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Mixture Models for the characterization of brain abnormalities in “de novo” Parkinsonian patients

Verónica Muñoz Ramírez

PhD directors : Michel Dojat & Florence Forbes



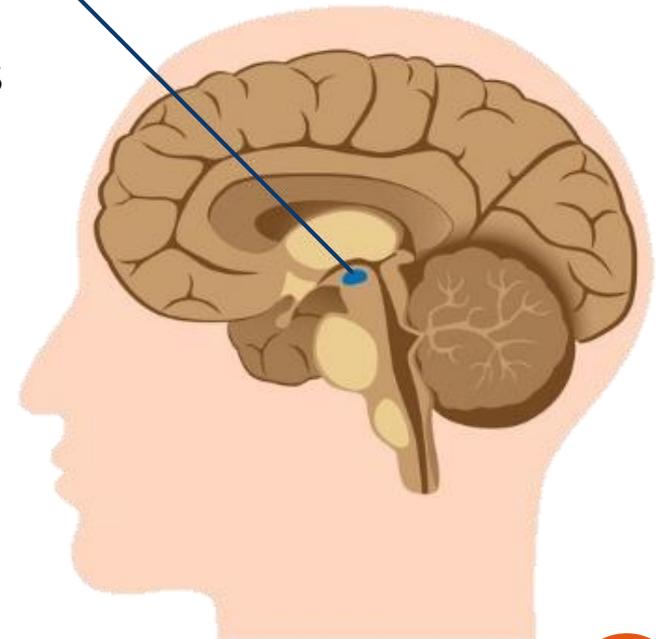
NeuroCoG
Univ. Grenoble Alpes





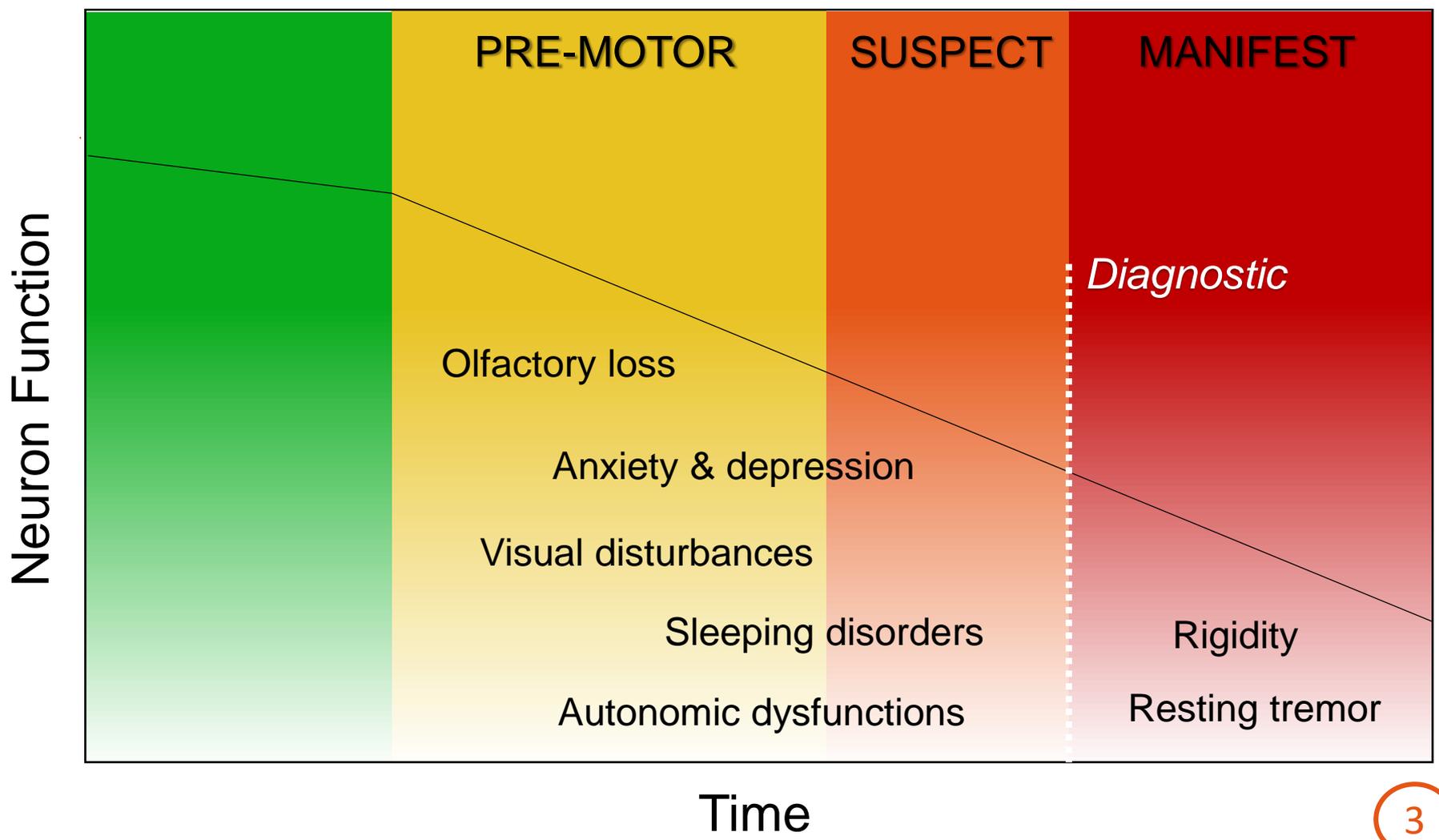
1. A brief introduction to PD

- ❖ Degenerative disease
- ❖ 10 million cases worldwide
- ❖ Loss of dopaminergic neurons in the *substantia nigra*
- ❖ Perturbation of other subcortical structures
- ❖ Non-motor (silent) phase
- ❖ Motor phase leading to handicap
- ❖ No cure, but symptom management





1. A brief introduction to PD





Objectives

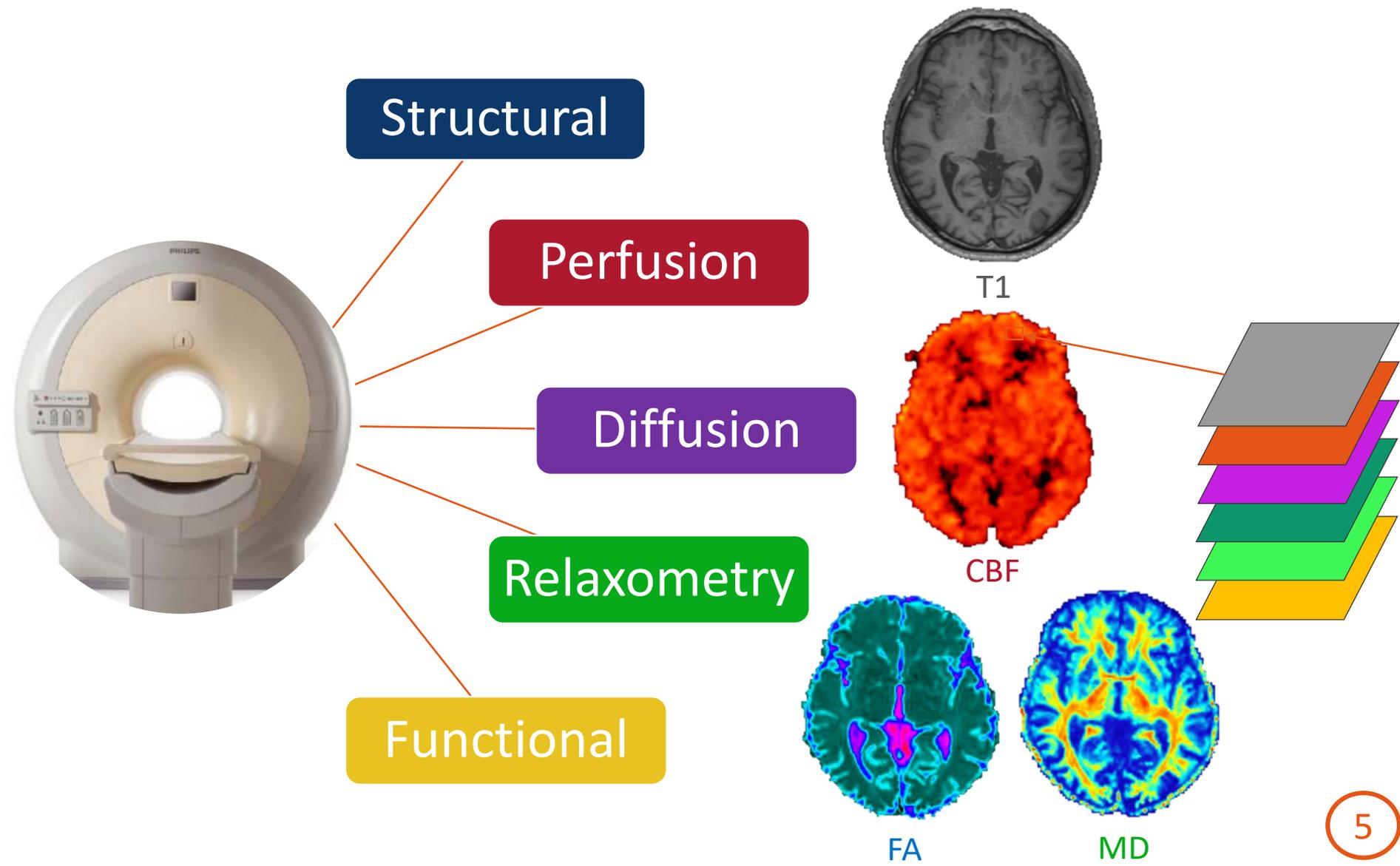
- To characterize the non-motor changes sustained by the Parkinsonian brain.*
- To find new biomarkers for the early diagnosis of Parkinson's disease.*
- To define specific classes of patients for personalized treatment*

Tools :

- MR imaging (anatomical and quantitative data)
- Statistical classification methods (Mixture models, data mining)



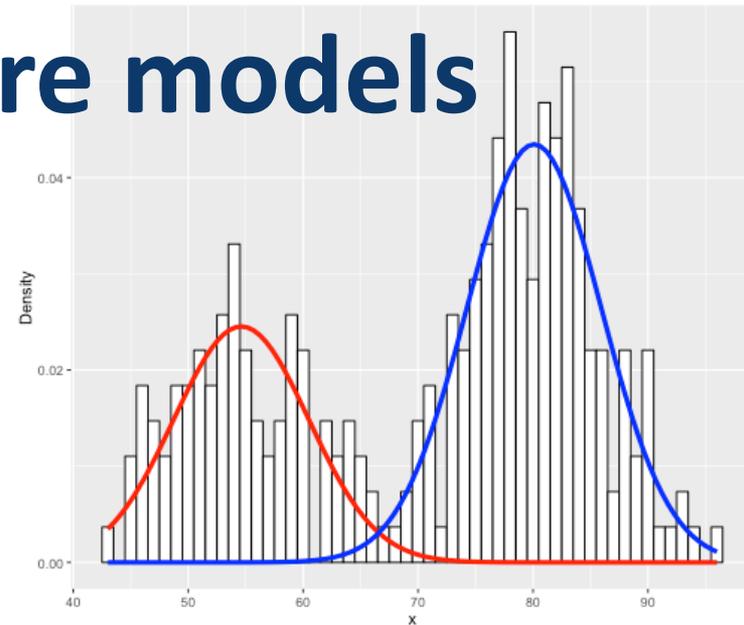
3. MRI parameters extraction





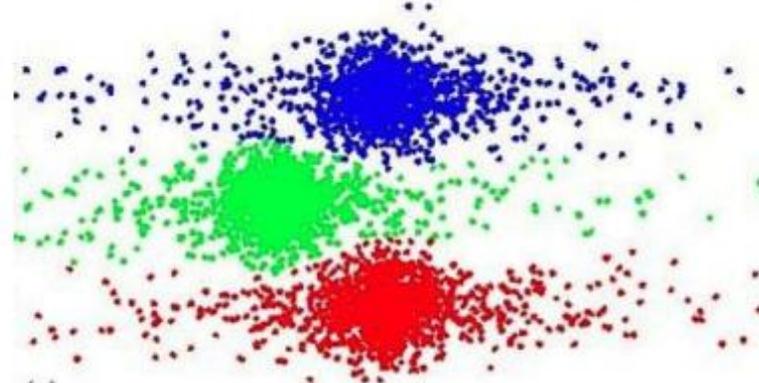
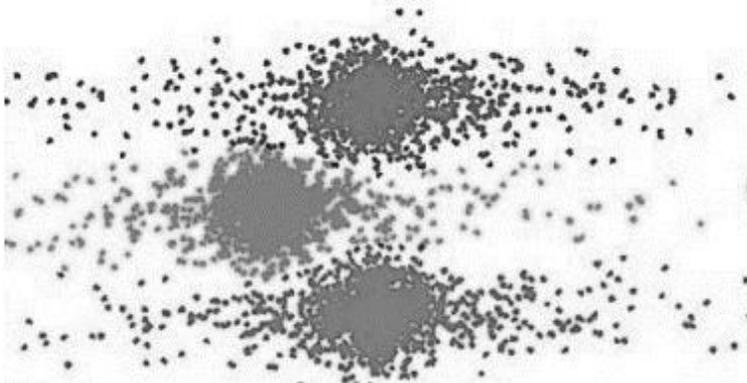
4. A word on mixture models

Mixture models are probabilistic models that represent subpopulations within an overall population.



Mixture of Multiple Scale t-distributions →

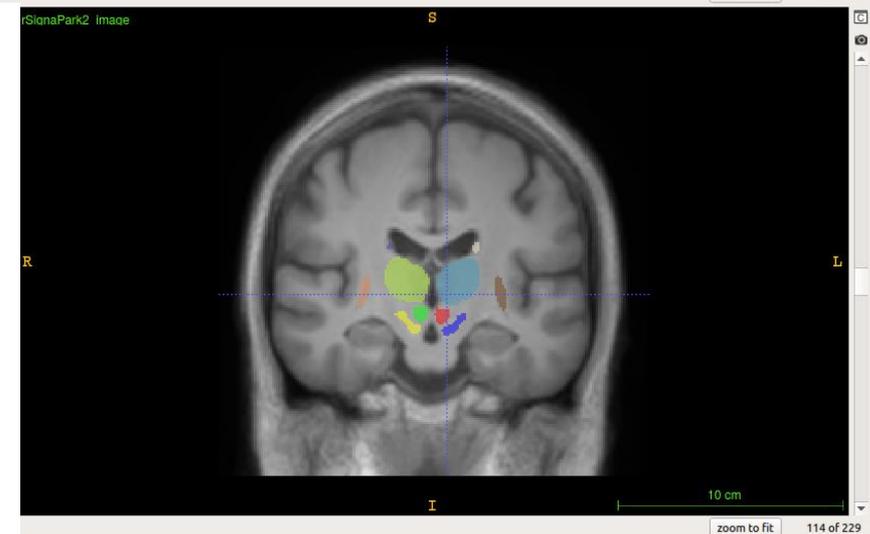
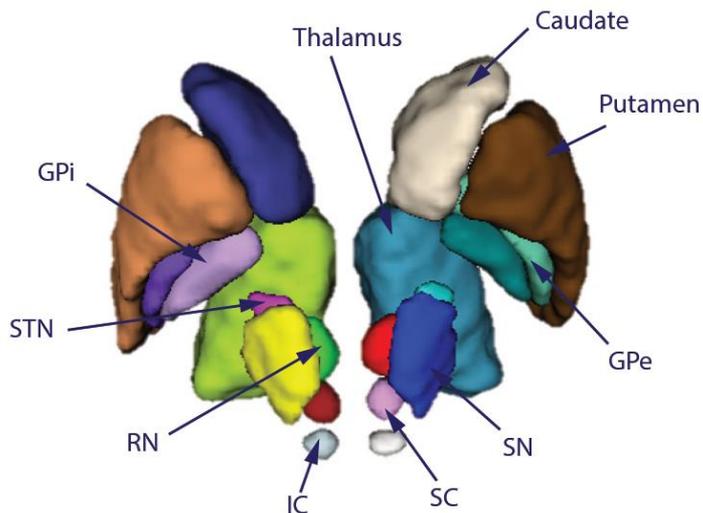
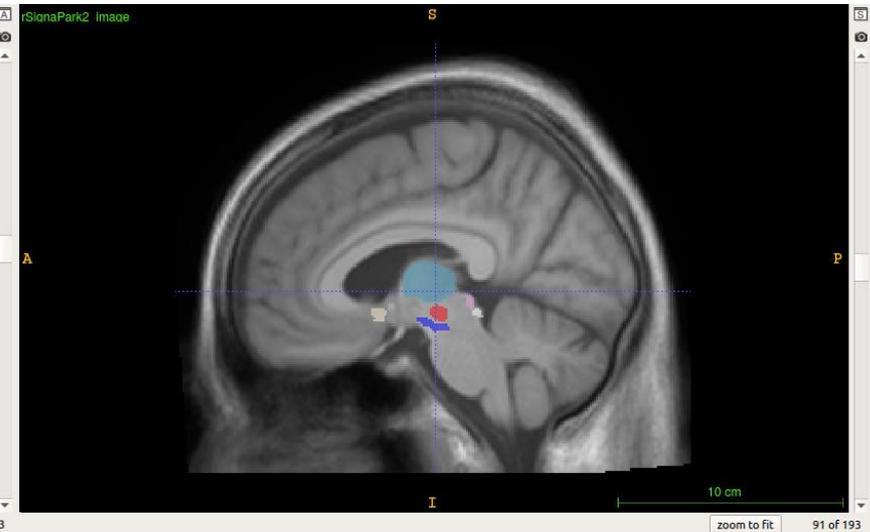
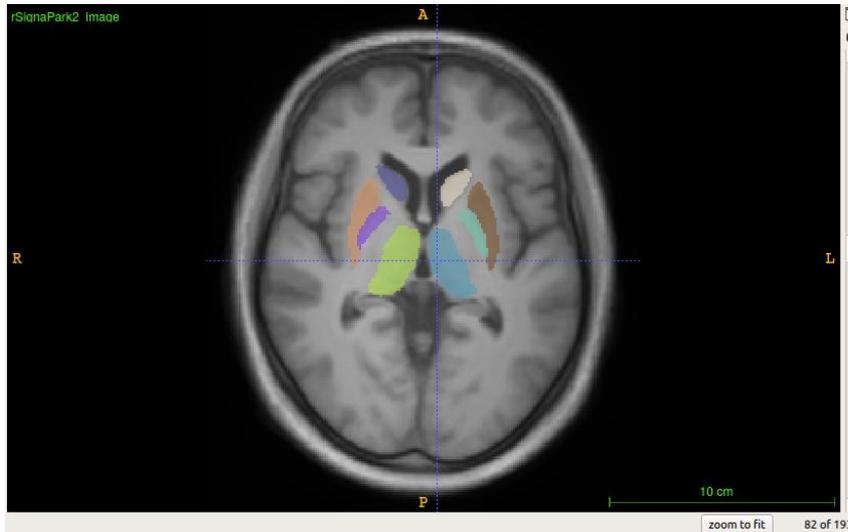
- More degrees of freedom
- Better classification of 'atypical values'



F. Forbes & D. Wraith (2014). A new family of multivariate heavy-tailed distributions with variable marginal amounts of tailweight: application to robust clustering. *Stat. Comput.*, vol. 24, 971–984.



5. Segmentation atlas



Xiao, Y., Collins, D. L. & al. (2015). Multi-contrast unbiased MRI atlas of a Parkinson's disease population. *International Journal of Computer Assisted Radiology and Surgery*, 10(3), 329–341.



6. Signatures extraction

Healthy MRI data



Mixture model for the healthy voxels



Reference Model

(Arnaud & al., 2017)

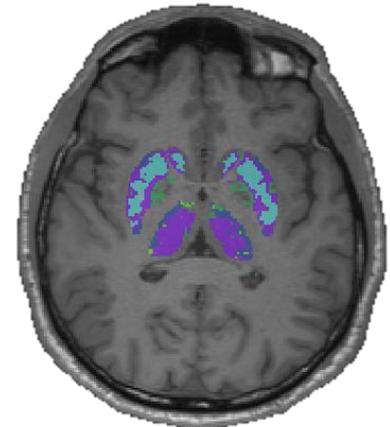
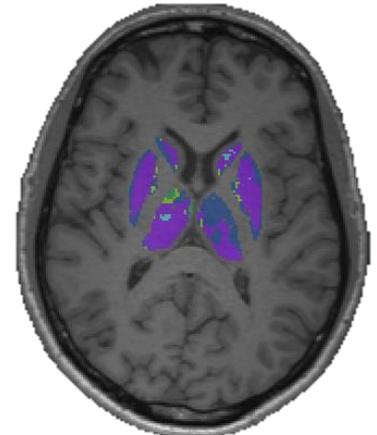
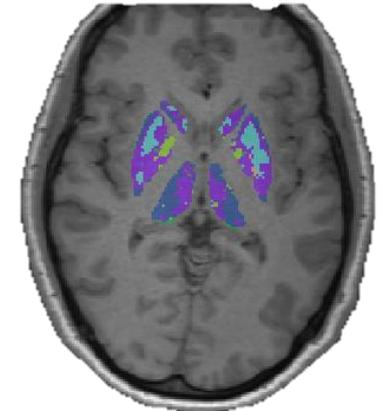
Healthy voxels group :

$$Y_H = \{y_v, v \in V_H\}$$

$$f_H(y|\pi, \theta) = \sum_{k=1}^{K_H} \pi_k \underbrace{MSD(y; \theta_k)}$$

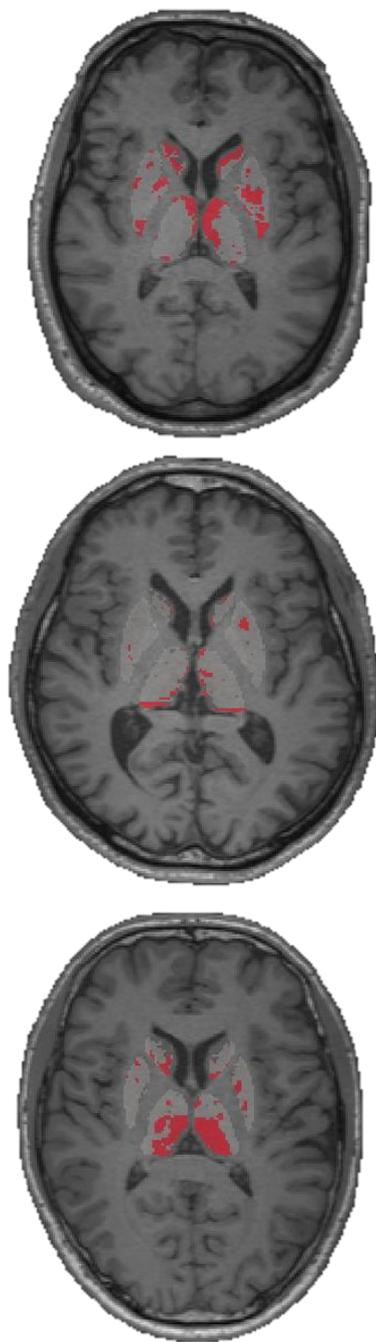
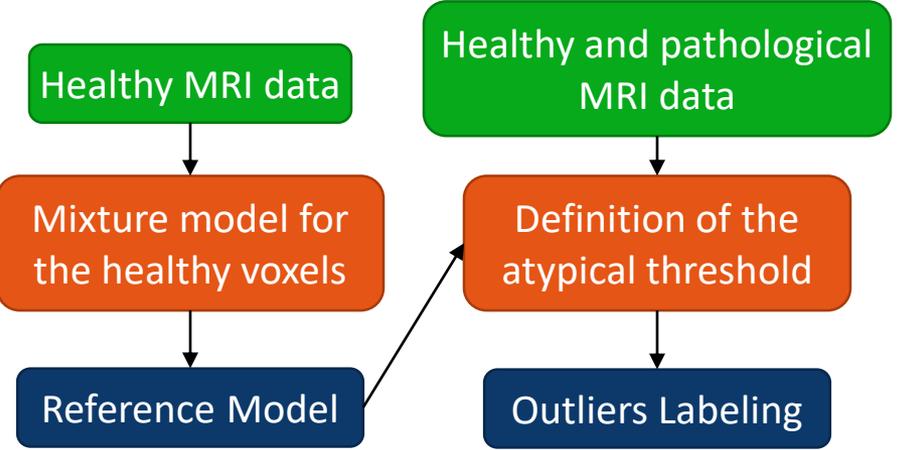
Probability distribution function of the estimated MMSD model

*K_H is determined by the BIC score
... or a slope heuristic*





6. Signatures extraction



Patient voxels group : $Y_P = \{y_v, v \in V_P\}$

$$P(\log(f_H(Y_v)) < \tau_\alpha) = \alpha$$

Where α is the FPR

6. Signatures extraction

Healthy MRI data

Healthy and pathological MRI data

Mixture model for the healthy voxels

Definition of the atypical threshold

Mixture model for the atypical voxels

Reference Model

Outliers Labeling

Atypical Model

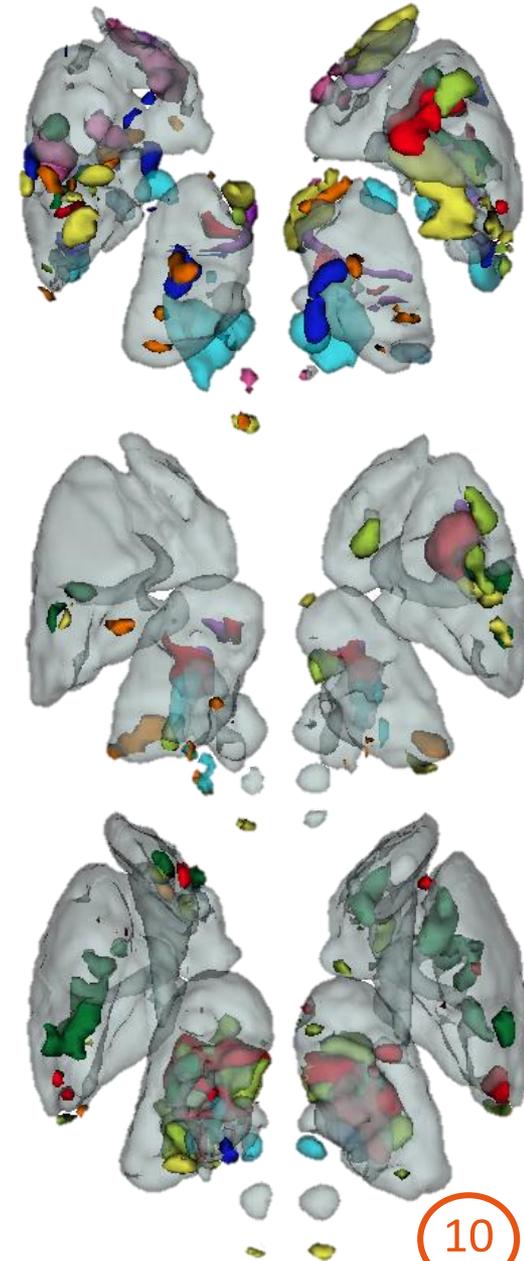
Atypical voxels group :

$$Y_A = \{y_v, v \in V_H \cup V_P\} \text{ such that } \log(f_H(y_v)) < \tau_\alpha$$

$$f_A(y) = \sum_{K=1}^{K_A} \eta_K MST(y; \phi_K)$$

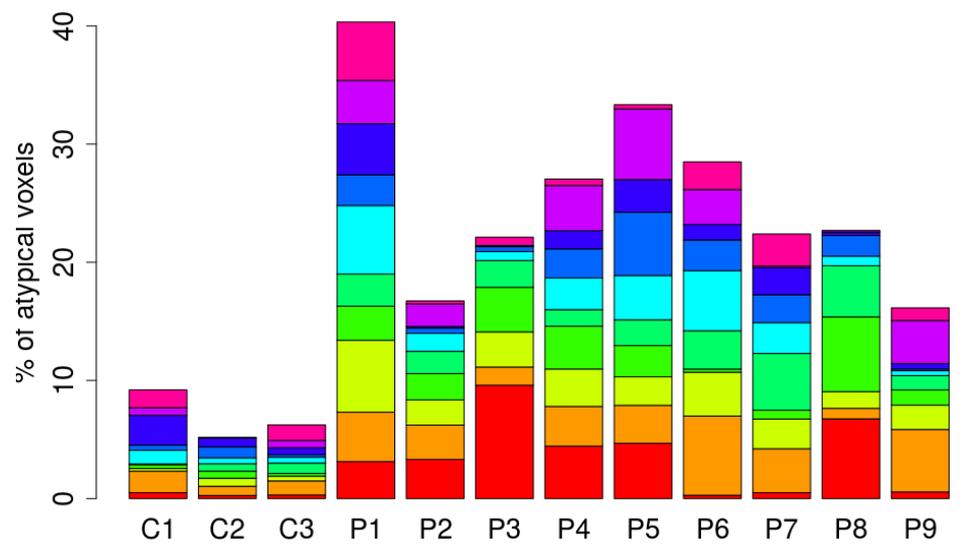
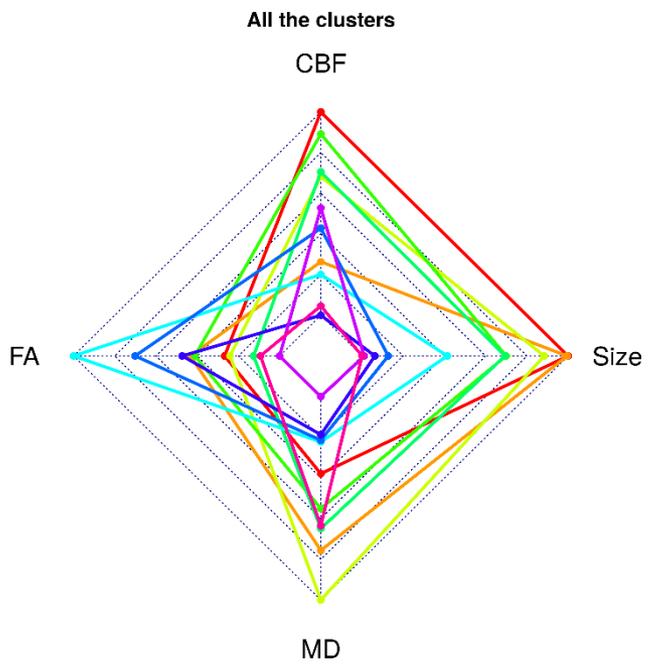
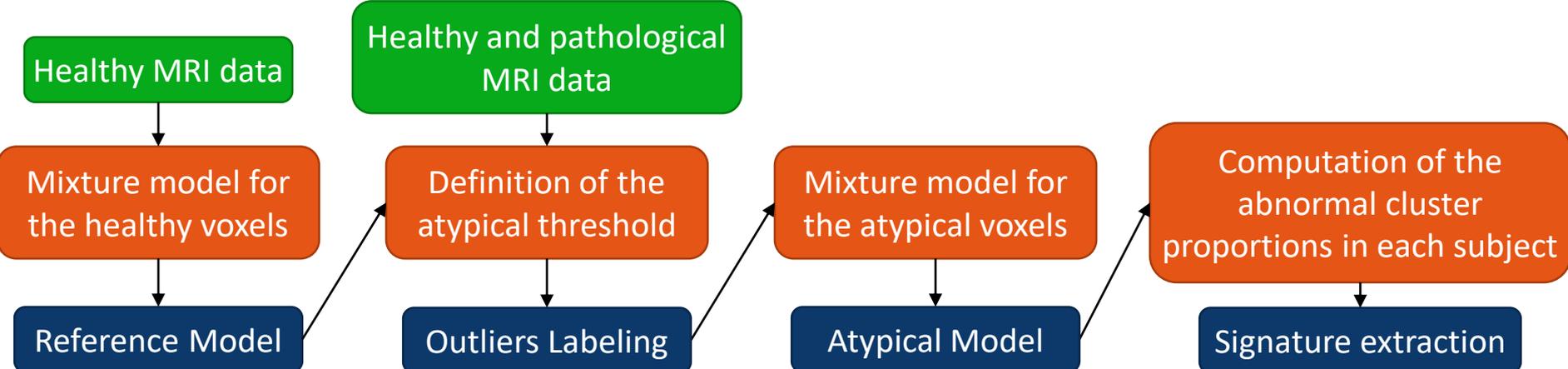
For each subject S

$$\rho^S = \{\rho_1^S, \dots, \rho_{K_A}^S\}$$



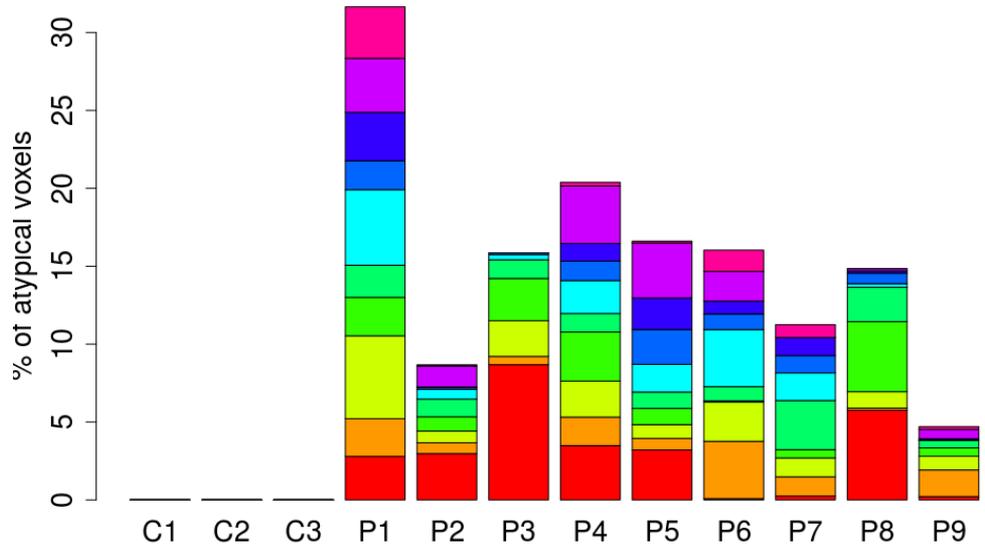
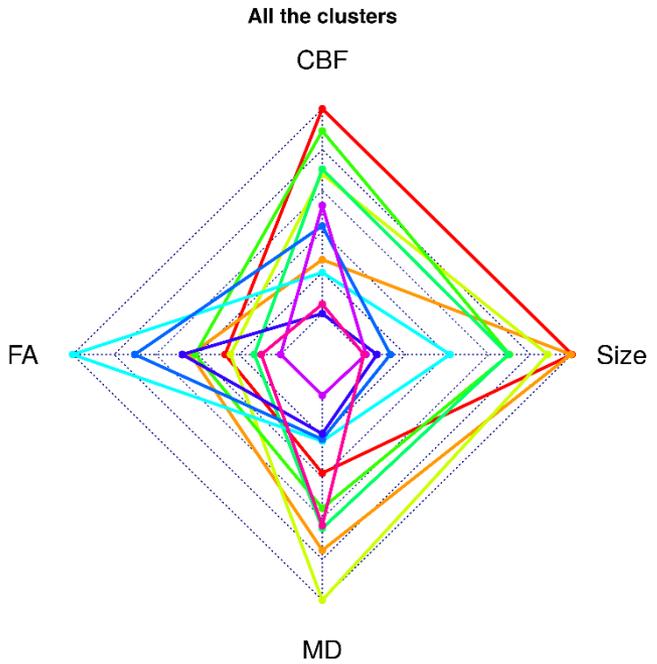
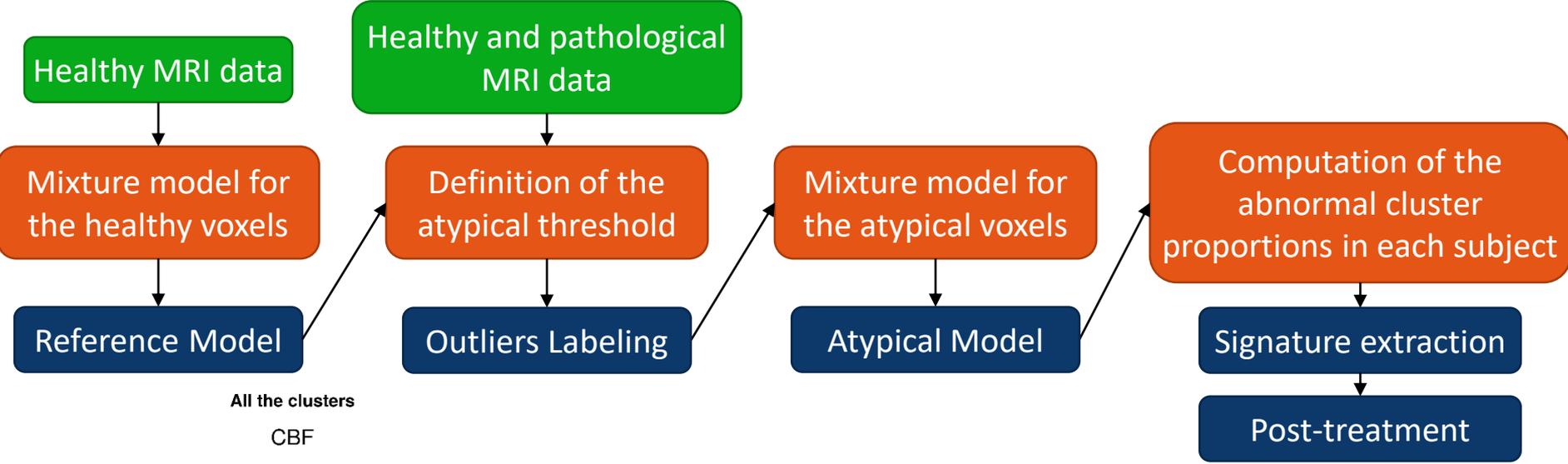


6. Signatures extraction





6. Signatures extraction



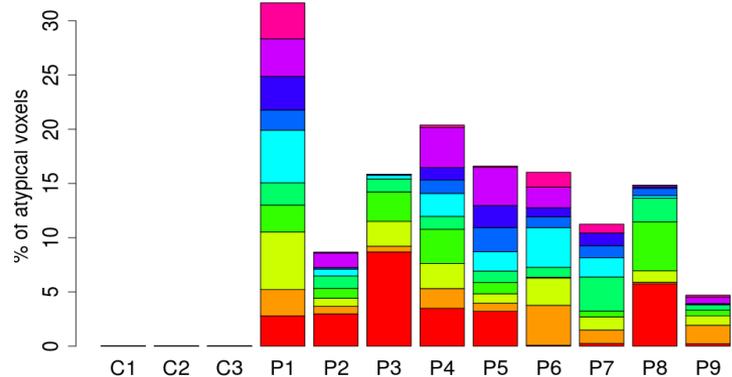
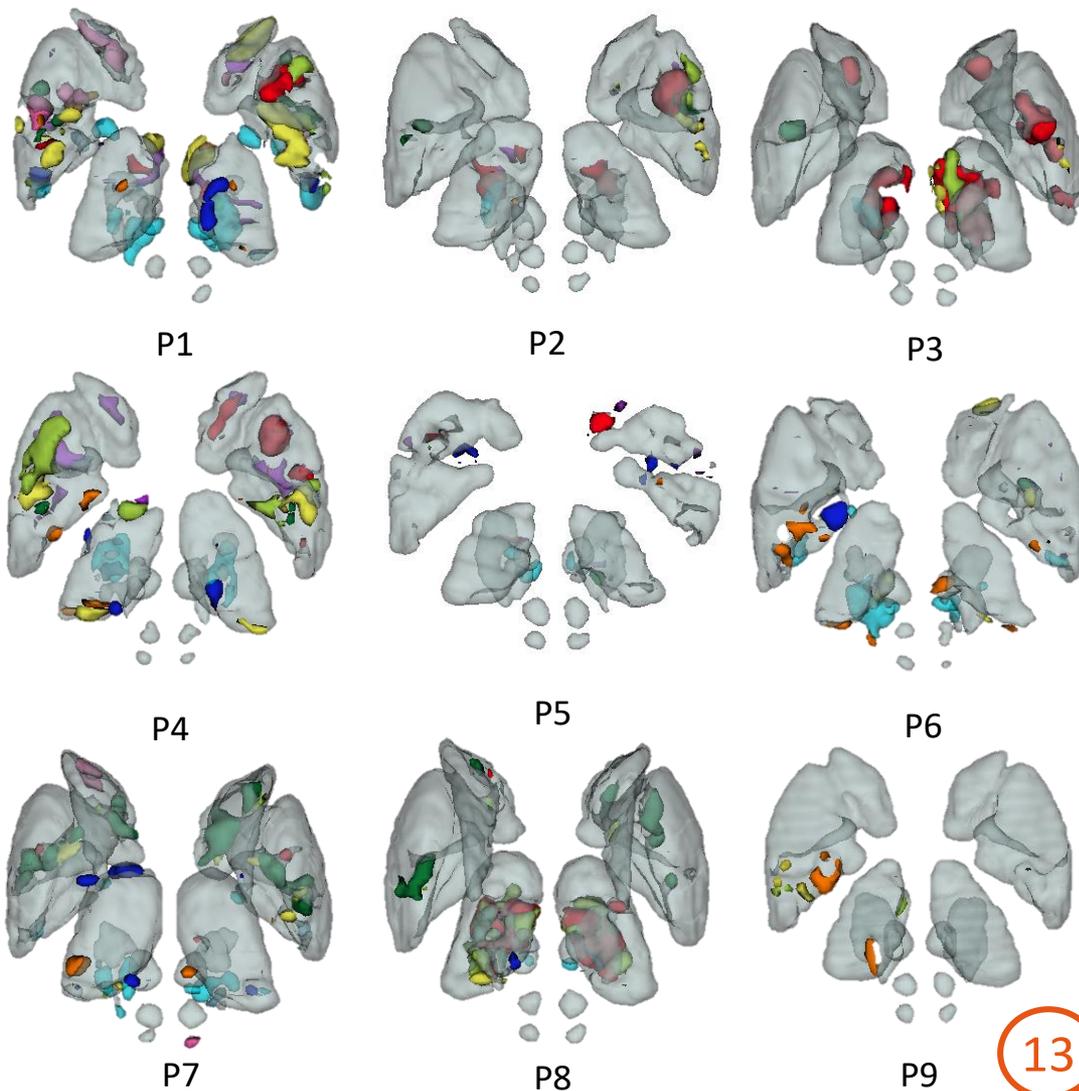


7. Results

Subcortical structures
CBF – FA – MD 9 patients K = 10

Highlighted regions :

- Substantia nigra
- Red nucleus
- Globus Pallidus



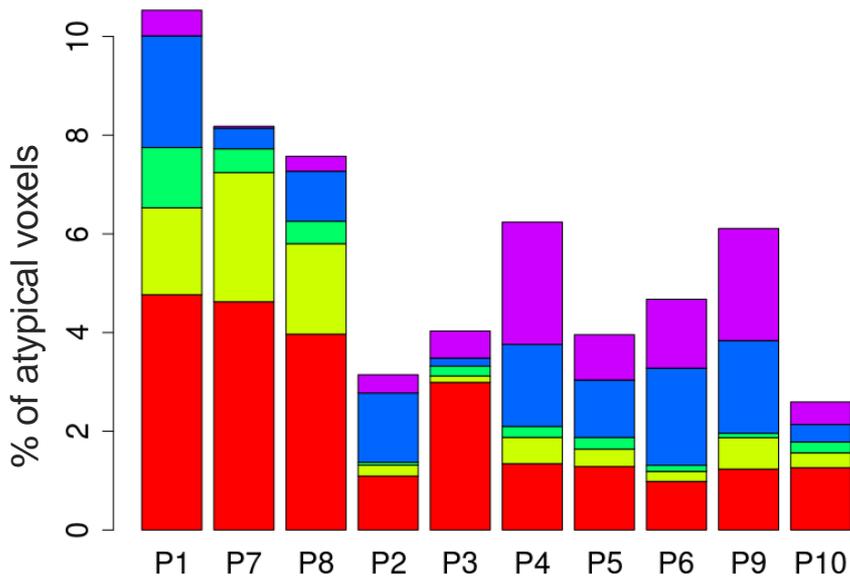
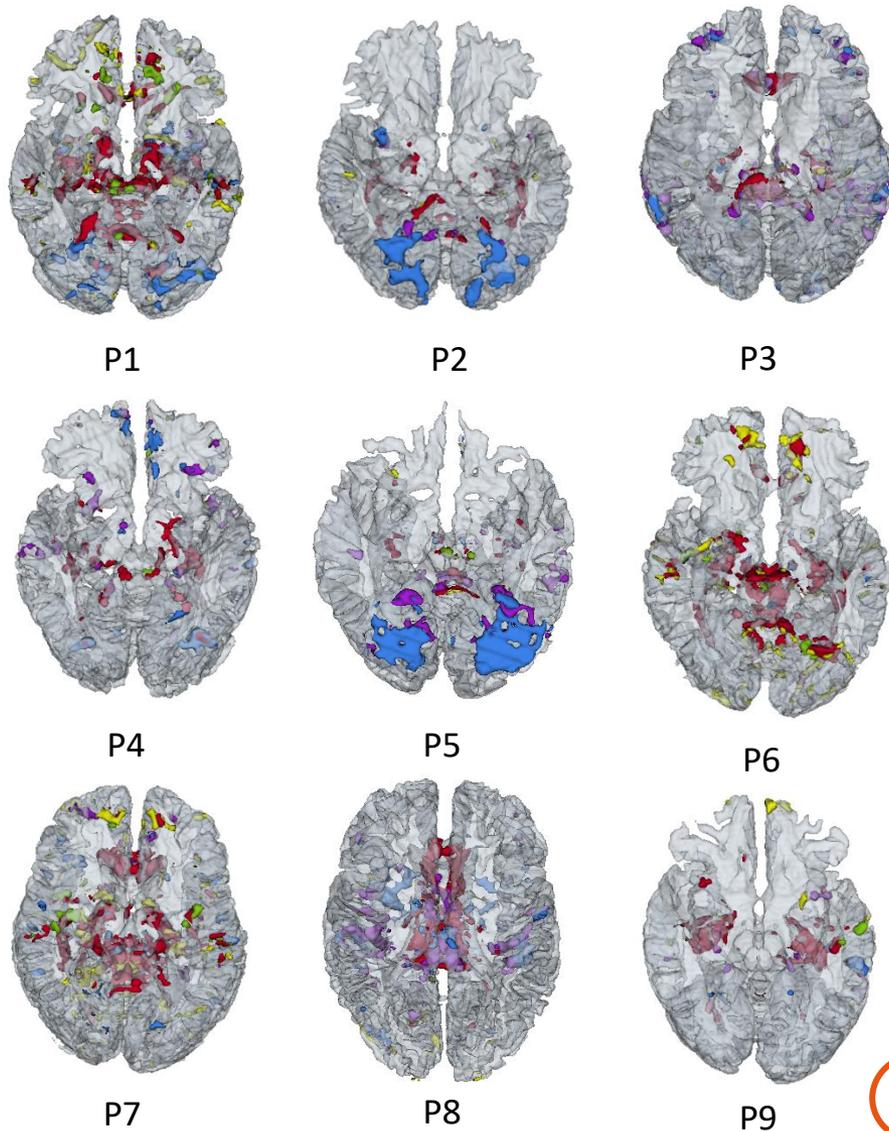


7. Results

Brain
CBF – FA – MD 9 patients K = 5

Highlighted regions :

- Brainstem
- Diencephalon
- Substantia nigra
- Transverse Temporal gyrus





8. Perspectives & Conclusion

Preliminary results show the potential of this approach, however we need to acquire more data to confirm our findings and build robust models.

WORK IN PROGRESS :

- Machine Learning approaches for anomaly detection
- Proof of robustness.
- Signature profiling



Thank you !

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NeuroCoG
Univ. Grenoble Alpes



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