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Functional activation during reading in relation to the sulci of the angular gyrus region.

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Abstract

Neurological studies suggest that the angular gyrus region of the inferior parietal lobule may be critical for reading. However, unambiguous demonstration of angular gyrus involvement from lesion and functional neuroimaging studies is lacking, partly because of the absence of detailed morphological descriptions of this region. On the basis of our recent anatomical examination of this region and a tightly controlled functional magnetic resonance imaging paradigm, the present investigation demonstrated reading-related activity in the region of the angular gyrus that lies between the central and posterior branches of the caudal superior temporal sulcus, namely cytoarchitectonic area PG. Analysis of functional connectivity showed increased functional coupling during reading of area PG with the language areas of Broca and Wernicke, and a region previously identified as the visual word form area. Thus, the parietal reading area has been precisely localized, and its interactions with other cortical areas during reading have been demonstrated.

Introduction

The classic neural model of reading considers the angular gyrus in the inferior parietal lobule (IPL) of the language-dominant hemisphere to be critical (Damasio & Geschwind, 1984). The model is based on case studies of patients showing reading and writing difficulties after brain injury (e.g. cerebrovascular accidents and brain tumours) involving the inferior parietal region, especially the angular gyrus (Dejerine, 1914; Geschwind, 1965a; Greenblatt, 1976; Warrington & Shallice, 1980; Damasio & Geschwind, 1984; Henderson, 1986). The angular gyrus is traditionally defined, loosely, as the cortex surrounding the caudal extension of the superior temporal sulcus (cSTS). We examined the morphological variations of this region in the human brain, and demonstrated that the cSTS is divided into three branches as it extends into the IPL: an anterior branch, a central branch (cSTS2), and a posterior branch (cSTS3) (Segal & Petrides, 2012b). It is unclear which one of these branches might relate to reading. The present study used functional magnetic resonance imaging (fMRI) to define precisely the critical locus for reading-related activity with reference to the three caudal branches of the superior temporal sulcus (STS) that define the angular gyrus region.

Many neuroimaging studies of reading in healthy subjects do not report activation within the IPL (Fiez & Petersen, 1998). Instead, activation in the middle part of the fusiform gyrus, near the lateral occipital temporal sulcus is often reported (Petersen et al., 1990; Cohen et al., 2000, 2002; Dehaene et al., 2002; McCandliss et al., 2003; Dehaene & Cohen, 2011). This mid-fusiform gyrus region in the language-dominant hemisphere (average xyz coordinates in Montreal Neurological Institute (MNI) standard space: -43, -54, -12) (Cohen et al., 2000) has been named the ‘visual word form area’ (VWFA), in order to emphasize its importance in word reading. However, the claim that the mid-fusiform region is dedicated to the processing of visual word forms has been called into question by several investigators (Price & Devlin, 2003, 2011; Hillis et al., 2005), who cite both neuroimaging and clinical evidence of the involvement of the midfusiform region in colour naming and visual object recognition, in addition to reading. These investigators propose that the VWFA may be involved in reading as a function of its interactions with other brain regions, including the angular gyrus in the IPL (Price & Devlin, 2011). The relative contributions to reading made by the mid-fusiform gyrus and the angular gyrus remain unclear.

The aims of the present study were: first, to provide a precise localization of reading-related functional activity within the angular gyrus based on our recent anatomical study of the morphology of the three cSTS branches that define this region; and second, to investigate the relative involvement of the angular gyrus and the mid-fusiform region (VWFA) in reading, and to examine their potential functional interaction during single word reading in healthy control subjects. Specifically, our hypothesis is that the visuo-spatial nature of words requires the contribution of the IPL, of which the angular gyrus is the critical part.

Materials and methods

Ethics Statement

The present study conformed with the Code of Ethics of the World Medical Association (Declaration of Helsinki), printed in the British Medical Journal (18 July 1964). This study was also approved the Montreal Neurological Institute's (MNI) Research Ethics Board. Informed, written consent was obtained from all participants according to the guidelines set forth by the Ethics Committee of the MNI.

Subjects

Nine healthy volunteer right-handed subjects fluent in English (six males), with an average age of 26 ± 3.72 years, participated. Although four of our subjects had learned English as a second language, including one subject who had learned a dialect of Chinese as a mother tongue, their competency in the English language was very high. At the time of testing, all subjects were functioning at university level in the English language, as demonstrated by the fact that they were studying at the anglophone McGill University.

Experimental design – reading minus pictures of objects; copying English words minus writing the names of pictured objects

To isolate brain activation related to reading, we compared an experimental condition requiring reading of single words with a control condition that did not involve reading. In both conditions, subjects wrote a word after seeing a visual stimulus on the screen. In the experimental condition, a written word was presented on the screen, the subject read it, and then wrote that word. By contrast, in the control condition, a picture of an object was presented on the screen, the subject saw it, and then wrote down the name of that object. Both conditions therefore required the writing of words, but the subjects read and copied the words in the experimental condition, whereas, in the control condition, the subject saw pictures of objects and wrote the names of those objects. Although, in the experimental condition, it was possible for the subjects to have viewed the words and copied them passively, i.e. like viewing the words as though they were linguistically meaningless designs, subjects were instructed to read silently the words on the screen and then write them. The university-educated subjects reported having performed all tasks as instructed. Note that the cognitive process of word retrieval was identical in both conditions, except that, in the experimental condition, it was happening through reading. Because, in both conditions, the subject was required to write down words, the motor processes for the common written output were strictly controlled. In addition, as both conditions involved the presentation of stimuli in the visual modality, basic visual processing in the occipital lobe (i.e. primary visual cortex, V1, and peristriate visual areas V2 and V3) should be subtracted out in the categorical comparison between the experimental and the control conditions. Thus, as both tasks required the writing of words, but differed in that, in the experimental condition, the words were accessed via reading, the categorical comparison should show activity related to the reading process as such.

Stimulus presentation

The present study was part of a larger investigation exploring reading and writing, which involved five task conditions. The isolation of writing-related activity, independent of reading, i.e. pure writing, has been described previously (Segal & Petrides, 2012a). All task conditions involved approximately 60 items (i.e. approximately 60 words or 60 pictures) (Table 1). Stimuli were counterbalanced across the runs. Stimulus items did not differ in terms of number of letters [F = 1.838, degrees of freedom (d.f.) = 4, 363, not significant (NS)] or number of syllables (F = 1.338, d.f. = 4, 363, NS). Items were selected to be high-frequency words, and the subjects reported that both tasks were equally easy to perform. For a detailed list of the stimuli used, see Table 1 in Segal & Petrides (2012a).

An instruction on the screen informed the subjects what task condition to perform for the next set of trials. The subjects knew that, after five trials, a new set of instructions would appear. Each trial lasted for 4.5 s. A variable intertrial interval (ITI) of 2.5–7.5 s allowed us to analyse individual trials for each condition as separate events during the event-related statistical analysis. Stimulus presentation was programmed and controlled with E-PRIME 1.1.

Subject training and task performance

On the day of scanning, the subjects received a short training session of 15 min, during which they practised all tasks that they would have to perform in the scanner. During the practice session, subjects were instructed to practise writing words while looking only at the computer screen and away from what they were writing, because, during the scan, they would not be able to view their responses, as they would be lying supine in the scanner with the writing pad at their right side and out of view. The subjects were instructed to write their responses on the same spot on the page (i.e. one word was written on top of the other) in order to limit hand and wrist movement, as well as to limit the recruitment of additional cognitive resources, such as monitoring the spatial layout of the page. Subject performance was monitored closely during the training session. All subjects performed at 100% accuracy.

During the scans, subjects were given a pencil with which to write, and a pad of paper that rested at their right side near their thigh. They could not see what they were writing, removing the possibility of visual interference. The subjects were instructed to write words in their normal writing style, more or less at the same spot on the page, just as they had practised. Before each scanning run, the experimenter gave the subjects a new sheet of paper, and collected the sheet of paper used during the previous run in order to verify that subjects were, in fact, performing the required task. All of the subjects reported that they easily could recognize the pictures of objects and retrieve their names, and that they were familiar with all of the English words that were presented to them. No condition was reported as being easier than any other.

Magnetic resonance image acquisition

All images were acquired on a 1.5-T Sonata MRI Scanner (Siemens, Erlangen, Germany). After a high-resolution T1 anatomical scan (whole head, 1-mm3 isotropic resolution), seven runs of 145 images each [38 oblique T2* gradient echo planar images covering the whole head; 3.4 x 3.4 x 3.4 mm; time to repeat (TR), 3.5 s; time to echo, 45 ms], sensitive to the blood oxygen level-dependent (BOLD) signal, were acquired. Each run comprised a total of 50 trials: the conditions were presented in blocks of five trials, which were repeated twice in a random counterbalanced order, giving a total of 10 trials per condition per run. For example, one condition began with an instruction that was followed by five trials, followed by new instructions for the next condition, which was followed by five trials, and so on, until the subjects performed the five different tasks twice. One run lasted for approximately 9 min. All of the subjects performed seven runs, except for one subject who performed six runs.

Statistical analysis

Medical Images NetCDF images were acquired from the structural T1 scan and the functional runs. The first three volumes of each functional run were excluded, owing to T1 saturation effects. Functional images were realigned with AFNI image registration software (Cox & Jesmanowicz, 1999), and smoothed with Medical Images NETCDF blur software, which applied a 6-mm full-width half-maximum (FWHM) isotropic Gaussian kernel. To correct for possible distortion resulting from motion, the functional images and the T1 anatomical image were linearly registered to the MNI standardized stereotaxic space with in-house software, which is based on multiscale, three-dimensional cross-correlation with an average magnetic resonance image volume aligned with the MNI stereotaxic space (Collins et al., 1994). Functional data for each subject were then superimposed onto the subject’s structural scan to visualize the anatomical regions that had a correlated increase in BOLD activity during the various tasks as measured by the functional scans.

Statistical analysis of functional data was performed with FMRISTAT (Worsley et al., 2002). The analysis model was a parametric event-related design with six conditions (five tasks plus the ITI). We excluded from the model the temporal period during which the instructions were presented. For all tasks, trial durations were 4.5 s, and ITI durations varied between 2.5 and 7.5 s. The scanner acquired whole brain images at a fixed TR of 3.5 s, producing desynchrony between TR and trial onset time, which allowed for there to be sufficient sampling across the haemodynamic response function. The statistical analysis of fMRI data was based on a general linear model (GLM) with correlated errors. The design matrix of the GLM was convolved with a haemodynamic response function modelled as the difference between two gamma functions timed to coincide with the acquisition of each slice. Temporal drift was removed by adding a cubic spline in the frame times to the design matrix (one covariate per 2 min of scan time), and spatial drift was removed by adding a covariate in the whole volume average.

The correlation structure was modelled as an autoregressive process of 1° (Bullmore et al., 1996). At each voxel, the autocorrelation parameter was estimated from the least squares residuals with Yule–Walker equations, after a bias correction for correlations induced by the linear model. The autocorrelation parameter was regularized by spatial smoothing with a 15-mm FWHM Gaussian filter, and then used to ‘whiten’ the data and the design matrix. The linear model was then re-estimated by the use of least squares on the whitened data, to produce estimates of effects and their standard errors, as well as t-statistics for each comparison of interest. Runs, sessions and subjects were combined by use of a mixed-effects linear model for the effects (as data) with fixed-effects standard deviations taken from the previous analysis. This was fitted by use of residual error maximum likelihood implemented with the estimation maximization algorithm. A random-effects analysis was performed by first estimating the ratio of the random-effects variance to fixed-effects variance, and then regularizing this ratio by spatial smoothing with a 15-mm FWHM Gaussian filter for runs and a 10-mm FWHM Gaussian filter for subjects. The variance of the effect was then estimated by multiplying the smoothed ratio by the fixed-effects variance to achieve higher d.f. More information on fMRI data analysis with FMRISTAT is available at http://www.math.mcgill.ca/keith/fmristat/.

The resulting t-statistic images were thresholded with the minimum given by a Bonferroni correction, random field theory, and the discrete local maximum, taking into account the non-isotropic spatial correlation of the errors. Significance was determined on the basis of exploratory and directed searches, and on the basis of the spatial extent of consecutive voxels.

For a directed search, a cluster volume extent of > 697 mm3 with a t-value of > 3 was significant ($P < 0.05$), corrected for multiple comparisons with the method of Friston et al. (1995). For a single voxel in an exploratory search involving all peaks within an estimated grey matter of 600 cm3 covered by the slices, the threshold for reporting a peak as significant ($P < 0.05$) was $t = 4.75$ (Worsley et al., 1996).

We performed an analysis of functional connectivity to examine increases, as a function of the task, in the correlation between a specified reference voxel and other voxels across the brain. The FMRISTAT method is based on the method described by Friston et al. (1997). Functional connectivity is computed as the correlation across time of the BOLD signal between a reference voxel and all voxels in the rest of the brain. The correlation as such is not of primary interest; the relevant investigation is about how this correlation is modulated by the task (how brain regions increase or decrease their correlation with each other as a function of a given task that the subject is being asked to perform). For example, we identified a reference voxel of interest in the left hemisphere of the IPL at the region between the cSTS2 and cSTS3. Its activity profile during the reading process was found to correlate with the activity profiles of other brain regions, which were then considered to be functionally connected with this reference voxel. The reference voxel values were extracted for each subject from native space after the application of slice time correction. We used the GLM, in which we added regressors for the task events and drift, and then added a regressor for the time course at the reference voxel. We then added an interaction (product) between the task events and the reference voxel time course as a regressor. Finally, we estimated the effect, standard error and t-statistic for the interaction in the same way as described above. Increased functional connectivity between the reference voxels and other voxels in the brain during the word copying task relative to during the picture name writing task is represented by positive t-values.

Results

Categorical comparison – reading (copying English words) minus pictures of objects (writing the names of pictures of objects)

The aim of this comparison was to isolate regions of the brain that support single word reading (see Experimental design). Activity was observed in the posterior part of the IPL within the angular gyrus region. The activity surrounded the cSTS2, but the greatest intensity was in its posterior bank, and spread onto the cortex that lies between the cSTS2 and cSTS3 (Fig. 1A; Table 2). The multi-subject average xyz coordinates in MNI standard stereotaxic space were as follows: for the left hemisphere, -58, -64, 26, t = 5.29; and for the right hemisphere, 58, -56, 26, t = 4.90. Activation within the angular gyrus region was then investigated on a subject-by-subject basis. The reading-related activity was clearly located between the cSTS2 and cSTS3 in every subject (Fig. 1B; Table 3). Our subjects, all of whom are fluent in English and studying at the anglophone McGill University, were divided into: (i) native English speakers; (ii) speakers with English as a second language; and (iii) one native Chinese speaker (i.e. a native language that is non-alphabetic). For group (i), native English speakers, the average xyz coordinates in MNI standard stereotaxic space were: -56, -64, 32, t = 3.63. For group (ii), English as a second language, the average xyz coordinates in MNI standard stereotaxic space were: -62, -66, 28, t = 4.27. For the native Chinese speaker, the xyz coordinates in MNI standard stereotaxic space were: -56, -62, 20, t = 4.54. In all subjects, the location of the functional peak was between the cSTS2 and the cSTS3 in the angular gyrus region (Fig. 1B; Table 3).

No other activity was observed in the multi-subject average anywhere else in the posterior parietal region. In other words, there was no activity in the postcentral gyrus, the superior parietal lobule, the intraparietal sulcus (IPS), or the anterior part of the IPL (i.e. the supramarginal gyrus). This observation is important, because it emphasizes the specificity of the reading-related activation in the parietal lobe. There was also no activation in Broca’s region (cytoarchitectonic areas 44 and 45) in the ventrolateral frontal lobe. By contrast, activation could be observed in the STS within the lateral temporal cortex (xyz coordinates in MNI standard stereotaxic space: -48, -38, 0, t = 4.45), in what is traditionally thought of as the receptive language zone (Rasmussen & Milner, 1975; Ojemann, 1979).

Functional connectivity

In order to examine interactions (changes in connectivity) during reading between the region in the angular gyrus in the left hemisphere and the rest of the brain, the voxel with the highest t-value in the peak that was isolated by the categorical comparison was entered as a reference for the functional connectivity analysis. This analysis showed that, during word reading (copying English words minus writing the names of pictured objects), the activity peak within area PG increased significantly in functional connectivity with the inferior frontal region that is involved in orofacial control and expressive language, including ventral premotor area 6 on the precentral gyrus (xyz coordinates in MNI standard stereotaxic space: -56, 2, 30, t = 2.17), area 44 on the pars opercularis (xyz coordinates in MNI standard stereotaxic space: -56, 12, 22, t = 2.46) (Tomaiuolo et al., 1999), and area 45 on the pars triangularis (xyz coordinates in MNI standard stereotaxic space: -38, 36, 4, t = 2.95). There was also an increase in the functional connectivity of this reading-related region of the angular gyrus with brain regions that comprise the ventral visual object processing stream, including the posterior occipito-temporal region (xyz coordinates in MNI standard stereotaxic space: -24, -92, -18, t = 3.64), the mid-fusiform gyrus (xyz coordinates in MNI standard stereotaxic space: -32, -38, -18, t = 2.85), and the posterior part of the superior temporal gyrus, bordering the posterior aspect of the Sylvian fissure (xyz coordinates in MNI standard stereotaxic space: -48, -38, 16, t = 2.56), in what is traditionally thought of as the receptive language zone (Rasmussen & Milner, 1975; Ojemann, 1979) (Fig. 2; Table 4).

Discussion

Precise localization of reading-related activity within the angular gyrus region

The first aim of the present study was to determine whether reading-related activity identified in the IPL in the left hemisphere could be located specifically within the angular gyrus region and to establish its relationship with the details of the morphology of this region, namely the sulcal patterns that recently have been examined (Segal & Petrides, 2012b). Three branches of the cSTS define the angular gyrus region (Segal & Petrides, 2012b), and any activity within the posterior IPL could, in principle, be related to any one of these precise landmarks. The present results demonstrated, first, that reading-related activity in the parietal region can be shown to be specifically related to the angular gyrus, with no other significant activity peak occurring in the parietal lobe, and second, that this reading-related activity is centred around the cSTS2.

This precise function–morphology relationship was based on each individual subject's anatomy (Fig. 1; Table 3). Further confirmation that reading activation is related to the cortex between the cSTS2 and cSTS3 came from entering the stereotaxic coordinates of the average parietal reading peak (xyz: -58, -64, 26) into our cSTS probability maps (Segal & Petrides, 2012b): the reading peak falls clearly posterior to the probability map of the cSTS2. This finding is important, because the cortex lying between the cSTS2 and cSTS3 is cytoarchitectonic parietal area PG (Economo & Koskinas, 1925; Caspers et al., 2008). Therefore, it can be concluded that area PG is the critical region for reading in the IPL. Note that the reading-related activation in the angular gyrus region starts where a short annectant sulcus separates the STS within the temporal lobe from the branches of the cSTS that rise into the parietal lobe. Reading-related activity therefore is located clearly in the angular gyrus region of the IPL between the cSTS2 and cSTS3, and not in the posterior temporal region. Also, note that reading-related activity involves the inferior region of the IPL occupied by area PG, and not the more dorsal region that is near the IPS.

Although the classic neurological model of reading based on clinical studies of neurological patients suggests that the angular gyrus region might be critical for reading (Dejerine, 1914; Geschwind, 1965b; Damasio & Geschwind, 1984), the extent of lesions in those studies prevented reading from being related to any precise part of the angular gyrus region. Furthermore, earlier neuroimaging studies either failed to report activity in the angular gyrus or reported activity more generally within the IPL (Bookheimer et al., 1995; Price et al., 1996; Horwitz et al., 1998; Turkeltaub et al., 2002; Joubert et al., 2004; Callan et al., 2005; Church et al., 2008), with the anterior–posterior coordinate, ranging from y -38 to y -72, covering most of the parieto-occipital region. This lack of precision relates both to the paradigms used to study such activity and the absence of detailed anatomical examination of this region of the brain (Segal & Petrides, 2012b). For example, most leading anatomical atlases of the human brain (Talairach & Tournoux, 1988; Ono et al., 1990; Duvernoy, 1999; Mai et al., 2007) have identified only two branches of the cSTS as it continues into the IPL whereas there are three branches. With the use of detailed morphological analysis in individual subjects and a reading paradigm, it could be shown in the present study that reading-related activity was restricted to a specific part within the angular gyrus region (area PG) (Fig. 1).

Reading-relating activity within the VWFA

The experimental and control task conditions used in the present study both involve stimuli that are presented visually, require subvocal rehearsal of the presented words or of the names of the pictured objects, and require written output. The main difference is that the experimental condition involved reading, whereas the control condition involved pictures of objects. Although reading-related activity in this study was observed in the angular gyrus after comparisons of the experimental and control task conditions (a finding that is consistent with the classic neural model of reading), no activity was observed in the middle part of the fusiform gyrus, i.e. the region previously identified as the VWFA (Dehaene et al., 2002; Dehaene & Cohen, 2011). Interestingly, however, results from the functional connectivity analysis showed that, during the reading of words, activation in area PG of the angular gyrus of the left hemisphere increases its functional interaction with the mid-fusiform gyrus in the inferior temporal region (along with other brain regions), regions), namely the region previously identified as the VWFA (Fig. 2).

The medio-lateral coordinate that is maximally associated with the VWFA has been reported, on average, at approximately x -43 in MNI standard space (McCandliss et al., 2003), corresponding to the anatomical location of the occipito-temporal sulcus, which forms the lateral boundary of the fusiform gyrus. The activation often spreads into the central part of the fusiform gyrus at various anterior–posterior coordinates (Cohen et al., 2000, 2002, 2008; Mc-Candliss et al., 2003; Cohen & Dehaene, 2004; Dehaene & Cohen, 2011; Szwed et al., 2011) (Fig. 2B). The functional connectivity results from the present study showing increased functional coupling between a region within the angular gyrus and the middle part of the fusiform gyrus during the reading of words are consistent with the interactive account of reading (Price & Devlin, 2011), which argues that the mid-fusiform gyrus may be involved in reading words through interactions with other brain regions, including the angular gyrus.

The VWFA in the middle part of the fusiform gyrus is likely to be involved in reading because it is part of the occipito-temporal stream that is specialized for processing many classes of visual forms (Vogel et al., 2012). Activation is found in the same region during the viewing of objects and of complex scenes (Malach et al., 1995; Grill-Spector, 2003; Grill-Spector et al., 2006; Kim & Biederman, 2011; Harel et al., 2012). There is a known anatomical connection that directly links posterior IPL with the middle part of the ventromedial temporal region in the macaque monkey (Seltzer & Pandya, 1994; Schmahmann et al., 2007). Therefore, it is possible that, in the human brain, a scene-analysis region of the mid-fusiform gyrus and the parietal reading-related angular gyrus region interact functionally to support the reading process (Turkeltaub et al., 2003; Hashimoto & Sakai, 2004). This notion is supported by studies showing that dyslexia is associated with reduced functional connectivity between the angular gyrus and other brain regions, including the fusiform and lingual gyri of the inferior temporal cortex, as well as Broca's area (Horwitz et al., 1998). According to our functional connectivity results, the mid-fusiform pattern perception region is not the only part of the cortex interacting with area PG during reading. There are significant interactions with Broca's region in the left ventrolateral frontal cortex, possibly via the superior longitudinal fasciculus (Petrides & Pandya, 2009), as well as interactions with the posterior superior temporal region (Wernicke's receptive language region) (Fig. 2A).

Reading-relating activity within the angular gyrus region

Studies of the effects of lesions on reading have suggested that posterior parietal lesions that involve the angular gyrus impair various aspects of the reading process, including phonological (Warrington & Shallice, 1980; Binder & Mohr, 1992) and semantic processing (Coltheart, 2000; Price et al., 2003). It is important to point out, however, that studies based on lesions resulting from brain disease cannot be localized to specific parts of the posterior parietal region, and even less to specific parts of the angular gyrus region (Brodmann, 1909; Economo & Koskinas, 1925; Critchley, 1966; Caspers et al., 2006; Seghier, 2013). Functional neuroimaging activity in combination with subject-by-subject analysis can provide precise information on whether reading-related activity is located in the angular gyrus and which specific parts (if any) of this large region contribute to the reading process. Our task paradigm isolated a focal peak of activation within the angular gyrus region that lies between the cSTS2 and cSTS3, i.e. the part of the angular gyrus that is related to area PG (Caspers et al., 2006, 2008).

What might be the reason for the involvement of area PG in reading, given that it is the endpoint of the dorsal visuo-parietal processing stream? Word reading is an exquisite example of retrieving semantic meaning from the analysis of visuo-spatial patterns (compare ba with da) in the context of directional movement through space (for example, we read words from left to right, and read paragraphs from top to bottom). Words and letters can be differentiated from one another according to the spatial arrangements of their elements (Vernon, 1957). For example, the words ‘eat’, ‘ate’ and ‘tea’are all composed of the same basic visual elements (i.e. the same letters), and what distinguishes these words from one another is the spatial order of the elements. Likewise, in words such as ‘pen’ and ‘den’ and in the syllables ‘ba’ and ‘da’, the fundamental distinction is the spatial orientation of certain letter elements (that is, p and d and b and d are rotations of the same visual objects). By contrast, unlike words and letters, objects may be differentiated from one another (e.g. an apple vs. a butterfly) on the basis of size, colour, texture, and form, features which may be apprehended sufficiently by the inferior temporal cortex. The subtraction of picture stimuli from word stimuli demonstrates the engagement of area PG, the endpoint of the visuo-spatial stream, during reading. In other words, aspects of orthographic processing that rely more on visuo-spatial analysis appear to be processed in this specialized part of the dorsal visual processing stream in the left hemisphere, whereas the overall visual object patterns of words may be processed within the ventral visual processing stream along the fusiform gyrus (previously called the VWFA). This conceptualization is in keeping with the well-known dissociation within the visual system of a dorsal pathway involved in the processing of spatial properties from a ventral pathway specialized for object recognition (Mishkin & Ungerleider, 1982; Ettlinger, 1990; Goodale & Milner, 1992). It is also supported by clinical evidence suggesting that the ventral occipito-temporal pathway is involved in early stages of reading, when words are detected quickly and at an unconscious level, whereas the dorsal parietal stream supports letter-by-letter assembly at a more conscious level (Gaillard et al., 2006).

Although, undoubtedly, the involvement of area PG in the left hemisphere of the human brain in the reading process is a uniquely human feature of area PG, it is of interest to note that the homologue of area PG in the non-human primate brain belongs to the dorsal stream of information processing. When this region is excised in nonhuman primates, specific visuo-spatial processing deficits can be demonstrated in the absence of impairment in the visual processing of objects in general (Petrides & Iversen, 1979; Mishkin & Ungerleider, 1982). Electrophysiological recording of neurons in area PG in macaque monkeys has also demonstrated that area PG is involved in specialized aspects of visuo-spatial processing, including the perception of spatial relations in complex visual stimuli (Mountcastle et al., 1975, 1987; Motter et al., 1987; Steinmetz et al., 1987). The results from the present study showing that area PG in the left hemisphere of the human brain is engaged during the reading of words, a process that requires the extraction of meaning from visuo-spatial forms are consistent with the known spatial properties of area PG.

The results presented here are also consistent with the pattern of results observed in a previously published study investigating the neural substrates of writing (Segal & Petrides, 2012a). That study demon strates that activity in the angular gyrus is canceled out when two task conditions involving English words as stimuli are compared. However, when a task condition involving words as stimuli is compared with a task condition involving pictures as stimuli, activation is observed in the angular gyrus, strengthening the argument that this area is involved in orthographic processing, which is largely visuospatial analysis. Additionally, the writing study shows that activity in the anterior portion of the superior parietal lobule (area PE) is associated with writing, and that area PE interacts with the angular gyrus when subjects write words that have just been read. Therefore, both the present study and the previous study are consistent in showing that activity in the angular gyrus is related to the reading of words. In conclusion, the present study is the first to identify a specific morphological feature of the IPL, namely the cortex centred around the cSTS2 (area PG), that is related to word reading. This finding adds to a growing literature showing that specific morphological features of the human brain can reliably predict the location of functional activation (Dumoulin et al., 2000; Amiez et al., 2006, 2013). The results of the present investigation indicate that area PG between the cSTS2 and cSTS3 in the left hemisphere of the human brain may be an important region that is specialized for the extraction of meaning from the analysis of the spatial features pertinent to words and may contribute to word reading by supporting orthographic processing.

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Abbreviations

area PE, anterior portion of the superior parietal lobule; area PG, cytoarchitectonic parietal area G; BOLD, blood oxygen level-dependent; cSTS, caudal extension of the superior temporal sulcus; cSTS2, central branch of the caudal superior temporal sulcus; cSTS3, posterior branch of the caudal superior temporal sulcus; d.f., degrees of freedom; fMRI, functional magnetic resonance imaging; FWHM, full-width half-maximum; GLM, general linear model; IPL, inferior parietal lobule; IPS, intraparietal sulcus; ITI, intertrial interval; MNI, Montreal Neurological Institute; NS, not significant; STS, superior temporal sulcus; TR, time to repeat; VWFA, visual word form area.

Tables

Table 1. List of stimuli

Copy the English Words	**Writing the names of Pictured Objects**
alley	anchor
banjo	bananas
belly	bat
blouse	belt
building	books
candle	boxes

canteen	broom
carpet	cactus
cheetah	cane
clock	cap
cow	carrots
curtain	cat
doll	chair
easel	cigar
elbow	cookies
ferry	croissant
fox	cup
glass	dog
graph	ear
hook	egg
insect	envelope
jeans	fence
kangaroo	flowers
kite	folder
koala	giraffe
leaf	gloves
map	grapes
mill	hammer
mountain	harp
nails	horse
needle	kettle
nymph	kleenex
orchid	ladybug
paintbrush	lemon
phoenix	lion
pool	luggage

quay	monkey
quill	mushrooms
receipt	pants
rhubarb	peanuts
saddle	penguin
sand	pie
satyr	plant
school	pylon
skiis	rabbit
spatula	ring
stove	scissors
sugar	shell
symbol	shorts
tattoo	slide
toes	snake
town	socks
urn	spider
vault	squirrel
walker	stapler
whale	telephone
window	throne
worm	toilet
wrench	tooth
zoo	tree
	umbrella
	wallet

Table 2. Focal peaks of activation related to reading (multi-subject)

Left Hemisphere	*x*	*y*	*z*	*t-value*
Anterior temporal area, inferior	-50	-2	-34	4.99
Anterior temporal area, superior	-60	2	-10	5.53
Middle temporal area	-48	-38	0	4.45
Angular gyrus region (between cSTS2 and cSTS3)	-58	-64	26	5.29
posterior intermediate parietal sulcus (pips)	-50	-72	44	4.99
Midline/Medial	*x*	*y*	*z*	*t-value*
Medial area PG	0	-60	42	6.74
Right Hemisphere	*x*	*y*	*z*	*t-value*
Lateral prefrontal area 9	20	44	40	6.80
STG, anterior region	58	8	-28	5.23
Anterior temporal area, inferior	66	-4	-20	5.78
ITG, anterior region	66	-22	-26	5.66
Angular gyrus region (between cSTS2 and cSTS3)	58	-56	26	4.90
Posterior intermediate parietal sulcus (pips)	48	-72	42	6.56

All *t* statistics are significant at $p < 0.05$ corrected for multiple comparisons. The stereotaxic coordinates are expressed in millimeters within the MNI stereotaxic proportional system.

Table 3. Location of the functional peak observed between the cSTS2 and cSTS3 for each individual subject during reading

Subject	*x*	*y*	*z*	*t-value*
Subject 1	-48	-72	22	3.33

Subject 2	-62	-66	30	4.93
Subject 3	-56	-62	20	4.54
Subject 4	-58	-66	29	3.27
Subject 5	-46	-68	24	2.54
Subject 6	-34	-56	24	3.43
Subject 7	-54	-70	20	3.20
Subject 8	-44	-58	40	3.36
Subject 9	-62	-60	20	3.18
Average coordinates	-51.56	-64.22	25.44	
Standard deviation	9.32	5.52	6.62	

All *t* statistics are significant at *p* <0.05 corrected for multiple comparisons. The stereotaxic coordinates are expressed in millimeters within the MNI stereotaxic proportional system.

Table 4. Functional Connectivity results of the cSTS2/cSTS3 peak during word reading

Left Hemisphere	*x*	*y*	*z*	*t-value*
ventral area 10	-28	60	-6	2.85
area 9	-30	28	38	2.66
anterior pars triangularis/area 45	-38	36	4	2.95
pars triangularis/area 45	-30	32	10	2.85
pars opercularis/area 44	-56	12	22	2.46
ventral premotor area 6	-52	4	0	2.95
dorsal premotor area 6	-36	0	50	2.36
ventral cingulate cortex	-2	8	34	2.56
dorsal cingulate cortex	-4	-24	72	2.66
primary motor cortex, area 4	-26	-18	76	2.95
superior temporal gyrus, middle region	-62	4	-6	2.95
inferior temporal gyrus, middle region	-56	-6	-26	2.46
temporal operculum of insula	-46	-12	-8	2.85
posterior region of superior temporal gyrus	-48	-38	16	2.56

AOCS-v	-56	-68	4	2.27
Fusiform, posterior and ventral part of area 37, dorsal to "VWFA"	-36	-56	-2	2.76
Fusiform, medial to OTS, anterior to "VWFA"	-32	-38	-18	2.85
extrastriate area 19, dorsal	-22	-80	44	2.46
extrastriate area 19, dorsal	-2	-82	48	2.56
extrastriate area 18, dorsal	-16	-74	28	2.66
retrosplenium	-8	-42	6	2.95
Midline	*x*	*y*	*z*	*t-value*
dorsal premotor 6	0	-6	70	4.61
Right Hemisphere	*x*	*y*	*z*	*t-value*
dorsal area 10	30	64	20	3.25
area 9	28	30	42	2.95
anterior insula	40	20	-8	3.24
pars triangularis/area 45	56	20	14	2.46
pars opercularis/area 44	60	6	30	3.54
anterior insula	30	20	-8	3.24
primary motor cortex, area 4	52	-8	56	3.05
ventral circular sulcus of insula	42	-18	-8	3.64
supramarginal gyrus, area 40	68	-32	24	2.95
posterior cingulate, ventral	6	-32	48	3.34
retrosplenium	8	-42	4	3.34
area 37	48	-74	8	2.76
AOCS-v	42	-68	12	2.76
SPL, area 7	24	-60	70	2.85
extrastriate area 19	12	-54	8	2.95
extrastriate area 18	12	-94	10	3.05
extrastriate area 18	4	-86	-10	2.66

All *t* statistics are significant at $p < 0.05$ corrected for multiple comparisons. The stereotaxic coordinates are expressed in millimeters within the MNI stereotaxic proportional system.

Figures

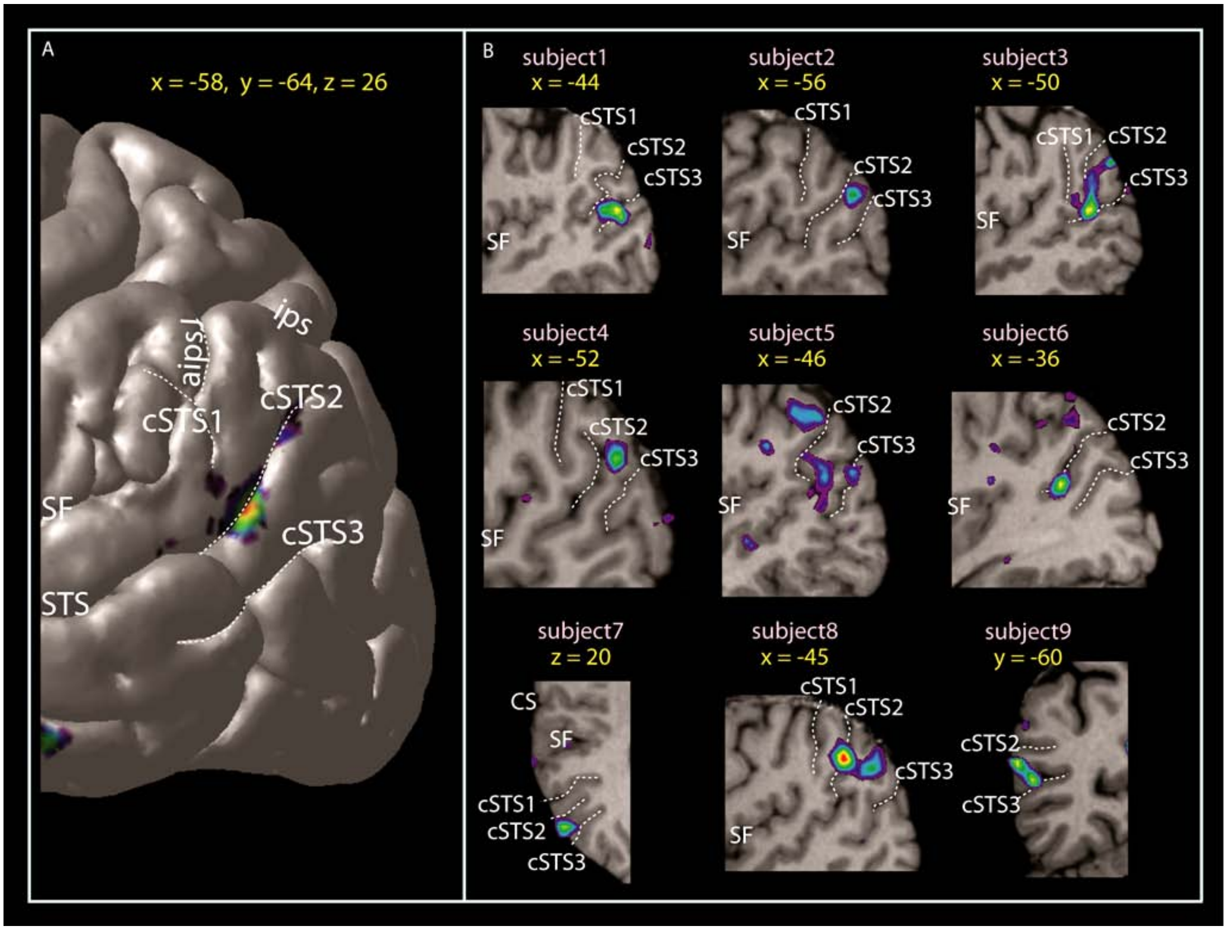

Figure 1. Reading-related Activation in the Angular Gyrus. Panel A. Multisubject average of the reading-related activation in the left angular gyrus, superimposed on the reconstructed 3D surface of the MNI average brain. The multi-subject average activation (xyz coordinates: -58, -64, 26, t = 5.29) falls within the central branch of the caudal superior temporal sulcus (cSTS2) and spreads towards the caudal branch (cSTS3). Thus, it is located in the central part of the angular gyrus. Panel B. 2D sections in the sagittal plane to show the reading-related functional data of each subject superimposed on his or her own anatomical MRI. Note that for subject 7 the activity is best displayed in a horizontal section (z = 20) and for subject 9 the activity is best displayed in a coronal section (y = -60). Abbreviations: aipsJ, anterior intermediate sulcus of Jensen; cSTS1, anterior branch of the caudal STS; cSTS2, central branch of the cSTS; cSTS3,

posterior branch of the caudal STS; IPS, intraparietal sulcus; SF, Sylvian fissure; STS, superior temporal sulcus.

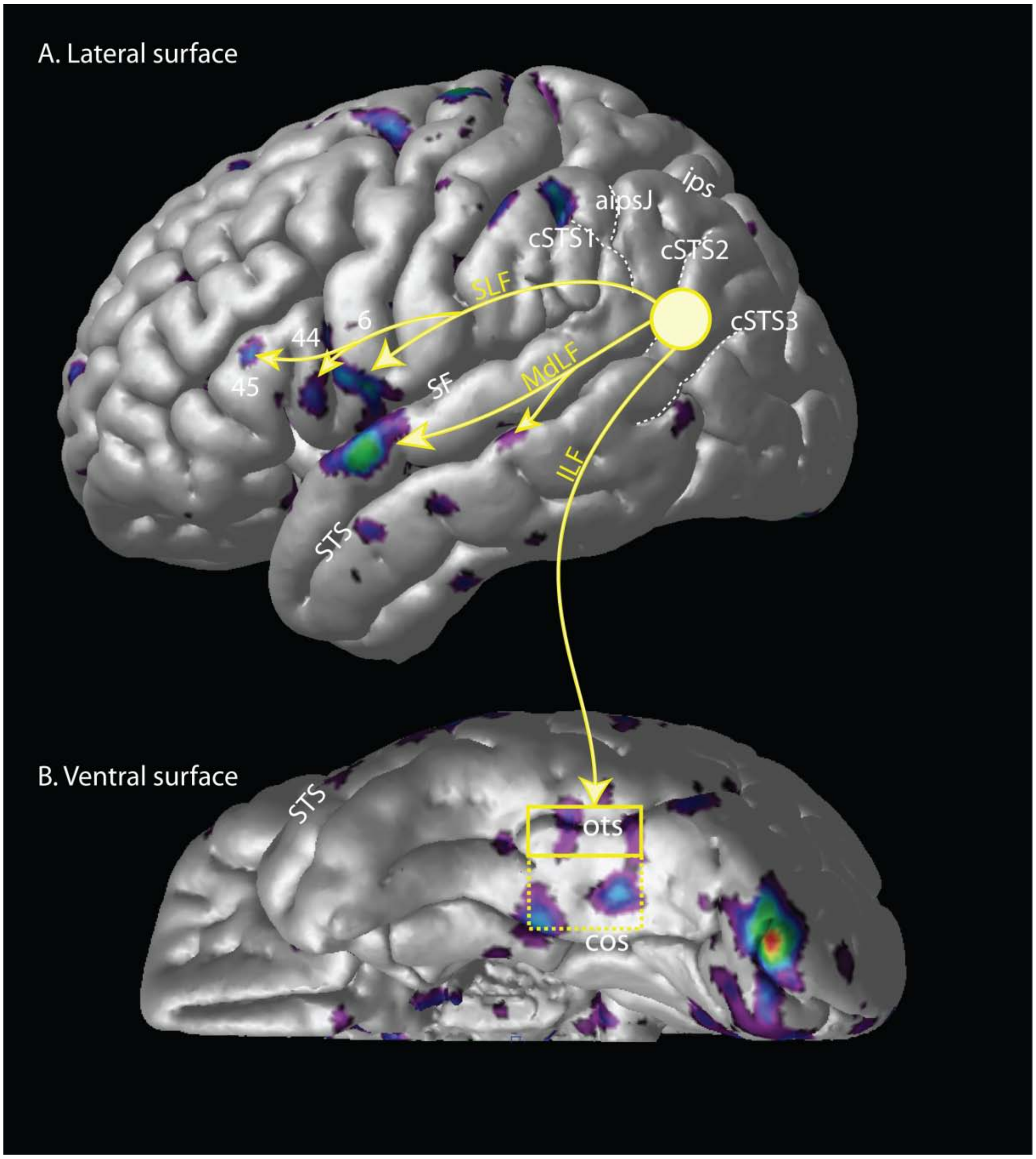

Figure 2. Functional interaction of the angular gyrus during reading. Panel A. The functional connectivity analysis demonstrated that, during reading, the region of the angular gyrus located between the cSTS2 and cSTS3 (indicated by the yellow circle) increased its interaction (i.e. functional connectivity) with the ventrolateral region of the frontal lobe that supports expressive

language (Broca’s region: areas 44 and 45) and the premotor region of the frontal lobe (area 6) that supports orofacial motor control. During reading, the angular gyrus also increased its interaction with parts of the superior temporal gyrus (Wernicke’s receptive language temporal region) and with the mid-fusiform region, an area previously described as VWFA. Panel B. The yellow boxes on the brain's ventral surface outline the extent of the coordinates that have been reported as representing the location of the VWFA. The coordinates associated with the maximum functional peak surround the ots, as outlined by the solid yellow box, but the functional activity spreads more medially and onto the middle part of the fusiform gyrus, as outlined by the dashed yellow box. The arrows indicate known anatomical connections from area PG in the angular gyrus to the regions showing increased interaction. Abbreviations: aipsJ, anterior intermediate sulcus of Jensen; cos, collateral sulcus; cSTS1, anterior branch of the caudal STS; cSTS2, central branch of the cSTS; cSTS3, posterior branch of the caudal STS; ILF, inferior longitudinal fasciculus; IPS, intraparietal sulcus; ots, occipital-temporal sulcus; MdLF, middle longitudinal fasciculus; SF, Sylvian fissure; SLF, superior longitudinal fasciculus; STS, superior temporal sulcus.

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