

Word Reading Processing In Children: A Functional MRI Study At 1.5 T

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Citation

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Abstract

Functional MRI is a tool for investigating brain function non-invasively. Our study addresses the question whether functional MRI can be used in children to differentiate activated brain areas in phonological tasks. A set of hierarchically structured reading tasks was used in 17 healthy right-handed children (median 14y 1m). fMRI was acquired during perception of letter strings, silent reading of non-words, silent reading of words, and during performance of a task with phonological transformation using a T2* weighted GRE sequence with three slices (TR/TE/α 68ms/50ms/10°). Postprocessing was done using SPM99. Activation was observed only in Broca's area while silent reading of real words. Phonological strategies (non-word reading and transformation task) resulted in activation in the frontal and temporal regions, as well as bilaterally in Broca's area in the inferior frontal gyrus.

Conclusion: The observed activation patterns in children are different to reported areas in adults. This could be caused by the stronger use of the grapheme-to-phoneme mapping as a serial process in children in contrast to adults.

INTRODUCTION

Until recently, studies of brain function in children have been limited to indirect techniques like electroencephalography (EEG) and event-related potentials, which provide information regarding the timing of sensory and cognitive events. Other brain imaging techniques, such as positron emission tomography (PET) and single photon emission computed tomography (SPECT) are available, but these techniques require exposure to radiation.

Consequently, these neuroimaging methods are limited in their use in pediatrics. In recent years, functional magnetic resonance imaging (fMRI) has been introduced to developmental research. The principle of this noninvasive technique is based on the so called BOLD-effect (blood oxygenation level dependent effect) which is caused by the different behavior of oxygenated and desoxygenated hemoglobin (HbO₂ and deHbO₂) in a magnetic field [1]. Neuronal activation causes an increase in regional blood flow and blood volume which in turn overcompensates for the increase in oxygen use. The result is a locally decreased concentration of paramagnetic deHbO₂ at the capillary venous level and, therefore, a smaller susceptibility difference between venous blood and brain parenchyma, which leads to a local signal intensity increase on T2*-

weighted sequences (gradient echo conventional sequences or echo planar imaging)[2]. Depending on the field of view, an in-plane resolution of up to 1mm is possible, which overcomes the restricted spatial resolution of SPECT or PET. Noninvasiveness, independence from any exogenous tracer, relatively high spatial and temporal resolution, and the possibility to acquire simultaneously activation and topographic data are the main advantages of functional MRI in comparison to other neuroimaging methods. Functional MRI may contribute to a better understanding of functional anatomy of reading in the intact human brain and its development. To date, only few pediatric functional MRI studies have been published [3].

Former functional imaging studies in adults using PET and fMRI have demonstrated that different brain areas are involved in reading processes [4,5,6,7,8,9,10,11,12,13,14]. These studies have also improved the knowledge about the functional specialisation of cortical regions that subserve different aspects of word processing in normal reading adults. With respect to pediatrics the functional mapping of language prior to neurosurgery was studied [15]. In a comparative fMRI study of dyslexic children and adolescents restricted activation of brain regions during

various language tasks could be shown compared to normal reading adults [16]. Significantly less activity in the inferior frontal gyrus and the supramarginal gyrus in the dyslexic group could be observed in a comparison of dyslexic adolescents and age-matched controls using a phoneme discrimination task [17]. These data supported the notion that functional MRI can play a role in localizing functional abnormalities in children but also underlined the importance of investigating normal development [3, 18].

The aim of our study was to investigate the possibility of functional MRI to discriminate functional brain areas which are involved in different, hierarchically structured reading tasks in children. Our hypotheses were that: (1) functional MRI can demonstrate brain activation in children following reading processes allowing a detailed anatomical description of the activated areas and (2) fMRI can demonstrate activation in different brain areas using hierarchically structured reading tasks requiring different phonological strategies.

MATERIALS AND METHODS

SUBJECTS

17 right-handed healthy children (9 girls and 8 boys; aged from 9 to 17 years; median 14 years and 1 month) was investigated. None of the subjects had any known history of neurologic or psychiatric disease. All had a similar sociocultural status. The nonverbal IQ was estimated using the progressive matrices tests by Raven [19]. All volunteers had normal or better than normal nonverbal intelligence test results (IQ >85; [median 101.2; range from 85 to 132]). All children showed normal results in a standardized German spelling paper-pencil test (IQ-S 99.2; range from 78 up to 103) [20] as well as in a normal reading test (IQ-R 107.1; range 82 to 120) [21]. Handedness was assessed by self-description of the subjects, by a relative motor proficiency of their right and left hands as well as by a hand dominance test [22]. Written informed consent was obtained from all parents. The study was approved by the local ethical review board.

STIMULATION PARADIGM

For stimulation we used a self-written PC-program which consisted of four different tasks. These four hierarchically structured contrasts (A-D) were chosen to isolate brain regions which are involved in different kinds of reading processes. In task A, – the baseline condition –, letter strings were presented. This task condition activate brain regions which are associated with perceptual visual processing. Since visual-perceptual processing is part of all other tasks,

task A can be subtracted from other word processing strategies. In task B, the volunteers had to read non-words without lexical content involving visual-perceptual plus phonological processing. Non-words conform to rules and can be read, but otherwise do not contain any meaning. In task C, frequent legal words had to be read silently. Direct lexical phonology is needed with this task including visual, addressed phonological, and semantic processing. In task D the volunteers had to perform a letter-transformation. They had to move the first letter of the presented word to the end and to add the suffix "ein" to this "new-word". This transformation requires visual, phonological, and semantic processing including working memory. Phonological awareness is needed at a distinctly more complex level than in task B.

Each task (A-D) was performed three times in a pseudorandomized order during the fMRI session. The stimulus material was presented with a Philips LC 2000 projector (Philips, Best, The Netherlands) on a rear screen placed in front of the scanner. The screen was visible for the volunteers by means of an angled mirror placed on top of the head coil. The volunteers were instructed to watch the screen carefully. All tasks had to be performed silently. There was no possibility to register the performance in the scanner, because subjects covertly generated responses in our study. The beginning of each new task condition was signaled to the volunteers. Each stimulus (letter string or word) appeared every 2000 ms and remained visible for 1800 ms. On the day before the fMRI measurement, a learning session of about 15min took place during which the volunteers were trained and the performance could be controlled.

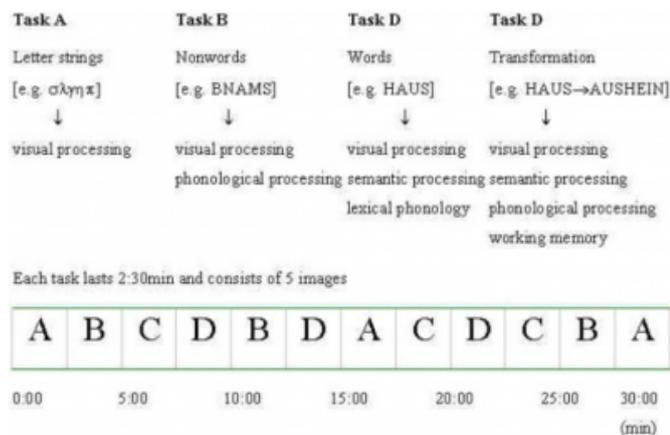
MRI MEASUREMENTS

Imaging was performed on a 1.5 T Gyroscan ACS II clinical MR-scanner (Philips, Best, The Netherlands) with a standard head coil. Ear plugs were used to reduce the noise level in the scanner. Head fixation was accomplished by a foam padding. Section selection was performed after acquisition of scout images with sagittal orientation by using a spin-echo sequence (FOV 230 mm, thickness 3 mm, gap 3 mm, 5 slices, TR/TE/ 300 ms/15 ms/90°). Since we were restricted to few slices for functional imaging, an orientation was selected fulfilling the following criteria: inclusion of regions presumably involved in reading processes, low susceptibility artifacts, reliability, and fast planning procedure. Careful planning of the slices guaranteed maximum reliability of the orientation and localization of imaging planes across subjects. The aim was to obtain images with the same

position and orientation in Talairach space. On the midline sagittal plane, the imaginary straight line between the anterior commissure (AC) and the posterior commissure (PC) was used to determine the orientation of the three slices used for functional MRI (Fig. 1).

Figure 1

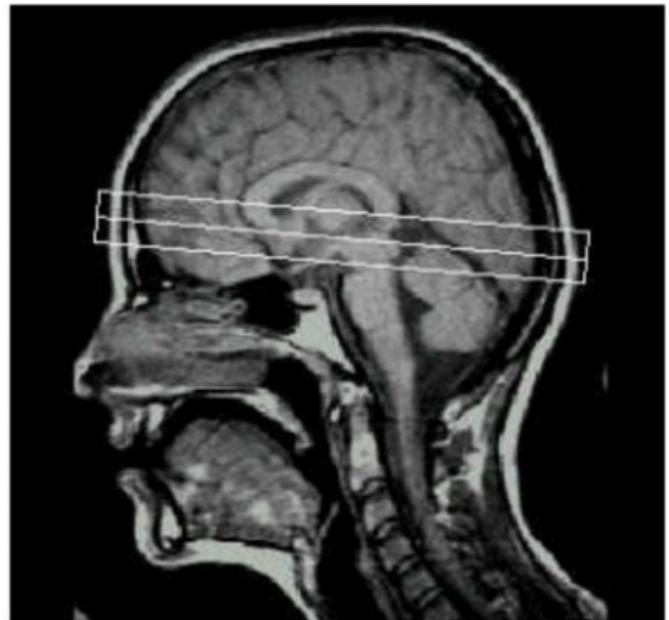
Figure 1: Paradigms used in the functional MRI study



The volume covered by the three slices ranged from z=-15 mm to z=+15 mm according to the coordinates from Talairach & Tournoux [23]. A T1-weighted sequence was sampled to acquire anatomical images with the same orientation (FOV 230 mm, thickness 10 mm, 3 slices, TR/TE/ 300 ms/15 ms/90°). To determine the location of major vessels, a time-of-flight MR angiogram was acquired covering the same volume. For functional imaging a T2*-weighted gradient-echo sequence was used with three consecutive slices (FOV 230 mm, matrix 128 x 128, NSA 2, section thickness 10 mm, 3 slices, TR/TE/ 68/50/10°). Each dynamic series consisted of 61 images. The first image (30 sec) was discarded to allow the MR signal intensity to reach steady state. Five images (30 sec for each image) were acquired per task resulting in 15 images per contrast during the whole fMRI-session.

Figure 2

Figure 2: Slice planning



Midline sagittal plane. The straight line between the anterior commissure (AC) and the posterior commissure (PC) was used to determine the orientation of the three slices used for functional MRI (slices ranged from z=-15 mm to z=+15 mm according to the coordinates from Talairach & Tournoux [23]).

DATA ANALYSIS

Postprocessing was done off-line on a Sun Sparc II workstation (SUN Microsystems, USA) including motion correction, spatial filtering, and normalization. Statistical analysis was performed using Statistical Parametric Mapping (SPM96b) implemented in MATLAB 4.2 (Mathworks Inc., Natick, MA, USA). SPM96b combines the general linear model and the theory of Gaussian fields [24].

Slight head motion during functional MR image acquisition can cause changes in T2*-weighted signal intensity unrelated to changes in BOLD contrast. To correct these effects prior to further analysis, the images were first realigned for each subject. Realignment was performed using a least square algorithm with the first scan of each slice as a reference. Motion was corrected using three parameters: translation x, translation y and rotation . Subjects whose images exhibited a translation of 2mm or a rotation of 2° were not included in the further analysis. The realigned images were transformed by SPM96b into a standard space [23] using 2D affine transformation. Then, the realigned and transformed images were smoothed with a

Gaussian isotropic kernel with full width at half maximum (FWHM) = 4mm for single-subject analysis and with a FWHM = 6mm for group analysis to accommodate variability in gyral anatomy and error of voxel displacement during normalisation. Statistical group analysis was performed with the SPM random effects toolkit. The design matrix was specified, including global activity as a confounding covariate. For analysis a simple subtractive design for each task contrast (task B vs. task A, C vs. A, D vs. A; C vs. B; D vs. B; D vs. C) was used. The images of each task condition for each volunteer were averaged into a single image. These averaged images were computed as the mean of the smoothed images and were used for the multisubject analysis with SPM. For each activated cluster, a p-value reflects the specific cluster-level inference based on the number of voxels comprising the cluster. The resulting SPM {Z} maps were thresholded at p=0.05 for height and corrected p=0.05 for the spatial extent. The SPM {Z} maps were then overlaid on the corresponding averaged anatomical images using a color scale. Activated voxels were color-coded and superimposed on the grey scale template.

RESULTS

None of the subjects had to be excluded from the analysis due to extensive head movements. After the functional MRI session all subjects were interviewed. None of them reported any difficulties in performing the reading tasks and the transformation task. The stereotactic coordinates of significant local voxel maxima and the results of the SPM analysis with corrected p-values of the contrasts non-word reading vs. perception of letter strings (B vs. A), word-reading vs. letter strings (C vs. A), and transformation task vs. letter strings (D vs. A) are given in Table 1.

Figure 3

Table 1: Local voxel maxima with corrected p-values (cluster-level)

Nonwords (task B) vs. letter strings (task A) -					
x	y	z	Z-score	p-corr	brain region
-47	13	10	3.97	0.004	IFG (BA 44) left
-23	5	10	3.46	0.004	Putamen left
29	-47	10	3.35	0.535	IT (BA 22) right
32	-77	0	2.72	0.805	OT (BA 18/19) right
36	9	10	3.21	0.188	IFG (BA 44) right

Words (task C) vs. letter strings (task A) -					
x	y	z	Z-score	p-corr	brain region
25	-43	10	2.92	0.696	IT (BA 22) left

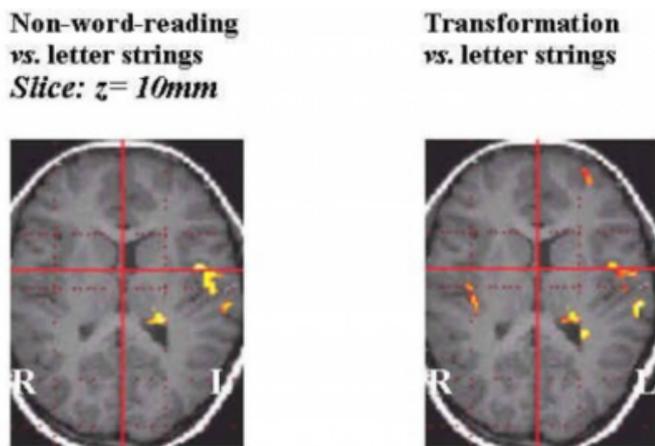
Transformation task (task D) vs. letter strings (task A) -					
x	y	z	Z-score	p-corr	brain region
-47	13	10	5.10	0.000	IFG (BA 44/45) left
-20	2	10	4.43	0.000	Putamen left
-34	-59	0	3.36	0.529	IT (BA 19/37) left
34	13	10	4.48	0.026	IFG (BA 44/45) right
31	-84	0	5.36	0.004	OT (BA 18/19) right
2	-81	10	3.40	0.497	BA 17 right

IFG = inferior frontal gyrus; IT = inferior temporal (hippocampus area); OT = occipitotemporal; BA = Brodmann area

x, y, z = Talairach coordinates (x coordinates are positive in the right hemisphere and negative in the left hemisphere)
 p-corr = corrected p-values with significance (p<0.05) were marked

With reference to the standardized space of Talairach and Tournoux x-, y-, and z-coordinates are listed (z corresponds to an average of a 10mm slice). Because individual activation maps for the single volunteers showed a relatively high variability, only the resulting Z-score maps for the group analysis are reported. Figure 3 shows an individual activation map and figure 4 the results of the group analysis (uncorrected Z-scores). The group analysis demonstrated significant activation with corrected p-values <0.05 for the phonologically relevant contrasts (task B vs. A and task D vs. A), particularly in the inferior frontal gyrus. For the non-word reading paradigm (contrast task B vs. task A) strong activation was observed in the left inferior frontal region (including Brodmann area 44) and in the left putamen. For the transformation task (contrast task D vs. task A) we obtained significant activations in the inferior frontal gyrus in both hemispheres (BA 44/45), in the left putamen, and in the right extrastriate, occipitotemporal region (BA 18/19). There were no significant results with corrected p-values in the contrast word reading vs. perception of letter strings (C vs. A) and in the other possible contrasts.

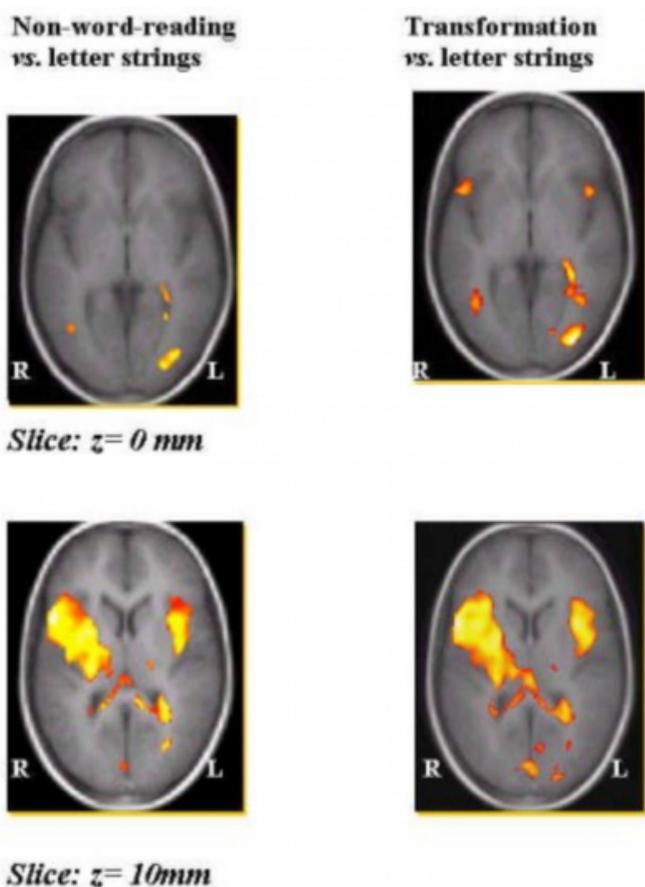
Figure 4



SPM {Z} maps were overlaid on the corresponding anatomical images using a color scale. Activated voxels (uncorrected p-values) were color-coded and superimposed on the grey scale template.

Figure 5

Figure 4: SPM Z-scores – Group analysis



SPM {Z} maps were overlaid on the corresponding averaged anatomical images using a color scale. Activated voxels (uncorrected p-values) were color-coded and superimposed

on the grey scale template.

DISCUSSION

In the past, serial models of the neural organization of reading have been suggested based on studies of the development of reading skills and their failure following cerebral injury [25]. A number of biologically based reading models resulting from studies of patients with acquired dyslexia demonstrated that reading involves three major elements: an orthographic processing system for information analysis concerning letter identification, a phonological system that encodes the phonemic constituents of a text, and a semantic or lexical system that extracts word meaning. In the dual-route model a direct route (semantic/lexical representation) and an indirect phonological route (phonological route) are integrated in the identification process of words [26]. The circuitry of beginning readers may be quite different from those of experienced readers. Beginning readers, like dyslexics, rely stronger on the indirect route while speaking out new words. In adolescents and adults the reading processing mechanisms are more developed [18]. These mechanisms use direct access to stored knowledge of words on the basis of letter configurations (lexical usage or addressed phonology). Unknown words require a sublexical analysis comprising conscious grapheme-phoneme transformations (segmented or assembled phonology) [27]. Functional neuroimaging studies postulated that oral word pronunciation engages a superior temporal/inferior parietal route [4, 9, 28]. Silent reading is less likely to utilize these temporoparietal areas and may more strongly utilize inferior temporal/extrastriate visual and inferior frontal cortical areas [25].

The present study examined cerebral responses to alternating periods of a control task (letter strings) and a hierarchically structured reading paradigm consisting of non-word reading, word reading and a letter transformation task. The observed activation maps during the hierarchically structured task conditions reflect the way of the phonological dual route processing. The addressed phonology, attributed to word reading, is assumed to be located in the superior temporal gyrus [7]. Non-words or pseudowords are orthographically word-like and require also straightforward computation of corresponding phonological representation. Unlike real words, they have no semantic representation. Phonological segmentation of words (assembled phonology) seems to happen in the beginning of the reading process as well as in the reading of non-words where no categorisation of words could be recognized. The cerebral areas of assembled

phonology were attributed to inferior frontal regions [7]. In a task that isolated assembled phonological processing both inferior frontal gyrus and temporal lobe activation was observed in a functional MRI [12].

Based on these studies we expected, that the non-word (task B) and the transformation task (task D) would produce spatially different activation than the word reading task. We observed no significant activation in the contrast word reading (task C) vs. letter strings (task A) in more temporal areas suggesting that these areas are involved in addressed phonology. Strong activation within the inferior frontal (in particular Broca's area) and extrastriate areas were detected in the contrast non-word reading (task B) vs. letter strings (task A) and transformation task (task D) vs. letter strings (task A). This supports the hypothesis that assembled phonology involves these brain regions. The activation in the frontal lobe was asymmetrically distributed in our study with a prevalence for the left hemisphere. Hemispheric differences have been observed in former functional MRI and PET studies of phonological processing [7, 29]. The transformation task (task D) produced significant activation in brain regions including the inferior frontal gyrus (areas 44 and 45), or Broca's area, a region known to be involved in language production. This is consistent with previous functional neuroimaging studies of verbal working memory tasks [30, 31, 32]. Broca's area is activated during rhyming tasks, if verbal stimuli are presented aurally [33] or visually [27] and if no overt speech is required reflecting inner speech [18].

In addition, the present study revealed activation in several other regions that have been shown to be involved in the performance of executive and memory tasks. We detected significant activation in the putamen in the contrast non-word reading (task B) vs. letter strings (task A) and letter transformation (task D) vs. letter strings (task A). This result supports the hypothesis that areas of the basal ganglia are involved in cortical networks for reading and language. In addition to its functional significance for learned motor behavior, the putamen appears to be involved in processes of implicit learning and the retrieval of implicit knowledge [34].

One of the limitations of the presented study is the single slice technique. Although three slices were acquired, a total thickness of only 30 mm was covered. Consequently, information about activation outside the covered volume was not available. Another limitation may be due to the fact that verbal responses were excluded. Overt responding, however,

may produce head movement artifacts and susceptibility-induced magnetic field homogeneity variations that increase the probability of errors in detecting activated regions [35].

In conclusion, different brain regions associated with reading processing could be shown to be activated in our functional MRI study. Thus, functional MRI may be a potential tool for the investigation of complex neurological function also in children. Using the structured design of the paradigms in our study we observed activation in different brain areas compared to a simple reading paradigm (word reading). Our findings suggest that the cortical systems that are associated with different types of orthographic and phonological coding in printed word identification are located in different brain regions [12]. A disconnection of these network structures may be responsible for the deficit in dyslexics in performing assembled phonology procedures. Keeping this in mind we anticipate that functional MRI should be able to differentiate between dyslexic and normal reading children using a structured reading test similar to the one used in the present study.

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