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Neurochemical–structural changes evaluation of brain in patients with obstructive sleep apnea syndrome

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ABSTRACT

Purpose: To evaluate neurochemical and structural changes in the patients with newly diagnosed obstructive sleep apnea syndrome (OSAS) by MR spectroscopy (MRS), T2 relaxometry, and diffusion weighted imaging (DWI).

Material and methods: Following the acquisition of routine cranial MR, MRS, T2 relaxometry, and DWI images; spectroscopic metabolite ratios and DWI–T2 relaxometry findings of the thalami, hippocampi, frontal white matter (FWM) and frontal cortex of 24 OSAS patients and 9 controls were statistically compared. The relationship between two groups was evaluated with Mann–Whitney test.

Results: Spectroscopic measurements in the frontal cortex and frontal white matter of the OSAS patients revealed significantly lower NAA/Cr ratios than those of the control group ($P = 0.004$ and $P = 0.006$, respectively). The measurements in the frontal white matter of the OSAS patients exhibited significantly lower NAA/Cho ratios compared with those of the control group ($P = 0.005$). Thalamic Cho/Cr ratios of the patient group were significantly higher than those of the control group ($P = 0.002$). In terms of the ADC–T2 relaxometry values, there was no significant relationship between the patient and the control groups ($P > 0.05$).

Conclusion: MRS is a useful and non-invasive modality in showing neurochemical changes in various regions of the brain but our data does not show any change on diffusion weighting or T2 quantification in the OSAS group. DWI and T2 relaxometry appear to be not effective techniques to evaluate the brain structural changes of the patients with newly diagnosed OSAS.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized with intermittent hypoxic episodes that repeat along the night [1]. OSAS patients demonstrate sleepiness and attention deficit during daytime which indicate disruption of the psychomotor functions. The structural and functional changes which may arise in the brain as a result of these hypoxic episodes may lead to cognitive deficits [2–4]. Many studies have shown that cognitive dysfunction in OSAS patients are associated with chronic intermittent hypoxia [3–6].

With the advance of magnetic resonance (MR) technology, various techniques such as magnetization transfer, diffusion weighted imaging (DWI), MR spectroscopy (MRS) and T2 relaxometry have been used to characterize the structural features of the brain tissue in various pathological situations [7,8]. DWI, T2 relaxometry, and MRS are neurochemical–structural techniques, which provide a quantitative and objective means for evaluating abnormal tissue conditions [7,8].

MRS is a non-invasive technique demonstrating some of the metabolites in the brain tissue. Decreased NAA/choline (Cho) and NAA/creatine (Cr) ratios suggest the presence of cerebral damage, probably caused by repeated apneic episodes [1–4]. Although it is commonly used in differentiating a variety of brain lesions, the number of articles evaluating its efficacy in the diagnosis of OSAS is limited [4,9–13].

DWI and T2 relaxometry can evaluate cerebral injury, and assess free water content in the cerebral tissue, a measure that increases with tissue injury, such as damage to the myelin and axons [3,14]. Increased T2 relaxation times and ADC values can result from subacute processes, such as vasogenic edema after hypoxia–ischemia,

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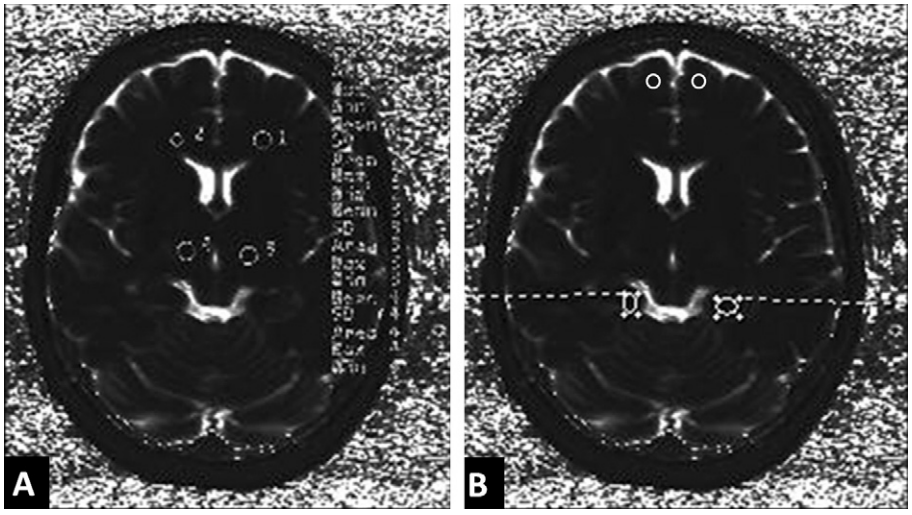

Fig. 1. Axial T2 map images. ROI (region of interest) sites, determined for T2 relaxometry measurements, are outlined from the frontal white matter-thalami (A) and the frontal cortex-hippocampi (B).

as well as chronic pathological conditions like chronic ischemia, gliosis, and demyelination [14]. As a result, DWI and T2 relaxometry may help detecting subtle structural abnormalities in 'routine cranial MR negative' OSAS patients [3,15].

In the literature, structural–neurochemical changes have been reported in many regions of the brain, with a strong emphasis on the structural changes particularly in the frontal cortex, frontal white matter (WM), thalamus, and hippocampus in OSAS patients [2–4]. In the current study, we aimed to detect the neurochemical and structural changes in those regions of the brain by non-invasive and quantitative MR imaging (MRI) methods (DWI, T2 relaxometry, and MRS). There are a limited number of studies in the literature evaluating the role of MRS and T2 relaxometry in OSAS [2,4,12,13]. As far as we know, there is no study on the use of DWI in the evolution of the structural changes in OSAS in the literature.

2. Materials and methods

2.1. Patient population

From June 2006 to December 2008, 24 patients with OSAS (23 males, 1 female, mean age: 52; age range: 38–68) and 9 age matched controls (6 males, 3 females; mean age: 48; age range: 41–61) underwent MRI protocol of our prospective study in our hospital. The patients suffering from newly diagnosed OSAS, who were sent to our radiology department for routine MRI, were included in the study. Sleep analysis full polysomnography (PSG) based on the guidelines of the American Electroencephalographic Society was performed for each patient during the last two weeks before our MRI study protocol [11,16]. Excessive daytime sleepiness was assessed by using the Epworth Sleepiness Scale (ESS) [9]. OSAS diagnosis was based on the criteria outlined by the international classification of sleep disorders [11,17].

The patients included in the control group had no pathological findings or additional illnesses. Control patients were selected from healthy individuals with no sleep disorder. Patients with trauma, malignancy, intracranial mass, psychiatric disease, were also not included in the patient group. The same MRI protocols were performed on control and patient groups. The study was approved by the Ethics Committee of our hospital. Written informed consent was obtained from all the individuals for participation in the study.

2.2. MRI examinations

MRI examinations were performed on a 1.5 T MR device (Magnetom Vision Plus, Siemens, Erlangen, Germany), covering T1-weighted (W) (TR/TE: 550/18, matrix: 192 × 256, FOV: 230 mm, slice thickness: 4 mm and slice gap: 1 mm), T2W (TR/TE: 5500/90 FOV: 230 mm, matrix: 345 × 512, slice thickness: 2 mm), proton-W (TR/TE: 5500/22) sequences, DWI, and T2 relaxometry. DWIs were obtained with single-shot, spin echo echo-planar imaging sequence (TR 6000, TE 139, number of acquisition (NEX) 1, matrix: 96 × 200, FOV: 240 mm, slice thickness 5 mm and slice gap 0 mm) in the axial plane. This sequence is labeled as 'b0-b500-b1000-apparent diffusion coefficient (ADC)' by the manufacturer. ADC values were obtained from automatically generated ADC maps with region of interest (ROI) evaluations. T2 relaxometry studies were conducted with axial Carr-Purcell-Meiboom-Gill multiple spin echo sequence (TR/TE: 2000/22.5–45 ms, slice thickness: 5 mm, NEX: 1, matrix: 154 × 256, FOV: 236 mm). From the obtained sixteen echo signals, mean T2 relaxation times of their pixels were measured. Images for ADC and T2 relaxometry studies were obtained as to encompass the hippocampi and thalami.

Following those sequences, MRS using PRESS sequence was performed by placing an $2 \times 2 \times 2\,cm^3$ volume of interest (VOI) in the frontal white matter, frontal cortex, thalamus, and hippocampal region (TE/TR: 135/2000, NEX: 136). Prior to the PRESS sequence, following placement of VOI in the appropriate site, automatic shimming was performed with 3–7 Hz line width for optimum intravoxel signal. Ninety degrees Gaussian pulse was applied after the spoiler gradient for water suppression. Following Fourier transformation, linear baseline values were corrected. Total duration of all MR examinations was about 25–30 min.

Following the acquisition of all the images: MRS, T2 relaxometry, and ADC maps were evaluated by two experienced radiologists (O.A., G.G.), blinded to the clinical and laboratory data, at the workstation of our MR unit. The ratios of NAA/Cr, Cho/Cr and NAA/Cr peaks for each region were calculated by commercially available software of our MR unit. T2 and ADC values were measured bilaterally in the hippocampal region, the frontal cortex, the frontal white matter, and the thalamus by placing a cursor over the region of interest (Figs. 1 and 2). By dividing the total of bilateral measurements by 2, the mean ADC and T2 relaxation time values for each region were calculated. The mean values of the metabolite ratios of MRS, T2 relaxometry–ADC values were statistically compared between two groups.