

DE LA RECHERCHE À L'INDUSTRIE

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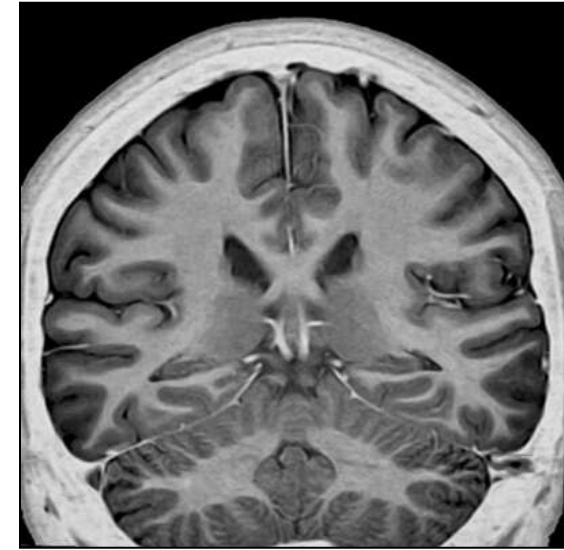
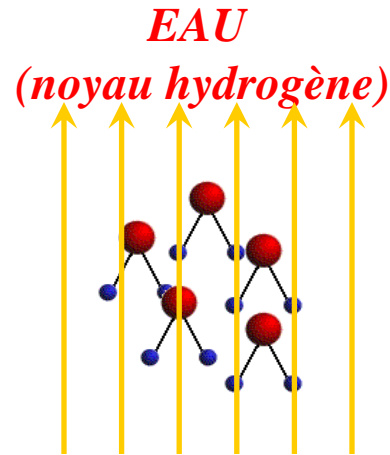
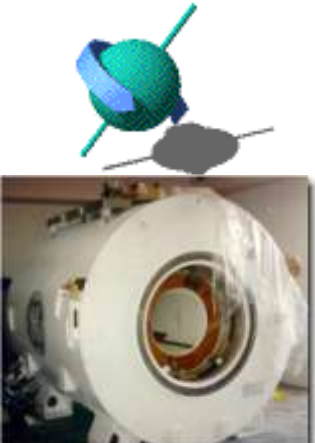
Le Cerveau de Cristal

Denis Le Bihan
NeuroSpin, CEA-Saclay, France

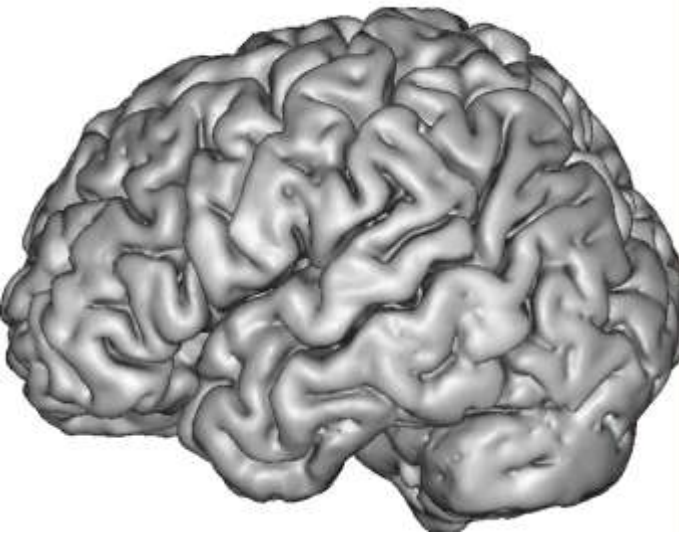


IMAGERIE PAR RESONANCE MAGNETIQUE

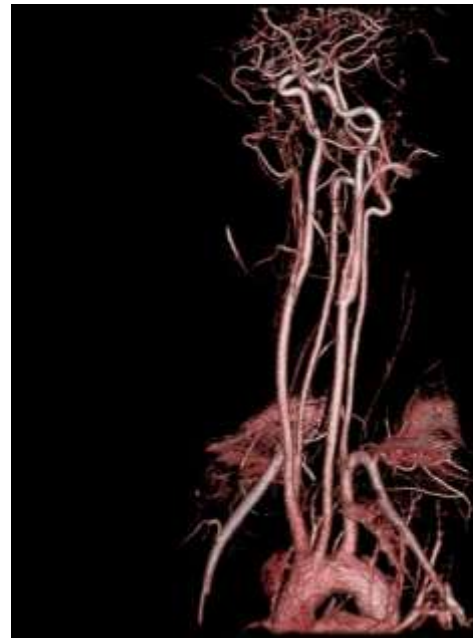
L'eau: une source de signal pour de multiples contrastes



Radiologues: Magiciens manipulant l'aimantation de l'**EAU** (et sa relaxation)!

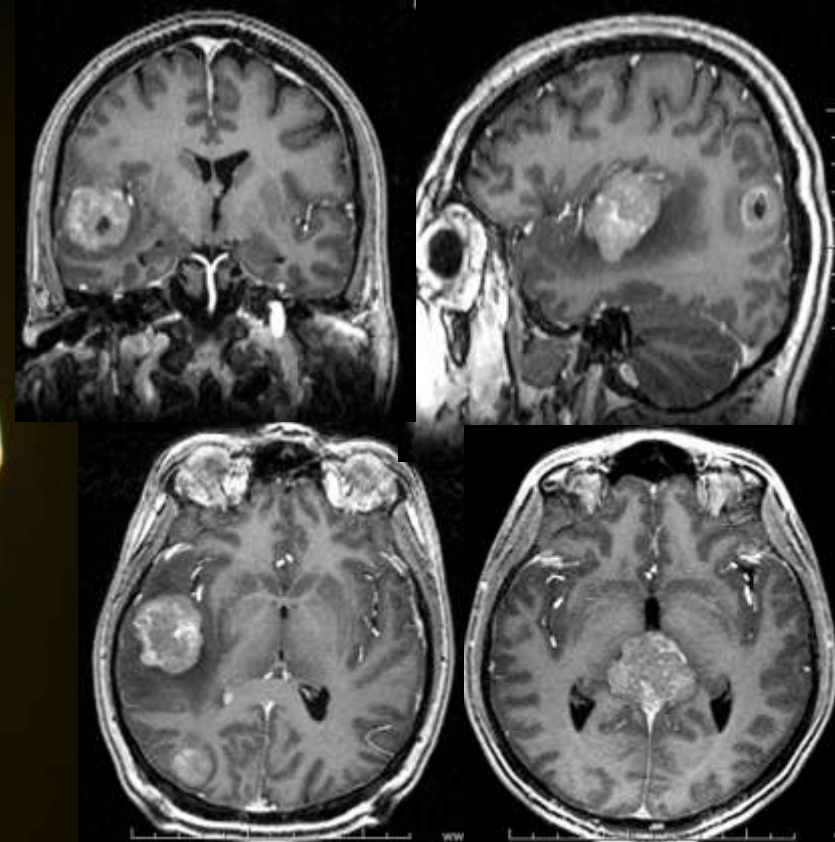
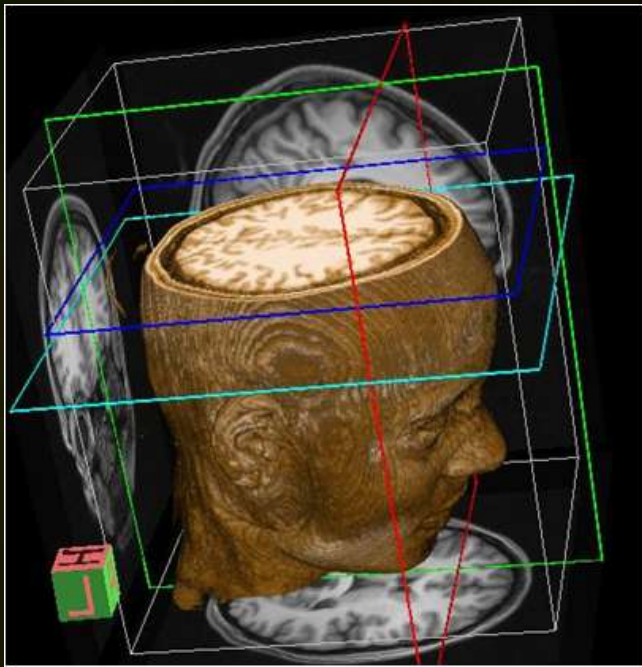


IRM: image virtuelle de l'aimantation des molécules d'eau du cerveau



La révolution de l'image...

fille de la physique et de l'informatique



Le cerveau *normal*

1972-82: Scanner-X, puis IRM:
dissection virtuelle du cerveau *malade*

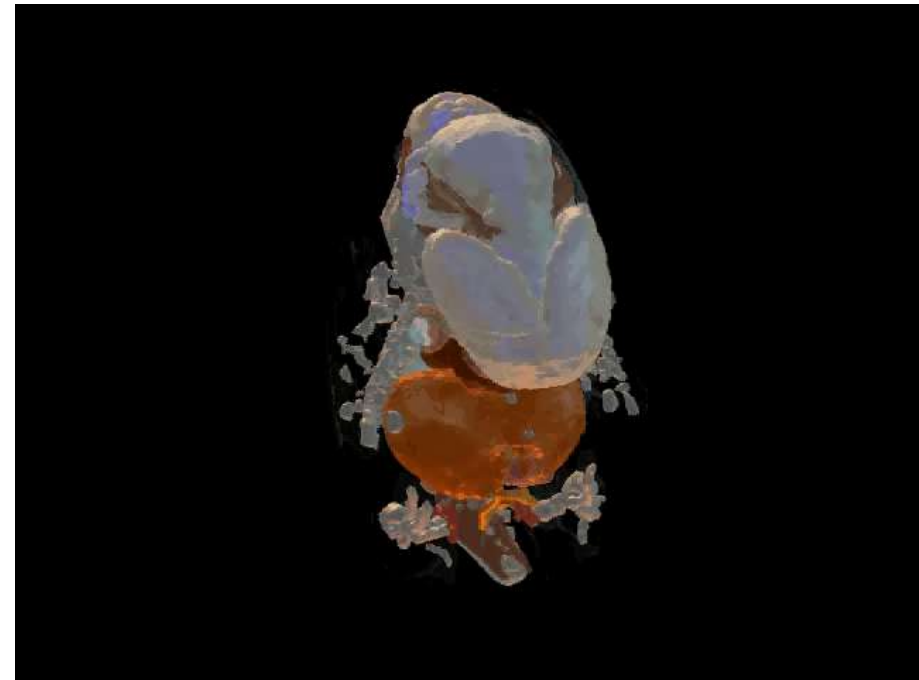
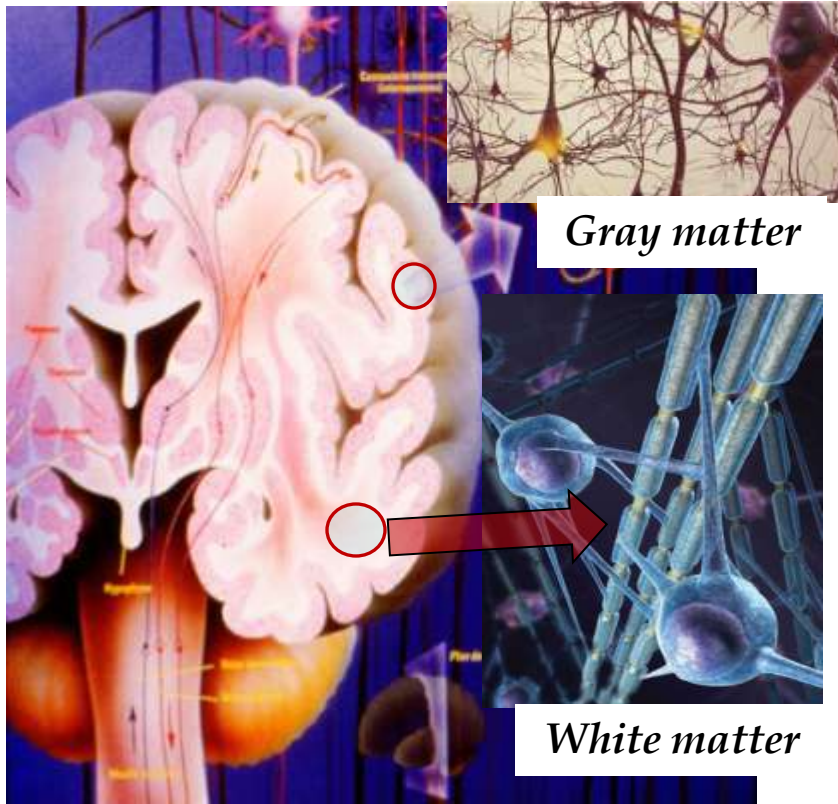
Un des secrets du cerveau réside dans son *architecture*: *fonction* et *localisation* sont intimement liés, à toutes les échelles, d'où l'importance de la *neuroimagerie*...

Development of the central nervous system

➤ At birth the brain weight is 350g
(1400g at the end of teenagehood)

➤ ALL neurons (100 billions...) are in place, mainly at the brain surface (2-4 mm cortical ribbon):
production of more than 250,000 neurons per minute during pregnancy.

➤ Connexions (synapses) develop during the last months of pregnancy, up to about 500 synapses/neuron (>10 000 in adults)

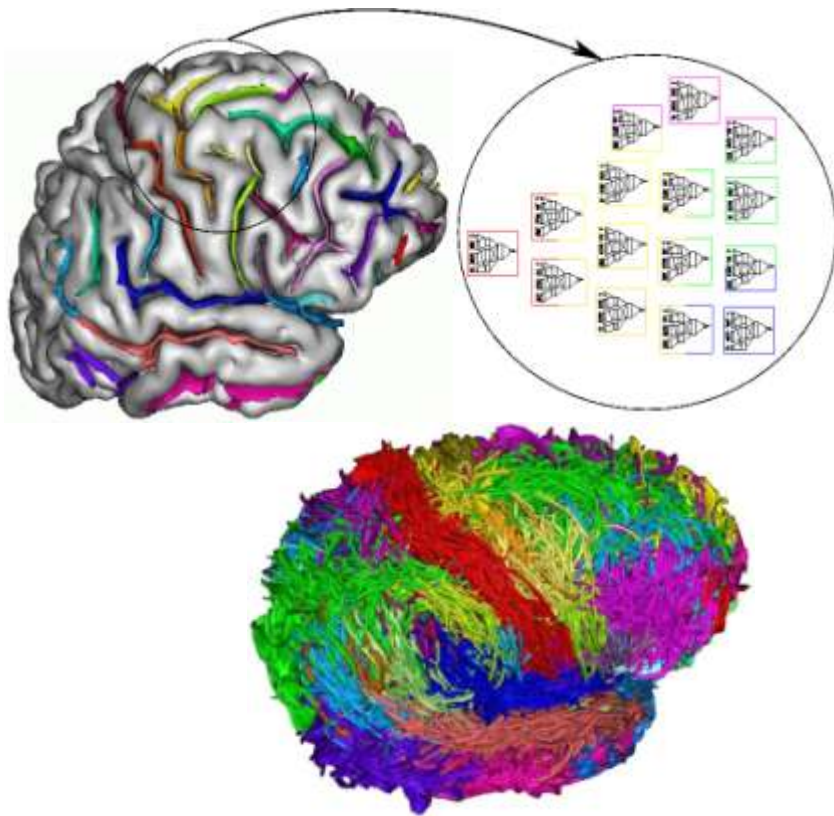


*Mouse embryo: 13.5 days after
conception (11.7T MRI)*



Mouse brain: 1gram!
100 millions neurons...

Gènes, Environnement & Plasticité



*La Timone Hospital + SHFJ/CEA +
McGill University (ICBM)*

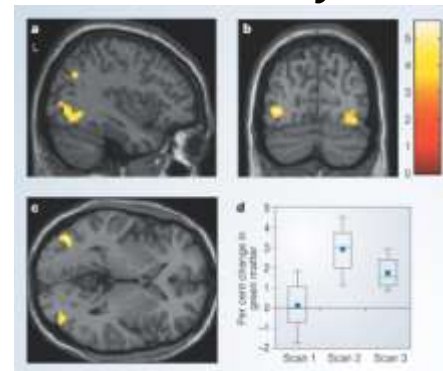
Hypertrophy of hippocampus in London taxi drivers

Long term
plasticity

*Maguire et al.,
PNAS, 2000*

The pianist's brain

Plasticity & learning: Jugglers

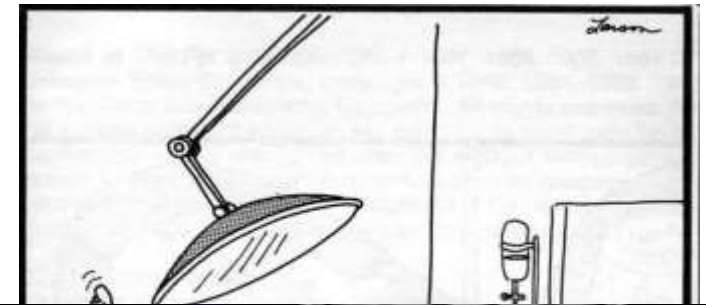
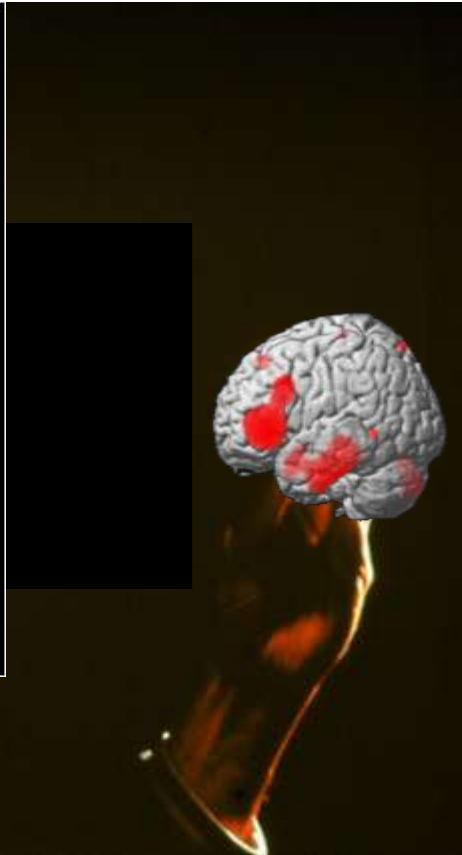
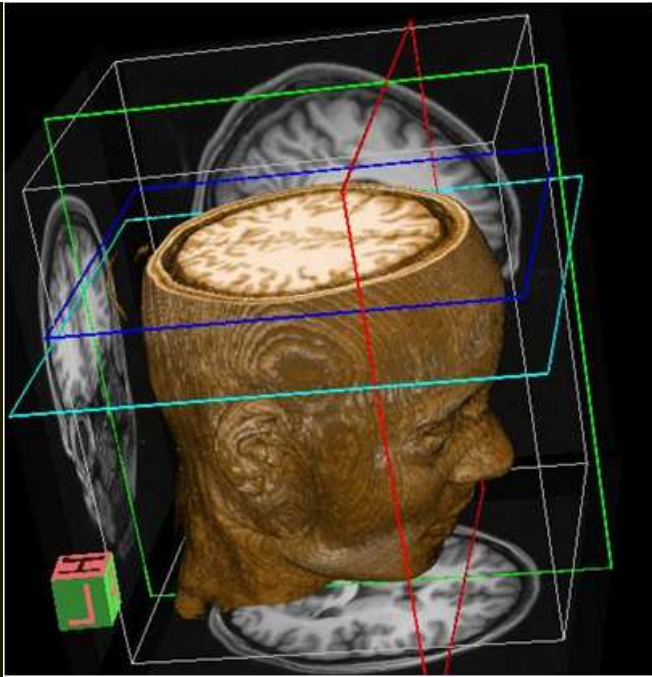


Short term
plasticity

*Draganski et al.,
Nature, 2004*

La révolution de l'imagerie...

voir le cerveau *normal* un *travail*



IRM: Fonction ↔ Structure

IRM fonctionnelle

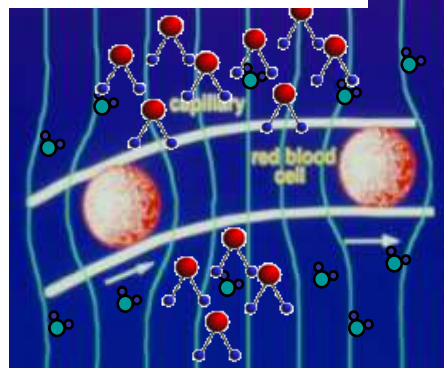
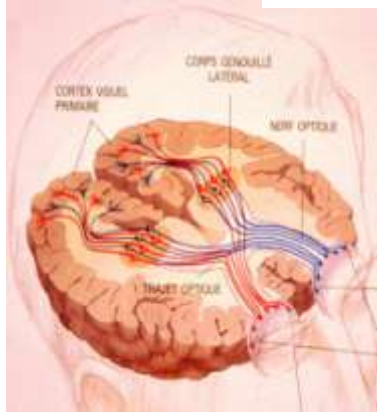
Voir c'est croire...

... "The brain possesses an intrinsic mechanism by which its vascular supply can be varied locally in correspondence with local variations of functional activity"...

Roy, C.W. & Sherrington, C.S. *J Physiol* 1890, 11: 85-108.

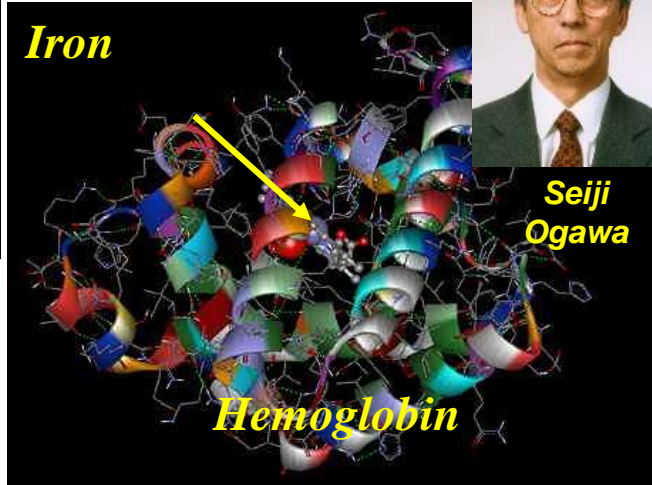
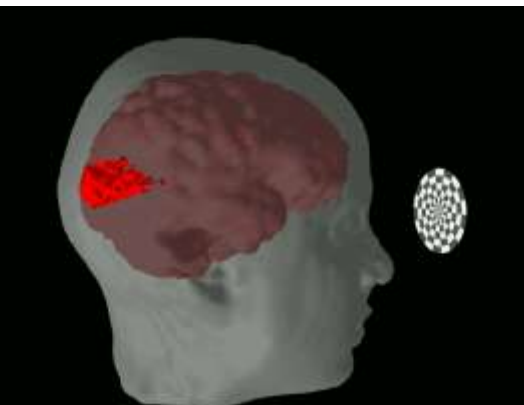
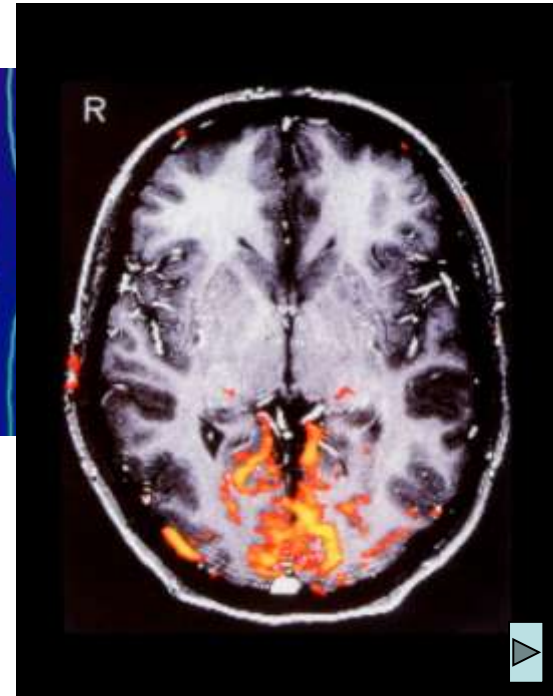
VISION

IRM fonctionnelle (fMRI)



Eau

(noyau hydrogène)



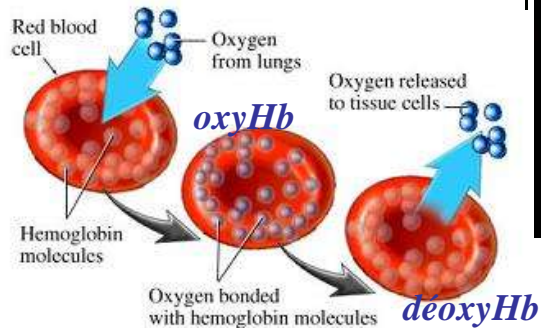
Iron

Seiji Ogawa

Hemoglobin

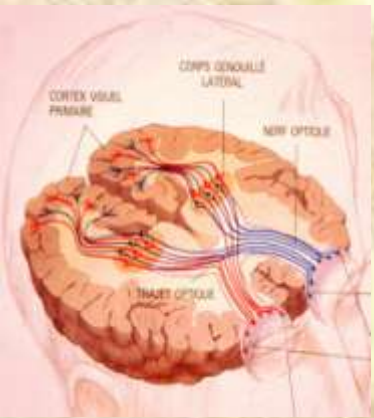
→ **Couplage neurovasculaire:**
Augmentation **débit sanguin** dans les régions activées

→ **Changement de l'aimantation de l'eau** près des capillaires sanguins des régions activées

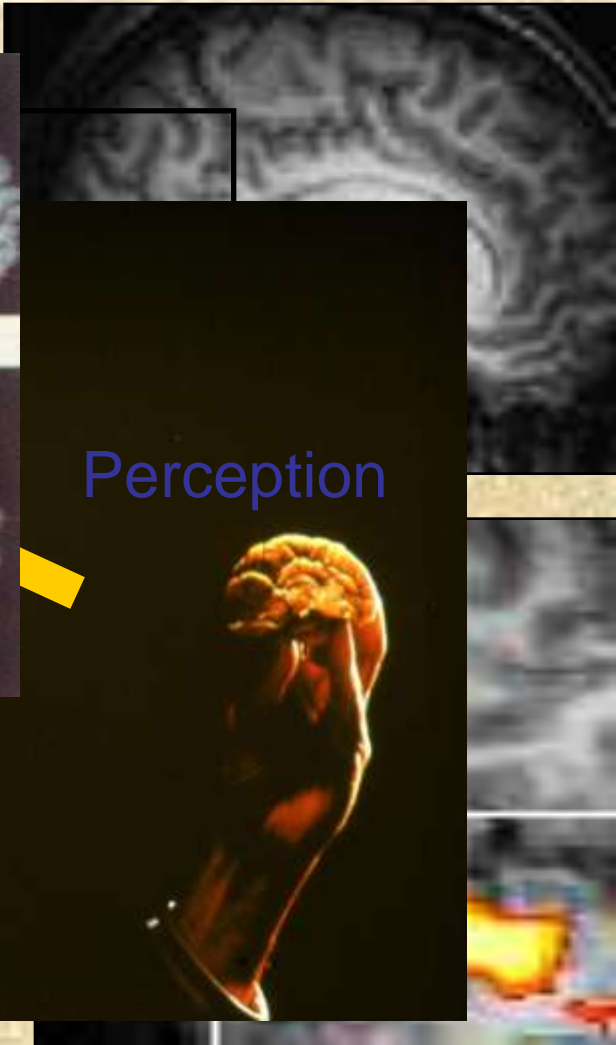
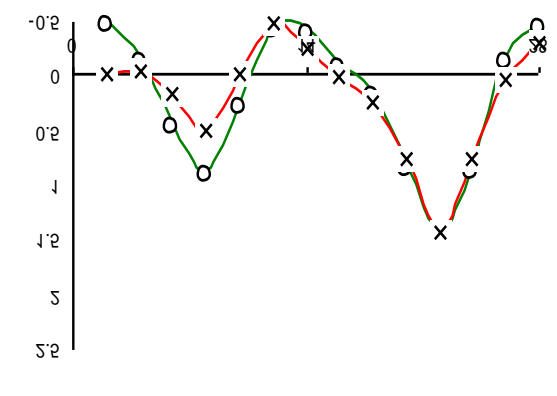
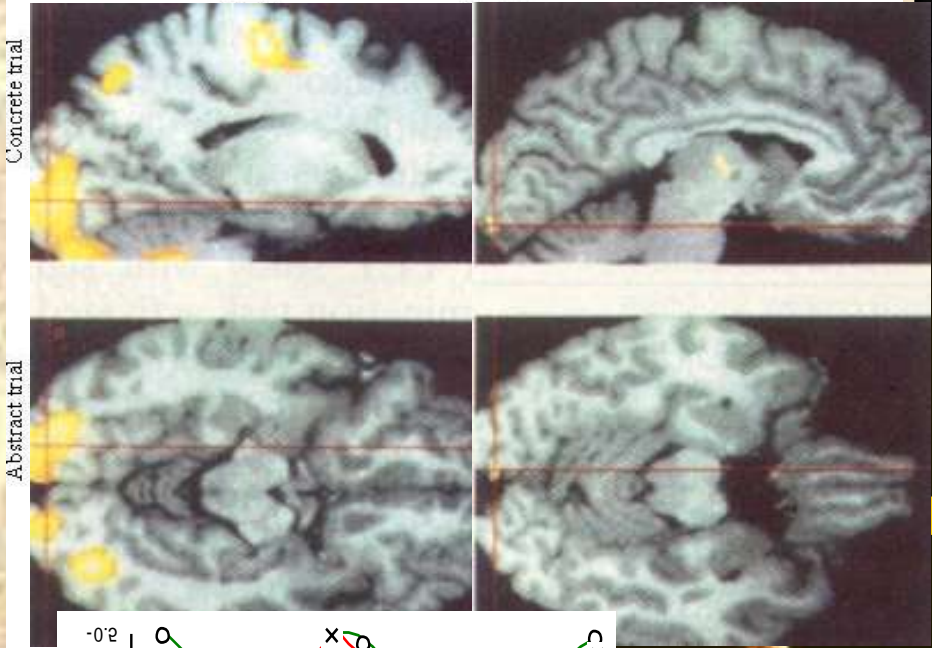


1990- ... **Blood Oxygen Level Dependent fMRI**

Voir notre monde interne: Imagerie mentale



VISION

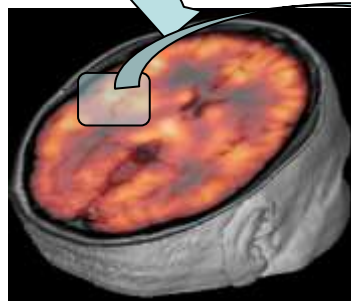
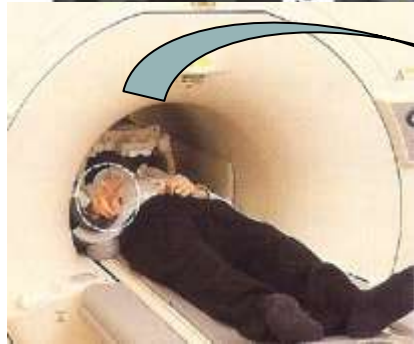
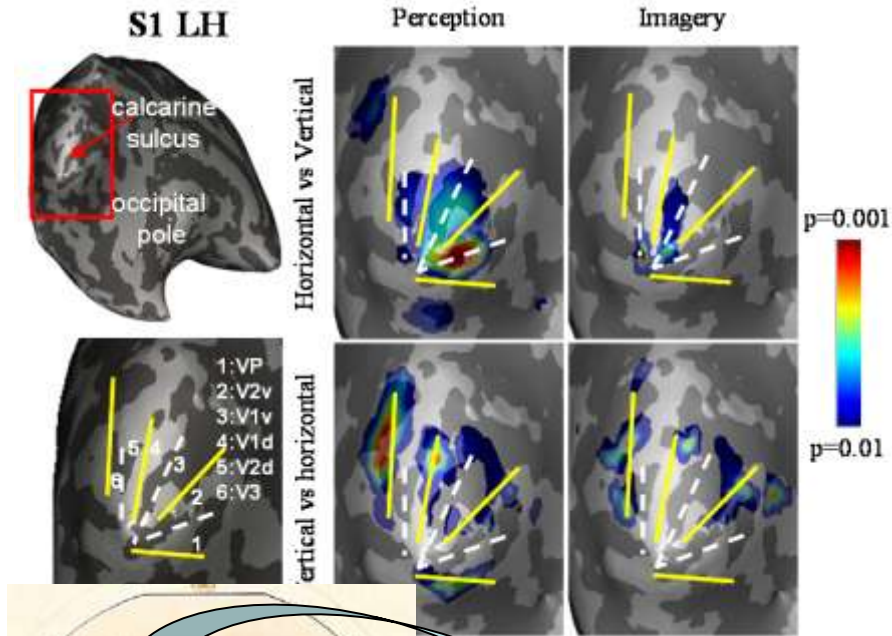


Klein I, Paradis AL, Poline JB, Kosslyn SM, Le Bihan D (2000). *J. Cogn. Neurosci.*

Visual activation during Braille reading in congenital blind people

(Sadato et al. *Nature*, 1995)

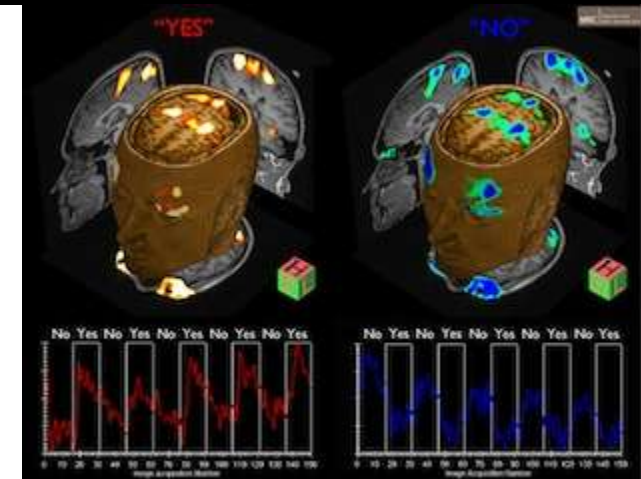
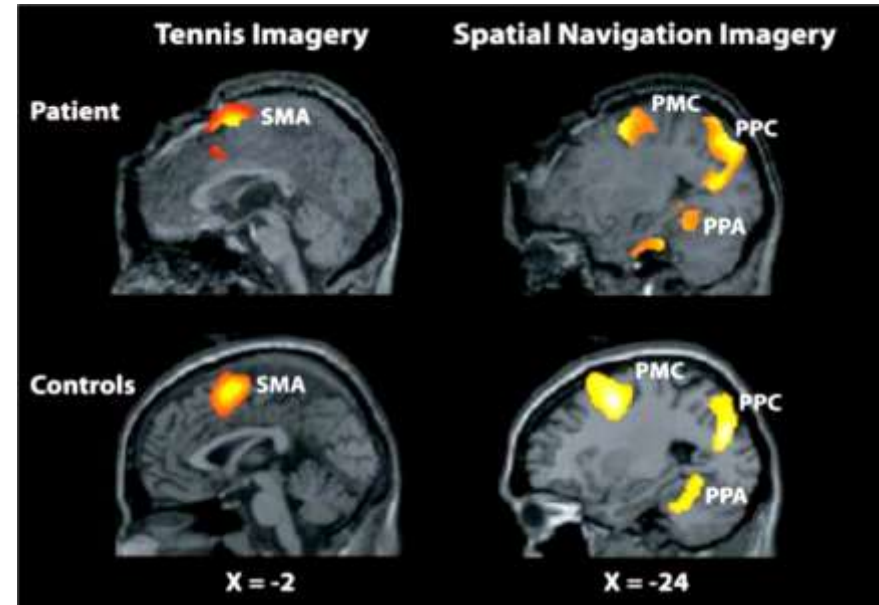
« Mind » reading... brain-machine interfaces



... consciousness Detecting Awareness in the Vegetative State

Adrian M. Owen,^{1*} Martin R. Coleman,² Melanie Boly,³ Matthew H. Davis,¹ Steven Laureys,³ John D. Pickard²

8 SEPTEMBER 2006 VOL 313 SCIENCE www.sciencemag.org

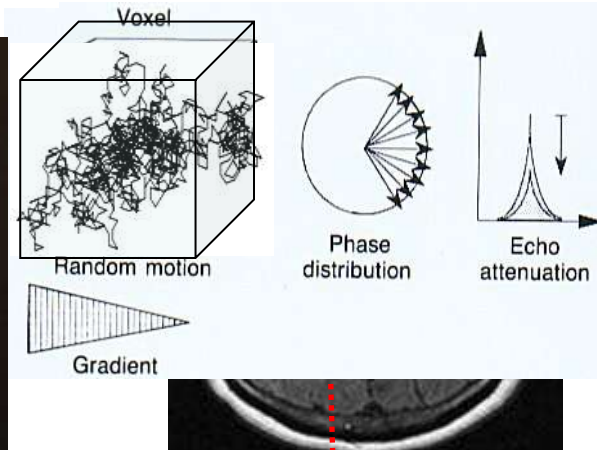




1985: WATER DIFFUSION MRI (from birth to adolescence)

→ Inferring microstructure from macroscopic resolution

Macroscopic scale



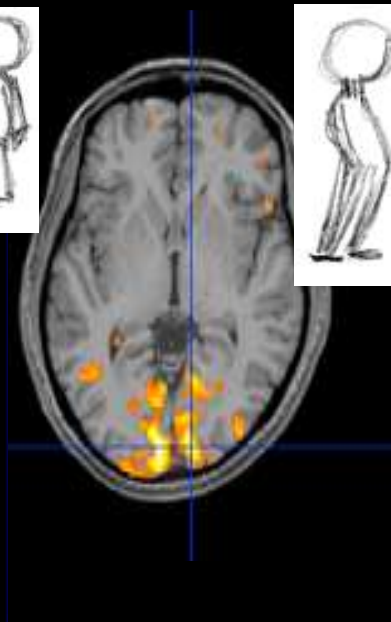
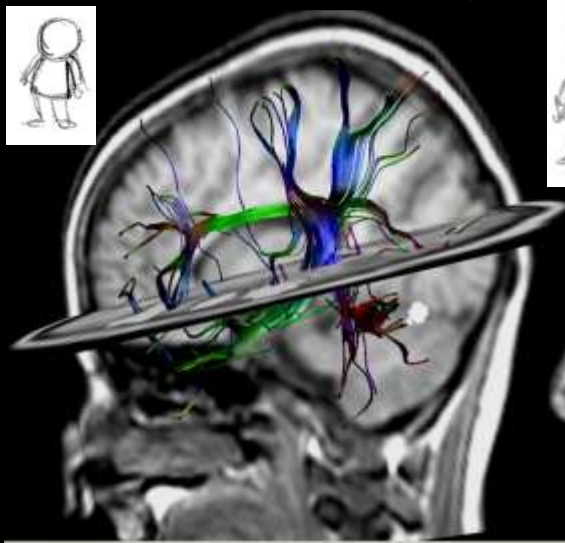
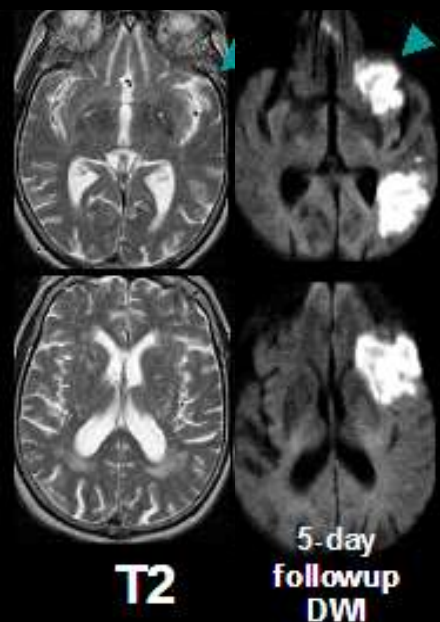
1985....1989... 1991... ..1992... 1994....1998... ..2004...2001....2006...

Stroke

Brain connectivity

Cancer

Brain functional MRI

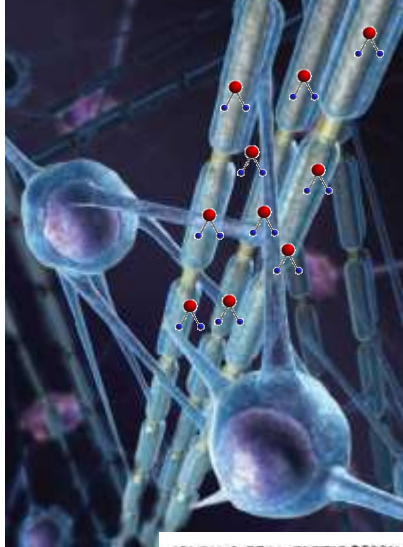


IRM de diffusion: anisotropie tissulaire

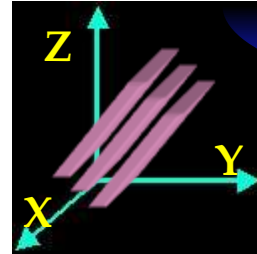
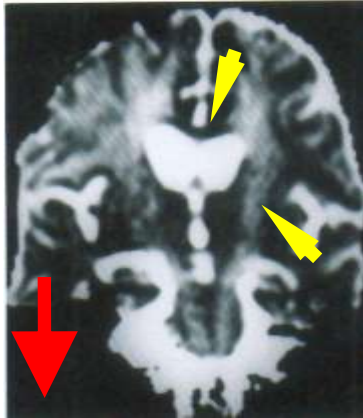
Anisotropie de diffusion

→ Baisse de la diffusion de l'eau ⊥ fibres de matière blanche
(Moseley 1990: cat brain & spine)

DTI

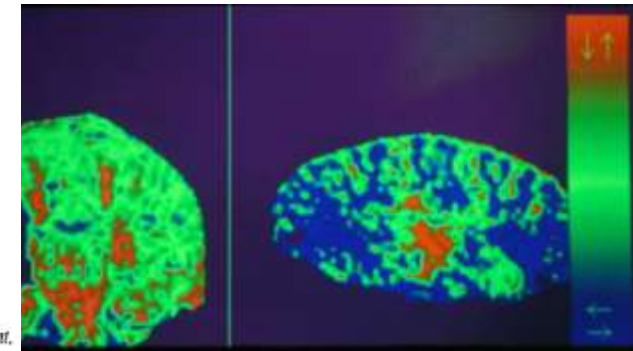
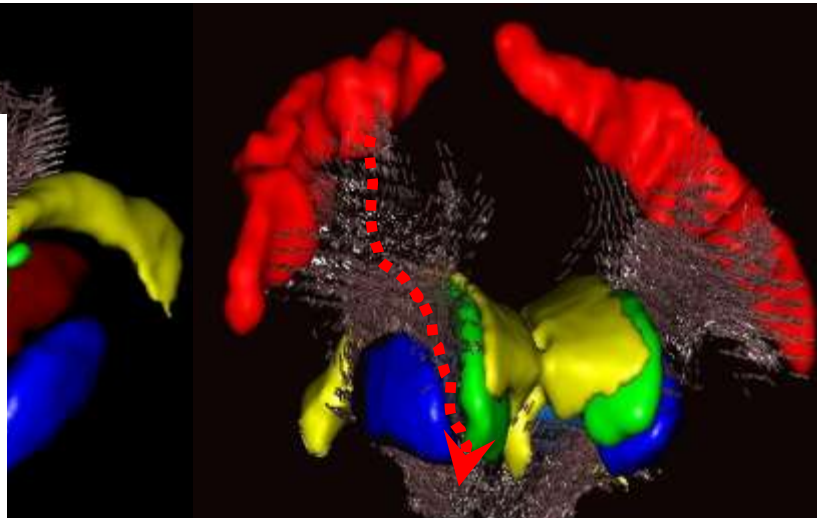
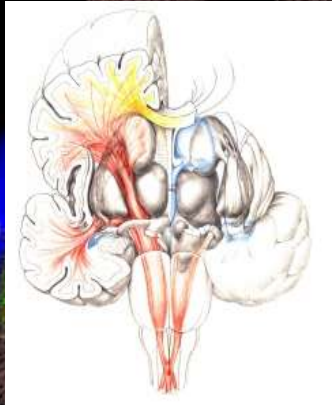
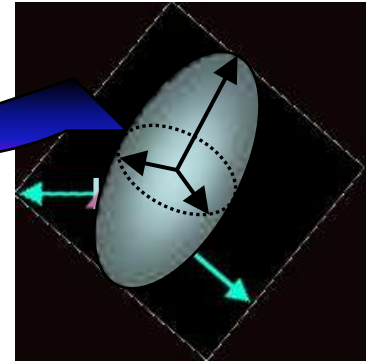


JOURNAL OF MAGNETIC RESONANCE. Series B 103, 247-254 (1994)

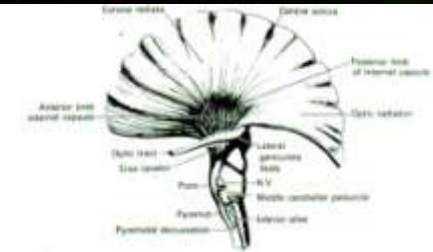


D =

$$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

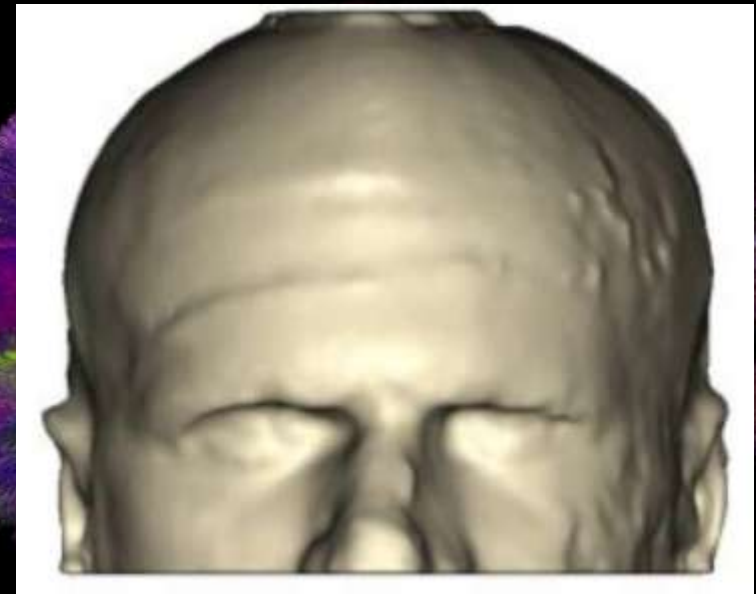
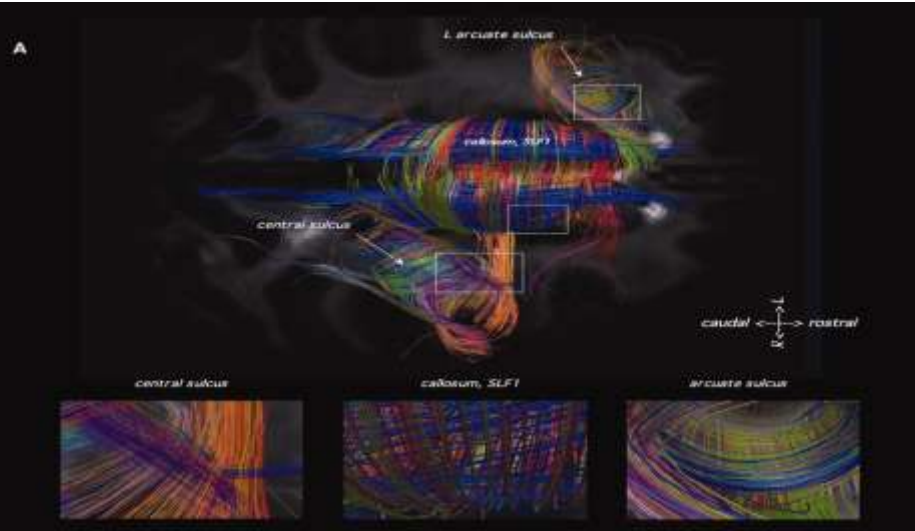


Department,



C. Poupon, J.F. Mangin et al., MICCAI, 1998 *fusivity axis*

IRM de diffusion: Du mouvement brownien au "Human Brain Connectome"



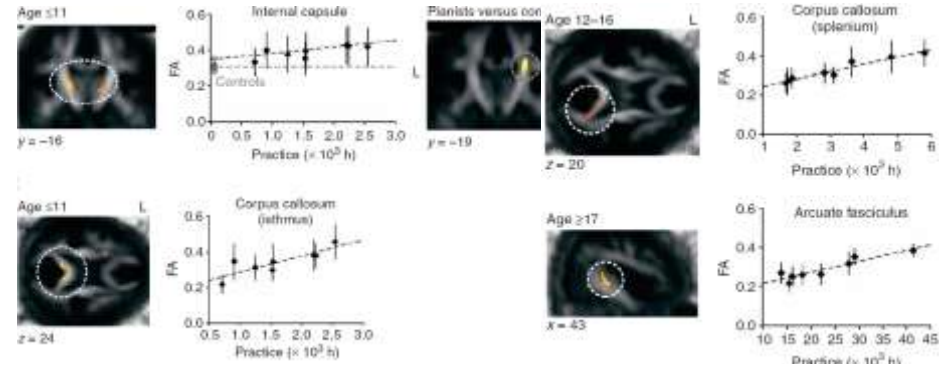
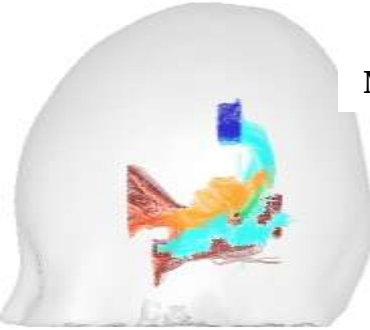
Poupon et al. (Connectomist/NeuroSpin)

IRM de diffusion: Développement cérébral, plasticité, dysconnexions



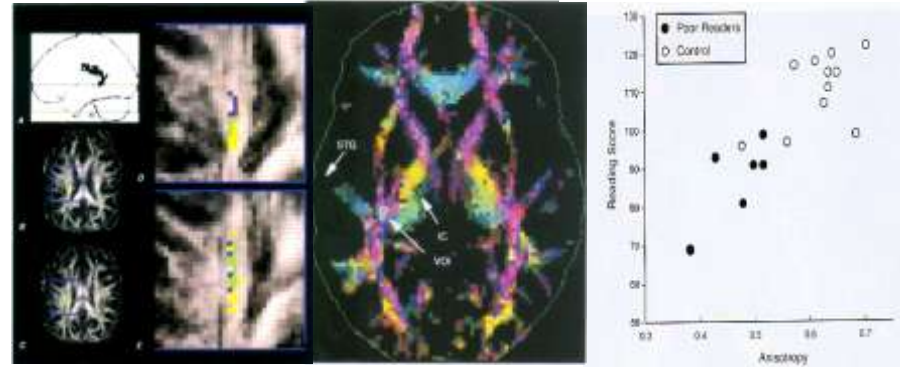
2-4 month babies

Maturation of language networks



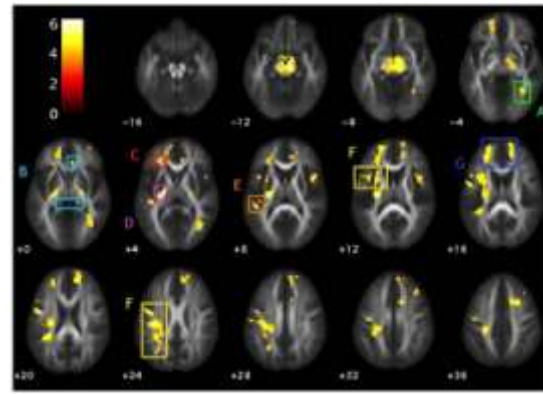
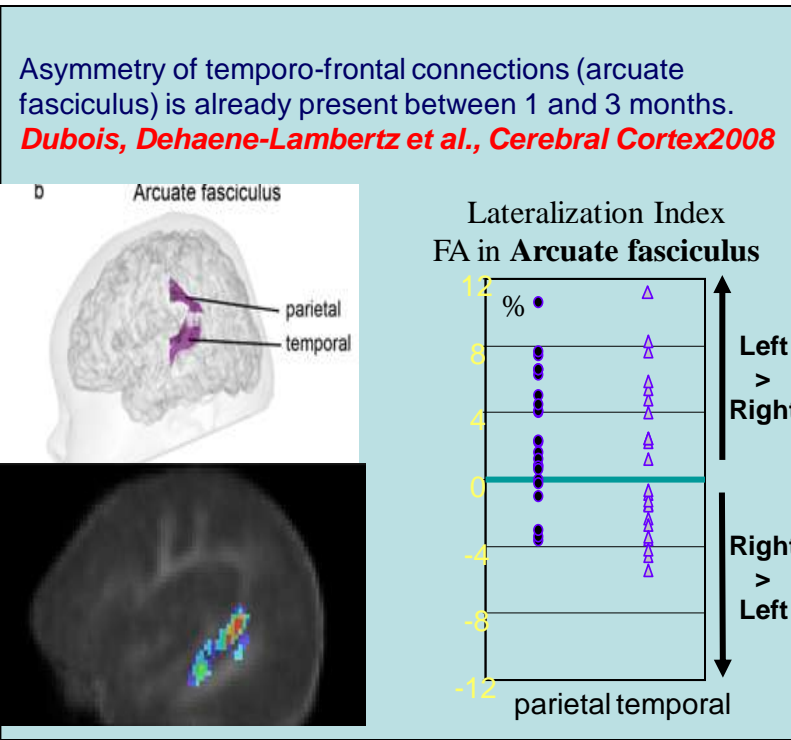
Pianist brains

Bengtsson et al. *Nat. NS.* 2008



Dyslexia

Klingberg T., et al. *Neuron* 2000



Schizophrenia

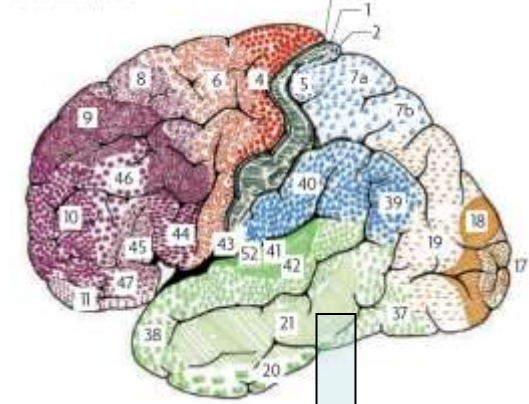
Skelly, et al. *Schizo. Res.* 2008



Neuroimagerie: Multiéchelle!



Brodmann, 1909

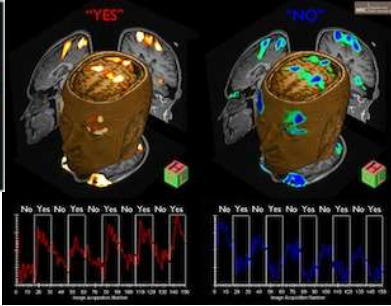
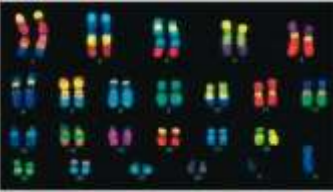


➤ Hier & aujourd'hui: architecture fonctionnelle

macroscopique:

-Codes cognitifs

-Connexions



➤ Aujourd'hui & demain: Gènes et cerveau

22000 gènes (10^{10} bits), 10^{11} neurones, 10^{15} synapses!

➤ Demain, le « code **neural**»:

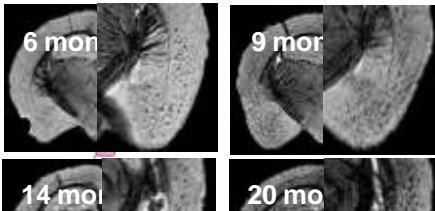
Set de clusters cellulaires assurant des briques de **fonctions élémentaires**, mises en **connexions** pour élaborer des fonctions « supérieures », → relation **mésoscopique dynamique** entre structure tissulaire et fonction



MESO

MICRO

0.000001 millimètre

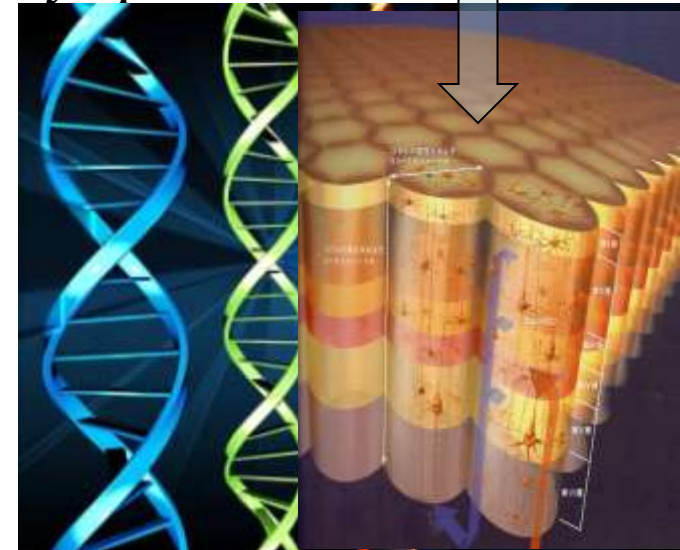


➤ La santé:

→ Prévention, diagnostic précoce (ALZ, psychiatrie)

→ Rééducation/reprogrammation (AVC, traumatismes)

→ Thérapies personnalisées



➔ Mésoscale & IRM (~100µm): Structure & Fonction

Instruments are key to groundbreaking science...

Large Instruments for science:

High energy, particles physics → Higgs boson
(CERN, RIKEN, etc)

Astronomy and astrophysics
→ Universe (Hubble telescope)



Neuro-physics → NeuroSpin...

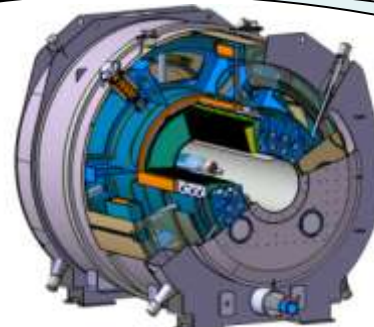
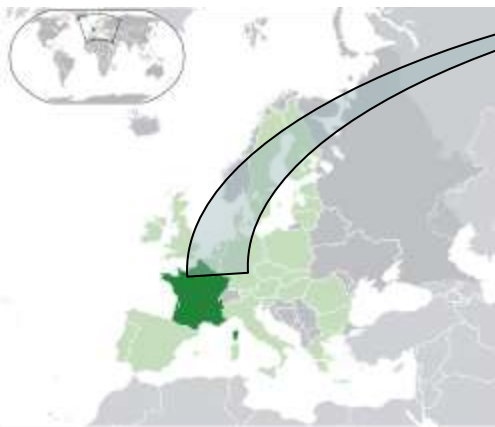
Aimed at ultra-high field MRI/MRS systems:

3T, 7T,

11.74T wide-bore for human studies

17.18T (rodents)

*Interdisciplinary effort
under one roof*



→ Human brain explorer



NeuroSpin, a concept unique in the world

**: world first*



Whole-body 3T MRI

Clinical care facility
(8 hospital beds, private examination rooms, MEG)

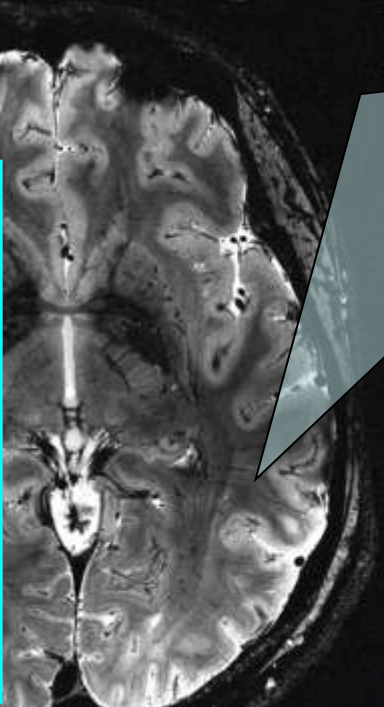
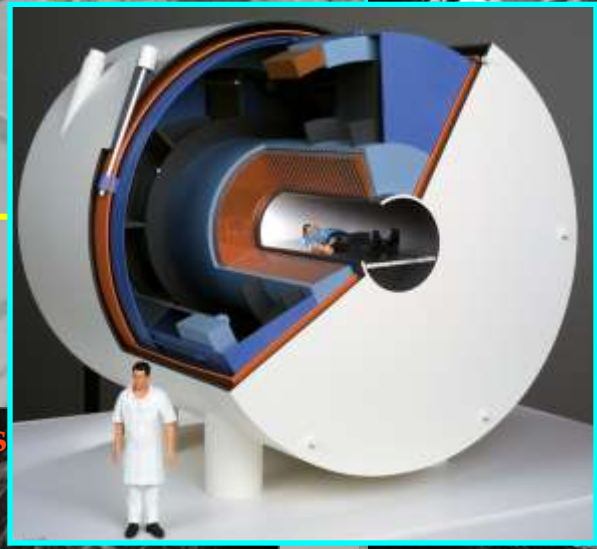
Whole-body 7T

11.74/900mm*

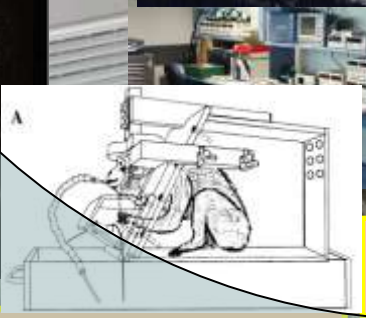
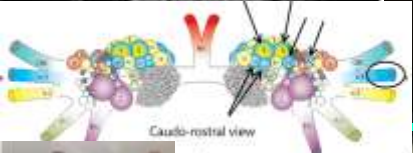
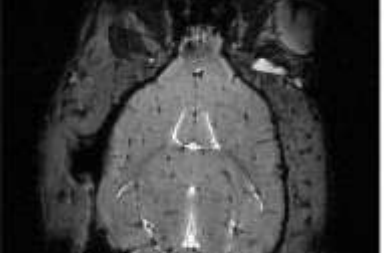
To be announced

17.2T/260mm*

Resolution: 80 micrometers



Library & Conference room

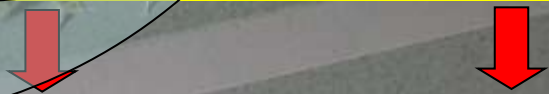


Laboratories, electronics, mechanics, chemistry shops and offices

Industry labs/offices

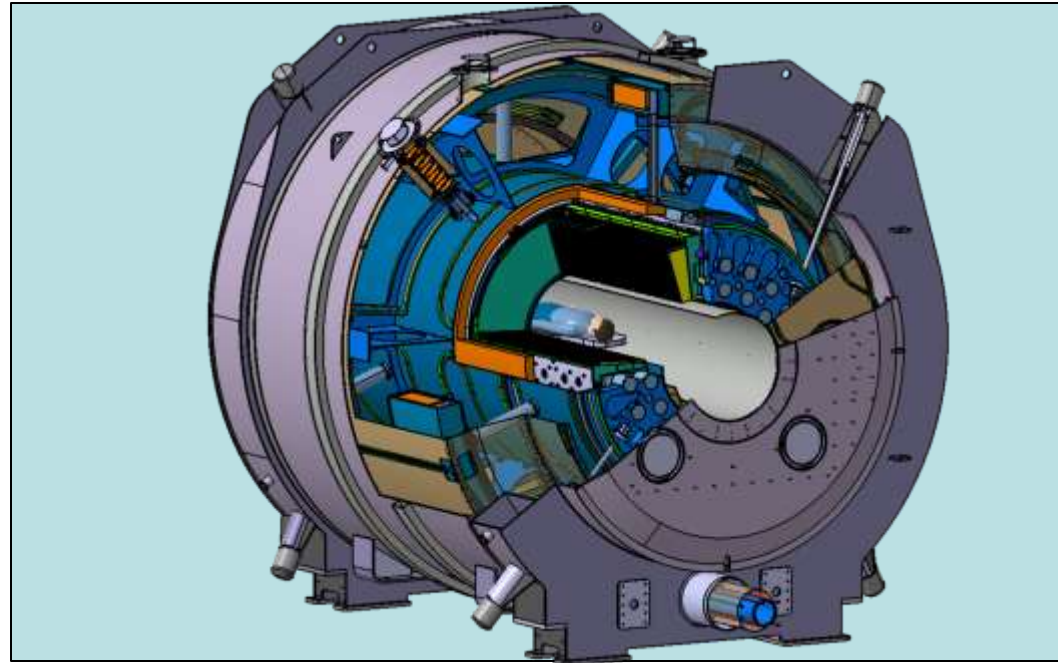
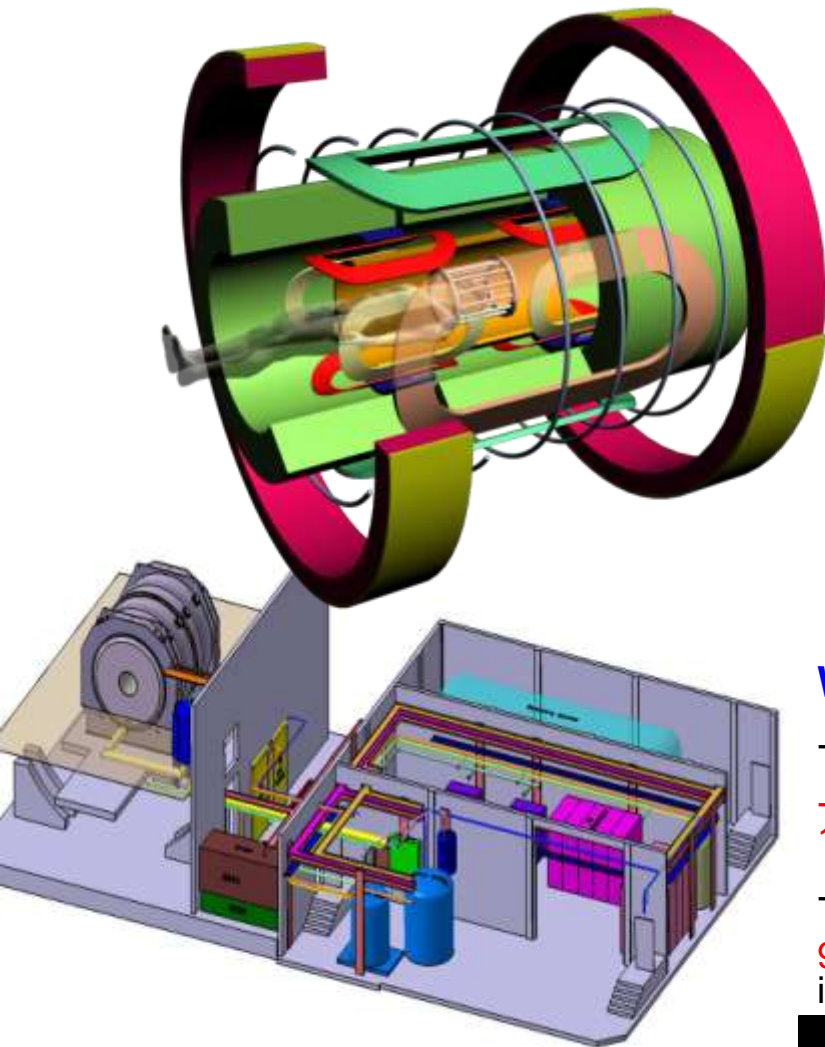
Animal care facility
(transgenic mice, primates, training rooms, surgical suit)

Accelerate translational research



CEA/Irfu design for NeuroSpin 90cm bore 11.74T magnet

They did not know it was impossible, so they made it... (Mark Twain)



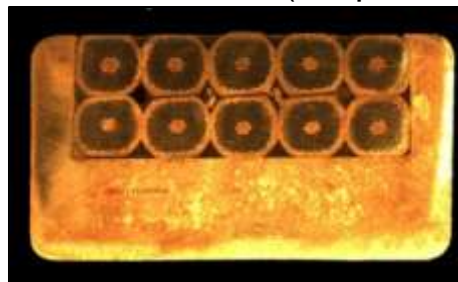
Whole-body actively shielded 11.74T/500MHz magnet:

- cryostat: 4.6x4.7x4.7m³, 900mm internal diameter, 150 tons

- wetted double pancakes in superfluid He:
1.8K pressured He II

- superconducting wire: 65t NbTi (182 km)

9.2x4.9mm² section, 1500 amp
in driven-mode (ext power supply)



Cryogenic satellite

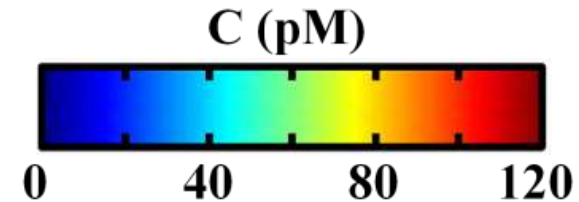
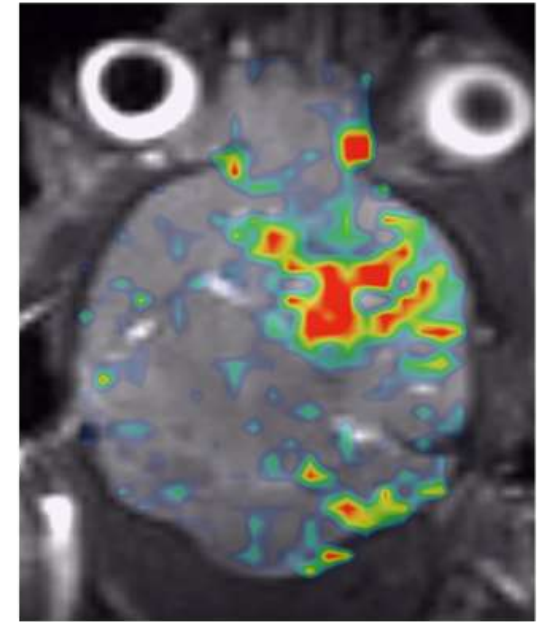
Hydraulic, vacuum and electrical links towards magnet cryostat are realised within multiple transfer line (*cryoline*)

Molecular Imaging



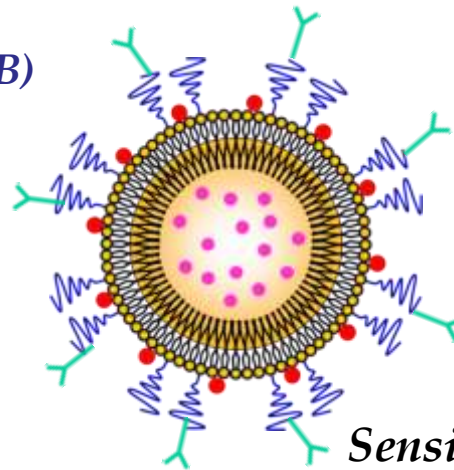
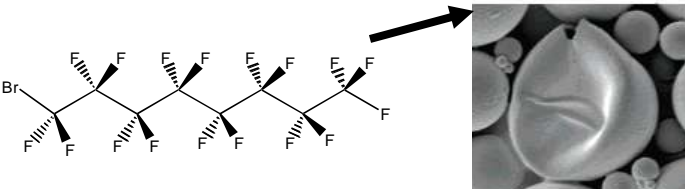
Rat brain tumor model

^{19}F MRI of $\alpha_v\beta_3$ receptors with RGD-functionalized PFOB NP in U87 mice



Sensitivity threshold is $\sim 100 \text{ pM}$

^{19}F PFOB based emulsion
perfluorooctylbromide nanoparticles (PFOB)
Alzheimer disease marker



Giraudeau C, Flament J, Marty B, Boumezbeur F, Mériaux S, Robic C, Port M, Tsapis N, Fattal E, Giacomini E, Lethimonnier F, Le Bihan D, Valette J. A new paradigm for high-sensitivity ^{19}F magnetic resonance imaging of perfluorooctylbromide. *Magn Reson Med*. 2010 Apr;63(4):1119-24

D. Le Bihan Nov 2012



● *International integration*

- Europe (CONNECT, ISEULT, EATRIS, EuroBioimaging/FLI, etc.)
- International teams/collaborations

- University of Freiburg, Germany
- Institute für Medizin, Jülich, Germany
- Max Planck Institute Tübingen, Germany
- University of Leuven, Belgium
- Kyoto University, Japan
- Tokyo University, Japan
- NIH, Bethesda, USA
- University of Minnesota, USA
- Nat. Research Council, Canada
- Tel Aviv University, Israel
- Nat. Yang-Ming Univ. Taipei
- ...



● *Industrial partners/clients*

- MRI and contrast agents:
Guerbet, Siemens, Bruker
- Pharmaceutical companies

● *Regional integration*

- Healthcare competitiveness pole (*cluster*) of the Paris region (*Medicen*)
- Orsay (Paris-South University), Paris-Saclay campus, NeuroSaclay campus
- Federative Research Institute (IFR 49) with Paris Hospitals

→ *Connecting basic research centers to research hospitals, leading schools and university*

DENIS LE BIHAN

LE CERVEAU DE CRISTAL

CE QUE NOUS RÉVÈLE
LA NEURO-IMAGERIE

