Imaging Hereditary Spastic Paraplegia: inputs from OCT and MRI.

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Introduction: *The in-vivo objective documentation of pathological changes in neurodegenerative disease is a major aim that will improve our diagnostic and prognostic ability and offer an efficient way to monitor disease progression and response to treatment.*
AIM: To explore the sensitivity of brain imaging by MRI (DTI, MRS) and retinal thickness by optical coherence tomography (OCT) to pathology specific changes in a cohort Hereditary Spastic Paraplegias (HSP) patients.

Methods: *22 molecularly defined HSP patients and 22 age-gender matched controls were recruited and studied. 1.5 T MRI protocol included DTI imaging and MRS focusing on the cortico-spinal tract and the pre-motor area (Fig. 1). Correlations with the clinical severity was tested using the Spastic Paraplegia Rating Scale (SPRS)(1).OCT protocol in 21 patients included papillary and macular scan by Spectralis.*

Risults: *DTI highlighted a significant alteration of FA and MD along the CST (Fig. 2) which correlated with SPRS scores (p<0.005) (2). SPRS significantly correlated to temporal variables such as age at onset and disease duration (model R2 = 0.327, p<0.0001, n=69; SC ß= - 0.276, p=0.014 for age at onset; SC ß= 0.408, p<0.0001 for the reported disease duration)(Fig.3). Inconclusive results were obtained by MRS.*
OCT was performed in a cohort of 21 HSP patients, n=20 had a molecular confirmed diagnosis (Table 1). All patients had performed a baseline OCT exam, and only 6 of them had another point of 6-12 months follow-up.
From the baseline data we observed that nearly 9/21 (42.8%) had a reduction of the nasal quadrant of RNFL on Right and Left Eye. In addition, 33% of the cohort had retinal nerve fibre layer (RNFL) reduction in the inferior quadrant of Right Eye (Fig. 4). The other quadrants appeared affected only in small percentages. From the OCT follow-up analysis (n=6), we observed that only one patient (SPG8) had a thinning of19% and 22% in the Superior and Inferior Right Eye RNFL respectively as compared to baseline data.

Conclusions: *Imaging by MRI and OCT can provide valuable biomarkers for HSP. The detected abnormalities provide expand the knowledge of the affected CNS areas and may contribute to the understanding of the pathophysiological mechanisms of the various SPG types.*

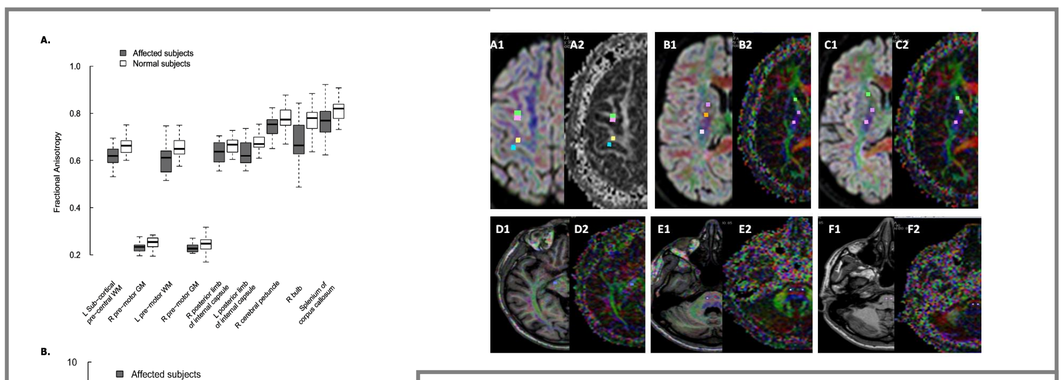

Figure 1. *Examples of ROIs manually positioned along the CST (squared colored dots) for analysis of the diffusion values.*

Figure 2. *DTI values in controls and HSP for FA (A) and MD (B). Only anatomical areas with statistically significant differences are reported (ANOVA, p-values not adjusted for multiple comparisons ranged between 0.002 and 0.048).*

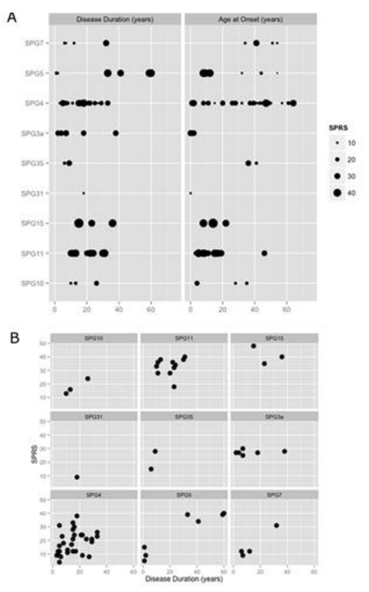

Figure 3. *The disease duration and age at onset for the various SPG forms. (A) Dot-plot illustrates the disease duration and age at onset size-scaled by the magnitude of SPRS score for patients in different HSP forms. (B) Scatter-plot with a matrix of panels, showing correlation between age of onset and disease duration and SPRS for different SPG forms.*

Table 1. *Demographic and clinical data on the OCT cohort.*

Demographics	
N=21	
Gender	11F; 10M
Clinical data, Mean ± SD (range)	
AAO	26.9 ± 21.7 (0-74)
Age at OCT	44.7 ± 18 (14-76)
DD	17.8 ± 13 (2-50)
SPRS	22.7 ± 10.2 (3-36)
Phenotype	20 Pure, 1Complex
Genotype, nr of patients	
SPG3A	5
SPG4	8
SPG5	1
SPG7	2
SPG8	2
SPG72	2
Unknown	1

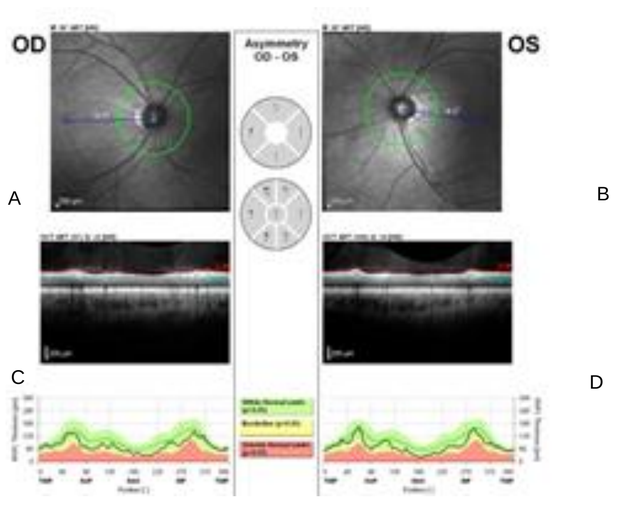

Figure 4. *Image of one HSP SPG3A patient Spectral Domain OCT. Top panels (A, B) show the optic nerve anatomy and peripapillary (green) ring scan of right (OD) and left (OS) eye. Panels C and D show virtual cross sections of peripapillary retina followed beneath from the quantitative spatial analysis (E, F) expressed in black line. In this patient a borderline level of RNFL was observed at the nasal quadrant of both eyes.*

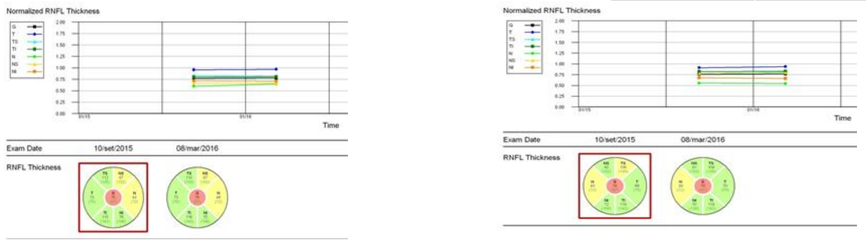

Figure 5. *RNFL thickness, confronting a patients at baseline and 1 year follow-up for right (A) and left (B) eye.*

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Bibliografia: *1. Schüle R et al., 2006 Neurology; Aug 8: 430-4. 2. Martinuzzi et al., 2016 PLoS One. Apr 14;11(4).*