Right hemisphere reading in a case of developmental deep dyslexia

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The right hemisphere hypothesis of deep dyslexia has received support from functional imaging studies of acquired deep dyslexia following damage to the left cerebral hemisphere, but no imaging studies of cases of developmental deep dyslexia, in which brain damage is not suspected, have been reported. In this paper, we report the first evidence of right hyperactivation in an adult case of developmental deep dyslexia. Hyperactivation was observed in the right inferior frontal cortex during fMRI imaging of the oral reading of imageable content words and nonwords to which imageable lexical responses were frequently made. No evidence of right hyperactivation was observed in the oral reading of function words, nor during the naming of imageable words in response to pictured objects. The results reveal strategic and selective use of right hemisphere functions for particular types of written stimuli. We propose that children with developmental deep dyslexia compensate for their lack of phonological skills by accessing right-hemisphere imageable associations that provide a mnemonic for linking written forms to spoken names.

Deep dyslexia is a profound reading disorder that is most commonly seen following wide-spread damage to the left side of the brain (acquired deep dyslexia) and is also occasionally observed in individuals with no clear brain pathology (developmental deep dyslexia). The theory that right hemisphere processes are responsible for the symptoms observed in acquired deep dyslexia (Coltheart, 1980a; Saffran, Bogyo, Schwartz & Marin,1980) has been supported by functional imaging studies (Coltheart, 2000; Price, Howard, Patterson, Warburton, Friston, & Frackowiak, 1998; Weekes, Coltheart, & Gordon, 1997) but the possibility of right hemisphere involvement in developmental deep dyslexia has not been explored (Johnston, 1983; Seigal, 1985; Yamada, 1995; Temple, 1988, 2003; Stuart, & Howard, 1995).

The cardinal symptom of acquired deep dyslexia is the semantic error (Marshall, & Newcombe, 1966; Coltheart, Patterson, & Marshall, 1980). Semantic errors (eg wrist-"watch"; dream-"sleep") lie at the core of an unvarying symptom-complex which also includes visually-related errors (eg shallow-"sparrow") and visual and/or semantic errors (eg incident-"accident"; next-"exit"). Words with imageable meanings (eg 'snow') are read most successfully; abstract words tend to elicit visually related imageable words; while function words are rarely read correctly and usually produce alternative words of the same class (Morton & Patterson, 1980). Nonsense words cannot be read aloud and either prompt visually similar imageable words (Saffran & Marin, 1975; Coltheart, 1980b) or fail to produce a response. Auditory-verbal memory span is always compromised.

A similar pattern of reading impairment has been reported in a few cases of developmental dyslexia. In all cases, verbal IQ scores were below average and in two cases were beyond -3sds below the mean, indicating widespread learning difficulties in some individuals. Semantic errors were observed in the oral reading of four single case studies of developmental dyslexia (Johnson, 1983; Temple, 1988; Temple, 2003; Stuart & Howard, 1995, Yamada, 1995) and in all six cases reported in a group study of six children (Seigal, 1985). As in acquired deep dyslexia, semantic errors were accompanied by visual, visual-semantic errors and function-word substitutions (Johnson, 1983; Temple, 1988; Temple, 2003; Stuart & Howard, 1995; Yamada, 1995). Imageable/concrete words were read more successfully than abstract words matched for word frequency (Johnston, 1983) but, in contrast to acquired deep dyslexia, function words were read relatively well (Johnson, 1983; Stuart and Howard, 1995) and in one case more successfully than imageable nouns (Temple, 2003). Nonwords could not be read aloud correctly and produced either omissions or visually similar words (Siegel, 1985; Temple 1991). These symptoms, which largely mirror those found in adult acquired dyslexia, have earned these cases the title of 'developmental deep dyslexia', although this classification has been disputed on the basis of the lack of purity of the symptoms (Jackson and Coltheart, 2001).

The right hemisphere hypothesis of deep dyslexia (Coltheart, 1975; Saffran, Bogyo, Schwartz and Marin, 1975) proposed that the symptoms reflect the characteristics of right hemisphere processes recruited to compensate for widespread damage to left hemisphere processes involved in normal reading. In support of this theory, functional imaging studies of acquired deep dyslexia have reported evidence of right hemisphere hyperactivition when compared with the neural activation found in controls. In one case, this hyperactivation centred on occipital areas involved in visual word recognition (Weekes, Coltheart, & Gordon, 1997), while in two further cases the hyperactivation centred on the pars opercularis of the right inferior frontal gyrus (Price, Howard, Patterson, et al, 1998), with weaker peaks of hyperactivation in right occipital and temporal areas, that in homologous left-hemisphere locations would be associated respectively with visual word recognition and semantic processing (Coltheart, 2000; Price, Howard, Patterson, et al, 1998). On the assumption of homology of function across hemispheres, it was assumed that the right pars opercularis has taken over the role of phonological word retrieval from the damaged pars opercularis in the left hemisphere (Coltheart, 1980a; 2000).

In this paper, we report the first functional imaging study of single-word reading in a case of developmental deep dyslexia. To date, studies of developmental deep dyslexia have either failed to consider right-hemisphere involvement or have rejected the possibility because brain abnormality is not suspected (Stuart and Howard, 1995). If the symptoms of deep dyslexic reading reflect the properties of right hemisphere activation, as the right hemisphere hypothesis predicts, we should find evidence of enhanced right hemisphere activation whether or not left hemisphere language areas are structurally impaired.

CASE HISTORY

We report the case of JPJ, a 29 year old female postgraduate student with a low reading-age and a deep-dyslexic pattern of reading. She has a family history of dyslexia and suffers from Ehlers Danlos syndrome, which affects the production of connective tissue. She reports an early history of learning and emotional difficulties and believes she began to read at 16 years of age. She writes with her right hand, but considers herself ambidextrous. Structural imaging using T1 MRI detected no cortical damage and diffusion weighted MRI showed white matter to be normal.

Psychometric assessments revealed above average WAIS-R verbal IQ of 106 and performance IQ of 117 making JPJ the first case of developmental deep dyslexia to be reported with an above average verbal IQ. She had obvious strengths in perceptual organisation (percentile 99) and verbal comprehension (percentile 73) but weaknesses in working memory (percentile 9) and processing speed (percentile 8). A good score (146/150 correct) was achieved on the British Picture Vocabulary Scale and an average score (17/30) on the Graded Naming Test, but auditory-verbal memory was very poor (3 digits forwards, 2 digits back). A below-average score (24/40 correct, >-2sd) was obtained on the Children's Test of Nonword Repetition and a zero score (0/20) on the Graded Nonword Reading Test. WORD, a standardised test of literacy development, revealed low age-equivalent values in oral reading (6 years 6 months), reading comprehension, (7 years 3 months), and spelling, (7 years). Oral reading errors included 1 semantic error, 1 visual error and 2 function word substitutions. Surprisingly, JPJ achieved an average score (16/30 correct) on the National Adult Reading Test which is composed of infrequent irregular words. Three words in this test JPJ recognised from her scientific work suggesting that her advanced academic studies have boosted her vocabulary of uncommon words relative to more common words that are generally learned at an earlier age.

Since a developmental analogue of acquired deep dyslexia has been questioned (Jackson, & Coltheart, 2001), we compared JPJ's oral reading with that of JG, a classic case of acquired deep dyslexia (Funnell, 1987) for whom there is evidence of enhanced activation in the pars opercularis of the right inferior gyrus during the reading of imageable words (Price, Howard, Patterson et al, 1998).

<u>Test 1.</u>

This test consisted of a mixed list of 38 highly imageable words (19 high frequency, 19 low frequency matched for syllable and letter length to 38 low imageable/abstract words (19 high frequency, 19 low frequency). These materials were presented to JG in 1985 and the results have not been published before.

Ten postgraduate controls with no history of reading difficulties were asked to read the test words aloud: eight controls read all 76 words correctly; one made two errors; and one made one error (mean correct 75.7 (99.6%), sd 0.68).

As Table 1 shows, JG read 43/76 (60%) words correctly and showed a significant advantage for imageable words (Fisher Exact two tailed p = 0.001) but no independent effect of word frequency (Fisher Exact two tailed p = 0.179). JPJ read 36/76 (50%) words correctly, a comparable score to that of JG. She showed a significant advantage for highly imageable words (Fisher Exacat two tailed p = 0.003) and also for words of high frequency (Fisher Exact two tailed p=0.001). Her advantage for high frequency words is not surprising since words that appear more often in script are likely to be learned most readily.

Table 1 about here

Table 2 presents the proportions of errors of different type made by JG and JPJ, which are very similar. Circumlocutions figured strongly in the responses of both subjects. Although circumlocutions are not usually included in lists of the characteristic of deep dyslexia, many such errors can be found in the Appendices to 'Deep Dyslexia' (Coltheart, Patterson and Marshall, 1980).

Table 2 about here

Test 2

In this test, we assessed the oral reading of function words to which we expected JPJ to produce a superior score, since function words are generally very high in frequency. JG scored 0/10 correct on a short list of very common function words (see

Funnell, 1987) while JPJ scored 71/86 (83%) correct on a longer word set. Although the distribution of errors differed, the pattern of errors made by JG and JPJ was very similar (see Table 3). JPJ made fewer substitution errors (eg who - "how") than JG, whose errors were confined to the grammatical class, and more visually-similar content word errors (eg (quite - "quick). She also made occasional semantic circumlocutions to these words (eg itself - "it, being on your own").

Test 3.

Here we compared the oral reading of sets of simple nonwords. JG read no nonwords correct in a set of 10 single-syllable nonwords (unpublished data), while JPJ read 4/30 correct nonwords in a test designed by Castles, & Coltheart (1993). As Table 3 shows, the distribution of errors of different types made by JG and JPJ is virtually identical. Visually similar, imageable word responses (eg stet-"street", nint-"mint") were typical of the errors made.

Table 3 about here

EXPERIMENTAL INVESTIGATION.

To explore the possibility that right hemisphere functions are hyperactivated in developmental deep dyslexia, we conducted two functional imaging experiments with JPJ using a 1.5T Philips Intera scanner. In both studies, the functional data were realigned within subjects to correct for head movements and subsequently normalized to an EPI template in line with the MNI space. High resolution T1 weighted structural imaging (3D MPRAGE, sagittal slices, flip angle 12º, TE 3.7ms, TR 8ms 1x1x1mm voxels) was obtained for JPJ and controls. For JPJ an additional diffusion weighted image (single-shot EPI, 2x2x3mm voxels, six directions, b=0 and 1000 s/mm2) was obtained also. For both functional imaging studies, one continuous series of whole brain T2* EPI volumes (single shot EPI, 64x64 matrix, 3x3x3mm voxels, 33 slices acquired in ascending order with no slice gap, TE of 60ms and TR of 3.5s) was obtained for controls and JPJ. The first couple of volumes in each series were discarded to allow for T1 effects (the number of volumes discarded varied but was approximately 5). The length of the task always exceeded the length of the scanning session.

EXPERIMENT 1.

Since imageability is strongly associated with correct reading responses in deep dyslexia, our first experiment used a visual object-naming task to investigate the pattern of neural activation associated with the retrieval of imageable words in a task other than reading. Tests showed that PJP's visual object naming was within the normal adult range on the Graded Naming Test (see above) and on the Age of Acquisition Naming test (Funnell, Hughes and Woodcock, unpublished) on which her score of 63/72 correct compared favourably with the average score of 62.48 correct obtained from a group of 45 adult female controls. We expected therefore that JPJ would be able to name without difficulty the pictured objects presented in the scanner.

Method.

39 coloured pictures of familiar objects were mixed at random with 36 coloured pictures of abstract art and presented in series to JPJ and to 10 right-handed adult controls (6 women, 4 men). Each picture was presented for 2000ms. The next trial began after an inter-trial interval that was randomized between 2004ms and 9966ms

and during which a fixation cross was presented. Subjects were asked to name the objects and remain silent to the abstract art. One continuous session of functional images was collected.

Results and discussion

One control subject (male) was excluded from further analysis because the amount of scan-to-scan head movement exceeded 1mm. Using statistical analyses to isolate brain areas associated with name retrieval we analysed the following volumes: JPJ, 171 volumes; 6 controls, 176 volumes; 2 controls, 175 volumes; and 1 control, 171 volumes. Statistical analysis of the functional data was performed on a trial-by-trial basis. Multiple regression analysis was used to identify voxels where the pattern of activity after convolution with a box-car function of the HRF and correction for small variations in temporal onsets of the HRF significantly correlated with the occurrence of the experimental trials.

We found no areas of the brain where the level of neural activation of JPJ differed significantly from the level of neural activation of the control subjects, showing that standard neural systems are activated to a normal level by JPJ when producing imageable words in response to pictured objects.

EXPERIMENT 2

In this experiment, we explored the cortical activation associated with naming three types of written stimuli: imageable content words and, for the first time in a case of deep dyslexia, function words and nonwords.

Method

Blocked lists of 18 familiar imageable words, 18 familiar function words and 18 nonwords were presented to JPJ and to 9 right-handed adult controls (5 women, 4 men) who had also taken part in the Experiment 1. All stimuli were four letters long. The imageable words had been read without error by JPJ on 2/2 occasions previously and the function words had been read without error on 1/1 occasions. We assume therefore that most, if not all, of these words will be identified correctly by JPJ in this experiment. The novel nonwords consisted of four letters and were orthographically legal (eg 'reth', 'hasp'). Previous tests have shown that JPJ is unable to pronounce nonwords correctly and instead produces visually similar imageable words. Levels of cortical activation produced by JPJ were compared to levels of neural activation of the controls in each experimental condition.

All stimuli were presented for 1200ms followed by the presentation of a fixation cross for 800ms. In each experimental block the complete stimulus set of 18 items was presented. Each block lasted 36 seconds and was alternated with a 10 second baseline block during which a row of 4 ‘X’’s was shown. Each of the 3 experimental condition blocks (function words, imageable words and nonwords) was presented 12 times, during which subjects were instructed to read aloud each stimulus.

Results

The following volumes were analysed: JPJ, 247 volumes; 7 controls, 251 volumes; and for 2 controls, 250 volumes. Statistical analysis of the functional data was performed on a block-by-block basis. Multiple regression analysis was used to identify voxels where the pattern of activity after convolution with a box-car function of the HRF significantly correlated with the occurrence of the experimental blocks.

A random effects analysis used a two-sample t-test to assess the significance of differences in condition means between the control subjects and JPJ. The statistical analysis applied a voxel-based threshold of $p < 0.05$ (FDR corrected for multiple comparisons) to determine which voxels were significantly activated in each statistical test.

Function word reading failed to result in a significant difference in neural activation between JPJ and controls, showing normal activation of standard neural systems for this word-class. In contrast, as Figure 1 and Table 4 show, responses to imageable content words (see Figure 1, Table 4) resulted in significantly enhanced activation in the pars opercularis of the right inferior frontal gyrus. Cytoarchitectonic probality mapping (Eickhoff, Stephan, Mohlberg, Grefkes, Fink, et al, 2005) assigned the peak voxel in this area to BA44 with a probability of 60%. Furthermore, when compared to controls, responses to nonwords (see Figure 1, Table 4) produced enhanced activation that peaked in the right insula and extended into the pars orbitalis and pars opercularis (ie in the region activated also by imageable words) of the right inferior frontal gyrus and into the superior temporal gyrus. Cytoarchitectonic probability mapping assigned both local maxima located in the right inferior frontal gyrus to BA 44.

Figure 1 and Table 4 about here

GENERAL DISCUSSION

JPJ is the first adult case of developmental deep dyslexia to be reported. By comparing her reading performance with that of JG, a classic case of acquired deep dyslexia, we have shown that her reading shares most of the characteristics of this disorder. JPJ and JG were both unable to pronounce novel letter strings to which they either failed to respond or they produced visually similar imageable words instead. They both read imageable words significantly more successfully than abstract words and made semantic errors; visual-semantic errors, visual errors, circumlocutions, and function word substitutions. Where JPJ's performance differed from JG was in the effects of experience on learning. While PJP showed an effect of word frequency on her ability to read words of different kinds, reflecting the positive effect of frequency of exposure on word recognition during learning, JG. (like other cases of acquired deep dyslexia) had lost the ability to read function words and his residual recognition of mainly imageable words was unaffected by word frequency.

The right hemisphere hyperactivation to imageable words observed in JPJ was focused in the pars opercularis of the right inferior frontal gyrus, which was also the main focus of right hyperactivation during JG's reading of imagable words (Price, Howard, Patterson, et al, 1998). Imaging studies of acquired deep dyslexia have assumed that the pars opercularis of the right inferior frontal gyrus has adopted the role of phonological lexical output in response to damage to the homologous area in the left hemisphere (Coltheart, 2000; Price, Howard, Patterson, et al, 1998). However, in JPJ, there was no decrement in activation in the left hemisphere, relative to controls, that would necessitate right hemisphere compensation. Also, no right hemisphere hyperactivation occurred when JPJ named imageable words in response to pictured objects or written function words, ruling out a left hemisphere problem with phonological lexical retrieval.

More importantly, an emphasis upon a right hemisphere role in phonological word retrieval fails to account for the characteristic features of deep dyslexia which the right hemisphere hypothesis seeks to explain. We suggest that the areas in the right frontal operculum that are activated by normal controls and hyperactivated by JPJ in response to written imageable words and nonwords are involved in an associative network of imageable meanings. The incidence of responses to written words that are semantically associated (eg 'geese'- "something white"; flax - "something to do with plant science") and circumlocutions that refer to perceptually-based episodic memories (eg 'security' - "I've seen it written big and bold on a car or a white van") suggests that this meaning system is not a lexicon confined to the representation of specific word-meanings but a memory system involved in the integration of imageable information from many sources and at many different levels of precision.

When novel written stimuli were presented, to which JPJ makes incorrect imageable word responses, more wide-spread right hemisphere hyperactivation was observed. This included the pars opercularis which was hyperactivated also by familiar imageable words. We propose that this wider activation is involved in finding lexical solutions to novel letter strings when contextual clues are unavailable. The high incidence of orthographically similar lexical responses with imageable meanings again testifies to the tolerance of this system to imprecise solutions, a characteristic that is likely to be essential to any associative memory system involved in the integration of novel information.

This study provides the first evidence of right hemisphere reading in a case of developmental deep dyslexia, and thus supports the right hemisphere hypothesis of deep dyslexia. In JPJ, who lacks phonological sub-lexical skills but has a structurally intact brain, the hyperactivation of right hemisphere processes during the reading of imageable words and novel letter strings indicates strategic use of right hemisphere imageable memory systems in order to connect orthographic patterns to spoken word forms. Since right hemisphere hyperactivation was found for imageable words that we know JPJ reads aloud reliably, we conclude that once established, reliance on these right hemisphere connections persists.

Most children with poor phonic skills do not develop deep dyslexia, but JPJ's exceptional perceptual organisation skills (at the 99th percentile) may have provided her with a mnemonic that enabled orthographic stimuli to be linked readily to perceptually realisable associations. This is not an efficient strategy: JPJ's reading vocabulary is low; she finds the task of reading difficult; and she avoids reading whenever she can.

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Figure legends

Figure 1: Areas of the brain that are significantly more activated for JPJ than for the controls. The top row of pictures shows results when subjects were reading imageable words. The bottom row of pictures shows results when subjects were reading nonwords. The pictures on the left show the results overlaid on a rendered standard brain. The pictures on the right shows a 3D view of the location of the peak activation. All images are in neurological convention and a significance threshold of 0.05 FDR corrected was used.

Table 1. Comparison of the number of correct oral reading responses by JG (acquired deep dyslexia) and JPJ (developmental deep dyslexia) to words varying in imageability and word frequency.

	Word sets			
	High Imageability		Low Imageabiltiy	
	High Freq.	Low Freq.	High Freq.	Low Freq.
Oral reading no. correct				
JPJ	16/19	9/19	10/19	1/19
JG	18/19	17/19	6/19	2/19
Imageability ratings				
Mean	594	589	374	345
SD	27	26	42	40
Frequency Counts				
Mean	163	1.7	164	1.8
SD	83	0.77	92	0.87

<u>Table 2.</u> Types of oral reading responses made to words in Test 1.

	JG		JPJ	
	N	(Proportion)	N	(Proportion)
Number Correct max = 76	43		36	
No response	5		25	
Total explicit errors	28		15	
Error types				
Visual	17 eg concept - "concert"	(0.61)	8 eg session - "season"	(0.53)
Visual-semantic	1 area -"acre"	(0.04)	1 teeth - "tooth"	(0.06)
Visual then semantic	0		1 glacier - "cherries"	(0.06)
Pure semantic	1 square - "inch"	(0.04)	1 hockey - "jogging"	(0.06)
Sem. circumlocution	6 eg gist - "German, ideas "	(0.21)	4 eg morphine - "something medical"	(0.27)
Phonological	1 morphine - "morphalin"	(0.04)	0	
Other	2	(0.07)	0	

Table 3. Distribution of reading errors made by JG and JPJ to function words and nonwords in Tests 2 and 3.

	JG	JPJ
Function words	n = 10	n = 86
Total errors	10	15
Substitutions	5 (0.5) *from-"who"*	4 (0.27) *where-"were"*
Visually similar content words	1 (0.1) *just-"justice, isn't but close"*	5 (0.33) *while-"white"*
Semantic circumlocutions	0	2 (0.13) *enough-"full, but it's not full"*
No response	4 (0.4)	4 (0.27)
Nonwords	n = 10	n = 30
Total errors	10	26
Other nonwords	1 (0.1) *ploon-"plink"*	5 (0.19) *toud – "trow"*
Visually related content words	7 (0.7) *cobe-"cobra"*	16 (0.62) *stet-"street"*
No response	2 (0.2)	5 (0.19)

Table 4. Areas of the brain significantly more activated for JPJ than for controls during the reading of imageable words or nonwords.

Brain area	Imageable words		Nonwords	
	MNI	probability	MNI	probability
R inferior frontal gyrus (pars opercularis)	57 12 6 (5.38)	BA44: 60% BA45: 10%	51 15 0 (4.85)	BA44: 30% BA45: 10%
			57 12 6 (4.64)	BA44: 60% BA45: 10%
R insula			42 18 -9 (5.12)	

Locations of the maxima are given in X Y Z mm (Z-score). Only local maxima more than 8mm apart in clusters larger than 5 voxels are reported. Coordinates are MNI coordinates. Probabilities are the probabilities of the maximum being located in a given Brodmann area according to cytoarchitectonic probability mapping (only available for the inferior frontal gyrus).

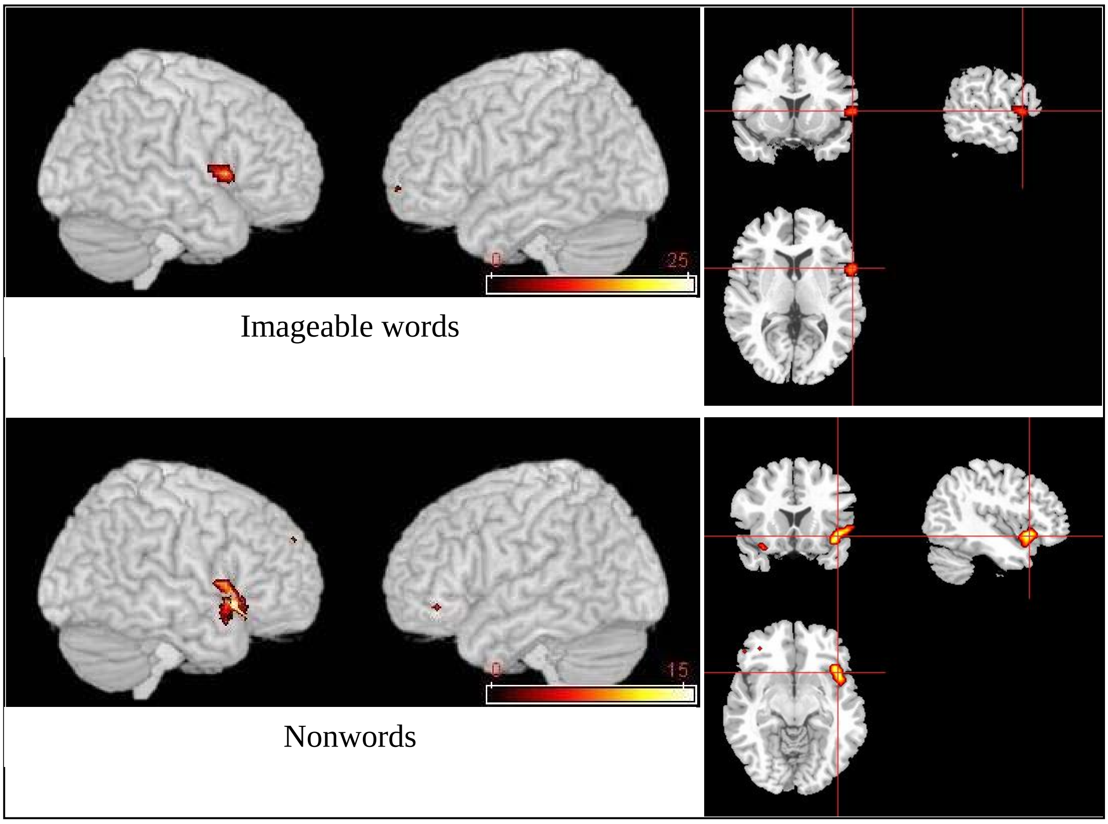

Figure 1 (see legend).