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ORIGINAL ARTICLE

Microstructural Changes in Absence Seizure Children: A Diffusion Tensor Magnetic Resonance Imaging Study

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Key Words
absence seizures;
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Background: Absence seizures are a subtype of epileptic seizures clinically characterized by transient alterations in states of consciousness and by electroencephalography indicating diffuse spike-wave discharges (SWD). Conventional brain magnetic resonance imaging (MRI) is not routinely used to establish the diagnosis, but rather to rule out other diseases. The present study investigated tissue integrity in children with SWD epilepsy using diffusion tensor imaging (DTI).

Methods: Magnetic resonance imaging (MRI)-DTI was conducted in 18 patients with absence seizures and 10 control participants. Brain areas were evaluated using diffusion maps, and fractional anisotropy (FA), mean diffusivity (MD), parallel diffusivity ($\lambda\|$), and perpendicular diffusivity ($\lambda\perp$) values were extracted and analyzed. Tractography at the regions of abnormal diffusion indices was then reconstructed in each group, and tract symmetry was evaluated by an index of asymmetry (AI). Statistical analyses were performed using nonparametric Mann–Whitney *U* tests, with p values < 0.05 indicating statistical significance.

Results: Compared to the control group, patients with SWD epilepsy had lower FA values and higher MD values at the genu of the corpus callosum. There was also a stronger negative correlation between MD and FA values at the genu of the corpus callosum in patients than in

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control participants. The AI for the fiber tracts through the genu of the corpus callosum in the SWD group was significantly higher than that of the control group, indicating that tract distribution was more asymmetric in patients with epilepsy. There were no significant differences between groups in diffusion indices for other brain areas.
Conclusion: We observed microstructural changes in the genu of the corpus callosum, as well as reduced FA values, increased $\lambda\perp$ values, increased MD values, and asymmetric distribution of fiber tracts, indicating that DTI is more sensitive than conventional MRI to detect brain abnormalities in children with absence seizures.

1. Introduction

Absence epilepsy (AE) is a specific type of brief, generalized nonconvulsive epileptic seizure disorder. The seizures are characterized by a transitory alteration in consciousness associated with electroencephalograms (EEGs) indicating bilateral 3—4 Hz spike-wave discharges (SWD) of variable duration.[1] There are three different types of absence seizures: childhood AE, juvenile AE, and epilepsy with myoclonic absences.[2,3] Although the prognosis is usually favorable in AE, cognitive changes as well as linguistic and behavioral problems may occur. In addition, improvements in cognition are observed only after patients are seizure-free and EEG no longer shows any SW complexes.[2]

Typical SWD in absence seizures is dependent on long-range corticothalamic and corticocortical network interactions.[1,4,5] In addition, the largest SWD amplitude typically occurs in the midline frontal region near the central sulcus, and in the occipital regions.[6—8] However, results from conventional magnetic resonance imaging (MRI) studies have not demonstrated specific pathology.[9] Advanced MRI sequences may provide more specific diagnostic information for use in investigating microstructural abnormalities in patients with AE.

Diffusion tensor imaging (DTI) noninvasively maps white matter tracts in the human brain.[10,11] DTI data is described by an anisotropic diffusion displacement-probability ellipsoid, characterized by three eigenvalues ($\lambda1$, $\lambda2$, and $\lambda3$) and three eigenvectors (e1, e2, and e3) in a local frame of each image voxel after matrix diagonalization. The average of the three eigenvalues is referred to as the mean diffusivity (MD), which is a directionally averaged measure of water diffusion that reflects tissue density. Fractional anisotropy (FA) quantifies the degree of preferred directionality for water displacement, and is a marker for diffusion anisotropy. These indices allow quantitative evaluation of the magnitude and degree of anisotropy for the random translational motion of water molecules. Both FA and MD are sensitive to a variety of brain pathologies affecting white matter integrity, including epilepsy.[12,13]

Although epilepsy is generally not considered a white matter disease, it occurs with increased incidence in patients with multiple sclerosis,[14] and can be associated with abnormal myelination.[15] Data from previous DTI studies have demonstrated abnormal diffusion indices in prefrontal areas of seizure patients,[13] including cortical malformation-related epilepsy and unilateral temporal lobe epilepsy.[16] In addition, Chahboune et al[17] found abnormal diffusion indices at the anterior corpus callosum in a rat model of absence seizure, suggesting that chronic SWD in the cortex may result in microstructural changes in white matter pathways.[17] However, generalized seizures involving the WAG/Rij rat may or may not be equivalent to human absence seizures.[2] Therefore, the present study investigated white matter integrity using DTI-derived FA, MD, and tractography in children with absence seizures and diffuse SWD, compared to control participants.

2. Methods

2.1. Patient selection

This prospective case—control study was approved by the Institutional Review Board of Far Eastern Memorial Hospital. Participant confidentiality and privacy were protected according to national standards. Informed consent was obtained from each participant and/or his or her parents. Eighteen right-handed patients with absence seizures and diffuse SWD were included in this study. Medical histories, neurological examinations, and routine EEG recordings were conducted for each participant, and diagnosis was then established according to the diagnostic criteria of the International League Against Epilepsy.[18] Inclusion criteria were as follows: (1) age of onset between 3 years and 18 years; (2) absence seizures as the main seizure type; (3) absence seizures associated with bilateral, synchronous, and symmetrical 3 Hz SWD with normal background; and (4) normal neurological examination. Ten patients were diagnosed with childhood absence epilepsy, five patients with juvenile AE, and three patients with drug-induced AE. The clinical data are presented in Table 1. Ten right-handed healthy participants [6 girls and 4 boys; mean age 10.6 years, standard deviation (SD) 3.8 years] with no history of neurological disorders and a normal neurological examination served as controls. When imaging yielded obviously detectable abnormalities or poor image quality, participants were excluded from the study ($n = 4$).

2.2. Image acquisition

All participants had MRIs within 6 months of diagnosis, and all exams were performed between ictal episodes and