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Major white matter fiber changes in medically intractable neocortical epilepsy in children: A diffusion tensor imaging study

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Summary This study aimed to investigate the extent of microstructural changes in the major white matter fibers and to evaluate whether diffusion tensor imaging (DTI) adds any lateralizing information in children with medically intractable neocortical epilepsy secondary to focal cortical dysplasia. Patient group included twenty-three consecutively enrolled patients with medically intractable focal neocortical epilepsy and focal cortical dysplasia histopathologically confirmed. Thirteen patients (56.5%) had no visible lesion on the conventional magnetic resonance imaging (MRI). Fractional anisotropy (FA) was measured for regions of interest (ROIs) in each major white matter fiber. FA in patients was compared with eighteen age-matched healthy controls. Patient group had lower FA values at corpus callosum, bilateral inferior frontooccipital fasciculus (IFO), bilateral inferior longitudinal fasciculus (ILF) and left superior longitudinal fasciculus (SLF) compared to controls ($p < 0.05$). In the left-side surgery group, the left SLF FA value was lower than controls, while in the right-side surgery group, the right SLF FA values were lower than controls ($p < 0.05$). In the patient group as a whole, ipsilateral SLF FA was significantly lower than the contralateral SLF ($p < 0.05$). Widespread decrease in FA values in the patients compared with the controls suggests that the pathologic changes extend diffusely to

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most major white matter tracts. In the patient group, the ipsilateral SLF to the seizure focus had greater change compared to the contralateral SLF. These data suggest that the detection of DTI abnormality has an added value to lateralization.

Introduction

Neuroimaging has advanced to the point where it can identify the location and extent of epileptogenic lesions undetected by conventional techniques (Duncan, 2010; Bernasconi et al., 2011). Identifying a lesion on magnetic resonance imaging (MRI) is important for developing a hypothesis for the potential location of the epileptogenic zone and planning of intracranial electrode implantation in epilepsy surgery. However, conventional magnetic resonance imaging (MRI) does not show apparent lesions in 20—30% of patients with medically intractable focal epilepsy (Duncan, 1997). Up to 42% of MRI-negative epilepsy surgery patients are found to have focal cortical dysplasia (FCD) (Chapman et al., 2005). FCD is often either invisible or so subtle as to be inconclusive on MRI (Palmini et al., 1991; Raymond et al., 1995; Krsek et al., 2009) and is the most common pathologic substrate in children with medically intractable focal epilepsy.

As the development of the gray and white matter is closely linked through neuronal migration process, developmental malformations including FCD can affect both the cortex and the underlying white matter. In focal epilepsy, the hyperexcitability associated with seizure activity propagates through the functionally and structurally connected cerebral network (Spencer, 2002). The major white matter tracts form the structural basis of these networks (Duncan, 2008).

Diffusion-tensor imaging (DTI) can examine the microstructural integrity of white matter with quantitative measures of diffusivity and fractional anisotropy. DTI measurements of pathological change in white matter tracts were discovered adjacent to FCD (Widjaja et al., 2007, 2009). DTI allows us to identify subtle FCDs by examing derangements in subcortical white matter fiber connections and specific functional propagation pathways in focal epilepsy.

We hypothesized that patients with medically intractable focal neocortical epilepsy would show microstructural changes affecting major white matter fibers, which are anatomically and functionally related to seizure onset zones. The ipsilateral major white matter fibers should be affected more than that contralateral to seizure onset zone, which may provide clinically useful information for epilepsy lateralization. This work assessed the lateralizing value of fractional anisotropy in the major white matter fibers of children with medically intractable epilepsy associated with histopathologically confirmed FCD.

Methods

Subjects

Epilepsy surgery candidates were evaluated at The Children's Hospital of Alabama utilizing a standardized protocol consisting of long term video-EEG monitoring, MRI, and functional imaging consisting of 2-[^{18}F]fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET), interictal and ictal single photon emission computed tomography (SPECT), and Magnetoencephalography (MEG). Each case was presented at a patient management conference and a consensus formulation for resection was achieved. For this retrospective observational study, cases were drawn from our consecutive surgical candidate population (02/2008—06/2010) and were selected based on the following criteria: (1) the resective epilepsy surgery for the focal neocortical epilepsy; (2) the histopathology revealing FCD; and (3) the postoperative follow-up duration of at least 6 months. Patients with tuberous sclerosis complex were excluded due to the likelihood of multiple lesions. Twenty-three patients (12 male, 11 female) were studied. The mean ages at seizure onset and at epilepsy surgery were 4.6 ± 3.8 years (3 months—13 years) and 10.7 ± 4.1 years (4 years 10 months—18 years 8 months), respectively. The mean duration of epilepsy was 6.7 ± 3.9 years (1 year—14 years 4 months). Nineteen patients (82.6%) were right-handed (11 left sided surgery, 8 right sided surgery) and 4 were left-handed (3 left side surgery; 1 right side surgery). Thirteen patients (56.5%) had no visible lesion or other diagnostic abnormality on preoperative brain MRI preoperatively. Nearly all patients (22/23) underwent intracranial EEG monitoring before the resective surgery; 13 had seizure onset zone in fronto-parietal regions and 10 in temporo-occipital regions. The mean postoperative follow-up duration was 22.5 ± 9.3 months (11—39 months). Histopathology revealed focal cortical dysplasia type Ia(2), Ib(1), IIa(14), and IIb(6) (Palmini et al., 2004). Postoperative seizure outcome was classified by Engel class (Engel Jr, 1993): 13 (56.5%) class I, 7 (30.4%) class II, and 3 (13.1%) class III. Twenty-two patients were analyzed; one case (case 5) was excluded because DTI acquisition was done during epilepsia partialis continua.

Control data were obtained from a database of raw data in a normal pediatric population (cmrm.med.jhmi.edu). This normative data set included eighteen age-matched subjects-12 between ages 4 and 11 years and 6 between ages 12 and 18 years. The institutional review board of the University of Alabama at Birmingham approved the acquisition and analysis portions of this study.

MRI protocol

For the patient group, MRI exams were acquired using a SENSE head coil on a 1.5T whole-body MR scanner (GE medical system, USA). The parameters for the DTI acquisition were as follows: axial 2D single-shot-spin-echo echo-planar imaging (EPI) diffusion weighted sequence with TE/TR = 88.2 or 90.7/1400—1700 ms, two *b*-values of 0 and 1000 s/mm^2, 25 directions. The field of view (FOV), the size of the acquisition matrix, and the slice thickness were 220 mm × 220 mm/128 mm × 128/3 mm without gap.