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What is This?

The Neurobiological Basis of Reading

Jane Joseph, Kimberly Noble, and Guinevere Eden

Abstract

The results from studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) in adults have largely revealed the involvement of left-hemisphere perisylvian areas in the reading process, including extrastriate visual cortex, inferior parietal regions, superior temporal gyrus, and inferior frontal cortex. Although the recruitment of these regions varies with the particular reading-related task, general networks of regions seem to be uniquely associated with different components of the reading process. For example, visual word form processing is associated with occipital and occipitotemporal sites, whereas reading-relevant phonological processing has been associated with superior temporal, occipitotemporal and inferior frontal sites of the left hemisphere. Such findings are evaluated in light of the technical and experimental limitations encountered in functional brain imaging studies, and the implications for pediatric studies are discussed.

In this society, where the quality of life is in large part determined by literacy, there has been a growing interest in understanding reading mechanisms and their development in diverse cultures. Until fairly recently, the neurological basis for reading had in most part been developed from case studies of brain lesion patients with selective reading deficits. As functional brain imaging tools have become more widely accessible, investigations into the neuroanatomical organization of reading and language have become more frequent, and the information gained about reading has become more detailed. Together, these lines of investigation have led to the development of theories of the modularity of language and reading. Today, functional brain imaging has a distinct advantage with its ability to noninvasively reveal information that will contribute to the study of reading acquisition and development. Although most of the brain imaging studies of reading to date have used adults, it is now possible to perform functional brain imaging studies on children. This information is crucial for an understanding of reading achievement, reading strategies,

and individual variation in mastering the reading process.

This article provides an overview of the current findings in functional neuroimaging research regarding the spatial localization of reading and reading-related tasks in the brain. Although many of the studies described in this article were designed to study language processing in a more general sense, most involved the presentation of written material, which allows us to make inferences about the functional specialization for single word processing. The various components of the reading process that are discussed have been extracted from existing models of reading, thereby providing a broad overview of the neurobiological basis of the reading process. However, we limit this review to neuroimaging studies of word decoding and do not fully address related processes such as comprehension, auditory language processing, working memory, and attention. Although significant progress has been made since the earliest neuroimaging studies of the reading process (Ingvar & Schwartz, 1974), many questions remain about the cortical specialization for various cognitive com-

ponents of reading. The present discussion attempts to find a consensus where possible. However, we also consider the limitations inherent in the various neuroimaging techniques as possible reasons for apparent discrepancies across studies. The results from these adult studies provide a useful foundation for the investigation of reading acquisition in children, which is currently still in its infancy.

Language and the Brain

Investigators have attributed language-specific processing to the areas that surround the Sylvian fissure, known as the perisylvian areas (see Figure 1). One of these areas, the temporoparietal cortex, receives projections containing but not limited to visual and auditory information. The posterior superior temporal gyrus, or Wernicke's area, has repeatedly been associated with a variety of language functions, usually involved in comprehension. Wernicke proposed, based on his observations in aphasia patients, that this area was specialized for auditory word recognition (Wernicke, 1887). Inferior parietal
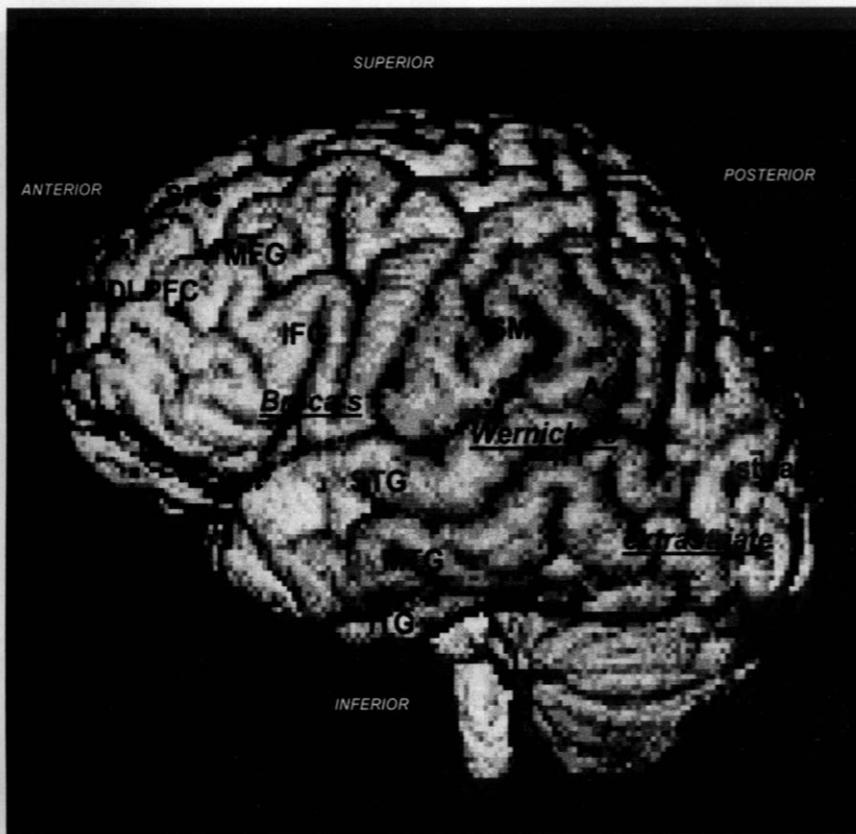
FIGURE 1. Lateral view of the left hemisphere of the human brain. For all figures in this article, the anterior portion of the brain appears on the left, and the superior surface appears at the top of the figure. Specific anatomical and functional regions (underlined) implicated in reading and reading-related tasks are indicated with labels. The Sylvian fissure is represented by a dotted line along the superior surface of the temporal lobe. AG = Angular gyrus; extrastriate = extrastriate visual cortex; IFG = inferior frontal gyrus (includes Broca's area); INS = insula; ITG = inferior temporal gyrus; MFG = middle frontal gyrus; MTG = middle temporal gyrus; SFG = superior frontal gyrus; SMG = supramarginal gyrus; STG = superior temporal gyrus (includes Wernicke's area). Although the insula (INS) is represented on the lateral surface of the brain in this figure, this cortical area actually lies buried in the depths of the Sylvian fissure.

classically associated with language, the analogous structures in the right hemisphere also appear to play a role. Moreover, noncortical structures such as the cerebellum, the cingulate, and the parahippocampal region have all been associated with various aspects of language processing. The functional neuroimaging studies reviewed here implicate a very wide network of regions associated with the reading process. These brain regions are referred to using the anatomical labels provided in Figure 1.

Physiological Basis of PET and fMRI

As proposed by Roy and Sherrington (1890), local cerebral hemodynamics in the brain are closely linked to local neuronal activity. Positron emission tomography (PET) allows the quantitative measurement of regional cerebral blood flow and blood volume. To assess task-related activity, which underlies sensory and cognitive processes, ^{15}O-water and butanol are commonly injected intravenously as freely diffusible tracers. The increase of regional cerebral blood flow (rCBF) in areas of high neuronal activity that are associated with the performance of a cognitive or sensory process can then be monitored by measuring the abundance of the tracer. This local increase associated with the task is typically compared to a baseline or resting condition that is believed not to engage the task under study (see Figure 2).

Functional magnetic resonance imaging (fMRI) can be achieved because of the paramagnetic properties of hemoglobin in its deoxygenated state. A local blood flow increase introduces more oxygenated blood than is required by the tissue, resulting in a relative decrease in deoxyhemoglobin (Belliveau et al., 1991; Ogawa, Lee, Nayak, & Glynn, 1990; Turner, Le Bihan, Moonen, & Frank, 1991). The relative concentration of deoxygenated hemoglobin relative to oxygenated hemoglobin acts as an endogenous, intravascular, para-

sites, such as the supramarginal gyrus and the angular gyrus, have been widely associated with written and spoken language comprehension. Dejerine argued that a disconnection of the angular gyrus from the primary visual areas would result in alexia, and direct damage to this area results in alexia with agraphia (Dejerine, 1892). Consequently, Dejerine proposed the angular gyrus to be the site of written language. The frontal lobe is also attributed with certain types of language processing. Most notable are the inferior frontal gyrus, which includes

Broca's area, and the dorsolateral prefrontal cortex. These areas are generally associated with organization, manipulation, and production of language, as well as grammar and syntax. However, it is probably oversimplistic to describe temporoparietal areas as those responsible for the reception of language whereas frontal regions are responsible for expressive language. On the contrary, it is most likely that a distributed network is responsible for full coherence of the language system. Although the aforementioned left hemisphere regions are those that are

PET

Task A   **Rest**   **Task B**   **Rest**   **Task A**   **Rest**   **Task B**   **Rest**

fMRI

Task A   **Task B**   **Task A**   **Task B**

Rest   **Rest**   **Rest**   **Rest**   **Rest**

FIGURE 2. A typical task design for PET and fMRI studies. In each case, two experimental tasks (Tasks A and B) and one rest task are used.

magnetic contrast agent by affecting the image intensity.

PET and fMRI techniques are similar in that they are based on the phenomenon of increased local blood flow during increased neuronal activity. To assess task-related signal change, both types of experiments usually employ task and control (resting) conditions. The signal changes that are associated with these conditions are contrasted to identify areas of the brain that show unique activation only during the task condition (see Figure 2). The accuracy of the resulting statistical maps in determining the location of task-related activity is, of course, dependent on the cognitive components involved and the strategies used during the task and control conditions. As we shall see, there are a number of ways to go about this for a task such as reading.

Component Processes of Reading

To study the neuronal correlates of cognition, investigators often aim to tease apart the components of a cognitive process. The complex process of reading involves several distinct components. Not all models of reading agree

on the number of components, the connectivity among the components (Is component A connected to component B?), or the flow of information among components (Is information relayed between components in a serial or parallel fashion? e.g., McClelland, 1979). However, in this article, we provide a survey of functional neuroimaging studies that deal with the component processes of reading that are typically shared among various models. Specifically, the components of the reading process that are reviewed in this article include processing of visual word forms, lexical orthography, semantic information associated with words, lexical and sublexical phonology, and phonological and phonetic encoding, each of which is addressed in a separate section.

Functional Neuroimaging Studies of Reading

Visual Word Form Processing

This component of reading involves visual analysis of letter and word stimuli to distinguish them from other visual patterns. Letters are translated into ab-

stract representations, which preserve the basic form of the letter despite stylistic differences such as size, font, or script. The tasks that have been used to isolate brain regions involved in visual word form processing have included passive viewing (Indefrey et al., 1997; Menard, Kosslyn, Thompson, Alpert, & Rauch, 1996; Petersen, Fox, Posner, Mintun, & Raichle, 1989; Petersen, Fox, Snyder, & Raichle, 1990; Puce, Allison, Asgari, Gore, & McCarthy, 1996); feature, color, or letter detection (Frith, Kapur, Friston, Liddle, & Frackowiak, 1995; Kapur et al., 1994; Price, Wise, & Frackowiak, 1996); and visual matching (Kuriki, Takeuchi, & Hirata, 1998; Pugh et al., 1996). Studies have employed words, pseudowords, letter strings, false fonts (i.e., letter-like stimuli), or symbols. Figure 3 summarizes the loci of activation across these studies. Some of these studies have shown greater activation in the left extrastriate cortex than in the right, using stimuli containing letters (e.g., Petersen et al., 1989; Price, Wiser, & Frackowiak, 1996; Puce et al., 1996). Also, letter strings and faces activate different regions of visual cortex (Puce et al., 1996), and different types of visual word forms may activate different cortical areas. Petersen et al. (1990) compared words, pseudowords, and consonant strings to false font strings. They isolated a region of the left medial extrastriate cortex that was activated by both words and pseudowords but not by consonant strings. Their conclusion was that this cortical area is involved in the recognition of visual word forms that obey English spelling rules. Pugh et al. (1996) have also shown that this region responds more to real words than to letter strings when a category judgement was made on real words and a case judgement was made on letter strings. Such findings support the proposal that the medial extrastriate cortex responds preferentially to word forms.

Other studies, however, do not support this proposal. Price, Wise, and Frackowiak (1996) demonstrated extrastriate activation using letter strings compared to false fonts only during a
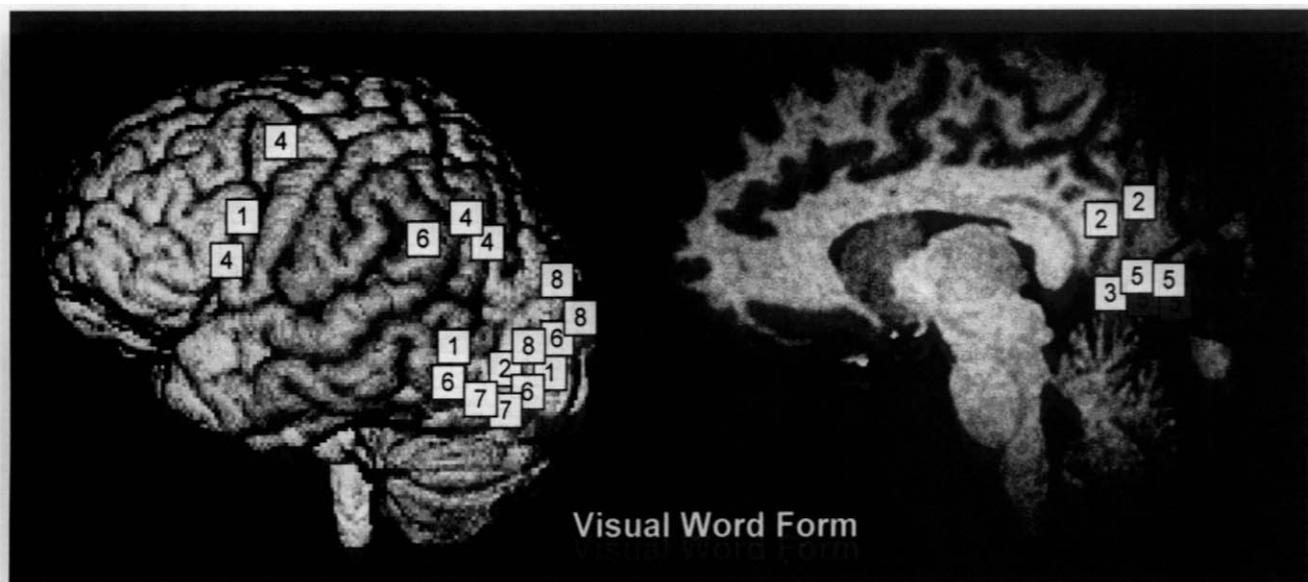
FIGURE 3. Functional loci associated with visual word form processing. 1—Frith et al. (1995); 2—Kapur et al. (1994); 3—Kuriki et al. (1998); 4—Menard et al. (1996); 5—Petersen et al. (1990); 6—Price, Moore, & Frackowiak (1996); 7—Puce et al. (1996); 8—Pugh et al. (1996). The placement of each locus in this figure and in Figures 4 through 7 was determined by Talairach coordinates (Talairach & Tournoux, 1988), Brodmann's areas (Brodmann, 1909), or gyral/sulcal anatomy provided in each study. The lateral view reflects loci more than 25 mm from the midline projected to the surface of the brain, whereas the medial view reflects loci less than 25 mm from the midline projected onto the medial plane.

feature detection task and not when words or pseudowords were compared to false fonts or letter strings. Consequently, extrastriate activation may not be specific to word forms. Likewise, Menard et al. (1996) failed to show consistent activation of any extrastriate visual area when participants passively viewed real words versus viewing pictures. More recently, Indefrey et al. (1997) demonstrated that the medial extrastriate activation associated with passive viewing of pseudoword strings was largely due to the length of the string; no medial extrastriate activation resulted from the comparison of pseudoword strings to length-matched false font strings.

In summary, whereas earlier studies pointed toward the specialization of left medial extrastriate cortex for visual word forms that obey English spelling rules, more recent studies have questioned this conclusion. Different cortical regions, such as the lingual and fusiform gyri, may be selectively involved in visual word form processing (Kuriki et al., 1998; Polk & Farah, 1998). Moreover, it is of great interest for the understanding of reading acquisition whether cortical circuitry is specifically dedicated to the recognition of visual word forms and how that cortical specialization may depend on an individual's experience with words. Such questions are just starting to be explored with functional neuroimaging.

Lexical Orthography

Orthographic units of language are abstract representations that indicate which letters compose a word and in which order the letters occur. Developing cognitive tasks that isolate orthographic processing from phonological or semantic processing is difficult. Some authors have compared single word reading to reciting a word in response to false font strings (Howard et al., 1992; Small et al., 1996) to isolate lexical orthography. This task, however, likely involves phonological decoding and processing as well as automatic semantic activation of word meanings (all of which are discussed in subsequent sections). Although posterior temporal and parietal areas were activated in these studies, these regions may also be involved in phonological processing, and their activation may not necessarily be attributed to lexical orthography per se.

Orthographic fluency (also called verbal, letter, or phonemic fluency) is another commonly used task. In this task, participants are given a single letter (presented either auditorily or visually) and asked to generate a word or words that begin with that letter. Access to the orthographic lexicon is required because the correct spellings of words must be retrieved. However, phonological strategies may also be used by converting the given visual letter into a corresponding sound and retrieving words from the phonological rather than the orthographic lexicon (L. Friedman et al., 1998). Despite notable differences across studies, nearly all of these orthographic fluency tasks have demonstrated activation of Broca's area, as shown in Figure 4 (Benson et al., 1996; L. Friedman et al., 1998; Paulesu et al., 1997; Rueckert et al., 1994). The second most commonly reported area across studies using orthographic flu-
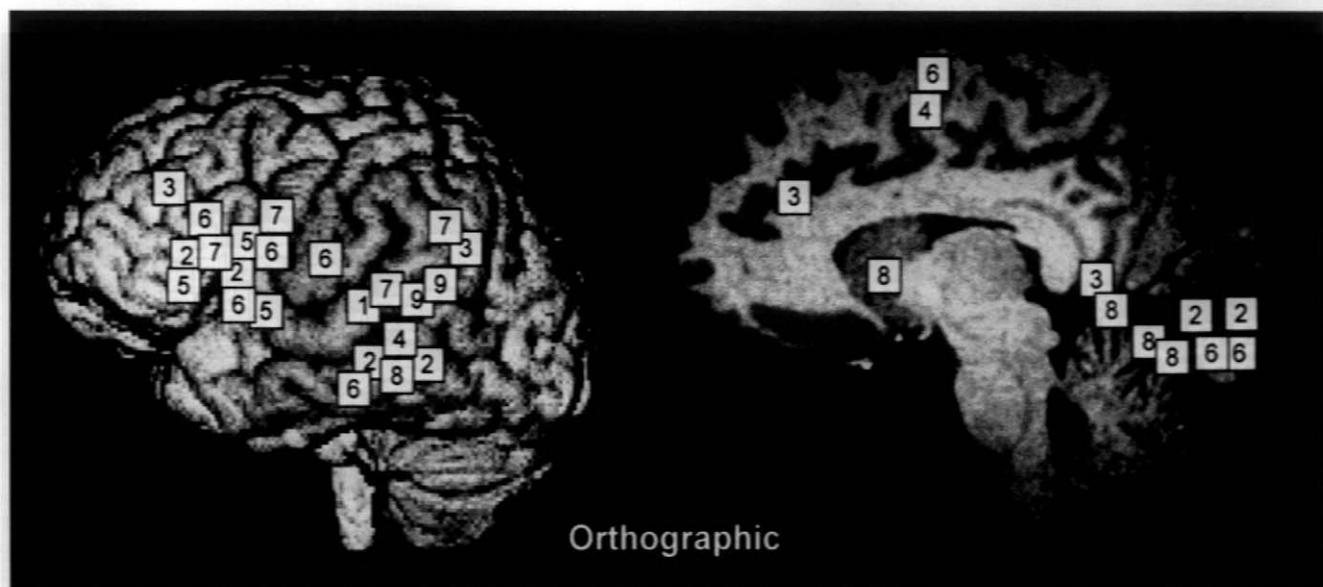
FIGURE 4. Functional loci associated with orthographic processing. 1—Flowers et al. (1991); 2—L. Friedman et al. (1998); 3—Frith et al. (1991); 4—Howard et al. (1992); 5—Paulesu et al. (1997); 6—Price et al. (1994); 7—Reuckert et al. (1994); 8—Rumsey, Horwitz, et al. (1997); 9—Small et al. (1996).

ency is the left posterior superior temporal gyrus (STG) or Wernicke's area (Benson et al., 1996; L. Friedman et al., 1998; Rueckert et al., 1994). It is not surprising for these two classically defined language areas to participate in orthographic fluency, given the linguistic nature of the task, but it is not entirely clear which components of fluency are subserved by which areas.

Spelling judgment tasks are another, perhaps less ambiguous, way to examine access to and functioning of the orthographic lexicon. In a PET study by Flowers, Wood, and Naylor (1991), participants decided whether auditorily presented words were four letters in length. This task involves access to information about the number of letters in a word, which is stored in the orthographic lexicon. Flowers et al. found that behavioral spelling performance was related to the magnitude of brain activation only in Wernicke's area (left posterior STG). Although the phonological representation of the word is undoubtedly used in this task, it is unlikely that the phonological word description would contribute significantly to determining the number of letters in a word. Nevertheless, pure

isolation of orthographic processing may not be best achieved with this particular spelling judgment task.

In the spelling judgment task developed by Rumsey and colleagues (Rumsey, Horwitz, et al., 1997; Rusmey, Nace, et al., 1997), a word and a pseudohomophone (e.g., *third* and *thurd*) were presented visually, and participants decided which of the two was a real word. This task successfully isolates orthographic processing from phonological processing because the spoken forms of the two stimuli are identical. Hence, participants can only rely on spelling, not phonology, to make the decision. This task was compared with a phonological decision task, in which participants decided which of two visually presented pseudowords sounded like a real word (e.g., *jope* or *joak*). Regions in the left lingual gyrus (extrastriate cortex) were more activated during the orthographic than during the phonological decision task, but it is also clear that orthographic and phonological tasks recruited similar regions of cortex, differing in magnitude of activation rather than in spatial localization.

In summary, studies that have attempted to isolate lexical orthography

from lexical phonology have implicated left temporal, left inferior frontal, and left inferior parietal cortex. However, many of the tasks that have presumed purely orthographic processing may have, in fact, also included phonological processing, making it difficult to attribute a brain region or network of regions to orthographic processing. One conclusion that can be drawn from these PET studies is that there is a great deal of overlap in terms of brain regions subserving the two kinds of processing, even when using tasks that more effectively isolate orthographic from phonological lexical processing.

Lexical Phonology

The phonological units of language specify the sound structure of words and the ordering of the phonemes that make up the pronunciation of a word. Access to the phonological lexicon has been studied with tasks that require perception and evaluation of the sound structure of words and letters. The most frequently used tasks in the neuroimaging literature have been rhyme judgments using letters (Paulesu et al., 1996; Sergent, Zuck, Levesque, & Mac-

Donald, 1992) or words (Petersen et al., 1989) and certain lexical decision tasks (Frith, Friston, Liddle, & Frackowiak, 1991; Rumsey, Horwitz, et al., 1997). Rhyme generation has also been used (Shaywitz, Pugh, et al., 1995).

As summarized in Figure 5, several perisylvian regions likely participate in phonological processing. The area most commonly reported across studies is the left posterior STG (including Wernicke's area). For example, rhyme judgment tasks using letters, which require participants to decide whether a visually presented letter rhymes with a target letter (e.g., B; Paulesu et al., 1996) or a target sound (e.g., *ee*; Sergent et al., 1992), result in activation of the left posterior STG. Further evidence for activation of the left posterior STG comes from Petersen et al.'s (1989) study using rhyme judgment with words and from Frith et al.'s (1991) lexical decision tasks using auditorily presented words and nonwords.

Another commonly reported area across tasks involving phonological processing is the left insula. Paulesu et al. (1996) reported left insular activation in a rhyme judgment task using letters. Rumsey, Hortwitz, et al.'s (1997) phonological lexical decision task required participants to decide which of two visually presented nonwords sounded like a real word (e.g., *jope* or *joak*? as described earlier). When this task was compared to the spelling judgment task described earlier (e.g., Which word is a real word, *third* or *thurd*?), the left insula, among other areas, was activated. Left insular activation was also reported as a major site for phonological processing in Shaywitz, Pugh, et al.'s (1995) rhyme generation task that required silent generation of words that rhyme with a given target word.

Finally, phonological tasks also involve the inferior frontal gyrus or Broca's area. The rhyme judgment tasks using letters (Paulesu et al., 1996; Sergent et al., 1992) and the phonological lexical decision task used by Rumsey and colleagues (Rumsey & Eden, 1997; Rumsey, Hortwitz, et al., 1997) resulted in activation of Broca's area. The two rhyme judgment tasks using letters also reported involvement of the left caudate (Paulesu et al., 1996; Sergent et al., 1992).

In summary, the neuroimaging evidence suggests that the lexical pho-nological network appears to be composed of the posterior superior temporal gyrus, left insula, and inferior frontal cortex. It is important to note, however, that many other cortical regions have been reported in these studies. Moreover, we have restricted our definition of phonological tasks to those that require evaluation of the sound structure of words. Production tasks, such as word and object naming, are also used to elucidate phonological retrieval (Price & Friston, 1997) and have led to the identification of a basal posterior temporal region that is recruited regardless of the mode of input of the stimulus to be named. For example, this basal temporal region is recruited even when blind participants are reading Braille (Buchel, Price, & Friston, 1998). Further experimentation is needed to determine which regions participate exclusively in phonological aspects of reading and which regions participate in phonological aspects of production.

Sublexical Phonology

This component of reading refers to the processing of the submorphemic sound
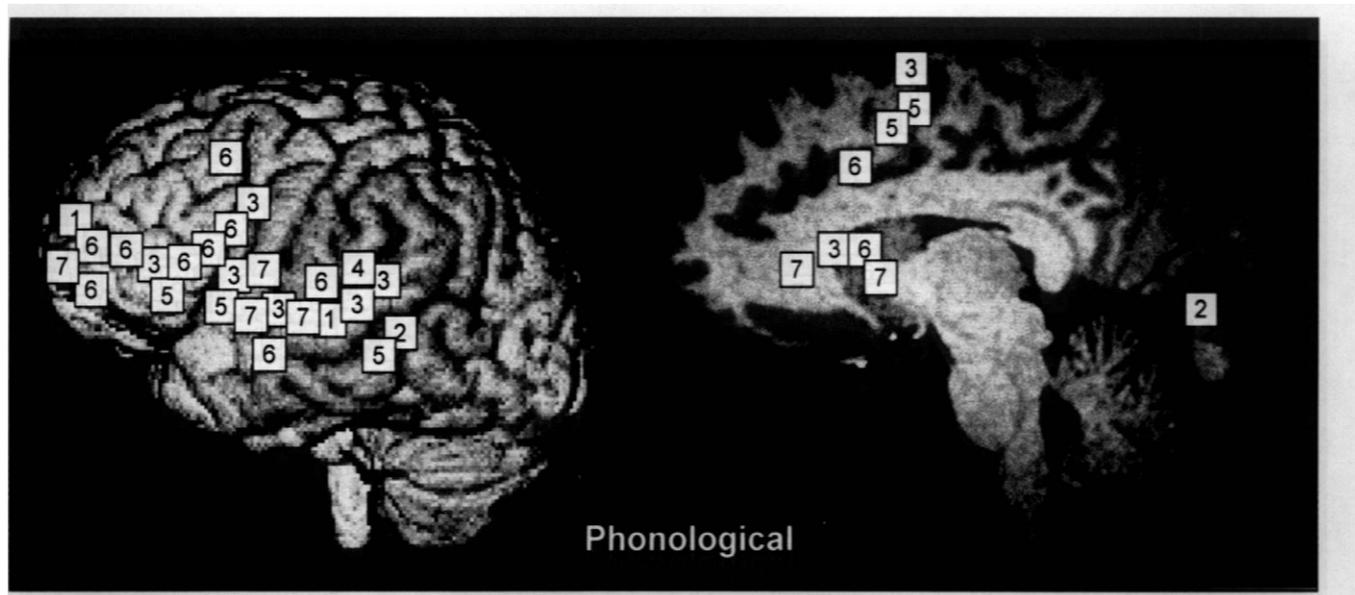
FIGURE 5. Functional loci associated with lexical phonological processing. 1—Frith et al. (1995); 2—Howard et al. (1992); 3—Paulesu et al. (1996); 4—Petersen et al. (1989); 5—Rumsey, Horwitz, et al. (1997); 6—Sergent et al. (1992); 7—Shaywitz, Pugh, et al. (1995).

units of phonological word descriptions, or *phonemes*. Phonemes alone generally do not have associated semantic information, unlike orthographic and phonological word descriptions. However, they can be accessed and manipulated separately from words, as in pseudoword reading, phonemic monitoring, and phoneme deletion. Figure 6 summarizes the loci of activation involved in sublexical phonology. Demonet and colleagues (Demonet et al., 1992; Demonet, Price, Wise, & Frackowiak, 1994a, 1994b) used phonemic monitoring, which requires monitoring auditorily presented nonwords for the phoneme /bee/ where the phoneme may occur at the beginning of the word (presumed to be simpler) or in the middle of the word (presumed to be more difficult). Even more difficult versions of this task involve detecting the phoneme /bee/ only if the word itself begins with the phoneme /dee/ or when it is preceded by the phoneme /dee/ anywhere in the word. The different versions of this task tend to activate left superior and middle temporal regions and areas along the occipitotemporal junction. Other investigators have confirmed activation of these temporal regions using nonword read-

ing (compared with irregular word reading; Rumsey, Horwitz, et al., 1997) and nonword rhyme judgment (Pugh et al., 1996). Both of these nonword tasks are presumed to be operating at a sublexical level, because nonwords should not have representations in the mental lexicon.

Investigators have also demonstrated the following frontal sites of activation involved in sublexical phonological processing: left inferior frontal (Demonet et al., 1992; Hagoort et al., 1999; Pugh et al., 1996), premotor cortex (Demonet et al., 1994b; Hagoort et al., 1999; Rumsey, Horwitz, et al., 1997), and left orbital frontal (Pugh et al., 1996). Although the brain regions involved in sublexical phonology overlap a great deal with those involved in lexical phonology, there are some notable differences (cf. Figures 5 and 6). First, lexical phonology appears to involve the insula, whereas sublexical phonology does not. Second, the temporal regions engaged during sublexical phonology include the occipitotemporal junction and appear to be more restricted to the middle temporal gyri, whereas those regions in the temporal lobes involved in lexical phonology are more superior. Third, frontal lobe

activations (both lateral and medial) appear to be more extensive during lexical than during sublexical phonological processing. Despite the range of tasks used during sublexical phonology, including visual and aural presentation paradigms, there is agreement that sublexical phonology elicits task-related activity in occipitotemporal, middle temporal, and inferior frontal regions of the left hemisphere.

Semantic Processing

The semantic system, for the present purposes, refers to conceptual knowledge about the referents of words, including the category to which an object or entity belongs, its associated attributes and functions, and other associated concepts. Although a number of functional imaging studies have explored the semantic system in and of itself, the present discussion is interested only in access to the semantic system from the written word.

Investigators have often used category judgment tasks, in which the participant decides whether a written word is a member of a certain semantic category, such as animals or tools (Demonet et al., 1992; Kapur et al., 1994;
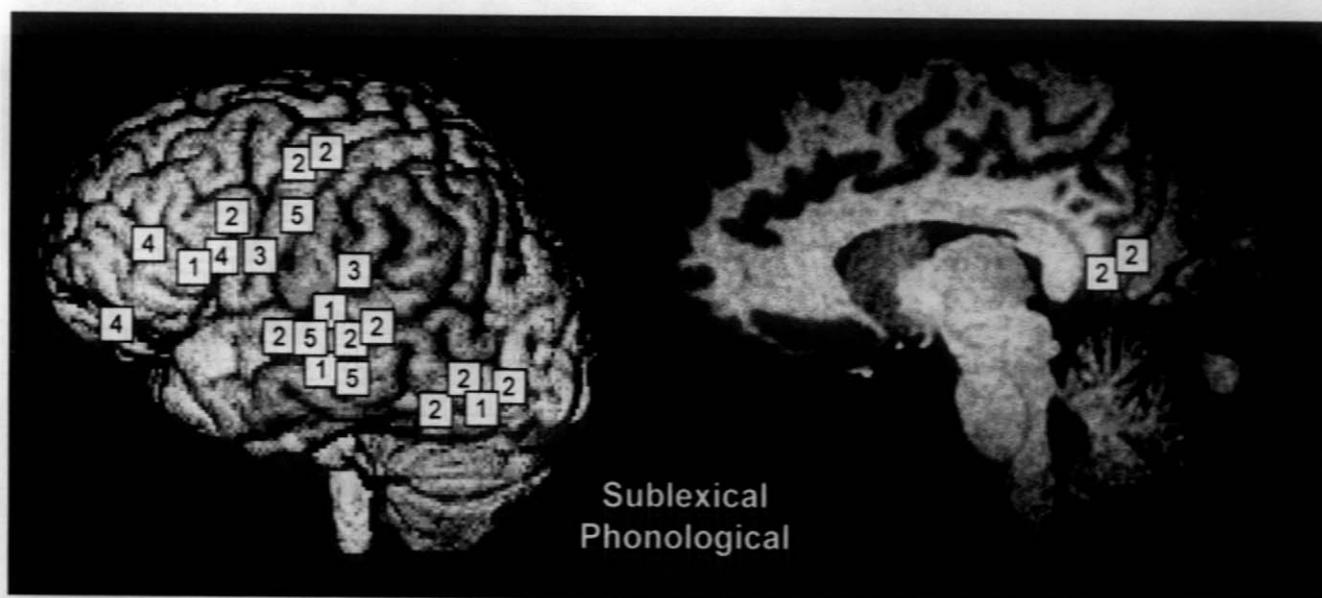
FIGURE 6. Functional loci associated with sublexical phonological processing. 1—Demonet et al. (1992); 2—Demonet et al. (1994a); 3—Demonet et al. (1994b); 4—Pugh et al. (1996); 5—Rumsey, Horwitz, et al. (1997).

Petersen et al., 1989; Price, Moore, Humphreys, & Wise, 1997; Pugh et al., 1996), or whether two stimuli of different parts of speech are semantically related (e.g., *apple* and *eat*; Warburton et al., 1996; Wise et al., 1991). In these tasks, the participant must attend to the meaning of the stimulus and determine whether its referent is a member of the designated category. Category judgment tasks have been associated with activation in superior (Demonet et al., 1992), middle (Demonet et al., 1992; Price et al., 1997), and inferior (Demonet et al., 1992; Pugh et al., 1996) temporal gyri, as well as in the temporal pole (Price et al., 1997) and the supramarginal gyrus (Demonet et al., 1992), as shown in Figure 7. However, there have been PET studies in which category judgment tasks did not activate the temporal lobe at all, but rather showed activation in the left frontal lobe (Petersen et al., 1989) including the left inferior frontal cortex (Posner & Pavese, 1998). Similar semantic monitoring tasks, such as verb–noun comparison, have also activated both temporal and frontal lobe structures (Warburton et al., 1996; Wise et al., 1991).

In other studies, semantic generation tasks have been used in which partici-

pants generate novel semantic coordinates for the stimuli presented. For instance, in a verb generation task, the participant is presented with a noun (e.g., *chair*) and must then generate a verb appropriate to that noun (e.g., *sit*; Fiez & Petersen, 1993; Fitz Gerald et al., 1997; Petersen et al., 1989; Snyder, Abdullaev, Posner, & Raichel, 1995; Warburton et al., 1996; Wise et al., 1991). Similarly, verbal fluency tasks, in which participants must respond with as many exemplars of the stimulus category as possible, also require the generation of novel, conceptually related items (Frith et al., 1991; Shaywitz, Pugh, et al., 1995). When comparing a verb generation task to rest, Wise et al. (1991) found activation in the superior temporal lobe, the left inferior and left middle frontal lobes, and the supplementary motor area. However, when Petersen et al. (1989) compared verb generation to the repetition of single nouns, they found activation in the left anterior inferior frontal cortex, the anterior cingulate, and the right inferior lateral cerebellum, but not in the temporal lobes. It is possible that no temporal activation was found in such a comparison because access to semantic knowledge was subtracted out in this

comparison (Petersen et al., 1989; Shaywitz, Pugh, et al., 1995; Wise et al., 1991). In contrast, when Warburton et al. (1996) compared the verb generation task to the aforementioned verb–noun comparison task, they continued to find both frontal and temporal regions of activation. Again, access to semantic knowledge was expected to be present in both tasks and thereby cancelled out with the subtraction, but this did not occur. These conflicting results are probably due to the use of different control conditions across studies, a point that is addressed more extensively in the discussion.

In summary, both category judgment and semantic generation using written words tend to activate wide regions of temporal and frontal cortex (see Figure 7). Although there are notable exceptions, category judgment has more often been found to result in activation of temporal structures, whereas semantic generation frequently leads to frontal activation.

Phonological and Phonetic Encoding and Articulation

Vocal word production involves a series of complex processes that are be-
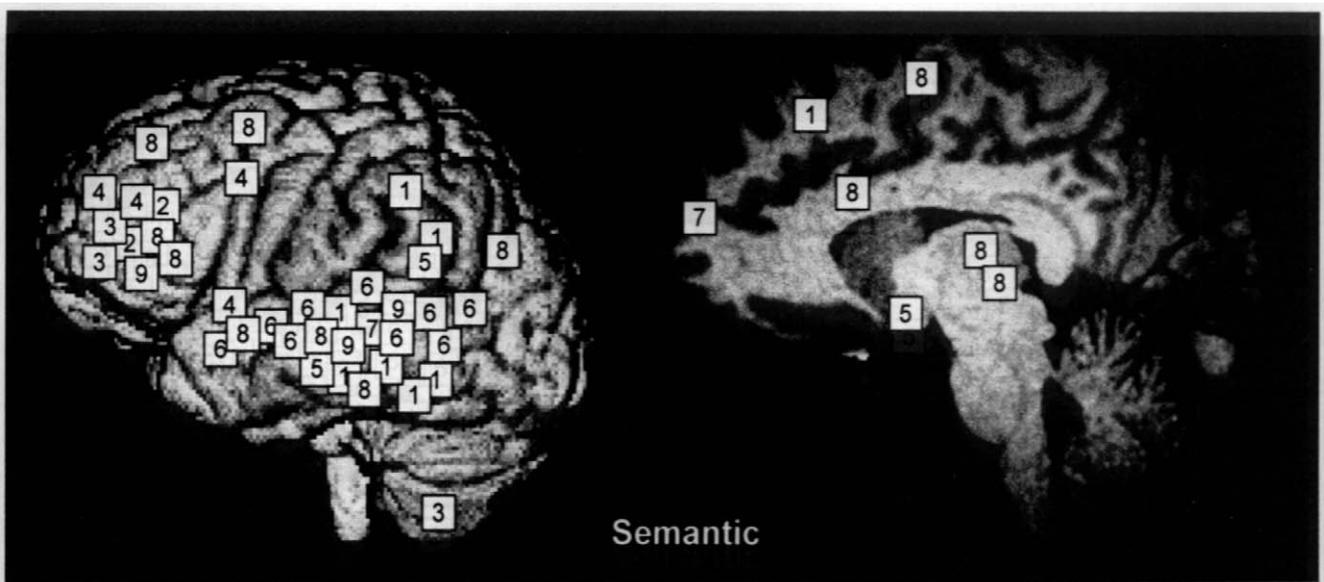
FIGURE 7. Functional loci associated with semantic processing. 1—Demonet et al. (1992); 2—Kapur et al. (1994); 3—Petersen et al. (1989); 4—Price et al. (1994); 5—Price et al. (1997); 6—Pugh et al. (1996); 7—Shaywitz, Pugh, et al. (1995); 8—Warburton et al. (1996); 9—Wise et al. (1991).

yond the scope of the present article (for more in-depth treatments of this topic, see Blumstein, 1995; Levelt, 1989). Although the present focus is on word decoding rather than word production, the encoding of a phonological representation into an articulatory program for overt speech is briefly reviewed here. Overt word production has been studied primarily with PET but not with fMRI. One reason for this is a technical limitation—articulation is associated with motion, and motion is detrimental to MRI data quality.

Using PET, Rumsey, Horwitz, et al. (1997) demonstrated that the covert or overt nature of the response strongly predicts the locus of activation in the brain. In their study, pronunciation tasks activated the superior temporal gyrus bilaterally, but decision-making tasks (responding *yes* or *no* with a button press) preferentially activated the left inferior frontal cortex. These findings are consistent with other studies comparing word pronunciation with silent reading (Bookheimer, Zeffiro, Blaxton, Gaillard, & Theodore, 1995; Price et al., 1994). An important confound to consider when comparing oral and silent reading is that oral reading may activate superior temporal regions close to the primary auditory cortex because individuals are hearing the sound of their own voices. Consequently, the STG activation may merely reflect auditory feedback from the task rather than access to phonological codes and execution of articulatory programs. Evidence against this proposal is that when reading aloud is compared to word articulation in response to a meaningless stimulus, STG activation remains (Moore & Price, 1999). Addressing such confounds is critical for illuminating cortical specialization for overt word production.

Functional Brain Imaging of Acquired Reading Disorders

Acquired reading disorder, or alexia, may result from a variety of postdevelopmental forms of brain damage, such as cortical insult, tumor, stroke, or de-

mentia. Reading may be disrupted in multiple ways, leading to a variety of behavioral deficits depending on the location of neural dysfunction (for a complete review of lesion studies, see R. B. Friedman, Ween, & Albert, 1993). Although the benefits of examining acquired disorders to elucidate the components of typical reading are limited (Snowling, Bryant, & Hulme, 1996), it is useful to examine some of the neural structures that may be functionally impaired in alexia. Two types of alexia are presented here: surface alexia and phonological alexia.

The acquired reading disorder known as *surface alexia* results in a patient having greater difficulty in reading words with exceptional spelling–sound correspondences (e.g., *gone*) than words with typical spelling–sound correspondences (e.g., *green*). The appearance of a surface alexia is possible evidence for reliance on a sublexical grapheme–phoneme route in oral reading. Although anatomical lesions producing surface alexia are diverse, they tend to involve the left temporoparietal cortex while sparing the occipital cortex (see Patterson, Marshall, & Coltheart, 1985). Functional neuroimaging data are in accord with this site being the locus of impairment. Parkin (1993) used PET to reveal regional hypometabolism at rest rather than examine relative neural activation during a specific task. Parkin showed that persons with surface alexia displayed regional hypometabolism in all three left temporal gyri as well as in the left posterior frontal gyrus.

Phonological alexia is defined as an inability to read pronounceable nonwords, or pseudowords, while the reading of both regular and exceptional real words is preserved. Patients with this disorder must use semantics to translate orthographic representations into phonological output, because the lexical route is impaired. Words without semantic representation (i.e., pseudowords) or with very little semantic representation (i.e., functors and low-frequency words) therefore pose a difficulty for these patients. Phonological alexia has been linked to lesions of the

superior temporal lobe and the angular and supramarginal gyri (Bub, Black, Howell, & Kertesz, 1987; Derouesne & Beauvois, 1985; R. B. Friedman & Kohn, 1990). Small, Flores, and Noll (1998) investigated the brain activation in an acquired phonological alexia patient (in this case with a large left frontotemporal lesion) during oral reading using fMRI. During the experimental condition, the patient was asked to perform a reading task, which when compared with a control false-font task, primarily activated the left angular gyrus. Also, the lingual gyrus, the lateral premotor area, the supplementary motor area, the precuneus, the middle temporal gyrus, and the prefrontal cortex all showed a lesser degree of activation. After engaging in therapy designed to teach the patient a set of rules for translating graphemes to phonemes, the patient was able to read pseudowords and functors. When retested using the same fMRI paradigm, the reading task preferentially activated the left lingual gyrus, with lesser activation occurring in the middle temporal gyrus, the lateral premotor area, the cuneus, the precuneus, and the precentral gyrus, and much less activation than in the initial scan in the angular gyrus. The authors proposed that during grapheme–phoneme conversion, the patient learned to visually decompose and convert orthography into phonology in order to read aloud. It is possible that functional reorganization of the brain followed therapy, such that circuits involving occipital areas, including the lingual gyrus, were unmasked to allow reading via the grapheme–phoneme route. These findings are consistent with task-related signal changes observed in typical reading populations, which assign the temporoparietal areas to orthographic and the occipitotemporal areas to phonological components of reading (described earlier and summarized in Figures 3 through 6).

Summary

Functional neuroimaging data that support the various components of the

single word reading process have been presented. Figures 3, 4, 5, and 6 show the loci of activation across a number of different studies for each component of reading. In general, left-hemisphere perisylvian regions are engaged across many of the subcomponents. More specifically, visual word form processing tends to engage posterior cortical regions, primarily in the occipital and occipitotemporal cortex. Orthographic processing primarily involves posterior temporal, inferior parietal, and inferior frontal regions. Lexical phonological, sublexical phonological, and semantic components recruit large regions of temporal and inferior frontal cortex. These are, of course, generalizations. As Poeppel (1996) has pointed out in his analysis of PET studies of phonological processing, and as is evident here, there is a great deal of variability across studies of brain and language relationships. The extant body of research on brain–behavior relationships within the reading domain needs to be substantiated and disambiguated with future research.

Discussion

PET and fMRI have enhanced our knowledge about how specific components of reading map onto the brain. As these techniques become more refined and technologically advanced, our knowledge of the brain structures that underlie reading will also advance. Improvements in experimental design and postprocessing of image data will help to improve the reliability of functional imaging data, allowing more precise and definitive conclusions about the neural underpinnings of the reading process. The following discussion evaluates the reviewed literature in light of the limitations and pitfalls of using the existing imaging techniques. These limitations are broadly classified into the following categories: technical limitations, experimental design issues, pediatric functional neuroimaging, and cognitive assumptions.

Technical Limitations

Most of the studies presented in this review have used the older functional imaging technique PET. The better spatial information gained with fMRI may help future studies in isolating separate but spatially proximal brain regions for tasks such as orthographic and phonological processing, which appear to overlap a great deal in terms of functional anatomy (e.g., Rumsey, Horwitz, et al., 1997).

In fMRI, the ultimate temporal limitation is the duration of the hemodynamic response, which is in the range of seconds; hence, the temporal resolution of fMRI (and PET) is poor. Other techniques with exquisite temporal information, such as evoked potentials (EPs) or magnetoencephalography (MEG), might be more useful for some of these questions. There are ongoing efforts to use techniques with higher temporal resolution in conjunction with fMRI in the same individuals performing the same tasks (Guy, ffytche, Brovelli, & Chumillas, 1999). This way, the strengths of each technique can be combined to provide good temporal and spatial information to elucidate brain mechanisms involved in reading and other cognitive functions.

Only partial brain volumes may have been collected in a number of these studies (depending on the equipment available and time constraints of the study), further hindering our ability to make comparisons across studies. For example, the cerebellum was often not included during data acquisition in many of these studies, yet in studies that have collected whole brain volumes, it appears that the cerebellum is often active during reading-related tasks (e.g., Rumsey, Horwitz, et al., 1997).

fMRI studies of reading aloud have rarely been conducted because of the resulting artifacts introduced by head and jaw movements. Alternating data acquisition with task execution can circumvent this problem (Eden, Joseph, Brown, Brown, & Zeffiro, 1999). With this approach, the jaw movement oc-

curs in a period different from the data acquisition interval. Because of the delay of the hemodynamic response, the signal is captured in the delayed acquisition period. Future developments in data acquisition techniques will inevitably improve neuroimaging studies of reading and address other issues such as noise contamination and inter- and intrasubject reliability.

Experimental Design

The choice of control task varies enormously across the studies reviewed here. As alluded to in earlier sections, the control task that is contrasted to the experimental task can have a tremendous impact on the cortical regions that appear to be activated by a task. Statistical contrasts that compare an experimental task such as reading words to a rest task such as visual fixation, for example, will not be as selective as comparing to a control task (e.g., pseudoword reading) that shares many of the same cognitive components as the experimental task. Interpreting results from functional imaging studies, therefore, requires an understanding of the control task that is used in statistical contrasts.

Another consideration in functional imaging studies of reading is the stimulus presentation rate. Blood flow and MRI signal changes can be modulated by the presentation rate and exposure duration of visual and auditory stimuli. Using PET, Price et al. (1992) showed that primary auditory cortex and middle STG were linearly modulated by the presentation rate of auditory speech stimuli, such that a faster presentation rate led to increases in blood flow. This linear relationship, however, did not hold for Wernicke's area. In the visual modality using PET, Price, Moore, and Frackowiak (1996) showed that when reading words aloud, blood flow in early visual areas increases with increased presentation rate and longer exposure durations. Such relationships have also been explored with fMRI. Binder et al. (1994) showed that the MRI signal increases

in a nonlinear fashion with respect to the rate of presentation of speech stimuli. However, in contrast with Price et al.'s (1992) work using PET, this relationship was not area-dependent. To ensure that the differences between PET and fMRI with respect to presentation rate were not due to differences in design, Rees et al. (1997) compared such relationships in PET and fMRI directly. Using passive listening to words, they showed that responses in primary auditory cortex linearly increased with presentation rate increases for PET, but that the relationship was not linear for fMRI responses. All of these studies show that the presentation rate of visual and auditory stimuli can significantly modulate cortical responses for both PET and fMRI. In general, increasing the presentation rate leads to increases in blood flow measures or MRI signal changes in primary sensory areas.

The functional neuroimaging studies of reading to date have often used very small samples of participants. Furthermore, the samples are rarely balanced for gender. Because some studies investigating reading-related tasks have suggested that there are differences between men and women (Shaywitz, Shaywitz, et al., 1995), the composition of the sample should be carefully considered when evaluating results from these studies.

Pediatric Functional Neuroimaging

Very few functional neuroimaging studies have been conducted with children, mainly because PET requires the application of radioactive material. Due to its noninvasive nature, fMRI can be used to study cognitive function in children. In early pediatric studies, fMRI was used to map language dominance in children with partial epilepsy (Hertz-Pannier et al., 1997). The results were in agreement with intracarotid amobarbital testing performed for presurgical evaluation. Recent studies have used fMRI to investigate nonlanguage cognitive tasks in children and

compare them to adults to yield developmental information (Casey et al., 1997; Thomas et al., 1999). Ongoing studies using fMRI to investigate language processing in typical volunteers age 5 years and older clearly demonstrate that children can tolerate the MRI environment for experimental and clinical purposes. Figure 8 shows an example of a 12-year-old child reading aloud versus visual fixation, as studied with fMRI in our laboratory. The activation pattern is similar to that seen in adults. The fact that multiple measurements can be made on the same individuals with fMRI allows for tracking developmental changes on both short- and long-term scales. One additional advantage of fMRI is the higher spatial resolution gained in these images. However, the quality of this finer resolution is highly dependent on the participant keeping his or

her head steady throughout the scan. Head movement is more noticeable in children compared to adults, and if the total amount of head motion exceeds a certain limit, artificial signal changes will be observed, resulting in data artifacts. Current solutions to the problem of excessive head motion are to provide pre-experimental training in keeping the child's head steady, using head restraining devices, and applying motion correction routines prior to data analysis. With the continued refinement and development of these procedures, pediatric functional brain imaging for cognitive research is becoming more feasible.

Cognitive Assumptions

Interpretations of the reviewed studies can be complicated by misattributing a cognitive function to a given task. For
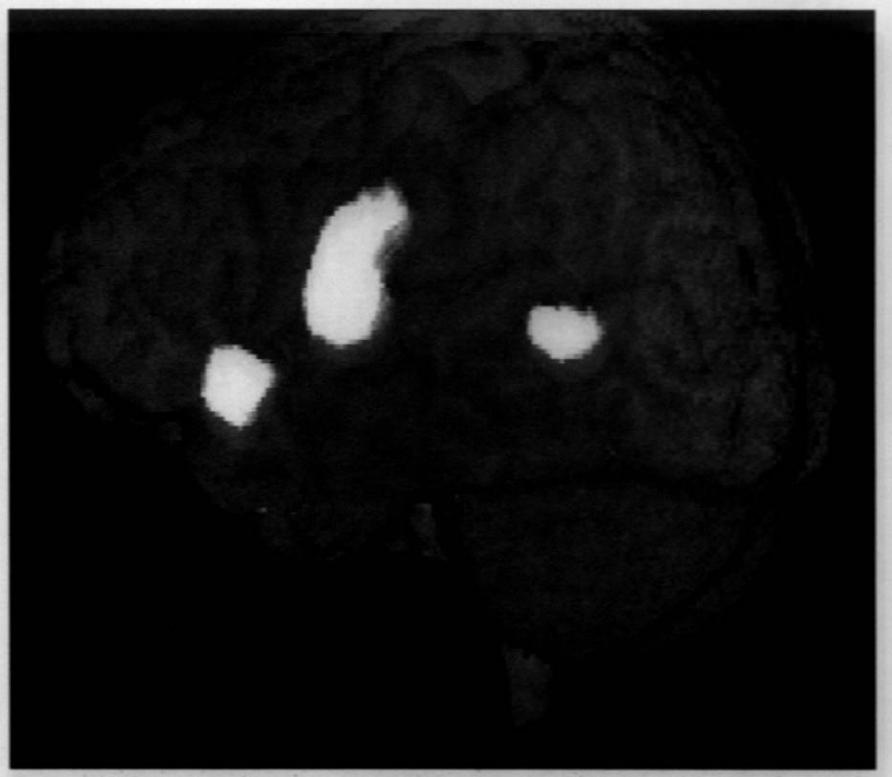
FIGURE 8. Functional loci associated with single word reading compared to fixation baseline in a 12-year-old child. The most anterior region of activation is in the inferior frontal gyrus and frontal operculum (i.e., the region of the frontal cortex that lies superior to the Sylvian fissure). The middle region of activation is in the precentral gyrus, in the most inferior portion of motor cortex. The posterior region of activation is in posterior middle temporal gyrus and superior temporal gyrus.

instance, because word generation is probably more demanding than word repetition, it is difficult to say whether increased activation in the former task is due to its semantic requirements or simply to increased effort. Studies comparing novel and overpracticed task-related activation have shown significant shifts in the location of activation loci (Raichle et al., 1994).

Another difficulty is devising a resting state task that does not involve cognitive processing of some sort. For instance, Binder et al. (1999) have proposed that it is incorrect to assume that a so-called "resting state" condition of an experiment is truly a state of neural inactivity (see Figure 2). They tested this by comparing a resting state, a tone perception task, and a semantic retrieval task. They found a network of left-hemispheric cortical regions that was more active during rest than during the perceptual task, but that had equal amounts of activity during the rest and the semantic task. These areas included a number of areas that feature prominently in the studies of reading described in this review. The investigators maintained that the semantic task and the rest condition both engaged general conceptual processing; therefore, these conceptual processing areas were seen in the rest–tone comparison and in the semantic–tone comparison, but not in the semantic–rest comparison. If processes involved in semantic retrieval and manipulation are engaged during conscious resting states, then studies designed to detect or manipulate these processes may lack sensitivity if a resting condition is used as a control comparison.

Conclusion

In conclusion, PET and fMRI are powerful tools for studying the brain–behavior relationships that underlie the reading process. The existing studies in adults have laid the groundwork for understanding single word decoding; however, future studies will enrich and expand these past efforts as tech-niques, experimental design, and data analysis become more refined. Promising future avenues of investigation include brain–behavior relationships that underlie the integration of single word decoding and comprehension of text, language dependencies in brain activation during reading and language, and reading acquisition in children.

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