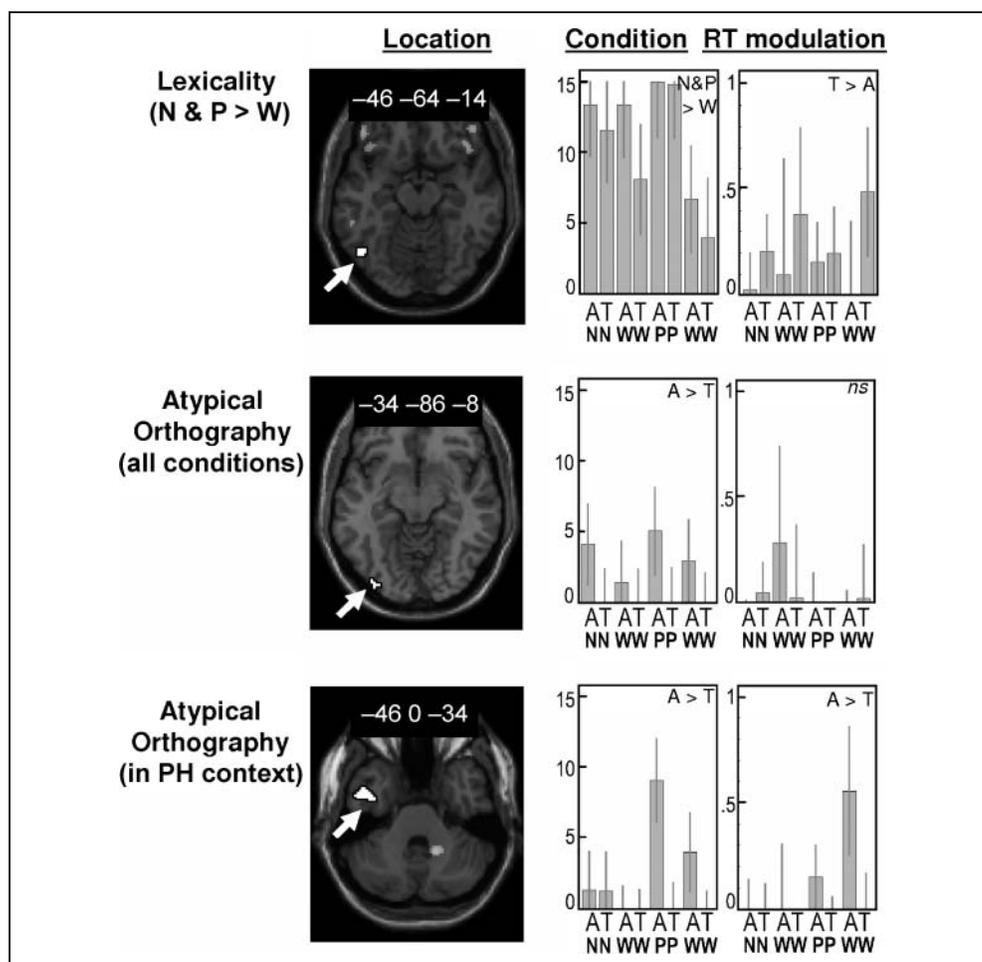
DISCUSSION

The goal of the present fMRI study was to localize the effects of orthographic typicality independently from the effects of lexicality. We therefore used a visual lexical decision task with nonword and pseudohomophone foils that were closely matched to the words in terms of the familiarity of their component letter combinations. Consistent with previous studies (Bruno et al., 2008; Kronbichler et al., 2007), we observed a lexicality effect in the posterior LvOT ROI, with higher activation for nonwords and pseudohomophones than words. In addition to this known effect of lexicality, we revealed a novel finding. The main effect of orthographic typicality was identified in a left inferior occipital region that was almost 30 mm *posterior* to the posterior LvOT area associated with lexicality. The effect of orthographic typicality was expressed as greater activation for stimuli with low relative to high typicality. Our study is therefore the first to isolate a discrete area of visual cortex that is specifically sensitive to the typicality of patterns of sublexical orthography in both words and pseudowords.

Across our eight conditions, activation in this left inferior occipital region was significantly higher for atypical than typical letter strings, irrespective of their lexical status. In

contrast, the behavioral data indicated slightly longer response times to typical than atypical items. The reason for this unexpected behavioral outcome is not clear, although it may be related to the experimental materials: Our efforts to match the word and the nonword stimuli very closely on subword patterns of orthographic typicality may have encouraged participants to engage in an orthographic checking strategy (Van Orden, Pennington, & Stone, 1990), meaning they would have looked very carefully at anything appearing especially wordlike. Indeed, in a previous study that involved a mixture of pseudohomophone and nonword foils carefully matched to words, a numerical trend toward slower responses to typical than atypical items was also observed (Hauk et al., 2006). In our study, we included pseudohomophones that would unambiguously be pronounced as a familiar word, meaning that the discrimination would have been even more difficult, and this is consistent with the slower response times obtained here relative to those reported by Hauk et al. (2006): 953 versus 759 msec, respectively. The disadvantage for typical relative to atypical items observed in the present study at these relatively slow RTs is consistent with previous research that has quantified orthographic typicality in terms of orthographic neighborhood, which has been shown to

Figure 2. The effects of typicality and lexicality in ROIs. Left column: Axial slice showing location of effects in ROIs ($p < .01$ uncorrected). The peak of each of these effects was significant ($p < .05$) after small volume correction for multiple comparisons. Middle column: Plots showing activation (mean and 90% confidence intervals) per condition. Right column: Plots showing the strength of the positive relationship between activation and RT for each condition. A = atypical orthography; T = typical orthography; N = nonwords; P = pseudohomophones; W = words; *ns* = not significant ($p > .05$ uncorrected).



be facilitatory when instructions stress speeded responding (Fiebach, Ricker, Friederici, & Jacobs, 2007) but inhibitory when accuracy is prioritized (Binder et al., 2003), as was the case in this study. The hypothesis that the disadvantage for typical relative to atypical items comes from an orthographic checking strategy for wordlike stimuli is supported by our observation that participants who were slower to respond to stimuli with typical orthography also had greater LvOT activation for stimuli with typical orthography (see top row of Figure 2). This is consistent with prior studies that have shown increased LvOT activation for discriminating between visually similar items (e.g., Rogers, Hocking, Mechelli, Patterson, & Price, 2005).

The second imaging finding of particular interest in this study was an interaction between typicality and context in the left anterior temporal ROI: Activation here was higher for atypical than typical items only in the context of pseudohomophones. Although we only observed a trend toward longer response times in the pseudohomophone foil context, we would suggest that this effect was diluted in the present study by the frequent switching between blocks of each foil type. The interaction between typicality and context seen in the left anterior ROI was not apparent in the behavioral data alone; however, longer response times for atypical items in the context of pseudohomophones resulted in more left anterior temporal activation (see bottom row of Figure 2), consistent with additional processing demands that were specific to both the condition and the region. We associate increased anterior temporal activation with greater reliance on semantic processing for atypical items on the basis of research involving patients with semantic dementia (Patterson et al., 2006; Rogers et al., 2004): These studies have demonstrated a strong association between the patients' degree of semantic degradation and their error rates in visual lexical decision for orthographically atypical words in the context of pseudohomophone foils. Indeed, the peak coordinates of the orthographic typicality effect in the pseudohomophone context observed here in anterior temporal cortex [$x = -46, y = 0, z = -34$] are very close to (a) the region reported to be most significantly damaged in semantic dementia by Mummery et al. (1999) ($x = -54, y = +9, z = -38$) and (b) the mean [$x = -46, y = +5, z = -35$] of the more distributed coordinates reported in Noppeney et al. (2007) as commonly damaged in semantic dementia and semantically impaired patients with herpes simplex encephalitis (HSE). This result is also consistent with the ERP findings of Hauk et al. (2006) but with more precise anatomical location.

The semantic interpretation of left anterior temporal activation for atypical items in the context of pseudohomophones is supported by behavioral studies of normal readers showing that a shift from nonword to pseudohomophone foils is accompanied by an increase in the size of meaning-level effects like polysemy (Pexman & Lupker, 1999) and semantic priming (Joordens & Becker, 1997). The interpretation in models of word recognition is that, when the lexical decision process cannot make use of phonolo-

gical information because the foils also sound like real words, semantic information plays an augmented role (Pexman & Lupker, 1999; Plaut, 1997; Van Orden & Goldinger, 1994).

The increased involvement of the left anterior temporal cortex for atypical items in the pseudohomophone context is particularly compatible with connectionist models of visual word recognition (e.g., Harm & Seidenberg, 2004; Plaut, 1997; Plaut, McClelland, Seidenberg, & Patterson, 1996) that emphasize distributed as opposed to localist orthographic representations. Within these models, information concerning familiarity at the whole-word level derives from higher order semantic representations, and the extent to which this information is used to inform lexical decision increases as the targets and foils become more difficult to distinguish on the basis of their orthographic and phonological properties (Plaut, 1997; Seidenberg & McClelland, 1990). Such accounts can therefore easily accommodate our finding that recognition of atypical items in the pseudohomophone foil context, where neither orthographic pattern nor phonological status was a reliable basis for lexical decision, yielded significant activation in the left anterior temporal region reliably damaged in semantic dementia. Given the strong association of the left anterior temporal lobe with semantic processing, we think it is highly unlikely that activation in this region reflects activation related to orthographic or phonological word form processing.

The observed contrast between the behavioral and the imaging results emphasizes the value of neuroimaging in understanding the word recognition process: Imaging can reveal early effects that may not be detected in behavior because the initial effects are obscured by the influence of subsequent processes, all of which combine to determine the accuracy and timing of actual responses. In this study, left frontal and temporal lobe activation was most strongly correlated with response times, but we also observed an interesting dissociation across typical and atypical items in the strength of the relationship between activation and response times. Specifically, response times correlated more strongly with posterior LvOT for typical than atypical items and with left anterior temporal activation for atypical than typical items. These contrasting effects of RTs show that activation in our ROIs cannot be associated with processing time per se but instead reflect specific types of processing demands.

Regarding the functions of our different ROIs, we suggest that the left occipital region is sensitive to familiarity of subword letter combinations with less activation for strings containing frequent than infrequent combinations during lexical decision. In the LCD model presented by Vinckier et al. (2007), the ROI in which we found effects of orthographic typicality has been associated with sensitivity to letter frequency, and it is certainly true that the present stimuli varied across typicality on this dimension. However, it is worth noting that Vinckier et al. reported higher activation for frequent than infrequent letters in this region, whereas we found significantly higher activation for

infrequent than frequent letters/bigrams, a difference we can only attribute to the variation in tasks used across the two studies (lexical decision vs. passive viewing). With respect to the anterior temporal lobe, we have argued that activation reflects the demands on semantic processing, which is greater for items with atypical orthography when presented in the context of pseudohomophones.

The functional contributions of LvOT are more contentious. Higher activation has been associated with pseudowords (Kronbichler et al., 2007), low-frequency words (Kronbichler et al., 2004), frequent bigrams (Vinckier et al., 2007; Binder et al., 2006), high demands on visual discrimination (Rogers et al., 2005), and the integration of abstract form processing with higher level processes (Devlin et al., 2006). The contrasting effects in LvOT require further investigations that systematically tease apart the influence of task and stimuli. For example, the contrasting effects of bigram frequency in our study and that of Binder et al. (2006) are likely to be due to differences in both the stimuli (much lower range of bigram frequency in Binder et al., 2006) and the task (lexical decision vs. visual feature detection on letter strings). Our study was not designed to determine the relative influence of these factors.

Moreover, although we observed an effect of lexicality on LvOT activation, this was confounded with significantly longer response times for nonwords and pseudohomophones than words. Therefore, it remains possible that higher LvOT activations for nonwords and pseudohomophones may simply reflect processing time (Binder, Westbury, McKiernan, Possing, & Medler, 2005). In contrast, the opposing effects of orthographic typicality on left inferior occipital activation and response times demonstrate that increased left inferior occipital activation for atypical items cannot simply be attributed to increased processing time.

In summary, the imaging results reported here demonstrate that activation in a posterior left inferior occipital region (at $y \approx -86$) is sensitive to word-like-ness (i.e., variations in orthographic typicality at the subword level) but not to word-ness (i.e., lexicality), the effects of which were observed in LvOT cortex at $y \approx -60$. In addition, when lexical decisions to orthographically atypical items became more difficult in the context of pseudohomophone foils, we observed an increase in activation in the left anterior temporal lobe for atypical items, consistent with data from semantic dementia patients and connectionist models of visual word recognition. Overall, our results provide the first clear dissociation between the neural regions sensitive to subword orthographic typicality and lexicality of letter strings.

Acknowledgments

This work was funded by the Wellcome Trust and grant MH64445 from the National Institutes of Health (USA).

Reprint requests should be sent to Dr. Anna M. Woollams, Neuroscience and Aphasia Research Unit, School of Psycho-

logical Sciences, University of Manchester, Zochonis Building, Brunswick Street, Manchester M13 9PL, England, or via e-mail: anna.woollams@manchester.ac.uk.

REFERENCES

- Baayen, H., Piepenbrock, R., & van Rijn, H. (1993). *The CELEX lexical database* [CD-ROM]. Philadelphia, PA: Linguistic Data Consortium, University of Pennsylvania.
- Behrmann, M., Nelson, J., & Sekuler, E. B. (1998). Visual complexity in letter-by-letter reading: "Pure" alexia is not pure. *Neuropsychologia*, *36*, 1115–1132.
- Binder, J. R., McKiernan, K. A., Parsons, M. E., Westbury, C. F., Possing, E. T., Kaufman, J. N., et al. (2003). Neural correlates of lexical access during visual word recognition. *Journal of Cognitive Neuroscience*, *15*, 372–393.
- Binder, J. R., Medler, D. A., Westbury, C. F., Liebenthal, E., & Buchanan, L. (2006). Tuning of the human left fusiform gyrus to sublexical orthographic structure. *Neuroimage*, *33*, 739–748.
- Binder, J. R., Westbury, C. F., McKiernan, K. A., Possing, E. T., & Medler, D. A. (2005). Distinct brain systems for processing concrete and abstract concepts. *Journal of Cognitive Neuroscience*, *17*, 905–917.
- Borowsky, R., & Masson, M. E. J. (1996). Semantic ambiguity effects in word identification. *Journal of Experimental Psychology: Learning Memory and Cognition*, *22*, 63–85.
- Bruno, J. L., Zumberge, A., Manis, F. R., Lu, Z. L., & Goldman, J. G. (2008). Sensitivity to orthographic familiarity in the occipito-temporal region. *Neuroimage*, *39*, 1988–2001.
- Cohen, L., Martinaud, O., Lemer, C., Lehericy, S., Samson, Y., Obadia, M., et al. (2003). Visual word recognition in the left and right hemispheres: Anatomical and functional correlates of peripheral alexias. *Cerebral Cortex*, *13*, 1313–1333.
- Dehaene, S., Cohen, L., Sigman, M., & Vinckier, F. (2005). The neural code for written words: A proposal. *Trends in Cognitive Sciences*, *9*, 335–341.
- Dehaene, S., Jobert, A., Naccache, L., Ciuciu, P., Poline, J. B., Bihan, D. L., et al. (2004). Letter binding and invariant recognition of masked words: Behavioral and neuroimaging evidence. *Psychological Science*, *15*, 307–313.
- Devlin, J. T., Jamison, H. L., Gonnerman, L. M., & Matthews, P. M. (2006). The role of the posterior fusiform gyrus in reading. *Journal of Cognitive Neuroscience*, *18*, 911–922.
- Fiebach, C. J., Ricker, B., Friederici, A. D., & Jacobs, A. M. (2007). Inhibition and facilitation in visual word recognition: Frontal contribution to the orthographic neighborhood size effect. *Neuroimage*, *36*, 901–911.
- Forster, K. I., & Shen, D. (1996). No enemies in the neighborhood: Absence of inhibitory neighborhood effects in lexical decision and semantic categorization. *Journal of Experimental Psychology: Learning Memory and Cognition*, *22*, 696–713.
- Harm, M. W., & Seidenberg, M. S. (2004). Computing the meanings of words in reading: Cooperative division of labor between visual and phonological processes. *Psychological Review*, *111*, 662–720.
- Hauk, O., Patterson, K., Woollams, A., Watling, L., Pulvermuller, F., & Rogers, T. T. (2006). [Q:] When would you prefer a sausage to a sausage? [A:] At about 100 msec. ERP correlates of orthographic typicality and lexicality in written word recognition. *Journal of Cognitive Neuroscience*, *18*, 818–832.
- Hodges, J. R., Patterson, K., Oxbury, S., & Funnell, E. (1992). Semantic dementia. Progressive fluent aphasia with temporal lobe atrophy. *Brain*, *115*, 1783–1806.

- Holcomb, P. J., Grainger, J., & O'Rourke, T. (2002). An electrophysiological study of the effects of orthographic neighborhood size on printed word perception. *Journal of Cognitive Neuroscience*, *14*, 938–950.
- Joordens, S., & Becker, S. (1997). The long and short of semantic priming effects in lexical decision. *Journal of Experimental Psychology: Learning Memory and Cognition*, *23*, 1083–1105.
- Kronbichler, M., Bergmann, J., Hutzler, F., Staffen, W., Mair, A., Ladurner, G., et al. (2007). Taxi vs. taksi: On orthographic word recognition in the left ventral occipitotemporal cortex. *Journal of Cognitive Neuroscience*, *19*, 1584–1594.
- Kronbichler, M., Hutzler, F., Wimmer, H., Mair, A., Staffen, W., & Ladurner, G. (2004). The visual word form area and the frequency with which words are encountered: Evidence from a parametric fMRI study. *Neuroimage*, *21*, 946–953.
- Leff, A. P., Spitsyna, G., Plant, G. T., & Wise, R. J. S. (2006). Structural anatomy of pure and hemianopic alexia. *Journal of Neurology, Neurosurgery and Psychiatry*, *77*, 1004–1007.
- Mechelli, A., Henson, R. N. A., Price, C. J., & Friston, K. J. (2003). Comparing event-related and epoch analysis in blocked design fMRI. *Neuroimage*, *18*, 806–810.
- Medler, D. A., & Binder, J. R. (2005). *MCWord: An on-line orthographic database of the English language*. Retrieved from www.neuro.mcgill.ca/mcword/.
- Mummery, C. J., Patterson, K., Wise, R. J. S., Vandenberg, R., Price, C. J., & Hodges, J. R. (1999). Disrupted temporal lobe connections in semantic dementia. *Brain*, *122*, 61–73.
- Mycroft, R. H., Behrmann, M., & Kay, J. (2009). Visuo-perceptual deficits in letter-by-letter reading? *Neuropsychologia*, *47*, 1733–1744.
- Noppeney, U., Patterson, K., Tyler, L. K., Moss, H., Stamatakis, E. A., Bright, P., et al. (2007). Temporal lobe lesions and semantic impairment: A comparison of herpes simplex virus encephalitis and semantic dementia. *Brain*, *130*, 1138–1147.
- Patterson, K., Lambon Ralph, M. A., Jefferies, E., Woollams, A., Jones, R., Hodges, J. R., et al. (2006). “Presemantic” cognition in semantic dementia: Six deficits in search of an explanation. *Journal of Cognitive Neuroscience*, *18*, 169–183.
- Pexman, P. M., & Lupker, S. J. (1999). Ambiguity and visual word recognition: Can feedback explain both homophone and polysemy effects? *Canadian Journal of Experimental Psychology*, *53*, 323–334.
- Plaut, D. C. (1997). Structure and function in the lexical system: Insights from distributed models of word reading and lexical decision. *Language and Cognitive Processes*, *12*, 765–805.
- Plaut, D. C., McClelland, J. L., Seidenberg, M. S., & Patterson, K. (1996). Understanding normal and impaired word reading: Computational principles in quasi-regular domains. *Psychological Review*, *103*, 56–115.
- Price, C. J., & Mechelli, A. (2005). Reading and reading disturbance. *Current Opinion in Neurobiology*, *15*, 231–238.
- Rogers, T. T., Hocking, J., Mechelli, A., Patterson, K., & Price, C. (2005). Fusiform activation to animals is driven by the process, not the stimulus. *Journal of Cognitive Neuroscience*, *17*, 434–445.
- Rogers, T. T., Lambon Ralph, M. A., Hodges, J. R., & Patterson, K. (2004). Natural selection: The impact of semantic impairment on lexical and object decision. *Cognitive Neuropsychology*, *21*, 331–352.
- Sears, C. R., Hino, Y., & Lupker, S. J. (1995). Neighborhood size and neighborhood frequency effects in word recognition. *Journal of Experimental Psychology: Human Perception and Performance*, *21*, 876–900.
- Seghier, M. L., Lee, H. L., Schofield, T., Ellis, C. L., & Price, C. J. (2008). Inter-subject variability in the use of two different neuronal networks for reading aloud familiar words. *Neuroimage*, *42*, 1226–1236.
- Seidenberg, M. S., & McClelland, J. L. (1990). More words but still no lexicon: Reply to Besner et al. (1990). *Psychological Review*, *97*, 447–452.
- Shulman, H. G., & Davidson, T. C. B. (1977). Control properties of semantic coding in a lexical decision task. *Journal of Verbal Learning and Verbal Behavior*, *16*, 91–98.
- Snowden, J. S., Goulding, P. J., & Neary, D. (1989). Semantic dementia: A form of circumscribed cerebral atrophy. *Behavioural Neurology*, *2*, 167–182.
- Van Orden, G. C., & Goldinger, S. D. (1994). Interdependence of form and function in cognitive systems explains perception of printed words. *Journal of Experimental Psychology: Human Perception and Performance*, *20*, 1269–1291.
- Van Orden, G. C., Pennington, B. F., & Stone, G. O. (1990). Word identification in reading and the promise of subsymbolic psycholinguistics. *Psychological Review*, *97*, 488–522.
- Veltman, D. J., Mechelli, A., Friston, K. J., & Price, C. J. (2002). The importance of distributed sampling in blocked functional magnetic resonance imaging designs. *Neuroimage*, *17*, 1203–1206.
- Vinckier, F., Dehaene, S., Jobert, A., Dubus, J. P., Sigman, M., & Cohen, L. (2007). Hierarchical coding of letter strings in the ventral stream: Dissecting the inner organization of the visual word-form system. *Neuron*, *55*, 143–156.
- Weiskopf, N., Hutton, C., Josephs, O., & Deichmann, R. (2006). Optimal EPI parameters for reduction of susceptibility-induced BOLD sensitivity losses: A whole-brain analysis at 3 T and 1.5 T. *Neuroimage*, *33*, 493–504.