fMRI Shows Atypical Language Lateralization in Children with Epilepsy

W. Yuan[1], S. K. Holland[1], J. Szaflarski[2], V. J. Schmithorst[1], A. W. Byars[1], R. H. Strawsburg[3]

[1]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, United States, [2]University of Cincinnati, Cincinnati, Ohio, United States, [3]Associates of Neurology, Valparaiso, Indiana, United States

Introduction

Hemispheric dominance of language is of interest with respect to brain development, injury, pathology, neuroplasticity and reorganization of neurological circuitry in support of critical neurocognitive functions. FMRI has been used to map hemispheric language dominance in both children and adults.[1-3] Several studies have demonstrated the correlation of fMRI language lateralization measures with more traditional approaches such as Wada or electrocortical stimulation.[4,5] In this study we report fMRI language lateralization findings in a cohort of children with epilepsy. This group is contrasted with an age matched control group of normal children. Our findings demonstrate atypical language lateralization in the pediatric epilepsy patients, reflecting a re-organization mechanism that is often observed in adults with various neurological pathologies.[6]

Methods

Twenty two epilepsy patients, ages 8-18 years, participated is an fMRI study using a block-periodic, covert verb generation paradigm on a 1.5 Tesla clinical MRI scanner. Five cycles of alternating 30-second periods of "stimulation" and "control" tasks were interleaved with each other. During the 30-second "stimulation" intervals a series of concrete nouns were presented over MR compatible headphones every 5 seconds and the subjects were instructed to silently generate as many verbs as possible connected with this object. During the "control" interval the subjects rested in silence. A total of 100 EPI gradient-echo images, each with six para-sagittal slices in each hemisphere (slice thickness=5mm), were acquired continuously during the execution of the behavioral paradigm (TR/TE=3000/40 msec, FOV=220x220mm, matrix=64x64, slice thickness= 5mm). Data was post-processed using cross-correlation of the time-series with a boxcar reference waveform and the threshold for activation was set at R=0.33. A language lateralization index (LI) was calculated as the ratio between the difference in the number of activated pixels in the two hemispheres to the sum of the activated pixel numbers: (LI = (Σpixels left - Σpixels right)/(Σpixels left + Σpixels right)). The normative LI data used for comparison in the present study was obtained from previous research by our group and details have been reported previously.[1,7] For the purposes of this presentation, LIs were computed from the normative control group using the same methodology as for the epilepsy patient cohort.

Results

Eighteen patients finished the auditory verb generation paradigm successfully. A standard two-sample t-test shows that there is a significant difference (t= 4.03, p=0.0001) in the mean lateralization index between the patients (mean LI = 0.06) and the normal control subjects (mean LI=0.23). A histogram analysis (Figure 1) shows that the distribution of LI from normal population (N = 211) follows closely to a bell-shape centered at the mean value of 0.23, suggesting a strong left hemispheric language dominance. The LI in the patient group however, spread out in a wider range with a more uniform distribution. A larger percentage of epilepsy patients had bilateral or right sided language dominance (n=9, 50%) as compared to the case in normal population (n=30, 14.2%).

Discussion and Conclusion

The neuroplasticity of language function associated with childhood epilepsy is of interest in several respects. The question remains as to whether language lateralization in epilepsy patients is atypical because of the chronic effect of seizures on the brain or whether preceding brain pathologies cause both the atypical lateralization and the epilepsy. This study focuses on the lateralization index computed from fMRI images to quantify the influence of childhood epilepsy on the re-distribution of language function in the brain. Our research shows that, similar to the conclusion from previous adult studies[4-6], LI can serve as a simple yet robust method for demonstrating the difference of the brain activation patterns between epilepsy patients and normal subjects during development. Compared to a normal age-matched population, pediatric epilepsy patients demonstrated a much wider variation and a more bilateral average value of lateralization index. These findings suggest that the influence of repeated seizure activity in epilepsy may cause redistribution of language function in the developing brain to compensate for injury to traditional left dominant language areas or connections to them. However, due to limitations in this study in terms of the variability in age of onset of seizure and pathologies in this patient group, we are not able to establish whether the atypical lateralization is a result of the epilepsy or related to its cause. Dependency of the neuroplasticity on age, gender, handedness, and /or other factors in children with epilepsy remains to be explored in further longitudinal studies.

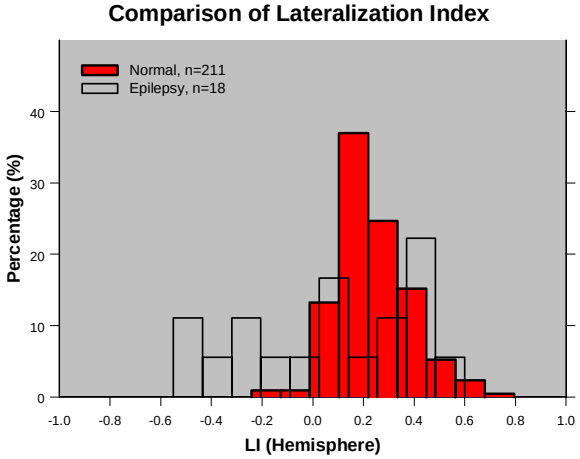

Figure 1: Comparison of Lateralization Index.

References

1. Holland, S. K. et al. Normal Brain Activation Patterns in Children Performing a Verb Generation Task. *Neuroimage* **14**, 837-843 (2001).
2. Holland, S. K. et al. in *SNR XVI/ASNR* 165 (1998).
3. Holland, S. K. et al. in *ISMRM 7th Scientific Meeting & Exhibition* 787 (Philadelphia, 1999).
4. Binder, J. R. et al. Determination of language dominance using functional MRI: A comparison with the Wada test. *Neurology* **46**, 978-984 (1996).
5. Desmond, J. et al. Functional MRI Measurment of Language Lateralization in Wada-Tested Patients. *Brain* **118**, 1411-1419 (1995).
6. Springer, J. A. et al. Language dominance in neurologically normal and epilepsy subjects: a functional MRI study. *Brain* **122**, 2033-46 (1999).
7. Holland, S. K. et al. in *ISMRM 10th Scientific Meeting & Exhibition* (Honolulu, Hawaii, 2002).