BRAIN REPRESENTATION OF PHONOLOGICAL PROCESSING IN ITALIAN: INDIVIDUAL VARIABILITY AND BEHAVIOURAL CORRELATES

C. PECINI1, L. BIAGI1, A. GUZZETTA1, D. MONTANARO2, D. BRIZZOLARA1,3, P. CIPRIANI1,3, A. CHILOSI1, M. TOSETTI1, G. CIONI1,3

1Department of Developmental Neuroscience, Stella Maris Scientific Institute, viale del Tirreno 331, 56018, Calambrone, Pisa, Italy, 2Institute of Clinical Physiology CNR-CREAS, Via Moruzzi 1, 56124 Pisa, Italy, 3Division of Child Neurology and Psychiatry, University of Pisa, via dei Giacinti 2, 56018, Calambrone, Pisa, Italy

ABSTRACT

Neuroimaging literature on phonological processing during reading lacks of studies taking into account orthographic differences across languages and behavioural variability across subjects. The present study aimed at investigating brain representation of phonological processing in reading Italian, a language with regular orthography, with particular regard to inter-individual variability and brain-behavioural correlates. Ten Italian adults performed a rhyme generation and a rhyme judgment task during fMRI acquisition and were tested with behavioural measures of phonological processing. Results for both tasks showed activations of the left inferior frontal gyrus and dorsolateral prefrontal cortex, likely underlying output sublexical strategies, for all or most of the subjects, while a minority of subjects activated the superior temporal sulcus and the temporo-parietal-occipital Junction. These results suggest that phonological processing of written Italian is based on the prevalent use of frontal structures. However, it is of interest that the activation of the Superior Temporal Sulcus, involved in phonological input, was associated to better behavioural performances in tasks of phonological processing. Our findings may contribute to understand neural correlates of phonological processing of languages with regular orthography.

INTRODUCTION

Phonological processing, that is the ability to represent and manipulate phonemes, is a fundamental component of written language. It requires multiple skills such as decoding phonological inputs, rehearsing the information in working memory and accessing phonological representation of the word (41). Common phonological mechanisms, consisting in the process of mapping orthography to phonology by assembling sublexical phonological codes (e.g. graphemes and phonemes), have been proposed for reading words and pseudowords (pronounceable non-words) (33, 39, 44). However, behavioural and neuroimaging
studies have also shown significant differences pointing to word reading as a more automatic and less demanding process, relative to pseudowords (23, 42, 46). This difference is thought to be related to the higher level of orthographic familiarity of words either leading to a more prompt grapheme-phoneme matching (33, 38, 43) or to a direct map onto lexical phonology, as words and not pseudowords have lexical representations in the language system (2, 18, 39, 40).

Cultural differences in the reading process have been interpreted within this theoretical framework (47). Learning to read in languages with deep orthography (e.g., English and French) is usually more difficult than in those with transparent orthography (e.g. Italian), where the mapping between letters, speech sounds, and whole-word sounds is highly consistent (9, 14) and a higher reading speed is usually found (15). It is conceivable that the specific characteristics of language orthographies may naturally drive the development of different reading strategies, with sublexical processes (based on grapheme-phoneme conversion) predominating in languages with transparent orthography, and semantic/lexical procedures predominating in those with deep orthography (32). This is also confirmed by functional neuroimaging studies. In tasks of reading languages with deep orthography, such as English or French, a stronger participation of structures known to be related to lexical-orthographic representations (left temporo-parieto-occipital junction), has been demonstrated. In contrast, a higher activation of regions involved in sublexical decoding (left superior temporal gyrus) has been found in readers of languages with transparent orthography (10, 11, 32).

The effect of cultural diversity found by behavioural and neuroimaging studies of normal reading is also reflected on the incidence and behavioural features of reading disorders across different countries, with a significantly lower incidence and the prevalence of reading speed deficits in dyslexics of languages with transparent orthography (3, 20).

Data on reading disorders support the hypothesis that transparent languages may allow a more flexible use of different reading strategies, leading to a wide variability in brain representation of phonological processing. Moreover, a potentially ineffective function of the phonological network is in principle not always associated to a corresponding apparent impairment. Most of neuroimaging studies however have been performed in English readers (5, 7, 27, 28, 45, 46), and no study in transparent languages has specifically assessed brain representation of phonological processing (16, 21, 32) or correlation between brain activation of phonological tasks and behavioural performance. We explored phonological processing in Italian subjects with the aim of contributing to answer the following questions: (i) What is the degree of inter-individual variability in the patterns of brain representation of phonological processing in Italian? (ii) Is there a correlation between pattern of activation and performance on behavioural tests?

For these goals two tasks tapping phonological processing of written stimuli were used. One task, recently applied to clinical populations (8, 19), requires silent generation of words rhyming with the stimulus and requires and actively involves several task involving several cognitive components such as phonological decoding, lexical access and phonological planning. The other task, requiring rhyme judgment on pseudowords, is a more passive task, used to stress mainly mechanisms of phonological sublexical decoding (24, 46).
METHODS

Ten young healthy volunteers (6 females and 4 males), aged between 22 and 36 years (mean age: 27.1) participated in the study. They all had Italian as first language and an education level higher than the secondary degree (their education ranged from 15 to 19 years). Before scanning, subjects were selected by a structured interview on motor and linguistic milestones, literacy acquisition and academic achievement in order to exclude neuromotor, psychiatric and learning disabilities.

According to the Edinburgh Handedness Inventory Laterality Quotients (30) all volunteers were right-handed (score > 0.85).

The research project was approved by the Ethical Committee of the Stella Maris Institute. Written consent was obtained from all participants.

1. - Behavioural tests.

The following three behavioural tests for the assessment of phonological processing were administered to all subjects.

Rhyme generation test.

Participants were instructed to read a two-syllable word, displayed on a computer screen, and find a new word rhyming with it. A total of 30 stimuli were presented at a frequency of one word every 5 seconds. The number of correct responses (from 0 to 30) was recorded. Word structure was regular for Italian (CVCCV or CVCCV). All stimuli were highly frequent words (Lexical Rank > 400) according to an Italian database (25). The neighbourhood size was computed for each word according to the ColFis database (mean = 6.8; sd = 2.8) (4).

Rhyme judgment test.

Participants were instructed to read a pair of two-syllable pseudowords (with legal structure) serially presented on a computer screen and to judge if they rhymed with a yes or no response. All stimuli were legal pseudowords (CVCCV syllable structure.) Given the transparency of orthography, rhyme judgment in Italian can be performed on the basis of the visual word form (e.g. /dane/ and /fane/), an upper-lower case condition (DANE-fane) was used, to force phonological encoding. A total of 15 stimuli were presented at a frequency of one pair of sequential pseudowords every 6 seconds (inter-stimuli interval: 1 sec; inter-trials interval: 3 sec). The number of correct responses (from 0 to 15) was recorded.

Spoonerism test.

Participants were orally presented with 18 pairs of two-syllable words (tasca - pocket and vela - sail). For each pair they were instructed to mentally transpose the first consonant and produce the two resulting words (vasca - bath and tela - cloth). The number of correct responses (from 0 to 36) was recorded (adapted from Marotta (26)).

2. - fMRI.

Imaging methods.

An 1.5 T MR system (Signa Horizon LX, Healthcare GE, Milwaukee, USA), equipped with Echo-speed gradient coils and amplifier hardware was used. Images were acquired by a EPI gradient-recalled echo sequence (flip angle 90°, TE = 50 ms, TR = 3000 ms, matrix: 128 x 128, FOV = 28 cm x 28 cm, spatial resolution in-plane = 2.2 mm). Each volume consisted of 13-15 contiguous axial slices 5-6 mm thick. Time-course series of 64 images were collected for each run and each period of the block design (30 sec task and 30 sec rest) was repeated three times. The first epoch always lasted 4 extra acquisitions (12 sec) to allow the signal to stabilise and this initial period was eliminated from any successive analysis.

A volumetric set of anatomical high resolution 3D FSPGR images (124 axial images, 1.1 x 1.1 x 1.1 mm³ voxels) was acquired at the end of the session in order to generate a 3-dimensional whole brain reconstruction and to estimate the anatomical localisation of activated regions.

The stimulus consisted of repeated cycles of “on” and “off” periods (30 sec in duration for each one) of the single task (block-design). Stimuli were generated as AVI movies in MATLAB and displayed through liquid crystal goggles (VisualStim XGA – Resonance Technology at a resolution of
800 x 600 voxels, subtending 30° x 22.5° at an apparent distance of 1.5 m, with mean luminance 30 cd/m². Luminance, colour, shapes (Arial font) and size (font 96) were carefully balanced both in task and rest conditions.

**Activation tasks.**

Two rhyme tasks analogous to the ones used in the behavioural test were applied in all subjects, using a new set of words and pseudowords equivalent, for syllable structure (CVCV or CVCCV), lexical frequency (> 400) and neighbourhood size (mean = 8.3; sd = 2.5), to those used in the behavioural measures. A short training session was performed before entering the magnet.

**Rhyme generation:** participants were instructed to read a two-syllable word and silently find a new word rhyming with it. Stimuli were presented at 0.2 Hz (1/5 sec), 6 words for block, for a total of 18 words. During the rest condition, participants were instructed to passively watch a string of capital x letters (XXXX) presented at the same time frequency of the stimuli.

**Rhyme judgment:** participants were instructed to read a pair of two-syllable pseudowords (with legal structure) serially presented and to judge if they rhymed. As in behavioural task, stimuli were written in upper-lower case (e.g. DANE - fane). A total of 30 stimuli were presented, 5 pairs for block for a total of 15 pairs (inter-stimuli interval: 1 sec; inter-trials interval: 3 sec). During the rest condition participants had to judge whether two sequences of Cyrillic characters matched (e.g. дджж - жждд). Cyrillic characters were chosen because of their low similarity to Italian alphabetic characters and were presented in strings of 4 elements. In order to prevent artefacts the judgment was silent and did not require motor actions.

Extreme care was taken to balance luminance, colour, shapes and size in the task and rest conditions.

**Imaging processing and data analysis.**

Data were analysed with Brain Voyager QX (Brain Innovation, Maastricht, the Netherlands). All volumes from each subject were realigned with the application of rigid body transformations for residual motion-related signal changes. Functional data were spatially (Gaussian kernel with a 4-mm full width at half maximum) and temporally smoothed (Gaussian kernel with a 2.8 sec full width at half maximum). Two types of analyses were performed, a group analysis and a single subject analysis.

**Group analysis:** To obtain activation maps across subjects, fMRI data of each subject were normalised to the Talairach’s target and combined in a General Linear Model analysis which is a less conservative and more sensitive approach to identify activated brain areas after different tasks (13). The maps were generated by the contrast of each activation task with the corresponding baseline condition.

A corrected threshold of p < 0.05 was applied at the voxel level (Bonferroni). A functional laterality index (λ) was also calculated on the basis of the extension in mm³ of the activation in the left and in the right hemispheres ((Left-Right)/(Left + Right)).

**Single subject analysis:** For each individual subject a statistical comparison between each voxel time course and the expected response waveform was performed. This was modelled in reference to a box-car waveform convoluted with a synthetic hemodynamic response function. Statistical activation maps were obtained using the General Linear Model analysis, thresholding at p < 0.005 (t > 3.6) and cluster size > 150 mm³. The same contrasts used in the Group analysis were obtained for each subject.

In order to express quantitatively the strength and reliability of the fMRI responses to different stimuli and in different subjects the Signal to Noise Ratio (SNR) was calculated as follows. For each region of activation the MR signal was extracted and separately analysed, calculating the percentage of signal change and using the Fourier Transform method. The signal was Fast-Fourier-Transformed (FFT) to yield the phase and amplitude of the harmonics in synchrony with the stimulus alternation. Then the amplitude of the fundamental component (respect to the stimulus design) was normalised to the mean signal over the full time-course to define the response amplitude. The SNR was calculated as the ratio of the fundamental component to the mean amplitude of all the other components asynchronous to the stimulus periodicity.
3. Correlation between fMRI and behavioural tests.

The correlations between performance at the behavioural tests and fMRI were explored with two different approaches. In a first analysis the behavioural performance was compared to the extension of the activation and the SNR of each one of the areas of the language network. In a second analysis the behavioural performance was compared to the fMRI results in terms of pattern of activation specifically considering the circuit usually involved in language processing. According to the existing literature (23, 24, 33, 35) three main regions of interest were considered in the left hemisphere: i) in frontal lobe, the left inferior frontal gyrus (IFG) and the left dorsolateral prefrontal cortex (DLPFC), ii) the left superior temporal sulcus (STS) and iii) the left temporo-occipito-parietal junction (TPJ/TOJ) (10, 17). Statistical correlations were obtained in both approaches by means of the Spearman correlation coefficient (SPSS version 12.0).

<table>
<thead>
<tr>
<th></th>
<th>Years of Education</th>
<th>Spoonerism</th>
<th>Rhyme Generation</th>
<th>Rhyme Judgment</th>
</tr>
</thead>
<tbody>
<tr>
<td>s1</td>
<td>17</td>
<td>31</td>
<td>28</td>
<td>15</td>
</tr>
<tr>
<td>s2</td>
<td>16</td>
<td>36</td>
<td>29</td>
<td>15</td>
</tr>
<tr>
<td>s3</td>
<td>19</td>
<td>36</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>s4</td>
<td>16</td>
<td>30</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>s5</td>
<td>18</td>
<td>36</td>
<td>31</td>
<td>15</td>
</tr>
<tr>
<td>s6</td>
<td>15</td>
<td>35</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>s7</td>
<td>18</td>
<td>34</td>
<td>25</td>
<td>15</td>
</tr>
<tr>
<td>s8</td>
<td>16</td>
<td>31</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>s9</td>
<td>18</td>
<td>33</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>s10</td>
<td>18</td>
<td>33</td>
<td>30</td>
<td>15</td>
</tr>
</tbody>
</table>

Fig. 1. Results of the group analysis. For each task, the statistical map of seven representative slices of a reference brain in Talairach’s space (at the top: the third coordinate) is reported. Images were obtained using a threshold of p < 0.05 corrected for the rhyme generation task and a less conservative threshold (p < 0.001 uncorrected) for the rhyme judgment task (*), as in the latter only the frontal activation was still present at more conservative thresholds (BA 44-45-6, extension 168 mm³, coordinates -53 ± 1.11 ± 1.22 ± 1).
Table 2. - Cortical regions identified by the group analysis (p corrected < 0.05) and used as region of interest in the single-subject analysis. They are listed from posterior to anterior and from caudal to rostral regions. For the Talairach’s coordinates, the averages and the standard deviations of the coordinates of the cluster are reported.

<table>
<thead>
<tr>
<th>Area name</th>
<th>BA</th>
<th>Rhyme Generation</th>
<th></th>
<th>Rhyme Judgment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Talairach</td>
<td>Cluster</td>
<td>Talairach</td>
<td>Cluster</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Coordinates</td>
<td>size</td>
<td>Coordinates</td>
<td>size</td>
</tr>
<tr>
<td></td>
<td></td>
<td>X</td>
<td>Y</td>
<td>Z</td>
<td>X</td>
</tr>
<tr>
<td>Superior Temporal Sulcus (STS)</td>
<td>21-22</td>
<td>LH</td>
<td>-52 ± 2</td>
<td>37 ± 1</td>
<td>-2 ± 2</td>
</tr>
<tr>
<td>Temporo-occipital Junction (TOJ)</td>
<td>19-37</td>
<td>LH</td>
<td>-45 ± 3</td>
<td>49 ± 5</td>
<td>17 ± 3</td>
</tr>
<tr>
<td>Temporo-Parietal Junction (TPJ)</td>
<td>39-40</td>
<td>LH</td>
<td>-43 ± 3</td>
<td>44 ± 3</td>
<td>37 ± 3</td>
</tr>
<tr>
<td>Supplementary Motor Area (SMA)</td>
<td>24-6</td>
<td>BH</td>
<td>-1 ± 4</td>
<td>12 ± 8</td>
<td>44 ± 6</td>
</tr>
<tr>
<td>Infraparietal Cortex (IPC)</td>
<td>7</td>
<td>LH</td>
<td>-27 ± 2</td>
<td>70 ± 3</td>
<td>42 ± 1</td>
</tr>
<tr>
<td>Primary Sensory Motor Cortex (M1S1)</td>
<td>1-2-3-4</td>
<td>LH</td>
<td>-24 ± 1</td>
<td>12 ± 1</td>
<td>47 ± 2</td>
</tr>
<tr>
<td>Dorsolateral Prefrontal Cortex (DLPFC)</td>
<td>8-9-6-46</td>
<td>LH</td>
<td>-44 ± 6</td>
<td>12 ± 6</td>
<td>28 ± 6</td>
</tr>
<tr>
<td>Inferior Frontal Gyrus (IFG)</td>
<td>44-45</td>
<td>LH</td>
<td>-41 ± 6</td>
<td>25 ± 6</td>
<td>10 ± 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RH</td>
<td>41 ± 3</td>
<td>20 ± 2</td>
<td>7 ± 5</td>
</tr>
<tr>
<td>Cerebellum</td>
<td></td>
<td>LH</td>
<td>7 ± 7</td>
<td>70 ± 2</td>
<td>22 ± 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RH</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BA = Broadman Area, LH = Left Hemisphere, RH = Right Hemisphere, BH = Both Hemispheres
Table 3.

a) Individual responses for each subject (s) obtained during the rhyme generation task: extension of activation (threshold p < 0.005; t > 3.6 and cluster size > 150 mm$^3$).

<table>
<thead>
<tr>
<th>s</th>
<th>STS</th>
<th>TOJ</th>
<th>TPJ</th>
<th>IPC</th>
<th>M1S1</th>
<th>DLPFC</th>
<th>IFG</th>
<th>STG</th>
<th>TOJ</th>
<th>TPJ</th>
<th>IPC</th>
<th>M1S1</th>
<th>DLPFC</th>
<th>IFG</th>
<th>SMA</th>
<th>Vis prim</th>
<th>Vis ass</th>
<th>R Cereb</th>
<th>L Cereb</th>
</tr>
</thead>
<tbody>
<tr>
<td>s1</td>
<td>3074</td>
<td>2494</td>
<td></td>
<td>725</td>
<td>1334</td>
<td>4814</td>
<td>203</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s2</td>
<td>348</td>
<td>290</td>
<td>1595</td>
<td>2059</td>
<td>2407</td>
<td>2465</td>
<td>406</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s3</td>
<td>377</td>
<td>377</td>
<td></td>
<td>1363</td>
<td>3567</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s4</td>
<td></td>
<td></td>
<td>174</td>
<td>609</td>
<td>1305</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s5</td>
<td>528</td>
<td>408</td>
<td></td>
<td>288</td>
<td>192</td>
<td>624</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s6</td>
<td>319</td>
<td>377</td>
<td>754</td>
<td>2204</td>
<td>2784</td>
<td>2755</td>
<td>174</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s7</td>
<td></td>
<td></td>
<td></td>
<td>986</td>
<td></td>
<td>435</td>
<td>174</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1189</td>
<td>232</td>
<td>203</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s9</td>
<td>840</td>
<td></td>
<td></td>
<td>1440</td>
<td>432</td>
<td>168</td>
<td>1824</td>
<td>1824</td>
<td>264</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s10</td>
<td>174</td>
<td></td>
<td></td>
<td>5394</td>
<td>1653</td>
<td>1827</td>
<td>6293</td>
<td>232</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
b) Individual responses for each subject obtained during the rhyme judgment task: extension of activation (threshold $p < 0.005$; $t > 3.6$ and cluster size $> 150 \text{ mm}^3$).

<table>
<thead>
<tr>
<th>s</th>
<th>STS</th>
<th>TOJ</th>
<th>TPJ</th>
<th>IPC</th>
<th>M1S1</th>
<th>DLPFC</th>
<th>IFG</th>
<th>STG</th>
<th>TOJ</th>
<th>TPJ</th>
<th>IPC</th>
<th>M1S1</th>
<th>DLPFC</th>
<th>IFG</th>
<th>SMA</th>
<th>Vis prim</th>
<th>Vis ass</th>
<th>R Cereb</th>
<th>L Cereb</th>
</tr>
</thead>
<tbody>
<tr>
<td>s1</td>
<td>2030</td>
<td></td>
<td></td>
<td>1189</td>
<td>2291</td>
<td>551</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s2</td>
<td>841</td>
<td>435</td>
<td>870</td>
<td>493</td>
<td>290</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s3</td>
<td>1305</td>
<td></td>
<td></td>
<td>2204</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s4</td>
<td>754</td>
<td>261</td>
<td>1334</td>
<td>406</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>203</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s5</td>
<td>480</td>
<td></td>
<td></td>
<td>144</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s6</td>
<td>377</td>
<td></td>
<td></td>
<td>435</td>
<td></td>
<td>1682</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s7</td>
<td>725</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s8</td>
<td>348</td>
<td></td>
<td></td>
<td>464</td>
<td></td>
<td>725</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s9</td>
<td>264</td>
<td></td>
<td></td>
<td>336</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>s10</td>
<td>232</td>
<td>957</td>
<td>4118</td>
<td>2639</td>
<td>4118</td>
<td>1363</td>
<td>1711</td>
<td>1798</td>
<td>319</td>
<td>1711</td>
<td>1798</td>
<td>319</td>
<td>1711</td>
<td>1798</td>
<td>319</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$s =$ subject; STS = Superior Temporal Sulcus; TOJ = Temporo-occipital Junction; TPJ = Temporo-parietal Junction; IPC = Inferior Parietal Cortex; M1S1 = Primary Motor and Sensory Areas; DLPFC = Dorso-Lateral Prefrontal Cortex; IFG = Inferior Frontal Gyrus; SMA = Supplementary Motor Area; Vis prim = V1, V2; Vis ass = V3; Cereb = Cerebellum; $R =$ right; $L =$ left.
RES U L T S

1. - Behavioural tests.

Table 1 shows the results of behavioural tests and the years of education for each subject. Years of education did not show significant correlation with any behavioural measure (spoonerism: r(10) = 0.34, rhyme generation: r(10) = 0.28). The number of correct responses in the rhyme generation test ranged between 23 and 30 (median = 28.5; quartile difference = 5.5). In the rhyme judgment test all subjects obtained the maximum score of 15. The number of correct responses in the spoonerism test ranged between 31 and 36 (median = 34; quartile difference = 4). Performances at spoonerism and rhyme generation tasks were significantly correlated (r(10) = 0.69, p < 0.05); this result was expected as both rhyme generation and spoonerism require active phonological procedures involving not only phonological processing but also lexical access and search. No correlation was found with the rhyme judgment task, probably because all subjects obtained the maximum score.

2. - fMRI.

Group analysis.

In rhyme generation task, group analysis showed a bilateral activation with a high degree of lateralisation in the left hemisphere (λ = 0.91). The main regions of activation and their relative Talairach’s coordinates are shown in Figure 1 and Table 2, respectively. They included IFG, DLPFC, supplementary motor area (SMA), STS, TOJ and TPJ in the left hemisphere, together with right cerebellar hemisphere.

In rhyme judgment task, group analysis showed activations only in the left hemisphere, at the level of IFG and DLPFC; the lateralisation index was thus equal to 1. Using a less conservative statistical threshold (p < 0.001 uncorrected), the larger number of activations found was consistent with the pattern observed in rhyme generation task (Fig. 1 and Table 2).

Single subject analysis.

For the analysis of individual data, the nine different Regions Of Interest (ROI) found in group analysis (Table 2), together with the visual areas, were identified in each participant by a neuroradiologist (DM) on the basis of anatomical landmarks.

In each ROI the presence/absence of activation, the extension of the ROI (mm³) and the SNR were recorded. Individual responses in both fMRI tasks are reported in Tables 3.

In all subjects rhyme generation task activated areas in the frontal lobe of left hemisphere, with particular regard to left IFG (10 subjects) and left DLPFC (8 subjects). Within the temporal lobe, STS was the most frequently activated (7 subjects), while activations in left TPJ and TOJ were less frequently observed (3 and 4 subjects respectively). Other areas of activation were found, particularly in SMA and right cerebellum (Table 3a).

Rhyme judgment task produced analogous results with all subjects showing areas of activation in the frontal lobe of the left hemisphere, with particular regard to left IFG (9 subjects) and left DLPFC (7 subjects). Within the temporal lobe, STS was the most frequently activated (5 subjects), while activations in left TPJ and TOJ were less frequently observed (2 subjects) (see Table 3b).

Correlation between single subject fMRI and behavioural tests

The first set of analyses investigated the relation between fMRI indices of activation...
In rhyme generation task, significant correlations were found between SNR values in STS (2.50-6.70) and DLPFC (2.35-6.75), and the number of correct responses at the rhyme generation (STS: \( \rho = 0.76, p < 0.005 \); DLPFC: \( \rho = 0.70, p < 0.01 \)) and the spoonerism behavioural tasks (DLPFC: \( \rho = 0.71, p < 0.01 \)). No correlations were found between rhyme generation test and the extension of global activation of the individual ROIs.

In rhyme judgment task, no significant correlations were found either for SNR (1.40-5.30) or for extension of activation, with any of the behavioural tasks. The lack of correlation may be due to the errors free performance obtained by all the subjects which could have acted as a sort of ceiling effect at behavioural and neurofunctional level.

The second set of analyses investigated the relation between patterns of fMRI activation and behavioural measures of phonological processing. On the basis of the three main regions of the language circuit considered for analysis, namely frontal regions (IFG/DLPFC), STS and TPJ/TOJ, only three possible combinations were found in our subjects: i) activation of frontal regions with no activation of the two posterior language regions; ii) simultaneous activation of frontal regions and STS, with no activation of TPJ/TOJ and iii) simultaneous activation of all three regions. The combinations observed reflected an antero-posterior gradient of activation; accordingly the three patterns were numbered on an ordinal scale, used for non parametric correlation analyses, with 1 for isolated frontal activation, 2 for additional activation of STS and 3 for activation of all three regions.
A statistically significant correlation was found between the gradient of fronto-temporal activation during the rhyme generation task and the number of correct responses at the rhyme generation (rho = 0.59, p < 0.05) and at the spoonerism task (rho = 0.66, p < 0.05): a higher number of correct responses was present in subjects who also showed activation of posterior areas. Three representative examples of the patterns observed are shown in Fig. 2.

No significant correlations were found between the gradient of fronto-temporal activation during rhyme judgment task and behavioural measures.

DISCUSSION

The results of our study revealed that within the neural network involved in phonological processing of written stimuli in Italian, the frontal lobe plays a relevant role regardless of the phonological task performed. Both during rhyme generation and rhyme judgment, two regions of the left frontal lobe, i.e. IFG and DLPFC, were significantly activated. The activation of IFG during tasks strongly demanding phonological processing is consistent with previous reports using rhyming tasks, indicating a relevant role of this structure in speech planning and execution (34, 37). Part of the activation of the frontal areas, in particular of DLPFC, could also reflect the use of phonological working memory (5, 46). This system is known to be involved in building a phonological representation matched to the orthographic input, by means of sublexical conversion rules, and in maintaining the phonological codes for speech output in the articulatory loop (1).

Group analysis showed differences in brain activation following the two tasks which may reflect a different involvement of sublexical and lexical mechanisms. Rhyme generation task activated a very extensive network involving left IFG and DLPFC, the supplementary motor area (SMA) and other relevant left posterior regions of the language circuit, including STS, TOJ and TPJ, and right cerebellar hemisphere. Rhyme generation from written words is assumed to tap not only phonological processing but also processes of lexical access necessary to read the word and verify the appropriateness in the lexicon of the rhyming word found (24). The activations in the rhyme judgment task were limited to frontal regions, namely left IFG and DLPFC. Rhyme judgment of pseudowords is considered a pure phonological task, based on sublexical processing since pseudowords do not have lexical and semantic representations, with visual matching strategies impeded by upper-lower case presentation (28, 34, 46).

Nevertheless, some of the differences found in our study may be due, as pointed out above, not only to the different cognitive components involved (phonological decoding, lexical access and output planning versus sublexical processing), but also to the different baselines used in the two tasks, one of which requiring an active judgment task.

The results of our group analysis need to be considered with caution as the number of participants only approaches the optimal limit for a group analysis (12). The main aims of our study however, were to explore the spectrum of individual variability in activation patterns and their relations to behavioural performance; we thus particularly focused on single subject analysis, which is more effective in addressing these issues.
Single subject analysis confirmed that the left frontal lobe was the only region constantly active in all subjects supporting the hypothesis of a relevant role of this structure for phonological processing of written words in a language with a regular orthography. When considering the activation of the posterior language areas, i.e. STS, TPJ and TOJ, our results show a high inter-individual variability.

In rhyme generation task about one third of our subjects did not show any activation of posterior language areas. In these cases, the main contribution of IFG might suggest the use of a specific strategy for phonological processing mainly based on output sublexical mechanisms. In the remaining seven subjects, who also constantly activated STS, the additional utilisation of input sublexical strategies might be hypothesised. Conversely involvement of regions, such as TPJ and TOJ, which have been related to lexically based mechanisms of phonological processing, was less consistently found in our subjects. These findings might be interpreted in the light of the specific properties of the language, as reported by Paulesu and collaborators in a PET study comparing cortical activations during reading tasks in Italian, French and English (32). It was found that left STS was preferentially involved in Italian readers, as opposed to languages with a less regular orthography. We hypothesise that in languages with regular orthography processes of lexical access may not be necessarily required in reading and rhyming tasks, therefore leaving more space for individual strategies of phonological processing.

When analysing rhyme judgment task, the other fMRI paradigm of our study, a similar general pattern of distribution of activations was found, i.e. a constant activation of the left frontal language areas associated to a more variable involvement of posterior language areas. In comparison to rhyme generation task, the posterior language areas were activated in a lower number of subjects, both for STS and for TPJ and TOJ. This finding is not surprising as the rhyme judgment of pseudowords is based on processing of strings that have no lexical and semantic representations, and therefore recruits mainly mechanisms of sublexical decoding and articulatory rehearsal.

Another important aim of our study was to investigate the possible correlations between the brain representation of phonological processing and the performance on related behavioural tests.

For the rhyme generation task, a significant positive correlation was found between the SNR of left STS and DLPFC and the number of correct responses at both rhyme generation and spoonerism behavioural tasks. This finding suggests a possible influence on task performance of the frontal structures mainly associated to phonological working memory and supports the role of the STS in the phonological analysis of language input.

The results of the second set of analyses, based on the identification of different patterns of activation of the language network, are in general accordance with these findings. For rhyme generation, an interesting correlation was found between the patterns of fMRI activation and the number of correct responses on the corresponding behavioural test. Although all subjects showed a high number of correct responses at the behavioural tests, as expected in a control group, the additional activation of the posterior language regions, in particular of STS, was significantly associated to better performances. This might indicate that optimal performance in rhyme generation tasks requires the contribution of a wider neural network related to both output and input strategies of phonological processing. Further support to this
hypothesis is provided by the significant correlation found between patterns of activation on fMRI and Spoonerism task, a behavioural test tapping several components of phonological processing, including phonological coding, maintaining the phonological representation and accessing the lexicon. We suggest that two main neurofunctional circuits are involved: the activation of inferior frontal gyrus may be associated to mechanisms of articulatory rehearsal and phonological output planning (1, 31), while the involvement of superior temporal sulcus provides a representation in input that works as an “inner phonological model” of the word. This hypothesis is in accordance with recent neuroimaging investigations suggesting that the temporal lobe is involved in the construction of a phonological representation in input (29, 35) and thus plays a crucial multifunctional role for linguistic and reading process (6).

In summary, our results seem to confirm that phonological processing in languages with regular orthography is mainly based on sublexical processes involving both rehearsal of output phonological codes and input phonology. Within this general framework however, inter-individual variability in the contribution of the different areas is observed, which interestingly appears to be related to the quality of behavioural performance. In this regard, the rhyme generation task in fMRI appears to be an effective tool for the exploration of the neural bases of phonology, as it addresses both sublexical and lexical components of phonological processing. Given some methodological limitations, mainly the use of behavioural results obtained out of scan and the small number of subjects, our data need to be further confirmed in larger cohorts that might better disclose different individual strategies and structure-function correlates of phonological processing. In this study we used both group analysis, which highlights common neuronal mechanism, and single subject analysis, more suitable to account for individual neurofunctional differences. This approach may be valuable not only for understanding of brain-behaviour relationships in normal subjects, but also to improve our knowledge on the neural correlates of different profiles of phonological disorders in languages with regular orthography (22, 36).

Acknowledgements. - This work was supported by grants FIRB 2001 from the Italian Ministry of University and Scientific Research (GC) and RC 1/2006 of the Italian Ministry of Health. The authors gratefully acknowledge all the subjects for the helpful cooperation. The authors would like to thank Lisa Saskia Arduino (Istituto di Psicologia, Università di Urbino) for her advice in the choice of the stimuli.

REFERENCES


