Reading and reading disturbance
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Recent functional neuroimaging studies are generating novel insights into our knowledge of skilled and disturbed reading. In neurologically normal subjects, a double dissociation in neural activation in response to reading words and pseudowords has been revealed that corresponds to that observed in the comparison of semantic and phonological tasks. In patients with acquired dyslexia, functional imaging is demonstrating re-organisation within the reading system; in developmental dyslexia, functional imaging is being used to identify the impact of rehabilitation. Together, these findings have implications for cognitive models of reading that have previously relied on input from behavioural data.

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Introduction
The ability to read letter strings requires the translation of visual codes (orthography) into pronunciations (phonology), with meaning (semantics) emerging when the pronunciation corresponds to a known word. During the course of learning to read, knowledge of the sounds associated with subword letter units is established, thereby enabling the pronunciation of new words that the reader has never encountered (e.g. 'heam' and 'ploon'). In experimental investigations, these novel word-like letter strings are referred to as 'pseudowords'. Reading is faster when lexical (whole word) and sublexical (word parts) pronunciations are consistent (e.g. 'pram', 'lamp' and 'sentiment') than when they are inconsistent (e.g. 'hymn'). We refer to words with consistent spellings as 'regular' and those with inconsistent spellings as 'irregular' or 'exception' words (see Glossary). Differences between these word types are particularly important for understanding reading disturbances (i.e. dyslexia).

Patients with acquired dyslexia caused by brain damage demonstrate a double dissociation in their ability to read exception words versus pseudowords. Phonological dyslexics have more difficulty reading pseudowords than exception words, whereas surface dyslexics display the opposite pattern (i.e. more difficulty with exception words than pseudowords; see Glossary). This suggests that there are different pathways for reading exception words (lexical processing) and pseudowords (sublexical processing) [1,2] and that these pathways can be selectively damaged. However, the neural correlates of these putative reading pathways are not well understood. Phonological dyslexia (poor pseudoword reading) is usually caused by large left hemisphere middle cerebral artery infarcts that affect temporo–parietal and frontal regions, whereas surface dyslexia (poor exception word reading) is associated with anterolateral temporal lobe atrophy [3]. In addition, a third type of dyslexia (pure alexia, or alexia without agraphia) is characterized by poor reading of both regular and exception words in the context of preserved writing skills, and typically occurs following left occipito–temporal damage. Notably, the pattern of behaviour in pure alexia has been quoted as evidence for the left occipito–temporal cortex being responsible for reading-specific processing [4].

Functional imaging techniques enable new and more detailed investigations of the biological foundation of reading. These studies have demonstrated that reading activates a widely distributed set of areas in occipito–temporal, posterior temporal, precentral and inferior frontal gyri [5], see Figure 1. We expect these regions to include, at a minimum, areas that sustain orthographic, semantic and phonological processing. In the review of functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies of reading that follows, we first discuss the results of experiments that have attempted to segregate brain areas involved in semantic and phonological processes during skilled reading. We then consider whether there are brain areas that are specific to reading (e.g. those involved in orthographic processing). Finally, we discuss functional imaging studies of developmental and acquired dyslexia. This review focuses on publications from 2003 onwards, with much of the earlier work being referenced in review papers only.

Segregating reading functions
Attempts to segregate the brain areas that are responsible for different reading processes have involved either task or word type manipulations. Task manipulations compare brain activation when attention is directed to one particular process or another [6,7]. For example, McDermott

Glossary

Exception words: When the pronunciation of a whole word is inconsistent with that of its parts (e.g. 'yacht').

Lexical: Refers to whole words.

Orthography: The combinations of visual letters that make up words.

Phonological dyslexics: Patients who have more difficulty reading pseudowords than exception words.

Phonology: The pronunciations of written words.

Pseudowords: Novel words that have not been encountered before (e.g. 'floop').

Regular words: When the pronunciation of a whole word is consistent with the sum of its parts (e.g. 'pram', 'lamp' and 'sentiment').

Semantics: The meaning of words.
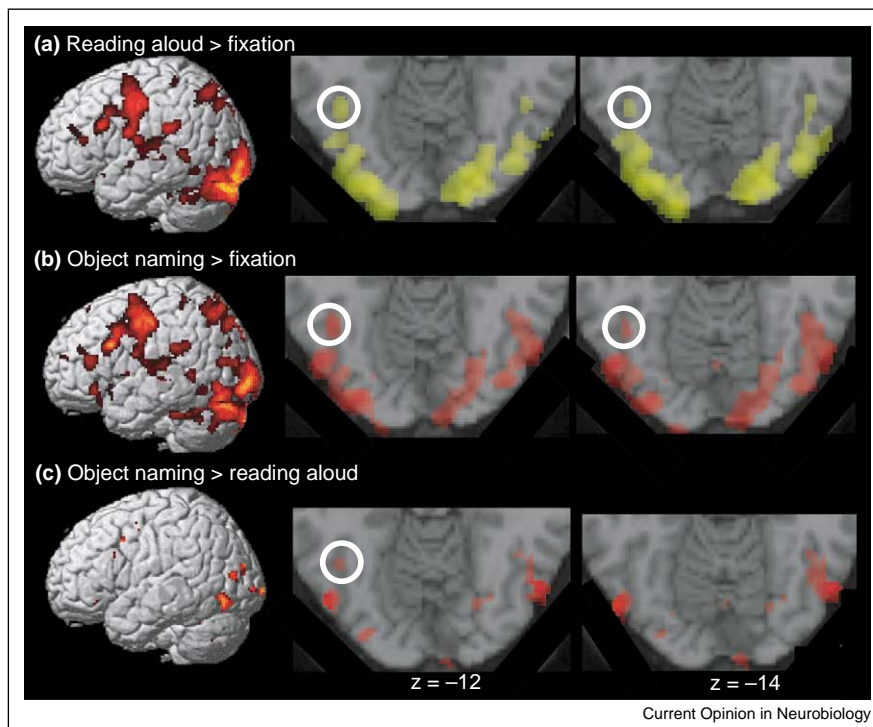
Sublexical: Refers to parts of words.

Surface dyslexics: Patients who have more difficulty reading exception words than pseudowords.

et al. [7] focused attention on semantics by instructing participants to decide which two of three words were most meaningfully related (e.g. tiger, circus and jungle) or focused attention on phonology by instructing participants to decide which two of three words sounded most similar (e.g. skill, fill and hill). When compared with phonological tasks, semantic tasks tend to increase left hemisphere activation in anterior left inferior frontal (LIF) regions (pars orbitalis and pars triangularis), the angular gyrus, the middle temporal cortex and the anterior fusiform gyrus [6–9]. Conversely, phonological compared with semantic tasks tend to increase activation in more dorsal and posterior LIF regions, including pars opercularis and premotor cortex, with bilateral activation occurring in the insulae and supramarginal gyri (see top row of Figure 2).

Word type manipulations compare responses to words and to pseudowords, with the expectation that they will tax the reading pathways differentially. For example, unfamiliar pseudowords are thought to increase demands on the sublexical conversion of orthography to phonology, whereas exception words that are not frequently encountered (e.g. yacht) rely on lexico–semantic processing. The effect of word type on brain activation appears to depend upon the task [10**,11,12*,13]. However, there is a growing consensus that words and pseudowords modulate activation in areas associated with semantic and phonological processing, respectively. For example, using lexical decision (decide if a letter string is a real word or not),

Figure 1

(a) Reading aloud > fixation
(b) Object naming > fixation
(c) Object naming > reading aloud

z = −12   z = −14

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Reading and object naming. The brain areas activated by **(a)** reading aloud compared with viewing a fixation point, **(b)** object naming compared with viewing a fixation point and **(c)** object naming compared with reading aloud. The left hand column is a surface rendering of activation in the left hemisphere. The second and third columns show the distribution of activation in bilateral occipito–temporal cortices on axial slices positioned 12 mm (z = −12) below the ACPC line (2nd column) and 14 mm (z = −14) below the ACPC line (3rd column). Data are from an fMRI study of a single subject (A Mechelli and CJ Price, unpublished) to demonstrate activations with high precision (see [5] and [23] for very similar effects at the group level). (a) and (b) are thresholded at p < 0.05 corrected for multiple comparisons; (c) is thresholded at p < 0.05 uncorrected to highlight greater activation for object naming than reading in the left mid-fusiform (within the white circle), which has been labelled the 'visual word form area' (see [27*]).

Figure 2
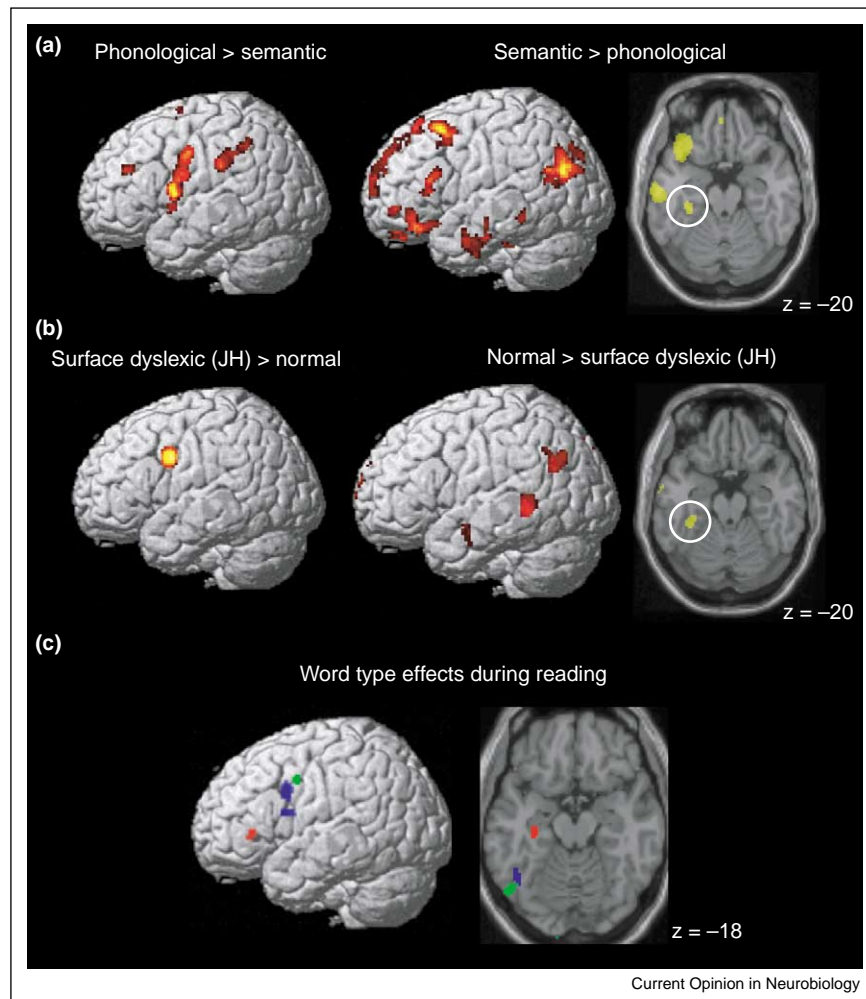
Segregating semantic and phonological processing. **(a)** The comparison of phonological and semantic tasks employing the same stimuli, using data from Mummery et al. [8], thresholded at p < 0.05 corrected for multiple comparisons. **(b)** The comparison of activation for reading aloud in a surface dyslexic patient (JH) with a group of 10 age-matched control subjects (normal) using data from Price et al. [19], thresholded at p < 0.05 uncorrected. In the first two images of (a) and (b), the surface rendering on the canonical brain illustrates the distributed nature of the activation. The images on the right of (a) and (b) are axial slices positioned 20 mm (z = −20) below the ACPC line that show the exact location of the anterior fusiform activation on the medial surface of the temporal lobe (see white circle). **(c)** The effect of word type. The left hemisphere rendering shows activation (at p < 0.05 corrected for multiple comparisons) for pseudowords compared to exception words (green), exception words compared to pseudowords (red) and exception words and pseudowords compared to regular words (blue) [14]. All are thresholded at p < 0.05 corrected for multiple comparisons. The axial slice on the right shows activation (at p < 0.005 uncorrected) for pseudowords compared to words (green), words compared to pseudowords (red) and words and pseudowords compared to falsefonts (blue) [18].

Binder et al. [10••] observed increased activation for words compared with pseudowords in left pars orbitalis, angular gyrus and middle temporal areas that are also activated by semantic compared to phonological tasks; however, there is increased activation for pseudowords compared with words in the left premotor area that is also activated by phonological compared with semantic tasks. Likewise, when participants are reading aloud, we have recently observed [14] increased activation for exception words compared with pseudowords in the pars triangularis; for pseudowords compared with exception words in the left premotor cortex; and for both pseudowords and exception words compared with regular words in the pars opercularis. This dissociation in inferior frontal activation for different word types mirrors that reported during task manipulations [6] (compare Figure 2a and c). Thus, task and word type manipulations are revealing similar effects, even though increased activation for words is more likely to be observed when the stimuli include exception words that are unfamiliar [15], and task effects are confounded by executive processes that are not required during skilled reading [16].

We can also use task effects to identify regions of interest in which the weaker effects of word type can be examined. For example, semantic compared with phonological tasks activate the left anterior fusiform [6,7], yet only one previous study [17] observed increased left anterior fusiform activation for words compared with pseudowords. By lowering the statistical threshold (to p < 0.005) [18], we also found that left anterior fusiform activation was greater for words compared with pseudowords. In addition, three subdivisions within the left fusiform gyrus become apparent (see Figure 2c), as hypothesised on the basis of previous studies [19,20]. First, a posterior area (66 mm behind the anterior commissure posterior commissure [ACPC] line) that is activated by pseudowords to a greater extent than it is by words [12•]. In this subdivision there is also orthographic but not semantic priming [21]. Second, a mid-fusiform region (54 mm behind the ACPC line) that is activated to a greater extent by both words and pseudowords compared with meaningless symbols (falsefonts) [17] and in which activation decreases with word familiarity [22]. Third, an anterior fusiform area (34 mm behind the ACPC line) that is activated to a greater extent by semantic compared with phonological tasks [6,8,23] and by words compared with pseudowords [16,18].

The focus of this review, so far, has been on the differential effects of either task or word type, but the dissociation is far from complete. Both semantic and phonological tasks activate inferior frontal areas with differential effects being reflected in relative, rather than absolute, activation differences [6]. Moreover, reading also increases activation in the left posterior superior temporal sulcus, but activation here is unaffected by word type, positively correlated with knowledge of the sound structure of words [24], linked to the integration of letters with their sounds [25] and observed for speech production in the absence of visual input [19,26]. This area therefore appears to contribute to phonological processing that occurs after orthographic-to-phonological conversion.

## What neuronal processes are specific to reading?

Reading is an acquired skill that takes many years to learn. But, what neuronal processes take place during this learning process? Does reading experience result in the generation of highly specialized neuronal populations that code specifically for visual word forms [4,20,27•]? Or does learning to read induce changes in synaptic connections among distributed neuronal populations that are also engaged in the processing of objects [28]? Ultimately, the answers to these questions will depend upon neurophysiological studies that are able to disambiguate the responses of individual neurons during the course of development; but, for the time being, functional imaging techniques limit us to the consideration of regional (>2 mm) responses that subsume large neuronal populations.

Left occipito–temporal areas are activated to a greater extent by reading than by auditory word processing [4,29], but when reading is compared with object naming, a different story unfolds. In a similar way to reading, object naming involves the identification of visual stimuli and the generation of spoken responses. However, unlike reading, objects do not comprise a limited set of canonical shapes that combine in predictable patterns and phonology cannot be generated on the basis of structural parts (i.e. sublexical conversion), but instead depends upon recognition of the whole object. Thus, the processes specific to reading include those involving orthographic word forms and/or sublexical conversion from orthography to phonology. Direct comparisons of reading and object naming highlight two crucial points. First, left occipito–temporal regions are activated to a greater extent by object naming than by reading [28] (see Figure 1). Therefore, the comparison of reading and object naming does not provide evidence for the presence of left occipito–temporal neuronal populations that are dedicated to orthographic processing [28]. Instead, this area might act as an interface in the retrieval of phonology from visual input [30–32]. Second, compared with object naming, reading activates the left posterior superior temporal and premotor regions that have been associated with phonological processing in the absence of orthographic input [23,33] (see Figures 3 and 4). This suggests that reading enhances the demands on phonological rather than on perceptual processes.

Developmental dyslexia

Recent studies have demonstrated that the acquisition of reading skills is reflected by progressively greater activation in left occipital, temporal and frontal regions and progressively less activation in posterior right hemisphere regions [34••,35]. Furthermore, the neural network for reading can be strongly left-lateralized by the age of six or seven years [36]. Neuronal abnormalities within this system, as observed in developmental dyslexia, are difficult to interpret because they appear to depend upon the task [37•,38], language [39], and type of dyslexia [37•]. Moreover, abnormal left occipito–temporal activations in developmental dyslexia have been observed during picture naming as well as during reading [32]. There are also difficulties interpreting the effect of intervention on abnormal neuronal responses. For example, although it has been demonstrated that abnormalities in brain activation during reading can be dramatically reduced following phonologically based intervention [40,41,42•,43], it remains unclear whether abnormal activation that occurred before intervention was related to abnormal functional anatomy or to the failure to engage the normal set of cognitive processes. Thus, it is difficult to distinguish effects that are the cause rather than the consequence of dyslexia. Likewise, although there is evidence for structural abnormalities in developmental dyslexia that correlate with the degree of impairment on

Figure 3
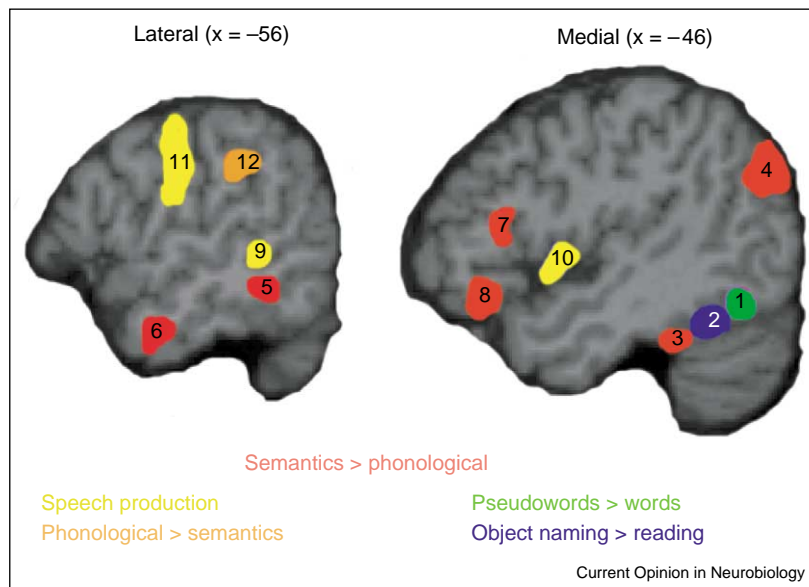
A summary diagram of reading areas. This is a schematic figure, created by copying the activation from five different contrasts on sagittal brain slices cut at x = −56 mm, and x = −46 mm in standard 3D space. The yellow areas are those activated during a speech production task that involved saying 'OK' in response to visual noise when compared with pressing a key pad in response to the same stimuli (data reported in Price et al. [19]). Each of these yellow areas are also engaged during reading aloud. The red areas are those activated in the comparison of semantic with phonological tasks (data from Mummery et al. [8]) but these areas are not consistently activated during reading aloud. The orange area is activated by phonological compared with semantic tasks (data from Mummery et al. [8]), but again it is not normally activated during reading aloud. The green area is activated to a greater extent by pseudowords than by words (data from Mechelli et al. [12•]). The blue area is activated by reading words and pseudowords compared with falsefonts (data from Brusnwick et al. [18]); but, also for object naming compared with reading [see Figure 1]. We use the following terminology for each area: 1, posterior occipito–temporal; 2, mid-fusiform; 3, anterior fusiform; 4, angular gyrus; 5, posterior middle temporal gyrus; 6, anterior middle temporal gyrus; 7, pars triangularis (in LIFG); 8, pars opercularis (in LIFG); 9, posterior superior temporal gyrus; 10, anterior insula; 11, premotor cortex; and 12, inferior (anterior) parietal.

behavioural scores [44,45•], several recent studies have shown that the brain structure changes with experience [46–49], again calling into question whether structural abnormalities in developmental dyslexia are the cause or the consequence of the reading disturbance.

Acquired dyslexia

Contrary to the case with developmental dyslexia, the cause of acquired dyslexia is usually clear, namely pathological or accidental focal brain damage. In the Introduction, we referred to three types of dyslexia: phonological dyslexia (particular difficulty with pseudowords), surface dyslexia (particular difficulty with exception words) and pure alexia (difficulty reading in the context of preserved language and writing). Pure alexics are sometimes able to compensate for their reading deficits by adopting a letter-by-letter reading strategy. Cohen et al. [50] have demonstrated that preserved reading in these patients, who typically have damage to the left occipito–temporal cortex, can be related to increased right occipito–temporal activation, and that the letter-by-letter reading strategy engages bilateral frontal and left parietal regions [51]. These findings suggest that an alternative right occipito–temporal pathway is able to sustain reading

following left occipito–temporal damage. The same right occipito–temporal pathway might also be responsible for object naming in these patients. This leads us to an alternative model of pure alexia: the greater impairment of reading compared with object naming reflects the more successful contribution of right occipito–temporal activation to object naming than reading [28]. This hypothesis is distinct from claims that greater impairment of reading reflects the loss of reading-specific neuronal populations in the left occipito–temporal cortex [4].

Finally, we note that a functional imaging study of reading short easy familiar words in JH, a patient with surface dyslexia [19], has revealed greater activation compared with normal control subjects in left premotor cortex and reduced activation compared with normal control subjects in the left angular gyrus, anterior fusiform, middle and anterior temporal areas. This dissociation corresponds to that observed in the comparison of phonological and semantic tasks discussed above (compare Figure 2a and b) and is precisely what might be predicted in surface dyslexics who have difficulty reading on the basis of semantics (67% accuracy for patient JH) but are able to

Figure 4
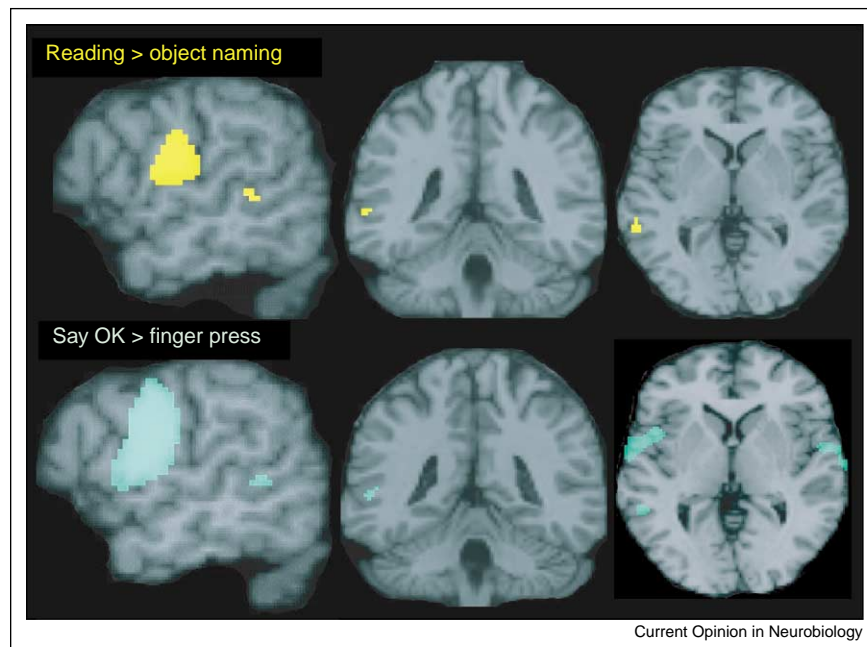
Enhanced activation for words in speech production areas. Sagittal, coronal and axial views showing the similarity between activations for **(a)** words compared with that for objects (yellow) [23,33] and **(b)** speech production (green) as revealed by comparing vocal (saying 'OK') with manual (finger press) responses, using data reported in Price et al. [19].

read a high proportion of pseudowords (96% accuracy for patient JH).

Conclusions

Reading engages a bilaterally distributed set of brain regions (see Figure 1). Within this system, some areas are more sensitive to semantically demanding stimuli or tasks (e.g. anterior fusiform, middle temporal, angular gyrus and anterior LIFG), whereas others are more sensitive to phonological manipulations (e.g. posterior LIFG and bilateral supramarginal gyri). Remarkably, this double dissociation is also mirrored in the neural activation pattern of a surface dyslexic patient who showed reduced activation in semantic areas and enhanced activation in a phonological area (see Figure 2). In other words, imaging data are characterizing the dissociations in reading processes that have been predicted on the basis of neuropsychological data.

The conversion of orthography-to-phonology requires left occipito–temporal activation that is also observed during object naming (a non-orthographic task). The conspicuous absence of brain areas that are dedicated to orthography challenges our understanding of how left occipito–temporal damage can impair reading more than it does object naming. We have proposed that selective impairments of reading might be explained in terms of right occipito–temporal activation that is able to sustain object naming better than it does reading. Future studies

are required to determine how reading areas interact with one another, particularly following brain damage. This should provide a better characterisation of the pathways that can sustain reading but it will require a fuller appreciation of both structural and functional connectivity.

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- • of special interest
- •• of outstanding interest

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