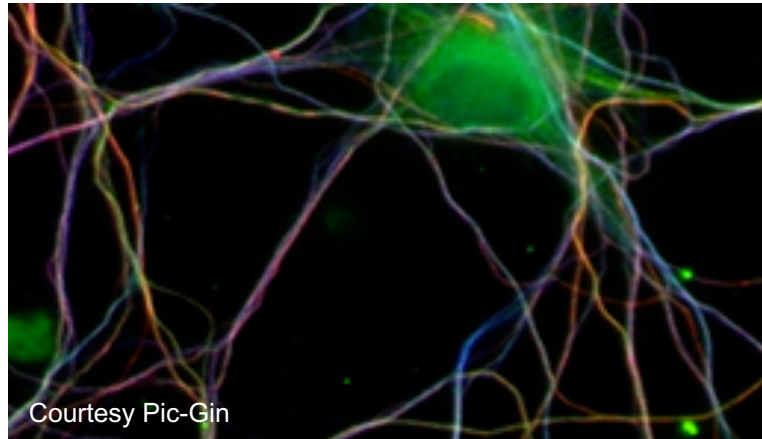


# Comprendre le fonctionnement cérébral : Apports de l'Imagerie

**Michel Dojat**

**[michel.dojat@inserm.fr](mailto:michel.dojat@inserm.fr)**

# Imager le cerveau



- ✓ Signaux chimiques (neuromédiateurs)
- ✓ Signaux électriques et magnétiques
- ✓ Variations métaboliques et hémodynamiques

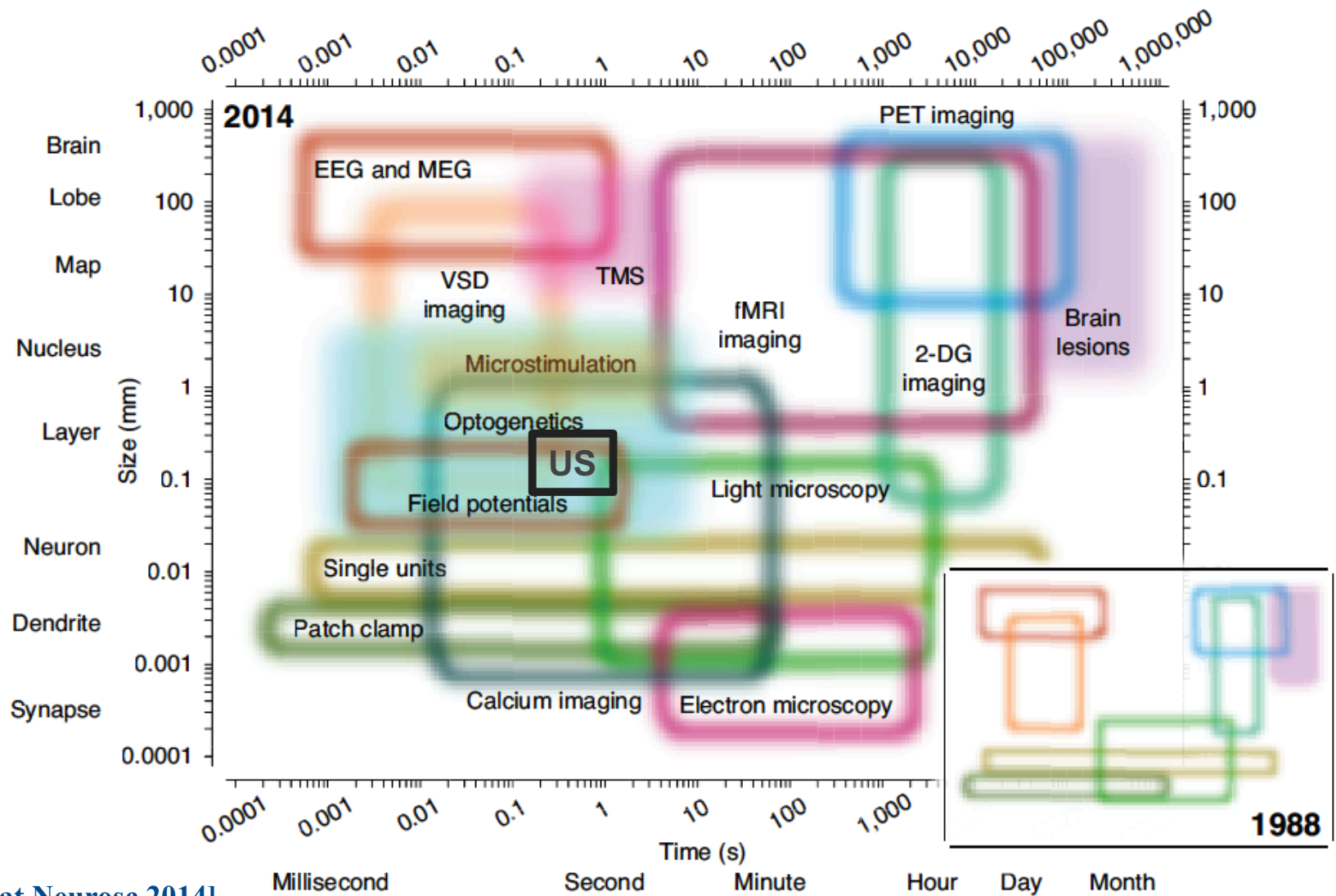
➔ Consommation O<sub>2</sub>, Glucose, émission Chaleur, H<sub>2</sub>O, CO<sub>2</sub>

**Cerveau = 2% du poids , 25% de consommation totale de glucose**

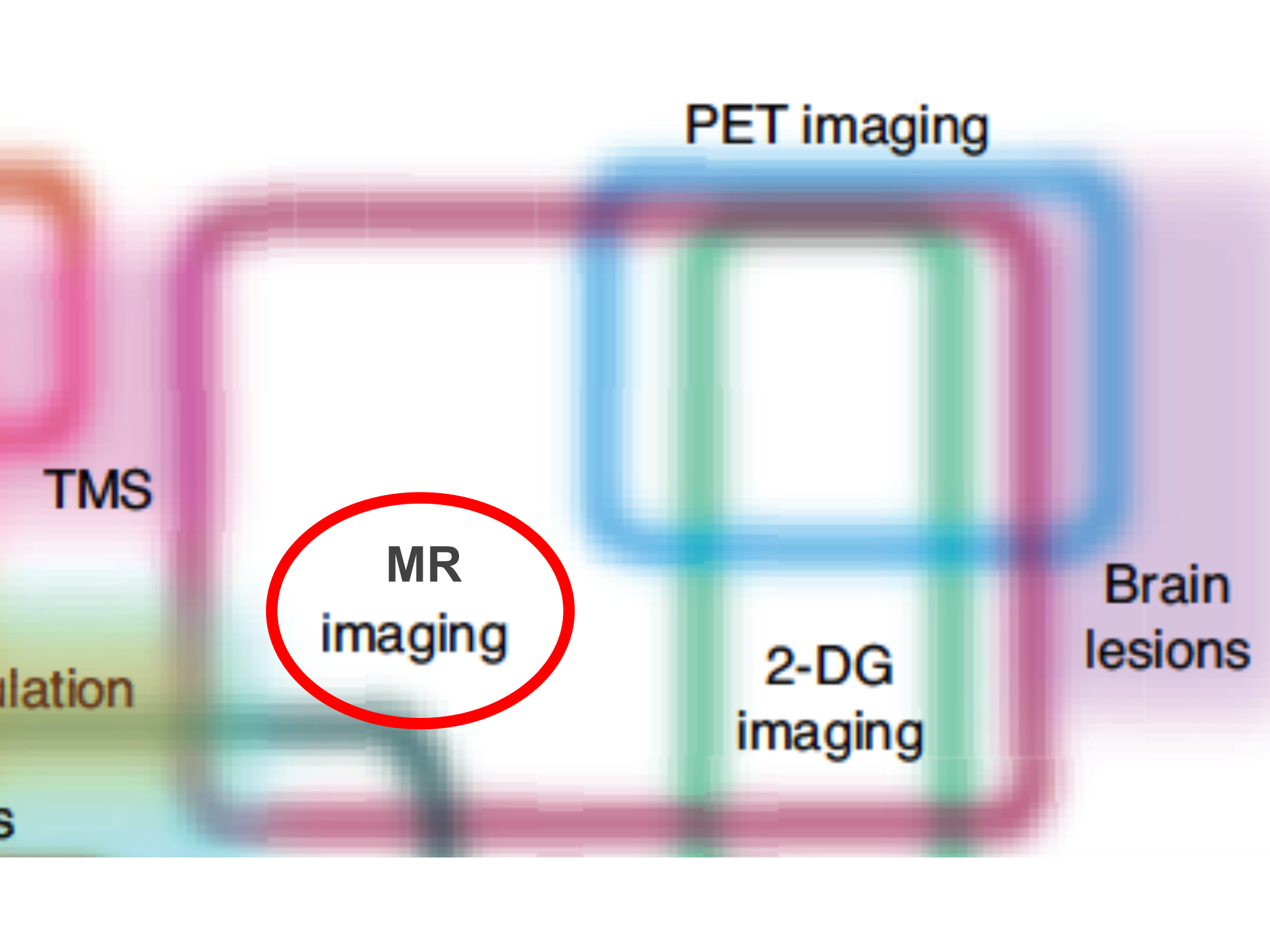
**12-15% du débit cardiaque, 20 % de la consommation totale d' O<sub>2</sub> !!!**



# Des techniques variées ...



[Sejnowski Nat Neurosc 2014]



PET imaging

TMS

MR  
imaging

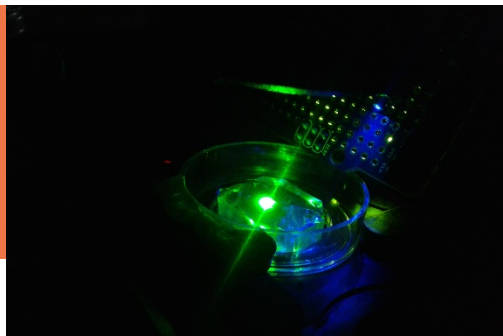
2-DG  
imaging

Brain  
lesions

ulation

S

# RESEARCH TOPICS AND EXPERIMENTAL APPROACHES



/ **Fundamental neurosciences**

*Cytoskeleton, Intracellular traffic, Synaptic plasticity, Mechanisms studied in normal and pathological conditions (neurobiological diseases, neurodegenerative diseases, myopathies)*



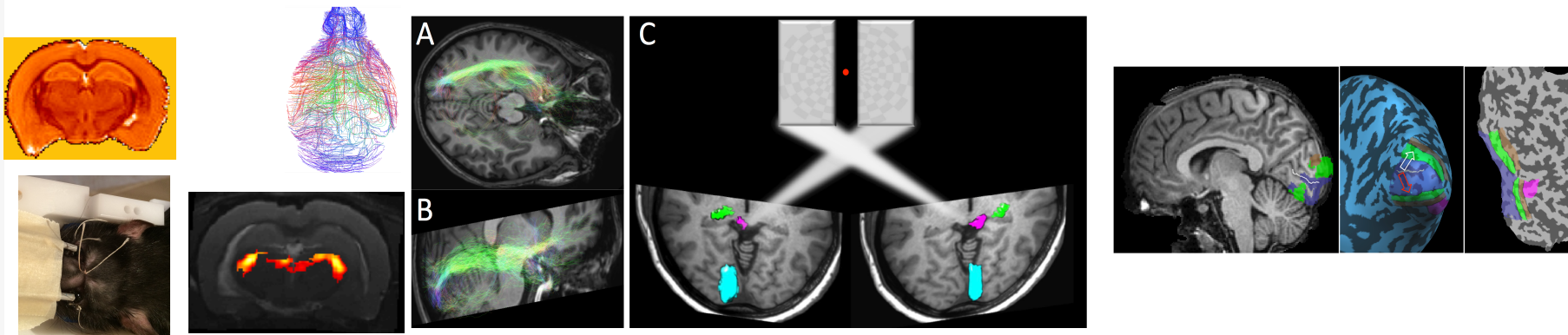
/ **Pre-clinical and clinical research**

*Developing tools and concepts  
Close links with networks such as GREEN, Neuropsynov, NeuroCoG...*



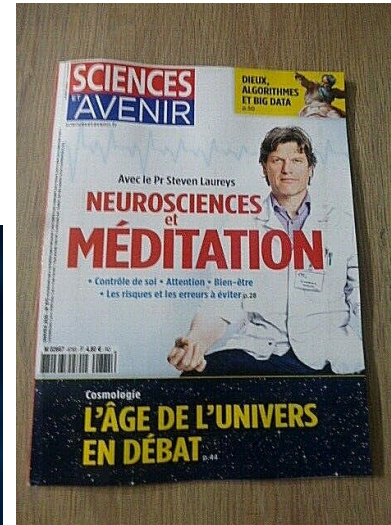
/ **Innovative technologies and treatments**

*Multidisciplinary approaches including human social sciences, and methodological developments (optogenetics, reconstruction of neural networks, electrophysiology...)*



# Le 21ème siècle sera neuroscientifique ou ne sera pas ...

Janvier 2020 ....





# Le 21ème siècle sera neuroscientifique ou ne sera pas ...

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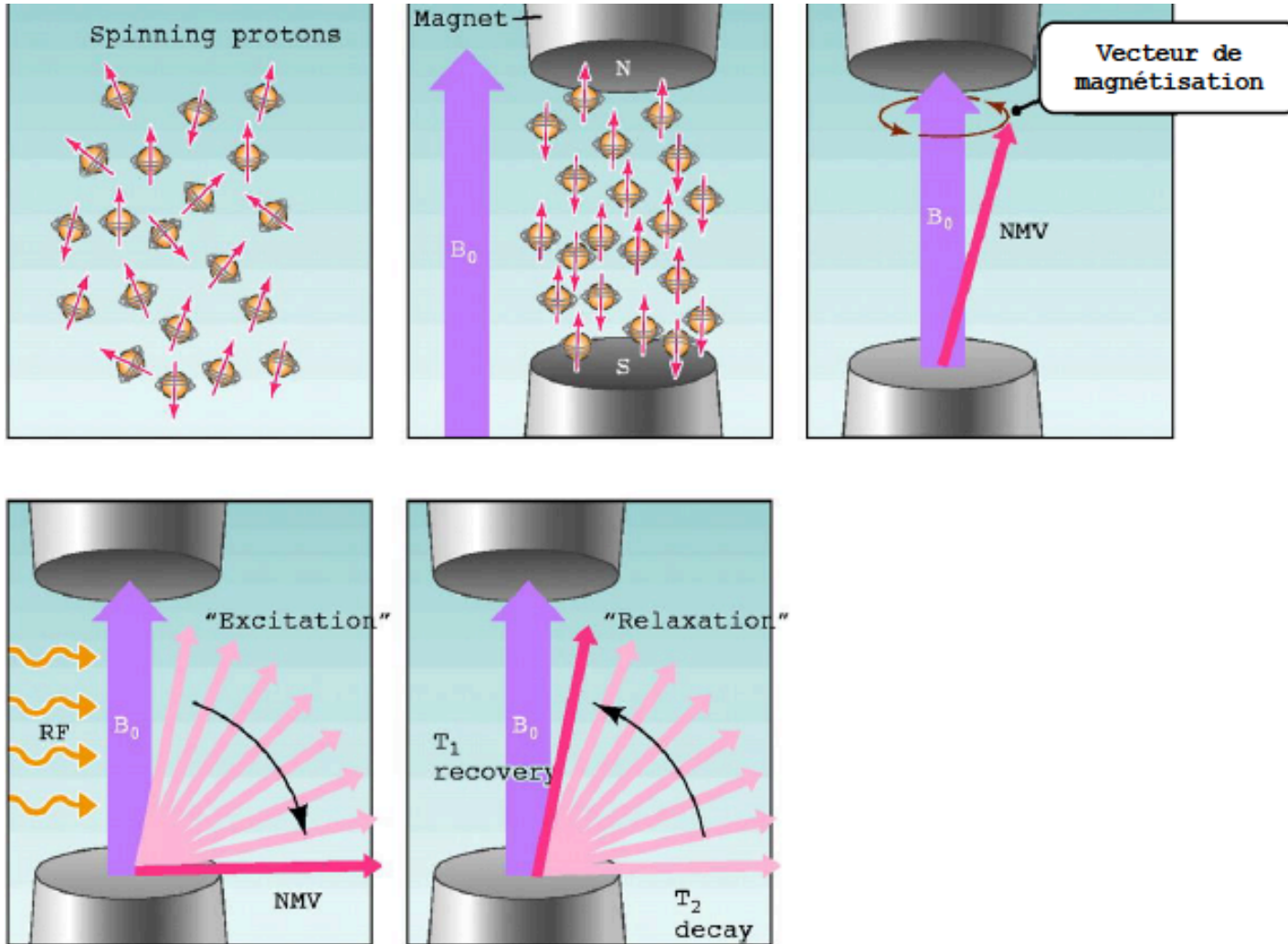
Il y a plus à comprendre dans un chapitre de **l'idiote de Dostoïevski** que dans les données cumulées de toutes les IRM du monde — car L'idiote de Dostoïevski résume des millénaires d'expérience mieux que tous les méta-articles des chercheurs en neuroscience.

2019 France Culture  
Aurélien Bellanger

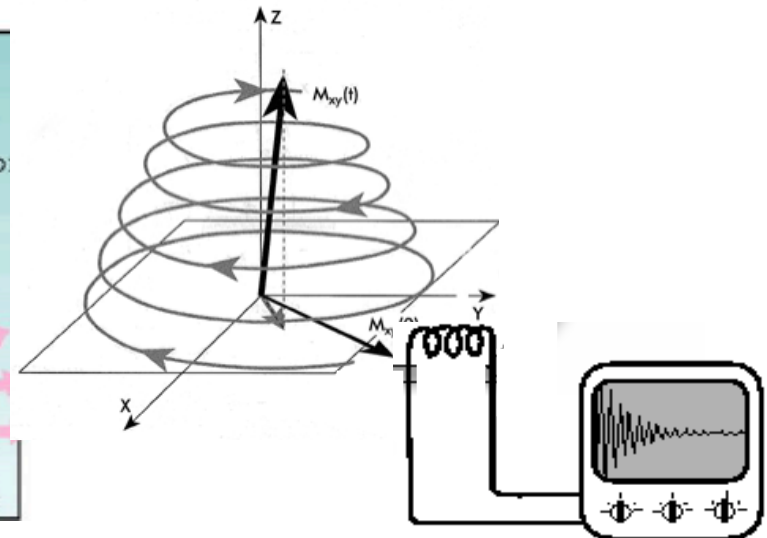
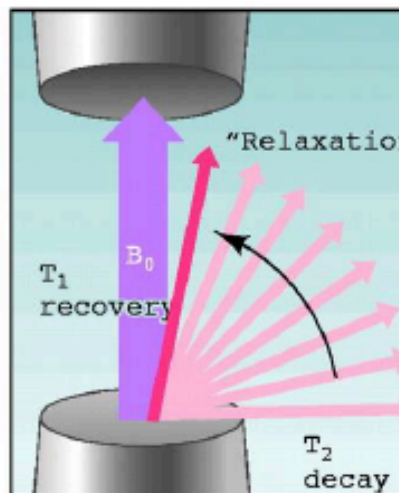
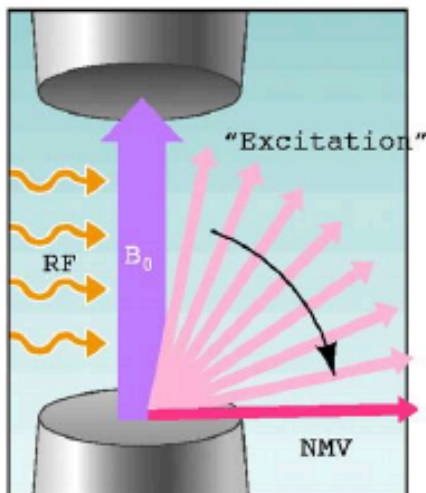
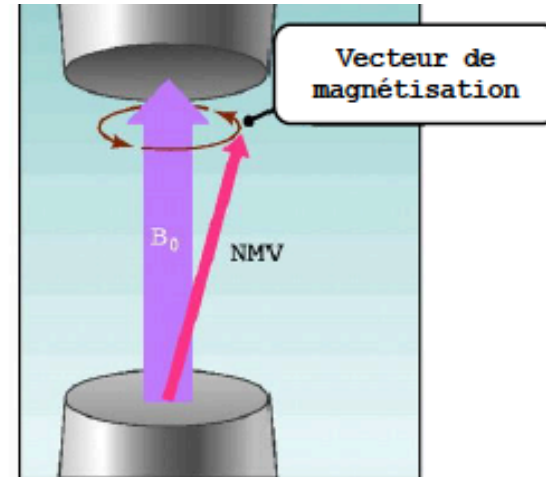
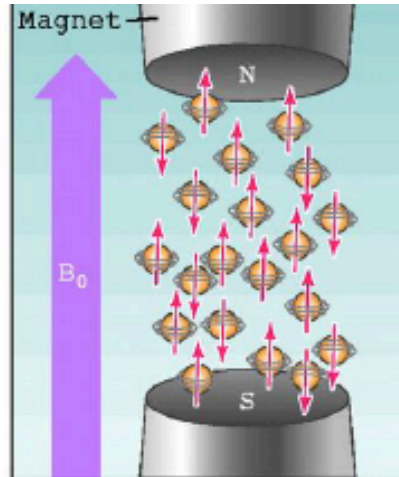
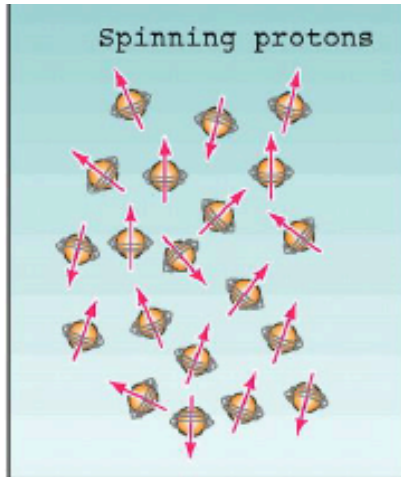


*MRI Principle*

# Un peu d'ordre ...

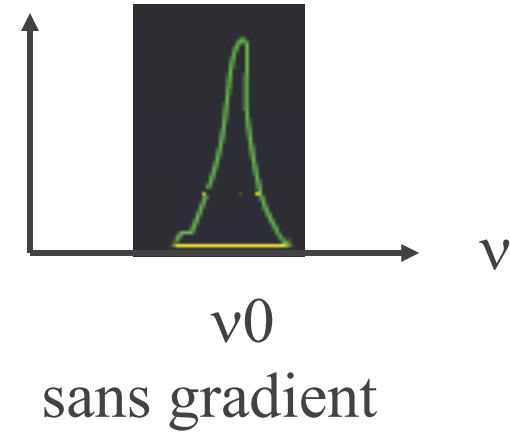
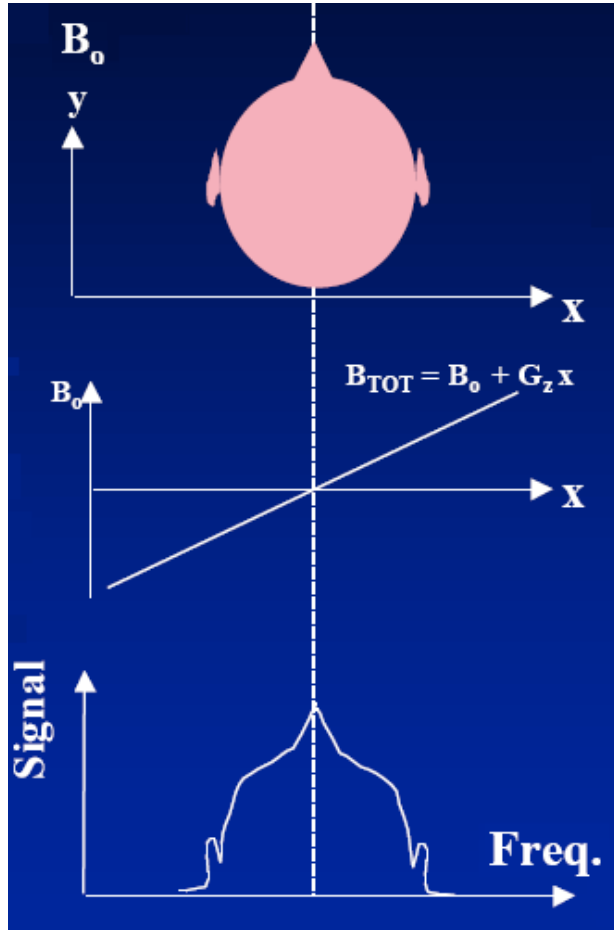


# Un signal spécifique ...





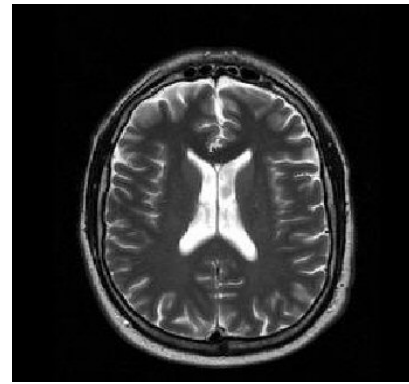
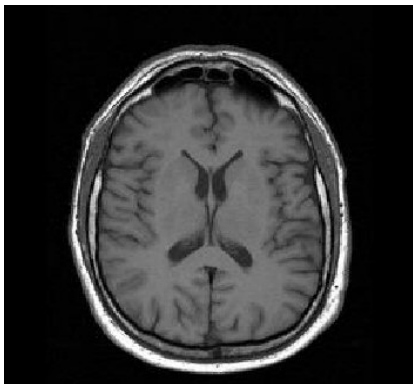
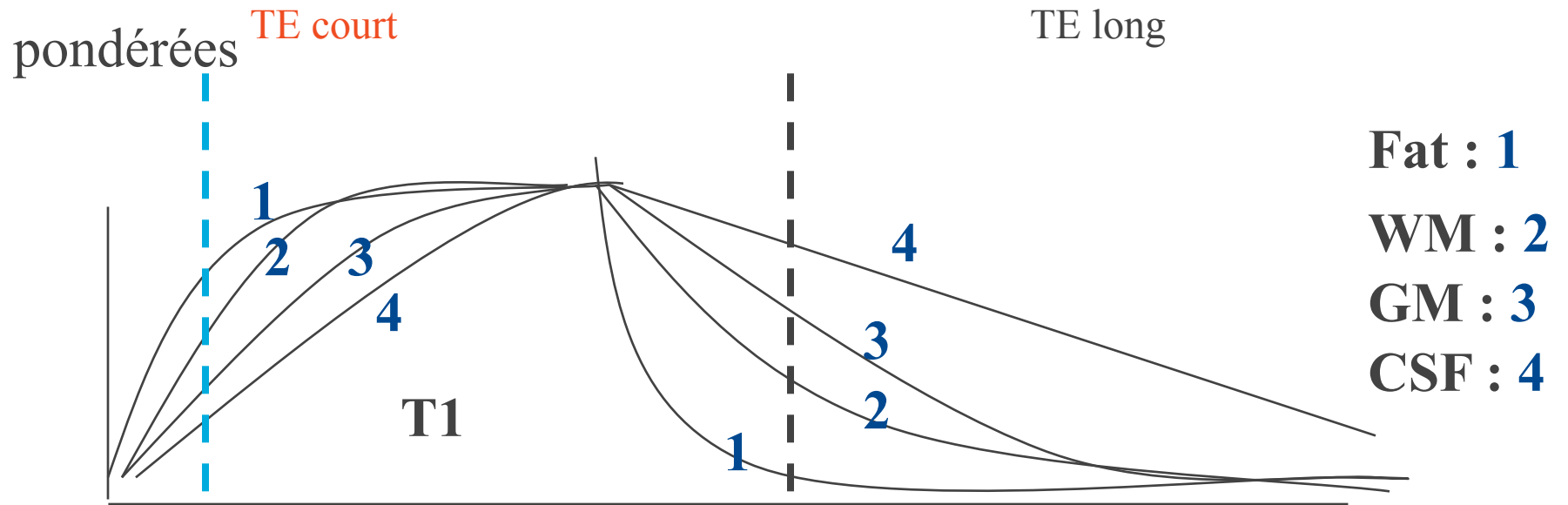
# Imager en 3D : Encoder la position par la fréquence



$$w(x) = \gamma [B_0 + xG_x]$$



# Des Images contrastées

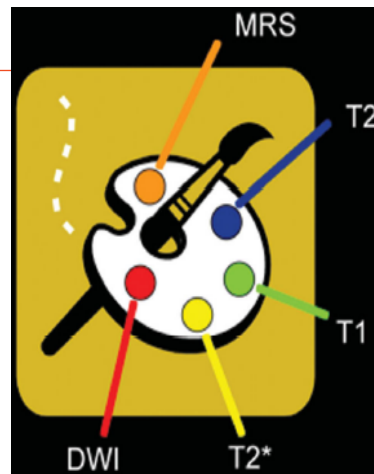
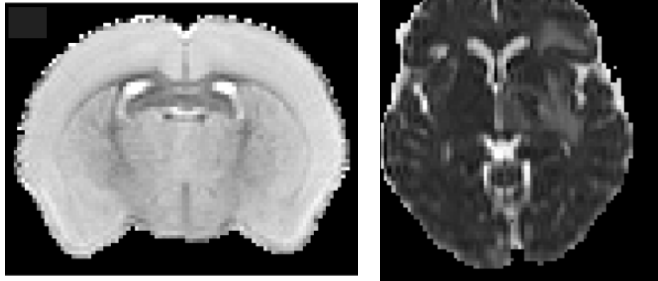


# Des modalités non invasives ...

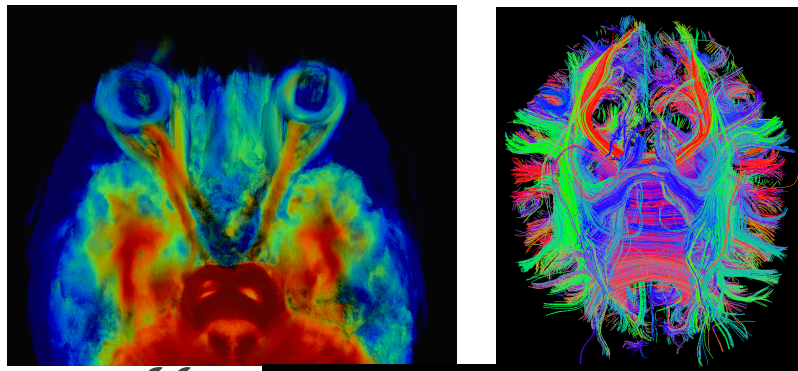
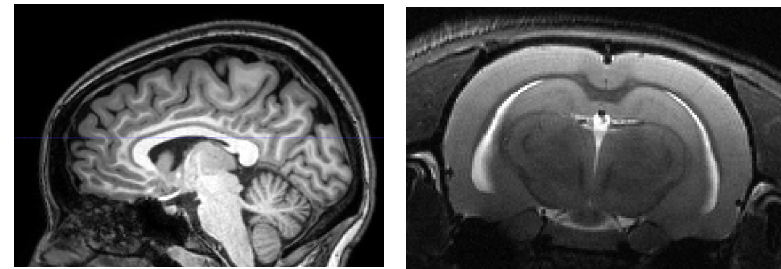


# Des modalités non invasives ...

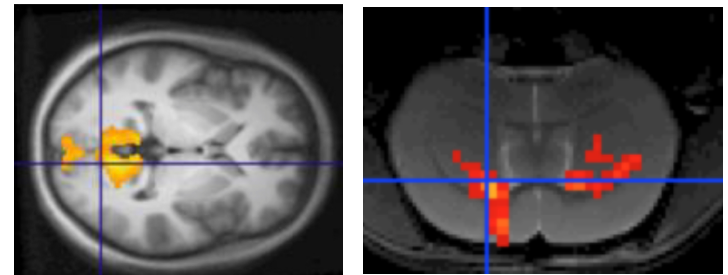
*Diffusion*



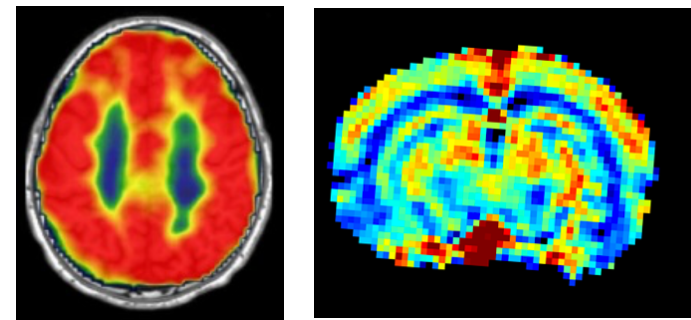
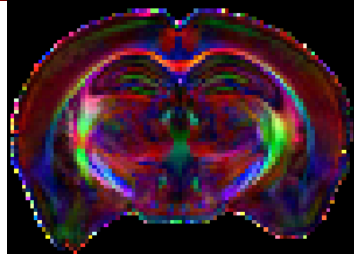
*Anatomie : tissus & structures*



*Fonction*



*Anatomie: fibres*

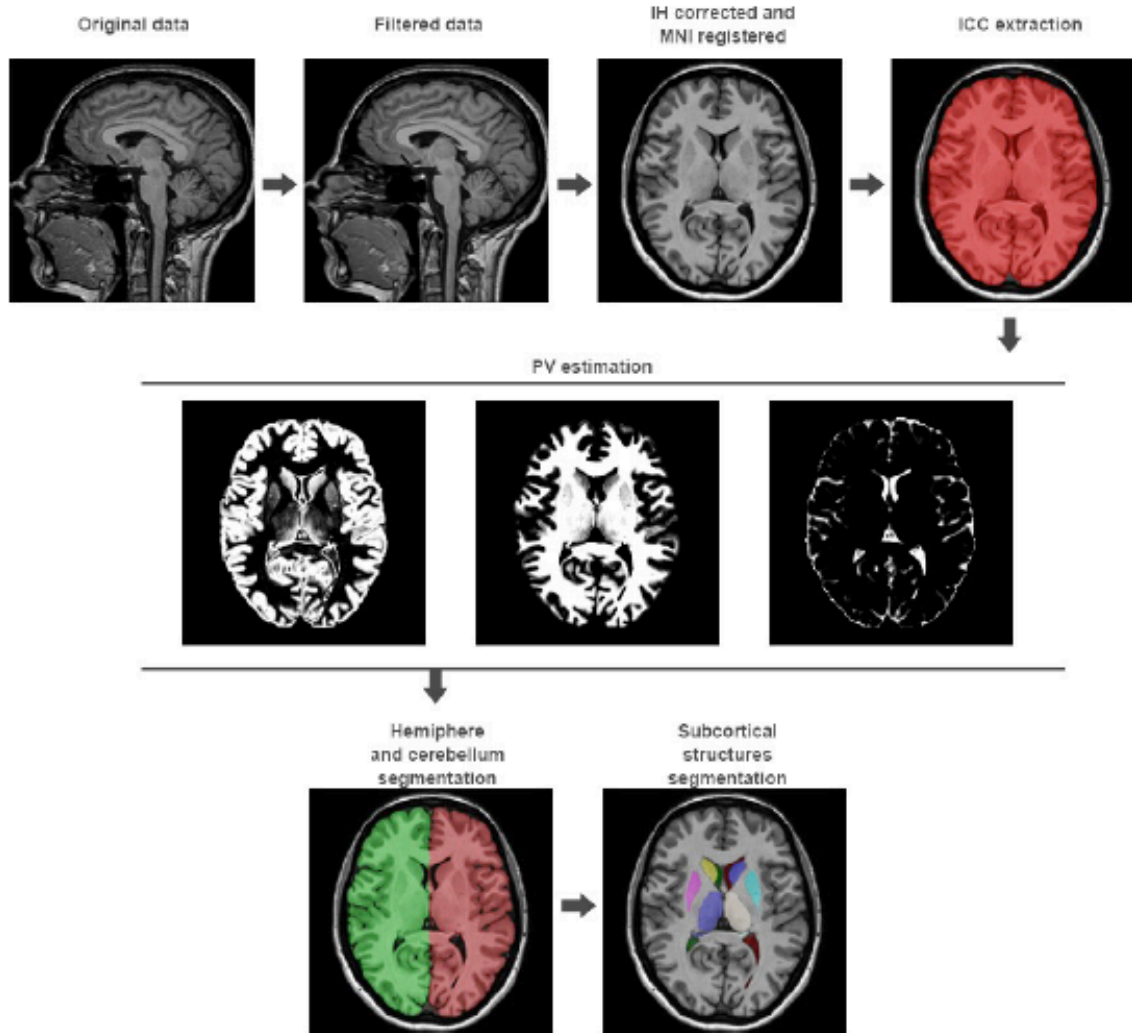


*Perfusion*



# *Anatomie Computationnelle*

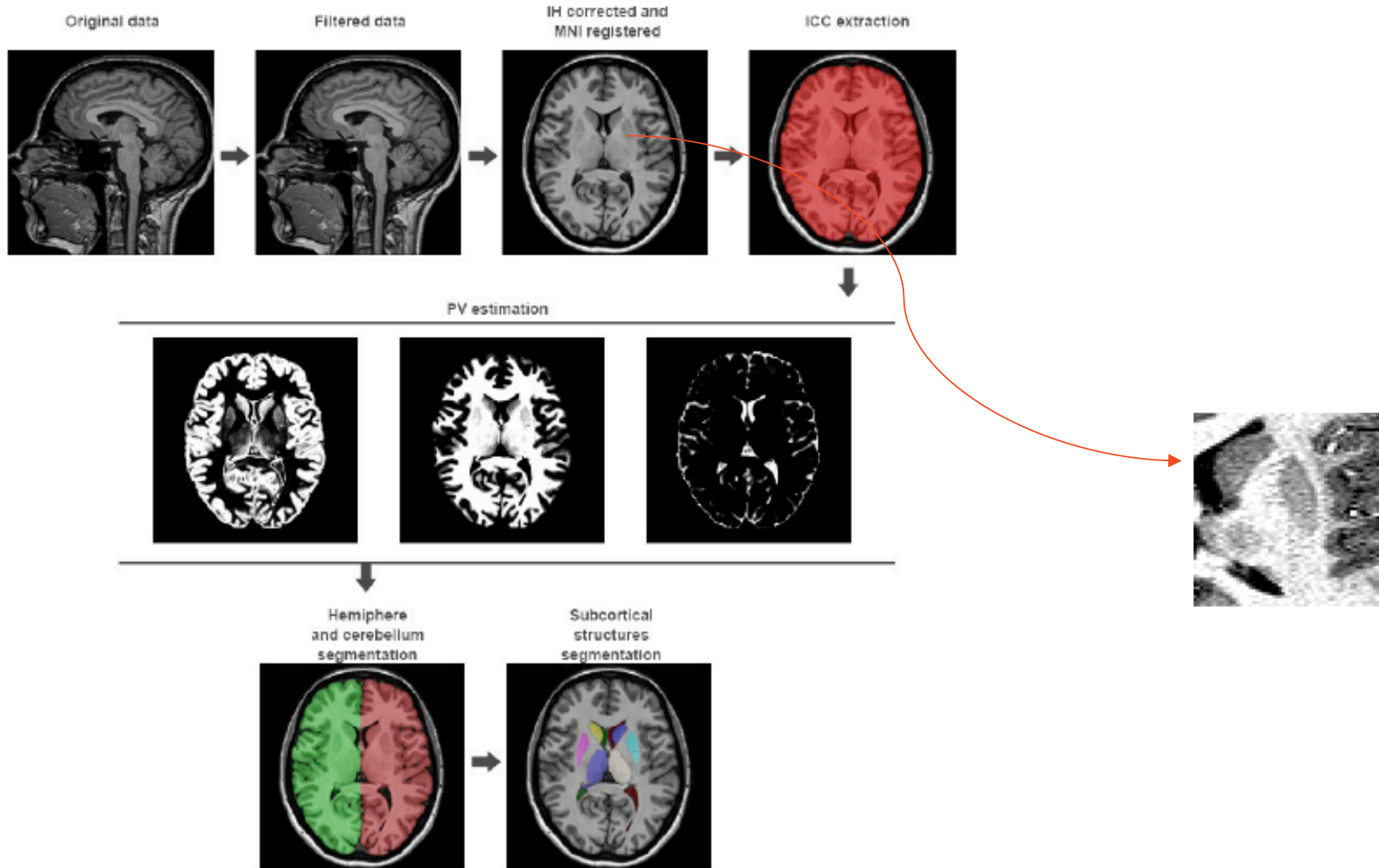
# Quantification automatique - Tissus & Structures



[Coupé HDR 2019]



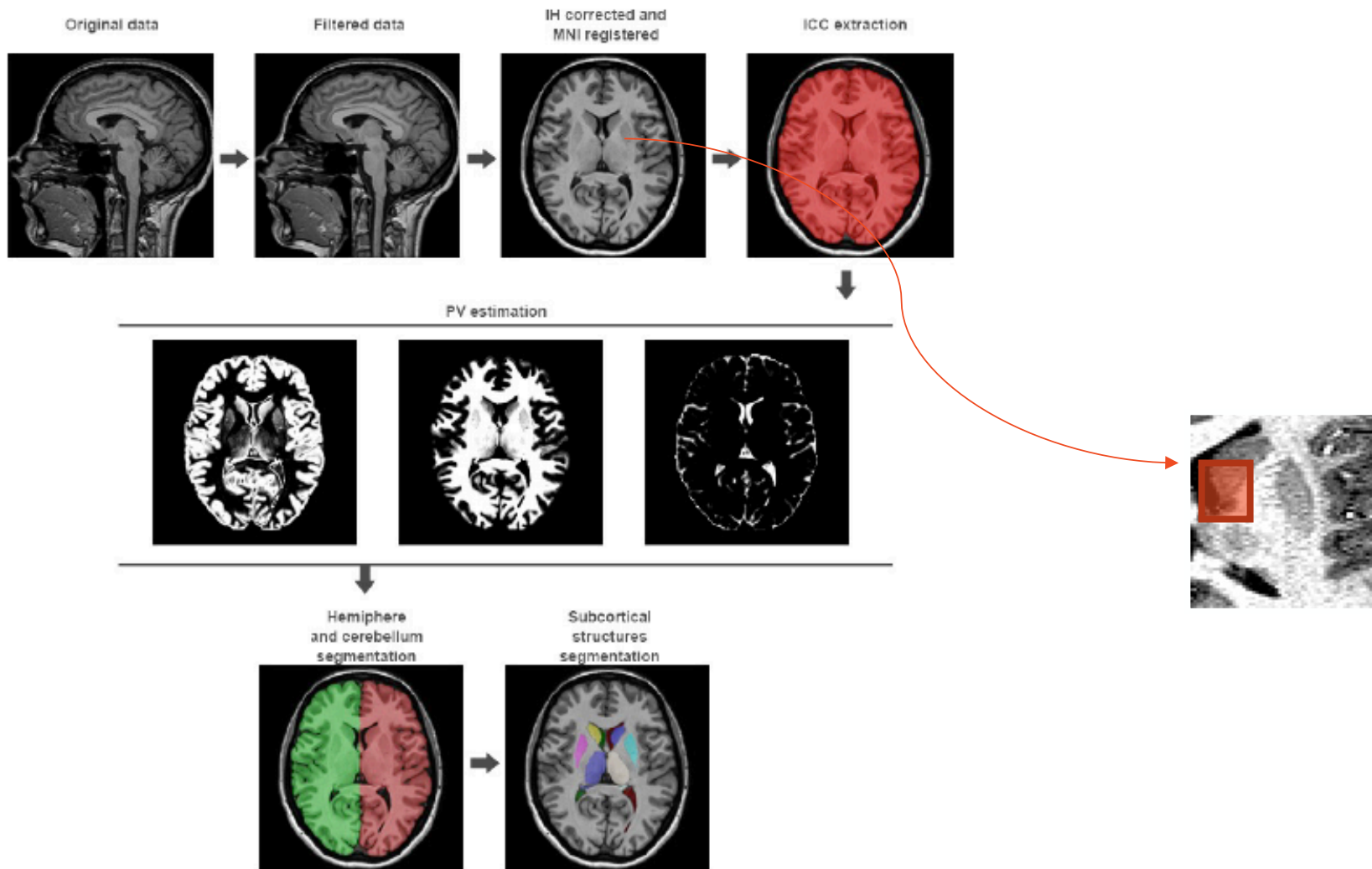
# Quantification automatique – Tissus & Structures



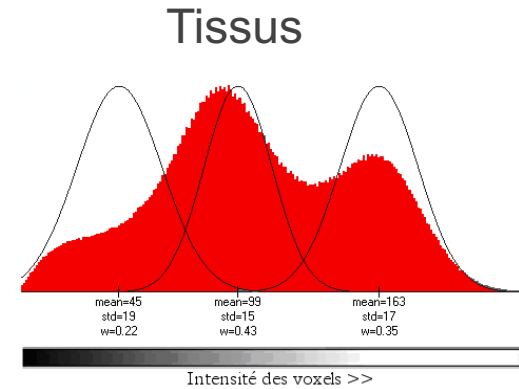
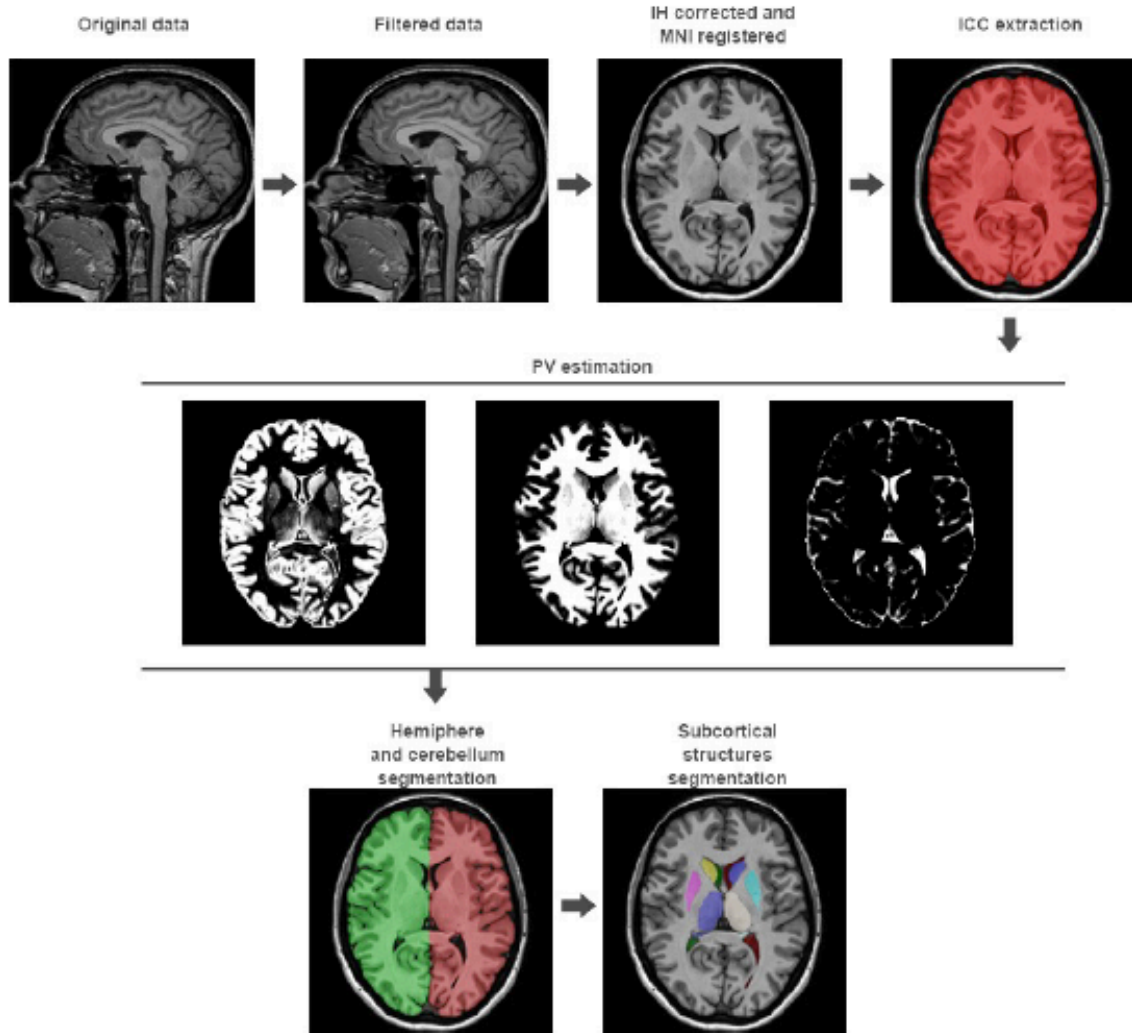
[Coupé HDR 2019]



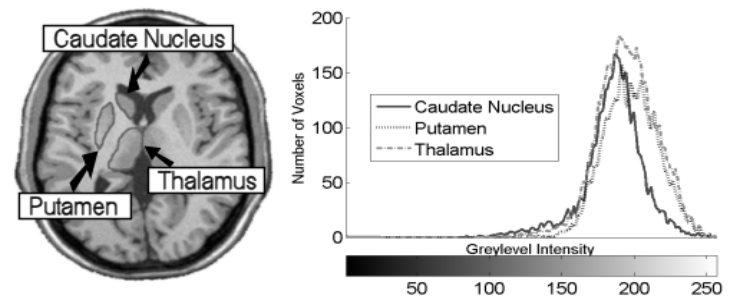
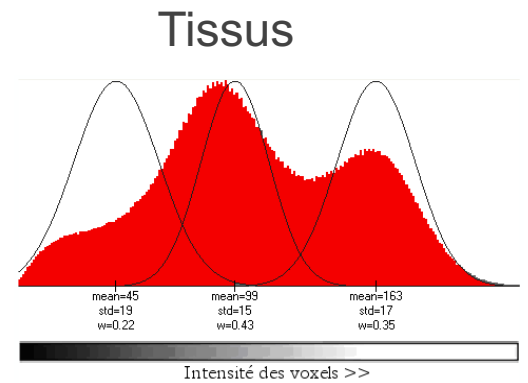
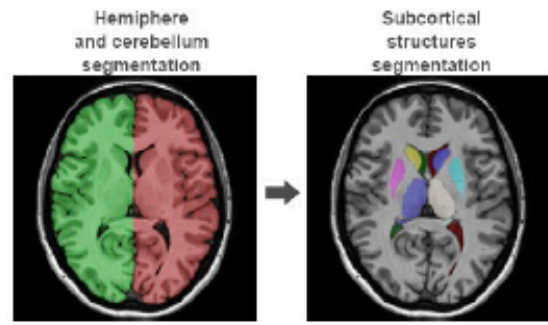
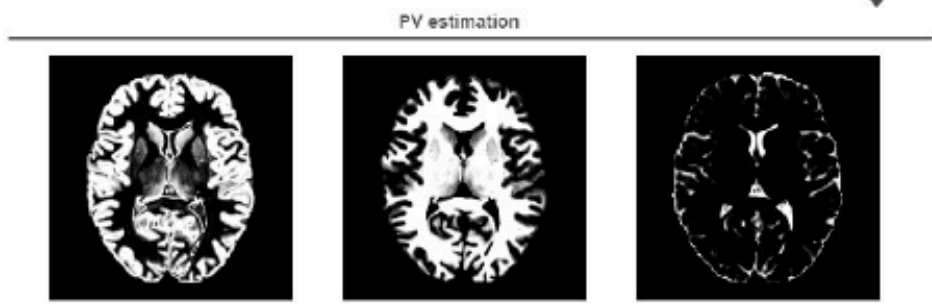
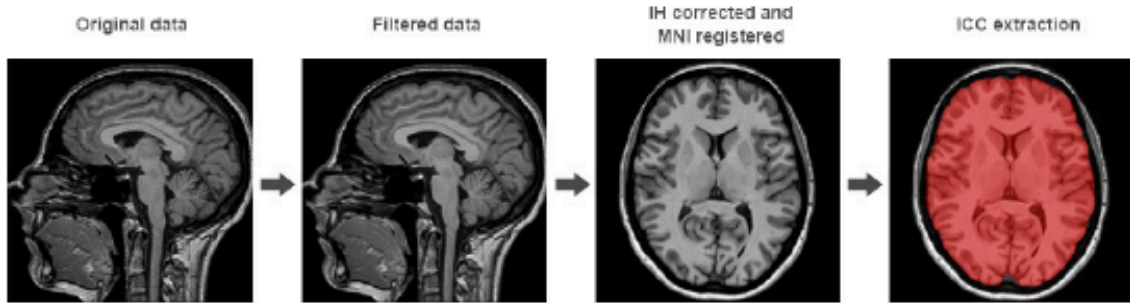
# Quantification automatique -II



# Quantification automatique -II

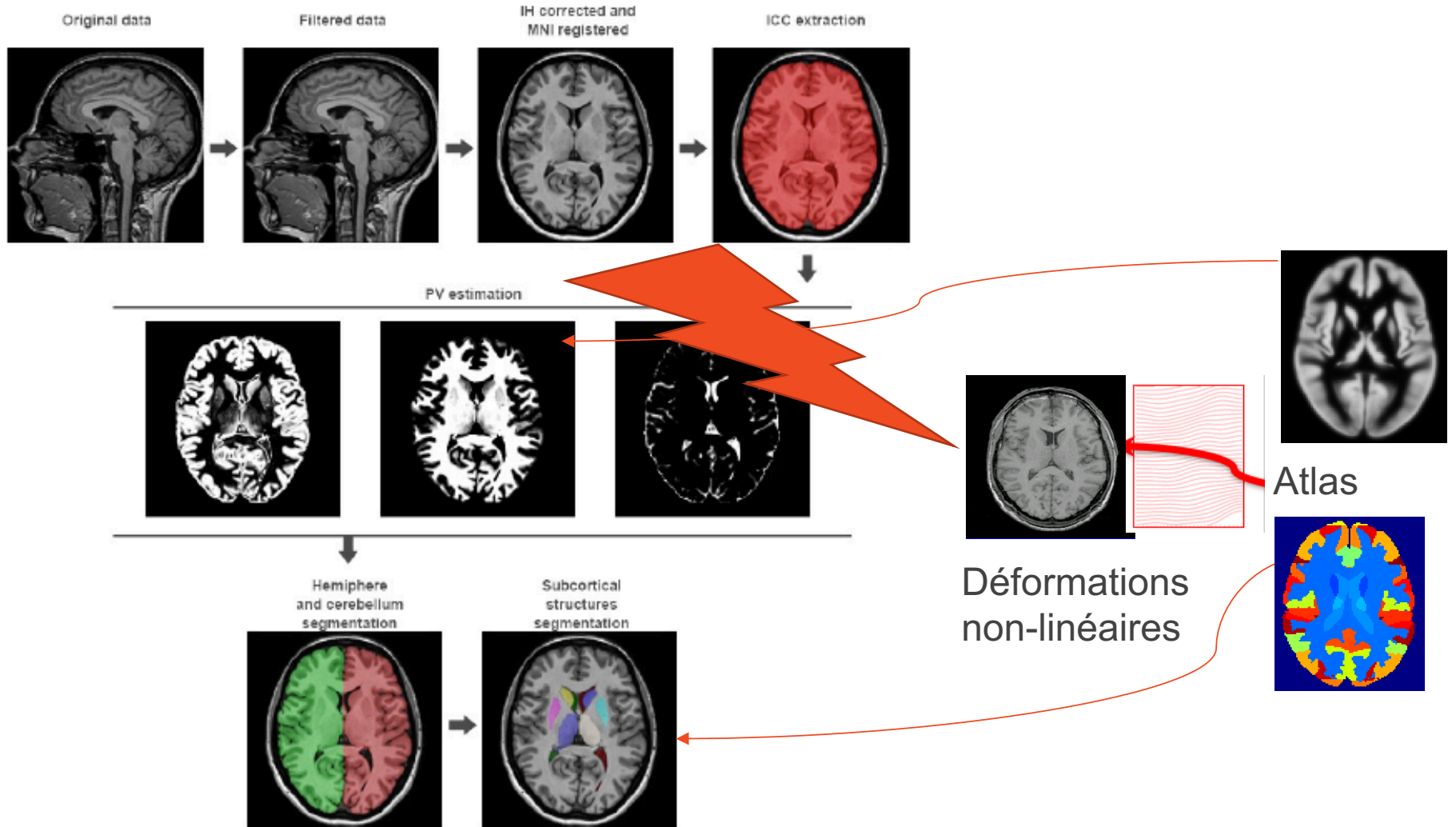


# Quantification automatique -II



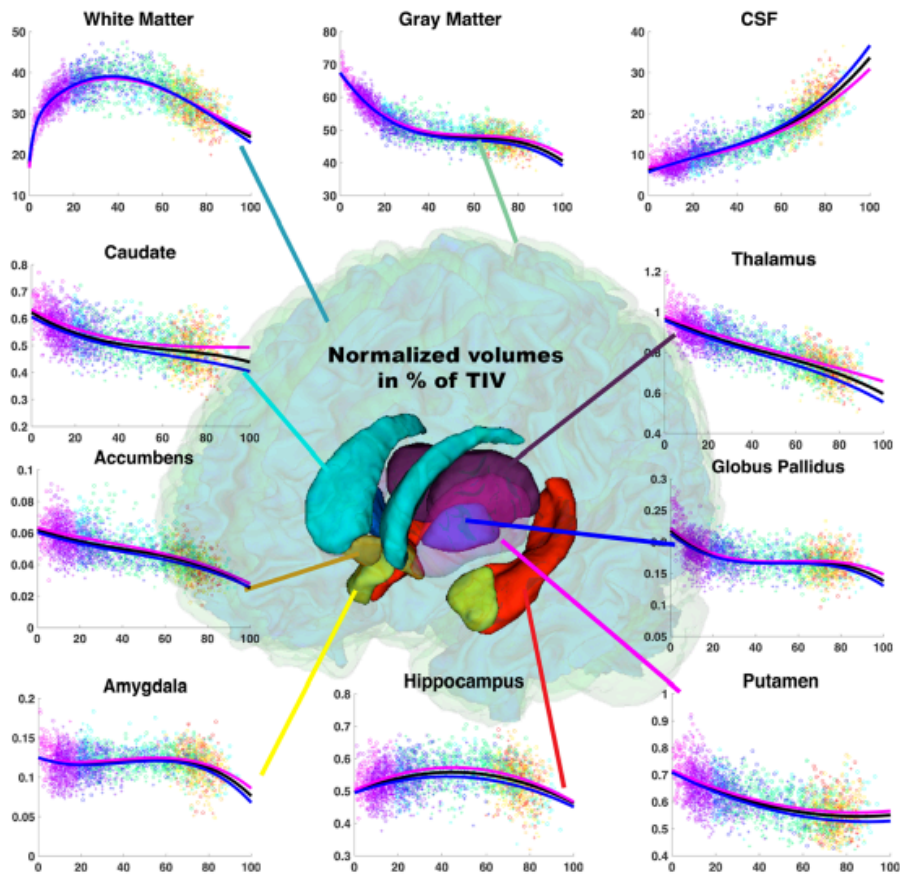
Structures

# Quantification automatique -II



# Détecter des formes atypiques

Sujets Sains : 2944

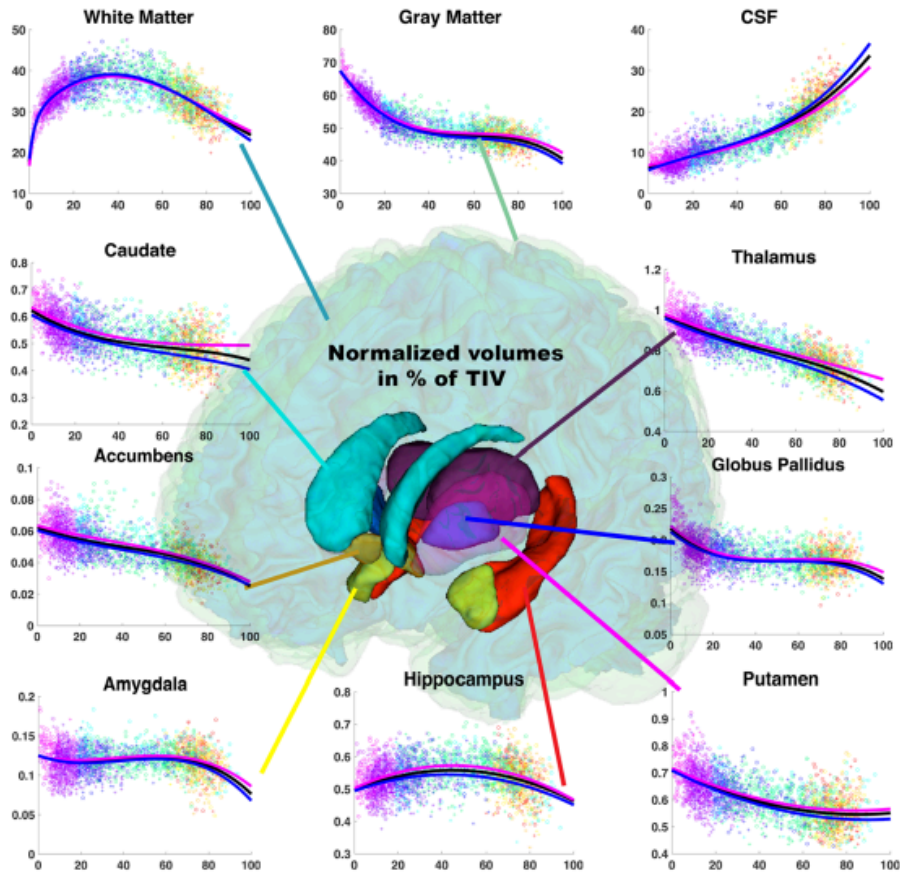


[Coupé HDR 2019]

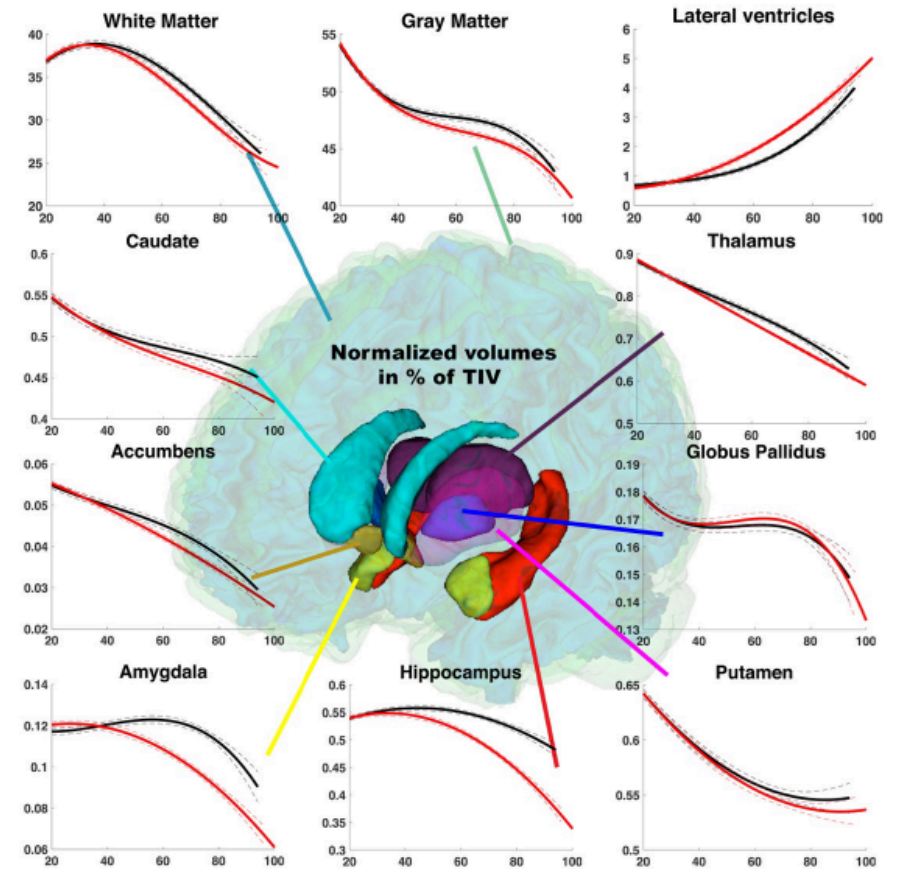


# Détecter des formes atypiques

Sujets Sains : 2944



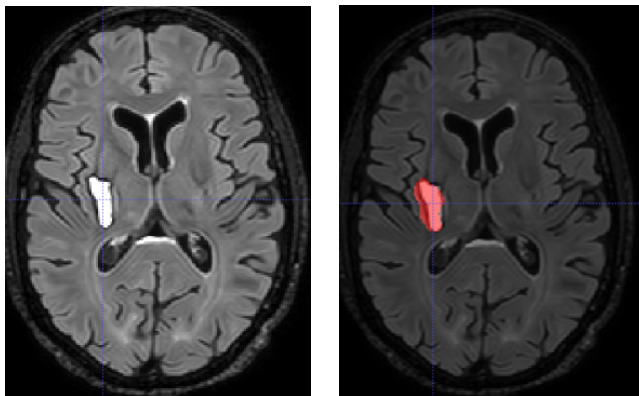
Patients Alz-MCI: 3262



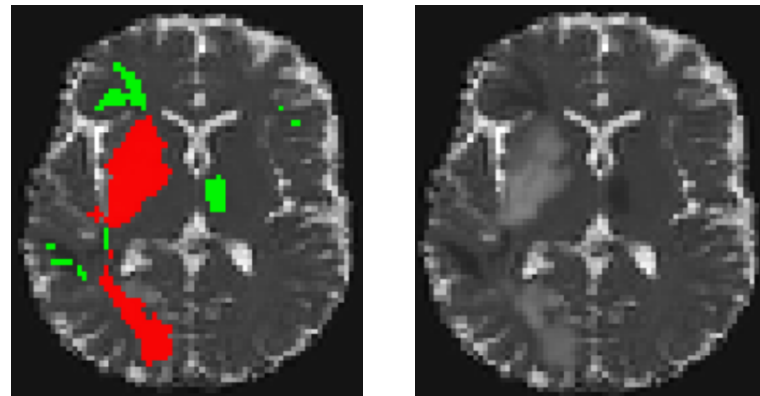
[Coupé HDR 2019]

# Détecter des zones atypiques

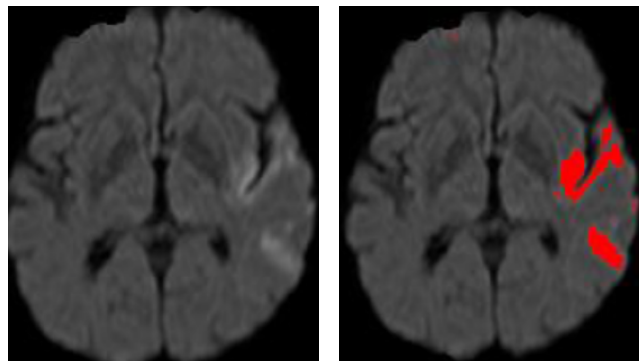
SEP



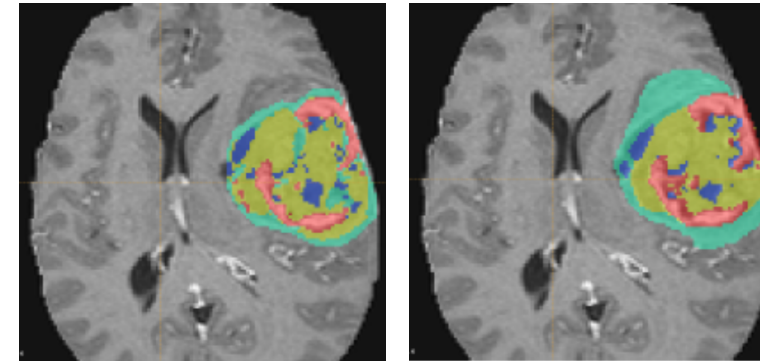
Trauma



AVC



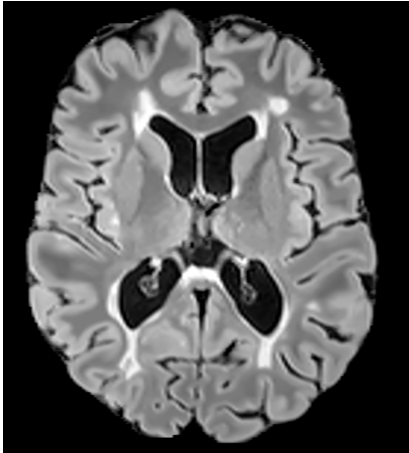
Tumeur



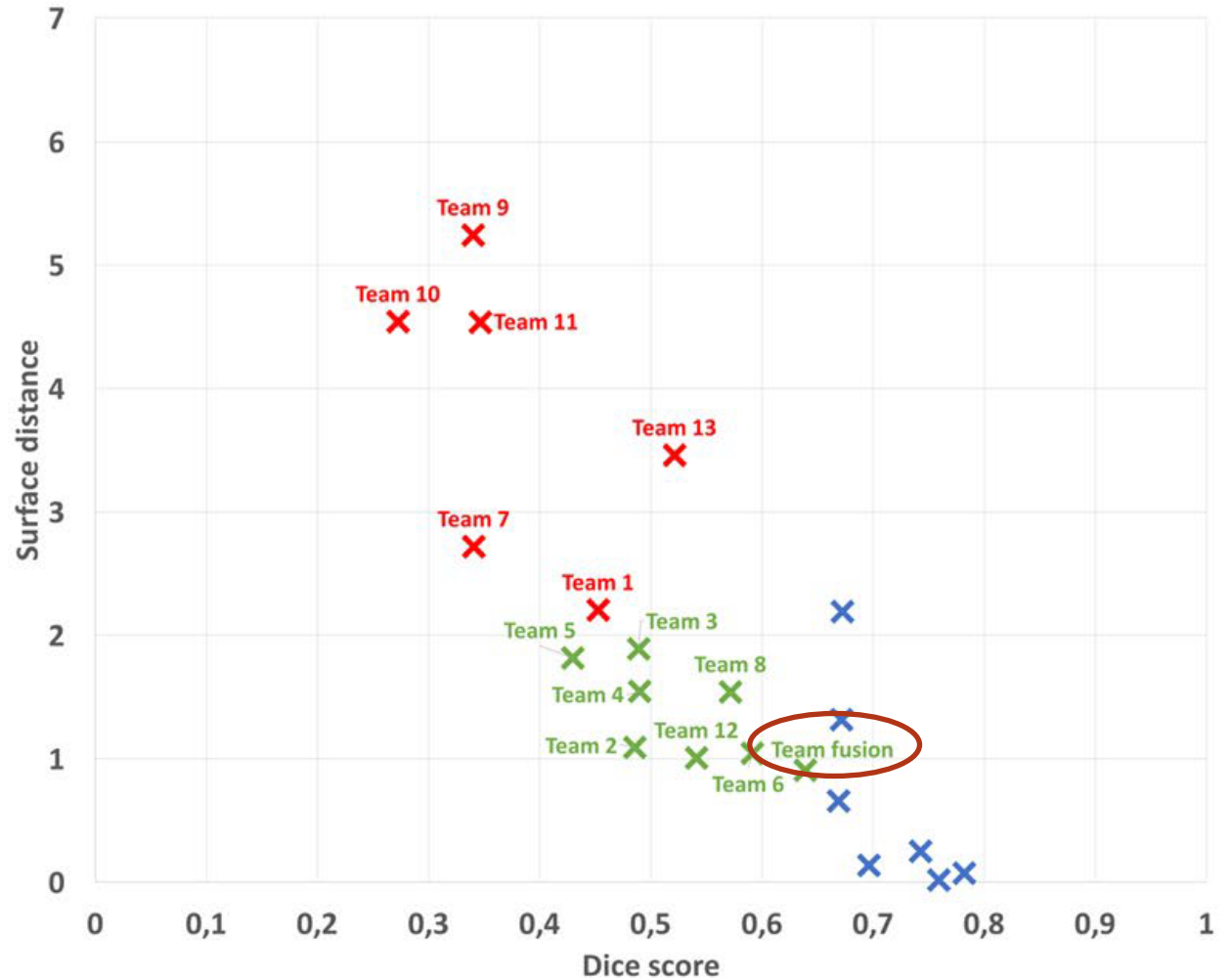
Automatique

Manuel

# Comparer les solutions




Challenge  
Miccai 2016



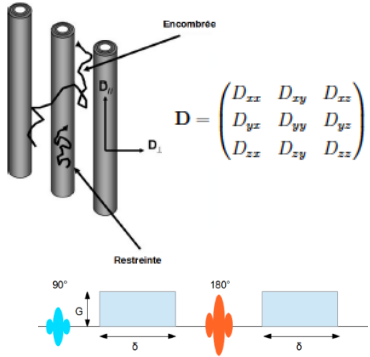
Commowick, O. et al. *Nature Scientific Reports*, 2018



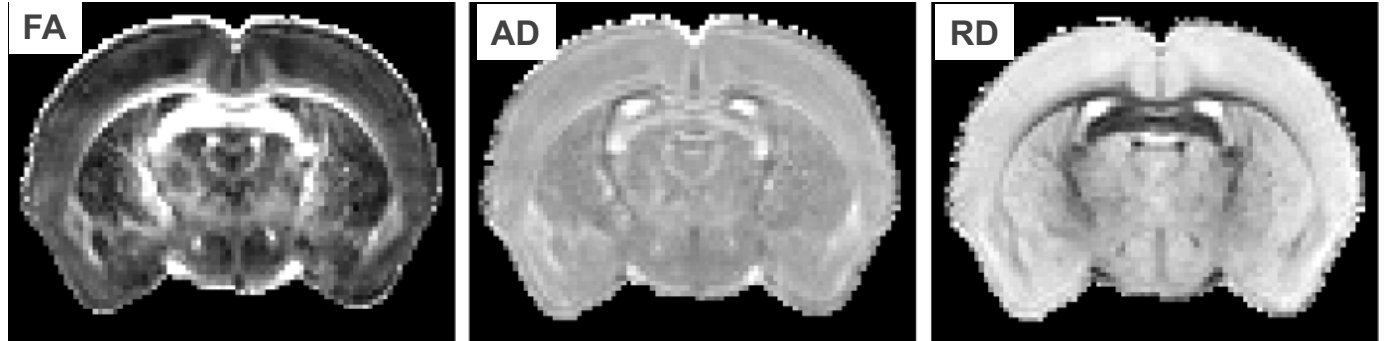


*Fiber Tracking*

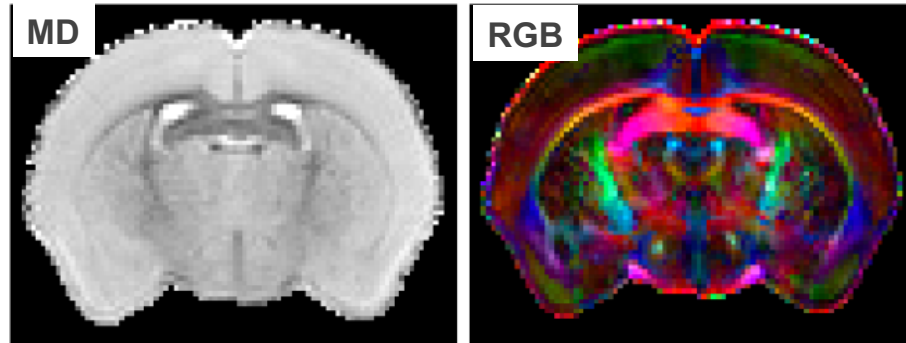
# Diffusion Tensor Imaging



$$D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yz} & D_{yy} & D_{yz} \\ D_{zx} & D_{xy} & D_{zz} \end{pmatrix}$$



9.4T

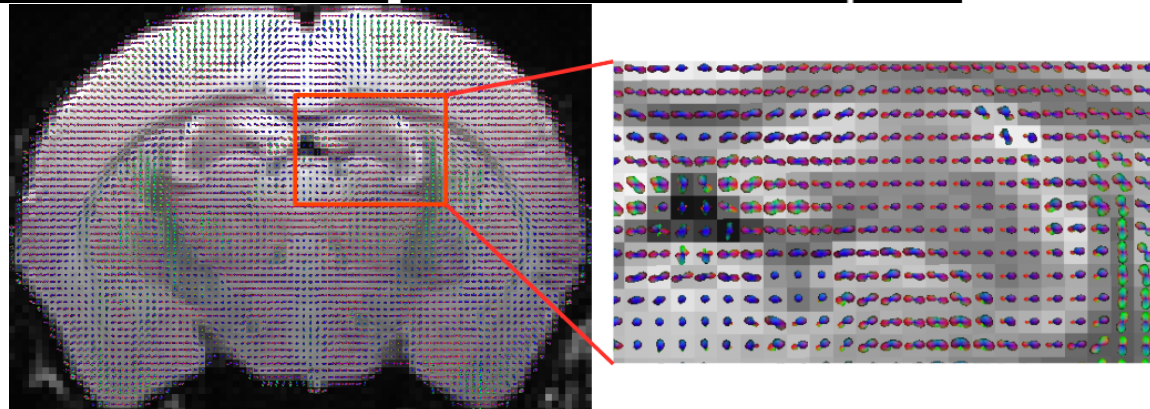


$$FA = \sqrt{\frac{3}{2}} \sqrt{\frac{(\lambda_1 - \bar{\lambda})^2 + (\lambda_2 - \bar{\lambda})^2 + (\lambda_3 - \bar{\lambda})^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

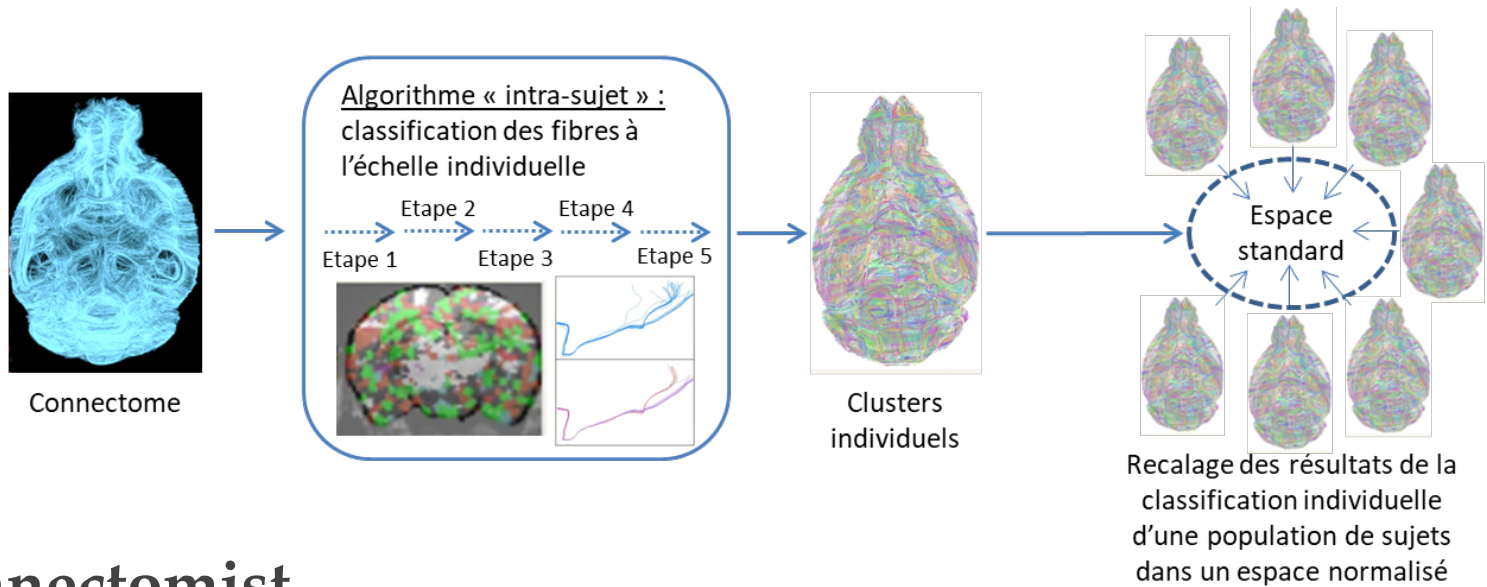
$$MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

$$RD = \frac{\lambda_2 + \lambda_3}{2}$$

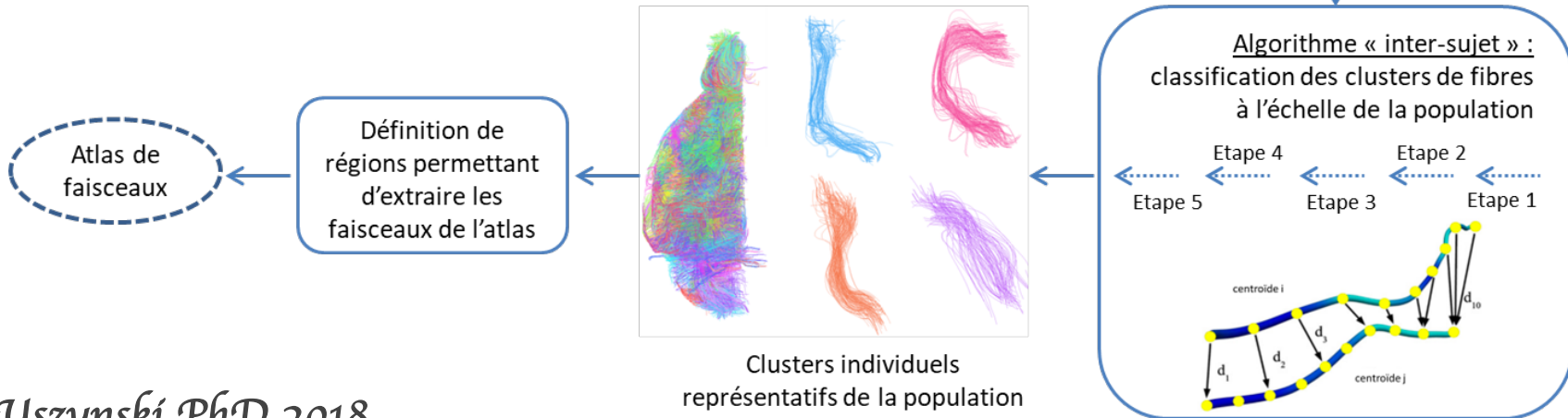
$$AD = \lambda_1,$$



# Towards an Murin brain fiber bundle atlas

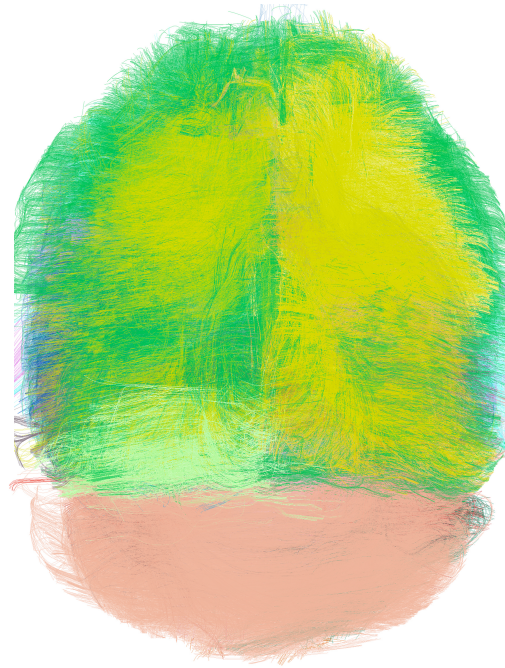
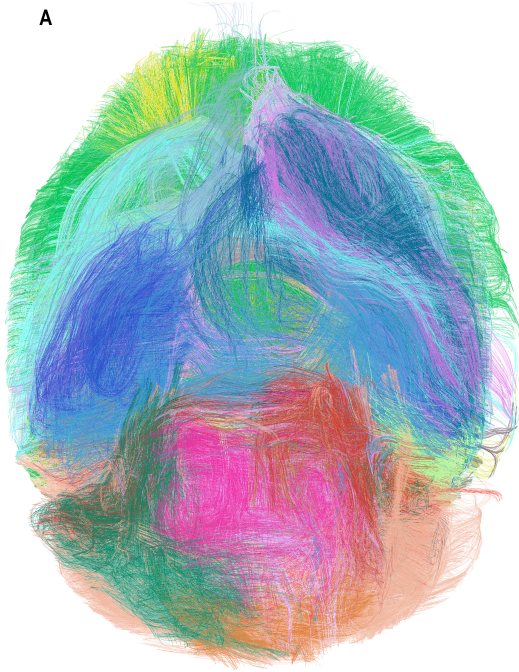


## Connectomist

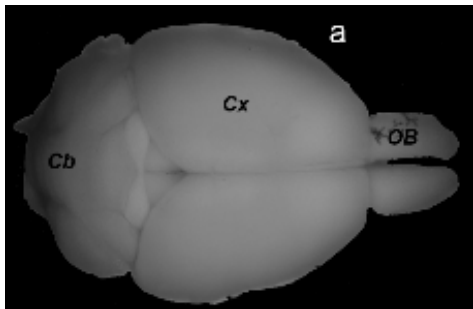


# C57Bl6 mouse brain

A



- Anterior Commissure
- Corpus Callosum
- Fimbria
- Inferior Colliculus Commissure
- Posterior Commissure
- Superior Colliculus Commissure
- Tectospinal Pathway
- Cerebellar Peduncle
- Cingulum
- Fasciculus Retroflexus
- Fornix
- Internal Capsule
- Inferior Cerebellar Peduncle
- Lateral Lemniscus
- Mammillothalamic Tract
- Medial Forebrain Bundle
- Medial Longitudinal Fascicle
- Pyramidal Tract
- Stria Terminalis
- Stria Medularis
- Ventral Spinocerebellar Tract
- Uncinate Fasciculus
- Arbor vitae
- Middle Cerebellar Peduncle



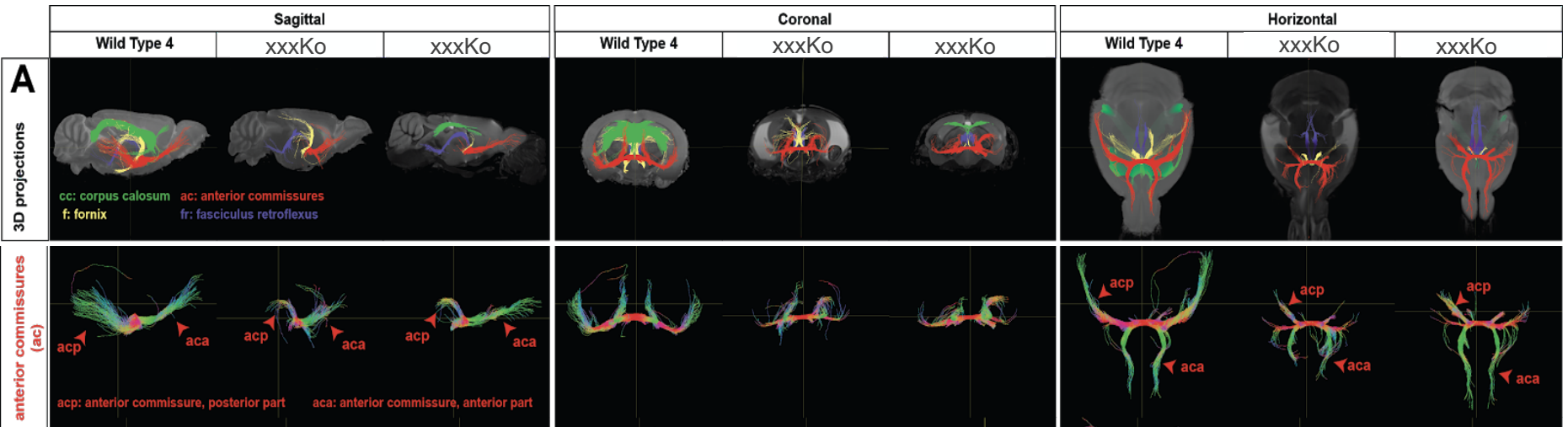
*1. Uszynski PhD 2018*



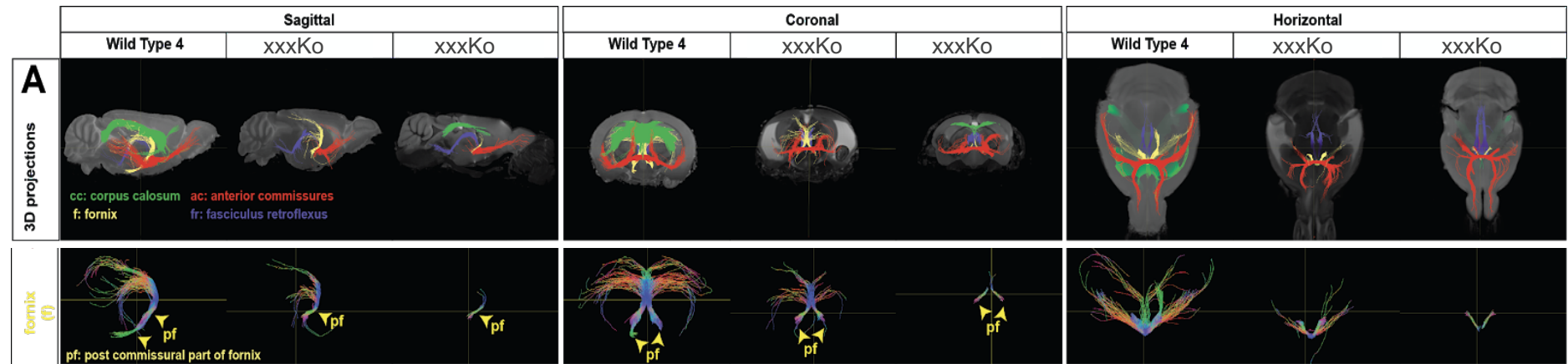
# Pathological model: xxx KO

Master 2019 D. Alves Rodrigues de Souza

## Anterior Commissure Global diminution

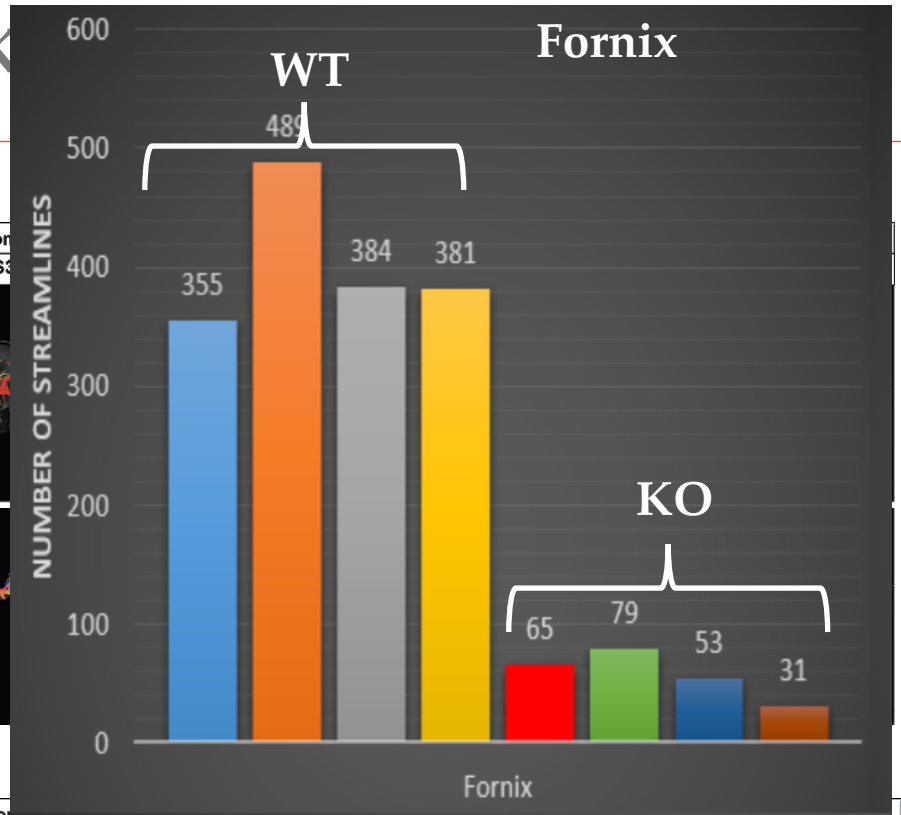
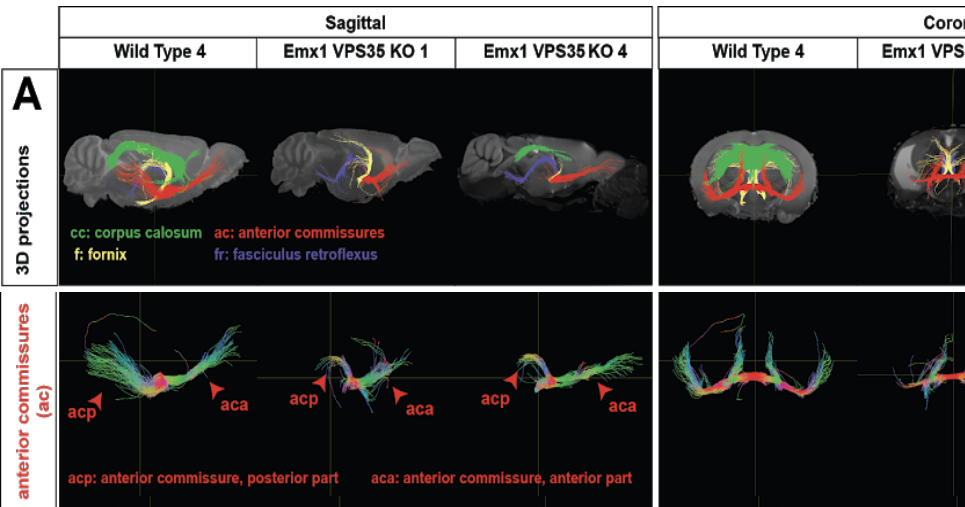


## Fornix

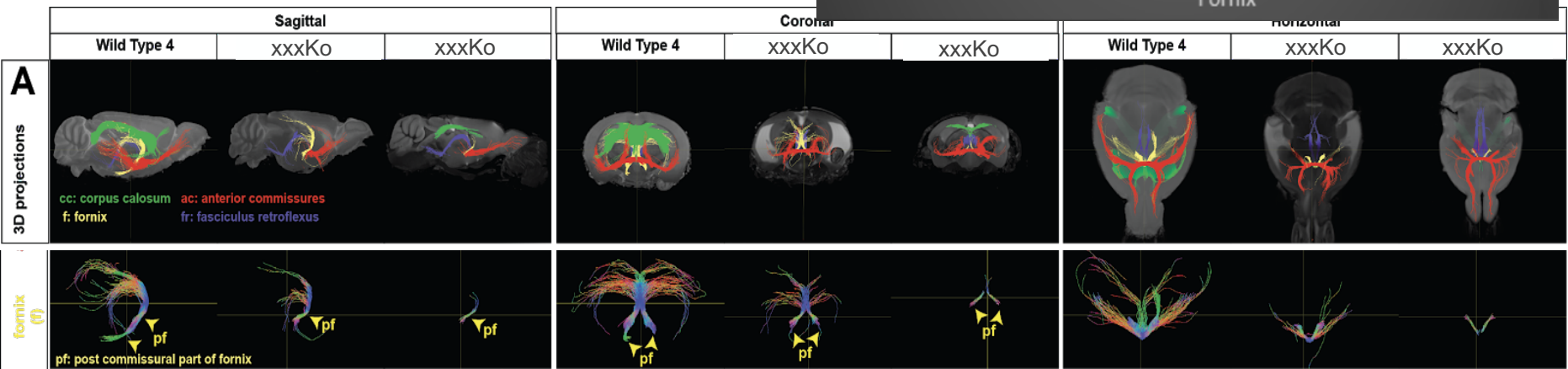


# Pathological model: VPS35 KO

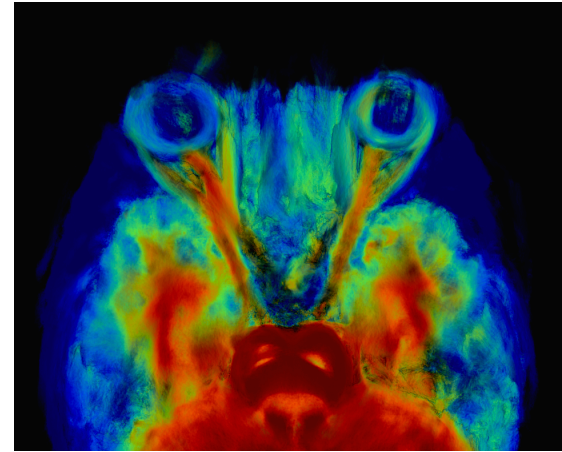
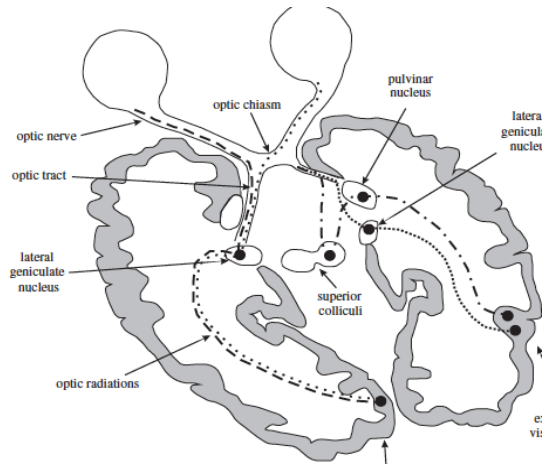
## Anterior Commissure Global diminution



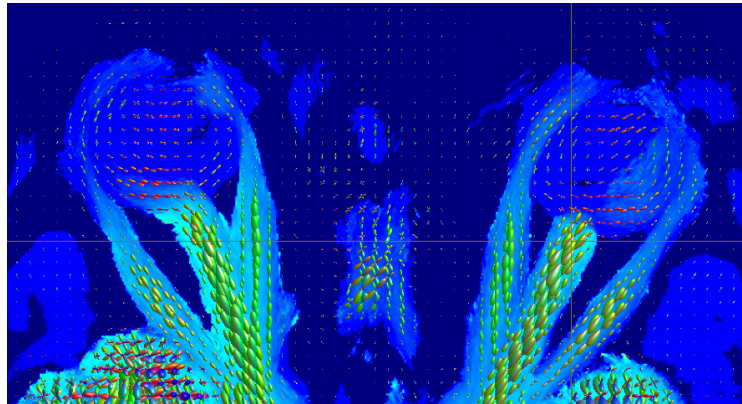
## Fornix



# DTI du système visuel chez l'homme - I

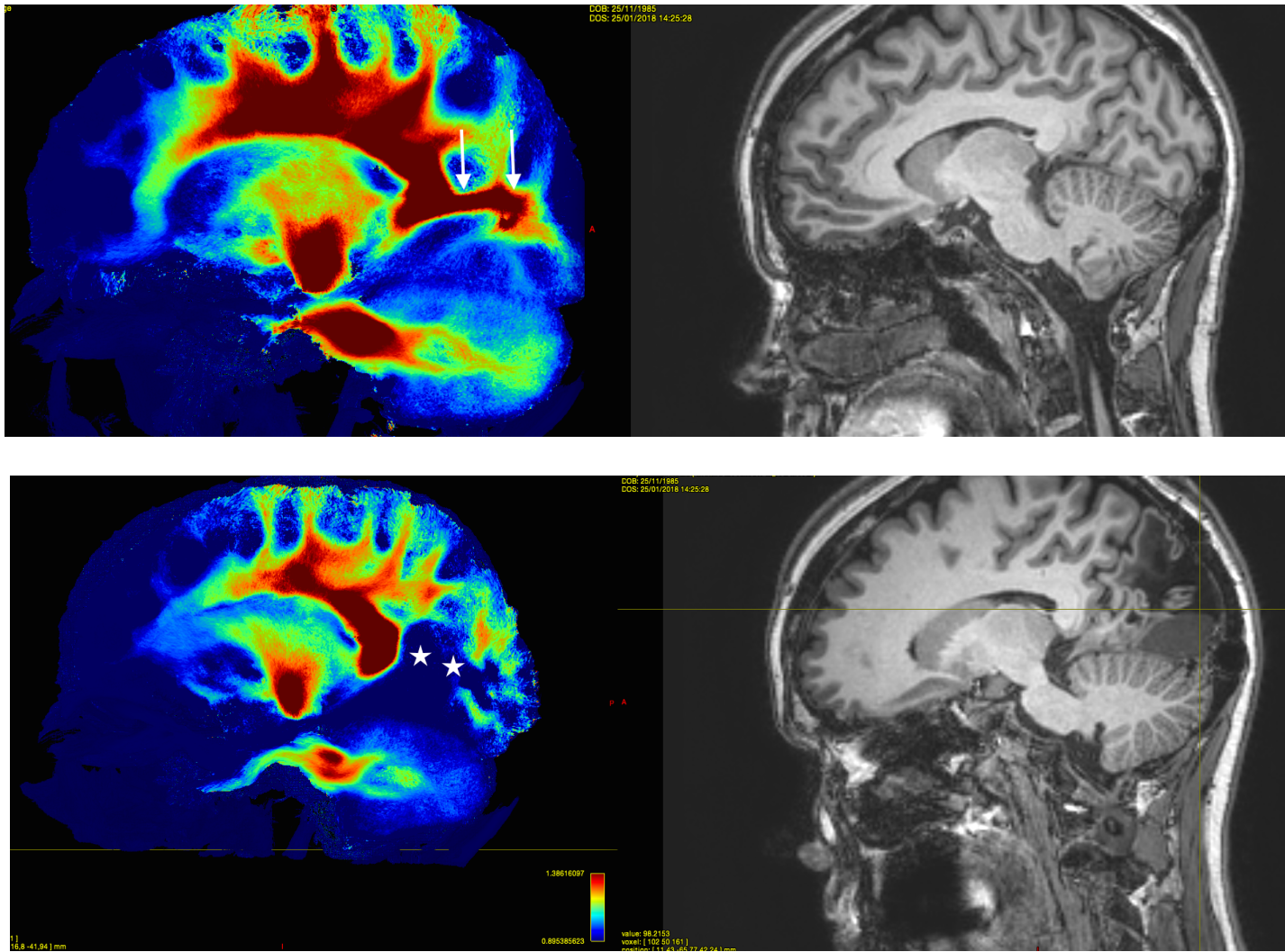


Control



Coll A. Attye

# DTI du système visuel chez l'homme - II



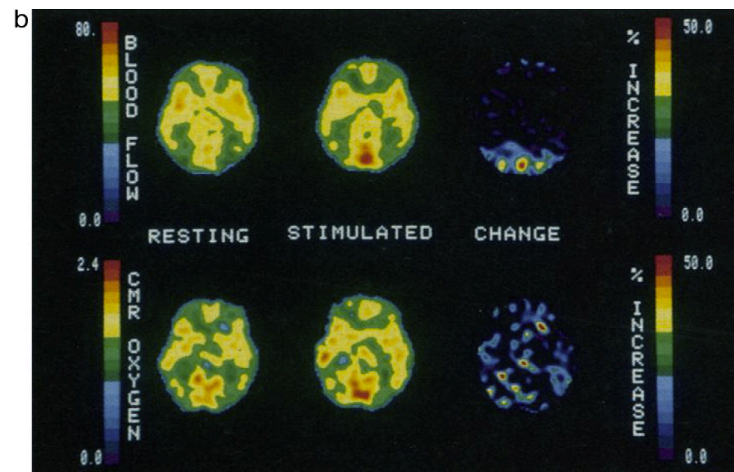
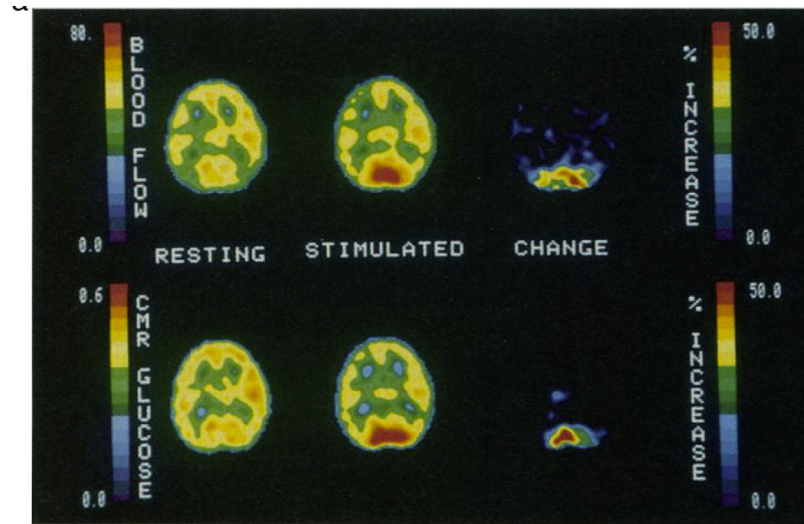
Passera et al HBM 2019





# *Functional Imaging*

# Principle

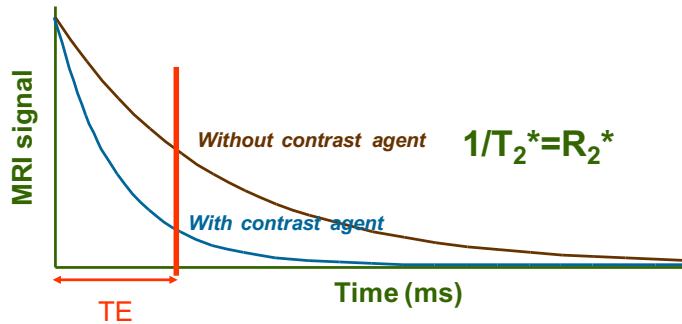


Fox and Raichle (1986), PNAS

# Blood Oxygen Level Dependent Contrast- I

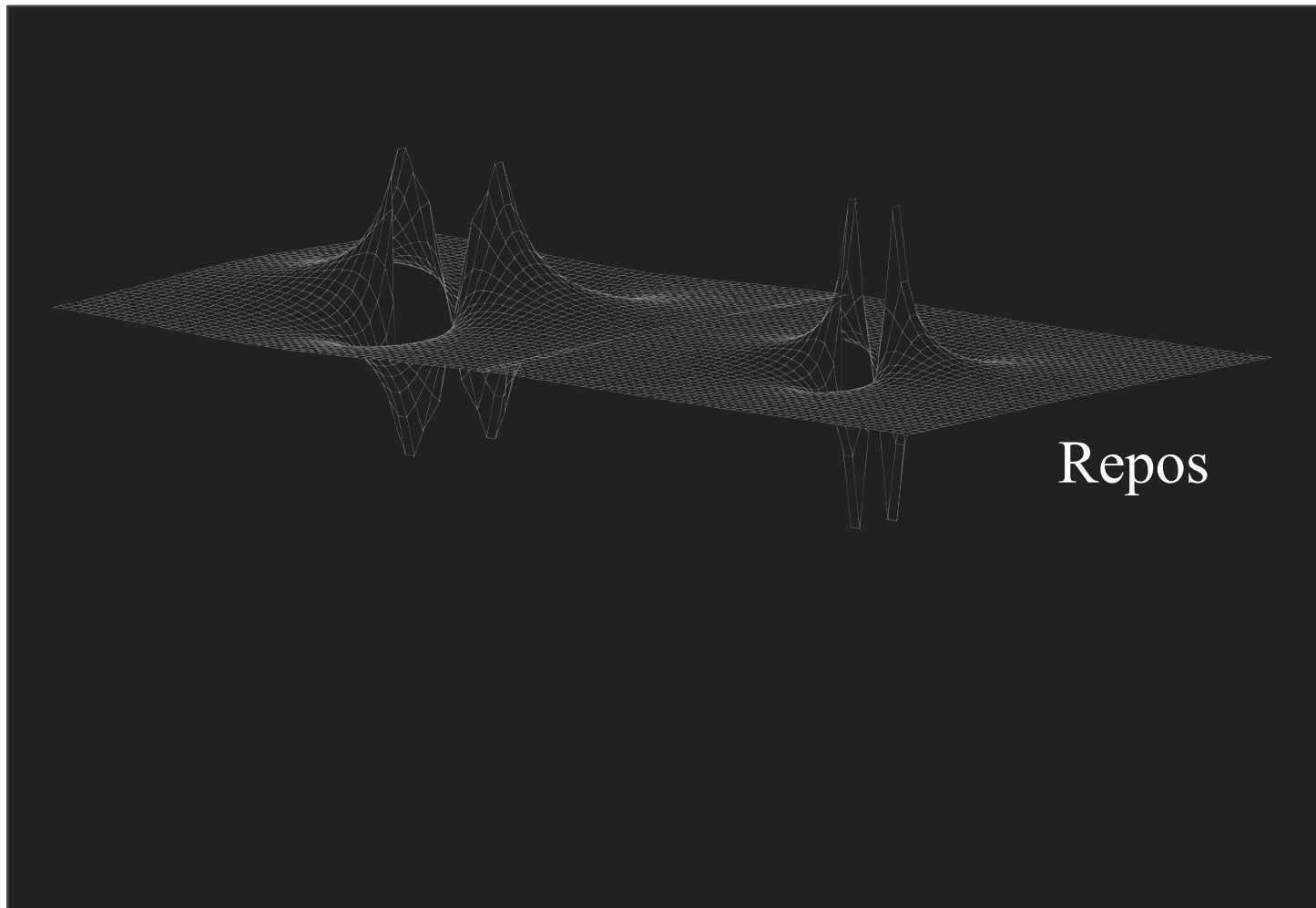


HbO<sub>2</sub>

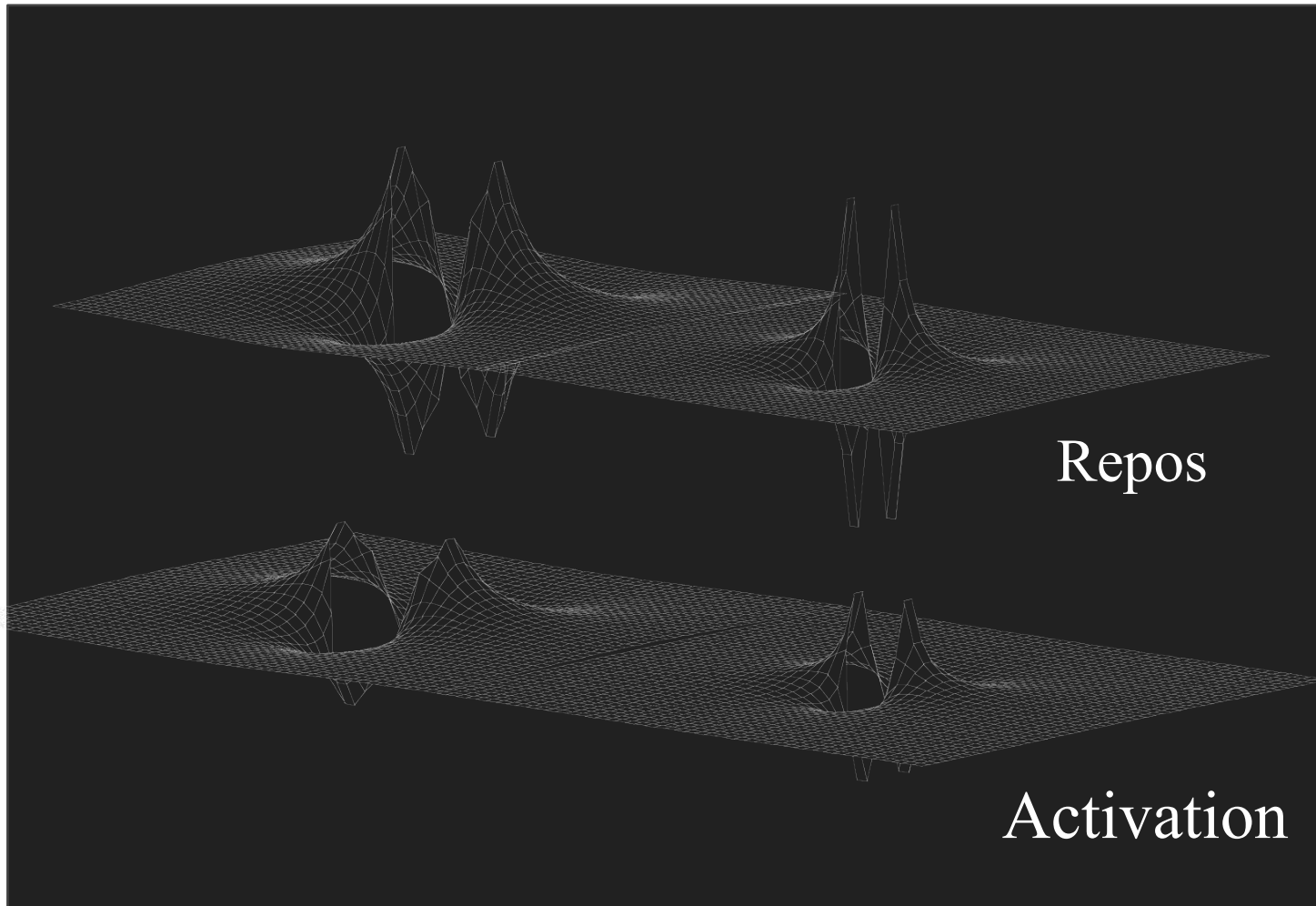


- Développement de la séquence EPI : Schmitt et al SMRM 1991
- Functional Brain Imaging basé sur EPI Kwong et al. 1992 PNAS
- Ogawa PNAS 1992

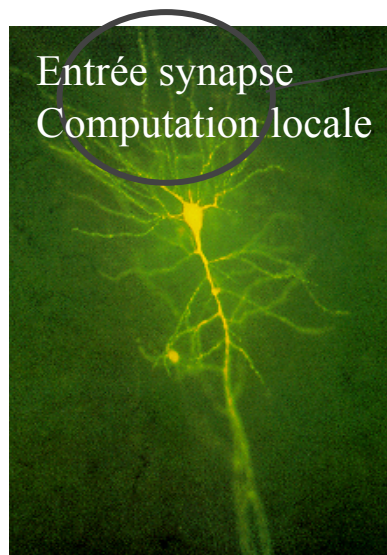
# Blood Oxygen Level Dependent Contrast - II



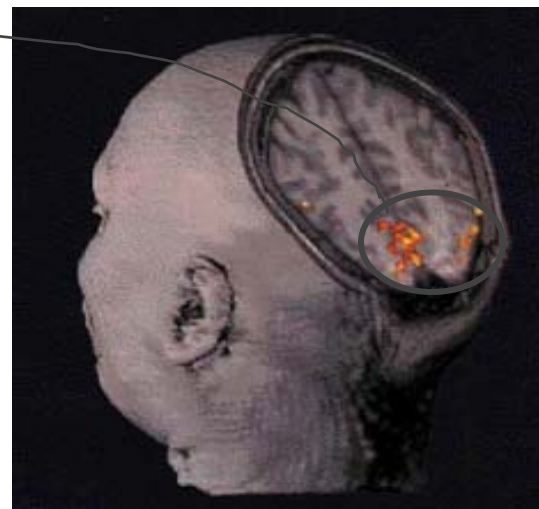
# Blood Oxygen Level Dependent Contrast - III



# Technique non-invasive & indirecte



Répercussions  
-métabolique  
-hémodynamique

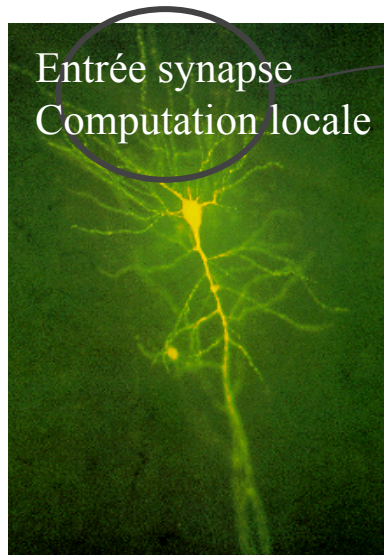


Activité neuronale

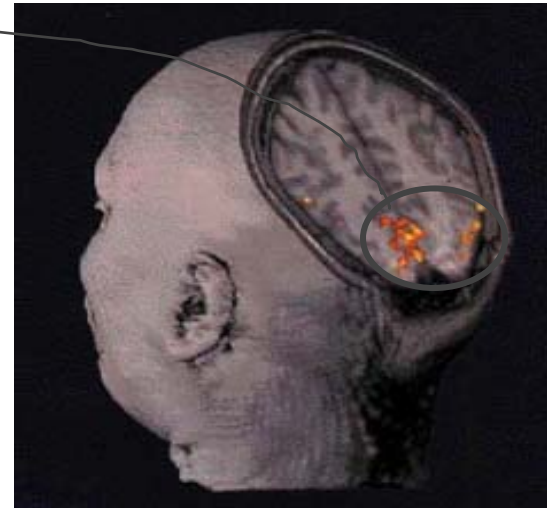
Imagerie par **effet BOLD**



# Technique non-invasive & indirecte



Répercussions  
-métabolique  
-hémodynamique



Activité neuronale

Imagerie par **effet BOLD**

**Couplage neuro-vasculaire** mal connu



1 voxel =  $3 \times 3 \times 3 \text{ mm}^3 = 5.5 \cdot 10^6$  neurones,  $10^{10}$  synapses, 22 Km dendrites, 220 km d'axones !!!

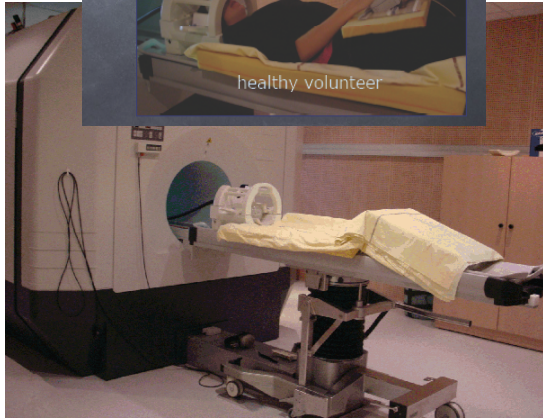
[Friston Science 2009]

Le signal est faible et dépend de nombreux facteurs

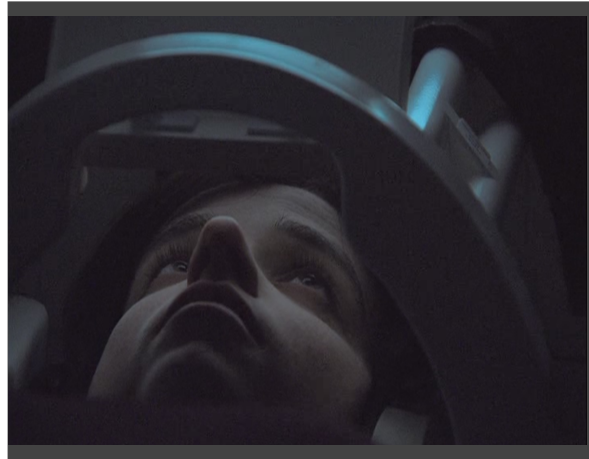


(vascularisation, pathologie, conditions de mesure, instrumentation ...)

# Une expérience en vision



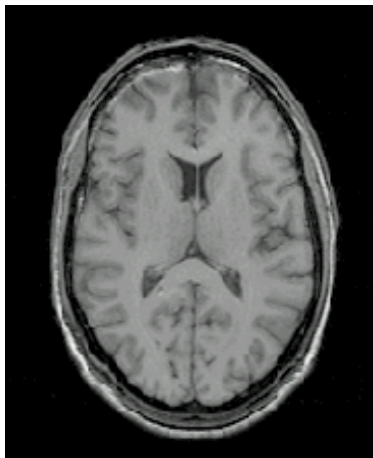
3T MR



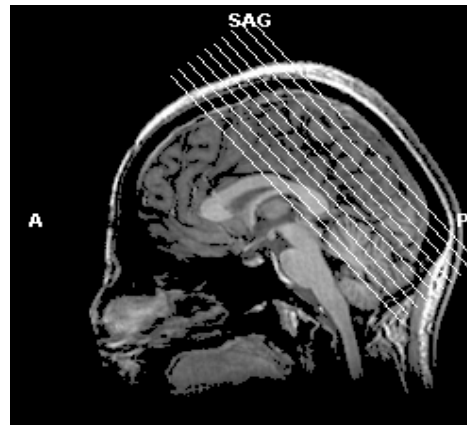
Structural



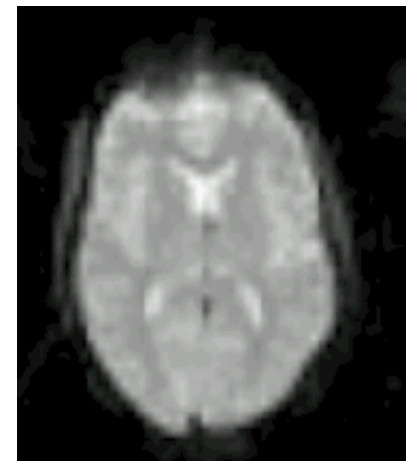
Fonctional



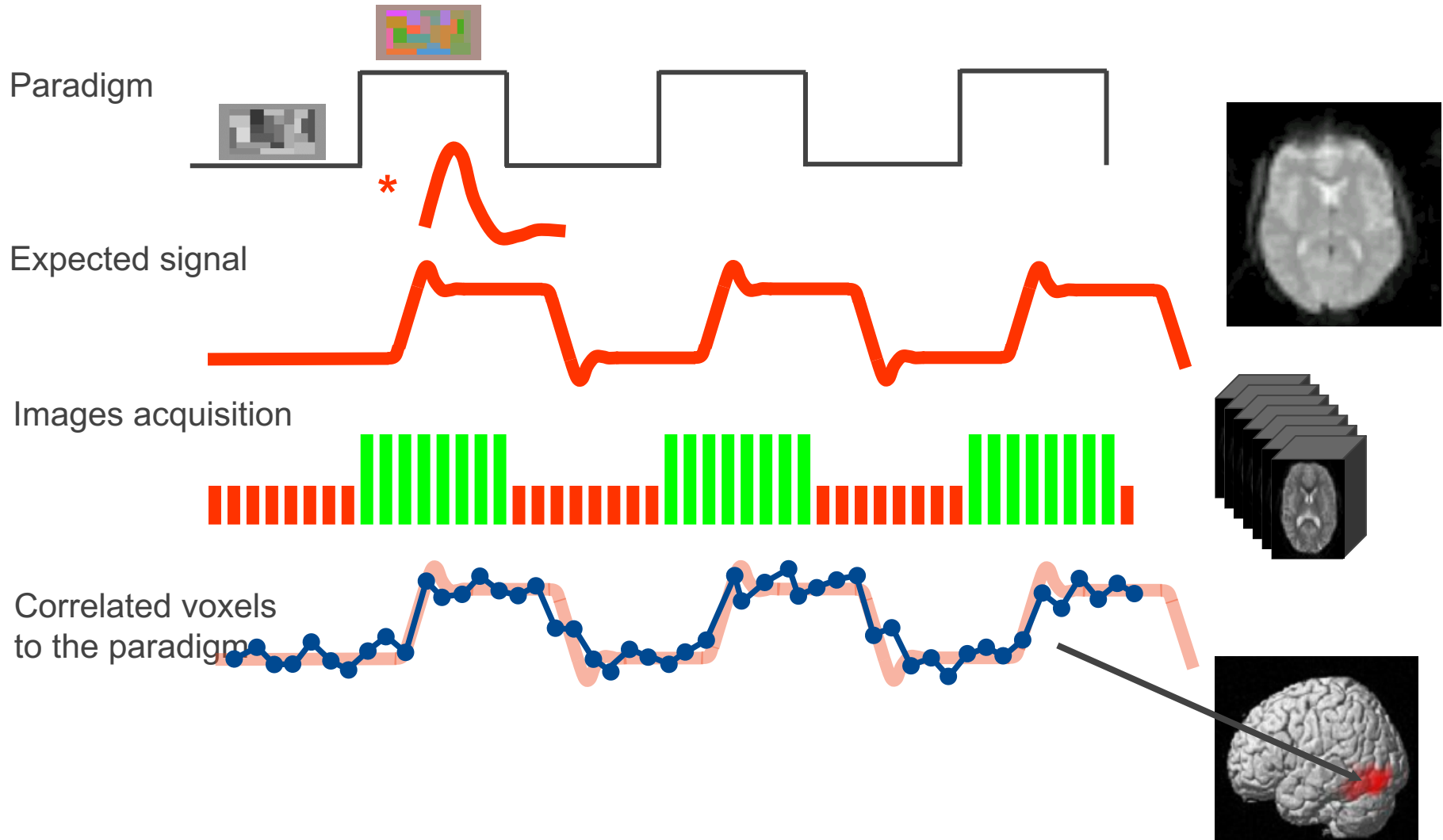
transverse



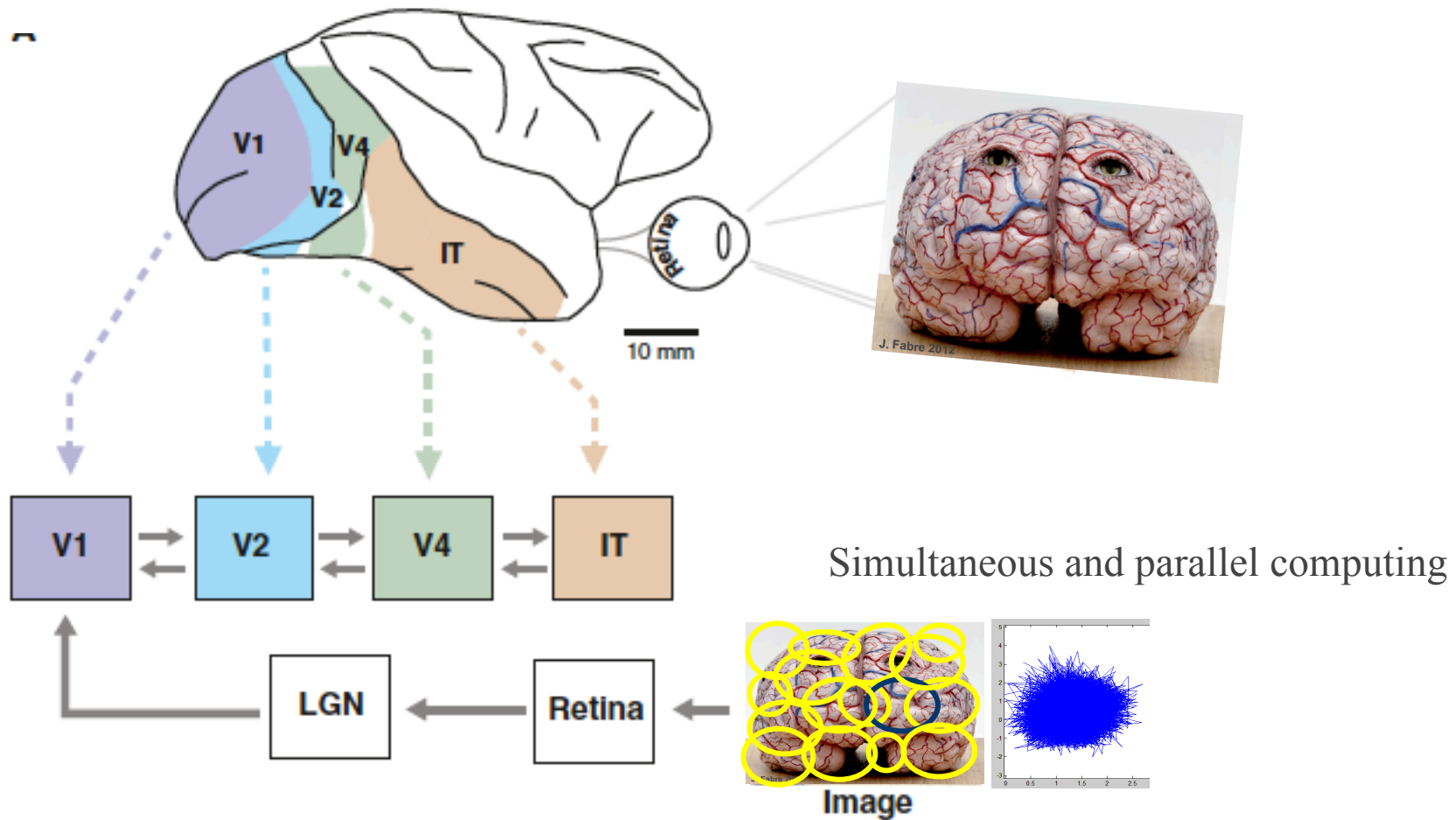
sagittal



# Recherche les zones activées



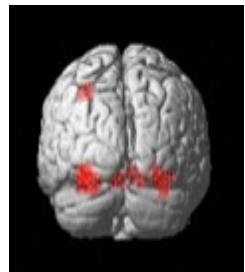
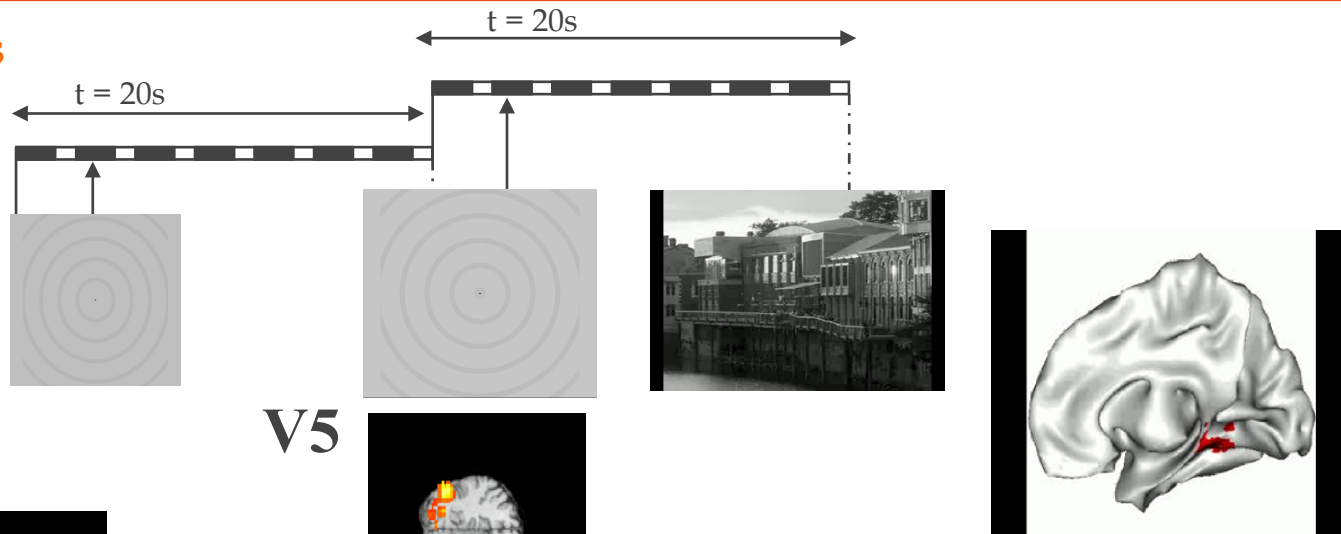
# Le système visuel humain



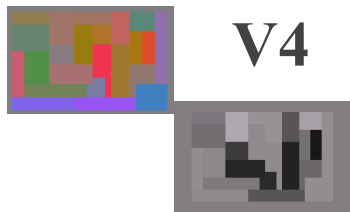
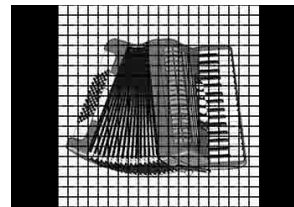
[adapted from Cox & Dean curr bio 2014]

# Some examples

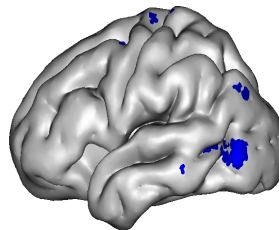
## Localizers



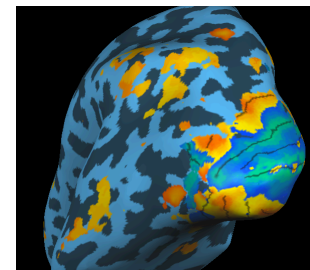
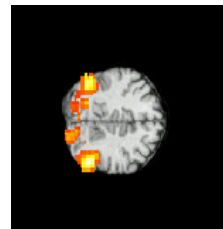
LOC



V4



V5



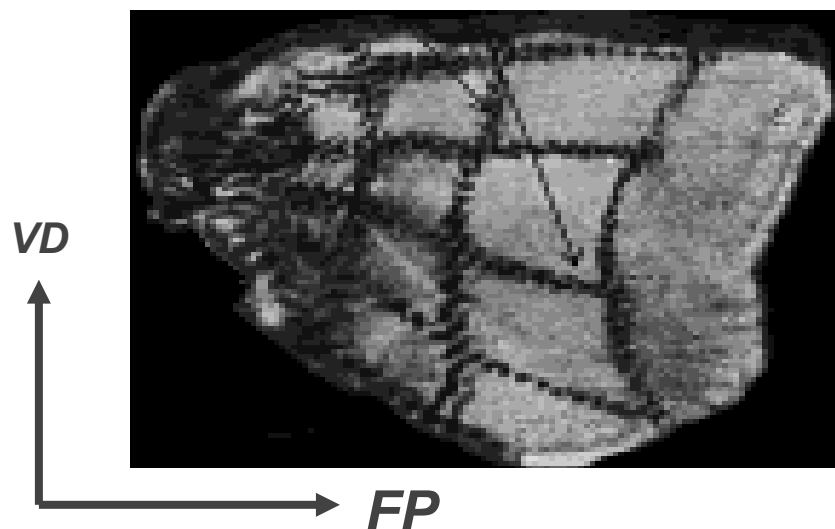
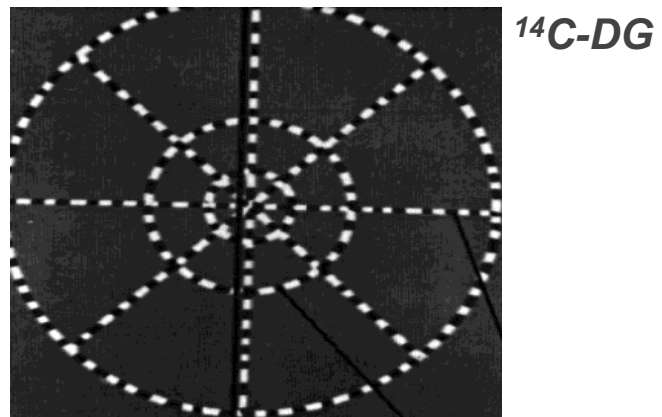
FFA



Bacon F 1976

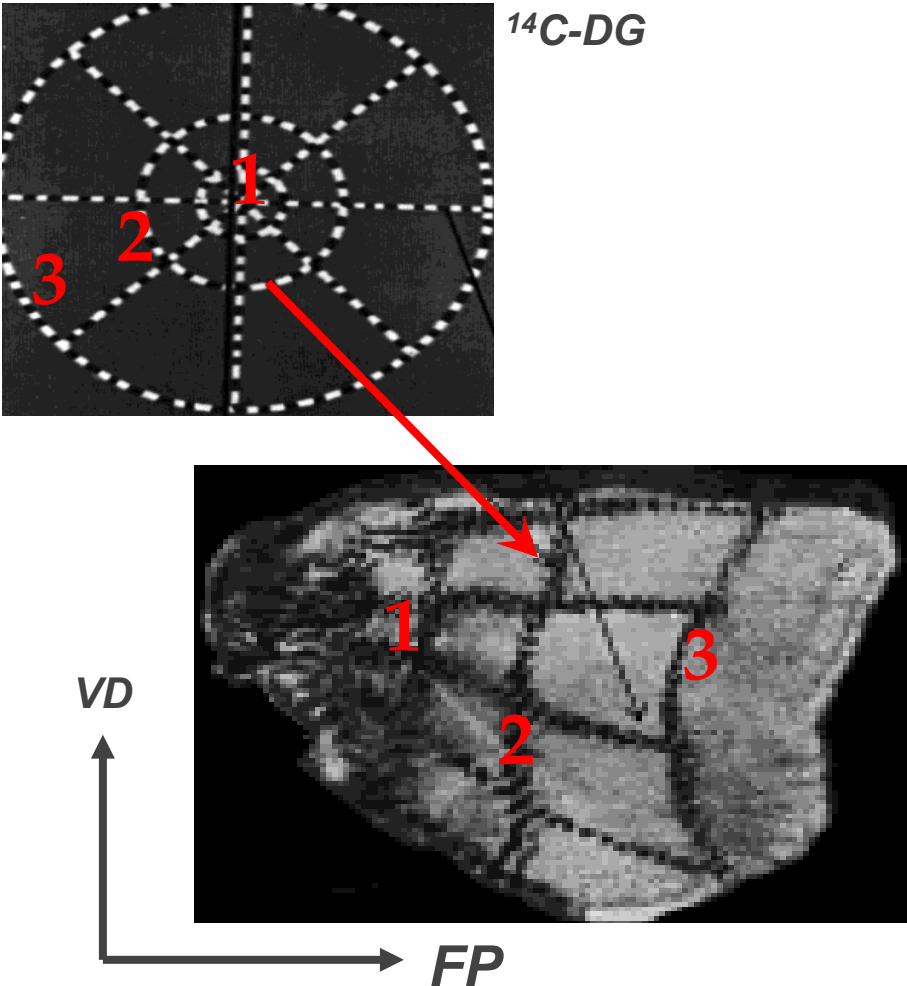


# Rétinotopie-I



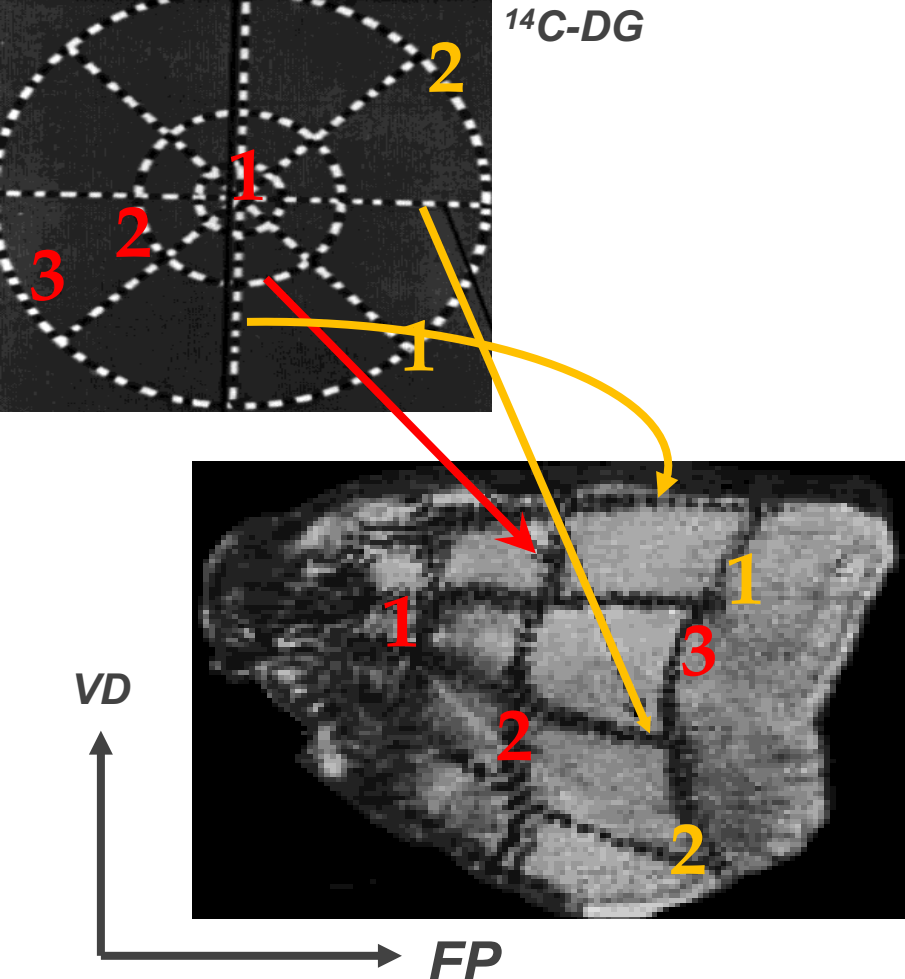
[Tootell et al, J Neurosci 8:1531 1988]

# Rétinotopie-II



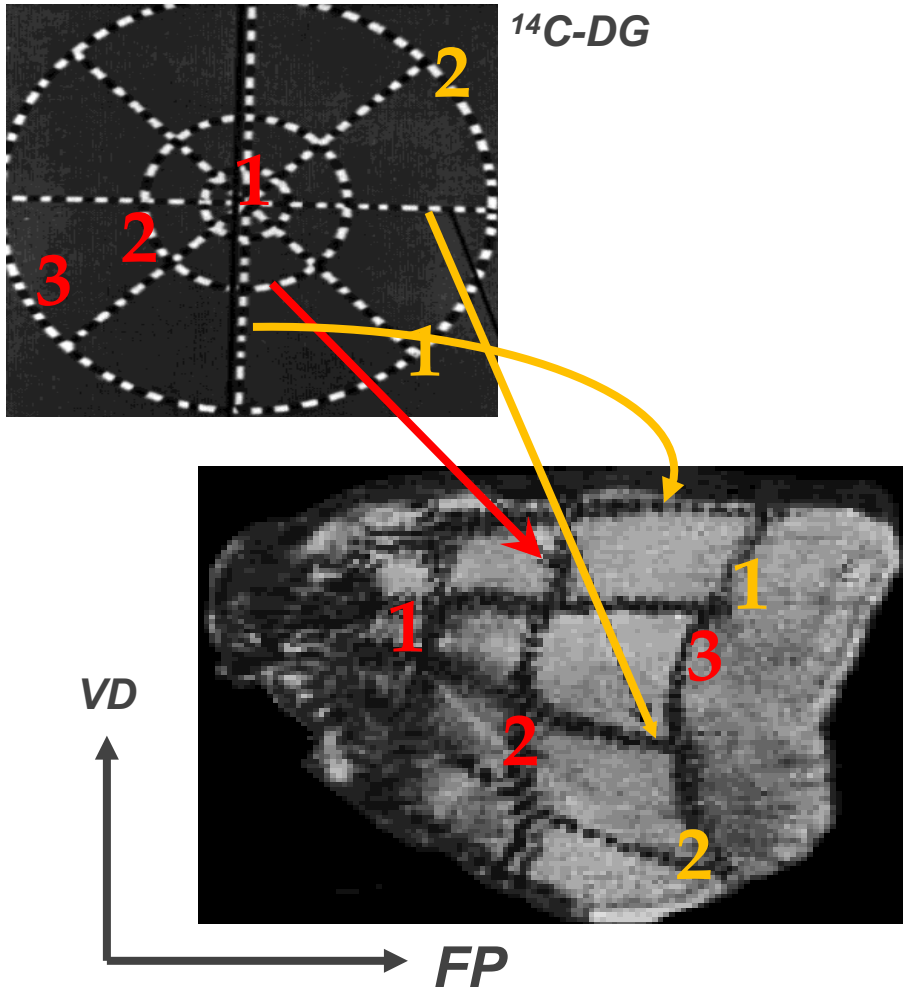
[Tootell et al, J Neurosci 8:1531 1988]

# Rétinotopie-II

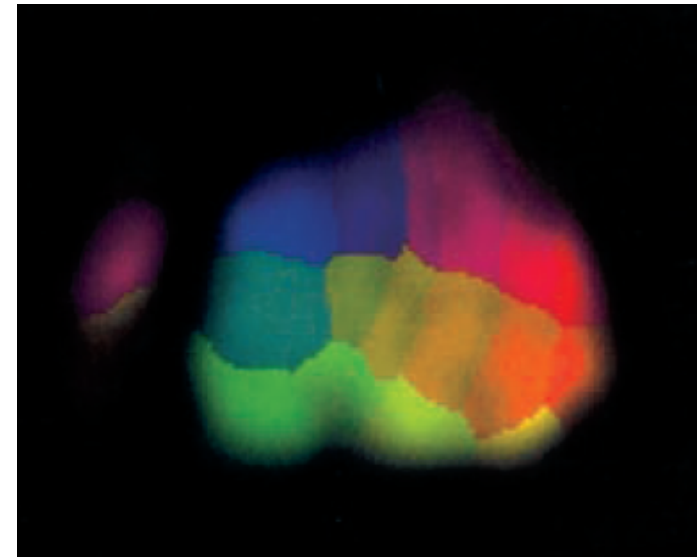
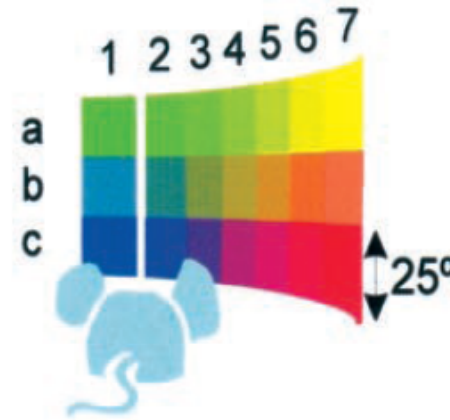


[Tootell et al, J Neurosci 8:1531 1988]

# Rétinotopie-II

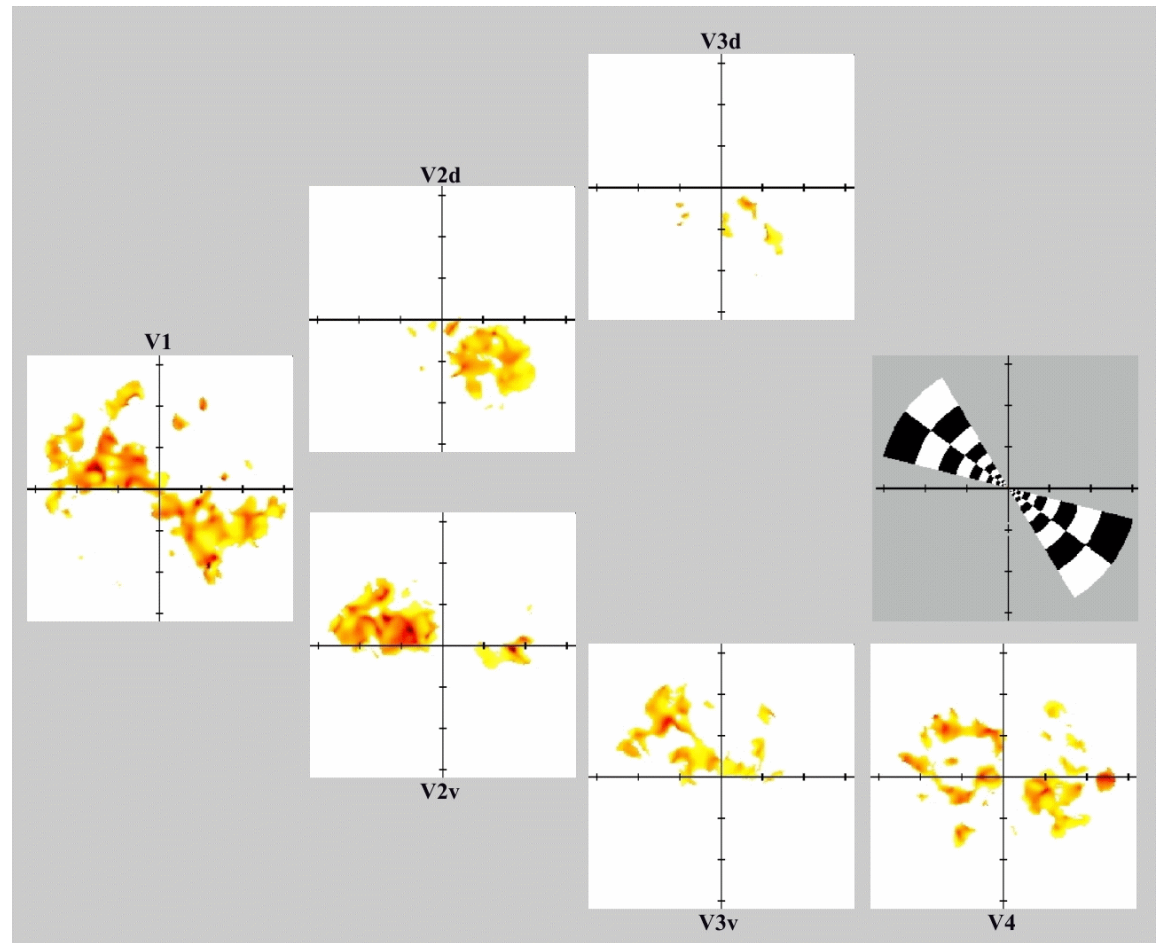
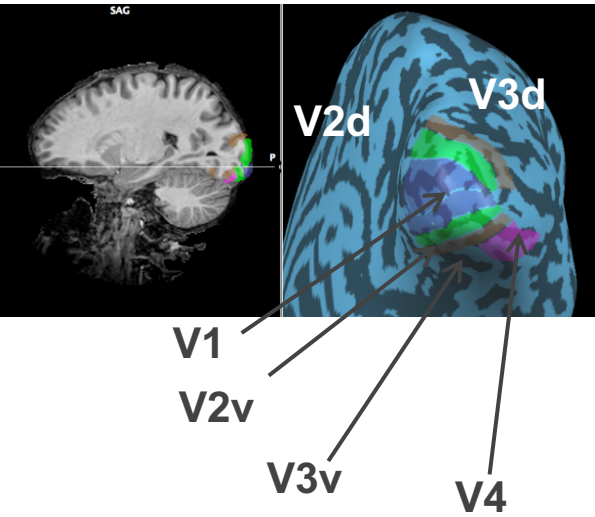


[Tootell et al, J Neurosci 8:1531 1988]



[Schuett J Neurosci 22:6549 2002]

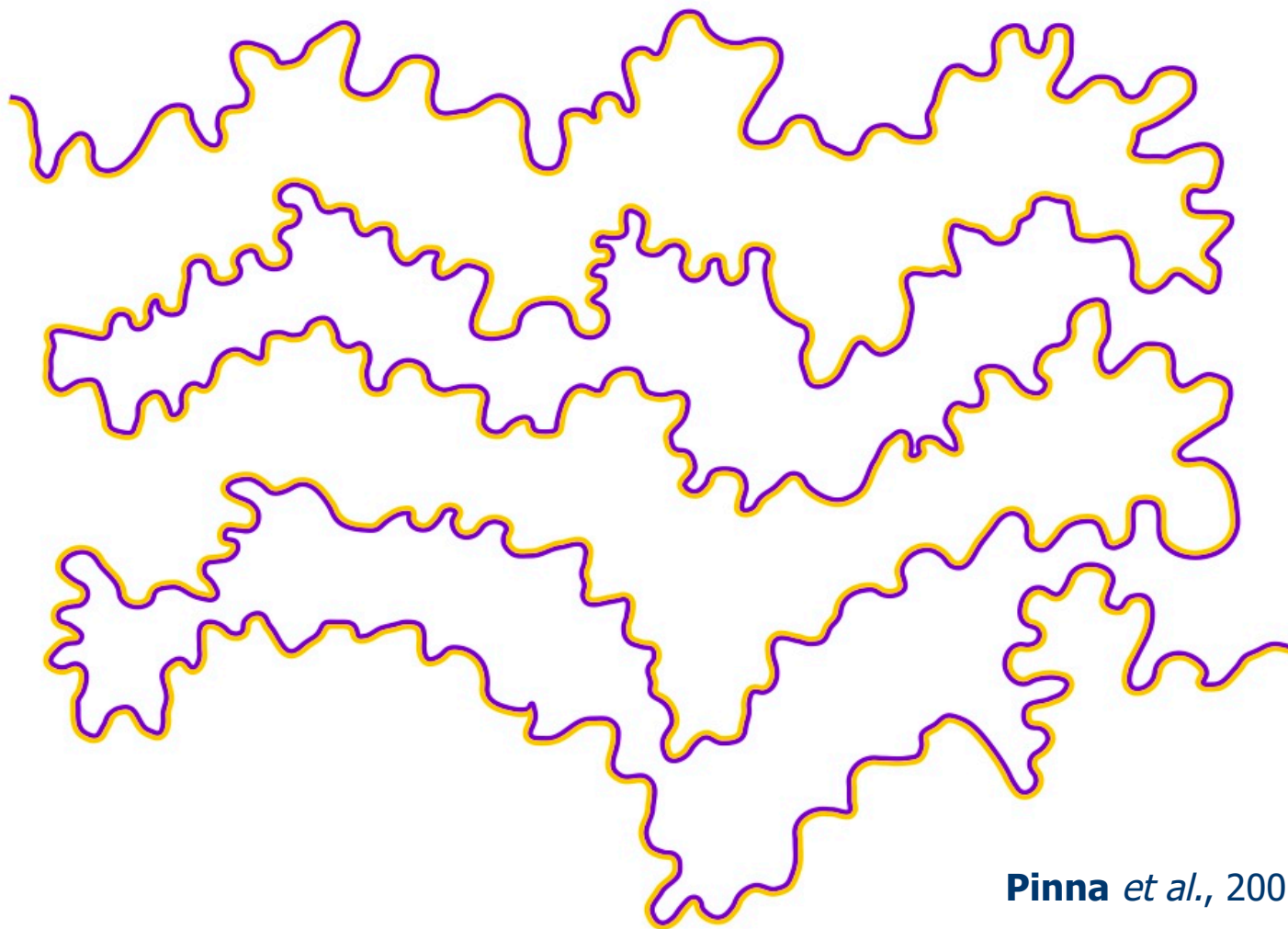
# Retinotopie chez l'homme



[Bordier C Postdoc 2015]

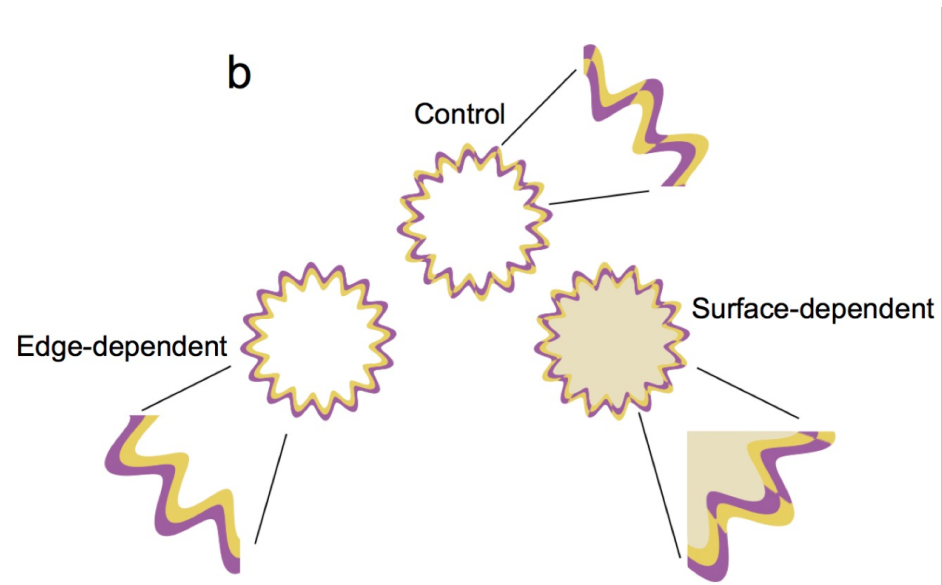


# Water color effect



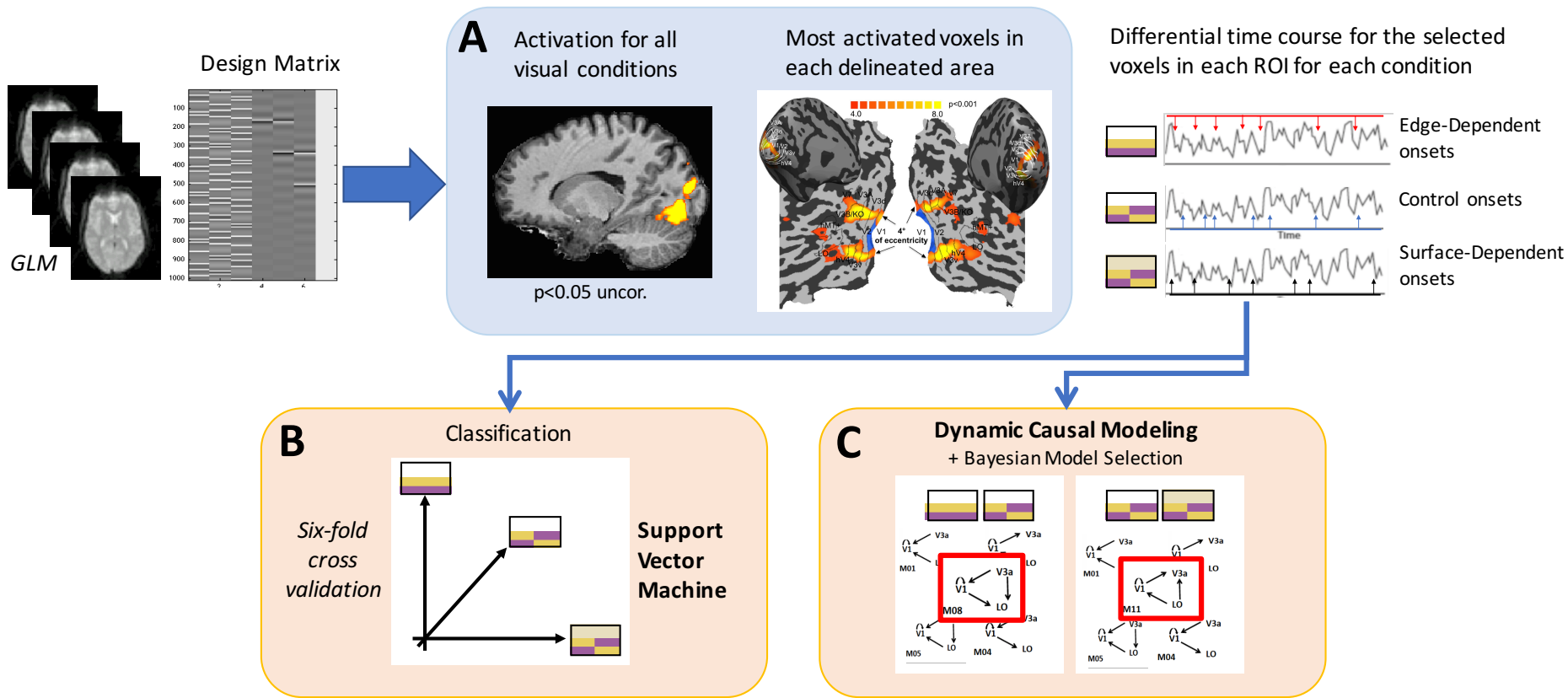
**Pinna** *et al.*, 2001.

# Water color effect



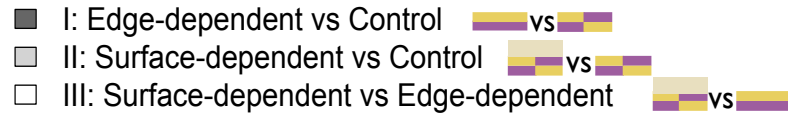
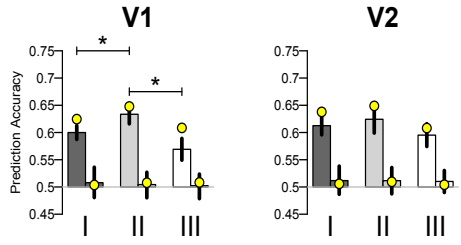
**Gérardin** *et al.*, Neuroimage 2018

# Method: Multi-Voxel Pattern Analysis (MVPA) from fMRI data.

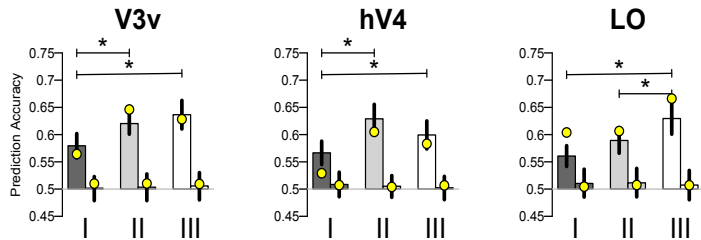


# Results

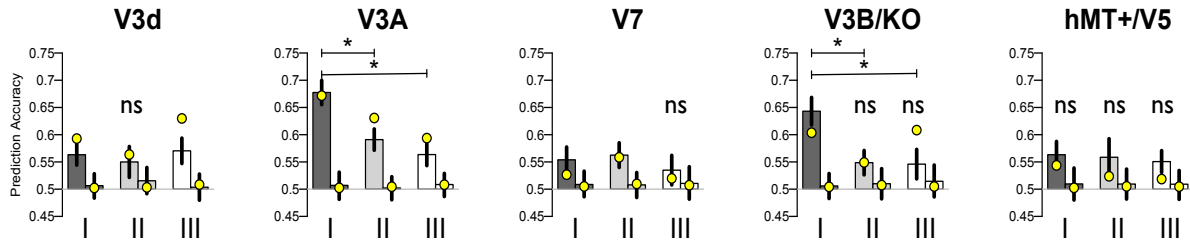
## Retinotopic areas



## Ventral visual areas



## Dorsal visual areas



# Conclusion



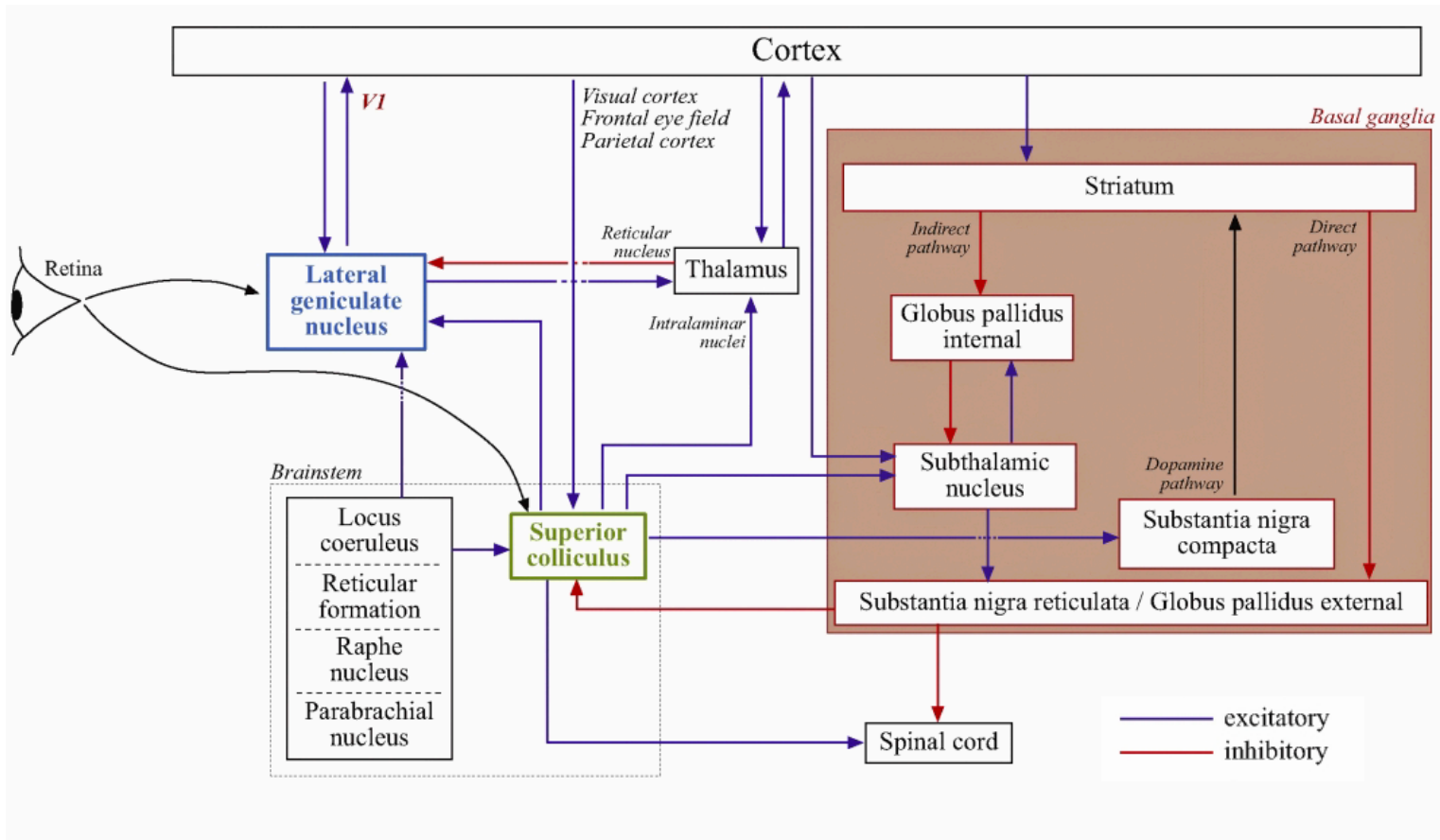
- Filling-in is best classified and best correlate with appearance by dorsal areas V3A & V3B/KO
- Uniform chromaticity by ventral areas hV4 & LO
- Feedback modulation from V3A to V1 and LO for filling-in
- Feedback from LO modulating V1 and V3A for uniform chromaticity



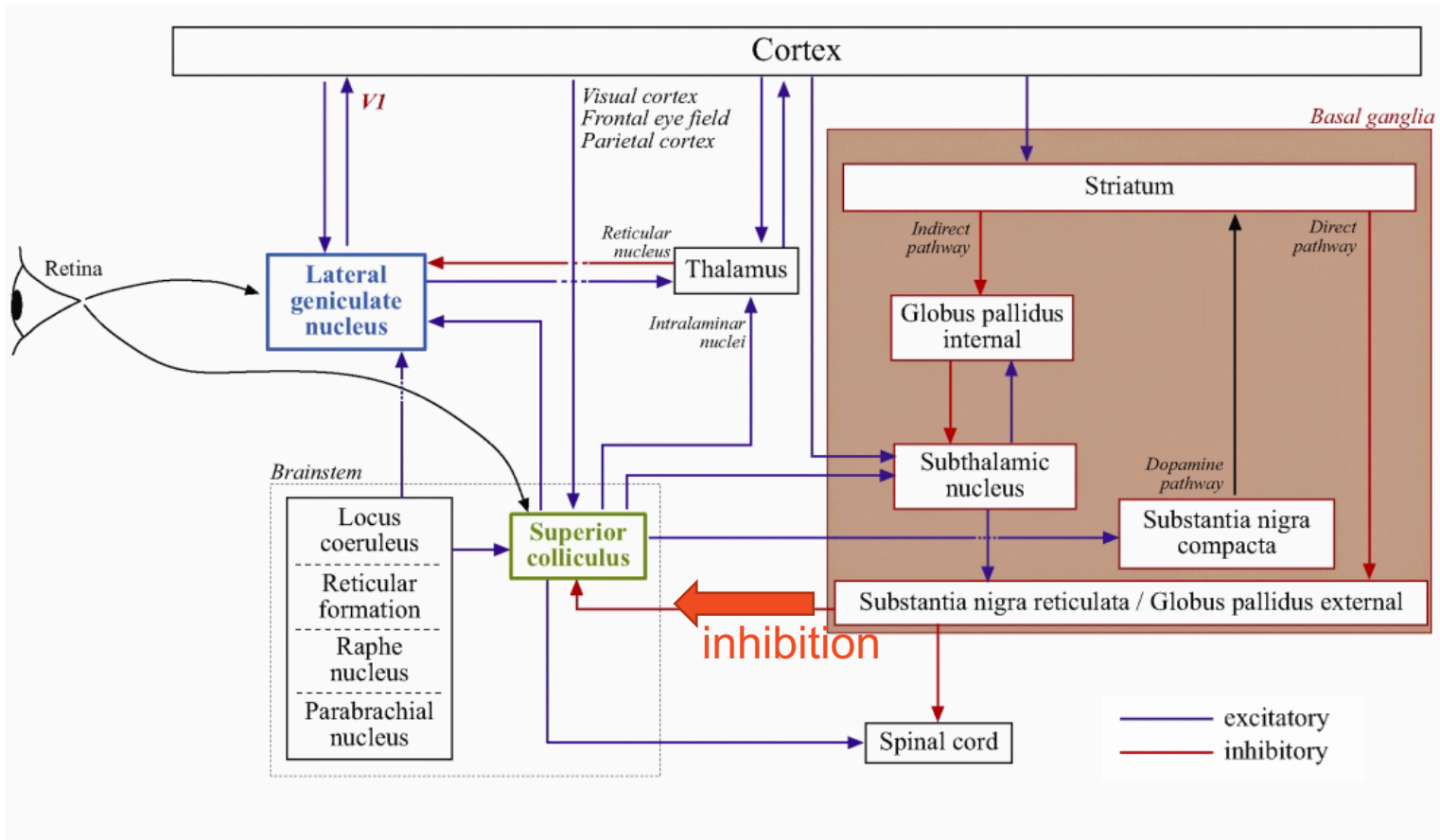
*InnoBioPark*



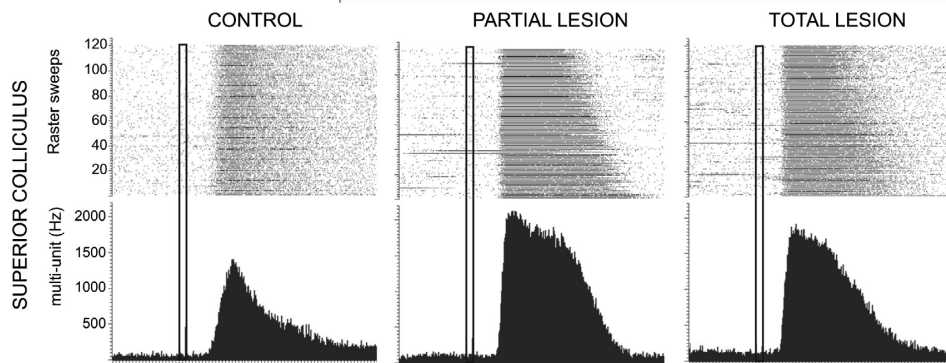
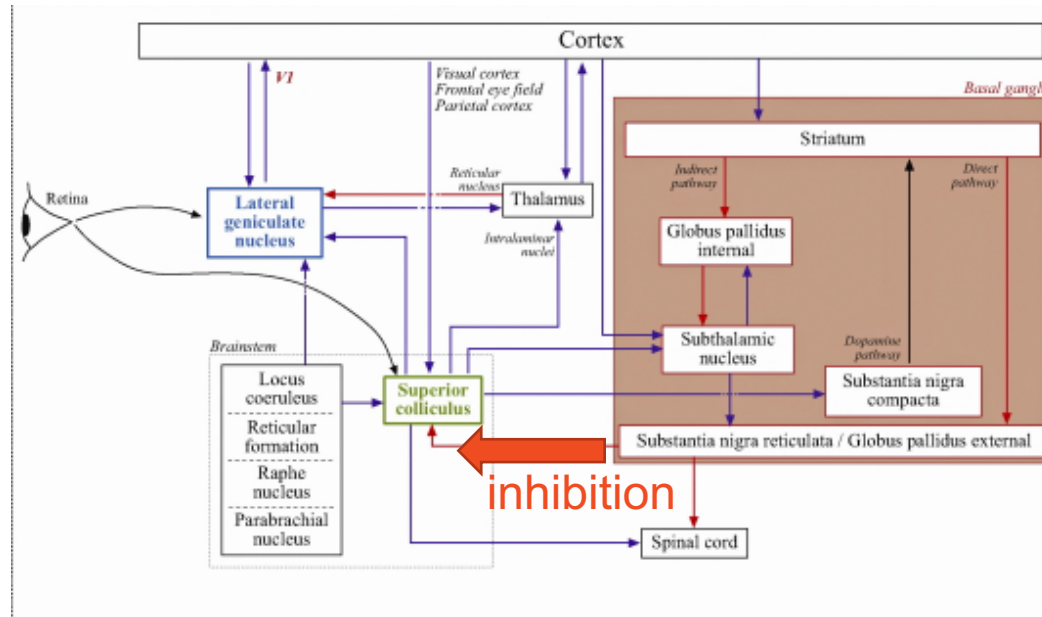
# Recherche translationnelle : Un bon exemple



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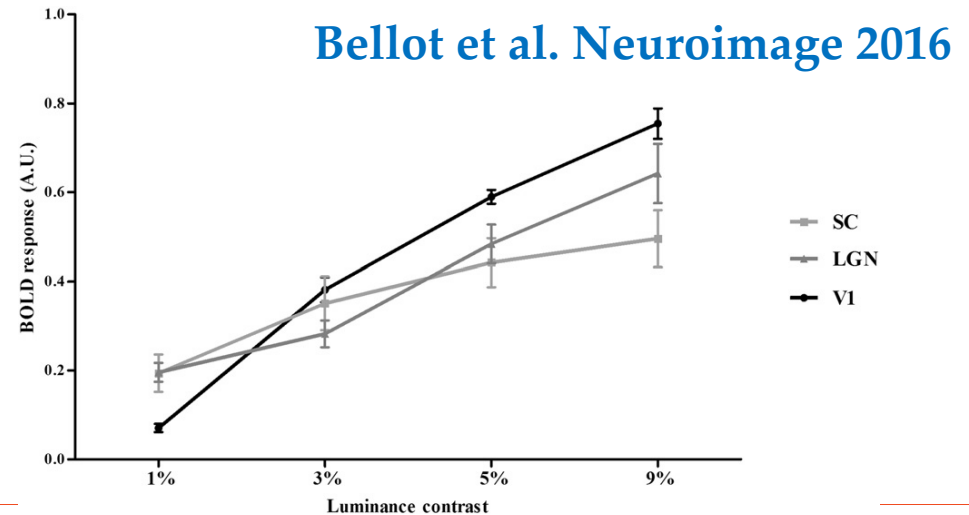
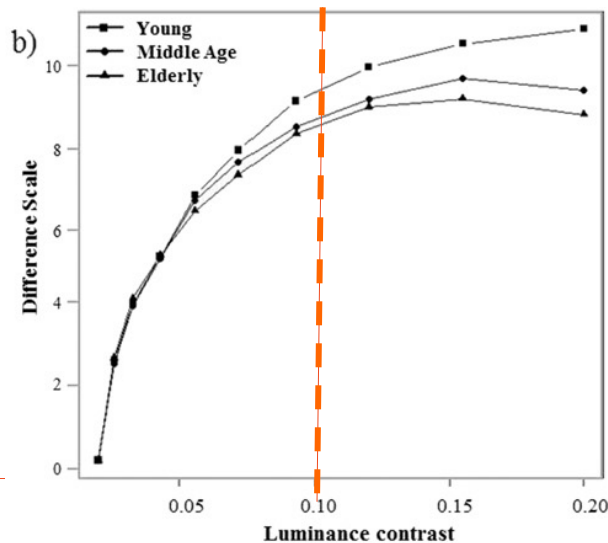
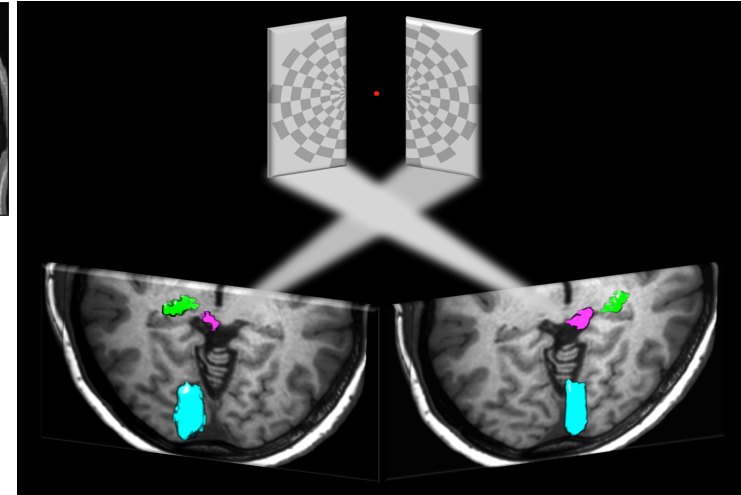
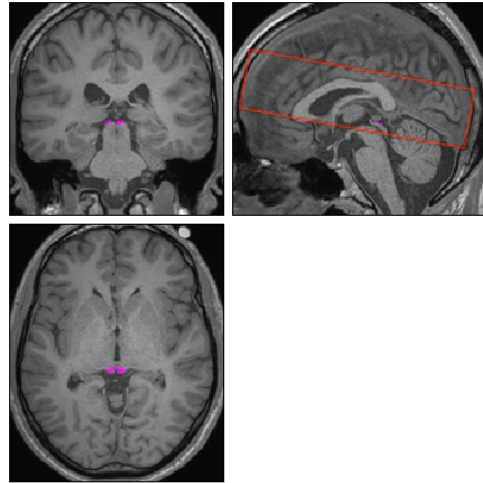
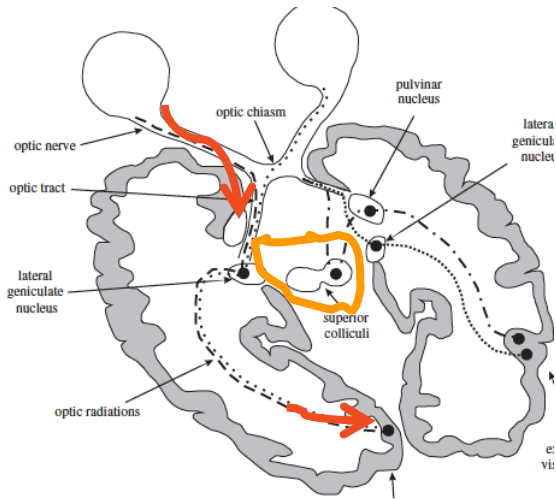


V. Coizet

Electrophysiology on rats

Rolland M et al Neuroscience 2013

# Translational research: a nice example, Parkinson Disease

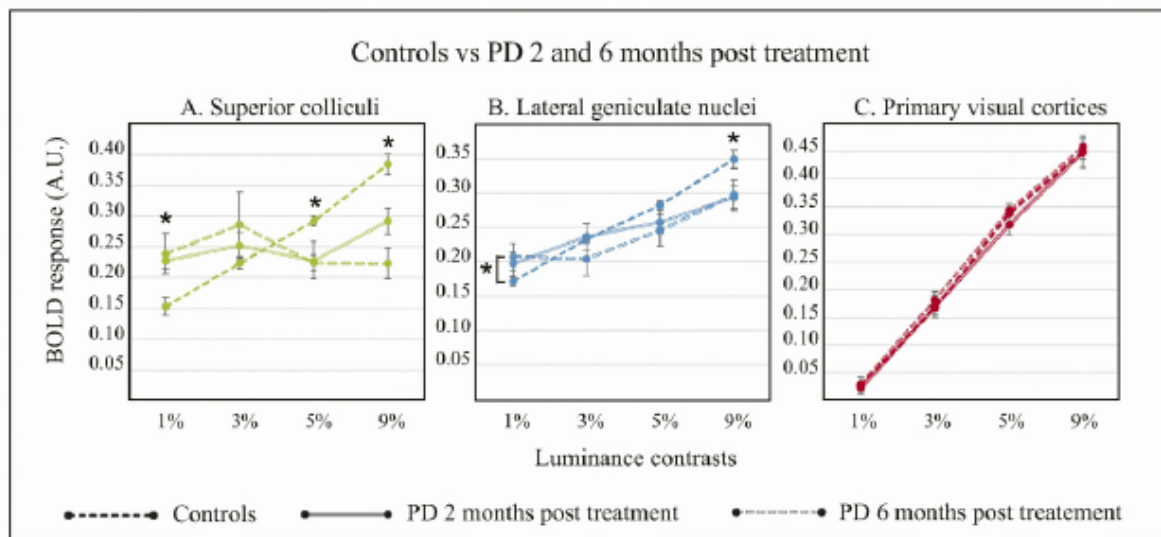
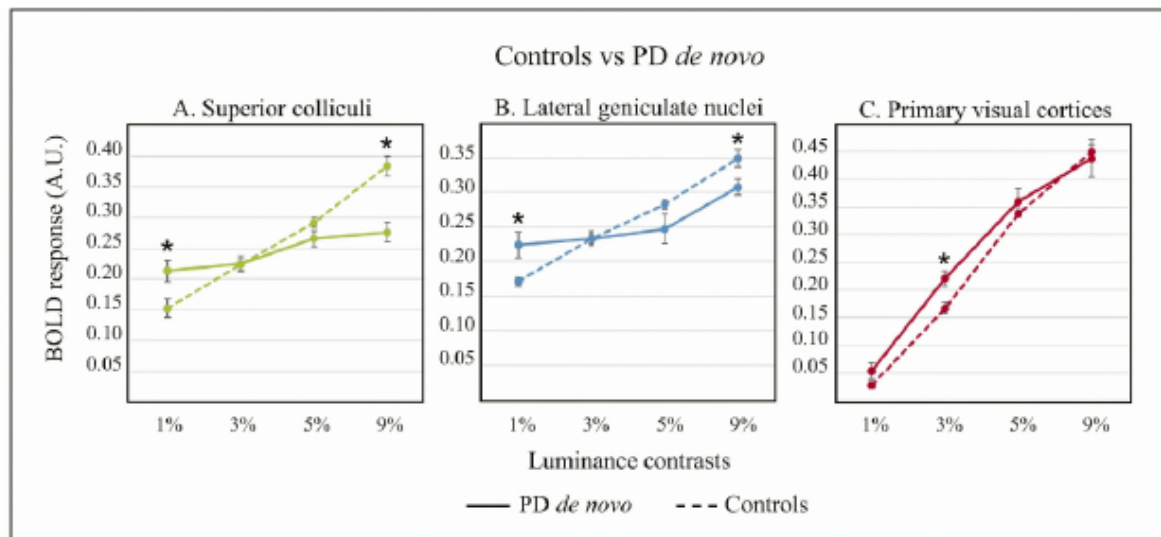


# To the patient bedside ...



E. Moro

Moro et al ANN 2020



**Objectifs : détection au plus tôt + personnalisation de la thérapie**

**Extraction de biomarqueurs d'imagerie**

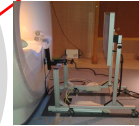
**Identification de profils de patients pour une thérapie + ciblée**

(antibody anti-  $\alpha$  synuclin, early surgery, ...)



**SIGNAPARK**  
Structural & Brain Perfusion

**Cohorts**  
2 x 60 patients & Controls  
4 y.



**EMOPARK**  
Emotion, cognition, vision & action



**EXCIPARK**  
Cortical excitability

Outils : Neuropsychologie – Neurologie – Ophtalmologie - IRM - EyeTracking – DATscan – TMS/EEG



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Cortical excitability



Outils : Neuropsychologie – Neurologie – Ophtalmologie - IRM - EyeTracking – DATscan – TMS/EEG

Recherche volontaires  
michel.dojat@inserm.fr



# *Challenges*

# Des difficultés

## CLINICAL REVIEW

Desperately seeking grey matter volume changes in sleep apnea: A methodological review of magnetic resonance brain voxel-based morphometry studies

Sébastien Celle <sup>a, b, \*</sup>, Chantal Delon-Martin <sup>c, d</sup>, Frédéric Roche <sup>a, b</sup>, Jean-Claude Barthélémy <sup>a, b</sup>, Jean-Louis Pépin <sup>d, e</sup>, Michel Dojat <sup>c, d</sup>

## RESEARCH ARTICLE

Magnetic resonance imaging does not reveal structural alterations in the brain of grapheme-color synesthetes

Michel Dojat<sup>1\*</sup>, Fabrizio Pizzagalli<sup>1\*</sup>, Jean-Michel Hupé<sup>2</sup>

**Multivariate pattern analysis of fMRI data for imaginary and real colours in grapheme-colour synaesthesia**

Mathieu J. Ruiz,  Michel Dojat,  Jean-Michel Hupé

doi: <https://doi.org/10.1101/214809>



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**we have not found any evidence of the involvement of the cortical colour network in the subjective experience of synaesthetic colours.**

# Des difficultés

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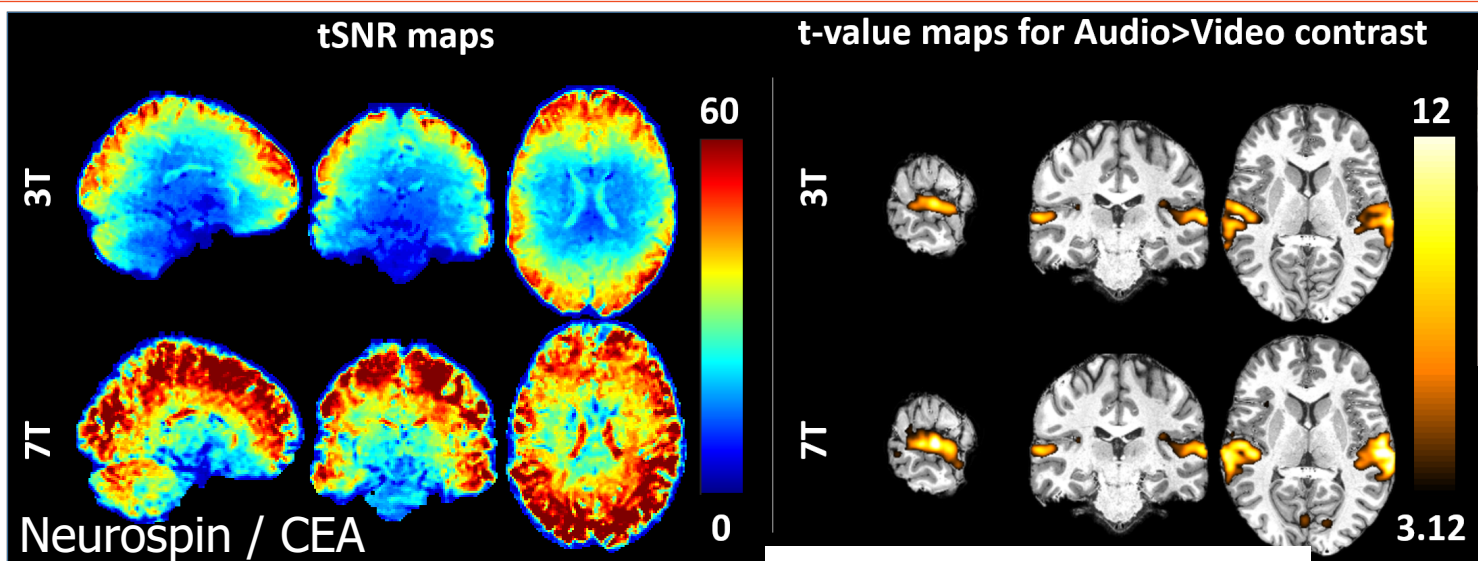
Mathieu J. Ruiz,  Michel Dojat,  Jean-Michel Hupé

doi: <https://doi.org/10.1101/214809>

**we have not found any evidence of the involvement of the cortical colour network in the subjective experience of synaesthetic colours.**

Signal / Bruit trop faible  
Manque de puissance statistique

# Toujours plus ...



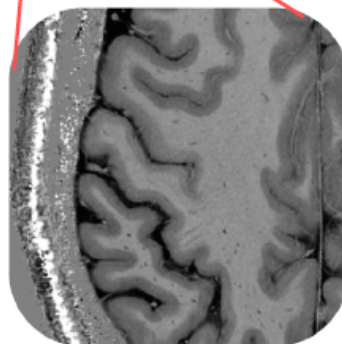
11.7 T

$RSB \propto B_0 \cdot V \cdot N_{acc} \cdot \frac{1}{2} \cdot T_e \cdot \frac{1}{2}$



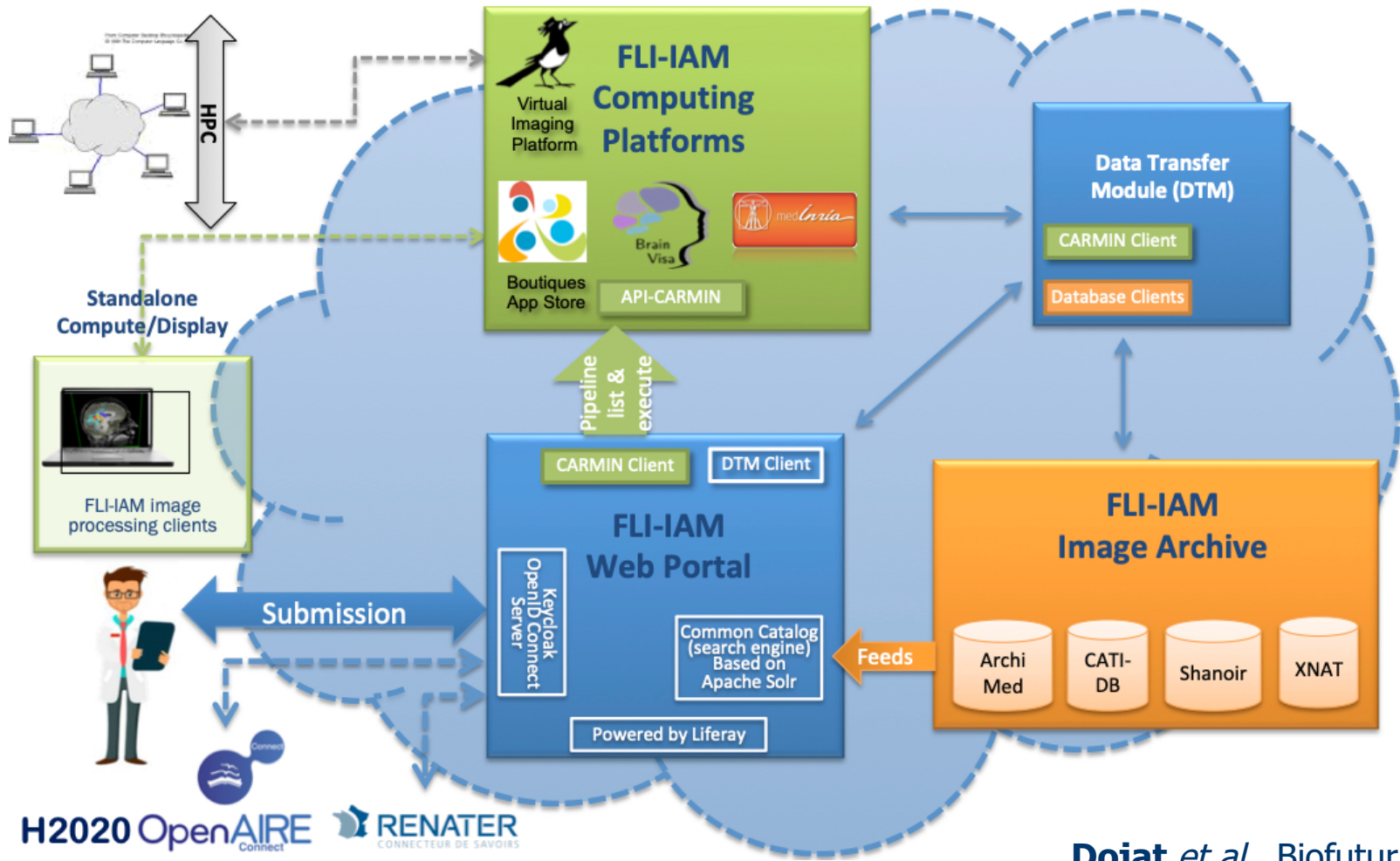
0.3 mm inplane  
1 mm slices  
(0.09 mm<sup>2</sup>)

3T 1mm<sup>3</sup>



Schluppeck et al.  
NeuroIm 2018

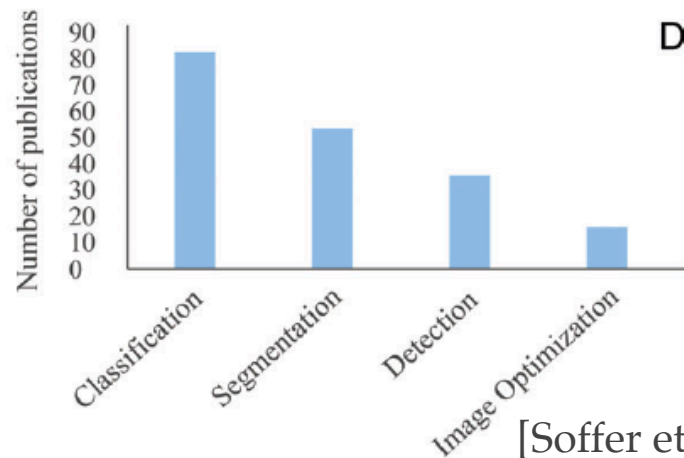
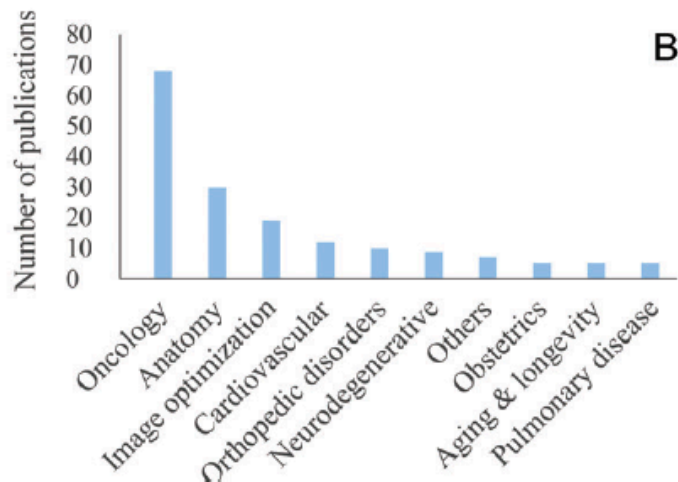
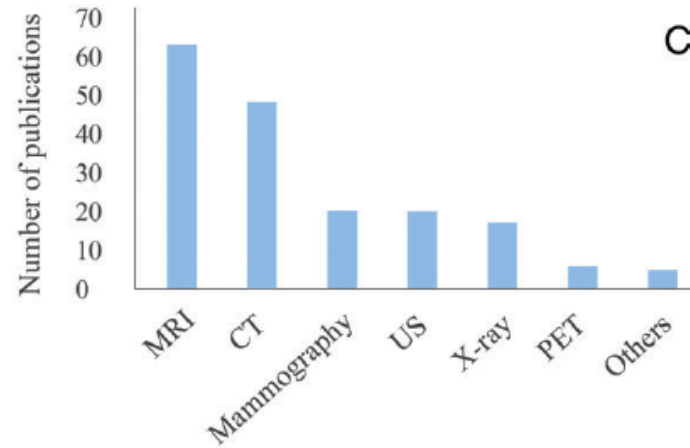
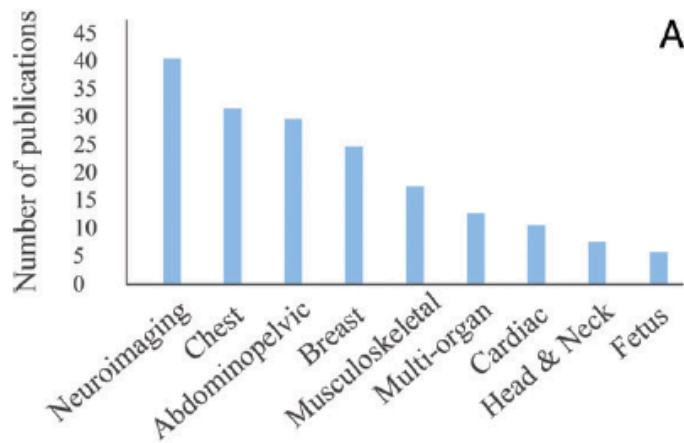
# Partager données et outils: Science ouverte





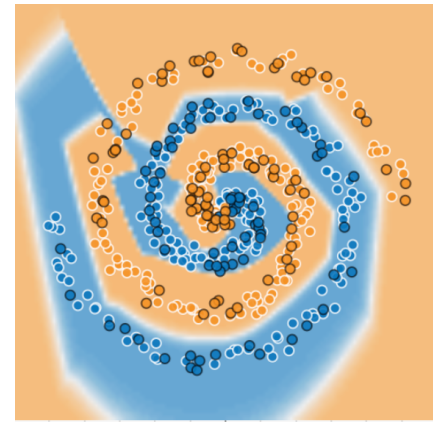
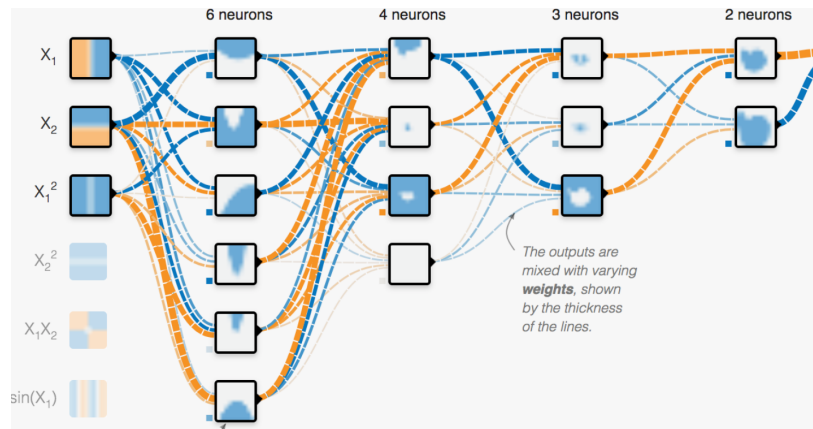
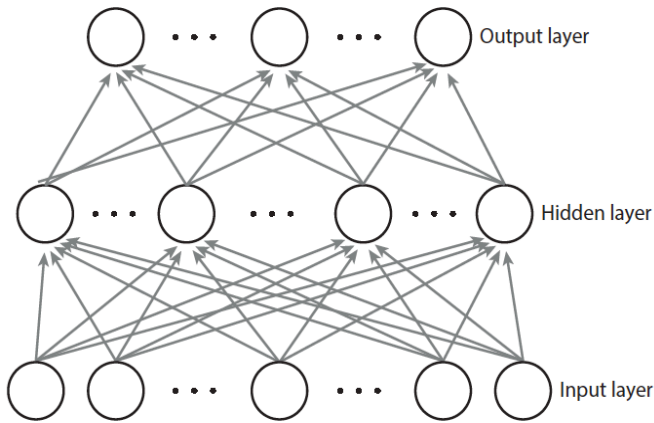
# NN in Radiology

- PubMed 2013-18 (“DL” or “CNN”) and (“image” or “imaging” or “radiology”)
- 744 art. 180 relevant

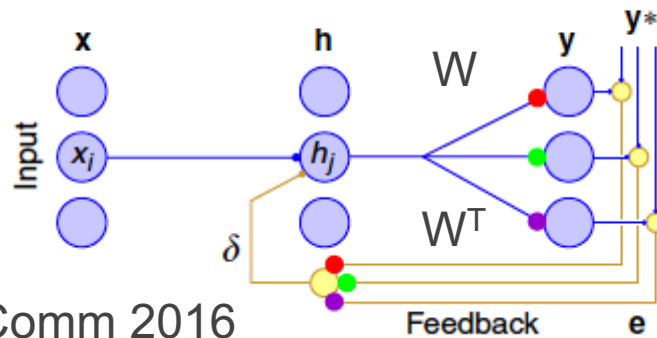


[Soffer et al 2019 Radiology]

# Multi-layer network

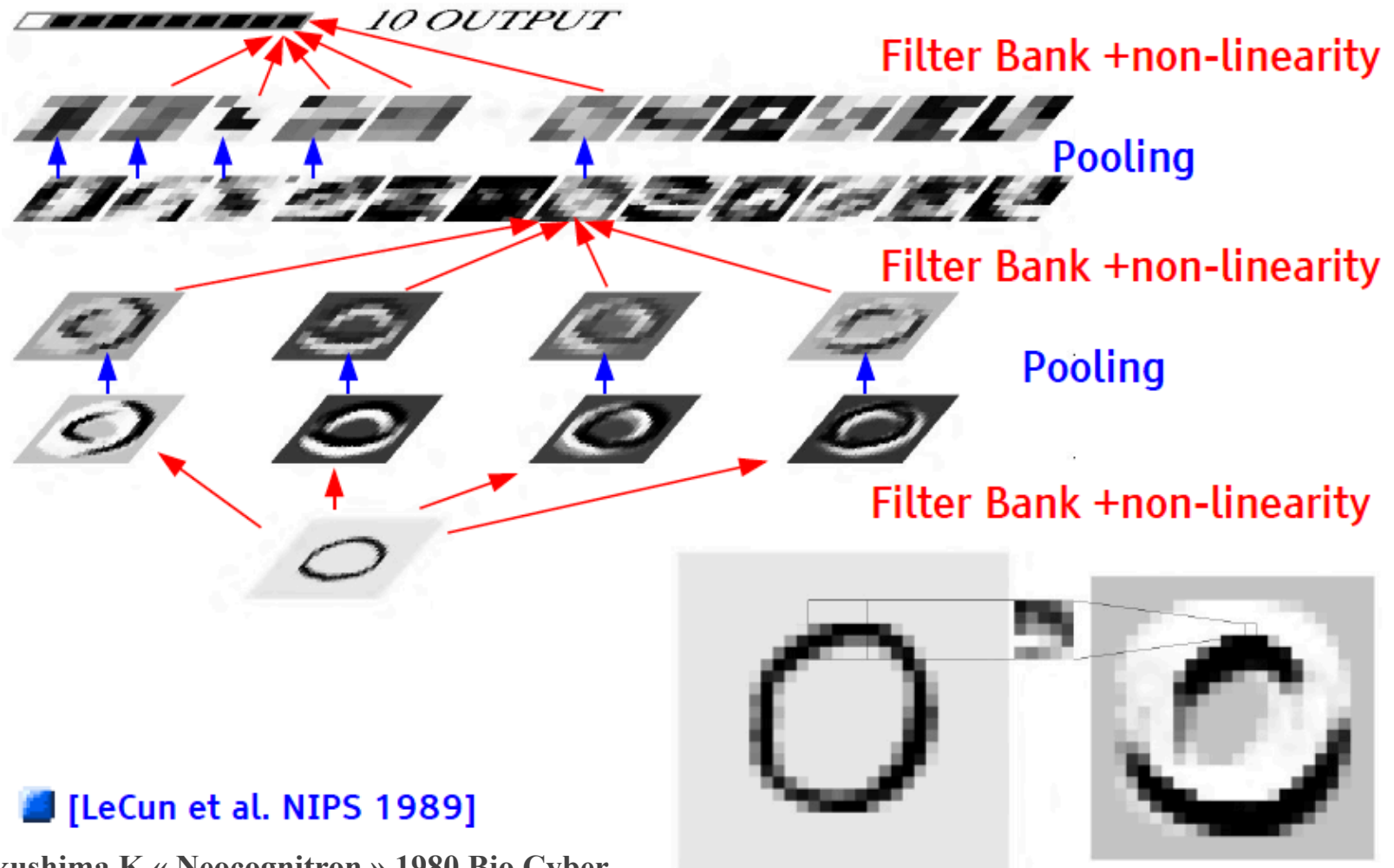


<https://www.tensorflow.org/>



Lillicrap Nat Comm 2016

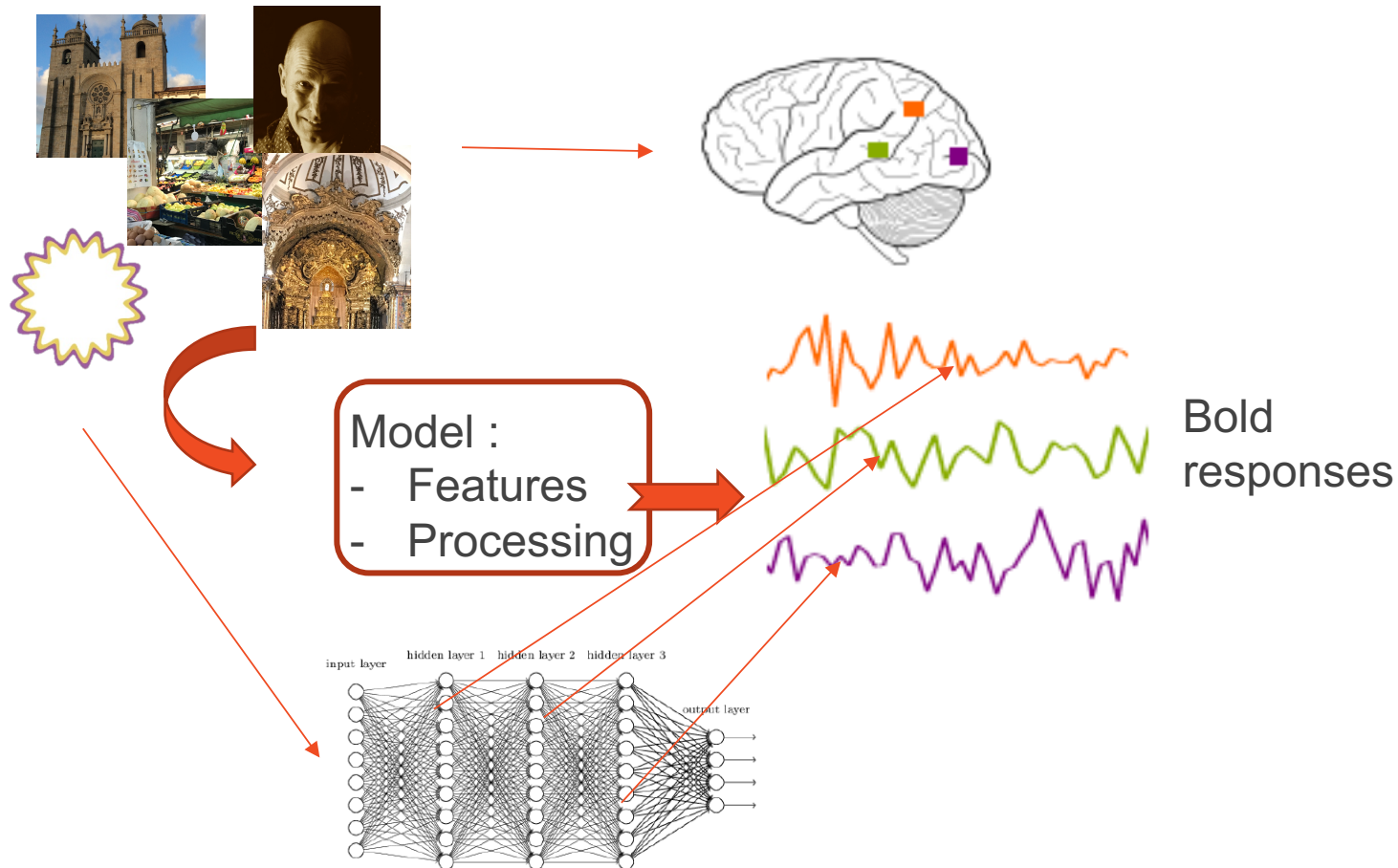
# Convolutional NN



■ [LeCun et al. NIPS 1989]

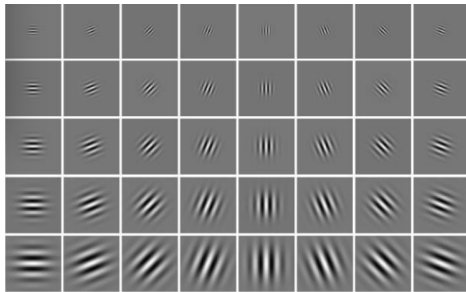
Fukushima K « Neocognitron » 1980 Bio Cyber

# CNN: a framework for modelling human vision?



# Natural “CNN”

- Gabor filter
- Local features



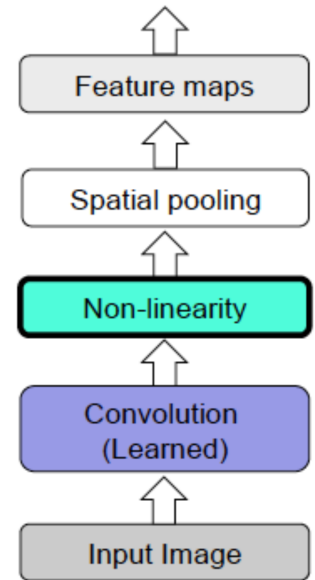
Input

- Hierarchical model
- Several areas (layers)
- Receptive field sizes increasing



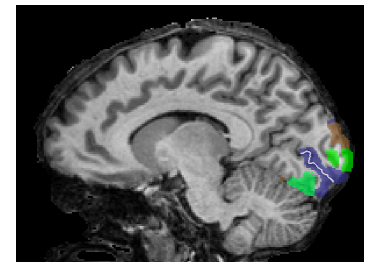
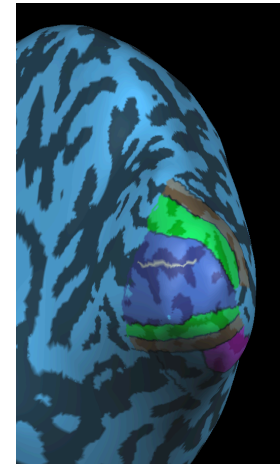
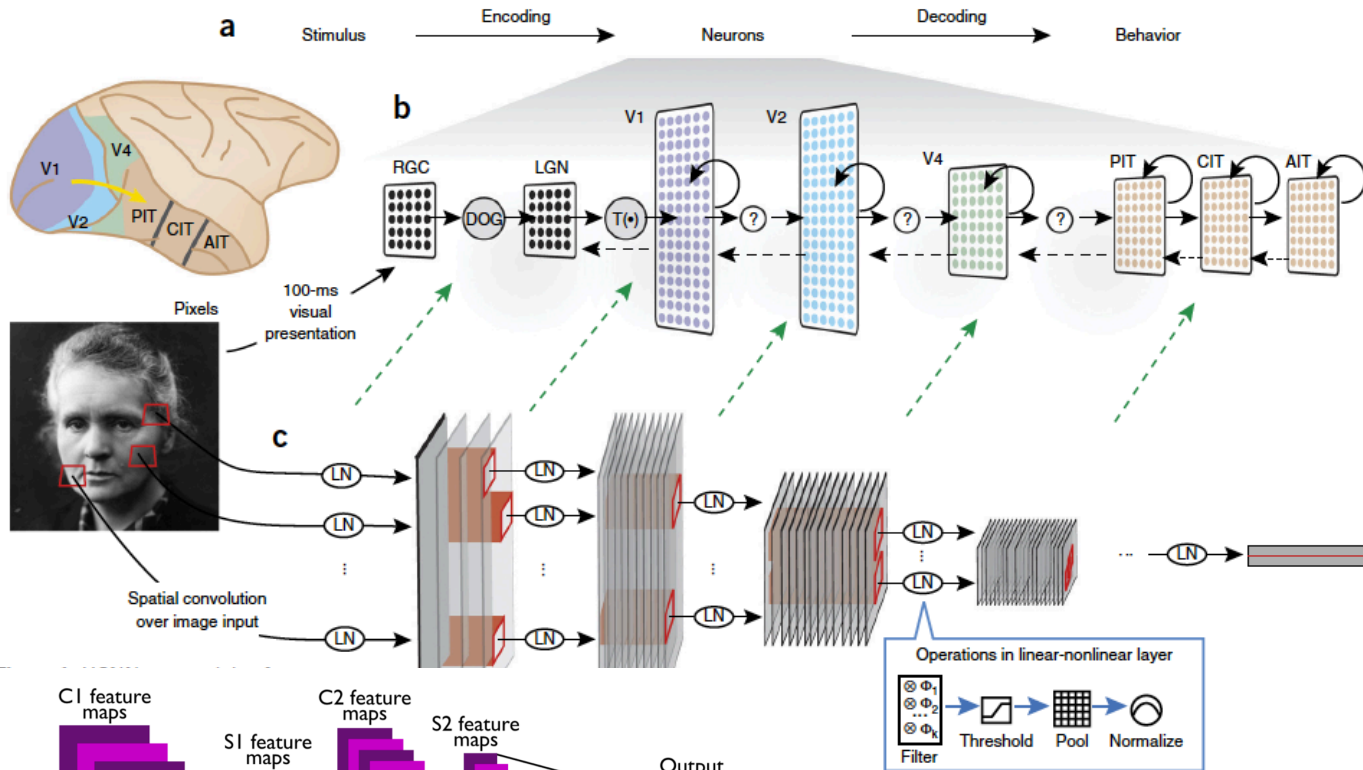
Feature Map

- Max pooling



# CNN as a model of the visual system ...

- ✓ Receptive field
- ✓ Hierarchical model
- ✓ Max pooling



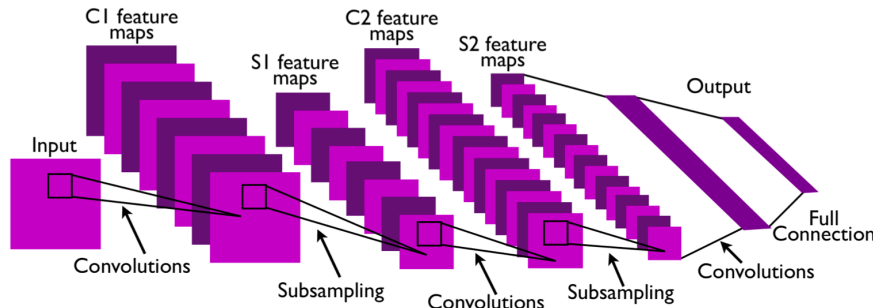
[Yamins and Dicarlo Nat Neuro 2016]

[Dojat Lavoisier ed. 2017]

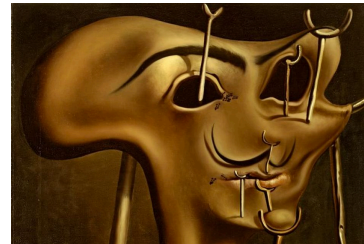
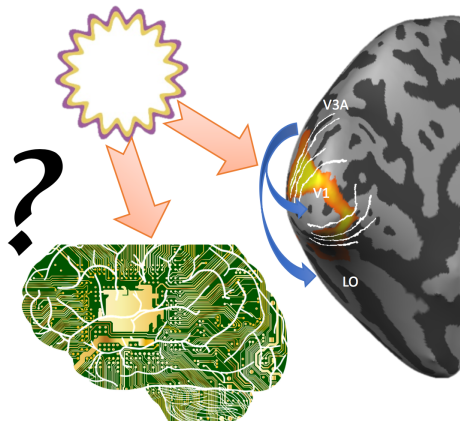
[Lecun et al ISCAS 2010]



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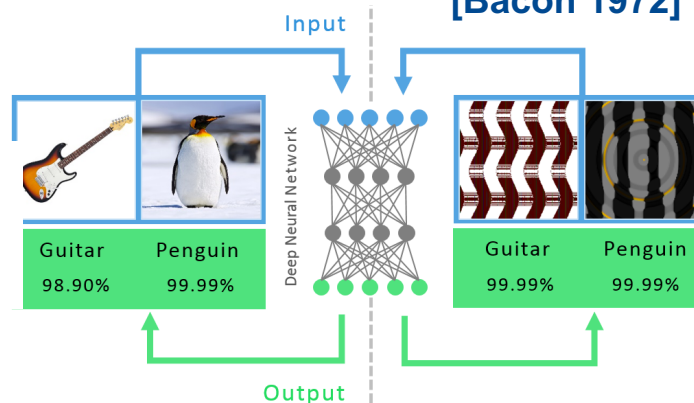
[Lecun et al 2010]



[Dali 1941]



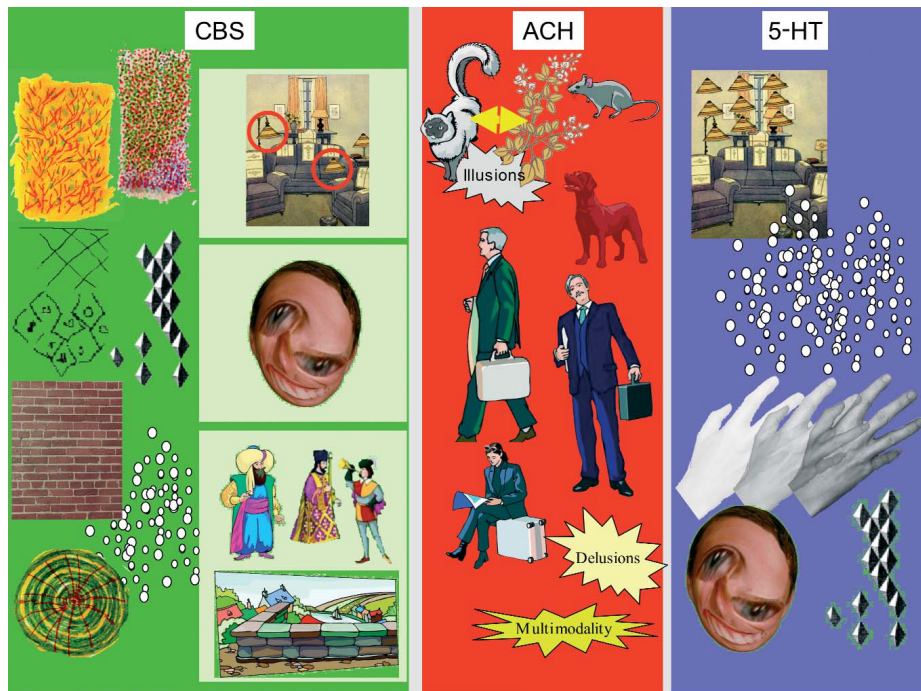
[Bacon 1972]



[Nguyen et al CVPR 2015]

- ✓ Receptive field
- ✓ Hierarchical model
- ✓ Max pooling
- ✓ Layer2layer conn.
- ✓ Magnitude factor
- ✓ Color
- ✓ Metamer
- ✓ Attention
- ✓ Local vs Global
- ✓ Perspective effects
- ✓ Learning
- ✓ Illusion
- ✓ Eye mvt
- ✓ Adversarial example

# Hallucinations



[Ffytche 2007 Dial Clin Neurosc]



DeepDream.com



[michel.dojat@inserm.fr](mailto:michel.dojat@inserm.fr)

