

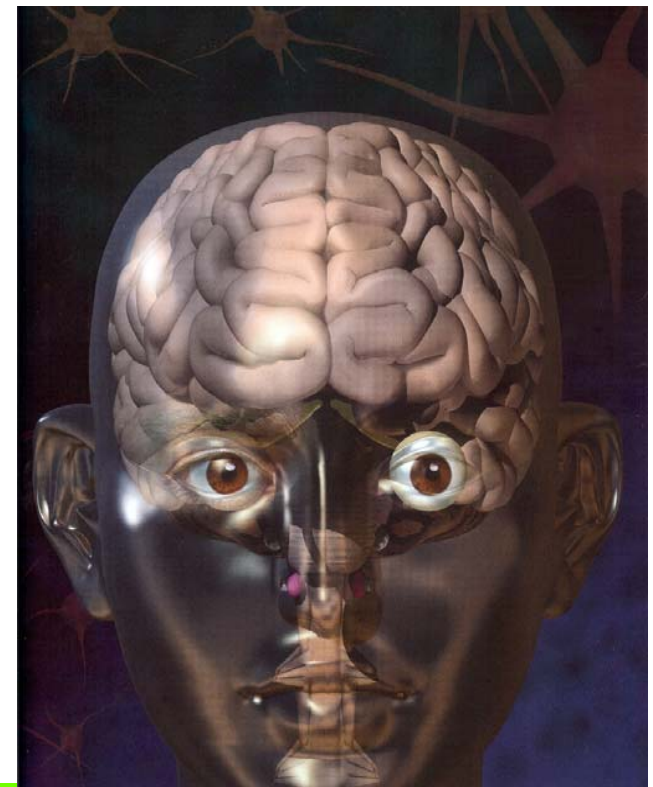
*NeuroSpin: An international infrastructure  
where physics meets neurosciences*

Denis Le Bihan

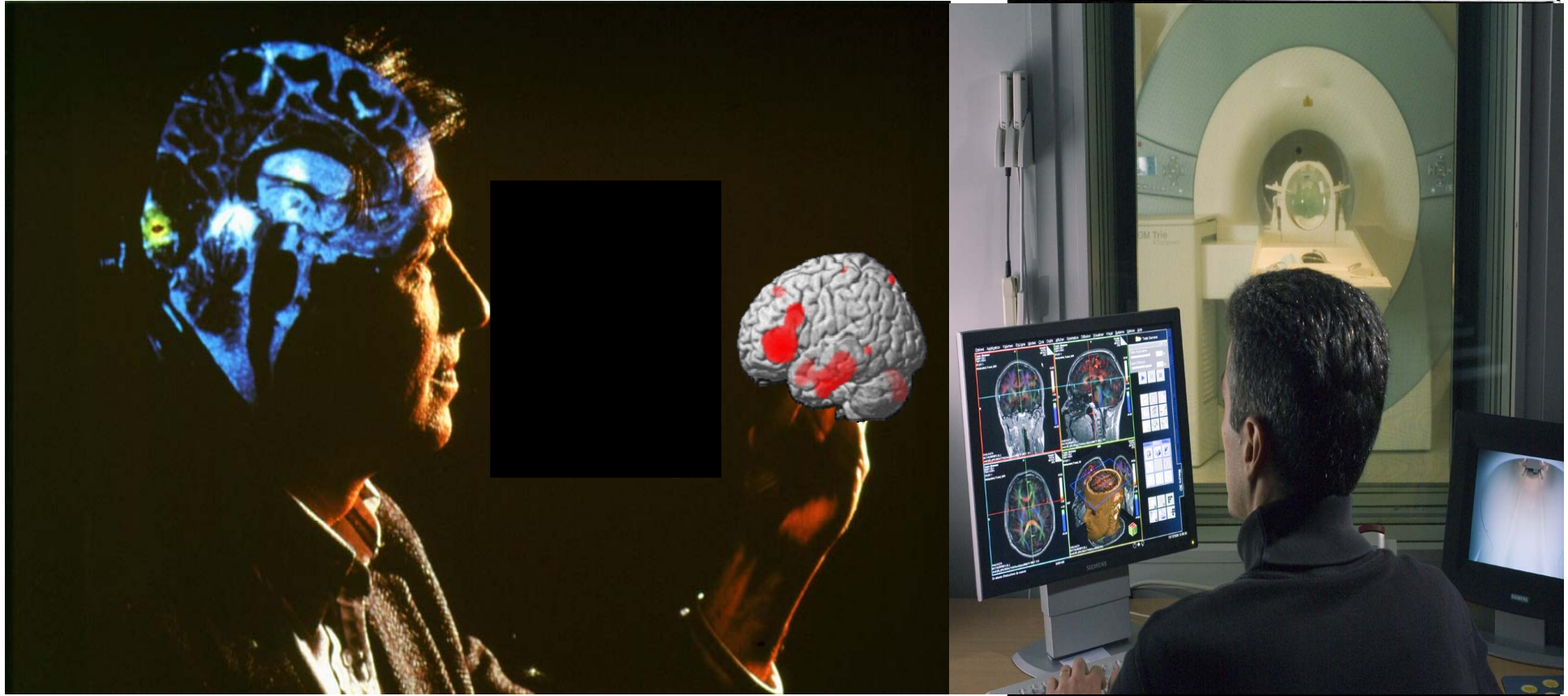
NeuroSpin Director, CEA-Saclay, France

Academy of Sciences

京都大学医学研究科附属高次脳機能総合研究センター



# The « image » revolution ... daughter of physics and computer sciences



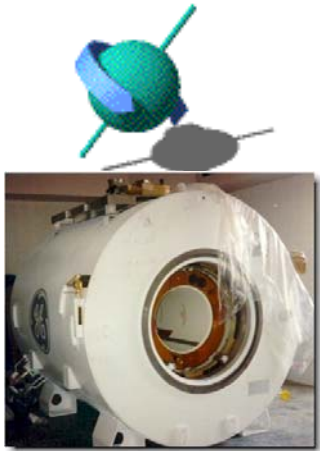
**MRI: Function ← Structure**  
The *normal* brain at work

1972-82: X-ray CT, then MRI:  
virtual dissection of the *diseased* brain

One of the brain secrets lies in its *architecture*: *function* and *localization* are intimately linked, at all scales, hence the importance of *neuroimaging*...

# MAGNETIC RESONANCE IMAGING: *Virtual magnetic images of the body*

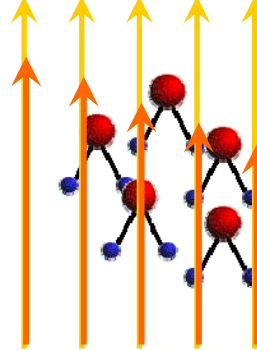
WATER: 90% of molecules,



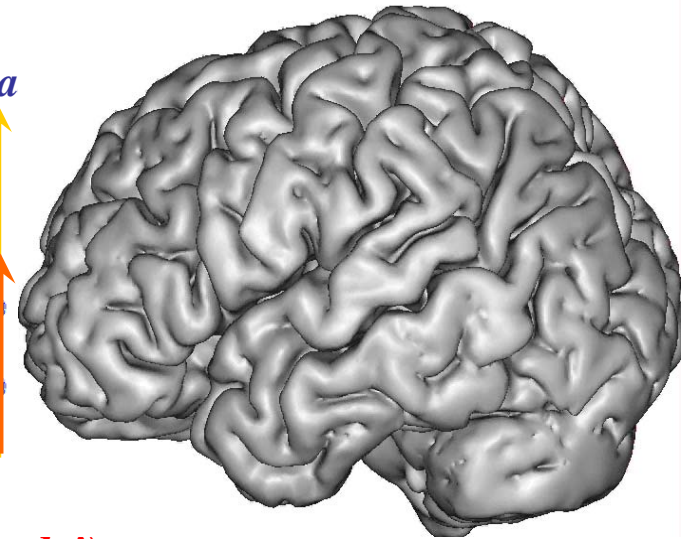
*Strong magnet*



*Magnetic field gra*



**WATER**

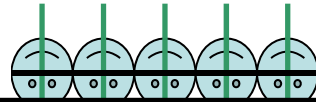


*Contrast:*

*≈1.5tesla (=15000Gauss)*

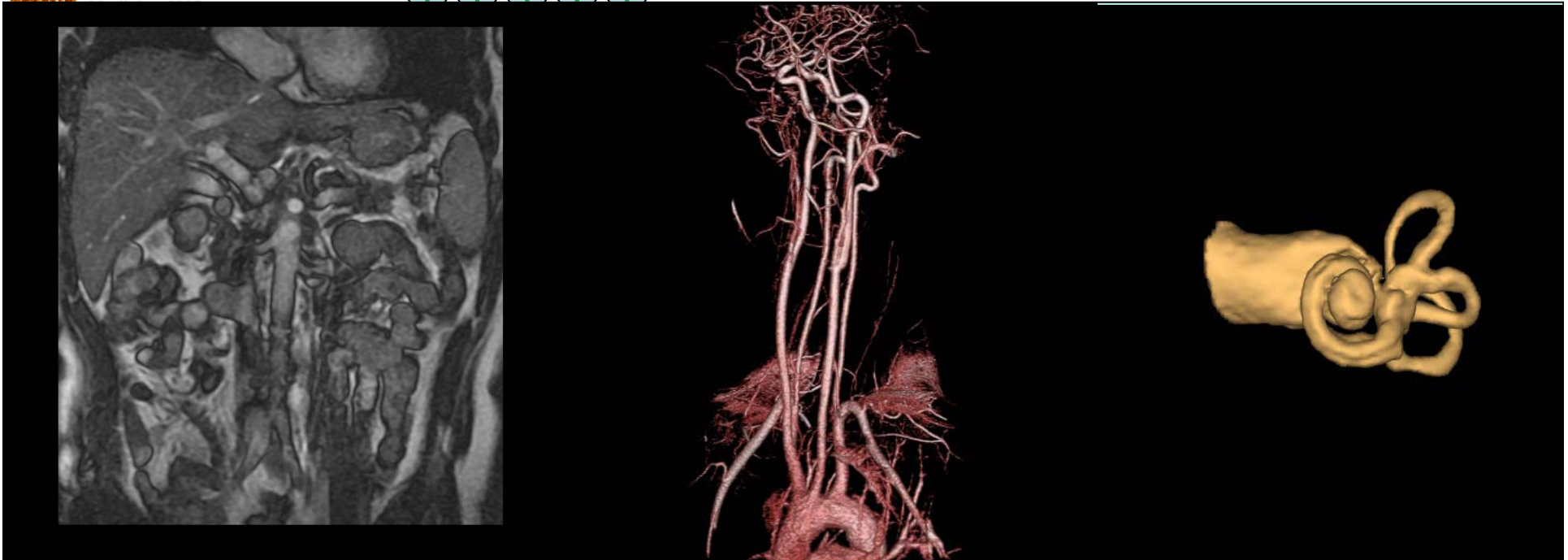


The Nobel Prize in Physiology or



$N_{high}$

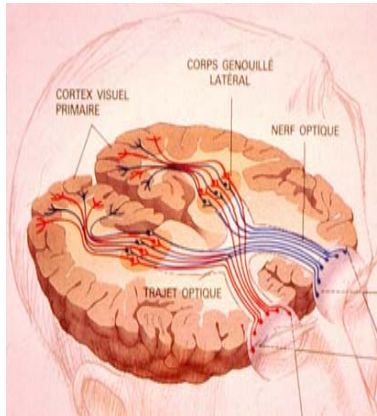
*(hydrogen nuclei)*



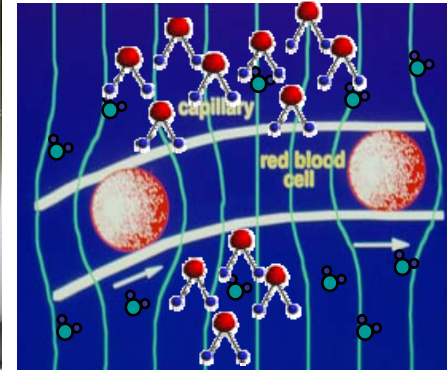
# Seeing is believing ...

*Coupling of blood flow and neuronal activation*  
 (Sherrington & Roy, 1890)

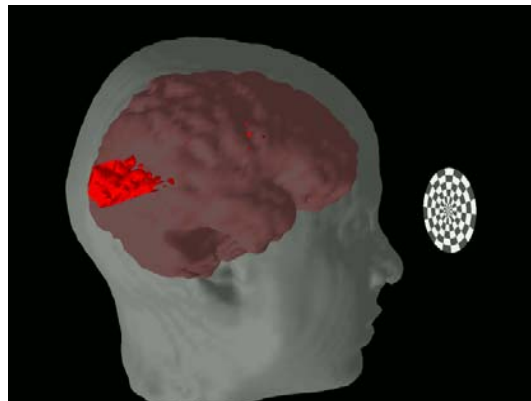
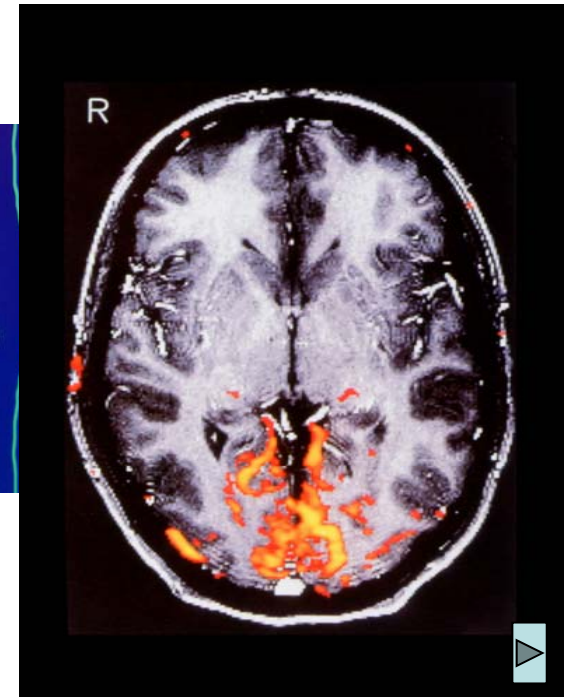
## VISION



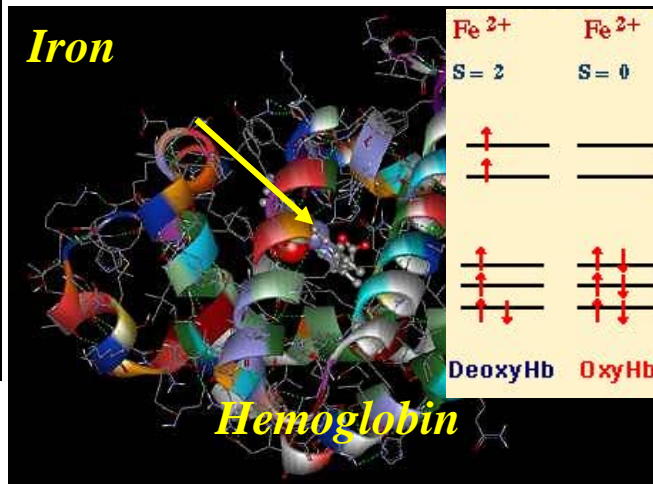
## Functional MRI (fMRI)



**Water**  
 (hydrogen nuclei)



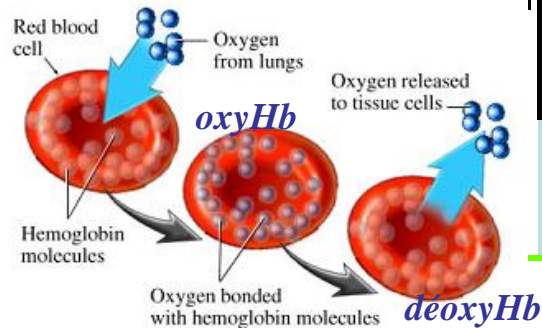
## Iron



## Hemoglobin

oxyHb: diamagnetic  
 deoxyHb: paramagnetic

→ Increase of cerebral blood flow in active regions  
 → Change in water magnetization near capillary blood vessels

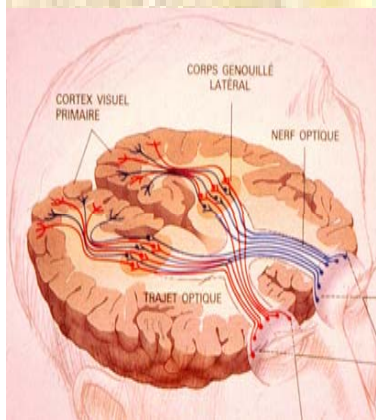


Seiji Ogawa



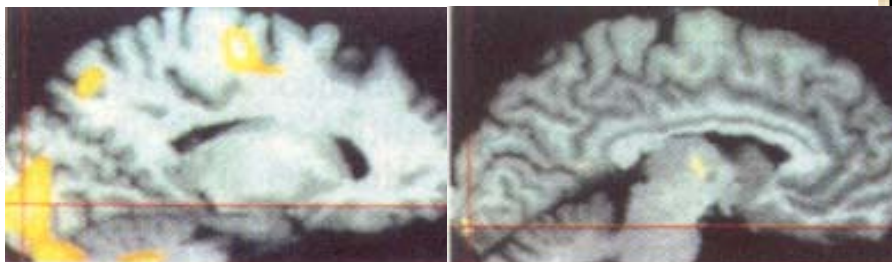
1990- ... Blood Oxygen Level Dependent fMRI

# Seeing the inner world: Mental imagery

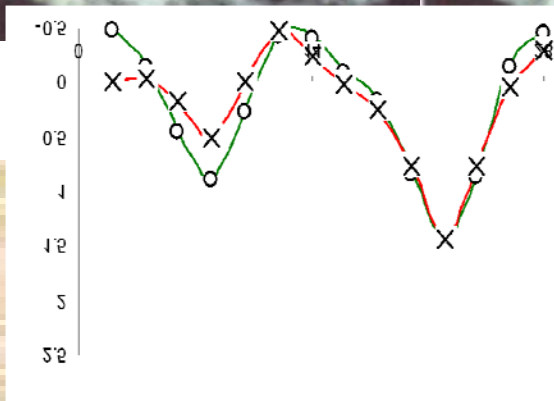
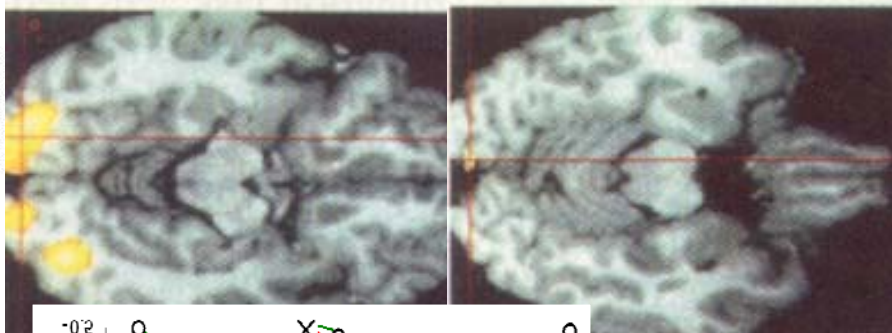


VISION

Concrete trial



Abstract trial



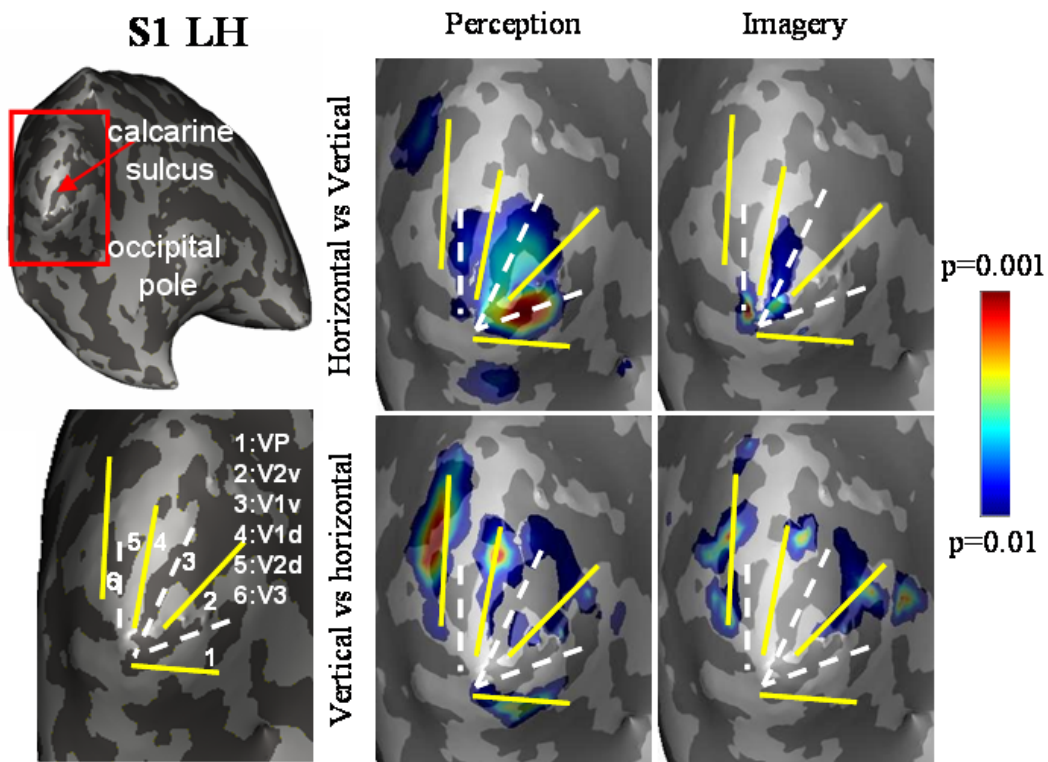
Perception



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

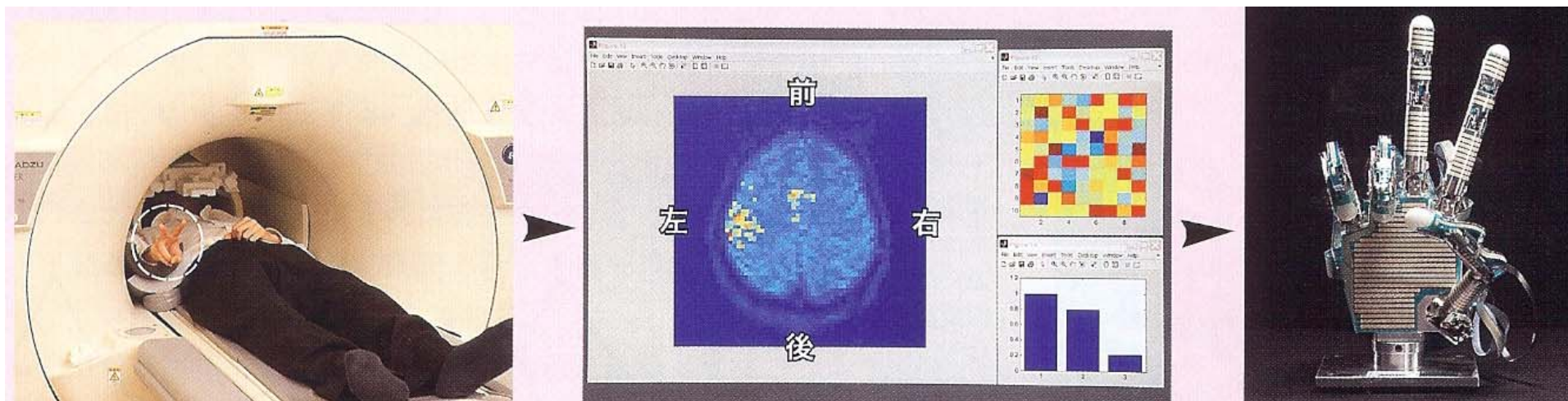
**Visual activation during Braille reading in congenital blind people**  
(Sadato et al. Nature, 1995)

# From mind reading to brain-machine interfaces



Klein I, Dubois J, Mangin JF, Kherif F, Flandin G, Poline JB, Denis M, Kosslyn SM, Le Bihan D.  
*Cogn.Brain.res.* 2004; 22:26-31

ATR labs. Nara





## 1905 - Einstein's "miraculous" year: *famous articles which changed the way we see the world*

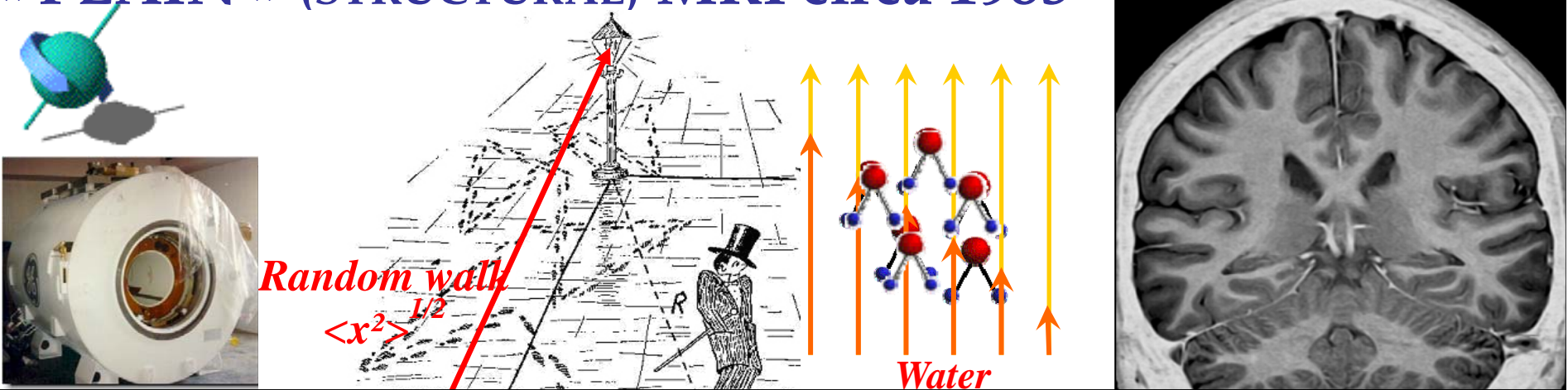
- ✓ "On a Heuristic Point of View on the Creation and Conversion of Light" (17 March 1905)  
(Photo-Electric Effect) → **Nobel prize in physics, 1921**
- ✓ "On the Electrodynamics of Moving Bodies"  
(30 June 1905)
- ✓ "Does the inertia of a body depend on its energy content?" (27 September 1905)  
(Theory of Special Relativity) →  **$E = m c^2$**
- ✓ "Investigation on the Theory of the Brownian Movement: On the motion of small particles suspended in liquids at rest ..." (11 May 1905)
- ✓ "A new determination of molecular dimensions" (PhD thesis, 30 April 1905)  
(Molecular-Kinetic Theory of Heat) → **diffusion theory**



**Albert Einstein, Circa 1905**

# WATER DIFFUSION MRI: 25th anniversary!

« PLAIN » (STRUCTURAL) MRI circa 1985



...1989... 1991... ..1992... 1994... 1998...

...2004...

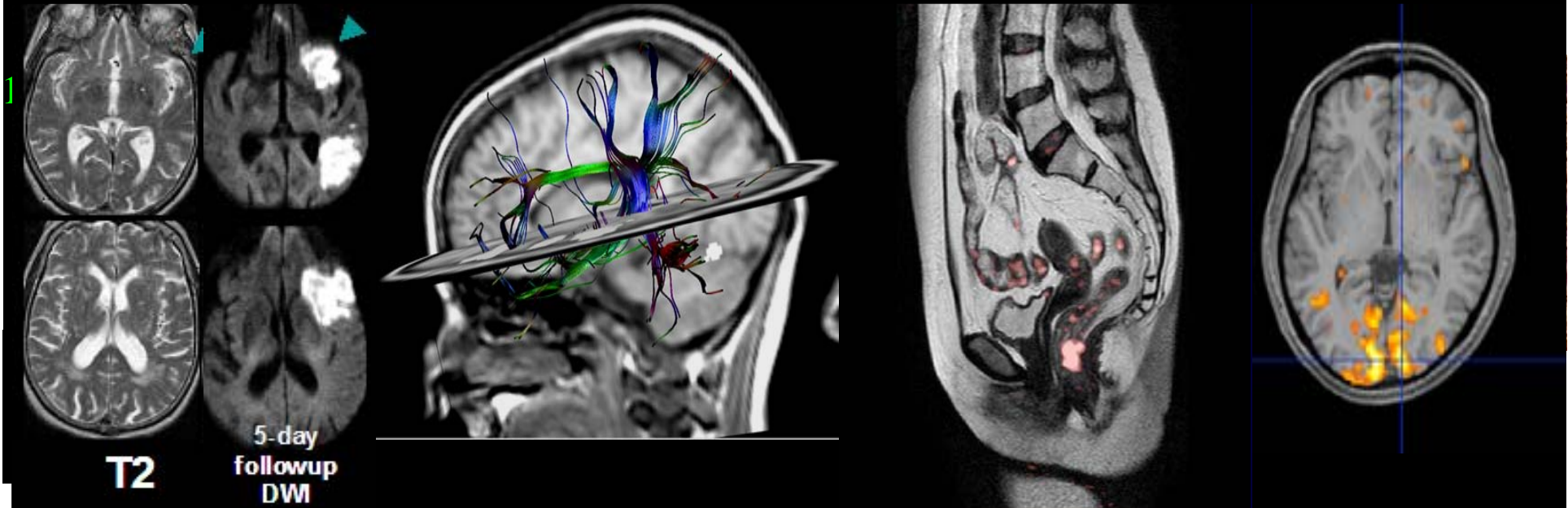
....2001... 2006...

*Stroke*

*Brain connectivity*

*Cancer*

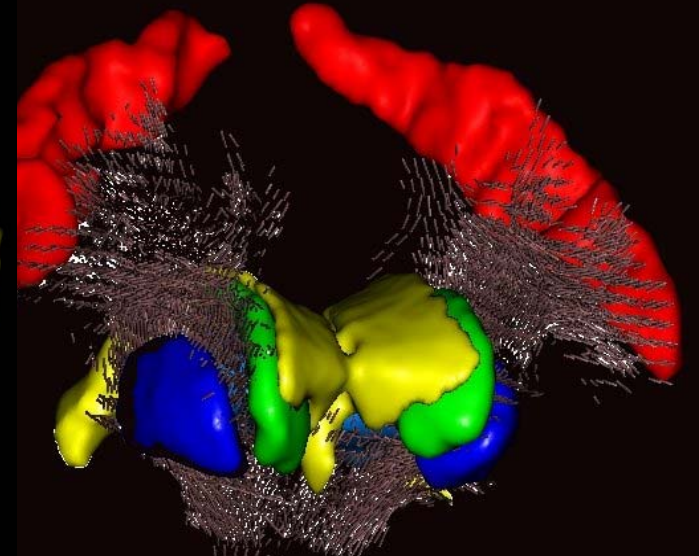
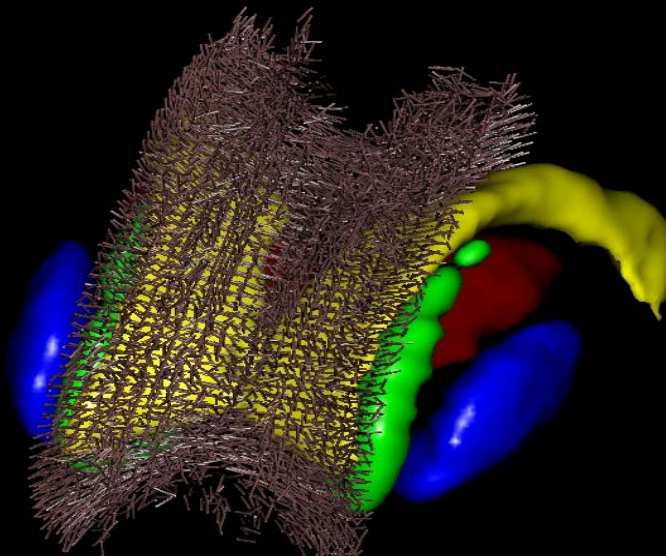
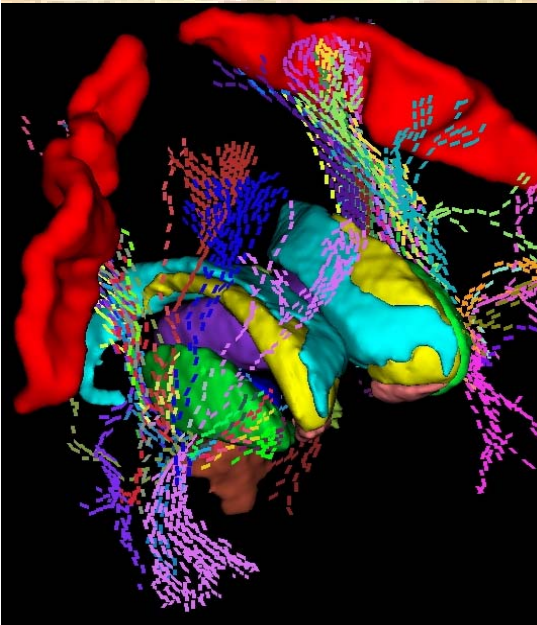
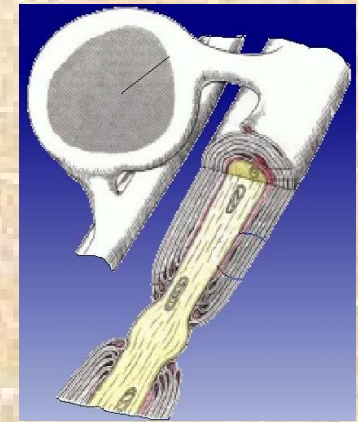
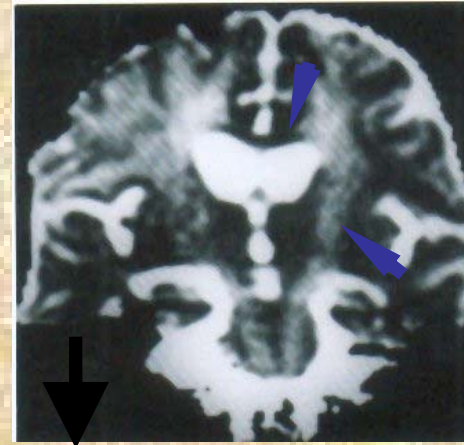
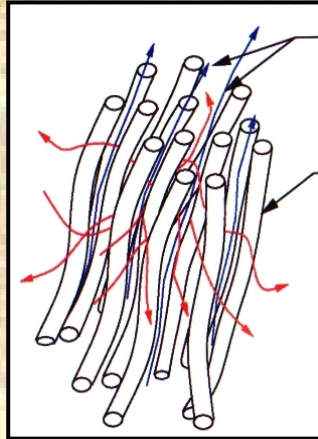
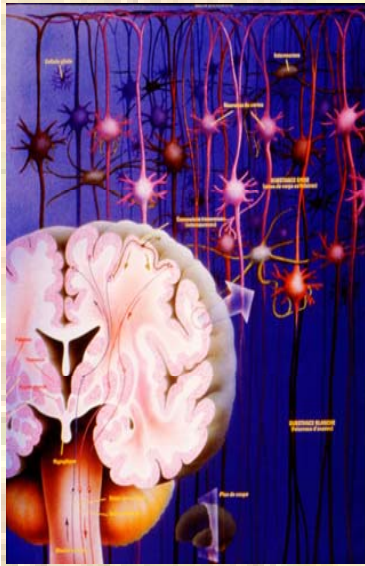
*Brain functional MRI*





# Diffusion MRI ...

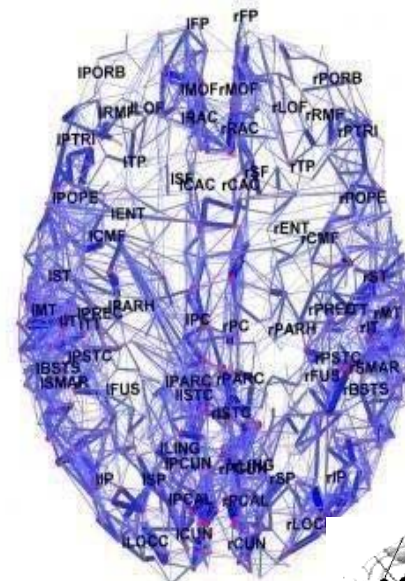
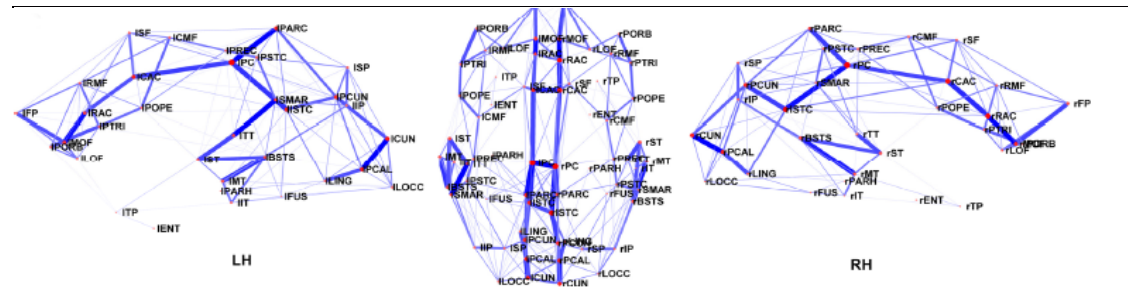
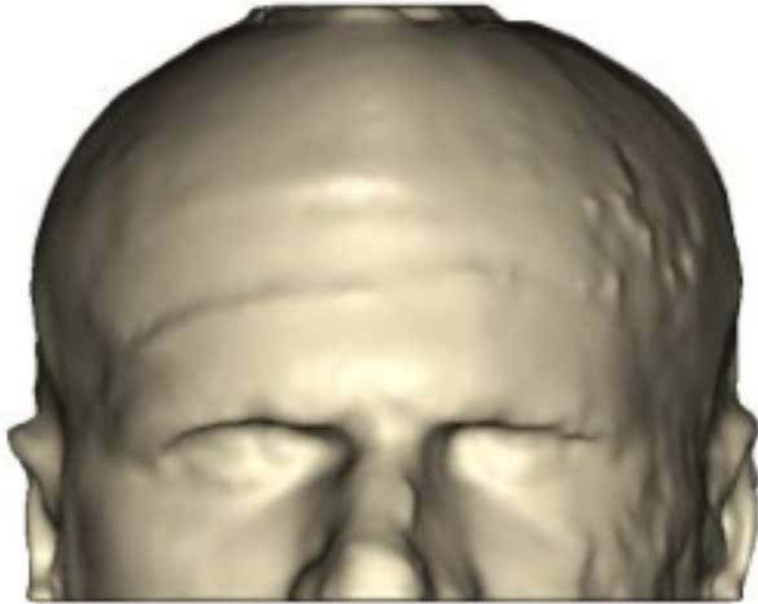
*Directional effects (anisotropy)...*



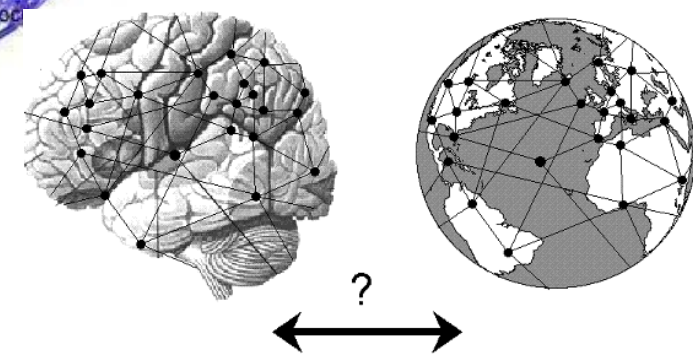
Mangin, Poupon et al. MICCAI 1998, NI 2000

*... towards connectivity in the brain*

# From brownian motion to brain connectivity: Diffusion Tensor MRI (Basser & Le Bihan, 1992-94)

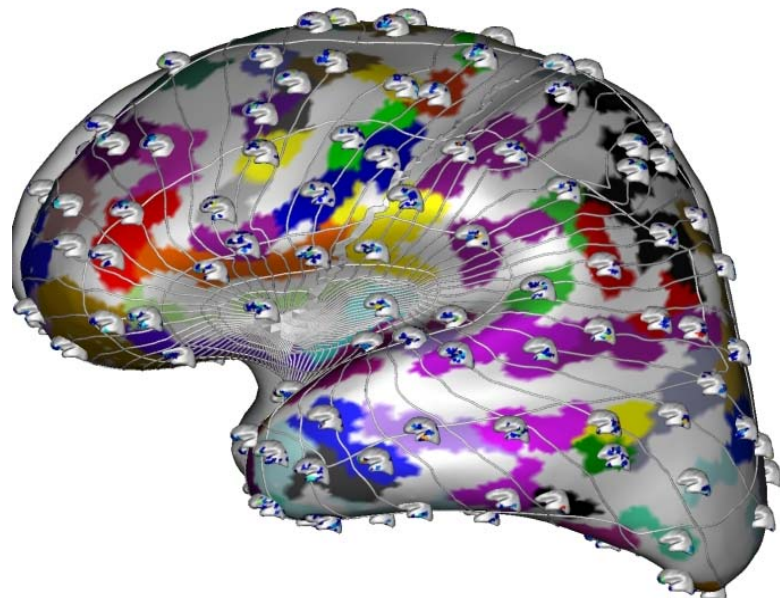


*Hagmann P. et al.  
PloS Biol 2008*



Human Brain

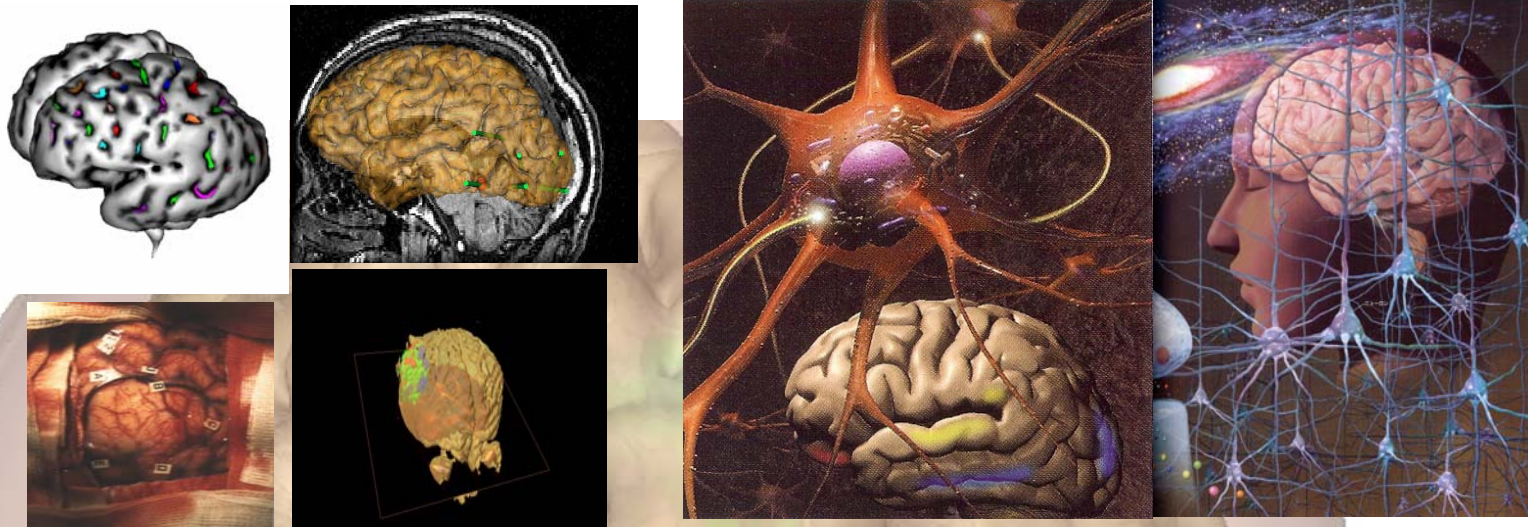
Global Network



ASEPS

# Investigating the Human Brain

体と心



- ✓ *Neurology/neurosurgery*
- ✓ *Development, aging, rehabilitation*
- ✓ *Psychiatry, mind disorders*

✓ *Neurosciences...*

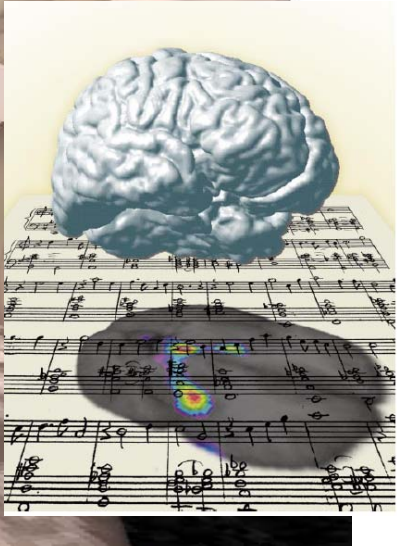
*Brain (organ) structure & function*

*Person level (health care)*

- ✓ *Social/cultural behaviors, art...*
- ✓ *Brain-machine interfaces*
- ✓ *Learning, education*

*Interaction, society level*

社交



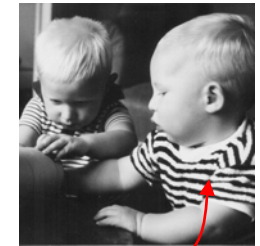
# The brain: A complex multiple scale assembly of 100 billions interconnected neurons

➤ *The « neural » code, a challenge for the 21st century:*

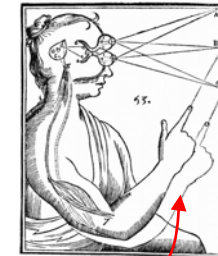
- *is there such a code?*
- *link with brain 3D microarchitecture?*
- *sensitivity to environment, learning & plasticity*

*Each mental state is the result of multiscale interactions, not the sum of sub-scale components (non-linear system)*

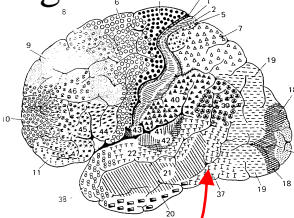
Culture & education



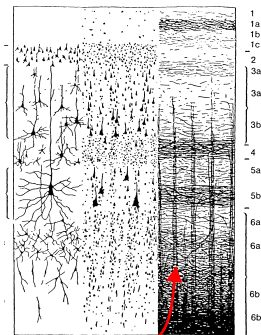
Comportments



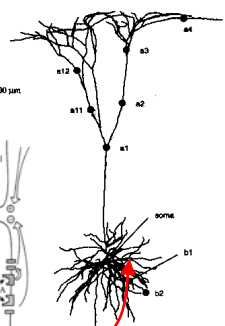
Regions & circuits



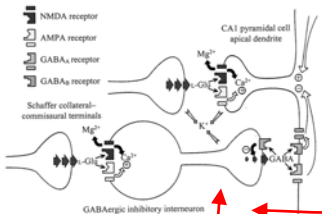
Cortical columns



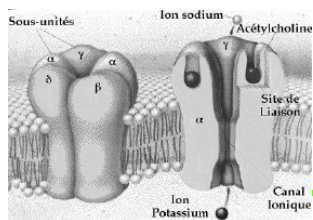
Neurons



Synapses



Receptors



Look for transition laws (space & time) between nested levels

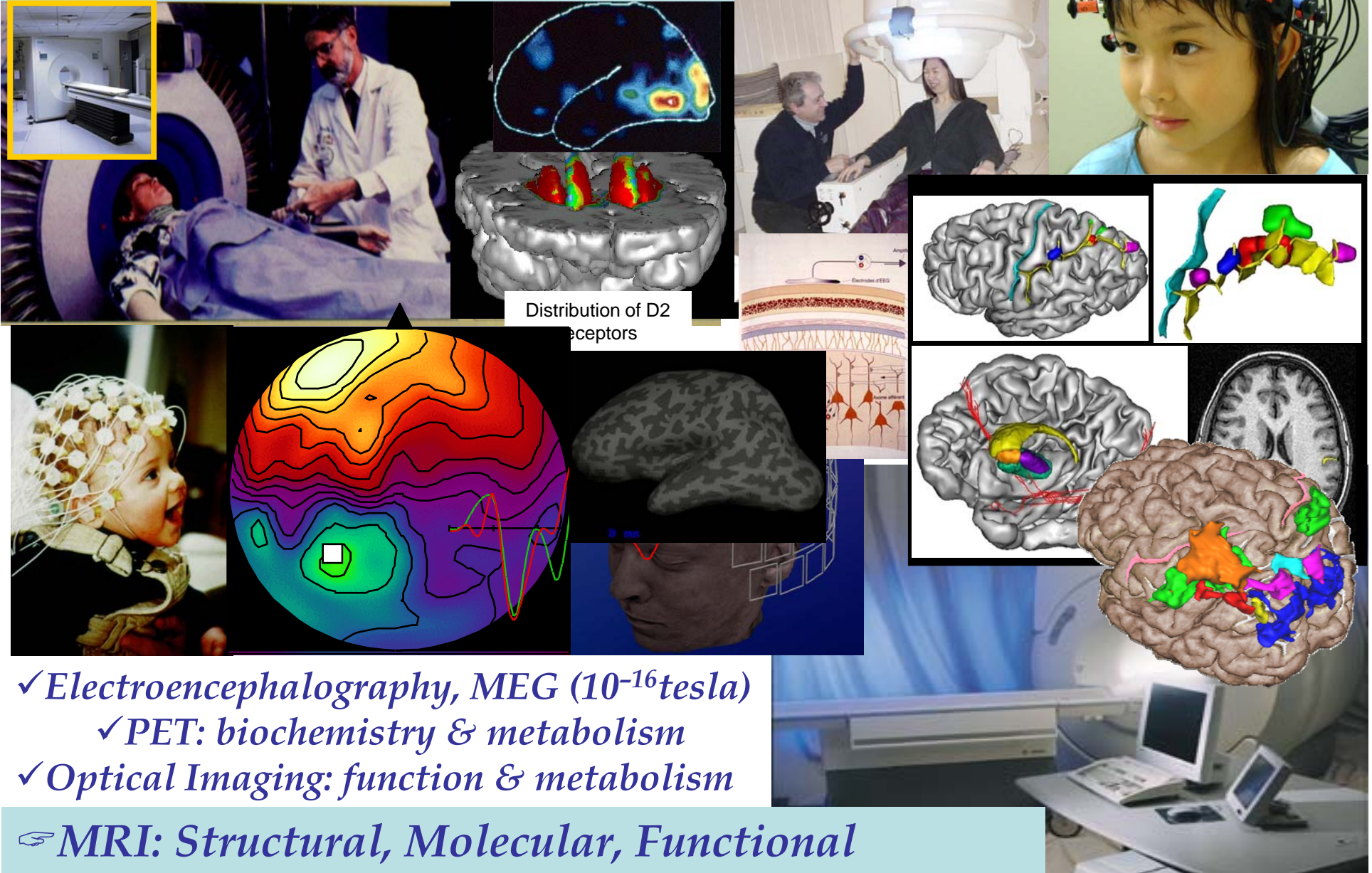
➤ *The genetic code, post-genomic era:*

- *25k genes (<10<sup>11</sup> bits), but 10<sup>11</sup> neurons, 10<sup>15</sup> synapses*

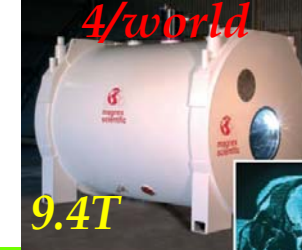
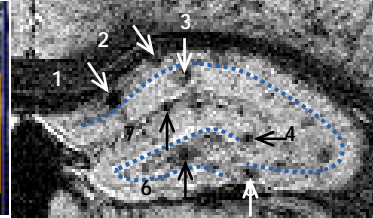
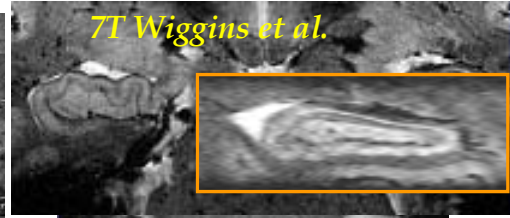
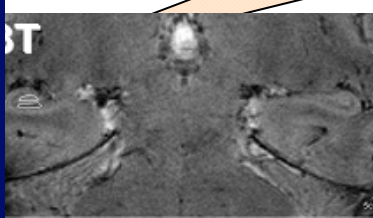
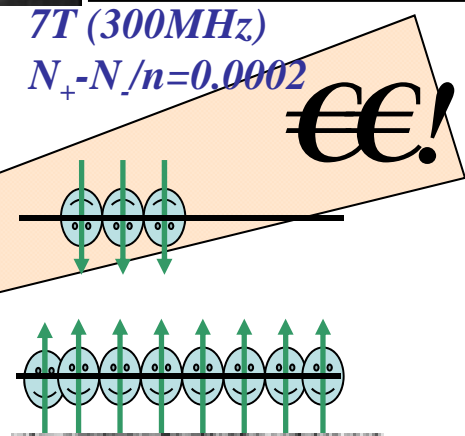
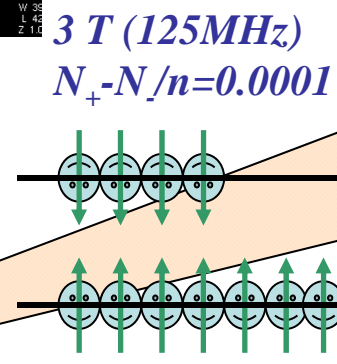
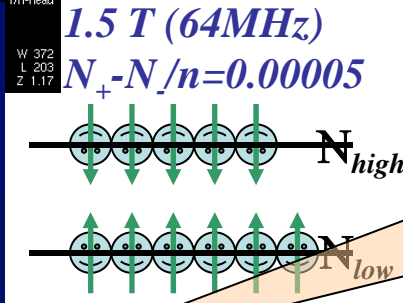
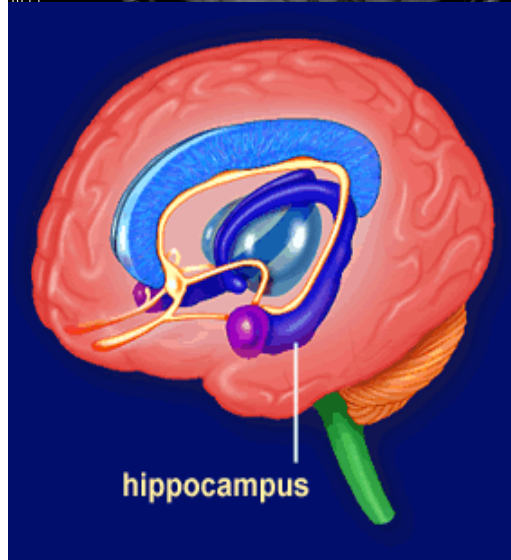
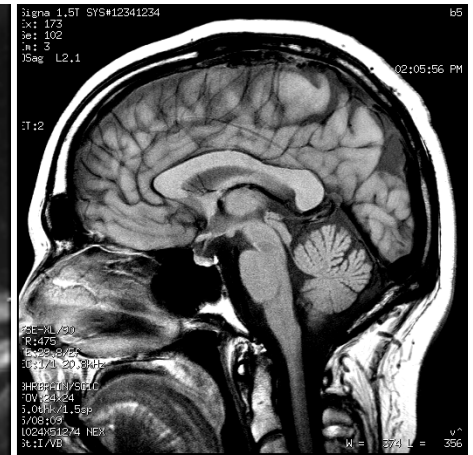
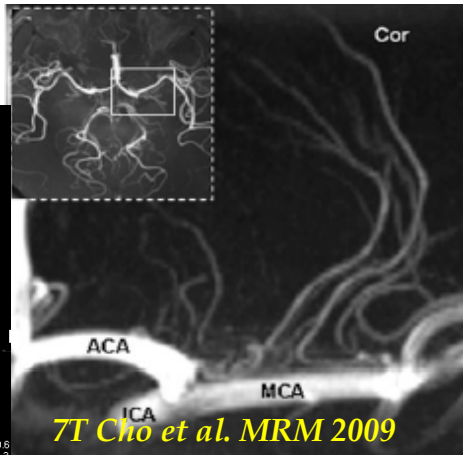
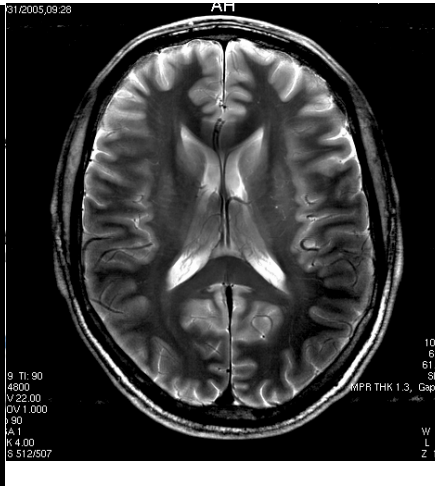
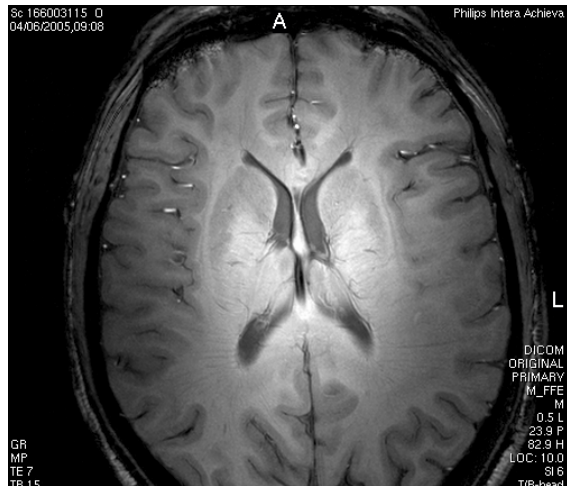
ASEF - *architecture/function relationship?*

# Human NeuroImaging:

*Non-invasive access to brain structure AND function*



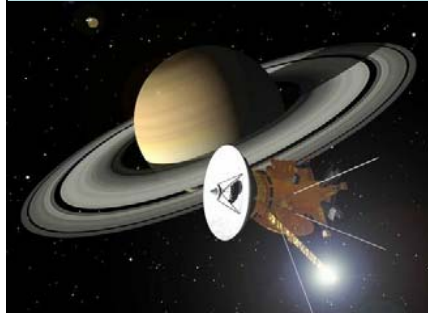
# ... Clinical Ultra-high field MRI:



# • Pushing the limits (*time, space, contrast*) of MRI



## Very Large Instruments for science:



High energy, particles physics  
→ CERN, RIKEN,...

Astronomy and astrophysics  
→ Hubble telescope,  
Huygens-Cassini probe...

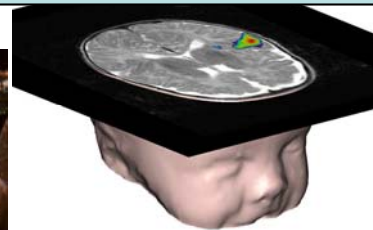
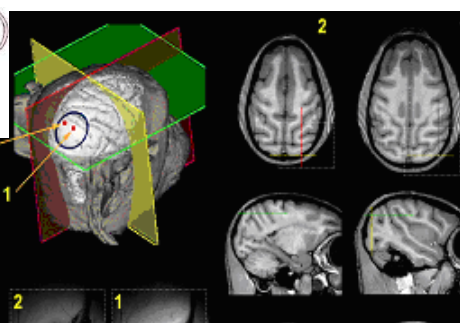


## Neuro-physics → NeuroSpin...

Aimed at ultra-high field MRI/MRS systems:

3T, 7T, **11.74T** wide-bore for human studies

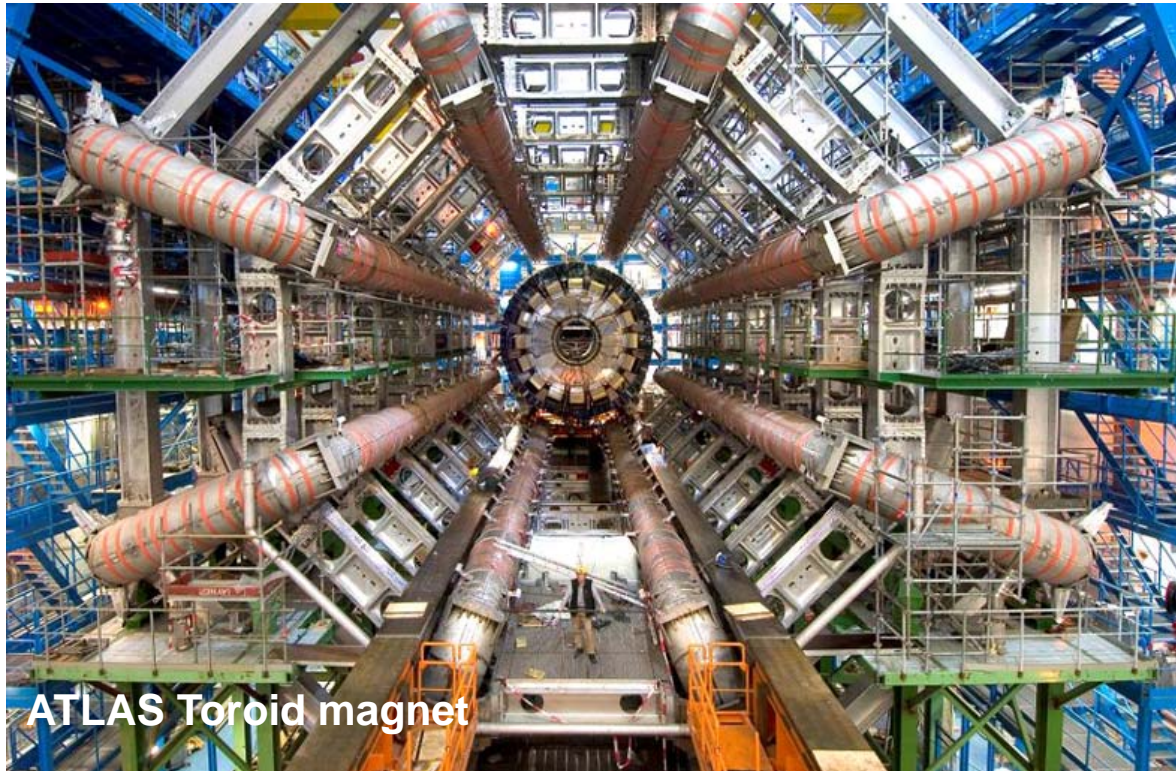
11.7T (primates) and **17.18T** (rodents)



## Validation and applications

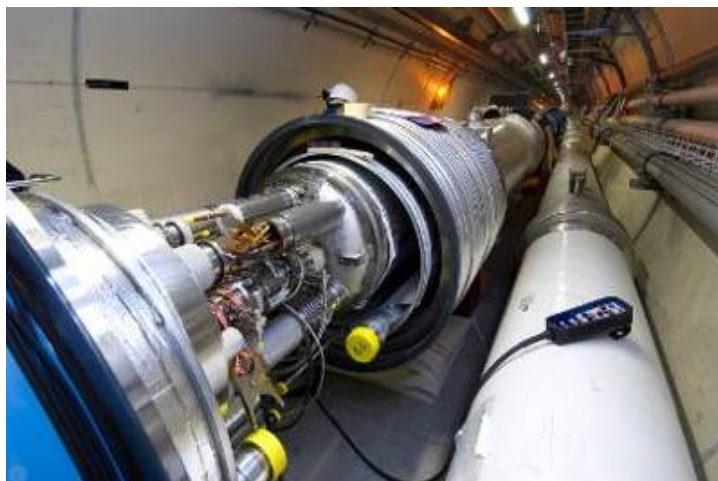
# Giant Particle Physics Superconducting Magnets

CEA/Irfu design



ATLAS Toroid magnet

LHC quadrupole magnet



ASEPS, Tsukuba, March 25



CMS solenoid magnet



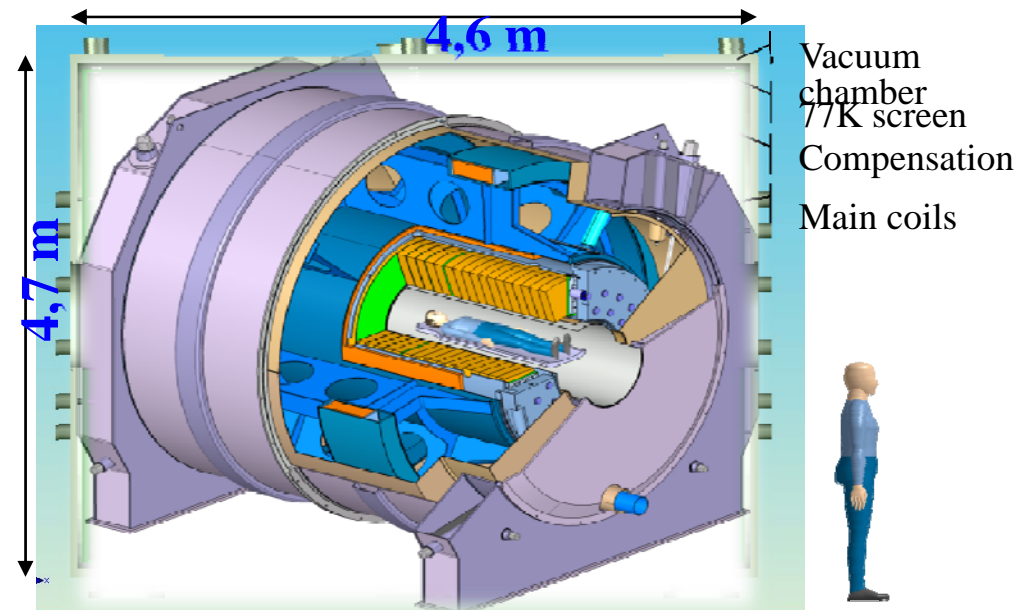
# CEA/Irfu design for NeuroSpin 90cm bore 11.74T magnet

(P. Vedrine, Project Manager)



## Cryogenic satellite

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



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

- cryostat:  $4.6 \times 4.7 \times 4.7 \text{ m}^3$ , 900mm internal diameter +++
- wetted double pancakes in superfluid He:  
1.8K pressured He II bath connected to a cryoplant
- superconducting wire: 65t NbTi (182 km),  $9.2 \times 4.9 \text{ mm}^2$  section
- nominal current: 1500 amp in driven-mode (ext power supply)
- stored energy: 328 MJ, inductance 304H,  $28.9 \text{ A/mm}^2$
- overall weight: 150 tons, 170MPa hoop stress on conductor
- actively shielded (5G line at 13m in axial direction, 9m radially)
- Field homogeneity: 0.5ppm over 22cmDSV
- Field stability:  $<0.05 \text{ ppm/h}$

# NEUROSPIN: UHF MRI temple....

*Claude Vasconi, Architect  
1940-2009*



*Who yearns for the impossible I love. Goethe*

# NeuroSpin: A Translational / Transnational Research Platform

## NeuroSpin:

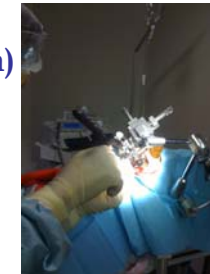
- Clinical suit (beds, test/examination rooms, neuropsychology, EEG/MEG...)
- Animal care facility (transgenic mice and **trained primates**, surgery suits, electrophysiology)
- Shops (mechanics, electronics, chemistry, histology, cell culture...)
- **Data processing center** (BrainVisa software, 150-terabyte data archiving system)



## Multidisciplinary environment

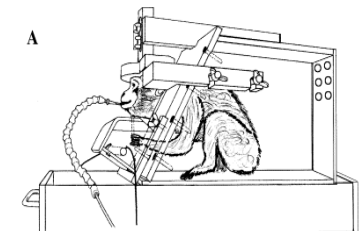
(staff: 120 → 160)

physicists, electronics, engineers, ...  
mathematicians, computer scientists, statisticians, ...  
neurophysiologists, neurobiologists,  
pharmacologists, neuropsychologists, ...  
neurologists, psychiatrists, neuroradiologists, ...



### Awake primate studies:

- Deep brain stimulation
- Optogenetics



## 5-laboratories:

- MRI physics
- Computer Assisted Neuroimaging
- Cognitive neurosciences
- Integrative biology
- Clinical/Translational research

offices, library, conference rooms, ...

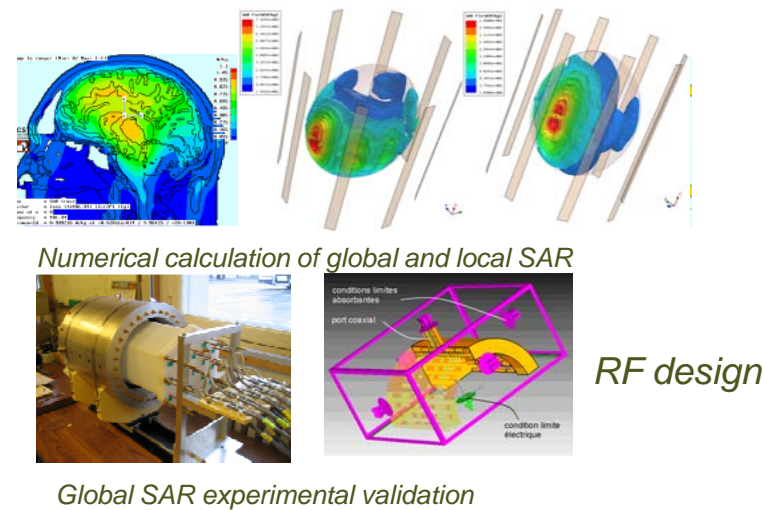
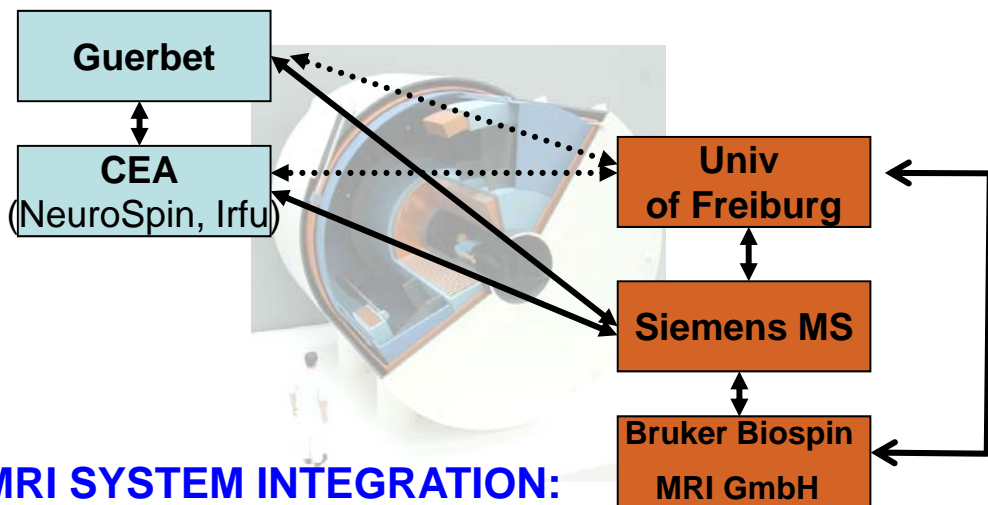


## 3-layer running mode:

- Resident teams (50%)  
(academic & industrial)
- Visiting (collab.) teams (25%)
- Support/service teams (25%) (contract)  
coverage of the complete chain, scientific knowledge, sophisticated instruments, project management

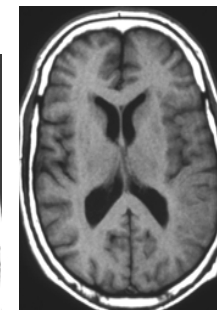
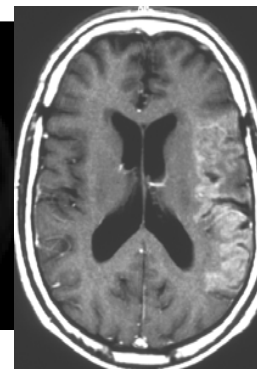
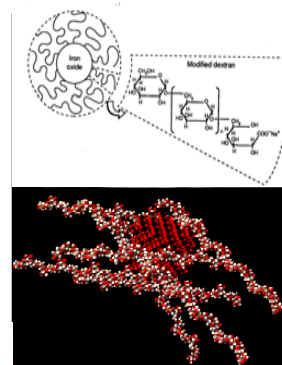
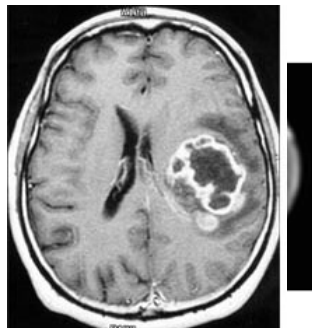
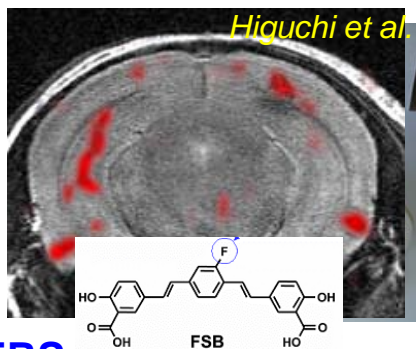
Training, build up qualified staff +++

**Iseult/Inumac:** A French-German industrial partnership to develop *High Field Molecular Imaging* financed partly by the partners and partly by the French Industrial Innovation Agency (Oséo) and the German BMBF.



**MRI SYSTEM INTEGRATION:**

- Develop MRI system at unprecedented performance (11.7T/900mm) for humans
- New rf pulses, coil design (CEA, Siemens, U. Tokyo), gradient system (Freiburg, Siemens)
- Biological effect of electromagnetic fields, safety (U. Tokyo, J-NIOSH)



Saleh A et al. Post USPIO

**TRACERS**

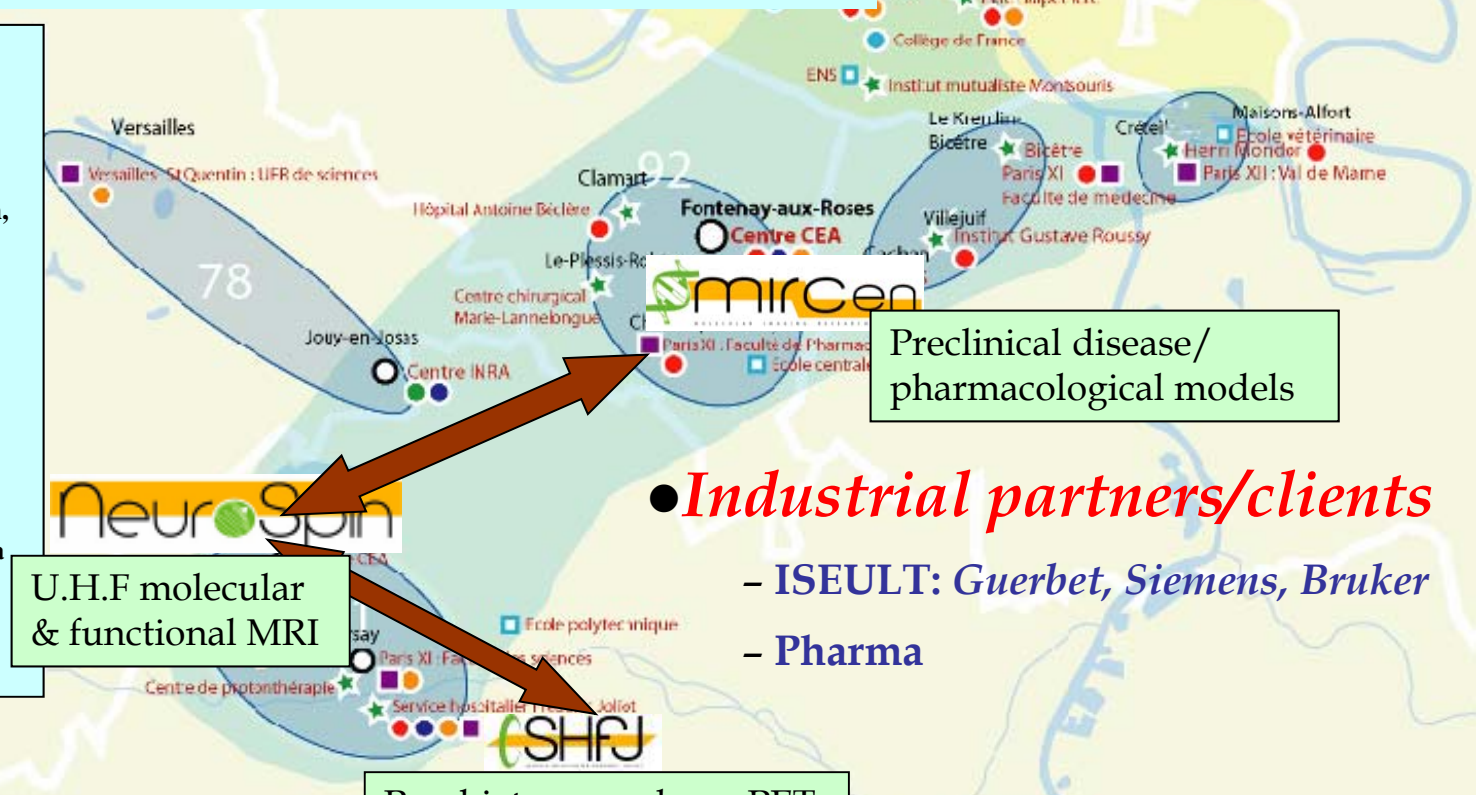
- Develop a new generation of tracers & biomarkers (Gd, CEST, USPIOs, <sup>19</sup>F,...) for high field MRI targeted on *Alzheimer's disease, brain tumors, stroke* (Guerbet, CEA)

## ● *International integration*

- Europe (CONNECT, ISEULT, EATRIS/ESFRI, EuroBioimaging, 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
- JNIOH, Japan
- MGH, Boston, USA
- NIH, Bethesda, USA
- University of Minnesota, USA
- Nat. Research Council, Canada
- Tel Aviv University, Israel
- Nat. Yang-Ming Univ. Taipei
- ...



## ● *Industrial partners/clients*

- ISEULT: Guerbet, Siemens, Bruker
- Pharma

## ● *Regional integration*

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

→ *Connecting basic research centers to research hospitals*

**LRMN**

C Wiggins  
L Ciobanu  
A Amadon  
N Boulant  
F Bouzmebeur  
J Valette  
S Mériaux  
F Poupon  
E Giacomini  
L Larivière  
...

**LNAO**

JF Mangin  
C Poupon  
D Rivière  
Y Cointepas  
JB Poline  
P Ciuciu  
A Roche  
...

**LBI**

M Dhenain  
C Wu  
B Jerraya  
...

**LBIOM**

L Hertz-Pannier,  
L Alliol  
Nurses  
Technicians

**LCOGN**

S Dehaene  
G Dehaene  
C Pallier  
A Kleinschmidt  
...

**Irfu/DSM**

P Védrine  
Ph Rebourgeard  
J Belorgey  
C Bériaud  
Ph Brédy  
FP Fuster  
A Hervé  
M Luong  
C Meuris  
F Nuno  
A Sinanna  
L Scola  
A Payn  
L Quettier  
T Schield  
...

**Kyoto University**

S-I Urayama  
T Aso  
S Kohno  
N Sawamoto  
H Fukuyama  
...

**Tokyo University**

S Yamaguchi  
M Sekino

