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## Imaging biomarker discovery in major depressive disorder with diffusion MRI multi-compartment models

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## Introduction

- Major depressive disorder (MDD) is a disease widespread all over the world associated with a large and increasing economic, societal, and personal burden [Ferrari 2013]
- Despite a large number of studies, the pathophysiology underlying MDD is not well understood
- We propose a tract-based pipeline analysis using multi-compartment models (MCM) that allows to model water diffusion under the voxel resolution

## Data

- Actidep: Major depressive disorder in the elderly population 40 patients and 28 controls
- Clinical interest: Depressive symptoms in late life are associated with an increased risk of developing dementia [Barnes 2012]
- MRI acquisitions
  - Cusp: DWI with 1.5 mm isotropic resolution, 60 gradient orientations and 7 b0 [Scherrer 2012]
  - MPRAGE: T1-weighted images 1 mm isotropic
  - Resting state fMRI

## Methods

### Input:

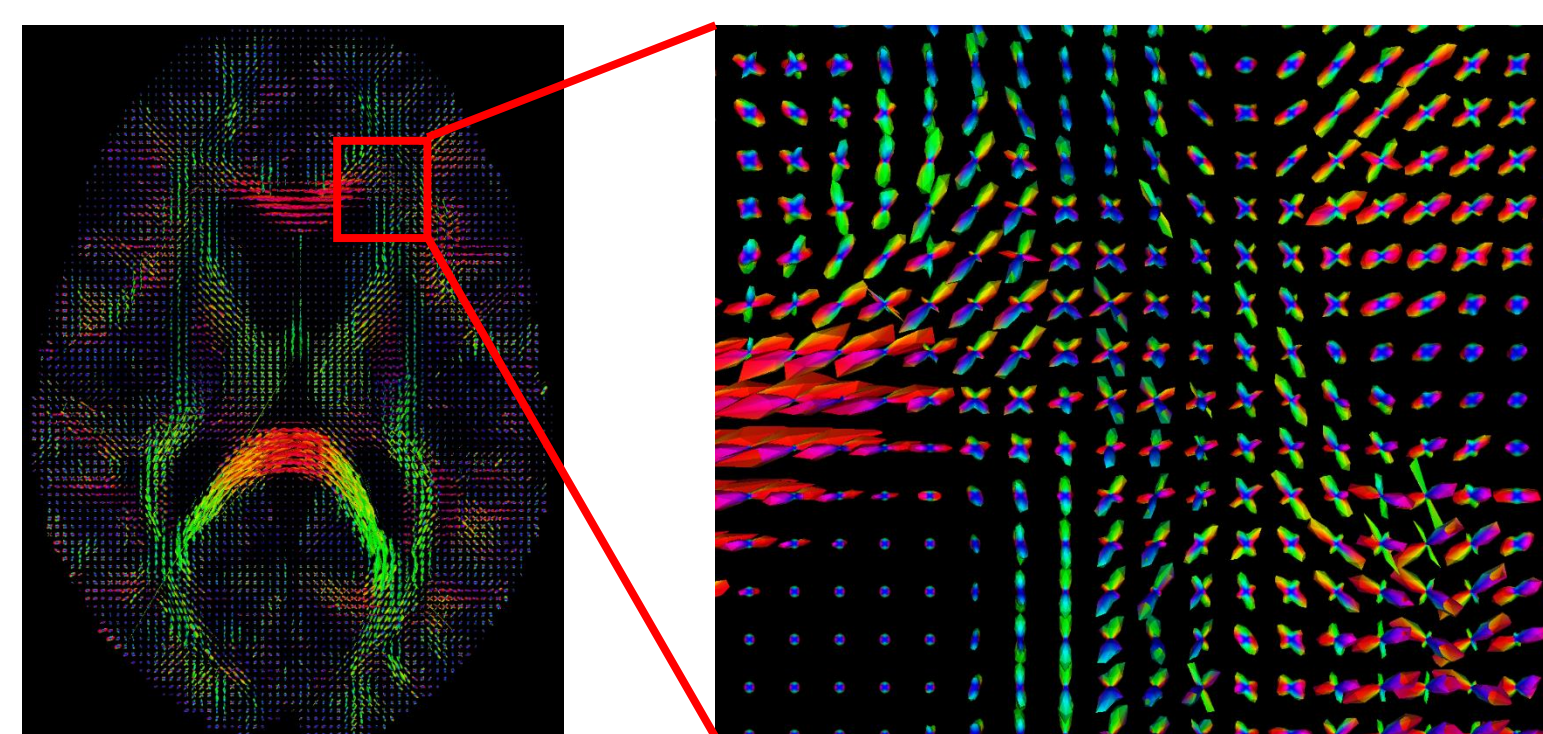
- DWI with several b-values to estimate complex models
- T1-weighted image for registration purpose

### DWI preprocessing



### Multi-compartments models

- Estimate MCM [Stamm 2016] that decomposes the water diffusion as a weighted sum of anisotropic and isotropic compartments



- Extract scalar maps (FA, MD, FW ...) from MCMs
  - ⚠ MCM FA is the average of each anisotropic compartment FA  $\neq$  DTI FA
- Rigid registration of preprocessed DWIs and scalar maps on MNI152 Atlas

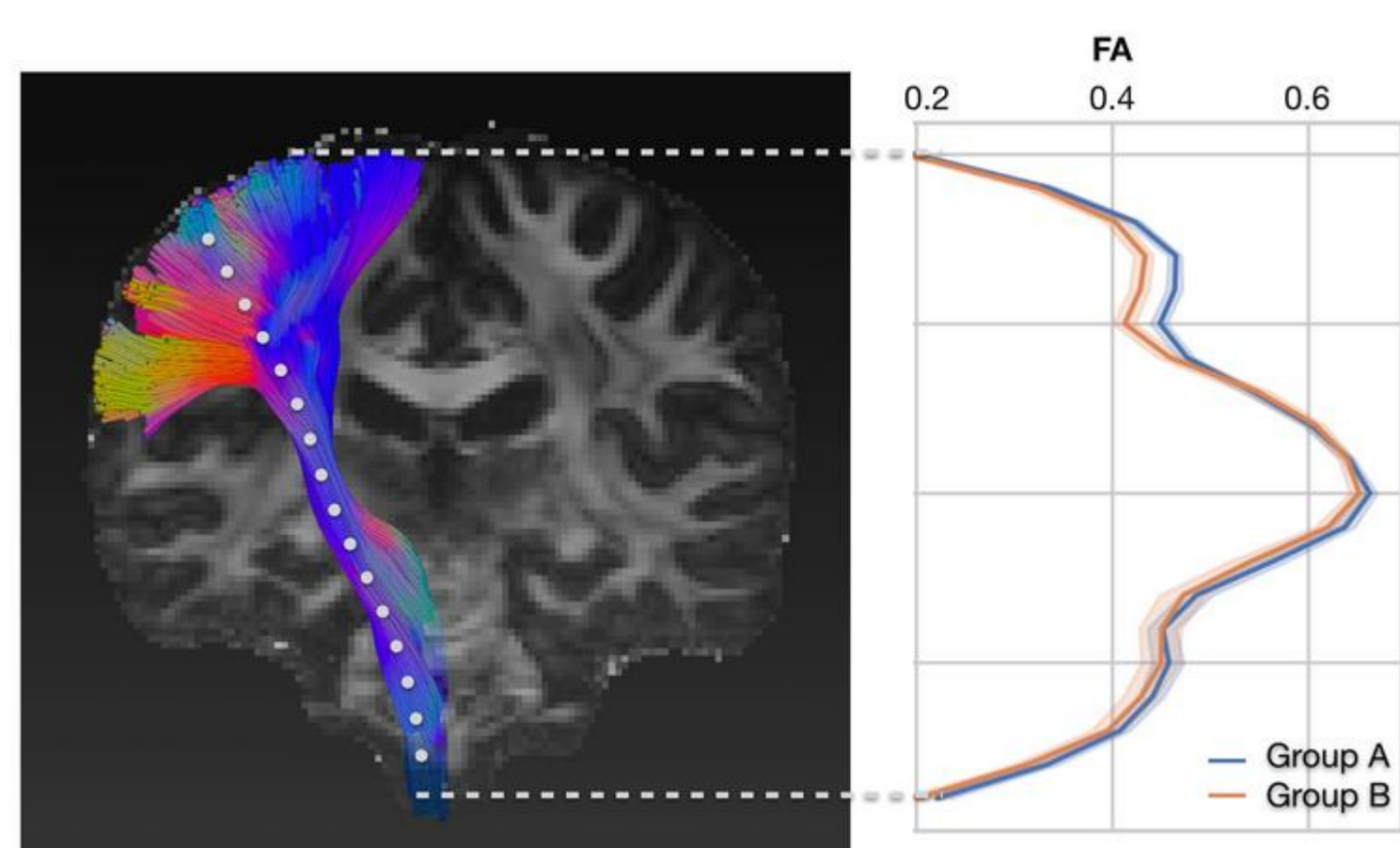
### Tractography

For each subject:

- TractSeg performs a tractography for all registered DWIs based on ODF resulting in 72 identified fiber bundles [Wasserthal 2018]
- For each bundle a centroid is estimated and values (FA, MD, ...) are provided [Chandio 2020]

### Statistics

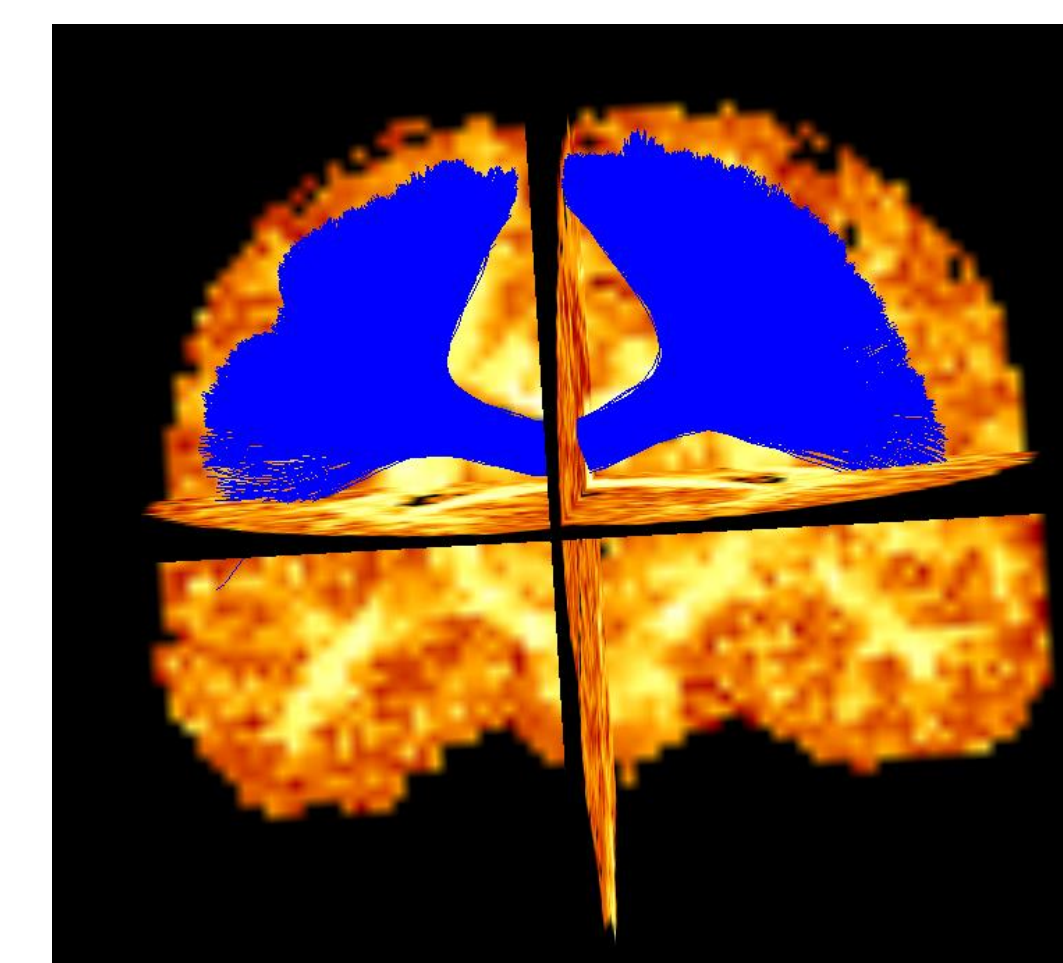
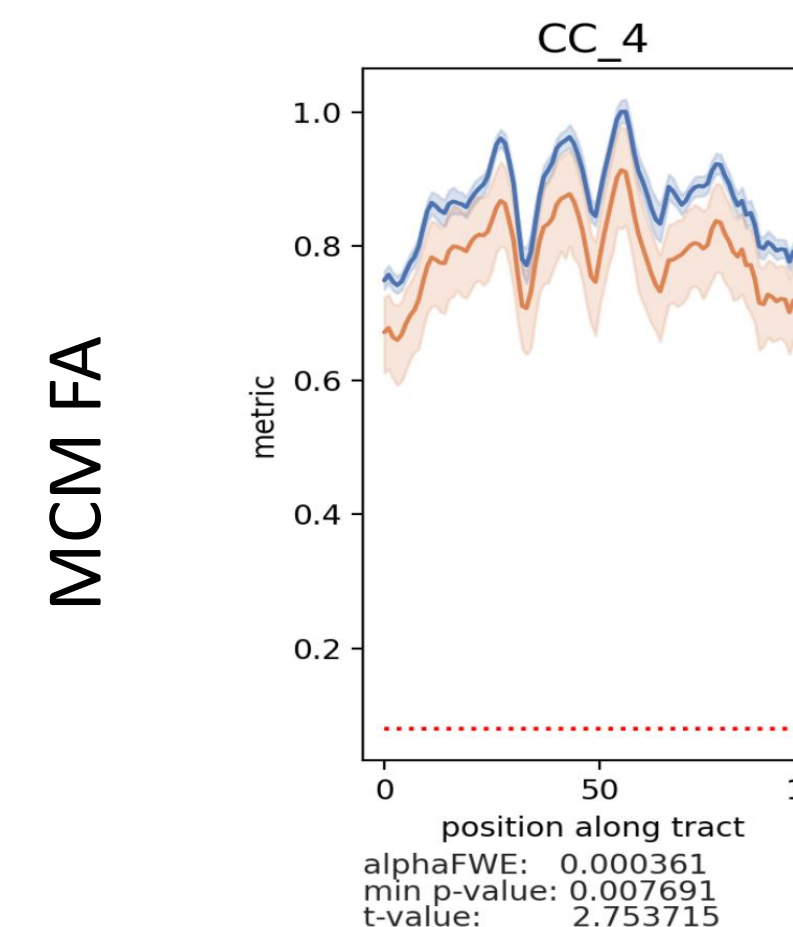
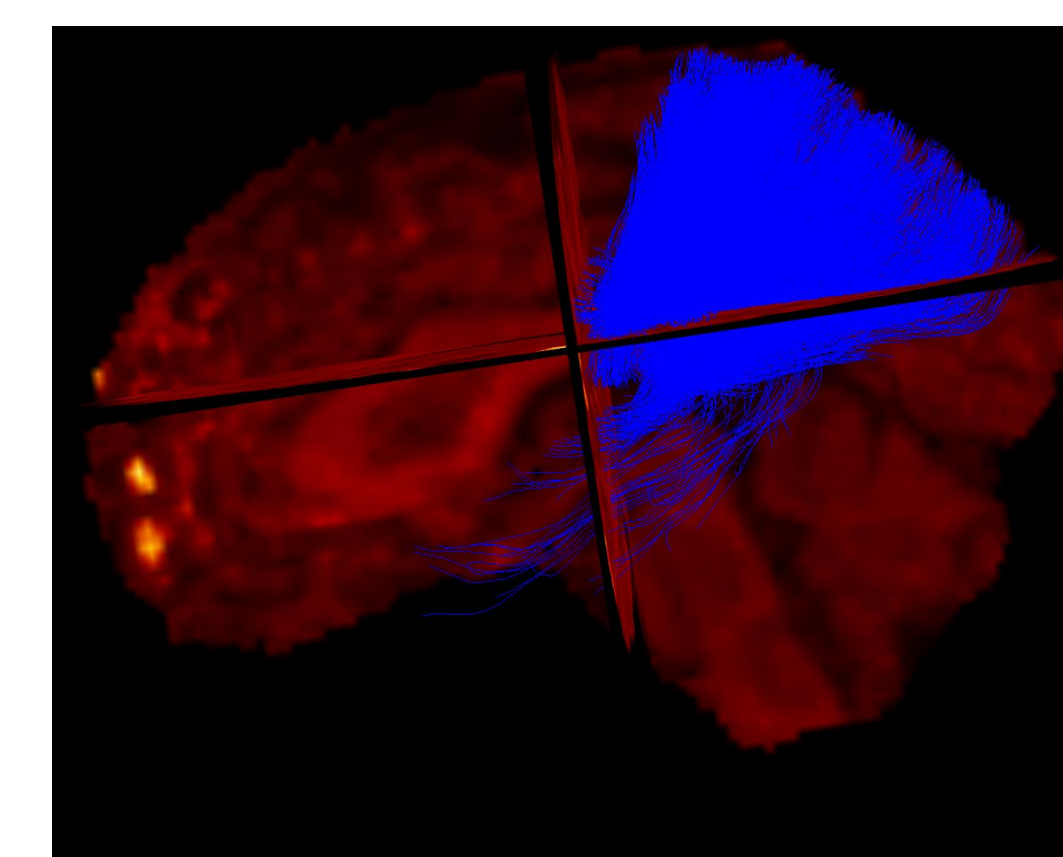
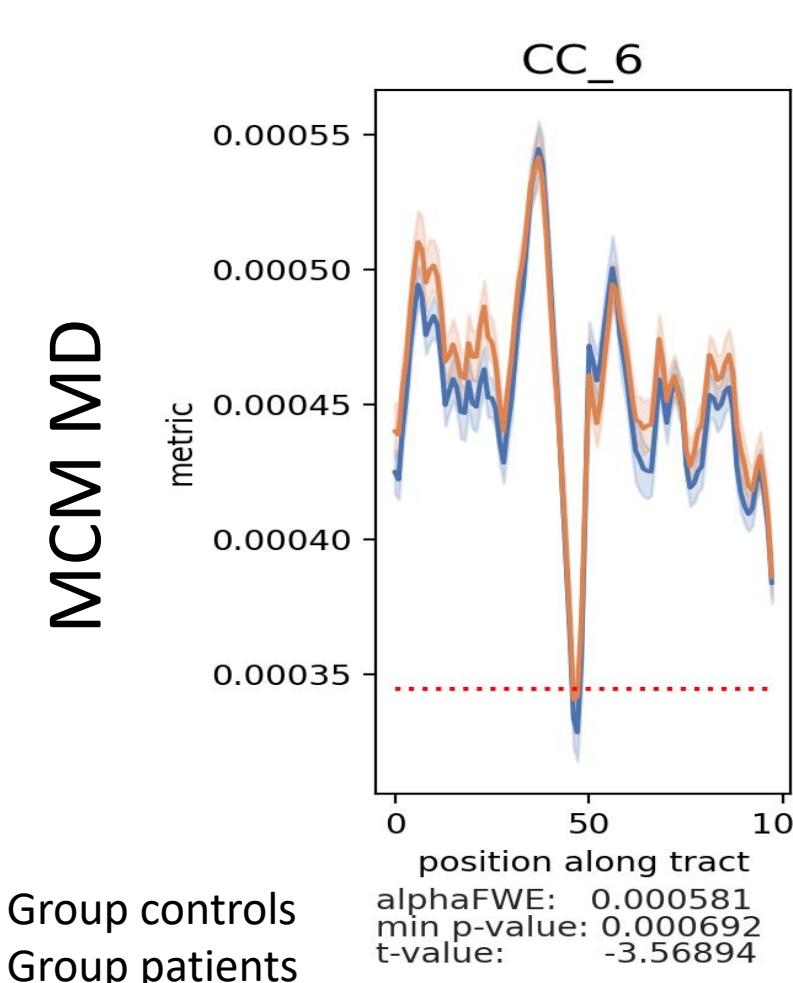
- Performs group to group comparison along tracts
- Covariable (age, sexe ...) can be removed



## Results

### Statistic along fiber tracts

- Pipeline tested on the Actidep database
- Group controls (26 subjects) vs group patients (39 subjects) for different MCM metrics
- Corrected for age, sex and duration of depression



- Expected highlight within the corpus callosum

## Conclusion & perspectives

- We developed a pipeline to perform tractography analysis using multi-compartments models
- We tested this pipeline on the Actidep database
- In the future we will extend this study to explore different database with additional MRI sequences, such as relaxometry, to derive new metrics and develop a multi-modal approach

Ferrari, Alize J., et al. "Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010."

Stamm, Aymeric, et al. "A Bayes Hilbert Space for Compartment Model Computing in Diffusion MRI, 2018.."

Wasserthal, Jakob, et al. "TractSeg-Fast and accurate white matter tract segmentation"

Chandio, Bramsh Qamar, et al. "Bundle analytics, a computational framework for investigating the shapes and profiles of brain pathways across populations."

Scherrer, Benoit, and Simon K. Warfield. "Parametric representation of multiple white matter fascicles from cube and sphere diffusion MRI."

Barnes, Deborah E., et al. "Midlife vs late-life depressive symptoms and risk of dementia: differential effects for Alzheimer disease and vascular dementia."