LENGTH EFFECT DURING WORD AND PSEUDO-WORD READING.

AN EVENT-RELATED FMRI STUDY

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SUMMARY

This event-related fMRI study has assessed the cerebral activations obtained during the reading of words and of pseudo-words of varying length (one, two and three syllables). Eight right-handed volunteers were examined. A pseudo-randomized fMRI paradigm with six types of stimuli was applied and the SPM'99 software was used for data processing. The number of cerebral regions involved in reading increased with the stimulus length, both for words and for pseudo-words. This concerned not only regions related to sensory-motor aspects of reading but also regions related to more "central" language processes. Independently of the length, the reading of words and of pseudo-words activated the same regions, an observation consistent with the connectionist models for reading. Considering the length of the stimuli, we obtained significant differences, in terms of cerebral regions, only between polysyllabic words and pseudo-words, not between monosyllabic words and pseudo-words. These results are in line with the connectionist view of reading, especially with the multi-trace connectionist model of Ans et al (3).

INTRODUCTION

Understanding cerebral correlates related to reading means knowing how the orthographic form of visual linguistic stimuli is translated into the phonological form. Several theoretical models were developed and tried to respond at this question. The classical cognitive "dual-route" model for reading postulates the existence of two completely isolated routes that work in *parallel* and rely on radically different computational principles: one "lexical-semantic" used for the processing of words and another "phonological" used mainly for the analytic processing of pseudo-words (grapheme-phoneme correspondence rules). According to the dual-route model, two different networks of cerebral regions will be expected to be activated, one for words and another one for pseudo-words,

independently on the item length. These differences are explained in terms of sublexical phonological processing required by pseudo-word reading with respect to word (even for monosyllabic stimuli).

Several connectionist models for reading were subsequently developed and they all proposed a unitary theory for reading (1-3). These models postulate that all orthographic items are read in the same way, that is the pronunciation is always computed from knowledge about previously experienced exemplars (familiarity). Among the connectionist approaches, the model developed by Ans et al (3) (thereafter ACV98), is the only one that can simulate reading of multi-syllabic items, the others being restricted to a monosyllabic processing. It postulates the existence of two *successive* reading procedures. According to it, any orthographical object (word or pseudo-word) is first submitted to a global processing which aims to find a "lexical familiarity" computed from previously experienced words. If it is found, the corresponding phonological form of the stimulus is activated and reading is performed. If it is not found, a subsequent analytical processing is performed within the input stimulus using the same route, in order to extract familiar orthographic components (typically, syllables) as well as their corresponding phonological forms. These syllabic phonological forms are successively and temporarily maintained into a phonological buffer, before being assembled into a whole phonological form. This model predicts that words and a number of monosyllabic pseudo-words are read by using the global procedure, while the multi-syllabic pseudo-words are read by using the analytical procedure. The simulations done with the ACV98 model have shown that monosyllabic pseudo-words also required a short analytical processing but the differences between monosyllabic words and monosyllabic pseudo-words have not been detected in behavioral experiments, in terms of time responses. This can be explained by the weak analytical procedure required by monosyllabic pseudo-words (only one syllable to be re-analyzed after the prior unsuccessfully global analysis) with respect to multi-syllabic pseudo-words. It is possible that by using fMRI, such a weak additional analytical procedure required for reading monosyllabic pseudo-words, can't be detected, which means that, in terms of global and sequential analysis, differences between words and pseudo-words should appear only during reading of multi-syllabic items.

The aim of the present fMRI study is to assess the cerebral substrate involved during reading of monosyllabic and multi-syllabic words and pseudo-words. If differences between words and pseudo-words reading are observed, independently on the item length, the dual-route model could be involved (two distinct networks whatever the item length). If differences are obtained only for multi-syllabic items, the results could be rather interpreted in accordance with the connectionist ACV98 model (global *vs* analytical procedure).

In accordance with the ACV98 model and in terms of anatomical substrate, the following aspects should be obtained during reading of words and of pseudo-words: (1) monosyllabic words and pseudo-words should commonly activate cerebral regions, either those related to more "central" language processing, such as orthography (left lingual gyrus) lexical access (temporo-occipital regions) phonology (left supramarginal gyrus), attention (cingulate gyrus, precuneus), or those in relation with sensory-motor aspects of reading such as visual analysis (visual associative areas) and articulation (motor and premotor cortex). (2) polysyllabic pseudo-words reading should induce more activation in regions responsible of visuo-orthographic analysis, lexical access, spatial attention. Furthermore, additional processes such as the phonological buffer within the framework of verbal working memory, could be involved.

ER-fMRI presents advantages such as the possibility to mix several types of stimuli and to use more flexible paradigms than the classical fMRI method uses. This technique is based on the measure of the haemodynamic response to each stimulus. If the neural activity is a very fast process, the haemodynamic response associated to it is very slow (average 15 s). Related to this aspect, it has been shown that two different ER-fMRI paradigm types could be used. The historically older (called deterministic) uses a constant inter-trial (inter-stimulus) interval (ITI), typically 15-20 sec, in order to prevent signal overlap from successive haemodynamic responses (4). However, under the hypothesis of a linear time-invariant (LTI) system, it has been shown that considerable gain in signal variance and thus in signal-to-noise ratio may be obtained by applying a second type of ER-fMRI paradigm that uses monosyllabic mean-ITI (m-ITI) called stochastic ER designs (5). In the optimization process, the distribution of the ITIs should be designed in such a manner that the haemodynamic response function (HRF) may be measured accurately, despite signal overlap from successive responses (6, 7).

MATERIALS AND METHODS

Subjects. Eight healthy volunteers, six males and two females, were examined. All were right-handed as assessed by the Edinburgh inventory (8) and they gave their informed consent. The study was approved by the local ethic committee.

Stimuli and paradigm. A pseudo-randomized ER-fMRI paradigm with six types of stimuli (words composed of 1, 2 and 3 syllables and pseudo-words composed of 1, 2 and 3 syllables), was used. Overall, 144 mid-frequency words and pseudo-words composed of one (3-5 letters), two (6-8 letters) and three (9-11 letters) syllables were presented during a single fMRI session. The words were mid-frequency regular words while the pseudo-words have been obtained by manipulating words. In addition to words and pseudo-words, 34 null-events (ten of them at the end of the session) composed of a blank screen and a fixation cross on the center of the screen were also included. A fixation cross was presented between stimuli on the center of the screen. The presentation time of each stimulus was

200 ms and the average interval between the stimuli of the same type was 14 seconds. The order of presentation of the stimuli has been optimized (6, 7). We therefore generated 10000 pseudo-random occurrences of the seven events. In order to get the same number of events of each type (i.e. 24), we randomly permuted the integers between 1 and 168. The series were divided in seven blocks of 24 numbers, each of them representing the occurrences of the different types of stimuli. As recommended by Friston et al (7) we choose an equal occurrence probability (.143) for each of the six events and the null event. The efficiency of each design was assessed with the following criterion (7): efficiency trace $(c^T (X^T*X)^{-1}*c)^{-1}$ where c is the vector of contrasts and X is the design matrix obtained by convolving a canonical haemodynamic response function (implemented in SPM99) with a series of delta functions representing the stimuli occurrences. In the procedure, we privileged optimization of the efficiencies related to the three contrasts between the words and the pseudo-words events respectively of one (W1-PW1), two (W2-PW2) and three syllables (W3-PW3). The subjects had to read each item, without articulating and vocalizing. The stimuli were generated by means of Psyscope V.1.1 (Carnegie Mellon Department of Psychology) on a Macintosh computer (Power Macintosh 9600). They were transmitted into the magnet by means of a video projector (Eiki LC 6000), a projection screen situated behind the magnet and a mirror centered above the patient's eyes.

MR acquisition. Functional MR imaging was performed on a 1.5 Tesla MR imager (Philips NT) with echo-planar (EPI) acquisition. Twenty-three adjacent, axial slices (thickness 5 mm each) were imaged. The imaging volume was oriented parallel to the bicommissural plane. Positioning of the image planes was performed on scout images acquired in the sagittal plane. An EPI MR pulse sequence was used. The major MR acquisition parameters of the EPI sequence were: TR = 2000 ms, TE = 45 ms, flip angle = 90 , field-of-view = 256x256 mm2, imaging matrix = 64x64, reconstruction matrix = 128x128. Subsequent to the functional scan, a high resolution 3D anatomical MR scan was obtained from the volume previously examined.

Data processing. Data analysis was performed using SPM-99 software (Wellcome Department of Cognitive Neurology, London, UK) running on a Unix workstation under the MATLAB environment (Mathworks, Sherbon, USA).

MR images were subjected to the following pre-processing steps. For each subject, in the first step, the fMRI scans were acquisition-corrected to correct for sampling bias effects caused by different slices being acquired at different times, relative to the haemodynamic response. In the second step, motion correction was applied. All images within a functional scan were realigned by means of a rigid body transformation. In a third step, the anatomical volume was spatially normalized into the Talairach and Tournoux reference space using as template a representative brain from the Montreal Neurological Institute series. The normalization parameters were subsequently applied to the functional images. Finally, to conform to the assumption underlying SPM that the data are normally distributed, the functional images were spatially smoothed.

Statistics: For all types of stimuli, regressors of interest were created by convolving a delta function at each event onset with a canonical haemodynamic response function, and its two partial derivatives. Contrasts between conditions were determined pixelwise using the General Linear Model. Clusters of activated pixels were then identified, based on the intensity of the individual responses and the spatial extent (k=10) of the clusters. Finally, a significance threshold of p=0.05 corrected for multiple comparisons, was considered for identification of the activated clusters. A fixed effect group analysis was performed. The contrasts evaluated were the following. First, we contrasted each type of stimulus *vs* fixation cross for obtaining the significant activated regions for each type of stimuli, with respect to baseline. Secondly, we have contrasted the previous calculated contrasts between them (for example the contrast between [mono-syllabic words *vs* fixation cross] *vs* [mono-syllabic pseudo-words *vs* fixation cross] allowed us to identify regions activated during mono-syllabic words reading and significantly more than during mono-syllabic pseudo-words reading).

RESULTS AND DISCUSSION

Figure 1 summarizes the results obtained in the present study. It represents the cerebral activations resulted from the group analysis, during the reading of monosyllabic (A), bi-syllabic (B) and three-syllabic (C) stimuli. The activations were projected onto 3D templates. As indicated in the caption of Figure 1, the activations induced by words are represented in red, those induced by pseudo-words in green and the overlapped activations, in yellow. The identification of the activated regions is represented by using indicative numbers. In the following section, we are describing the activated regions and the related processes.
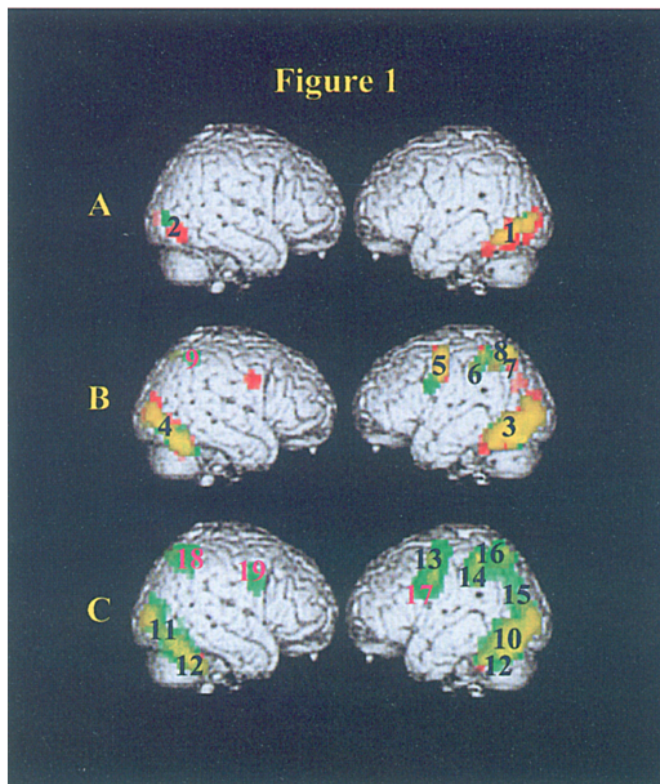

Figure 1 represents functional activations resulting from the group analysis (p= 0.05 corrected), during reading of monosyllabic (A), by-syllabic (B) and three-syllabic items (C). They are projected onto 3D templates (lateral views of the hemispheres). In all these images, the activations induced by words are represented in red, those induced by pseudo-words are represented in green and the common activation induced by both, words and pseudo-words, in yellow. The activated regions are indicated by using colored numbers (dark blue numbers indicate regions activated in common by words and by pseudo-words, while pink numbers indicate regions activated during reading pseudo-words with respect to words). The cerebral activated region corresponding to each number is specified in Table 1. The Talairach coordinates (x,y,z) refer to the strongest activated voxel of each cluster. The corresponding significance value (p) of each cluster is given.

Table 1

Figure 1A
1. Left inferior (-48, -77,-2) and middle (-50,-65,4) occipito-temporal regions (BA 18,19,37) p<0.001
2. Right middle (53,-78,5) occipital gyrus (BA 19)   p<0.001
Figure 1B
3. Left inferior (-35,-80,1) and middle (-52,-63,4) occipito-temporal regions (BA 18,19,37) p<0.001
4. Right middle (53,-76,4) occipital gyrus (BA 19)   p<0.001
5. Left premotor cortex (-60,-5,28) (BA 6)   p<0.001
6. Left supramarginal gyrus (-50,-35,32) (BA 40)   p<0.001
7. Left angular gyrus (-52,-63,35) (BA 39)   p<0.001
8. Left superior parietal lobule (-35, -61, 45) (BA 7)   p<0.001
*Bilateral cerebellum (left:-40,-60,-20; right: 35,-50,-20) not indicated on these images p<0.002
9. Right superior parietal lobule (37,-55,46) (BA 7)   p<0.001
Figure 1C
10. Left inferior (-35,-77,2) and middle (-50,-65,4) (occipito-temporal   regions (BA 18,19,37) p<0.002
11. Right middle (51,-72,3) occipital gyrus (BA 19)   p<0.001
12. Bilateral cerebellum (left:-40, -55, -20; right: 31, -47, -23)   p<0.002
13. Left premotor cortex (-59,-4,26) (BA 6)   p<0.001
14. Left supramarginal gyrus (-47,-35,32) (BA 40)   p<0.002
15. Left angular gyrus (-51,-60,33) (BA 39)   p<0.001
16. Left superior parietal lobule (-35,-60,43) (BA 7)   p<0.003
17. Broca's area (-53, 10, 28) (left BA 44)   p<0.002
18. Right superior parietal lobule (43, -63, 45) (BA 7)   p<0.003
19. Right premotor cortex (57,-6,28) (BA 6)   p<0.001

A. Cerebral regions activated during monosyllabic words and pseudo-words reading (Figure1A)

Reading monosyllabic words and pseudo-words activated a very limited number of cerebral regions. No statistical differences in activation were obtained between monosyllabic words and pseudo-words reading. The bilateral activation of the extrastriate cortex (BA 18, 19) and of the left lateral temporo-occipital junction (BA 37, 19) were related to visual analysis and lexical access. It is well accepted that left inferior occipito-temporal region is activated in relation with visual word and pseudo-word form analysis (9). Left BA 37 (fusiform gyrus) was also involved in retrieval phonology (10). Thus, the bilateral but left predominant activation of the posterior temporo-occipital region depicted during monosyllabic words and pseudo-words reading, is explained in terms of visual analysis and lexical orthographic and phonological access. These results suggest that not only

monosyllabic words but also monosyllabic pseudo-words address phonology directly via left posterior temporo-occipital lobe, without implication of the phonological graphemes-phonemes analysis. This observation is not in line with the dual-route model predicting a sublexical phonological analysis required by pseudo-words, but rather close to connectionist view that suggests that words and pseudo-words are processed by a unique way (2, 11). We should underline that the small number of activated regions during monosyllabic items reading could be related to the weakness of the activation induced by short length stimuli, activation maybe not detected at the used threshold. The event-related design of the present study offers the advantage of allowing randomization of conditions, but it is less sensitive in detecting activation when compared to blocked designs.

B. Cerebral regions activated during bi-syllabic words and pseudo-words reading (Figure 1B).

With respect to monosyllabic items, bi-syllabic words and pseudo-words activated more numerous regions, meaning that supplementary cerebral processes are necessary for reading multi-syllabic stimuli. The bilateral occipito-temporal regions (especially the fusiform gyrus), commonly activated during bi-syllabic words and pseudo-words and related to visual analysis and lexical access were more intensively activated during bi-syllabic, as during monosyllabic items reading. Mechelli et al (12) used positron emission tomography in order to investigate how fusiform and lingual gyrus are modulated by word length (three, six and nine letters) and perceptive similarity to the background (high and low contrast). The authors have shown that the increasing of both, word length and visual contrast had a positive monotonic effect on activation in the bilateral fusiform gyrus, increasing the demands on visual analysis. The motor preparation of articulatory codes was suggested by the activation of the premotor cortex (13) activated during reading of both types of stimuli. The left supramarginal gyrus (BA 40) was activated for both, bi-syllabic words and pseudo-words. The activation of this region was classically attributed to the sublexical phonology necessary for reading multi-syllabic low-frequency words or unfamiliar items, such as pseudo-words. In accordance to the connectionist ACV98 model, the activation of the left supramarginal gyrus could be interpreted as temporarily maintaining the phonological form of syllables composing the orthographic items. The bilateral cerebellum has also been activated for bi-syllabic stimuli. Cerebellum has traditionally been associated with motor performance (14). Recently, there has been considerable interest regarding the contributions of this subcortical structure to aspects of cognition. In particular, both the basal ganglia and cerebellum have been hypothesized to be involved in the control of attention (15). Thus, the activation of cerebellum may serve as a modulator of the attentional processes. Furthermore, the right

cerebellum was associated to the output of phonological processes (16). The left precuneus and the left angular gyrus were activated for both, words and pseudo-words. Fletcher et al (17) have suggested that memory-related imagery was associated with significant activation of the precuneus, especially to the left. The precuneus was also related to semantics processing. The activation of the left angular gyrus (BA 39) was usually related to semantics (18). Other studies have shown that semantics is activated not only by words but by pseudo-words too. Price et al (19) have interpreted this observation as the evidence that the activation is directly proportional with the unlikely to find representations, that being the case for pseudo-words. This explanation is close to the connectionist view of reading rather to a hierarchical model as dual-route. The right superior parietal lobule was activated only by pseudo-words. Among its different roles, the superior parietal lobule is involved in spatial attention (20, 21). Its activation only during pseudo-words reading is explained by the increase of spatial attention demand within the framework of the sequential analysis of pseudo-words, as the connectionist model for multi-syllabic reading (3) suggests.

Overall, reading bi-syllabic words and pseudo-words activated common cerebral regions related to visuo-orthographic processing, lexical access, phonology, semantics, motor articulation and attention. Additionally, reading bi-syllabic pseudo-words activates the right superior parietal lobule, suggesting more spatial attention toward stimulus processing. In general, the extent of the activation within common activated regions was similar for words and for pseudo-words: the predominant color representing activations induced by bi-syllabic items on Figure 1B is yellow, that means a good overlapping between activations induced by words (represented in red) and pseudo-words (represented in green). With respect to monosyllabic stimuli reading, bi-syllabic stimuli activated more extensively visuo-orthographic, lexical access regions, phonology, semantics, premotor function and attention.

C. Cerebral regions activated during three-syllabic words and pseudo-words reading (Figure 1C).

Three-syllabic words and pseudo-words activated a certain number of common cerebral regions, such those involved in visuo-orthographic analysis, lexical access, phonological processing, programming of articulation and attention, largely discussed earlier. Furthermore, these common regions were more extensively activated by pseudo-words than by words (on Figure 1C, the green color is dominant on functional maps obtained during reading of three-syllabic stimuli). With respect to bi-syllabic items, three-syllabic stimuli induced more activation. This is particularly true for

regions classically implicated in phonological analysis (left supramarginal gyrus), articulatory processes (premotor cortex, cerebellum), semantics (angular gyrus). Broca's area (left BA 44) was activated only during three-syllabic pseudo-words reading. It could be related to the articulatory loop (keeping "on line" of the phonological form of syllables before being assembled into the output phonology). In the same context it is explained the increase of the activation of the left supramarginal gyrus during reading of three-syllabic pseudo-words with respect to three-syllabic words. It has been shown that Broca's area and supramarginal gyrus are particularly involved when a pseudo-word input is used (22-25). Furthermore, Fiez et al (26) suggested that Broca's area could have a role in grapheme-phoneme transformation. In this context, it is involved in reading especially when pseudo-words or low-frequency irregular words are used as visual input. Our results are in line with these findings because only the pseudo-words activated Broca's area and not the words. Three-syllabic pseudo-words additionally activated a more important part of the right cerebellum. Only three-syllabic pseudo-words and not three-syllabic words, activated the right superior parietal lobule, suggesting the high spatial attention level during reading multi-syllabic pseudo-words.

The results obtained in this study allow making some main observations. The number of cerebral regions involved in reading increases with stimulus length, for both words and pseudo-words. This observation concerns regions related to sensory-motor aspects of reading (visual analysis, articulatory processes) and regions related to more "central" processes of language (orthography, lexical or sublexical phonology, lexical access, semantics). Overall, reading words and pseudo-words activates a common network of cerebral regions, as the connectionist models postulate, and not two distinct networks, as dual-route model predicts. There were no differences between monosyllabic word and pseudo-word reading. Bi- and three-syllabic pseudo-words induced, with respect to bi- and three-syllabic words more extensively activation of regions activated in common and the activation of additionally regions (Broca's area and right superior parietal lobule). These additional regions suggest the involvement of the articulatory loop (Broca's area) and the increase of the spatial attention (right superior parietal lobule). The differences obtained between multi-syllabic words and pseudo-words and not between monosyllabic words and pseudo-words are well predicted by the connectionist ACV98 model. Our results suggest that reading is better explained by the connectionist view of reading, especially by the ACV98 connectionist model. In accordance with this model, the global analysis required for reading words and monosyllabic pseudo-words is demonstrated by the activation of common cerebral regions, while the subsequent analytical process required for reading multi-syllabic pseudo-words is suggests by more extensively activation of common activated regions and

the additional involvement of regions responsible for the phonological loop and the spatial attention, key aspects of the analytical procedure predicted by this model. The evaluation of reading by using orthographic stimuli varying in length, could allow a better understanding of cerebral correlates of reading function which could be explained either close to the dual-route model or close to the connectionist view. These models of reading are not exclusive and fMRI provides information permitting only to situate reading *close to* one or to another model and not to exclusively "validate" one model and exclude another one.

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