Language lateralization and reorganization in subjects with early-onset brain focal lesion: an fMRI study

L. Biagi[1], C. Pecini[1], M. Tosetti[1], D. Brizzolara[1], A. Chilosi[1], G. Cioni[1]
[1]Department of Developmental Neuroscience, Stella Maris Scientific Institute, Pisa, Italy

Introduction

Studies of language development in children with early focal brain injury concordantly report relatively mild impairments in contrast to the severe deficits seen in adults with comparable lesions. This evidence supports the concept of cerebral plasticity that is the capacity to compensate for damage to specific brain areas which is higher in the developing brain. It has been hypothesized that cerebral plasticity depends on several factors such as timing, size and localization of the lesion, presence of epilepsy, maturational state of the injured areas. For cognitive functions, which rely on lateralized neural systems such as language, damaged areas of the left hemisphere could be functionally substituted by undamaged regions of the right hemisphere. Whether language reorganization after an early lesion occurs inter- or intrahemispherically, has been traditionally addressed with behavioural techniques, such as the dichotic listening paradigm. These studies have supported the concept of a compensatory role of the right hemisphere for language. However, behavioural techniques cannot localise the neural circuits and the cortical regions involved in plasticity. Recently, language reorganization has been investigated by means of PET and fMRI in children and young adults candidates for neurosurgery because of intractable epilepsy and with early-onset lesions (Duncan et al. 1997; Gaillerd et al. 2002; Staudt et al. 2002; Liégois et al. 2004). The results suggest that, especially in language perception tasks, early left hemisphere lesions are associated with enhanced activation of some anterior and posterior areas of the right hemisphere, whereas recruitment of regions ipsilateral to the lesion is limited. However, the relationship between lesion characteristics and the pattern of language lateralization need further investigation, as the effects of lesion side, site and size on the pattern of language reorganization vary across studies. With the specific aim to investigate the relationship between these characteristics and language lateralization at fMRI during language tasks, we conducted an fMRI study on a group of children with congenital or early (<3 yrs) acquired focal lesions.

Methods

Eleven Italian subjects were selected from a larger sample of patients with early brain vascular accidents, followed by the Department of Developmental Neuroscience of the Stella Maris Scientific Institute. The group was composed by 3 subjects with focal lesion in the right hemisphere (aged from 6 to 17 years) and 8 subjects (aged from 7 to 24 years) with focal lesion in the left hemisphere. Patients performed phonological tasks previously tested on normal Italian adults and children, involving the anterior and posterior language areas (Biagi, ISMRM 2004). Depending on the age of test, the phonological task was a rhyme generation and/or a rhyme judgement task on word, pseudo-words or a letters matching task. In the rhyme generation task, participants had to find a word rhyming with the visually presented target and, in the rest condition, they had to passively view strings of four 'x'. In the rhyme judgement tasks participants had to judge whether two words, visually presented, rhymed and, in the rest condition, they had to judge whether two Cyrillic strings matched. In the letters matching task, participants had to judge whether two letters (activation) or two Cyrillic characters (rest) matched. Patients laid on their backs and view binocularly stimuli displayed in a virtual reality sep-up (VisuaStim XGA - Resonance Technology). BOLD responses were acquired by 1.5 T General Electric Signa Horizon LX System (GE, Milwaukee, USA), equipped with Echo-speed gradient coil and amplifier hardware. Activation images were acquired using echoplanar imaging (EPI) gradient-recalled echo sequence (TR/TE/flip angle = 3 s/50ms/90°, FOV = 280x280 mm, matrix = 128 x 128, 3-4 mm thick slices). Time-course series of 64 images for each volume were collected usually in 6 epochs alternating between control and active conditions, each 30 seconds in duration. The first epoch always lasted 12 sec more to allow the signal to stabilise. This initial period was eliminated from any successive analysis. An volumetric set of data (3D FSPGR: TR/TE/TI/flip angle = 21.1 ms/3.8 ms/700 ms/10°; FOV = 280 x 280 mm, matrix = 256 x 256) was acquired to generate a 3-dimensional whole brain reconstruction. BOLD maps for signal intensity changes were generated by using the software package BRAIN VOYEGER. The effective probability has been set to a value less than 0.001, with the additional requirement of a cluster size of 5 voxels. A Fourier analysis was conducted on the signal obtained in some selected ROI. Patients were also tested with behavioural tasks aimed to measure phonological processing skills and the hemispheric specialisation for language (dichotic listening paradigm).

Results and Discussion

In the evaluation of the cortical areas involved in the phonological tasks, we focused on the cerebral circuits which were activated in our group of normal Italian controls, i.e. the inferior frontal gyrus (IFG), the dorsolateral pre-frontal cortex (DLPFC), the infrapartietal cortex (IP), the supplementary motor cortex (SMA), the Wernike's areas (22 and 39-40) and the cerebellum hemispheres.

Preliminary results show that patients with congenital (pre- or peri-natal) lesion in the left hemisphere, involving the cortical-subcortical structures, have a shift of activation of language areas into the homologous cortical regions of the right hemisphere. These subjects did not show any language disabilities. A normal language development was also documented in the only case of our series with the lesion in the periventricular white matter; this subject preserves the activation of the cerebral areas in the left hemisphere. The cases with post-natal brain injury (occurred before 3 years) of the left hemisphere showed a peri-lesional reorganization of language areas, accompanied with some disabilities in learning, reading or phonological processing. All patients with a lesion in the right hemisphere maintain the activation of cerebral areas of the left hemisphere.

These results of this preliminary study seem to confirm the hypothesis that the mechanism of cerebral plasticity involved in language reorganization depends on several factors, in particular timing and localization of the lesion.