

WHITE MATTER CHANGES IN PRIMARY PROGRESSIVE APHASIA: A TRACT-BASED SPATIAL STATISTICS ANALYSIS

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INTRODUCTION

The purpose of this study was to evaluate the extent and localization of white matter (WM) damages in individuals with primary progressive aphasia (PPA) by using Tract-Based Spatial Statistics (TBSS, <http://fsl.fmrib.ox.ac.uk/fsl/tbss>). Voxel and tract-based analyses of multi-subject Diffusion Tensor Imaging (DTI) studies can suffer from possible misalignment errors of images and they can leave a certain arbitrariness of choices. TBSS is a standardized tool that has been proposed to overcome this arbitrariness. The aim of this work was to extend the findings of previous Voxel and tract-based studies that described the WM involvement in the 3 major subtypes of PPA: non-fluent/agrammatic PPA (PNFA), characterized by agrammatism, motor speech errors and left inferior frontal damage; semantic variant PPA (SD), characterized by single-word comprehension and retrieval deficits, loss of semantic knowledge, surface dyslexia and anterior temporal atrophy; the logopenic variant PPA (LPA), characterized by word-finding deficits, phonological errors in spontaneous speech and naming, sentence repetition impairment and left posterior temporal and inferior parietal damage [1, 2, 3].

MATERIALS AND METHODS

Data Acquisition: 27 PPA patients (9 LPA, 9 PNFA, 9 SD) and 21 age-matched healthy controls (48 subjects, 29 f, 19 m, mean age 64.3 ± 5.6 years, recruited through the Memory and Aging Center at UCSF) underwent a single-shot spin-echo echo-planar diffusion weighted imaging (DWI) acquisition on a 3T Siemens Trio Tim system equipped with a eight-channel head coil (repetition time/echo time= 8000 ms/109 ms, 55 slices, $2.2 \times 2.2 \times 2.2$ mm³ resolution, GRAPPA parallel acceleration factor 2, 64 diffusion gradient directions, $b = 2000$ s/mm²).

Data Analysis: After the correction for eddy current distortion and motion, fractional anisotropy (FA) and mean diffusivity (MD) maps were computed from the DWI datasets using the FSL FDT tool. Each of the 3 PPA variant groups was separately compared to the healthy controls (HC) group. A spatial normalization was performed by transforming all maps to a target FA image (in each of the HC/patients subgroup) that was affine-aligned to the MNI152 standard space. TBSS analysis was carried out on FA and MD maps projected into a common WM skeleton using randomize (10000 permutations) with the Threshold-Free Cluster Enhancement option [4] and the statistical maps were family wise error (FWE) corrected for multiple comparisons.

RESULTS

The different PPA variants showed FA and MD significant effects on white matter pathways implicated in language processing with patterns characteristic of each variant. In LPA patients, while FA was not significantly different from HC, in the left hemisphere increased MD ($p < 0.05$) was found in the Corpus Callosum (CC), in the posterior parieto-temporal components of the superior longitudinal fasciculus (SLF), in the posterior components of the inferior longitudinal fasciculus (ILF) and in the inferior fronto-occipital fasciculus (IFOF) (Fig.1). SD and PNFA variants showed relevant and quite spread effects on WM that became very focused by decreasing the statistical threshold ($p < 0.001$). While for SD patients very significant FA reductions (Fig.2) and MD increases were evidenced mainly in the left anterior temporal portions of the ILF and uncinate fasciculus (UF), for PNFA patients strong FA reductions (Fig.3) and MD increases were mainly evidenced bilaterally in the CC and on fronto-angular and fronto-supramarginal components of the left SLF. An increase of MD was also found on the anterior part of the left IFOF and of the left thalamic radiation. In all the figures the common WM skeleton is reported in green superposed to the target FA image. The significant regions are reported in red-yellow (increasing significance level).

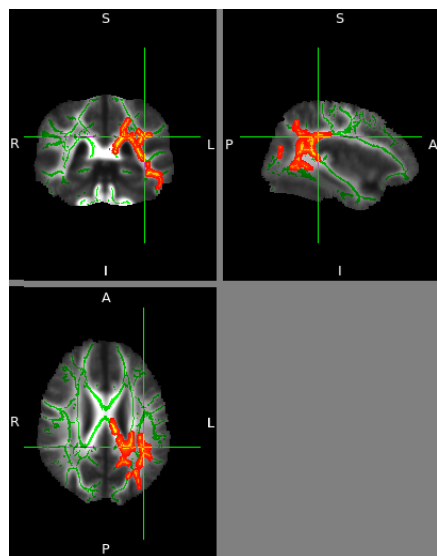


Fig.1: LPA subjects. Significant increase of MD ($p < 0.05$) in patients compared to controls.

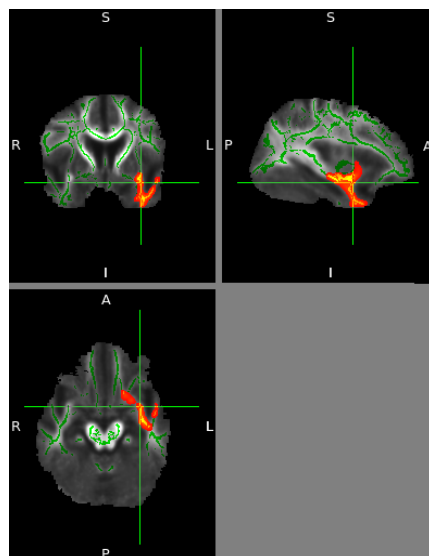


Fig.2: SD subjects. Significant reduction of FA ($p < 0.001$) in patients compared to controls.

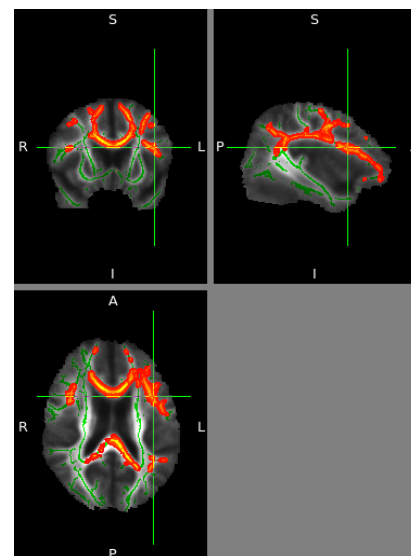


Fig.3: PNFA subjects. Significant reduction of FA ($p < 0.001$) in patients compared to controls.

DISCUSSION AND CONCLUSIONS

Characteristic patterns of WM damage in the three major variants of primary progressive aphasia were evidenced and characterized by means of TBSS, that showed to be a useful standardized technique to investigate WM integrity in PPA pathologies. WM damage was found to be less pronounced and limited to left parieto-temporal pathways in LPA variant, while SD and PNFA patients showed spreader WM damage, with very remarkable effects on the anterior temporal portion of the left ILF and UF for SD, and of the fronto-parietal components of the left SLF and in the CC for PNFA. Since strong gray matter atrophy is present in PPA patients, a careful check of co-registrations in critical regions and the introduction of a parameter as covariate to check for atrophy effects in the statistical analysis are further steps. This will complete the results obtained with a canonical TBSS analysis and here reported.

REFERENCES: [1] Gorno-Tempini M.L. *et al.*, *Ann Neurol.* **55**, 335-46 (2004) [2] Gorno-Tempini, M.L. *et al.*, *Neurology* **71**, 1227-34 (2008) [3] Galantucci S. *et al.*, *Brain* **134**, 3011-29(2011) [4] Smith S.M. *et al.*, *Neuroimage* **44**, 83-98 (2009)