Apparent diffusion coefficient of the superior cerebellar peduncle differentiates progressive supranuclear palsy from Parkinson's disease.

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Introduction

The early diagnosis of progressive supranuclear palsy (PSP), a sporadic neurodegenerative disorder, may be challenging, because of clinical overlapping features with Parkinson's disease (PD) and other parkinsonian syndromes [1]. Conventional MRI can help in differentiating parkinsonian disorders but its diagnostic accuracy is still unsatisfactory [2]. On the basis of the pathological demonstration of superior cerebellar peduncle (SCP) atrophy in PSP patients [3], we assessed the SCP apparent diffusion coefficient (ADC) values in PSP and PD patients in order to evaluate its feasibility, reproducibility and diagnostic value *in vivo*.

Methods

Forty-three patients presenting with parkinsonian syndromes and sixteen healthy controls were studied. According to the UK Brain Bank Criteria [4] fifteen patients had typical PD, and, on the basis of National Institute of Neurological Disorders and Stroke criteria for PSP [5], twenty-eight patients had PSP. Subjects were studied in a 1.5T GE (Milwaukee, Wisconsin) Signa Horizon LX whole-body scanner. T1-weighted structural and diffusion-weighted axial MR images were acquired with 5 mm thickness and 1 mm inter-slice gap. As previously reported [6,7], diffusion-weighted MRI was conducted using a spin-echo single-shot EPI sequence and diffusion weighting gradients were applied along three orthogonal axes and at three gradient strengths (b-values= 300, 600, and 900 s/mm^2). In addition, T2-contrast EPI images without diffusion weighting were acquired. The ADC trace map was generated as the mean value of three orthogonal directions, determined pixel-wise using a least-squares fit, after registration to correct for eddy current distortions using software FLIRT (www.fmrib.ox.ac.uk/fsl). The T2-weighted image was segmented using the FAST algorithm (www.fmrib.ox.ac.uk/fsl) to exclude pixels containing significant amounts of CSF. Finally, using FLIRT, the diffusion data was registered onto the T1 scan. The left and right SCP were manually selected on T1-weighted images (Figure 1).

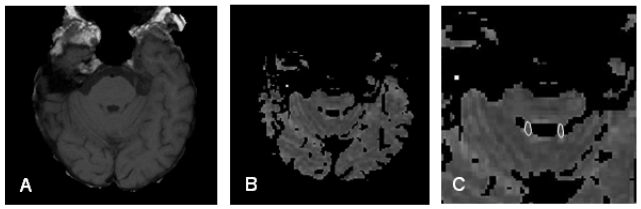

Figure 1. (A) T1-weighted SE scan; (B) CSF-masked apparent diffusion coefficient (ADC) map; and (C) zoomed superior cerebellar peduncles on the ADC map from a normal subject. Regions of interest were defined on T1-weighted SE scans and then pasted onto registered ADC maps.

Two independent raters blinded to the patient's diagnosis separately evaluated all MR and DWI images. To assess the intrarater reliability, a second evaluation was made two weeks after the first evaluation by one of the two raters. Sensitivity, specificity and positive predictive values for differentiating PSP from PD and PSP from controls were calculated using the optimal cut-off values determined by ROC (receiver operating characteristic) curve analysis [8]. Optimal cut-off level was considered the value that has the highest sum of sensitivity and specificity. All tests were two-tailed and the α level was set at $p<0.05$. Statistical analysis were performed using SPSS for Windows (version 12.0, Chicago, IL).

Results

The intra-class correlation coefficients showed strong agreement between left and right SCP ADC values ($r=0.96$; $p<0.001$). The intra-rater reliability showed strong agreement between the first and the second evaluation for the first operator ($r=0.98$, $p<0.001$). The inter-rater reliability of the measurements procedure was 0.96 for SCP mean values ($p<0.001$). Comparing the SCP ADC mean values between the three groups, the Kruskal-Wallis test showed a highly significant ($p<0.001$) difference: the SCP ADC mean values were higher in PSP patients (median=0.98 x 10^{-3}mm^2/s, range=0.95-1.15) than in PD patients (median=0.79 x 10^{-3}mm^2/s, range=0.77-0.84) and controls (median=0.80 x 10^{-3}mm^2/s, range=0.75-0.86). No difference was found in SCP ADC mean values between PD patients and control subjects. SCP ADC mean values in PD patients or in the controls did not exceed the lowest SCPs values observed in the PSP group (Figure 2). Using a cut off value of 0.89 x 10^{-3}mm^2/s, the sensitivity of SCP ADC values to correctly diagnose PSP (proportion of PSP patients with a value greater than the threshold) was 100%. The specificity (proportion of PD patients with SCP ADC values less than 0.89) was 100%; the positive predictive value of SCP ADC (likelihood of a subject with SCP ADC values higher than 0.89 to have PSP) was 100%.No correlations were found between ADC SCP values and clinical findings (age at examination, age at onset, duration and severity disease quantified by standardised clinical scale evaluation) in PSP or PD patients.

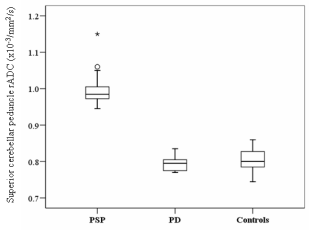

Figure 2. Box plot of the superior cerebellar peduncle (SCP) apparent diffusion coefficient (ADC) values (10^{-3} mm^2/s) from patients with PSP, PD, and controls. Note that none of the SCP ADC values in the PSP group is lower than the highest value in the PD or control group.

Conclusions

An increase in mean SCP ADC values in PSP but not in PD patients was detected, showing a diagnostic accuracy of 100% in differentiating between patients with PSP and PD. The higher values of ADC in SCP of PSP patients indicate *in vivo* microstructural changes that likely correspond to atrophy as detected in previous post-mortem study [3]. These results provide a new MR marker to be included in the early diagnostic assessment of patients with parkinsonisms.

References

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