The Egyptian Journal of Radiology and Nuclear Medicine (2016) 47, 1009–1018

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

www.elsevier.com/locate/ejrnm
www.sciencedirect.com

ORIGINAL ARTICLE

Correlation of Apparent Diffusion Coefficient to cognitive impairment in Relapsing remittent multiple sclerosis (plaque, peri-plaque and Normal appearing white matter)

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Received 9 September 2015; accepted 25 April 2016
Available online 7 July 2016

KEYWORDS

DW-MRI;
ADC map;
Multiple sclerosis;
Cognitive impairment

Abstract The purpose of this study was to determine diffusion coefficient (ADC) in plaque, peri-plaque and normal-appearing white matter (NAWM) in multiple sclerosis (MS), compare them with the control and correlate findings with cognitive state.

Subjects and methods: Sixty-five participants were included and categorized into MS patients with normal cognition ($n = 25$); MS with mild cognitive impairment ($n = 20$) and control group (no MS and normal cognition; $n = 20$). The Montreal Cognitive Assessment was used to determine cognitive state. Mean ADC was measured in plaque, peri-plaques and NAWM, compared with ADC from corresponding white matter in control and correlated with cognitive scores. Chi Square and Pearson correlation coefficient were used.

Results: The mean ADC of peri-plaque and NAWM in MS group with cognitive impairment was significantly higher than MS group with normal cognition ($p < 0.001$) and control group ($p < 0.05$) respectively. In MS patients with impaired cognition, the mean ADC in peri-plaque and NAWM demonstrated inverse correlations with cognitive state ($r = -0.64$, $p < 0.001$) and ($r = -0.56$, $p = 0.01$) respectively.

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Peer review under responsibility of The Egyptian Society of Radiology and Nuclear Medicine.

http://dx.doi.org/10.1016/j.ejrnm.2016.04.018

Conclusions: ADC values in peri-plaque and NAWM have an inverse correlation with cognition in MS. The ADC is useful for detecting subtle abnormalities in white matter and can be used as a predictor of cognitive state.

1. Introduction

The characteristic abnormalities of multiple sclerosis (MS) in the brain consist of multiple white matter lesions (plaques) with high signal intensity (SI) on fluid attenuation inversion recovery (FLAIR), Proton density (PD) WI, and T2-WI and low SI on T1-WI. Lesions are found predominantly in a periventricular distribution, centrum semioval, and the calloso-septal interface. Additional sites of involvement include other parts of the cerebral white matter such as the subcortical white matter, optic nerves, corpus callosum, internal capsule, cerebellar peduncles, brainstem, and spinal cord (1).

Demyelinating lesions appear smaller on T1-WI than on T2-WI. Occasionally, they show a hyperintense border on T1-WI. Lesions in MS can be small, large, or confluent. The typical configuration is that of an ovoid lesion extending perpendicularly from the ventricular surface (Dawson's finger). This probably reflects the perivascular inflammation along a penetrating medullary vein. Atypical lesions and mass-like lesions occur with sufficient frequency to cause diagnostic errors (1).

Recent years have witnessed increasing interest in the prediction of neuropsychological (NP) impairment in patients with MS. Approximately 50% of MS patients exhibit some degree of NP impairment. Deficits in processing speed, memory, and higher executive function are particularly common, affecting the quality of life and employment (2).

A cognitive impairment substantially impacts the lives of patients with MS and their families. More than 50% of people with MS are unemployed within ten years of diagnosis (3).

Identifying patients at risk for NP disabilities on the basis of MRI would enhance the quality of care. It is also increasingly recognized that early microstructure changes in the normal-appearing brain tissue (NABT) may also predict cognitive impairment in MS (4).

Diffusion-based imaging techniques, particularly diffusion-weighted imaging (DWI) and diffusion-tensor imaging (DTI), provide measures of increased pathologic specificity over conventional MRI. They are able to assess in vivo the presence of tissue damage occurring outside visible lesions, in the so-called normal-appearing tissue (5).

Diffusion techniques measure the random movement of water molecules in all tissues and fluid. Enhancement of such movement in brain parenchyma probably reflects the destruction of cell membranes, and in the case of MS, demyelination, and microscopic cell damage. Numerous studies have found increased translational movement of water in both active lesions and NABT in MS samples. As a result, diffusion-related measures may account for clinical signs independent of variance explained by more conventional, macroscopic MRI measures (6).

The purpose of this study was to utilize DWI and ADC values as a marker for early detection of MS patients susceptible to cognitive impairment and determine the most correlated sites (plaque, peri-plaque or normal-appearing white matter (NAWM)) for early prediction of cognitive impairment and to explore the correlation between water diffusion and cognition state.

2. Subjects and methods

This prospective study was carried out during the period from December 2014 to July 2015 in Radiology and Psychiatry department, Zagazig University, and included 45 MS patients and 20 matched age healthy volunteers as a control. Approval for the study from ethics committee board of our institute was taken, as well as, a written consent from all participants after explanation of the procedure.

2.1. Subjects

Forty-five patients (15 males and 30 females; mean age 34.22 ± 7.09 year) with a clinical and radiologic diagnosis of MS according to the McDonald criteria (7) were included in the study. The duration of clinically evident disease was 2–11 y (mean 4.89 ± 2.6) at the time of imaging and the number of attacks ranged from 2 to 7.

Inclusion criteria: Relapsing remittent MS patients with no relapse for at least 3 months before the study.
Exclusion criteria: (1) MS patient in active stage; (2) Other intracranial pathology; (3) psychotic patients; (4) Other major medical conditions or substance abuse; (5) Patients on antidepressants psychoactive steroids, or immunosuppressive drugs; (6) Patients with delirium; (7) The presence of any contraindications to MRI examination.

The control group 20 healthy volunteers (6 males, 14 females, mean age 35.4 ± 6.12 years) with no neurologic disability or intracranial pathology proved by clinical and conventional MR examination were included.

All the patients (n = 45) and the controls group (n = 20) underwent cognitive state assessment and MR examination including conventional MR imaging, DW-MR imaging, and its corresponding ADC map.

2.2. Cognitive state assessment

The Montreal Cognitive Assessment (MOCA) (8) was designed as a rapid screening reference for mild cognitive impairment. It is sensitively widespread and more easily used. MOCA assesses different cognitive domains: visuospatial/exec-