Journal of Neuroradiology xxx (2017) xxx–xxx

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Original Article

Can MRI water apparent diffusion coefficient (ADC) value discriminate between idiopathic normal pressure hydrocephalus, Alzheimer's disease and subcortical vascular dementia?

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ARTICLE INFO

Article history:
Available online xxx

Keywords:
ADC
Normal pressure hydrocephalus
Alzheimer
Subcortical vascular dementia

ABSTRACT

Numerous similarities in MRI and clinical symptoms exist between Alzheimer's disease (AD), subcortical vascular dementia (sVD) and possible idiopathic normal pressure hydrocephalus (iHPN). The aim of this study is to explore mean apparent coefficient diffusion (ADC) difference between theses diseases in different periventricular and deep white matter areas, as compared to healthy controls. This retrospective study analyzed mean ADC values of 120 patients in normal appearing deep white matter and lenticular nuclei, frontal, caudate nuclei corpus and parietal periventricular and deep white matter areas INPH group showed significantly lower ADC than sVD group in frontal periventricular region (1567.10^{-6} mm²/s vs 1755.10^{-6} mm²/s; $P=0.0009$) and in parietal deep region (1087.10^{-6} mm²/s vs 1271.10^{-6} mm²/s; $P=0.0052$), but showed significantly higher ADC in lenticular nuclei ROI (834.10^{-6} mm²/s vs 753.10^{-6} mm²/s; $P=0.002$). The comparison between iNPH and sVD showed a cut-off value of 1676.10^{-6} mm²/s (sensitivity 0.70, specificity 0.77) in periventricular frontal area. INPH group, in comparison with NA group, showed significantly higher ADC in all ROIs. The iNPH group also showed significantly higher ADC than AD group in all ROIs. AD group showed significantly lower ADC than sVD group in all regions, except in normal appearing lenticular nuclei and caudate nuclei corpus deep ROI. SVD group showed significantly higher ADC than NA in all ROIs, except in normal appearing lenticular nucleus ROI. Different patterns of ADC values can differentiate between AD, sVD and iNPH, even when other MRI sequences appear morphologically similar.

Introduction

As the European population gets older, the incidence of neurological disorders is increasing, with an ever-increasing impact on social costs [1]. Despite differences in disease etiology, several brain disorders in the elderly, e.g., Alzheimer's disease (AD), subcortical vascular dementia (sVD) and idiopathic normal pressure hydrocephalus (iNPH), share dementia as a common clinical feature. The current treatment for the majority of these diseases is merely symptomatic and does not modify the course of the illness. The only symptoms that may be modified are those of iNPH, provided they are recognized in time and treated appropriately [2]. It has been suggested that other dementias, including AD and sVD, may coexist with, or be misdiagnosed, as iNPH. Patients with AD or sVD may demonstrate large ventricles as a result of cerebral atrophy and may also have normal pressure hydrocephalus-like symptoms, such as gait disturbance or urinary incontinence, related to various degrees of white matter ischemia [3].

White-matter hyperintensities (WMHs) are typically observed in patients affected by sVD, but can also be present in patients who fulfill the clinical diagnostic criteria for typical AD or iNPH. In iNPH, white matter changes appear as confluent periventricular hyperintensities (PVH) on MRI, most pronounced around the frontal horns. The extent of PVH correlates with the severity of clinical symptoms and cerebro-spinal fluid (CSF) markers of neuronal degeneration [2].

In recent years, there have been numerous diffusion-weighted MR imaging (DWI) studies describing an increased water diffusivity in T2-weighted hyperintense areas and in normal-appearing white

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http://dx.doi.org/10.1016/j.neurad.2017.08.001
0150-9861/

matter (NAWM), in patients with impaired cognitive performance [4]. Diffusion-weighted imaging, dependent on the motion of water molecules, provides information regarding tissue integrity [5]. DWI allows assessment of the water apparent diffusion coefficient (ADC), a measure of tissue water diffusivity. ADC depends on the interactions between water molecules and the chemical environment, as well as the structural barriers at cellular and sub-cellular level hindering their motion in vivo. An increase in water diffusivity may be caused by degeneration of microstructural barriers, such as loss of membrane integrity and myelin, or decreased cellular density [6–8].

It remains unclear if ADC can discriminate between the different types of dementia. The aim of this study was to explore the difference in periventricular and deep white matter diffusion patterns in patients diagnosed with AD, sVD, normal aging (NA) and with possible iNPH.

Materials and methods

Patients

This is a retrospective, case-control study conducted over a two-year period from August 2014 to August 2016, at a university-affiliated hospital in Martinique (French West Indies). Thirty-five consecutive patients with a diagnosis of iNPH were identified by electronic search of the hospital PACS and RIS using the search term "Normal pressure hydrocephalus". Two of the 35 patients were excluded because of artifacts degrading image quality and a further three were excluded due to secondary causes of hydrocephalus (one meningitis, two subarachnoid hemorrhage). This left 30 patients in the iNPH group. The last 30 consecutive patients with clinical and radiological characteristics of AD [9,10] and sVD [11,12] were identified from our database and matched with 30 patients in the normal aging control group. Therefore, a total of 120 patients were included. All patients underwent MRI with a 1.5 Tesla magnet (General Electric Optima MR450 W). The groups were defined as follows:

- idiopathic normal pressure hydrocephalus (iNPH) (group 1);
- Alzheimer's disease (AD) (group 2);
- subcortical vascular dementia (sVD) (group 3);
- age-matched normal aging brain (NA) (group 4).

Idiopathic normal pressure hydrocephalus (iNPH) (group 1)

The diagnosis of possible idiopathic normal pressure hydrocephalus (iNPH) (group 1) (mean age: 77.4 ± 8.38; male: 17; female: 13) was based on the presence of the following criteria, based on the guidelines drawn up by Relkin et al. [13]:

- clinical suspicion of iNPH addressed by neurologist or geriatrician (one or more symptoms of dementia, gait disturbance or urinary incontinence, progressive over time, with a minimal duration of at least 6 months);
- enlarged lateral ventricle with Evans index > 0.3 (maximal width of frontal horns/maximal width of inner skull);
- posterior callosal angle (angle between lateral ventricles on coronal T1WI slice crossing posterior white commissure) < 90°;
- tight high-convexity and medial subarachnoid spaces with expanded sylvan fissure on coronal T1-weighted MRI;
- absence of known or visible disorders (i.e. subarachnoid hemosiderin deposit, meningitis, obstruction) causing ventriculomegaly.

Alzheimer's disease (AD) (group 2)

The diagnosis of Alzheimer's disease (AD) (group 2) (mean age: 76.1 ± 10.1; M: 14; F: 16) was based on the presence of the following:

- clinical suspicion of AD addressed by neurologist or geriatrician following the National Institute of Neurological and Communication Disorders and Stroke-Alzheimer's Disease and Related Disorders Association Criteria, as described in McKhann et al. [14];
- thinned gyri, widened sulci, and enlarged ventricles; medial temporal lobe, particularly hippocampus (high Scheltens scale[10,15]: 3 or 4/4) and entorhinal cortex disproportionately affected;
- no or slight periventricular and deep white matter disease (Fazekas scale[12] 0 or 1/3).

Subcortical vascular dementia (sVD) (group 3)

The patients with subcortical vascular dementia (sVD) (group 3) (mean age: 80.5 ± 9.6; M: 14; F: 16) met clinical criteria of the Diagnostic and Statistical Manual of Mental Disorders-IV for vascular dementia [16]. They had significant white matter hyperintensities on MR imaging in accordance with modified criteria of Fazekas et al. [12]: irregular periventricular T2 hyperintensity extending into the deep white matter, with large confluent areas, classifying Fazekas 3/3.

Normal aging control patient group (group 4)

The normal aging control patient group (group 4) (mean age: 72.1 ± 7.9; M: 12 F: 18) had no history of neurologic or psychiatric illnesses. This group underwent MRI for investigation of peripheral vertigo. All examinations were negative for cerebral and otological pathology.

All MRI examinations were reviewed by two radiologists in consensus (AA and AG) with 12 and 2 years of experience in neuroradiology respectively.

MR imaging protocol

For all patients, the following sequences were performed in the axial bi-commensural plane:

- diffusion-weighted imaging measured in 3 directions (*x*, *y* and *z*) with *a b* value of 0 and 1000 s/mm^2 (SE-EPI) (Repetition Time: 6500 ms; Echo Time: 76.1 ms; Flip Angle: 90°; thickness: 5 mm; space: 1 mm; FOV: 250 × 250 mm; Imaging matrix: 128 × 192; NEX: 2). Apparent diffusion coefficient maps were performed and measured in different regions of interest (ROI) mentioned above;
- axial T2-weighted image (WI) Fluid-Attenuated Inversion Recovery (FLAIR) (Repetition Time: 9800 ms; Echo Time: 164 ms; Thickness: 5 mm space 1 mm; FOV: 250 × 250 m: Imaging matrix: 320 × 256; NEX: 1) merged to the ADC slice, in order to correctly position the ROI from the ADC map, evaluate Evan's index and Fazekas scale;
- 3D Inversion recovery T1-WI (Repetition time: 11 ms; Echo time: 4.4 ms; Inversion time: 500 ms; Flip angle: 12°; thickness: 1.40 mm; space: 0.7 mm; FOV: 240 × 190 mm; Imaging matrix: 288 × 256; NEX: 1) in order to measure the posterior callosal angle and Scheltens scale.

Three transaxial slices were used for image analysis, as seen in Fig. 1:

Please cite this article in press as: Goujon A, et al. Can MRI water apparent diffusion coefficient (ADC) value discriminate between idiopathic normal pressure hydrocephalus, Alzheimer's disease and subcortical vascular dementia? J Neuroradiol (2017), http://dx.doi.org/10.1016/j.neurad.2017.08.001