

# STRUCTURAL CONNECTIVITY OF THE LEFT ANTERIOR TEMPORAL LOBE: A DIFFUSION TENSOR IMAGING STUDY

Nico D. Papinutto<sup>1,2</sup>, Sebastiano Galantucci<sup>2,3</sup>, Roland G. Henry<sup>2</sup>, Jorge Jovicich<sup>1</sup>, and Maria Luisa Gorno-Tempini<sup>2</sup>

<sup>1</sup>CIMEC, University of Trento, Mattarello, TN, Italy, <sup>2</sup>University of California San Francisco, San Francisco, CA, United States, <sup>3</sup>Scientific Institute and University Hospital San Raffaele, Milano, MI, Italy

## INTRODUCTION

The anterior temporal lobe (ATL) is crucial for higher order language functions, such as semantic memory, and it is involved in behavioral regulation [1,2,3]. Evidences of ATL damage are found in many neurological diseases, but little is known about the structural connections of this area with the rest of the brain. The aim of this study was to explore the architecture of the left ATL connectivity with many ipsilateral regions of the brain (in particular the areas known to have a key role in language) and to segment the left ATL based on these connectivity patterns, by using diffusion tensor imaging (DTI).

## MATERIALS AND METHODS

**Data Acquisition:** Using a 3 T Siemens Trio Tim scanner equipped with a eight-channel multi receive system, 21 healthy subjects recruited through the Memory and Aging Center at UCSF (8m, 13f, mean age  $65.3 \pm 3.6$  years) underwent a standard T1-weighted structural acquisition (3D MPRAGE,  $1 \times 1 \times 1 \text{ mm}^3$ ) and a diffusion weighted image (DWI) acquisition (2D SE-EPI sequence, 55 axial slices, resolution  $2.2^3 \text{ mm}^3$ , TR/TE 8000/109 ms, b-value= 2000  $\text{s/mm}^2$ , GRAPPA acceleration factor 2, 1 image without diffusion sensitizing gradient (b0) and 64 DWI with gradients along independent directions).

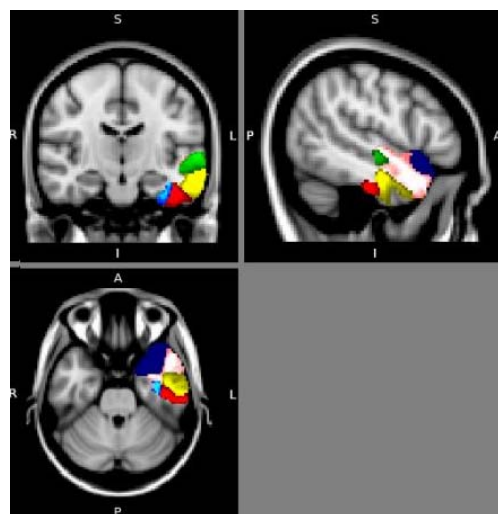
**Data Analysis:** All data analyses were performed using the FMRIB's FSL library tools (<http://www.fmrib.ox.ac.uk/fsl/>). 9 regions of interest (ROIs) including cortical gray matter (GM) and the underlying white matter (WM) were defined in the MNI-space using the FSL Harvard-Oxford (H-O) cortical structures atlas. The ROIs selected in the left hemisphere for this study were: the ATL, the posterior inferior temporal gyrus (ITG), the posterior middle temporal gyrus (MTG), the posterior superior temporal gyrus (STG), the posterior fusiform gyrus (Fus), the angular and supramarginal gyri (AG/SmaG), the occipital pole (OP), the triangularis and opercularis inferior frontal gyri (IFG) and the orbitofrontal cortex (OFC). After brain extraction, the diffusion-weighted datasets were corrected for eddy current distortions and motion and the tensor quantities calculated using the FSL FDT tool. Each subject's fractional anisotropy (FA) image was transformed to the MNI space using the T1-weighted image as an intermediate step (with both linear (flirt) and non-linear (fnirt) transformations). These transformations were inverted and applied to the 9 ROIs to work in the native diffusion spaces.

Using the ATL ROI as seed and the other ROIs as targets, probability levels for connectivity and the related segmentation of the left ATL were computed by using the probabilistic algorithm implemented in FSL (probtrackx) and based on Bayesian estimation of diffusion parameters (bedpostx) [4,5].

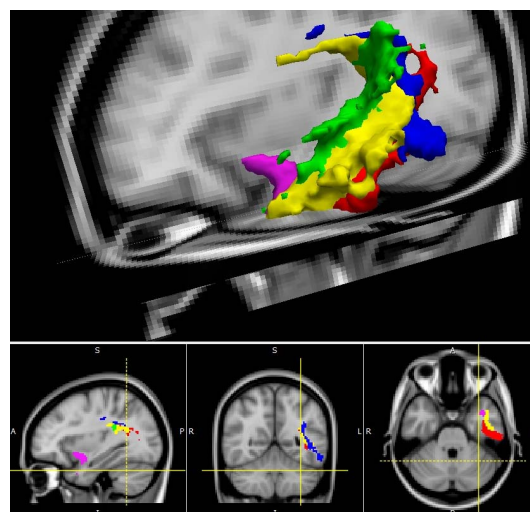
In parallel, connectivity distributions (hereafter called tracts) were obtained using various couples of the 9 ROIs as seed and target. For each subject and each voxel of the ATL ROI, the relative probability of connectivity with one of the 8 targets was created in 8 separate masks. These masks were transformed to the MNI space using the linear and non-linear transformations. Each voxel of the left ATL was then classified as mainly connected to one of the 8 different targets when its average level of connectivity on the 21 subjects group was higher than 30% (Fig.1). Tracts were thresholded to a value equal to 40% of the 95<sup>th</sup> percentile of the distribution of the number of streamlines passing in the voxels included in the tracts and then binarized. In the MNI space a normalized tract was finally created with the voxels belonging to a particular tract in at least 15% of subjects (Fig.2).

## RESULTS

No part of the ATL was found to be more connected to the IFG or AG/SmaG ROIs than to the other 6 target ROIs. The following pattern was defined in the segmentation (Fig.1): besides an anterior dorsal part of the left ATL connected to the OFC (through the uncinate fasciculus (UF)) and a more lateral and inferior region connected to the occipital pole through the inferior longitudinal fasciculus (ILF), 4 regions of the ATL were found to be mainly connected with the posterior sections of Fus, ITG, MTG and STG. Regarding the tracts (Fig.2), besides the UF and the ILF (not reported in figure, but basically parallel to the ATL-ITG connection reported in red), 3 tracts of interest were evidenced: a connection of the ATL with the SmaG/AG regions that remains in the STG WM (supporting the existence of the middle longitudinal fascicle in humans [6]), a long connection between the ATL and the IFG (that passes through the MTG and that could be an extension of the arcuate fasciculus to the ATL), and a posterior temporo-parietal connection between the posterior ITG and the AG/SmaG areas (that could correspond to the temporo-parietal subsection of the SLF previously described [7, 8]).



**Figure 1 (left):** Segmentation of the left ATL (21 subjects, MNI space) based on the highest probability of connectivity to 6 targets ROIs: light blue=Fus, red=ITG, yellow=MTG, green=STG, pink=OP, blue=OFC.



**Figure 2 (right):** High probability levels of connectivity of the left ATL (21 subjects, MNI space) with the ipsilateral OFC (violet), AG/SmaG (green), IFG (yellow), posterior ITG (red). In blue the connection of the lateral ventral posterior temporal pole with the parietal AG and SmaG regions is reported.

## DISCUSSION AND CONCLUSIONS

Using DTI on a group of 21 healthy subjects, possible connections of the left ATL with areas involved in language processing (middle/superior temporal gyri, angular gyrus, supramarginal gyrus, inferior frontal gyrus) were evidenced. We think the architecture of these possible connections and the ATL segmentation based on them can offer new insights into the understanding of the involvement of the left ATL in many higher order brain functions.

**REFERENCES:** [1] Warren J.E. *et al.*, Brain **132**, 3428-42 (2009) [2] Rankin K.P. *et al.*, Brain **129**, 2945-56 (2006) [3] Gorno-Tempini M.L. and C.J. Price, Brain **124**, 2087-97 (2001) [4] Behrens T.E. *et al.*, Magn Reson Med **50**, 1077-88 (2003) [5] Behrens T.E. *et al.* Neuroimage **34**, 144-55 (2007) [6] Makris N. *et al.*, Cereb Cortex **19**, 777-85 (2009) [7] Catani M. *et al.*, Ann Neurol **57**, 8-16 (2005) [8] Frey S. *et al.*, J Neurosci **28**, 11435-44 (2008)