Journal of Clinical Neuroscience 22 (2015) 166–172

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

An investigation of diffusion imaging techniques in the evaluation of spinocerebellar ataxia and multisystem atrophy

Michael N. Rozenfeld [a,*], Alexander J. Nemeth [b,e], Matthew T. Walker [c], Prasoon Mohan [d], Xue Wang [b], Todd B. Parrish [b], Puneet Opal [e,*]

[a] Department of Radiology, University of Chicago, 5841 S. Maryland Avenue, Chicago, IL 60637, USA
[b] Department of Radiology, Northwestern University, Chicago, IL, USA
[c] Northshore University Health Systems, Department of Radiology, Evanston, IL, USA
[d] St. Francis Hospital, Department of Radiology, Evanston, IL, USA
[e] Ken and Ruth Davee Department of Neurology, Northwestern University, Chicago, IL, USA

ARTICLE INFO

Article history:
Received 20 August 2014
Accepted 30 August 2014

Keywords:
Diffusion tensor imaging
Diffusion weighted imaging
Multisystem atrophy
Q-ball imaging
Spinocerebellar ataxia

ABSTRACT

Multisystem system atrophy and spinocerebellar ataxia are rare neurodegenerative ataxias that can be difficult to diagnose, with important prognostic and treatment implications. The purpose of this study is to evaluate various methods of diffusion imaging and tractography in their effectiveness at differentiating these diseases from control subjects. Our secondary aim is determining whether diffusion abnormalities correspond with clinical disease severity. Diffusion imaging and tractography were performed on five patients and seven age-matched controls. Fractional anisotropy, generalized fractional anisotropy, and apparent diffusion coefficient values and corticospinal tract volumes were measured within various diffusion and probabilistic tractography models, including standard diffusion tensor and Q-ball tractography. Standard diffusion based fractional anisotropy and apparent diffusion coefficient values were significantly altered in patients *versus* controls in the middle cerebellar peduncles and central pons. Tractography based fractional anisotropy and generalized fractional anisotropy values were significantly lower in patients *versus* controls when corticospinal tracts were drawn in a craniocaudal direction (bilaterally using Q-ball imaging, only on the right using diffusion tensor imaging). The right corticospinal tract volume was significantly smaller in patients *versus* controls when created using Q-ball imaging in a caudocranial direction. There was no correlation between diffusion alteration and clinical symptomatology. In conclusion, various diffusion-based techniques can be effective in differentiating ataxic patients from control subjects, although the selection of diffusion algorithm and tract growth technique and direction is non-trivial.

1. Rationale and objectives

The neurodegenerative ataxias are a heterogeneous group of disorders that affect the cerebellum and its connections. Two groups of disorders that are especially difficult to diagnose are the autosomal dominant spinocerebellar ataxias (SCA) and the sporadic multisystem atrophy (MSA). A diagnosis of SCA is made via genetic testing, however only 60–75% of patients have a known genetic locus and when identified sporadically, only 20% have an identifiable locus [1,2]. A diagnosis of MSA is made per clinical criteria [3]. For both diseases, MRI is currently used mainly to exclude other diseases.

For both MSA and SCA, the roles of diffusion, diffusion tensor imaging (DTI) and Q-ball imaging (QBI) have not been thoroughly evaluated as a diagnostic tool to our knowledge. A handful of studies have been performed over the past 10 years, however, the current knowledge base is limited due to significant differences in technique, and varying results. Additionally, there is little data comparing the efficacy of the various techniques tested. The purpose of this study is to evaluate various methods of diffusion imaging and probabilistic tractography (DTI and QBI) including tract growth methods in their effectiveness at differentiating these diseases from control subjects. Some of the techniques tested have not previously been applied in this population. Secondary aims include determining whether diffusion abnormalities correspond with clinical disease severity.

* Corresponding authors. Tel.: +1 773 834 9980; fax: +1 773 834 6237 (M.N. Rozenfeld), tel.: +1 312 503 4699; fax: +1 312 503 0872 (P. Opal).
E-mail addresses: michael.rozenfeld@uchospitals.edu (M.N. Rozenfeld), p-opal@northwestern.edu (P. Opal).

http://dx.doi.org/10.1016/j.jocn.2014.08.006
0967-5868/

2. Materials and methods

Five patients (three MSA cerebellar type, one MSA parkinsonian type, one SCA 2; normal allele 28 repeats, abnormal allele 42 repeats) and seven age-matched controls were prospectively recruited. Ataxic patient age and sex were as follows: 60-year-old woman, 36-year-old man, 65-year-old woman, 55-year-old man, and 65-year-old woman. One patient died during the study, with confirmation of her MSA cerebellar type with additional pathologic features of MSA parkinsonian type. Control subject exclusion criteria included extensive cerebral and cerebellar atrophy. One control subject was removed from the study for this reason as he represented an outlier that would have adversely affected the statistical analysis. Informed consent was obtained from all study participants. The diagnosis was confirmed by a senior neurologist subspecialized in movement disorders. The same neurologist examined patients on the day of the MRI using the Scale for the Assessment and Rating of Ataxia [4]. Institutional Review Board approval was granted on 10 December 2009.

2.1. MRI protocol

T1-weighted anatomical brain image and DTI were collected on a Siemens 3.0 Tesla Trio Tim whole body system with a 32-channel head coil (both Siemens Medical Solutions, Erlangen, Germany). T1-weighted anatomical images were acquired using magnetization-prepared rapid acquisition with gradient echo with the following parameters: voxel size, 1 mm isotropic; repetition time (TR)/echo time (TE), 2300/2.91 ms; flip angle = 9^0; in-plane matrix resolution, 256 × 256; slice, 176. DTI parameters were as follows: voxel size, 2 mm isotropic; TR/TE, 9400/89 ms; flip angle = 90^0; in-plane matrix resolution, 128 × 128; slice, 72; b = 1000 s/mm^2, GRAPPA with acceleration factor of 2. Diffusion was measured in 64 directions with one b0 image.

2.2. Imaging analysis

2.2.1. Standard fractional anisotropy/ADC ROI analysis

Analyses were conducted using FSL 4.1 (www.fmrib.ox.ac.uk/fsl/). T1-weighted anatomical image was skull-stripped using the brain extraction tool (BET; part of FSL tools), and regions of interest (ROI) were created for each subject based on the anatomical image using FSLview. A radiology resident blinded to the clinical data drew the ROI and a neuroradiologist with 6 years of experience then confirmed their placement. The ROI were placed in the bilateral frontal and cerebellar white matter as well as bilaterally in the posterior limb of the internal capsules, cerebral peduncles (CP), superior cerebellar peduncles, and middle cerebellar peduncles (MCP). ROI were also placed in the ventral pons, central medulla and the body, genu, and splenium of the corpus callosum (Fig. 1). All ROI measured 5 mm^2 except within the internal capsule (4 mm^2) and superior cerebellar peduncles (2 mm × 4 mm) – these were altered due to the size constraints of the location. Diffusion images were eddy current corrected, and b0 images were co-registered to their anatomical images using FLIRT. Fractional anisotropy (FA) maps were estimated by the Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB) (www.fmrib.ox.ac.uk) Diffusion Toolbox (FDT). Average FA and apparent diffusion coefficient (ADC) values within each ROI were calculated.

2.2.2. DTI versus QBI based tractography

In DTI based tractography, a diffusion tensor model was fitted at each voxel by FDT. We applied the Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques (BedpostX) tool that accounts for two crossing fibers per voxel. A burning period of 1000 iterations was performed before starting the sampling. In Q-ball based tractography, using a real spherical harmonics basis, single q-shell constant solid angle orientation distribution function (ODF) estimation (50 samples, peak threshold = 30% of maximum ODF value, SH l_{max} = 4) was performed by the Qboot command in

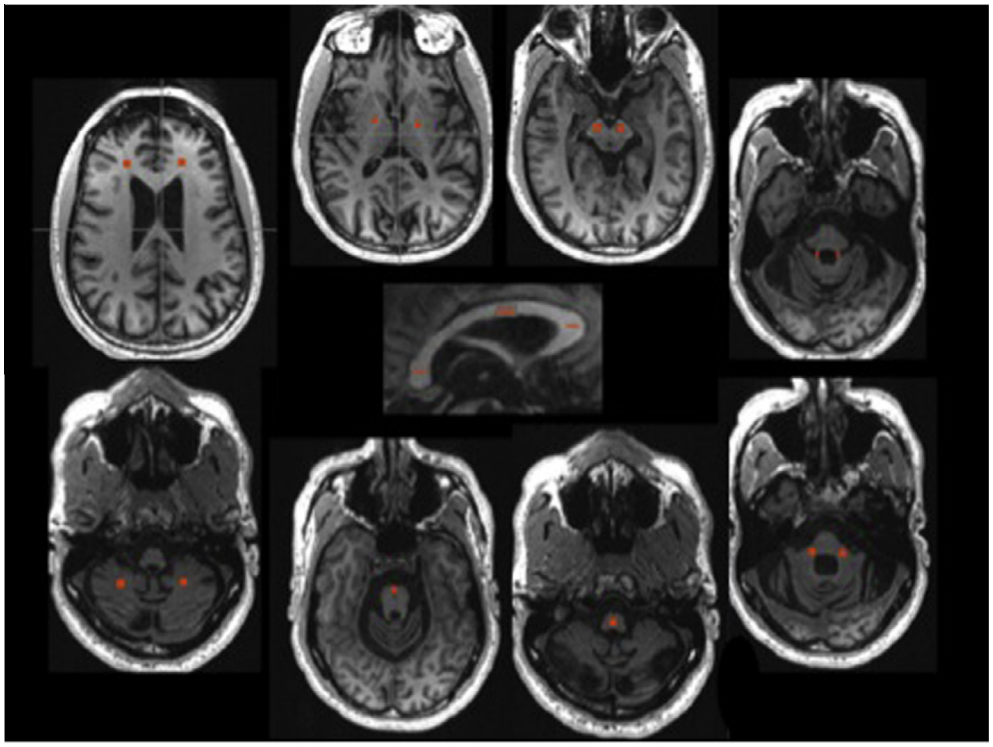

Fig. 1. Region of interest placement on a sample patient's axial (surround) and sagittal (center) T1-weighted MRI for fractional anisotropy/apparent diffusion coefficient analysis.