

# Brain Mechanisms for Reading Words and Pseudowords: an Integrated Approach

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**The present study tested two predictions of dual-process models of reading: (i) that the brain structures involved in sublexical phonological analysis and those involved in whole-word phonological access during reading are different; and (ii) that reading of meaningful items, by means of the addressed phonology process, is mediated by different brain structures than reading of meaningless letter strings. We obtained brain activation profiles using Magnetic Source Imaging and, in addition, pronunciation latencies during reading of: (i) exception words (primarily involving addressed phonology and having meaning), (ii) pseudohomophones (requiring assembled phonology and having meaning), and (iii) pseudowords (requiring assembled phonology but having no meaning). Reading of meaningful items entailed a high degree of activation of the left posterior middle temporal gyrus (MTGp) and mesial temporal lobe areas, whereas reading the meaningless pseudowords was associated with much reduced activation of these two regions. Reading of all three types of print resulted in activation of the posterior superior temporal gyrus (STGp), inferior parietal and basal temporal areas. In addition, pronunciation speed of exception words correlated significantly with the onset of activity in MTGp but not STGp, whereas the opposite was true for pseudohomophones and pseudowords. These findings are consistent with the existence of two different brain mechanisms that support phonological processing in word reading: one mechanism that subserves assembled phonology and depends on the posterior part of STGp, and a second mechanism that is responsible for pronouncing words with rare print-to-sound correspondences and does not necessarily involve this region but instead appears to depend on MTGp.**

## Introduction

It has been proposed that reading is subserved by two independent mechanisms [for a review, see Coltheart *et al.* (Coltheart *et al.*, 1993)]. This 'dual-route' model is based mainly on evidence for a double dissociation in the ability to read pseudowords and real words in patients with acquired dyslexia secondary to brain damage (Marshall and Newcombe, 1973; Shallice and Warrington, 1980). According to this model, an *addressed* or lexical mechanism mediates the conversion of visual input to a whole-word phonological representation by means of access to a word-specific, lexical representation. Presumably, this route can only be used for reading aloud real words, and is required for pronouncing words with peculiar print-to-sound correspondences, such as PINT and COLONEL (i.e. exception words). In contrast, the *assembled* or sublexical mechanism involves mapping of individual orthographic segments onto the appropriate phonological elements to arrive at a complete phonological representation (a process also referred to as 'phonological decoding'). Assembled phonology is required for reading unfamiliar letter strings (pseudowords), as well as pseudohomophones (i.e. letter strings, such as BURTH, which are pronounced the same as their real-word counterparts, but have different spellings).

Recently, in the context of an electrocortical stimulation

study, we obtained evidence that the two purported mechanisms for reading may differ in at least one important feature. The mechanism that subserves assembled phonology depends on the activity of the posterior part of the left superior temporal gyrus (STGp), whereas the mechanism that is responsible for addressed phonology does not necessarily involve this region (Simos *et al.*, 2000a). Unfortunately, the extent of the cortical area that can be examined in the operating room, with cortical stimulation techniques, is very limited. Functional brain imaging techniques, on the other hand, do not share this limitation and are therefore capable of providing a more complete picture of the cerebral mechanism of complex linguistic functions such as reading.

Previous approaches to this problem using functional imaging methods have relied on data from a single source, namely the spatial profile of brain areas that show increased levels of activity during reading tasks, obtained using a particular functional imaging technique (Pugh *et al.*, 1996; Price *et al.*, 1996; Rumsey *et al.*, 1997). To be successful, however, this undertaking requires additional information on: (i) how different activated brain areas may operate together during reading tasks, and (ii) the degree and type of contribution of each area to reading performance.

The present report describes an attempt to integrate data derived from two noninvasive techniques. These techniques are, first, magnetic source imaging (MSI) performed in neurologically intact volunteers during reading tasks and, second, monitoring of reading performance (naming speed) in the same participants. MSI is unique among other functional imaging techniques for its ability to provide brain activation profiles with high spatiotemporal resolution. It can be used to determine not only which areas participate in reading, but also *how* these areas might interact with each other in real time to enable this function (Breier *et al.*, 1998, 1999a). In addition, the capacity of MSI to provide accurate and detailed maps of language-specific cortex has been validated in the context of two large clinical studies against invasive cortical mapping techniques (Breier *et al.*, 1999b, 2001; Papanicolaou *et al.*, 1999; Simos *et al.*, 1999, 2000a).

This study addresses two issues: first, the dual-process hypothesis that the brain mechanism for reading words that require assembled phonology, in experienced readers, is different from the mechanism for reading words that do not; and second, whether different brain structures mediate reading of meaningful versus meaningless words. If such distinct regions exist, they may be involved in lexical access, which according to dual-route models mediate pronunciation of exception words. To address both issues we obtained MSI-derived brain activation profiles during reading of three types of print: exception words (relying more on addressed phonology and having meaning), pseudohomophones (requiring assembled phonology and also

having meaning) and pseudowords (requiring assembled phonology but having no meaning). The prediction was that activity in posterior temporal and inferior parietal structures known to be involved in reading (Breier *et al.*, 1998, 1999a; Pugh *et al.*, 1996; Simos *et al.*, 2000b,c) would differentiate processing of (i) meaningful versus meaningless items and (ii) letter strings that require assembled phonology versus those that do not.

## Experiment 1

### Materials and Methods

#### Participants

Sixteen adults (10 males, mean age: 29, range: 25–42 years), who had no history of neurological or psychiatric disorder, learning disability or visual impairment were studied. In addition, all participants were right-handed with English as their primary language. They were paid \$30.00 for their participation. This study (as well as the one reported below in Experiment 2) had been approved by the University of Texas Institutional Review Board. All participants were asked to sign a consent form after the nature of the procedures involved had been explained to them.

#### Stimuli and Tasks

Each participant was tested on three word pronunciation tasks involving (i) exception words, (ii) pseudohomophones and (iii) pseudowords. Each list contained 80 monosyllabic letter strings ranging in length from four to six letters. Pseudowords and pseudohomophones were the same stimuli used by McCann and Besner in their Experiment 1 (McCann and Besner, 1987). Words in the exception list were adapted from Pugh *et al.* (Pugh *et al.*, 1997) and Glushko's (Glushko, 1979) exception inconsistent word lists and were generally items with very rare print-to-sound correspondences. Mean frequency of occurrence for the exception words was 138 (range: 3–1700) per million in the Kucera and Francis corpus (1967) and 100 (range: 2–1264 occurrences) per million for the words from which pseudohomophones were derived ( $P > 0.61$ ).

#### Procedure

The MSI scan was performed during all three tasks within a single session in a different random order across participants. Printed stimuli were presented for one second in order to prevent potential contamination of the event-related field (ERF) record by visual offset responses. The interstimulus interval varied randomly between 3 and 4 s across trials. The stimuli were presented in lowercase letters through a Sharp LCD projector (Model XG-E690U, Sharp Electronics Corporation, Mahwah, NJ, USA) controlled by a Macintosh G3 portable computer running SuperLab Pro. They were projected on a white screen located ~1.5 m in front of the participant and subtended 1.0–2.0° and 0.5° of horizontal and vertical visual angle, respectively.

The principles underlying the MSI method as well as MSI data collection and analysis methods are described in detail elsewhere (Papanicolaou *et al.*, 1999) and will only be briefly outlined here. MSI data were recorded in a magnetically shielded room with a whole-head neuromagnetometer (WH2500, 4D Neuroimaging, San Diego, CA) consisting of 148 magnetometer coils. The precise location of the intracranial sources of the observed evoked fields were computed at successive 4 ms intervals for a period of 1 s after the onset of the stimuli using standard algorithms (Sarvas, 1987). Source estimation was performed separately for each hemisphere and was attempted only when the surface distribution of magnetic flux was dipolar, i.e. consisted of a single region of magnetic outflux and a single region of magnetic influx. This surface map configuration usually indicates the presence of a single underlying active cortical patch that can be modeled as an equivalent current dipole (ECD). Occasionally, two distinct dipolar distributions were discerned, typically, over the left hemisphere, one over anterior frontal regions and the second over temporo-occipital areas. In that case, source estimation was performed for both dipolar distributions independently. To avoid localization errors produced by smearing of the magnetic flux produced by one source by the flux induced by the

other source, two simultaneous source solutions were retained only if the corresponding dipoles were at least 5 cm apart. Using this method, no more than two sources in different anatomical regions can be computed in each hemisphere at each 4 ms time bin. In this way a maximum number of  $1000 \text{ ms}/4 = 250$  sources can be computed for each hemisphere during the entire recording epoch. Reliably localized activity sources [i.e. those passing a 0.90 best-fit correlation criterion, see (Breier *et al.*, 1999b; Simos *et al.*, 1999)] were co-registered on structural MRI scans, and the anatomical location of each source was determined using a standard MRI atlas (Damasio, 1995).

The sum of all acceptable sources localized in a particular area (i.e. left STGp), starting at ~150 ms after stimulus onset, when the first 'wave' of activity in the primary visual cortex has subsided, and ending 1 s later, served as a metric of the degree of stimulus-locked activation of that area. The validity of this measure as an index of regional activation has been established in several studies involving neurologically intact volunteers and patients (Simos *et al.*, 1998, 1999; Breier *et al.*, 1999b, 2001; Papanicolaou *et al.*, 1999). On the basis of previous MSI studies on reading (Breier *et al.*, 1998; 1999a; Simos *et al.*, 2000b,c), we examined the following areas in each hemisphere: posterior third portion of the superior temporal gyrus (STGp), posterior third portion of the middle temporal gyrus (MTGp), supramarginal gyrus (SMG), angular gyrus (ANG), mesial temporal lobe (MTL) including the hippocampus and parahippocampal gyrus, and basal temporal cortex (BTC) comprising the fusiform and lingual gyri. Activity sources were also noted in the inferior frontal gyrus (IFG), predominantly in the left hemisphere (Broca's area) and in sensorimotor cortex, bilaterally. The proportion of subjects who showed activity in either of the two areas in at least one condition and hemisphere was not significant (9/16 subjects,  $P < 0.81$  for inferior frontal and 10/16 subjects,  $P < 0.45$  according to the binomial test), and data pertaining to these regions will be mentioned separately in the Results section.

## Results

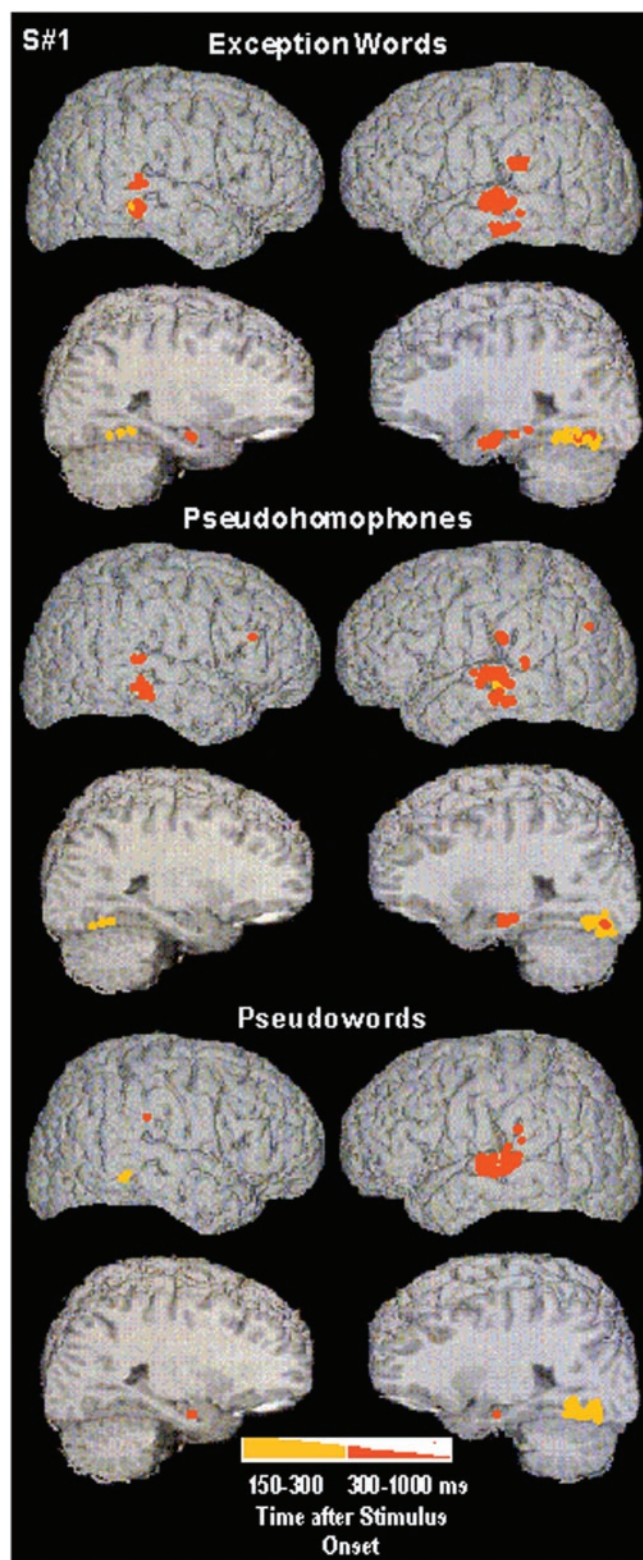
Reading error rates were too low to allow further analyses: group mean error rates were 2.3% (range: 1–4%), 4.2% (range: 2–5%) and 5.1% (range: 3–7%) for exception words, pseudohomophones and pseudowords, respectively.

Individual brain activation profiles obtained during reading of all three types of stimuli closely resembled those observed in previous MSI studies in the context of silent reading tasks (see Fig. 1). They feature initial activation of the mesial occipital cortices bilaterally (within the first 150 ms after stimulus onset), followed by activity in basal temporal cortices predominantly in the left hemisphere (starting within 200 ms post-stimulus onset). In the next several hundred milliseconds, the profiles entailed activation of posterior temporal and inferior parietal and, in some cases, frontal areas as well as of mesial temporal regions. With the notable exception of MTGp, the degree of activity in all other temporal areas was strongly left-hemisphere dominant.

Across reading tasks, the most striking pattern that could be discerned by mere visual inspection of brain activation profiles in each participant was the near complete absence of activity sources in MTGp and MTL during pseudoword reading. In contrast, activity in these regions was detected in every participant during reading of exception words. In the left MTGp and MTL, greater activation was found for exception as compared with pseudowords in 15/16 participants. In both areas the degree of activity was greater during reading of pseudohomophones as compared with pseudowords in 14/16 participants.

The data were analyzed using a multivariate approach to ANOVA with three within-subject variables [Type of Letter String (exception, pseudohomophone, pseudoword), Area (STGp, MTGp, SMG, ANG, BTC, and MTL) and Hemisphere (left, right)]. The Bonferroni method was used for maintaining





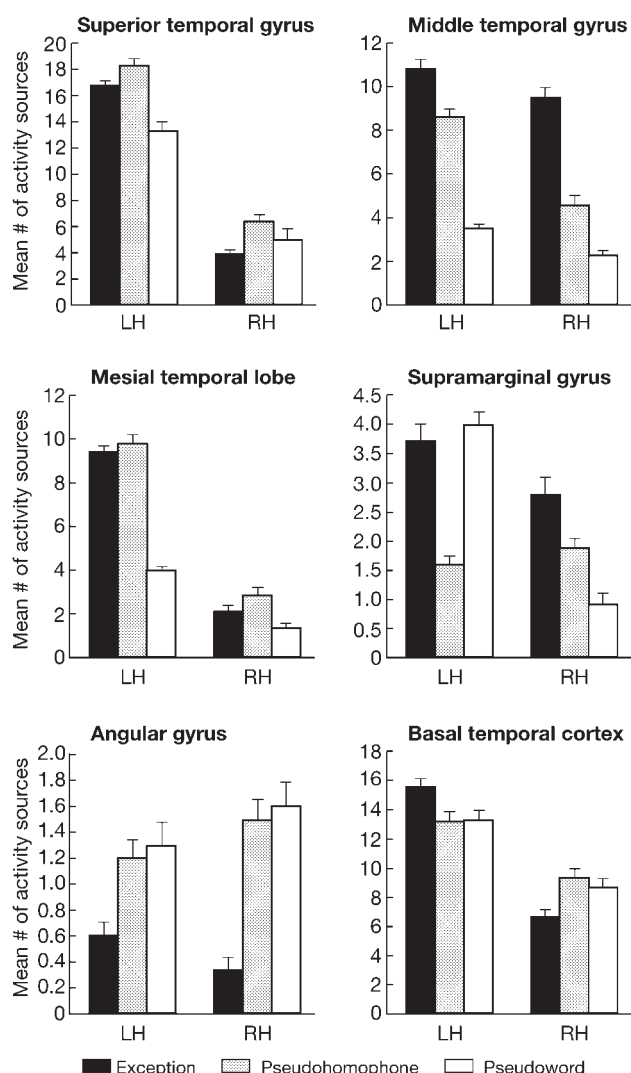
**Figure 1.** Activity sources from one representative case projected on a 3-D rendering of the participant's MRI (Experiment 1). Clusters of activity sources computed at 4 ms intervals after the presentation of each printed stimulus were projected on the brain surface for easier visualization. Sources occurring between 100 and 300 ms after stimulus onset (shown in yellow) were typically localized in basal temporal cortices. Posterior temporal and inferior parietal sources (shown in orange) usually became active later between 300 and 1000 ms after stimulus onset. Note the abundance of activity sources in the left middle temporal gyrus and mesial temporal cortex during exception word and pseudohomophone reading and the lack of activity sources in these areas during reading of meaningless letter strings.

family-wise Type I error under 0.05 when pairwise means comparisons were performed. Pairwise comparisons that followed a significant Stimulus Type by Area interaction were based on data collapsed across hemispheres for each area and task. Pairwise comparisons that followed a significant Area by Hemisphere interaction were based on data collapsed across tasks for each area and hemisphere. The main ANOVA yielded a significant Type by Area interaction,  $F(10,150) = 2.06$ ,  $P < 0.031$ , and a significant Area by Hemisphere interaction,  $F(5,75) = 6.24$ ,  $P < 0.0001$ . Pairwise comparisons revealed that activity in MTGp was significantly increased during reading of exception words,  $t(15) = 4.27$ ,  $P < 0.001$ , and pseudohomophones,  $t(15) = 3.95$ ,  $P < 0.001$ , as compared with pseudowords. Reading of exception words and pseudohomophones was associated with approximately twice or three times as much activity in MTGp as compared with pseudoword reading. A similar (nearly two-fold) increase in activity was noted in MTL, although the results of the pairwise comparisons did not satisfy our stringent  $P$  value criterion of 0.0028 [ $t(15) = 2.02$ ,  $P < 0.061$  for pseudohomophones versus pseudowords, and  $t(15) = 3.06$ ,  $P < 0.008$  for exception words versus pseudowords]. These differences in degree of activation across reading tasks are presented graphically in Figure 2.

A closer look at hemisphere differences at each area revealed a significant left hemisphere predominance in the degree of activation for STGp [ $t(15) = 4.46$ ,  $P < 0.0001$ ], BTC [ $t(15) = 3.60$ ,  $P < 0.003$ ] and MTL [ $t(15) = 5.88$ ,  $P < 0.0001$ ] regardless of stimulus type. These differences were highly consistent across participants: greater left than right STGp activation was found in 94% of participants for exception words, in 82% for pseudohomophones and in 92% for pseudowords. Corresponding figures for MTL were 94, 82 and 90%, and for BTC, 75, 67 and 67%, respectively.

Given that the proportion of participants who showed activity sources in IFG and sensorimotor areas was not significant, data from these areas were examined separately and resulting findings should be considered as preliminary. A two-way ANOVA conducted on data from IFG with Task (3) and Hemisphere (2) as the within-subject factors revealed a significant Hemisphere main effect,  $F(1,15) = 5.19$ ,  $P < 0.038$  and a marginally significant Task main effect,  $F(2,30) = 3.38$ ,  $P < 0.071$ . These results reflected the predominantly left hemisphere IFG activation and a trend for stronger activation during the pseudohomophone and pseudoword tasks compared with the exception word reading task. None of the ANOVA effects approached significance for activity sources in sensorimotor areas ( $P > 0.1$ ).

The results outlined above supported our first prediction, namely that meaningful items entailed high degree of activation of the MTGp and MTL regions, whereas reading meaningless letter strings entailed greatly reduced activation of these two regions. However, the degree of activity in superior temporal and temporoparietal areas did not differentiate between exception words and pseudohomophones (i.e. stimuli that are meaningful, yet differ in the amount of assembled phonology processing that they require). This was somewhat unexpected given the results of our previous electrocortical stimulation study (Simos *et al.*, 2000a), which suggested that at least one temporal lobe area (STGp) is a key component of the mechanism for reading aloud items that require assembled phonology, although pronunciation of exception words may not depend on STGp. Therefore, it appeared likely that STGp activation observed in the present study during exception word reading may indicate automatic engagement of this region. This may be part of an attempt to apply assembled phonology operations or,



**Figure 2.** Mean number of activity sources in six posterior temporal and inferior parietal areas for each of the three stimulus types in Experiment 1. Vertical bars represent standard error values. Significant task differences were found in the MTGp and MTL. A near three-fold increase was found in the degree of MTGp activation (bilaterally) between exception words and pseudowords. This pattern was apparent in all but one participants. On average, the left MTL showed approximately twice as much activity during reading of exception words and pseudohomophones than during pseudoword reading. Again, this pattern was observed in the vast majority of individual brain activation profiles (i.e. in 14/16 participants).

alternatively, reflect a process that is secondary to whole-word phonological access. In a similar manner, MTGp activation during pseudohomophone reading would appear to reflect lexical access that is secondary to phonological assembly. Activity in IFG, although present in only a subset of the participants, was clearly lateralized to the left hemisphere, and there were indications that Broca's area showed increased activation in tasks that required explicit phonological decoding operations. This is in agreement with previous reports using MSI (Breier *et al.*, 1999a) and functional magnetic resonance imaging (fMRI) studies (Pugh *et al.*, 1996).

If the above explanation regarding the relative roles of STGp and MTGp in reading is correct, it should follow that the onset of STGp activation would not correlate with the speed of articulation of exception words. Moreover, if STGp activation indeed reflected operations of assembled phonology for pseudoword

and pseudohomophone reading, its onset should correlate with the speed of articulation of these stimuli. Further, if addressed phonology operations depend upon access to whole-word representations, and if MTGp and MTL are involved in the retrieval of such representations, onset of activity in these areas should correlate with speed of articulation of exception words. Finally, if MTGp activation is only secondary to the process of reading aloud pseudohomophones, then its onset latency should not correlate with articulation speed for this type of letter string. To assess these predictions, we obtained pronunciation latencies for each of the three types of stimuli used in Experiment 1 from a subgroup of the participants in that experiment.

## Experiment 2

### Materials and Methods

#### Participants

Fourteen of the participants in Experiment 1 agreed to visit the laboratory for a second testing session (nine males, mean age: 29, range: 25–42 years). They were paid \$30.00 for their participation.

#### Stimuli and Tasks

A subset of 30 stimuli was randomly selected to form each of the three lists used in this session. Mean word frequencies for these shorter lists were not significantly different from those used in the corresponding MSI sessions (mean = 128 and 119 for exception words and pseudohomophones, respectively,  $P < 0.48$ ). To avoid practice effects, this part of the study was conducted at least 1 month after the MSI scan.

Each participant was seated in a quiet room at a distance of 30 cm in front of the computer screen and asked to read aloud letter strings presented once every 3–4 s as rapidly as possible without neglecting accuracy. The letter strings remained on the screen until the computer registered the participant's vocal response. Pronunciation errors were also recorded by an experimenter seated next to the participant. The order of task presentation was again counterbalanced across participants.

### Results

Again, reading errors were too low to allow further analyses (1.8, 3.0 and 4.5% for exception words, pseudohomophones and pseudowords, respectively). Pronunciation latencies are presented in Table 1. On average, exception words were pronounced 60 ms faster than pseudohomophones, which were pronounced 22 ms faster than pseudowords. The latter difference is essentially identical to that reported by McCann and Besner for the same stimulus lists (McCann and Besner, 1987). A one-way ANOVA, computed on mean pronunciation latencies from each participant, with Type of Letter String as a within subjects variable, was significant,  $F(2,26) = 6.88$ ,  $P < 0.004$ . Pairwise comparisons revealed a significant difference between exception words and both pseudohomophones [ $t(13) = 2.17$ ,  $P < 0.049$ ] and pseudowords [ $t(13) = 3.57$ ,  $P < 0.003$ ]. The difference between pseudohomophones and pseudowords, although highly consistent across participants (with 11/14 cases showing the effect), did not reach significance.

Although differences in mean word frequency between exception words and pseudohomophones were small, we wanted to ensure that they did not exert a significant influence on naming speed. For this purpose, we computed, for each participant, the correlation between naming latency and word frequency for exception words and pseudohomophones according to the Kucera and Francis norms (Kucera and Francis, 1967). For the latter, the frequency of the real word from which the pseudohomophone was derived was used. Pearson correlation coefficients ranged between  $-0.16$  and  $0.14$  across



**Table 1**

Mean pronunciation latencies and mean latencies of onset of regional activation in Experiments 1 and 2 (in ms after stimulus onset; SD values in parentheses)

Left hemisphere	Pronunciation latency	STGp	MTGp	SMG	ANG	MTL
Exception	771 (106)	467 (170)	410 (138)	580 (118)	420 (170)	500 (140)
Pseudohomophone	831 (115)	470 (134)	420 (120)	480 (66)	460 (190)	521 (148)
Pseudoword	853 (118)	450 (135)	409 (83)	600 (117)	400 (180)	560 (123)

STGp: posterior portion of the superior temporal gyrus, MTGp: posterior portion of the middle temporal gyrus, SMG: supramarginal gyrus, ANG: angular gyrus, MTL: mesial temporal lobe regions (hippocampus and parahippocampal gyrus), BTC: basal temporal cortices (fusiform and lingual gyrus).

**Table 2**

Pearson correlation coefficients between onset latency of activation in areas STGp, MTGp and MTL, and pronunciation latency

Left hemisphere	STGp	MTGp	MTL
Exception	-0.37	0.57*	-0.40
Pseudohomophone	0.61*	-0.07	-0.35
Pseudoword	0.55*	-0.21	-0.16

STGp: posterior portion of the superior temporal gyrus, MTGp: posterior portion of the middle temporal gyrus, MTL: mesial temporal lobe regions (hippocampus and parahippocampal gyrus).

\* $P < 0.05$ .

participants, indicating a negligible relation between these variables.

### Relation between Naming Latency and Onset of Regional Activation

Onset latency of activation of a particular area was defined at the earliest latency (4 ms time bin), after stimulus onset, in which the first of at least two consecutive activity sources was found in a particular area. The mean onset latency of the activation of each area is also shown in Table 1 for comparison. The relation between onset latency of activity in each area and naming latency was examined by computing the Pearson  $r$  correlation coefficient separately for each type of letter string. As shown in Table 2, the onset latency of activity in STGp accounted for a moderate proportion of the variability in naming latency for pseudowords and pseudohomophones ( $R^2 = 0.31$ , and  $R^2 = 0.37$ , respectively). In contrast, a significant proportion of the variance in naming speed of exception words ( $R^2 = 0.32$ ) was accounted for by the onset latency of activation in MTGp. Onset of activity in MTGp and naming latency for the other two types of letter strings were negatively correlated (see Fig. 3). Correlations between naming latency and onset of activity in mesial and basal temporal areas were either negligible or even negative. Also negligible were correlations between the onset of activity in homologous right hemisphere areas and pronunciation latencies.

### Onset of Activation Across Regions

An ANOVA conducted on the onset of activation with three within-subject variables [Type of Letter String (Exception, Pseudohomophone, Pseudoword), Area (STGp, MTGp, SMG, ANG, BTC and MTL) and Hemisphere (Left, Right)] revealed a significant Area main effect,  $F(4,60) = 44.75$ ,  $P < 0.0001$ . Pairwise comparisons confirmed our initial observation (see Table 1) that activity in basal temporal regions was detectable earlier than activity in all other temporal and inferior parietal

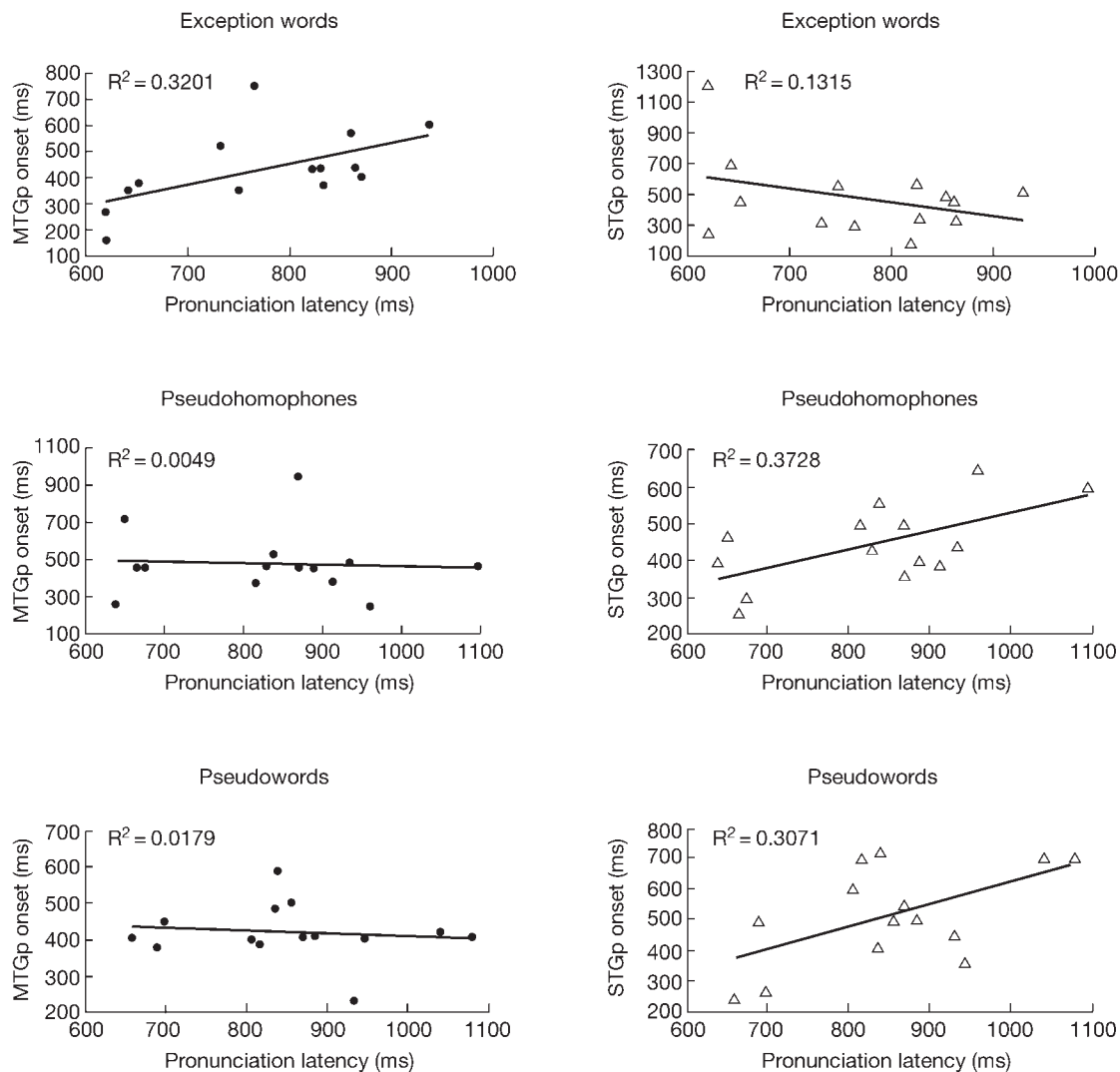
areas (in all cases  $P < 0.0001$ ). There were no significant differences across participants in the onset of activation in the following areas: STGp, MTGp, SMG, ANG and MTL.

To summarize, the results from Experiment 2 were in accord with electrocortical stimulation data reported previously (Simos *et al.*, 2000a) in that: (i) there was no significant relation between STGp activation onset and pronunciation latency for exception words; (ii) there was a substantial correlation between the onset of activity in STGp and pronunciation latency for pseudowords and pseudohomophones; (iii) there was a significant correlation between onset of MTGp activation and pronunciation latency of exception words; and (iv) there was no significant relation between onset of MTGp activation and pronunciation latency for pseudohomophones.

## Discussion

The spatiotemporal activation profiles associated with reading aloud each of the three different types of print displayed a number of common features: first, the regular progression of activation from occipital to basal temporal areas within the first 150–200 ms after stimulus onset; second, the subsequent ‘spread’ of activation to postero-lateral temporal regions; and third, the strong left hemisphere predominance in the degree of activation in both basal and lateral temporal regions. One should note that in all three tasks used in the present study subjects were asked to produce a vocal response to each printed word stimulus. Therefore, the tasks involved speech as well as reading (i.e. conversion of graphemic input into a phonological representation). However, the close similarity between the activation maps obtained in the context of these tasks and those observed in previous studies in our laboratory using silent reading of real words as well as pseudowords with several groups of non-impaired readers (ranging in age between 7 and 45 years) (Breier *et al.*, 1998; 1999a; Simos *et al.*, 2000b,c) suggest that these profiles are specific to reading, regardless of the particulars of the experimental task used to obtain the activation profiles. Direct comparisons between silent and reading aloud tasks, in the same group of subjects, are now under way to examine subtle differences in the spatiotemporal activation profiles that may reflect the engagement of neurophysiological processes specific to the vocal response and unrelated to reading *per se*.

The stimuli used in the present study allowed us to identify additional features of these profiles that are specific to two important attributes of print: (i) meaningfulness and (ii) dependence on assembled phonology operations. Specifically, it is generally assumed that meaningful stimuli are associated with word-specific (lexical) mental representations. It has been proposed that the mechanism responsible for pronouncing real words, especially those with rare print-to-sound correspondences, initially involves access to a lexical representation that subsequently mediates the retrieval of the word’s name (Coltheart *et al.*, 1993). Both exception words and pseudohomophones (by virtue of their phonological similarity to real words) possess entries in the hypothetical ‘mental lexicon’, whereas pseudowords do not. Based on this premise, we hypothesized that the mechanisms involved in reading exception words and pseudohomophones would share at least one common component, namely a process related to lexical access. This process would not be part of the mechanism for reading pseudowords. Our findings were consistent with this notion, showing that a prominent feature of the activation profile associated with reading aloud both exception words and pseudohomophones involved the left middle temporal gyrus and mesial temporal



**Figure 3.** Regression plots that demonstrate the relation between onset latency in the left STGp and MTGp and pronunciation latency for each of the three types of letter strings used in the study ( $n = 14$ ).

regions. However, reading aloud pseudowords involved very sparse activity in these regions. Thus, MTGp shows reduced neurophysiological activity as well as reduced regional cerebral blood flow during pseudoword as compared to real word reading (Hagoort *et al.*, 1999). Moreover, it appears that the left MTGp plays a special role in exception word reading. The significant correlation between onset of activity in the left MTGp and naming latency indicated that the earlier the engagement of this area following word presentation, the faster the pronunciation of the letter strings. The fact that MTGp activity did not predict pronunciation speed for pseudohomophones suggests that engagement of this area may be a byproduct of phonological access achieved through the assembled route for nonwords that sound like real words. Involvement of the MTGp in lexical/semantic analysis is suggested by several independent sources of evidence, including noninvasive functional imaging investigations (Mummery *et al.*, 1998; Hart *et al.*, 2000; Kuperberg *et al.*, 2000) and lesion studies (Damasio and Damasio, 1989).

Both pseudowords and pseudohomophones, on the other hand, require assembled phonology operations. By definition, pseudohomophones and pseudowords not only require phono-

logical decoding, but they are also orthographically unfamiliar. This feature is what makes their pronunciation unequivocally dependent upon phonological decoding. In principle this difference could account for the relation between onset latency of activity in the left STGp and reading speed of these two types of letter strings. However, given that pseudohomophones possess familiar phonological representations, this assumption would imply that the left STGp is primarily involved in visual/orthographic processing of unfamiliar graphemic patterns. To our knowledge, there is no evidence to support this claim.

In contrast to pseudowords and pseudohomophones, reading aloud words that contain rare print-to-sound correspondences does not require these operations. In experienced readers, pronunciation of exception words that occur with a relatively high frequency in print is likely to be highly automatized and depend little on assembled phonology. In a previous study (Simos *et al.*, 2000a), we obtained evidence that the brain mechanism for reading engages different areas depending upon the regularity (or frequency) of print-to-sound correspondences displayed by the words used. Specifically, we ascertained, using an invasive technique (electrocortical stimulation mapping), that the left STGp plays a crucial role in pseudoword pronunciation,

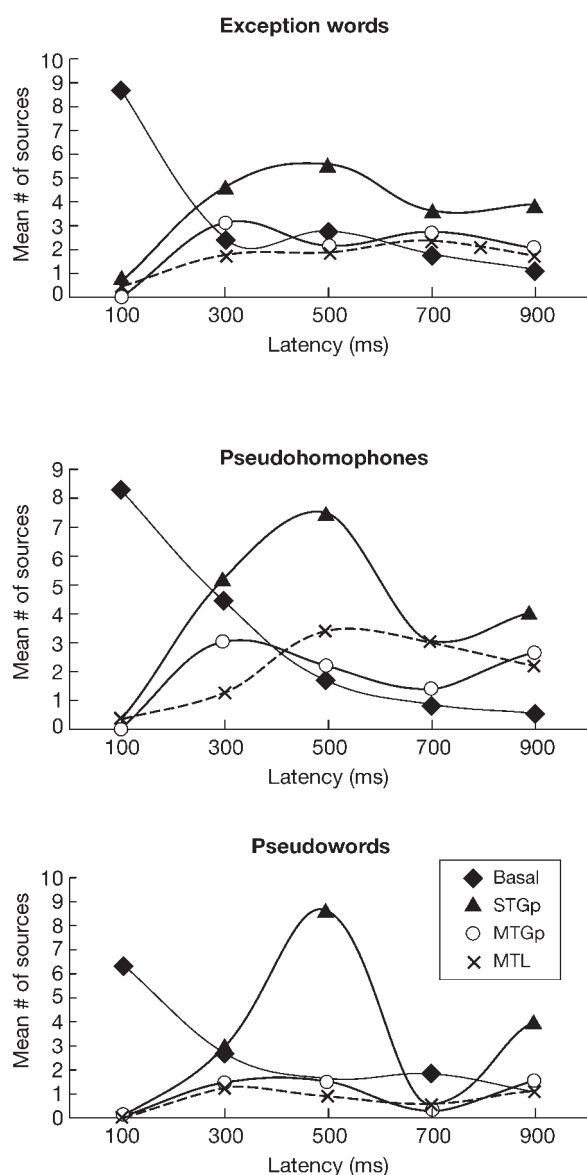
but may not be an indispensable component of the mechanism responsible for reading aloud exception words (Simos *et al.*, 2000a). However, inspection of the brain activation profiles obtained from the same patients during reading of both regular and exception words (using MSI) indicated that the left STGp showed significant activation in all participants. In agreement with this finding, activity in the left STGp was an invariable feature of the activation profiles obtained in the present study during reading of all three types of print. We did not observe reliable differences in either the degree or the onset latency of STGp activation across the three types of letter strings. Closer inspection of the data, however, indicated that the contribution of STGp in the brain mechanism of reading may change as a function of the presumed amount of sublexical phonological processing required to pronounce items in each list. Thus, the onset of activity in STGp was the only reliable predictor of naming speed for pseudowords and pseudohomophones, a finding consistent with the purported role of this area in assembled phonology. In contrast, no significant relation between the onset of MTGp activity and naming speed for these items was found. Taken together our data demonstrate that, at least in experienced readers, the posterior portion of STGp, although routinely activated during reading of real words, is not an indispensable component of the mechanism for reading aloud words that do not contain common print-to-sound correspondences. An alternative mechanism that could support access to phonological representations for pronouncing real words may involve engagement of the middle temporal gyrus.

Data regarding the progression of activation across different regions provides information regarding the temporal course of regional engagement in the experimental task that, in turn, reflects the functional connectivity among the areas that compose the mechanism of reading. A closer inspection of the spatiotemporal activation profiles obtained in the present study reveal the following regarding regional interactions that may occur during reading. First, visual association areas located in the basal surface of the left hemisphere appear to serve as an intermediate station between modality-specific visual cortices (areas 17 and 18) and tertiary association regions in the temporal lobe. Second, posterior temporal, inferior parietal, and mesial temporal areas appear to become engaged either in parallel, or at least in very close temporal proximity to each other, so that a consistent temporal succession of activation is not discernible. Third, areas that may not be directly involved in the operations required for a particular function may nevertheless show increased levels of activity during performance of this function. Three areas showed automatic activation although their engagement did not appear to be a key component in the mechanism of reading a particular type of print: STGp during reading of exception words, MTGp during pseudohomophone reading, and MTL during reading of exception words and pseudohomophones. Assuming that MTGp is directly involved in lexical/semantic access, engagement of this region during word reading may reflect automatic semantic analysis of meaningful stimuli. Regional increases in blood flow/metabolism in this region, associated with implicit word processing, have also been found in Positron Emission Tomography (PET) and fMRI studies (Price *et al.*, 1996; Hart *et al.*, 2000). Automatic engagement of semantic representations is consistent with parallel and distributed models of reading (Seidenberg and McClelland, 1989). Further, assuming that STGp is directly involved in assembled phonology, then activation of this region during exception word reading may reflect phonological decoding that occurs in parallel with addressed phonology operations.

Automatic activation of STGp in tasks that do not require phonological decoding, but tap primarily into word recognition processes, has been reported in other imaging studies as well (Hart *et al.*, 2000). This possibility is consistent with the view that even words with rare sound-spelling correspondences (such as LAUGH) can be pronounced via a non-lexical route as postulated by connectionist models of reading (Seidenberg and McClelland, 1989). Finally, with respect to MTL, the results are consistent with findings from other imaging modalities and support the notion that activation of this area may occur even in tasks that do not pose explicit demands for semantic analysis or even for encoding for subsequent retrieval (Martin *et al.*, 1997).

A final note is in order regarding the interpretation of timing data. The source modeling approach adopted in this and our previous investigations can only accommodate a maximum of two (usually only one) sources at each 4 ms bin per hemisphere. Theoretically, several, simultaneously active, sources can be distinguished on the basis of MSI data. The technique we routinely use in our lab is the standard method employed in all clinical applications of MSI worldwide. Further, we have ascertained the validity of this procedure in the context of a series of combined MSI-electrocortical stimulation studies (Papanicolaou *et al.*, 1999; Simos *et al.*, 1999, 2000a; Castillo *et al.*, 2001). Although it is in principle possible to differentiate sources located at a smaller distance from each other, we do not have cross-validation data that support this approach. Based on our combined MSI-electrocortical stimulation studies, we have ascertained that the location of clusters of activity sources represent cortical patches that play a crucial role in certain component operations, such as phonological analysis. Taking these studies into account we can safely conclude that, at any point in time, the activity sources that meet the criteria adopted in our source modeling procedure represent the most *prominently* active cortical patch in a given hemisphere.

Using this method, we observed, in a given subject, clusters of temporally contiguous activity sources in a particular area running for 8–100 ms at a time, which were preceded and followed by source clusters in different areas. Accordingly, in the spatiotemporal maps constructed for each subject, anatomical areas within each hemisphere appeared to become active sequentially. Collapsing spatiotemporal profiles across participants is necessary in order to derive a more realistic representation of the temporal course of regional activation associated with a given task. The group spatiotemporal profiles displayed in Figure 4 were derived using this procedure. The observation that the three main cortical areas discussed above (STGp, MTGp, MTL) became active at one time or another during the same 400 ms latency window (300–700 ms) may have two alternative, but not mutually exhaustive, explanations: first, that these regions were all active simultaneously but activity in only one area at a time could be modeled in each participant; and second, that these regions became engaged strictly sequentially. It is difficult to distinguish between the two alternatives solely on the basis of functional imaging data. Methods that rely on measures of regional blood flow or metabolism simply lack the temporal resolution necessary to monitor neurophysiological activity in real time. MSI, on the other hand, possesses adequate temporal resolution, but it is currently limited by validity considerations, to the use of source modeling techniques that permit reliable identification of no more than two simultaneously active cortical patches. One way to resolve this issue would be to combine data from MSI and electrocortical stimulation in the same patients. This approach is generally very promising as an adjunct to any non-invasive functional imaging method, but is difficult to



**Figure 4.** Temporal course of activation in each of the three brain regions (left hemisphere) that showed significant print-type related effects and in basal temporal areas for the group of 16 participants. Note the clear temporal distinction between activation of basal temporal and all other areas, and the significant overlap in the course of activation among the latter.

implement, mostly due to time constraints and patient safety considerations associated with direct cortical stimulation studies. In this approach, MSI data could be used to identify cortical patches that appear to be essential for the performance of a particular experimental task. Subsequently, during the electrocortical stimulation study, MSI-derived cortical patches may be stimulated with brief pulses delivered at different delays after stimulus onset to determine the critical time window that stimulation of a particular cortical region disrupts task performance.

To summarize, the present investigation integrates three types of evidence to provide unique insights into the role of various temporal lobe regions in reading, namely information on: (i) the degree; (ii) the temporal course of the engagement of various brain areas during tasks that exemplify word reading; and (iii) the effects of transient interference with one of these regions on

the ability to read different types of print. This approach meets a number of critical requirements for any investigation of the brain mechanisms of complex cognitive or linguistic functions. First, it utilizes a noninvasive functional imaging technique (MSI) that has the capacity to provide reliable images of the working brain of individual subjects. Secondly, this technique captures critical aspects of brain activation (i.e. neuronal signaling, as opposed to secondary delayed effects of neuronal activity such as regional blood flow or metabolism). Thirdly, the functional significance of activated brain areas is verified in patients undergoing functional mapping using invasive techniques (Simos *et al.*, 2000a), thereby ascertaining the external validity of activation profiles obtained non-invasively through MSI. Fourthly, MSI captures the spatial as well as the temporal features of regional activation in real time.

As discussed above, MSI (like any other functional imaging method) may fail to detect certain details of the activation profiles, it appears to be capable of capturing the essential features of this profile, as indicated by the results of direct comparisons with invasive mapping techniques (Breier *et al.*, 1999b; Simos *et al.*, 1999, 2000a). A comparison of the results presented here with those from functional imaging studies that use measures of cerebral blood flow or metabolism reveals many similarities, but some notable differences as well. The present data are consistent with reports of increased activation in MTG during reading of real words, implicating this region in whole-word (i.e. lexical) processing (Price *et al.*, 1996; Hart *et al.*, 2000) and with reports of automatic activation of STGp even in tasks that do not require addressed phonology (Hart *et al.*, 2000). Activation in the left frontal operculum, which has been found in several PET and fMRI studies (Herbster *et al.*, 1997; Hagoort *et al.*, 1999; Fiez *et al.*, 1999; Pugh *et al.*, 1996), was not as consistent in the present study as activation in temporal and temporoparietal regions. This discrepancy may reflect a peculiarity of the functional imaging modality used in the present study: in our experience MSI appears to be more sensitive to neurophysiological activity produced in the temporal (including mesial temporal), parietal and occipital lobes than in the frontal lobe. When detected, prefrontal activity showed the expected left hemisphere lateralization and modulation by task demands, i.e. increased activity in tasks that require phonological decoding, in agreement with previous reports (Pugh *et al.*, 1996; Fiez and Petersen, 1998; Breier *et al.*, 1999a; Hagoort *et al.*, 1999).

Future studies should examine more closely the role of stimulus (such as degree of regularity, consistency, and relative frequency) and subject variables (such as age and reading skill) on the degree and timing of neuronal activity in the brain regions identified in this report. Among other issues, such studies would address, in a more systematic manner, the neurological validity of theories postulating single versus dual mechanisms for reading words.

## Notes

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