

# BRAIN DISCONNECTION AND ATROPHY IN NORMAL TENSION GLAUCOMA

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## Objectives

To assess in normal tension glaucoma (NTG) the possible presence of brain changes within and beyond the visual system, which we have previously demonstrated in both early and advanced stages of primary open angle glaucoma (POAG) [1,2].

## Materials

Multimodal brain MRI was acquired in NTG patients (n=17, age=58.9±13.7 years, stage: mild [n=10], moderate [n=2], severe [n=5]) and age-matched normal controls (NC, n=29, age=57.9±9.9 years).

## Methods

Anatomical connectivity (AC) along white matter (WM) tracts was assessed, at group level, with TBSS after using, in single subjects, DTIPrep for artefacts removal and FDT to obtain images of fractional anisotropy (FA), axial and radial diffusivity (AD and RD).

Functional connectivity (FC) within each resting state network (RSN) (short-range FC) was evaluated, in single subjects, with ICA-AROMA for motion correction and then, at group level, with MELODIC followed by dual regression (spatial maps and timecourses). FC between the different RSNs (long-range FC) was carried out with FSLNets. FSL-VBM was used to assess local grey matter (GM) volumes. Voxelwise statistics was performed with nonparametric permutation testing ( $p < 0.005$  uncorrected, cluster size  $\geq 30$  voxels).

## Results

### Anatomical connectivity

Compared to NC, NTG patients showed abnormal AC in both visual and nonvisual WM pathways. In particular, there was lower FA ( $0.23 \pm 0.03$  vs  $0.28 \pm 0.03$ ) in the optic tracts (Fig. 1a), higher AD ( $1.13 \pm 0.08$  vs  $1.01 \pm 0.02$  mm<sup>2</sup>/s) along the optic radiations, inferior lateral occipital cortex and lingual gyrus WM (Fig. 1b-c), but also in the superior longitudinal fascicle and precuneus cortex WM (Fig. 1f), and higher RD ( $0.65 \pm 0.08$  vs  $0.53 \pm 0.04$  mm<sup>2</sup>/s) in the superior parietal lobule WM and inferior frontal gyrus (Fig. 1g-h).

## Grey matter volumes

In terms of GM volumes, NTG patients showed regional atrophy ( $860 \pm 120$  vs  $1094 \pm 128$  mm<sup>3</sup>) mapping on the visual cortex (temporo-occipital fusiform cortex) (Fig. 1d) but also in distant regions (precentral gyrus, inferior frontal gyrus) (Fig. 1i).

## Short-range functional connectivity

Intranetwork FC was also altered in NTG patients compared to NC, being lower in the primary visual network (VN) (occipital pole,  $-0.89 \pm 3.3$  vs  $4.13 \pm 6.64$ , arbitrary units [au]) (Fig. 1e) and higher in the ventral attention network (VAN) (inferior frontal gyrus,  $3.42 \pm 3.3$  vs  $-0.86 \pm 3.48$  au) (Fig. 1l).

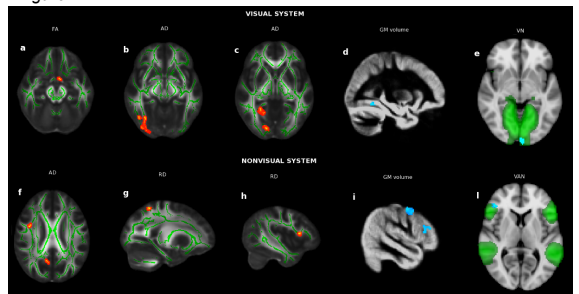
## Long-range functional connectivity

No differences in internetwork FC were found.

## Correlations

In NTG, lower thickness of the retinal nerve fiber layer, derived from Optical Coherence Tomography, correlated with lower FA in the OT ( $r = 0.75$ ,  $p = 0.001$ ).

Figure 1



## Conclusions

Similarly to POAG, both altered brain connectivity and GM atrophy occur in the NTG brain not only in the visual system but also beyond it. This provides evidence that widespread brain damage in glaucoma may be independent of the high eye pressure and further suggests glaucoma as a neurodegenerative condition [3].

**References** [1] Frezzotti P, Giorgio A, Motolese I, De Leucio A, Iester M, Motolese E, Federico A, De Stefano N. Structural and functional brain changes beyond visual system in patients with advanced glaucoma. PLoS One. 2014;9:e105931. [2] Frezzotti P, Giorgio A, Toto F, De Leucio A, De Stefano N. Early changes of brain connectivity in primary open angle glaucoma. Hum Brain Mapp. 2016 Aug 9. doi: 10.1002/hbm.23330. [3] Hardy J, Revesz T. The spread of neurodegenerative disease. The New England journal of medicine. 2012;366:2126-8.