# Le ‘immagini’ del dolore
# Imaging pain


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# Pain and Imaging

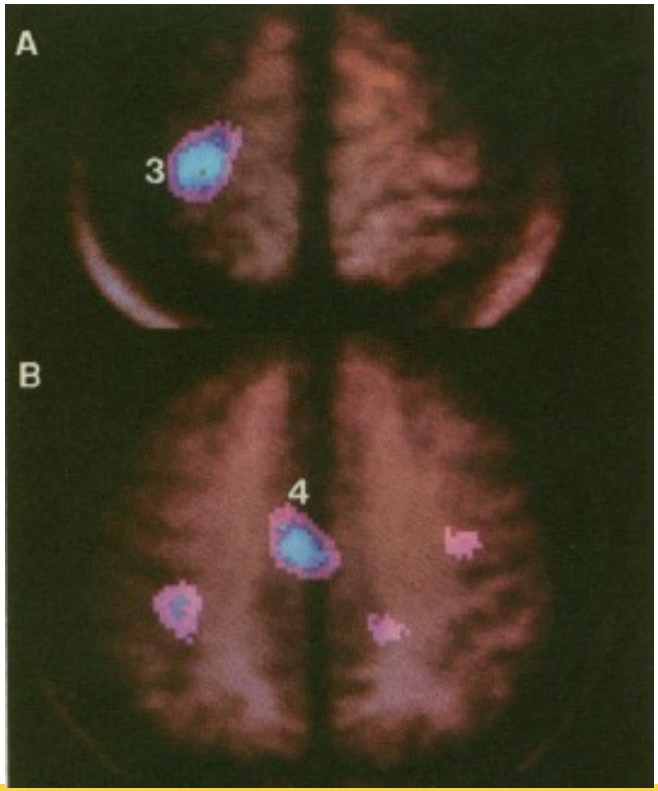
## Multiple Representations of Pain in Human Cerebral Cortex

JEANNE D. TALBOT, SEAN MARRETT, ALAN C. EVANS, ERNST MEYER, M. CATHERINE BUSHNELL, GARY H. DUNCAN*

SCIENCE, 15 MARCH 1991

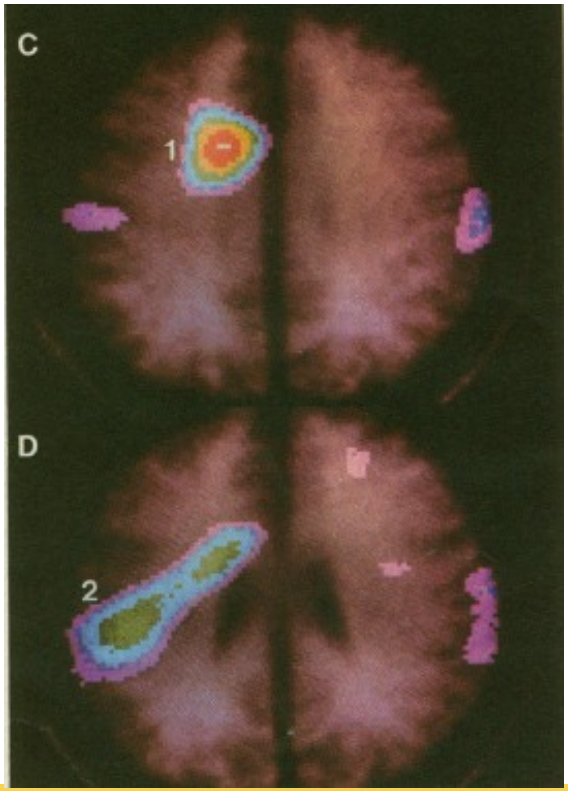
SI

AC

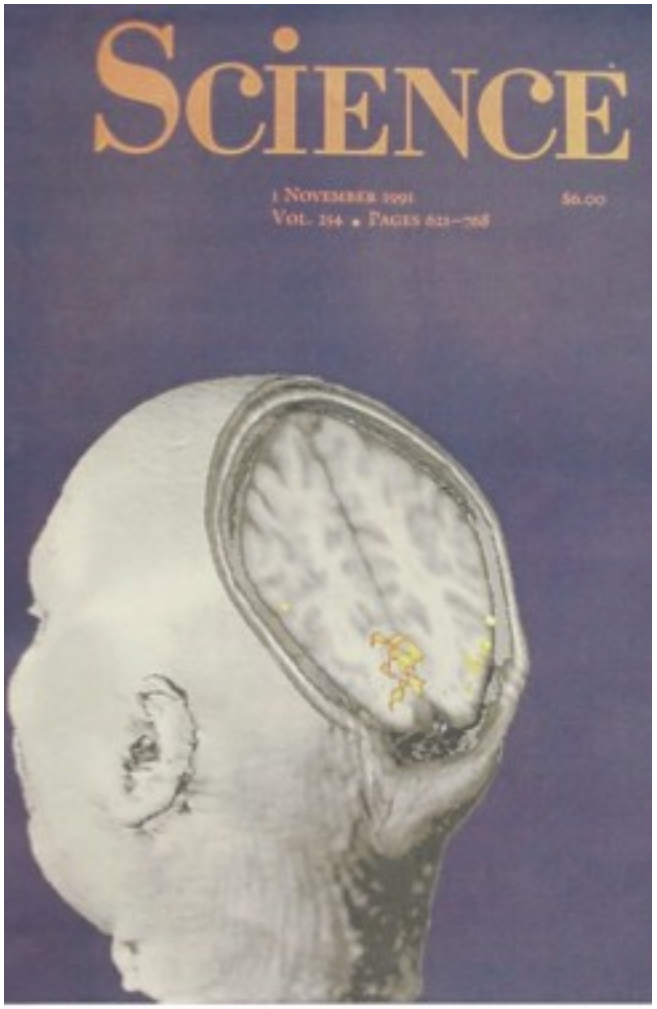



AC

SII



# Functional Imaging (fMRI)



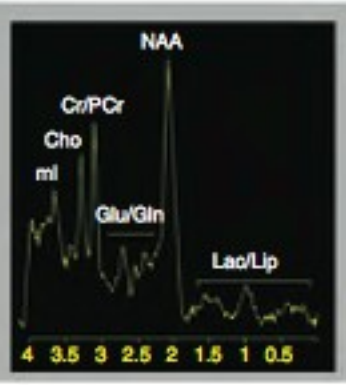

Functional Mapping of the Human Visual Cortex by Magnetic Resonance Imaging

J. W. BELLIVEAU,* D. N. KENNEDY, R. C. MCKINSTRY, B. R. BUCHBINDER, R. M. WEISSKOFF, M. S. COHEN, J. M. VEVEA, T. J. BRADY, B. R. ROSEN

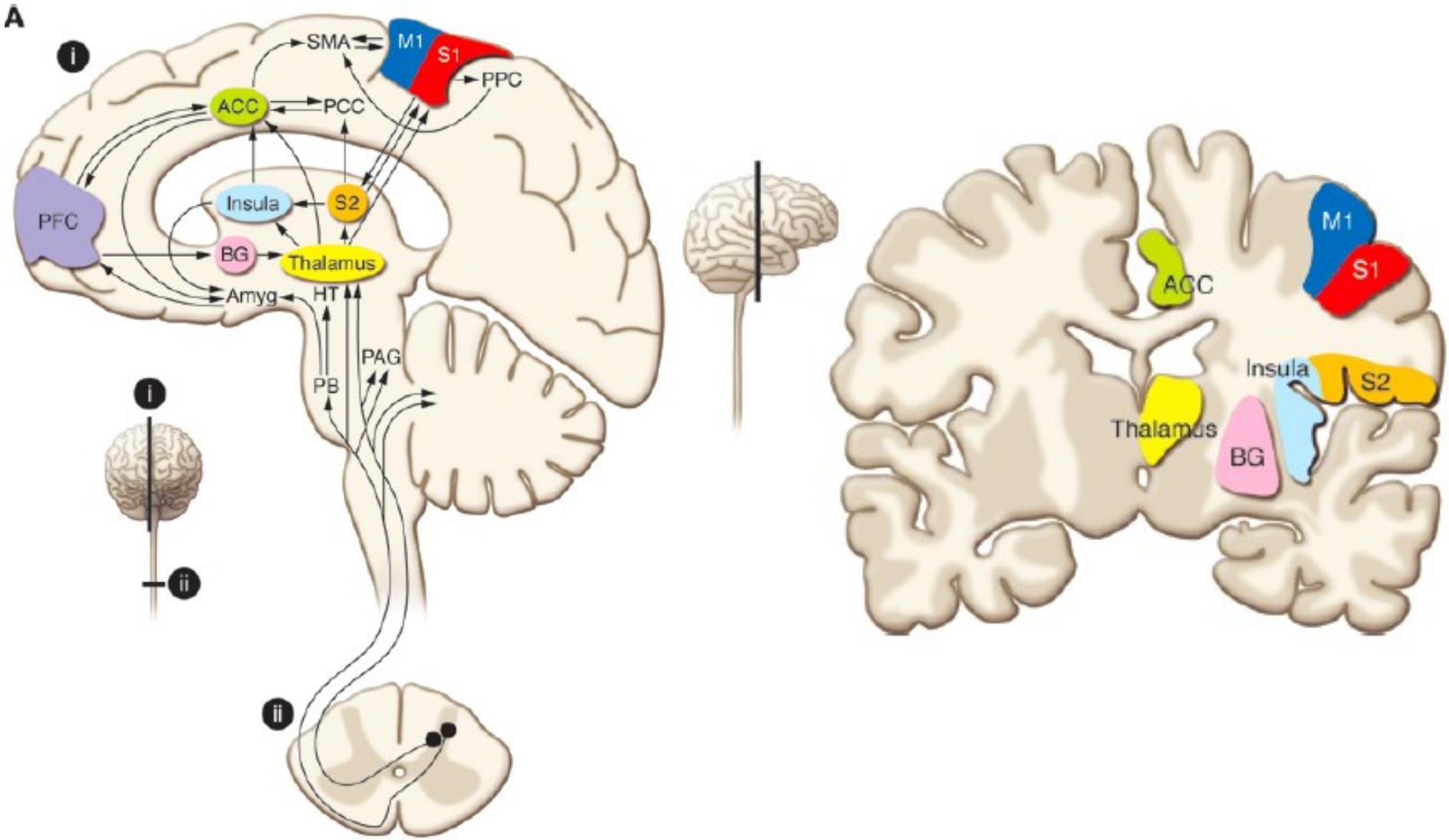
# Pain and Imaging

# Pain and Imaging

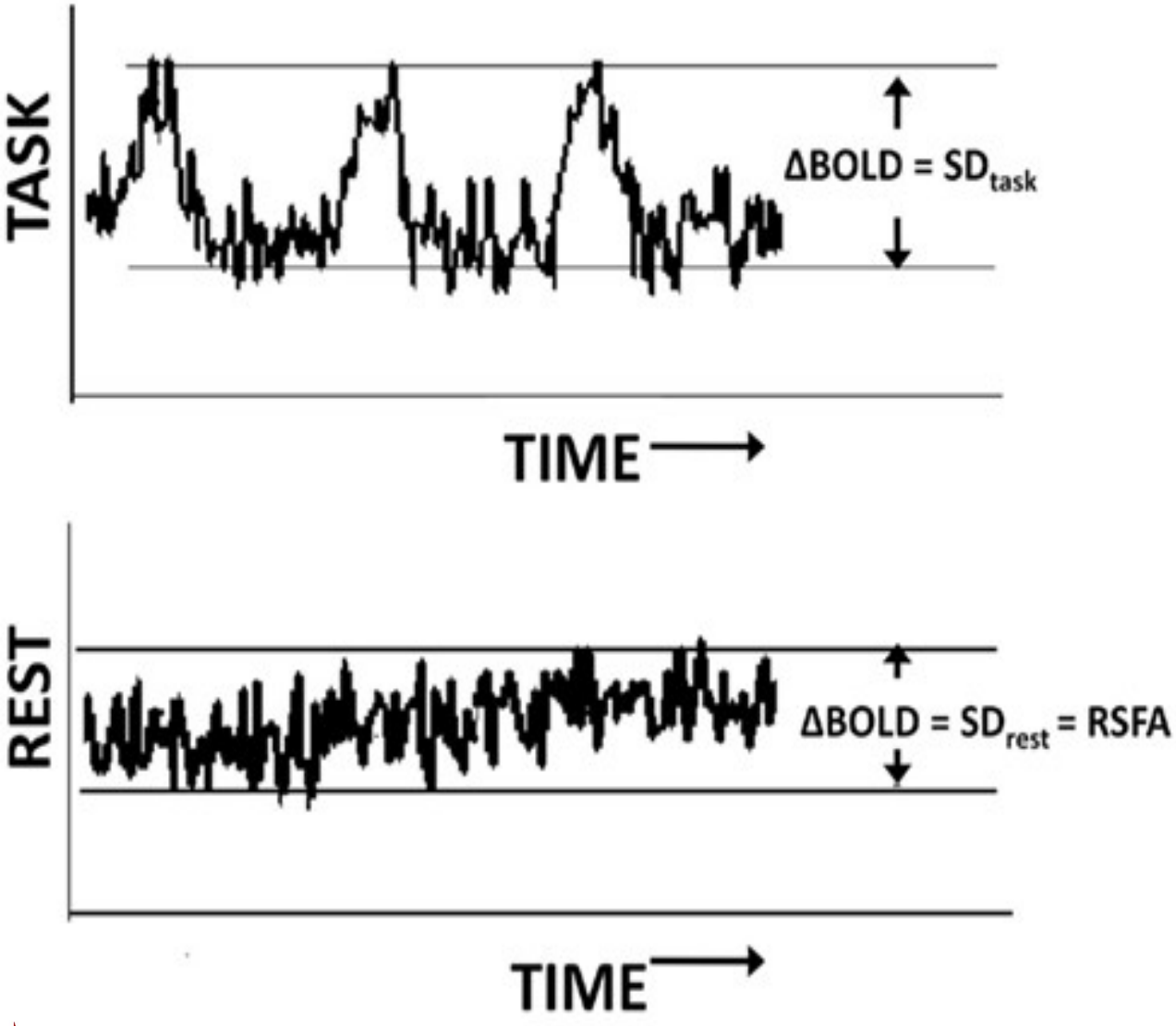
| MRI-modality | Physiological measure |
| --- | --- |
| Neurochemical<br>*MRS* | Brain metabolites |

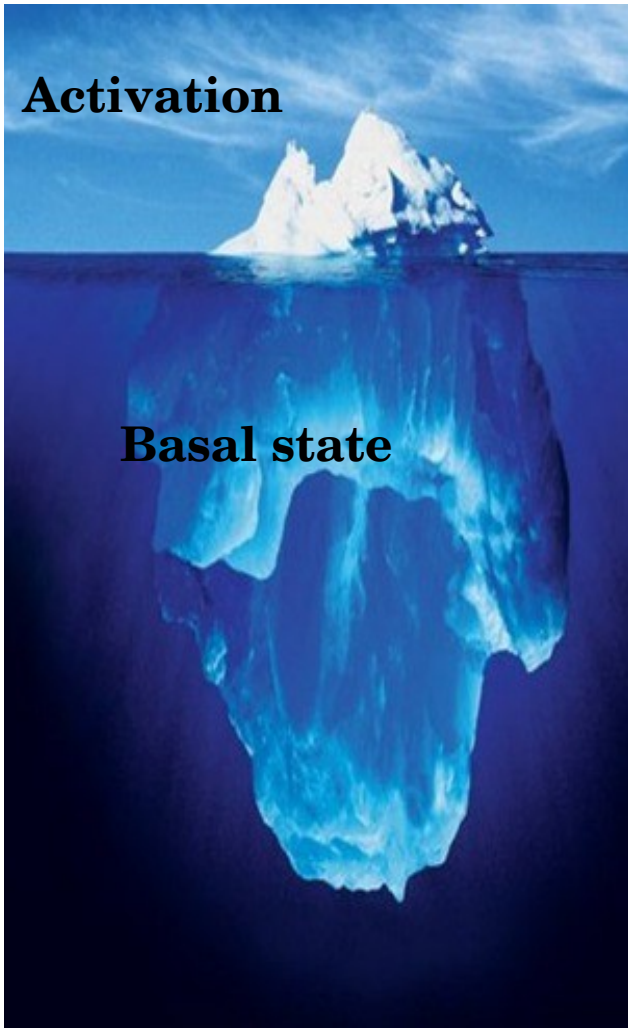


# Pain and fMRI



# fMRI → Studi di connettività



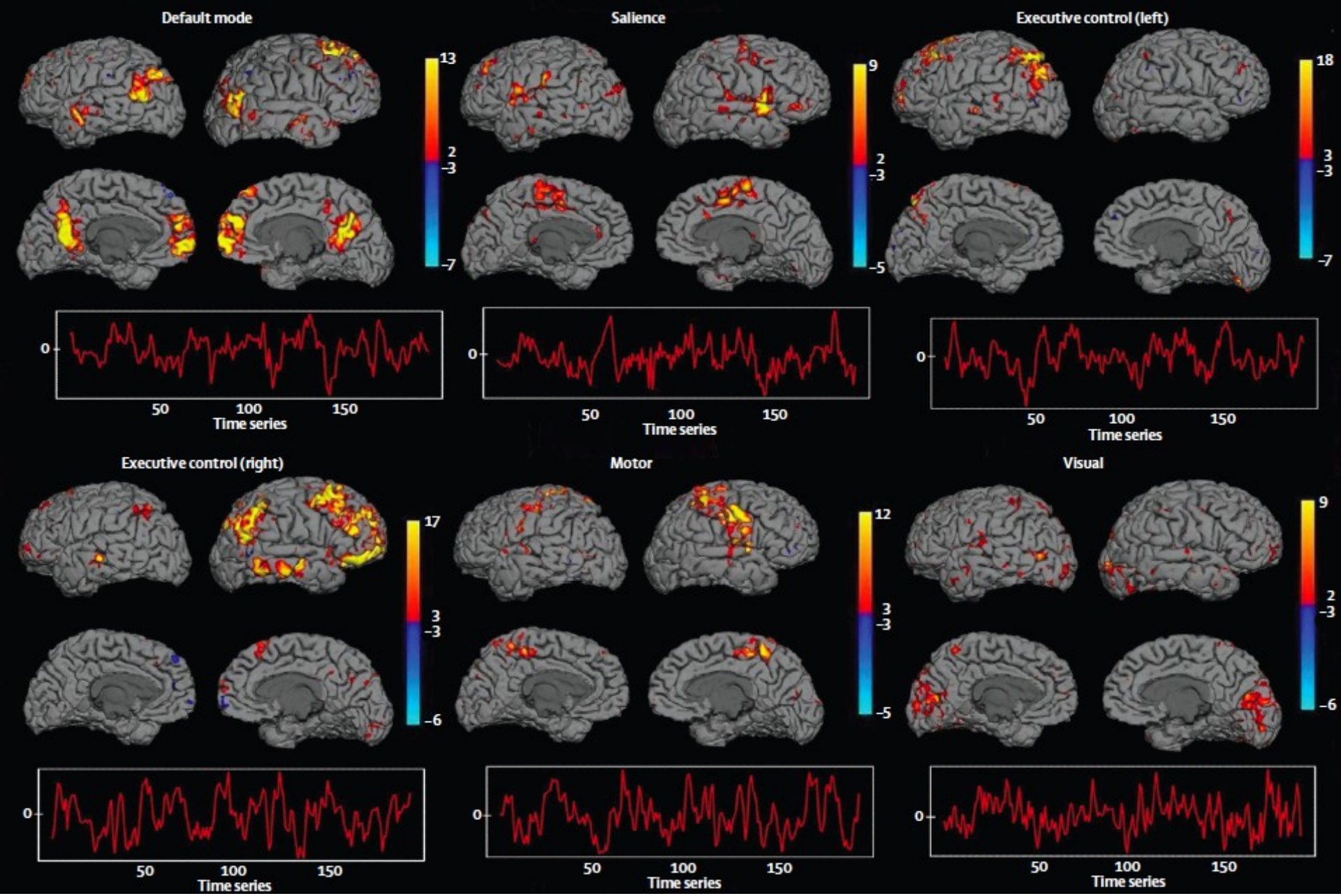

Courtesy F. Barkhof

# Resting-state fMRI - technique

- EPI scans acquired every 2-3 seconds
  - 200 or more volumes

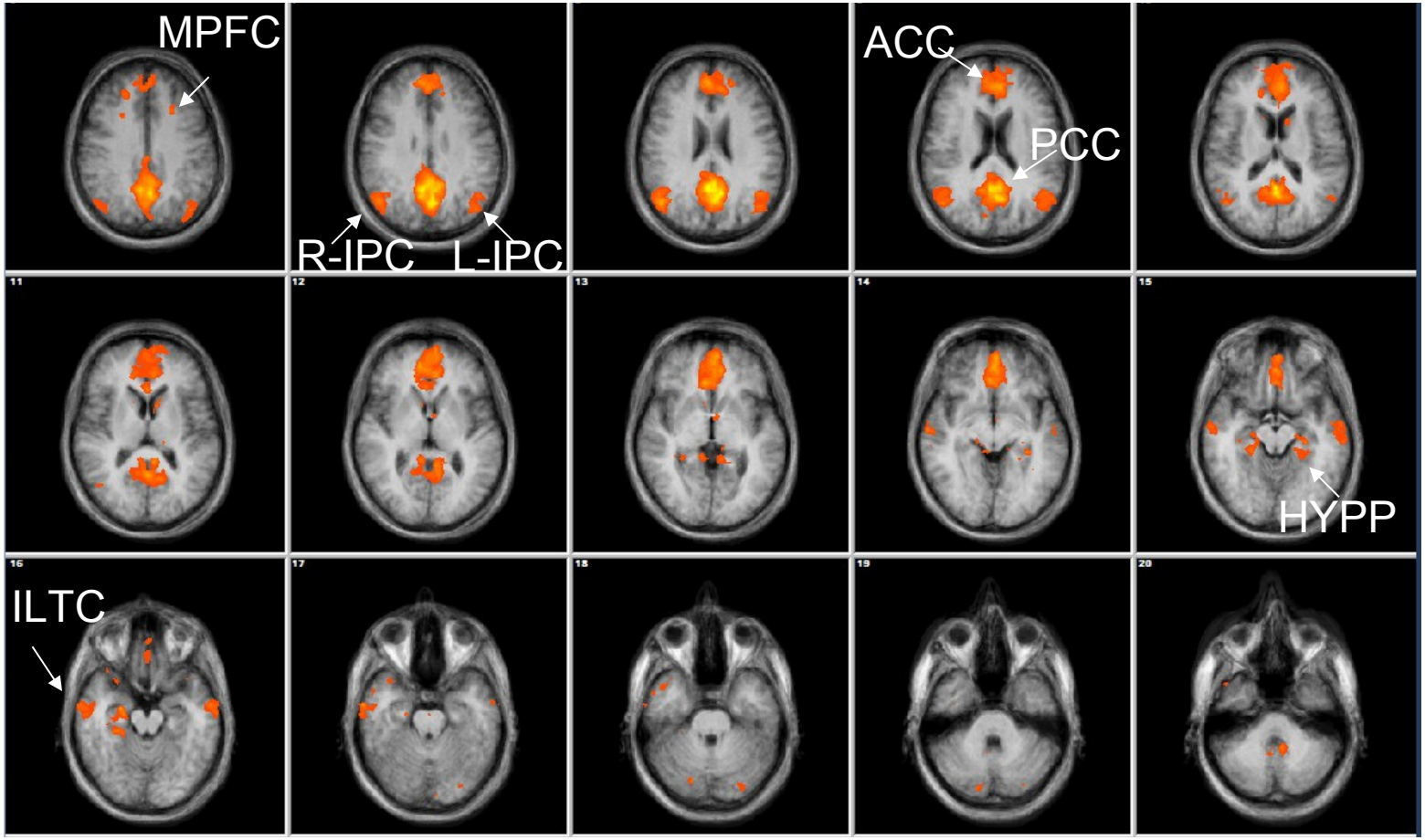
- **No-task condition: rest, eyes open/closed**
  - instruction not to think of anything in particular

- Preprocessing
  - movement correction, signal scaling, standard space
  - optional – cardiac/respiratory signal regression
- Post-processing techniques (FSL, GIFT, SPM)
  - **seed-based** (with additional nuisance regressors)
  - **ICA** (independent component analysis)
  - **network (graph) analysis**




Pievani M et al. Lancet Neurol 2011

# The “Default-mode” network (DMN)




- The main nodes of the **DMN** are in the **Anterior and Posterior cingulate cortex (ACC/PCC) and right/left inferior parietal cortex (IPC)**

- Typically, **DMN** also recruits bilateral **Hyppocampus**, **Medial Pre-frontal cortex (MPFC)** and **infero-lateral temporal cortex (ILTC)**

# Pain related connectivity

Researchers are now using imaging techniques to examine connectivity among pain-related regions and possible disruptions of such connectivity in chronic pain patients.

In healthy individuals undergoing experimental heat pain, Ploner and colleagues used this method to determine that the individual functional connectivity between the anterior IC and brainstem, regions thought to be related to the subjective perception of pain and the modulation of pain, respectively, predicted whether a potentially noxious event would be perceived as painful.

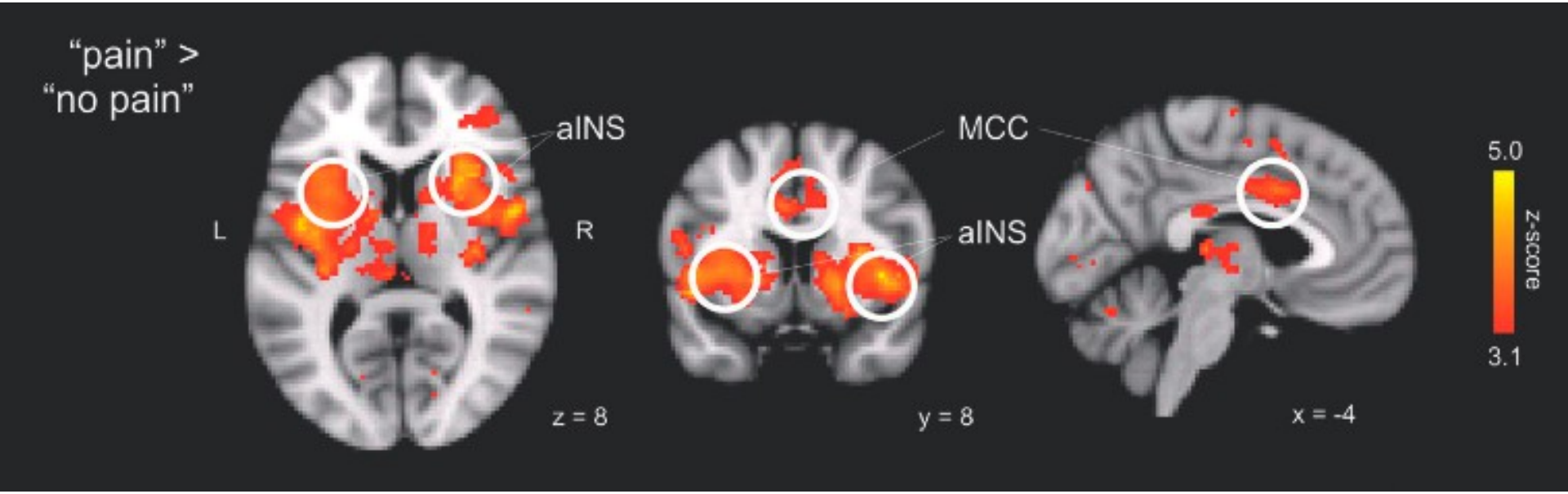
# Pain related connectivity

## Prestimulus functional connectivity determines pain perception in humans

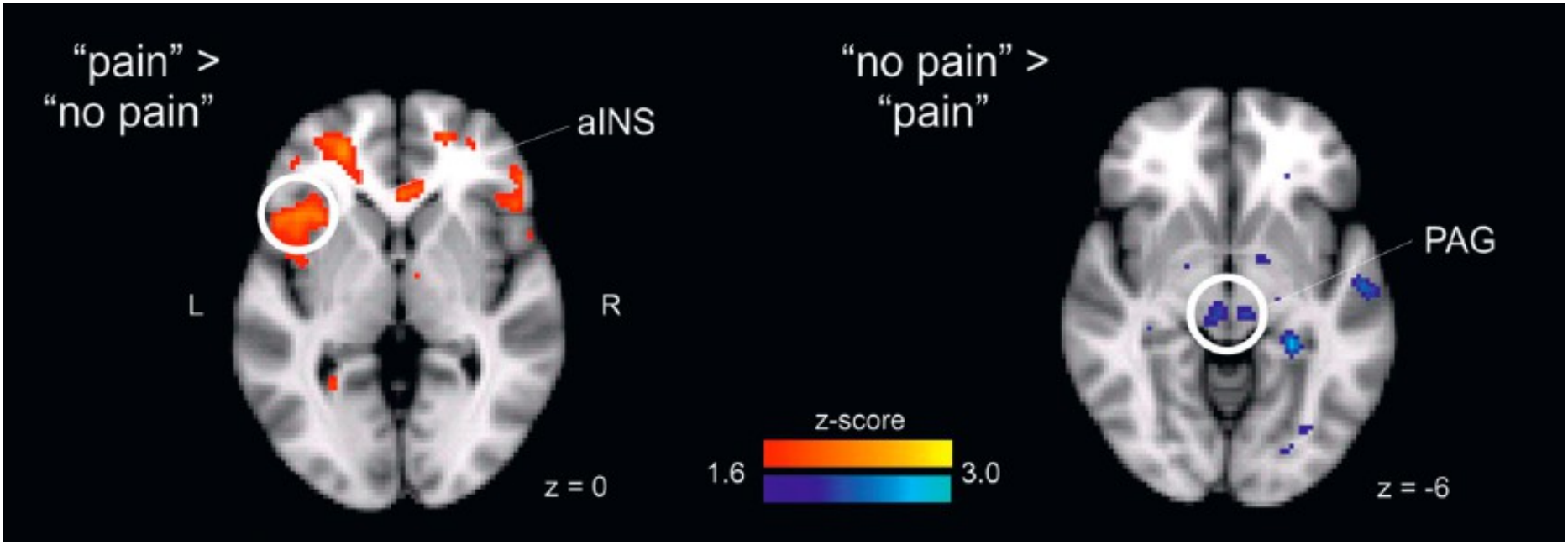
Markus Ploner[a,b,1], Michael C. Lee[a], Katja Wiech[a], Ulrike Bingel[a], and Irene Tracey[a]

[a]Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, Department of Clinical Neurology and Nuffield Department of Anaesthetics, University of Oxford, UK; and [b]Department of Neurology, Technische Universität München, Munich, Germany

PNAS | January 5, 2010 | vol. 107 | no. 1 | 355–360

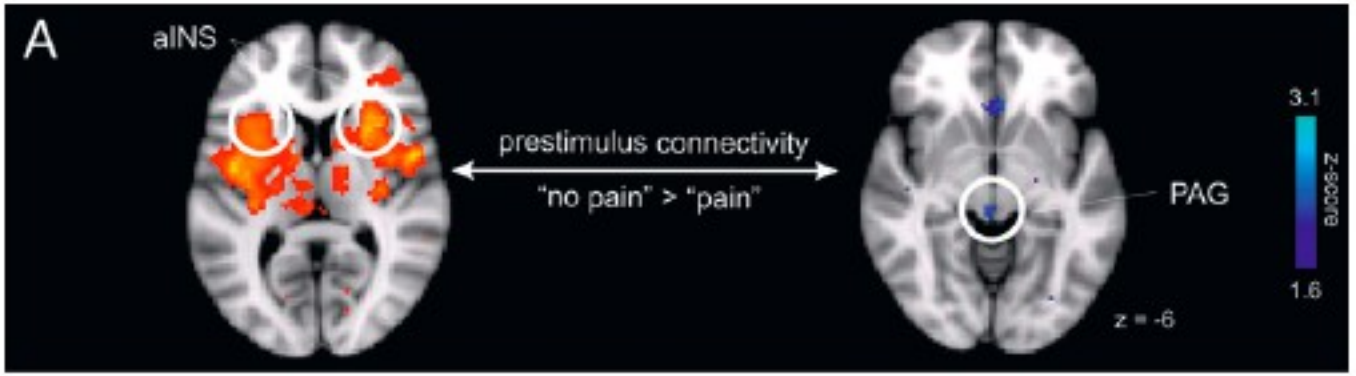


# Pain related connectivity




Pre-stimolo

# Pain related connectivity




connettività

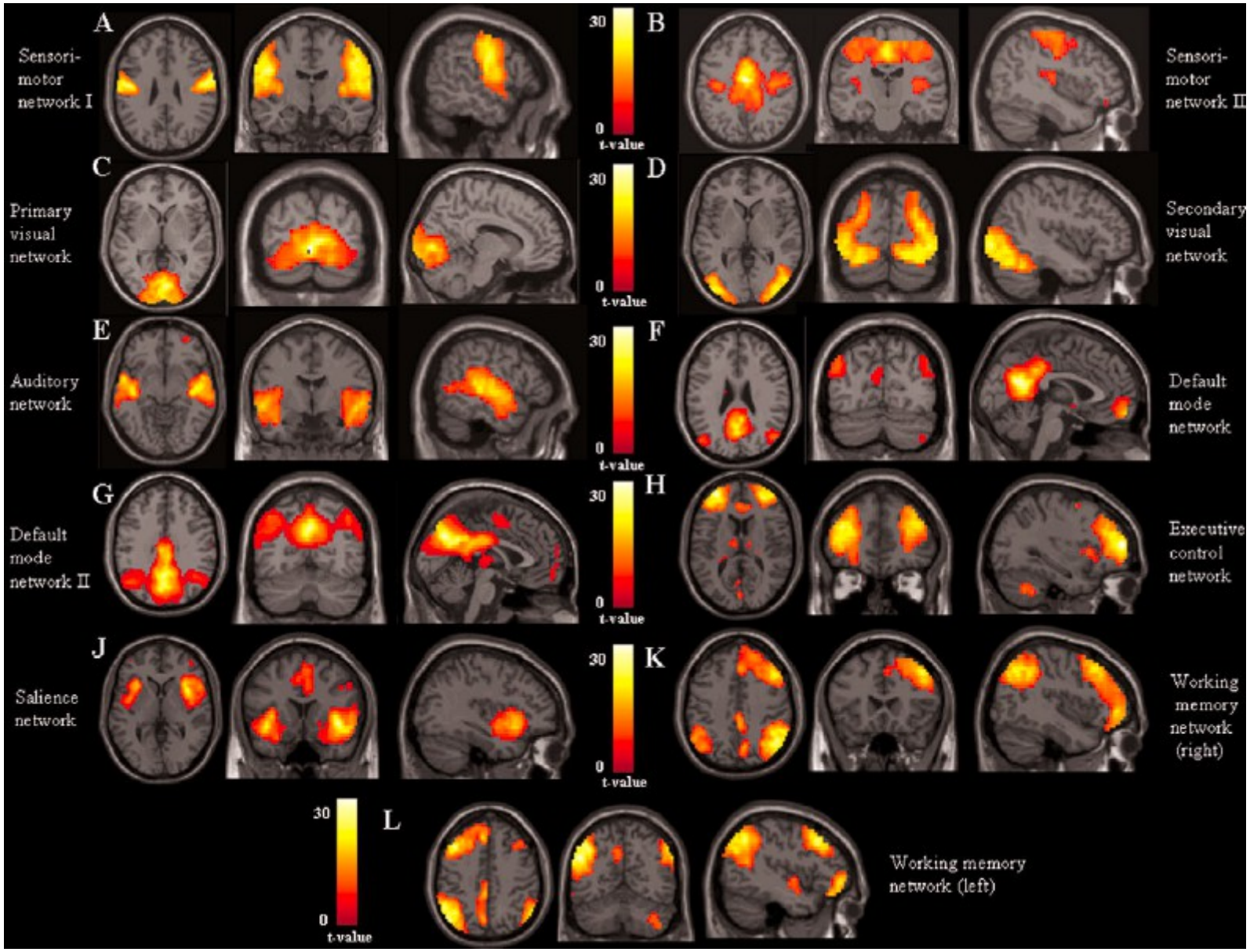
# Connectivity in polyneuropathy

## Brain Connectivity Abnormalities Extend Beyond the Sensorimotor Network in Peripheral Neuropathy

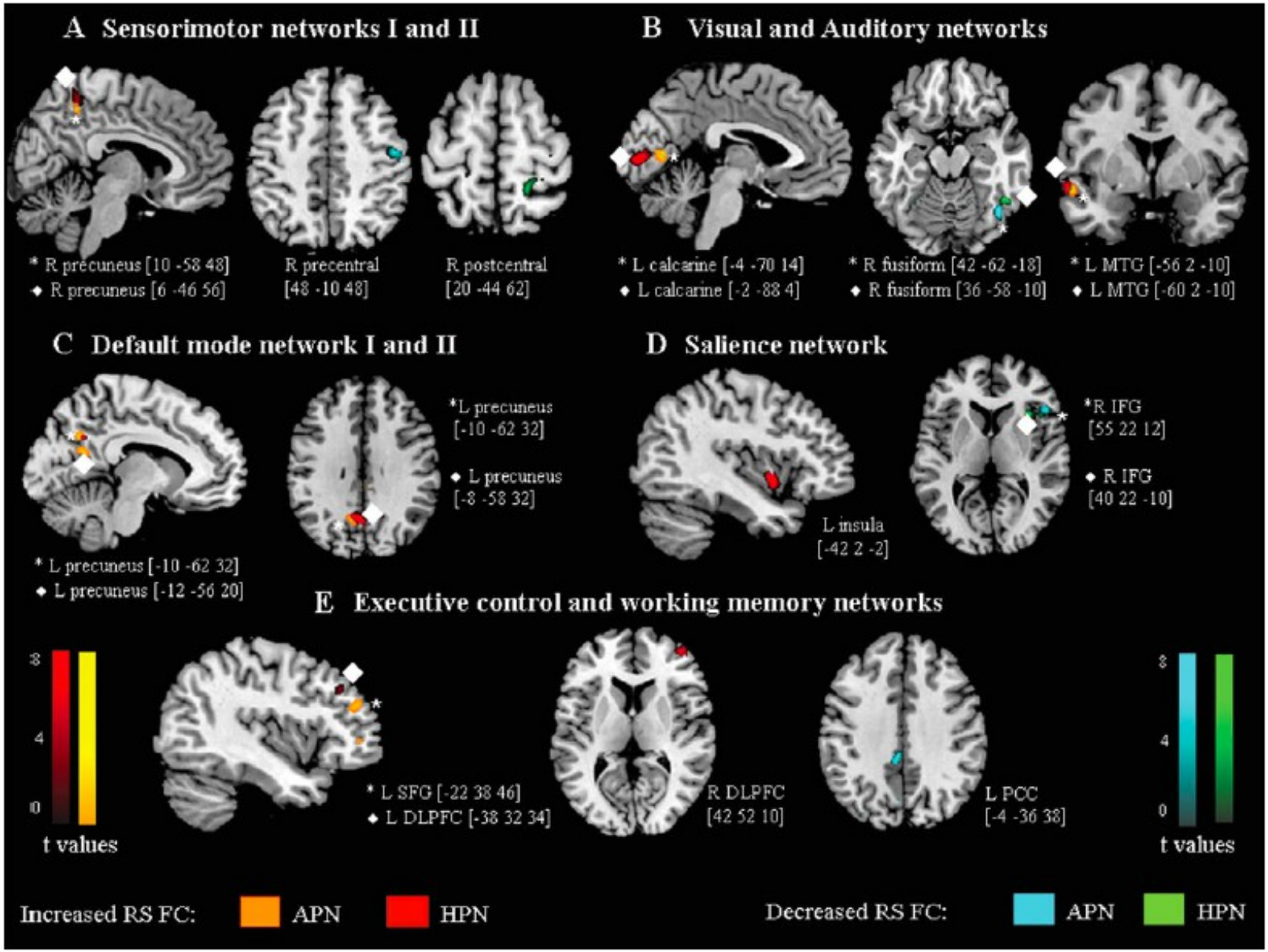
Maria A. Rocca,[1,2] Paola Valsasina,[1] Raffaella Fazio,[2] Stefano C. Previtali,[2] Roberta Messina,[1,2] Andrea Falini,[3] Giancarlo Comi,[2] and Massimo Filippi[1,2]*

◆ Human Brain Mapping 35:513–526 (2014) ◆

# Resting state networks



# Connectivity in polyneuropathy



# Studi di attivazione midollare

ORIGINAL RESEARCH

N.F. Ghazni
C.M. Cahill
P.W. Stroman

## Tactile Sensory and Pain Networks in the Human Spinal Cord and Brain Stem Mapped by Means of Functional MR Imaging

**BACKGROUND AND PURPOSE:** Touch and brush sensory stimuli elicit activity in discriminative touch pathways involving specific regions in the spinal cord and brain stem. However, no study has mapped normal sensory activity noninvasively in healthy humans. The purpose of this study is to map the neuronal activity of sensory input to understand abnormal sensory transmission.

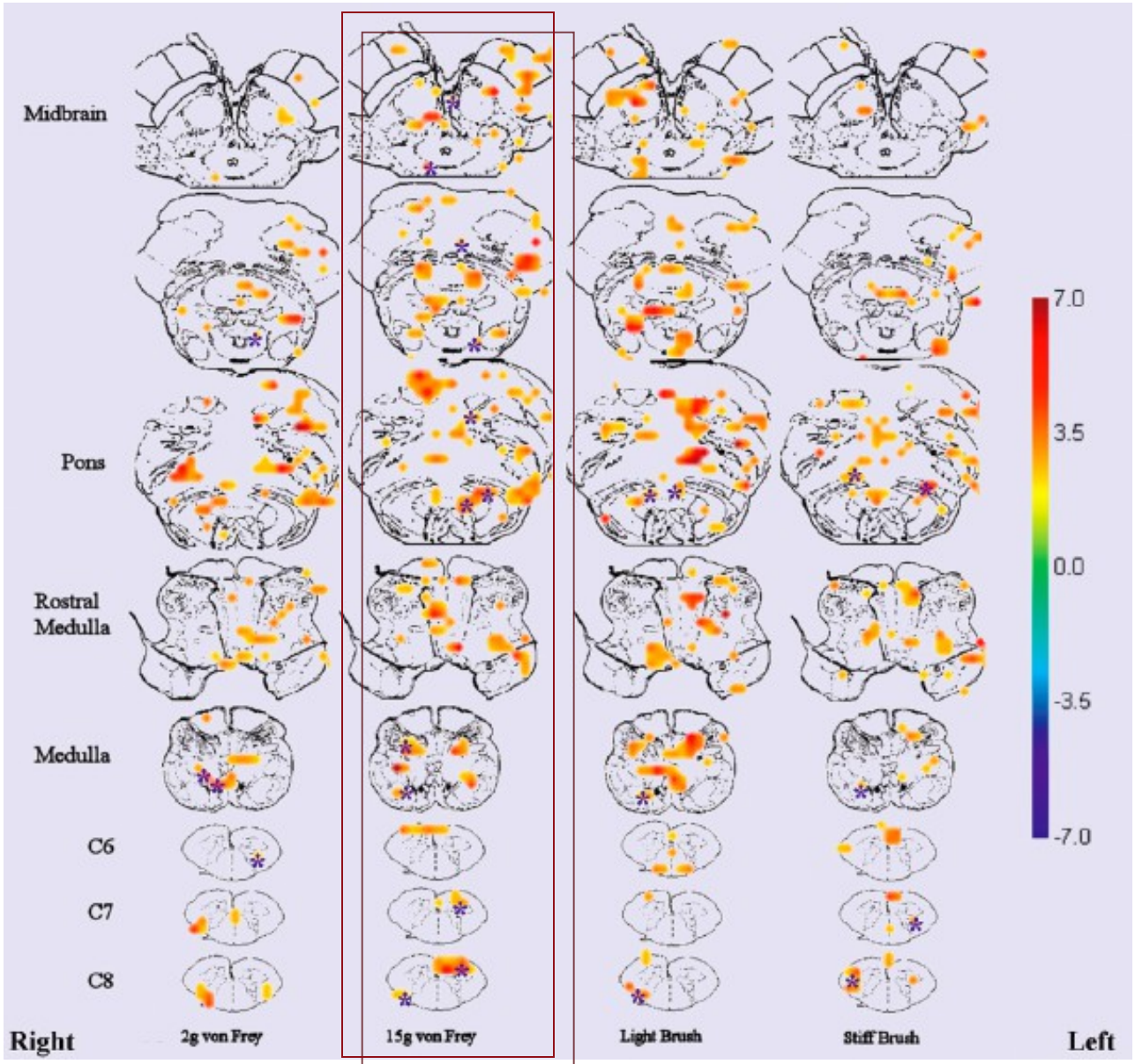
**MATERIALS AND METHODS:** In the present study, spinal fMRI (by using SEEP) was used to map the activity involved with light touch (2 g and 15 g von Frey filaments) and brush stimuli in the brain stem and spinal cords of 8 healthy volunteers. The results were spatially normalized and analyzed with custom-made software. Areas of SEEP activity were identified by using general linear model analysis.

**RESULTS:** The 2 g von Frey filament showed predominant activity in the medulla around the ipsilateral dorsal gracile and cuneate nuclei. The 15 g filament elicited significant activity in the ipsilateral dorsal and contralateral ventral gray matter areas of the spinal cord, areas around the olivary nuclei, pontine reticular formation, periaqueductal gray, and raphe nuclei in the rostral pons and midbrain. The brush stimuli elicited more activity in the medulla around the ipsilateral cuneate and gracile nuclei.

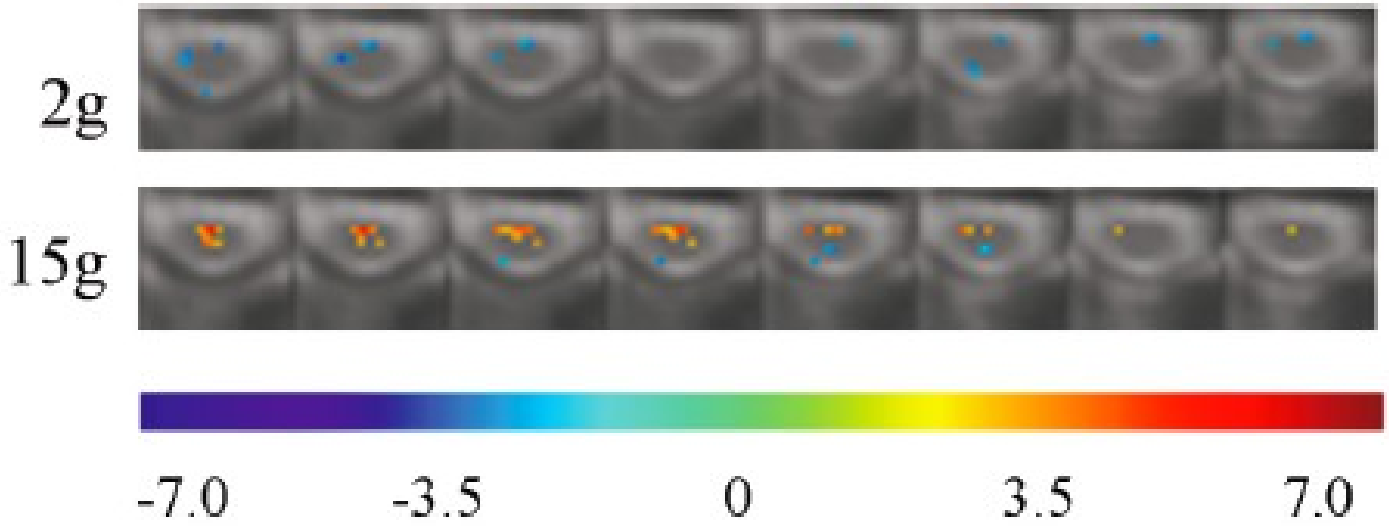
**CONCLUSIONS:** The 2 g filament and brush stimuli activated areas associated with a touch response. The 15 g filament activated areas associated with a pain response. The results from this study identify specific neuronal regions in the brain stem and spinal cord involved in sensory transmission and help understand altered sensory and pain states.

AJNR Am J Neuroradiol 31:661–67 | Apr 2010

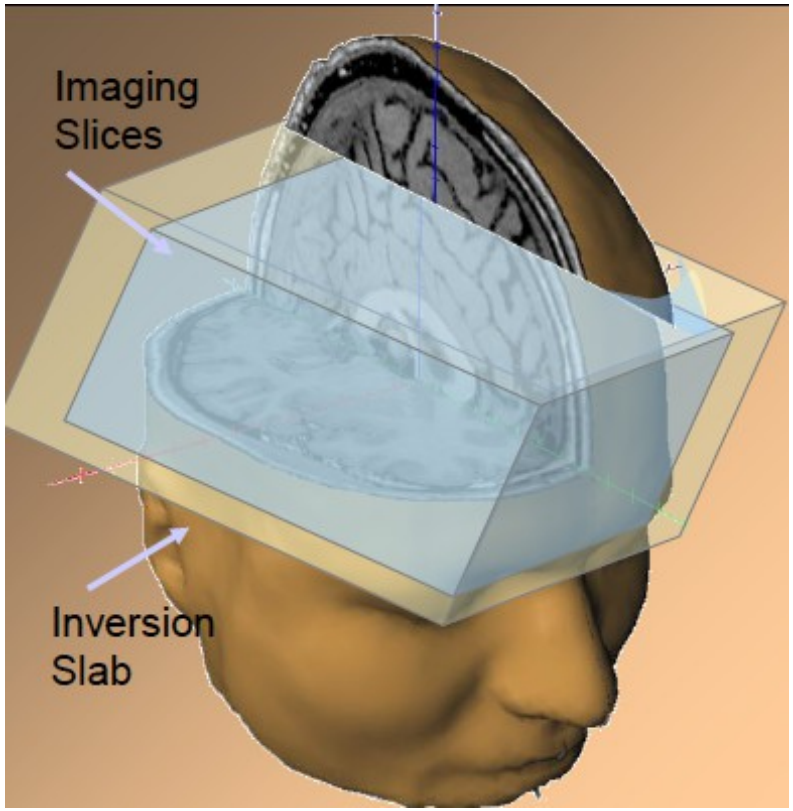
# Studi di attivazione midollare

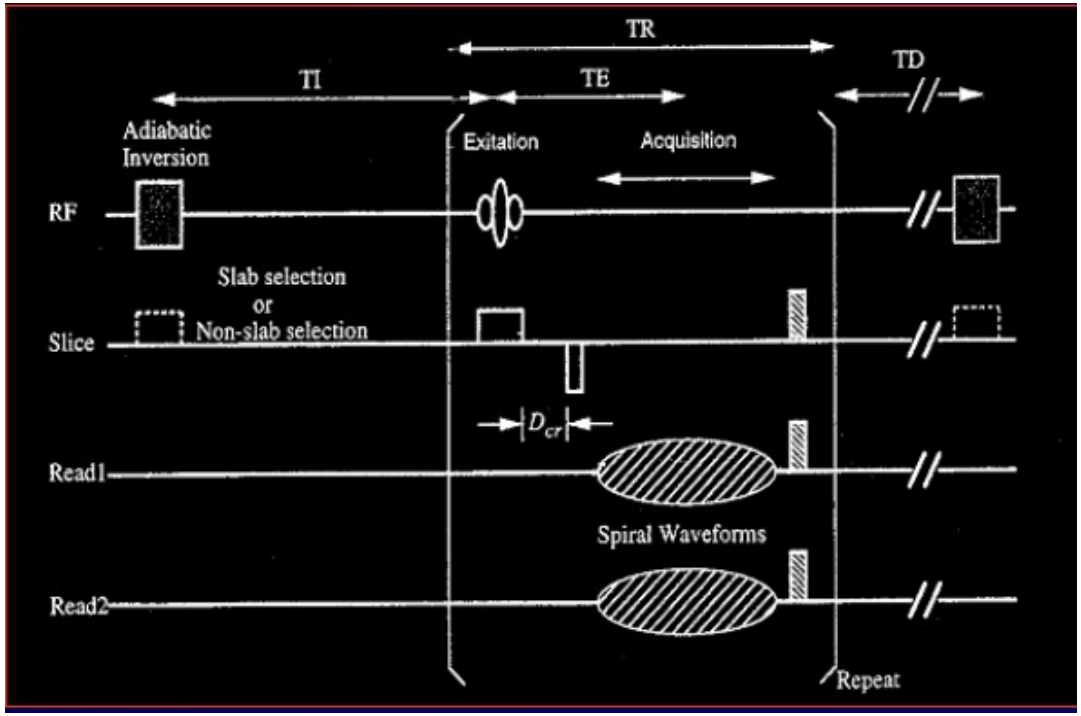


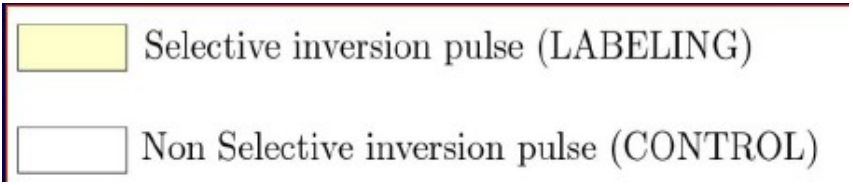
# Studi di attivazione midollare

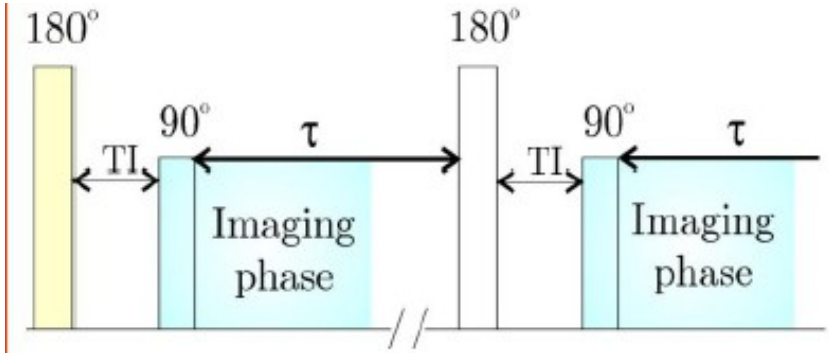


# Arterial Spin Labeling (ASL)



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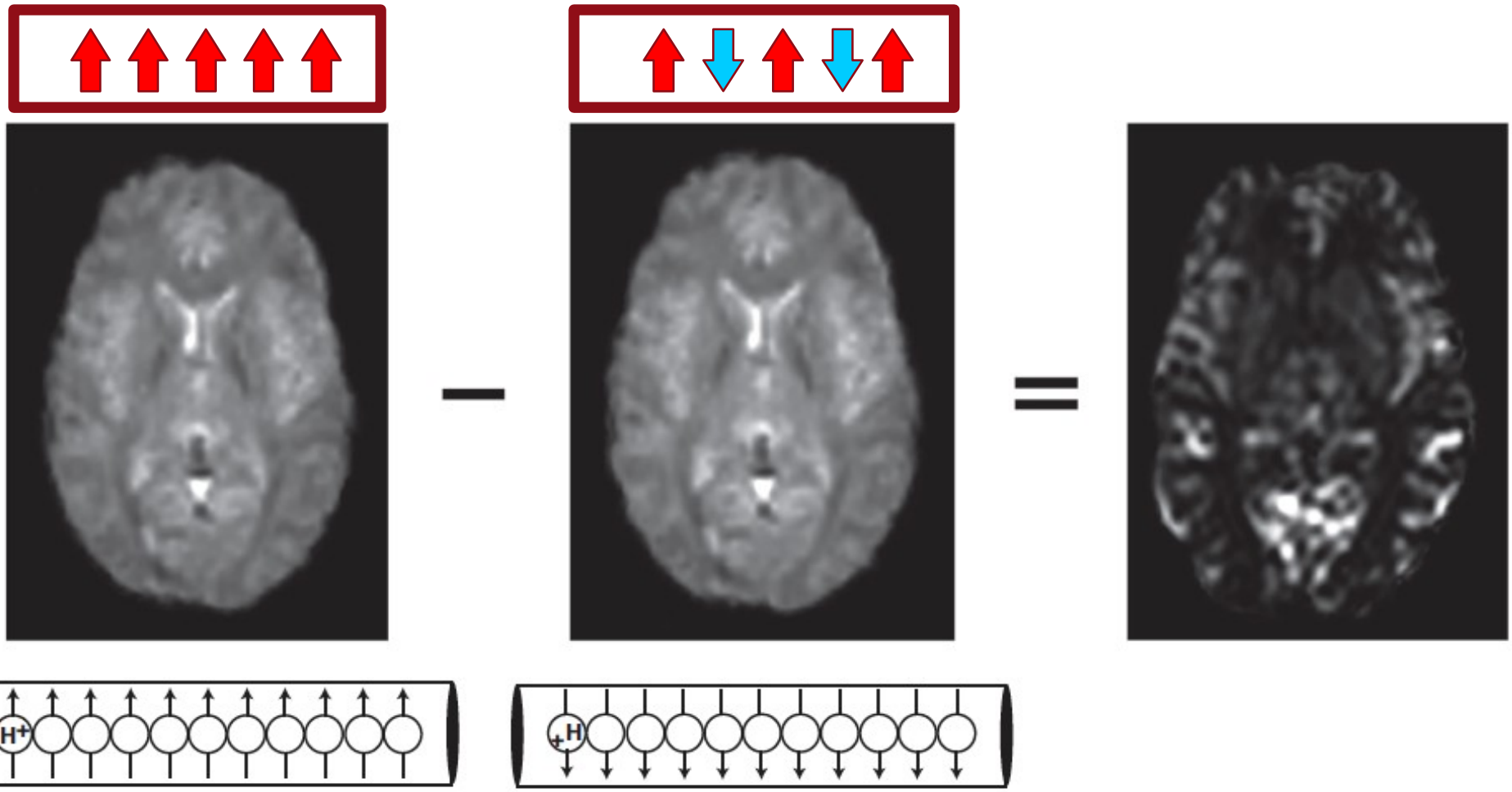

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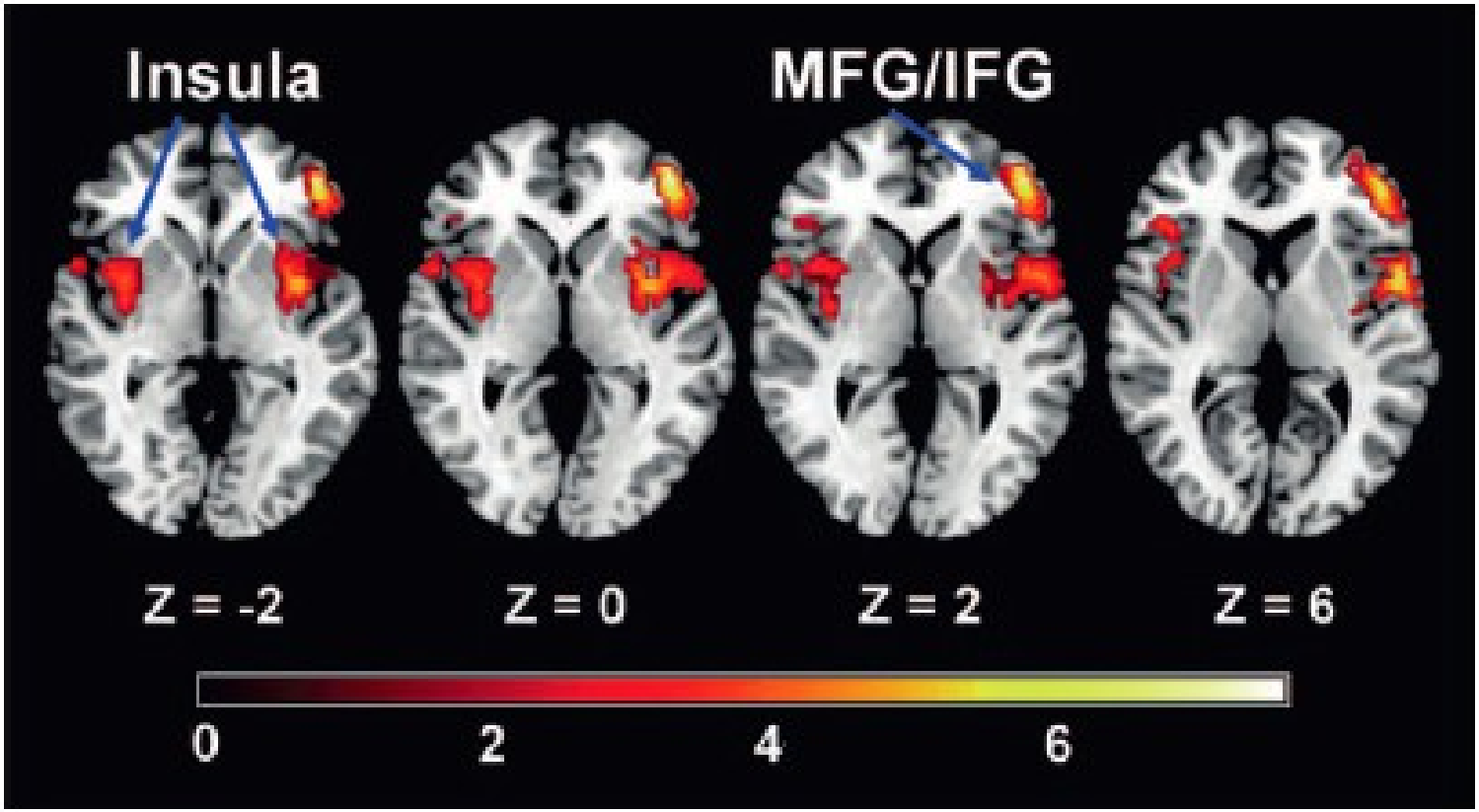
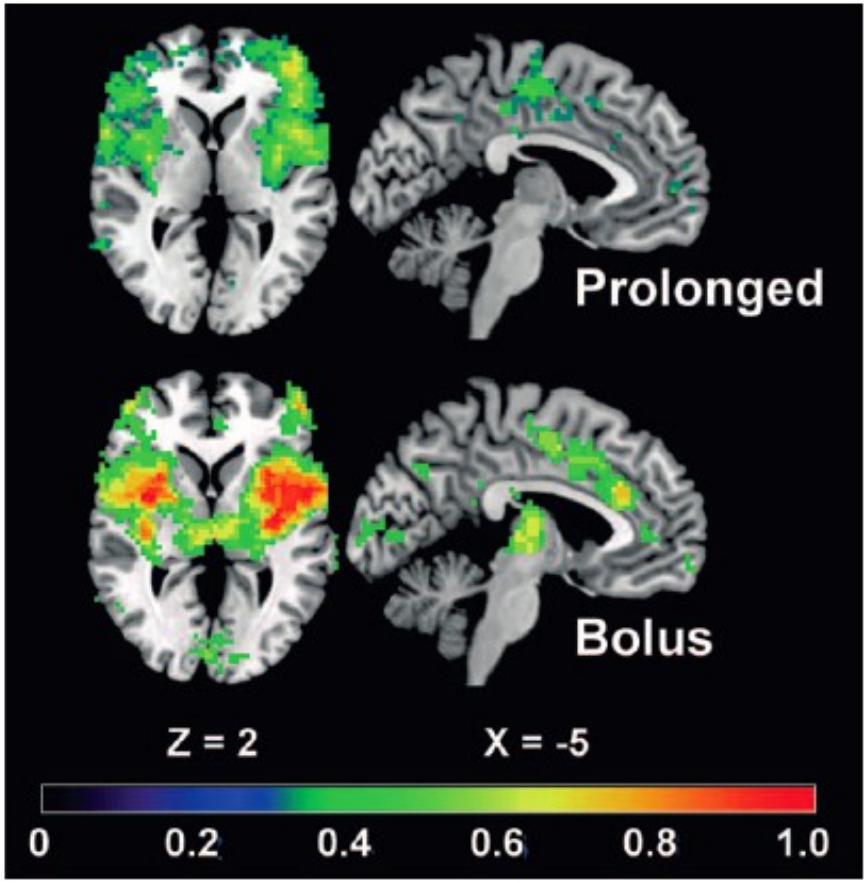


# Arterial Spin Labeling (ASL)


Pain. 2010 Mar;148(3):375-86. Using perfusion MRI to measure the dynamic changes in neural activation associated with tonic muscular pain.



# Studi strutturali

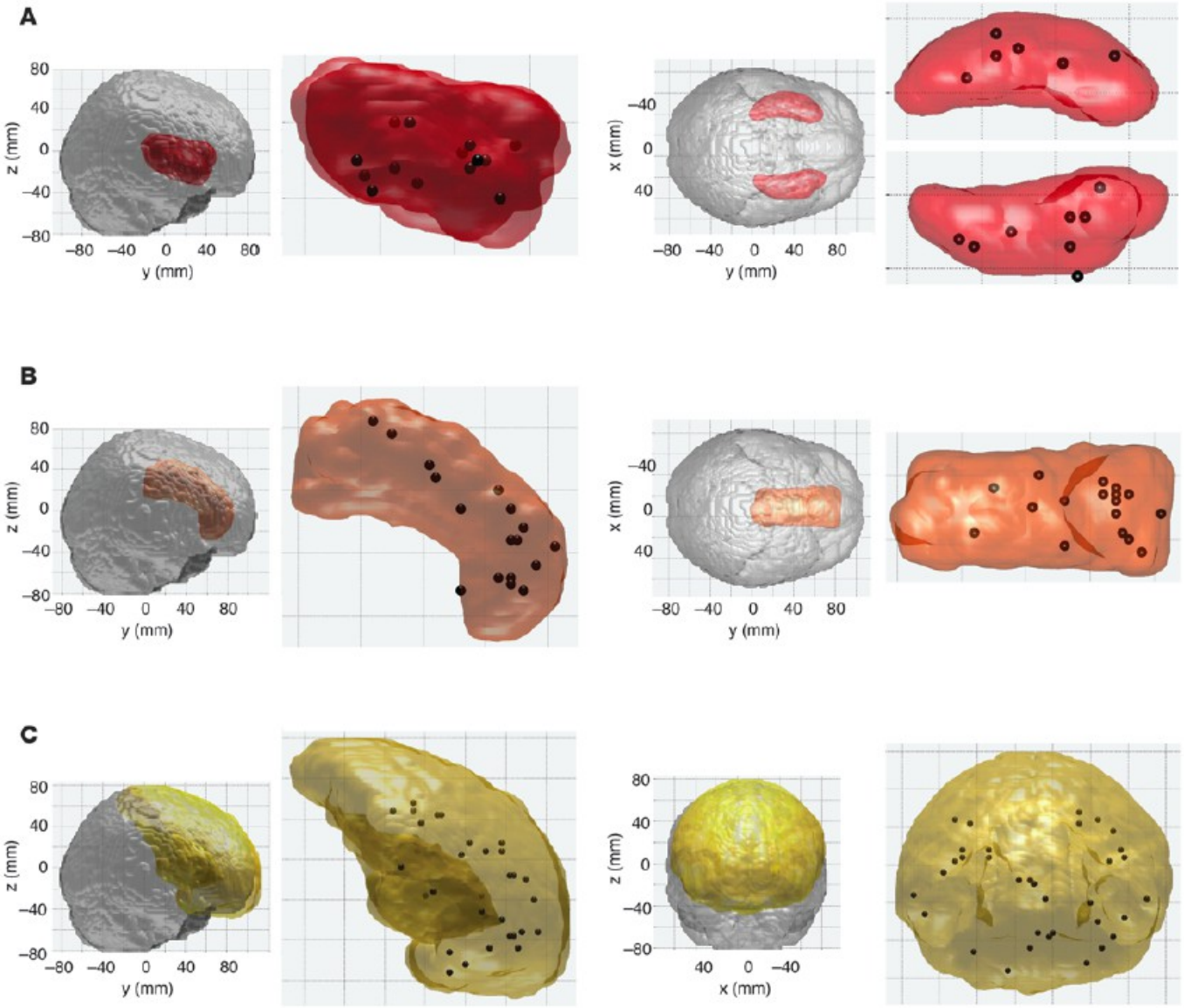
Alterazioni strutturali sono state descritte in soggetti con dolore o stimoli nocicettivi prolungati:

fibromialgia, emicrania o osteoartrite

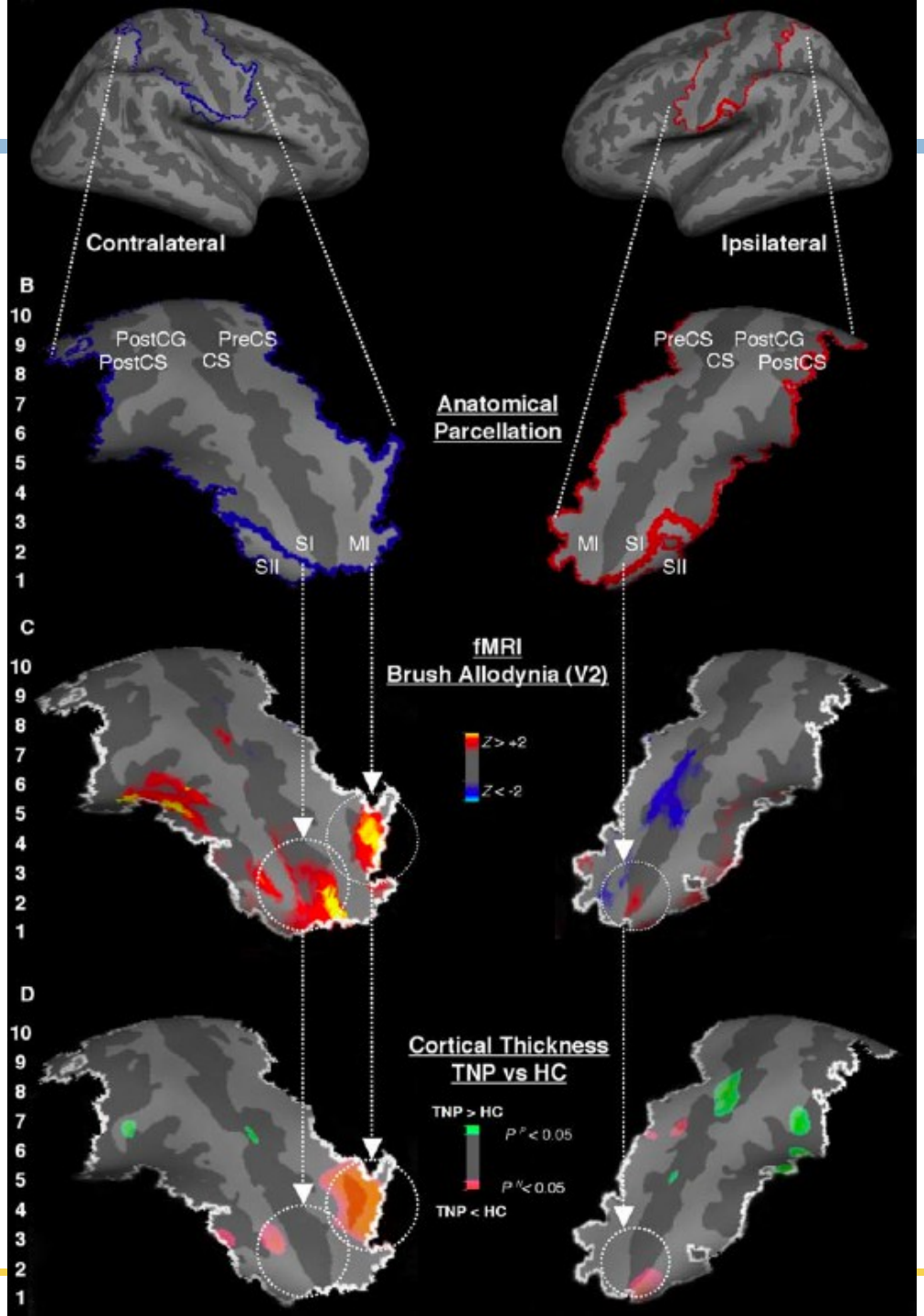
>> riduzione della sostanza grigia:

- ACC, IC, talamo e corteccia frontale, paraippocampo

# Studi strutturali nel dolore cronico




The Journal of Clinical Investigation Volume 120 Number 11 November 2010

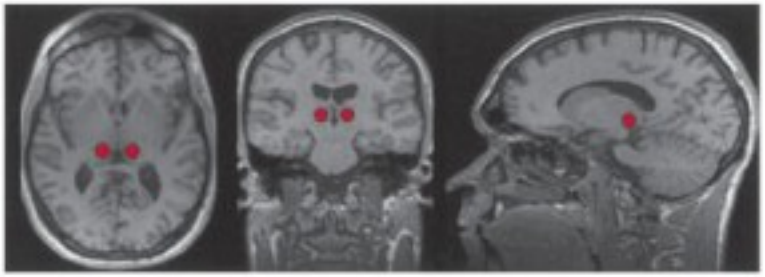



DaSilva AF et Al.PlosOne2008

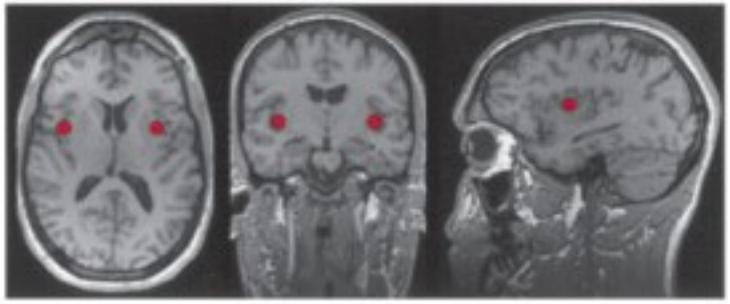
# Diffusione tensoriale

Some clinical significance of decreased diffusion directionality was provided by a study in fibromyalgia patients that demonstrated a relationship between decreased fractional anisotropy in the thalamocortical tract and the degree of stiffness

Thalamus



Insula



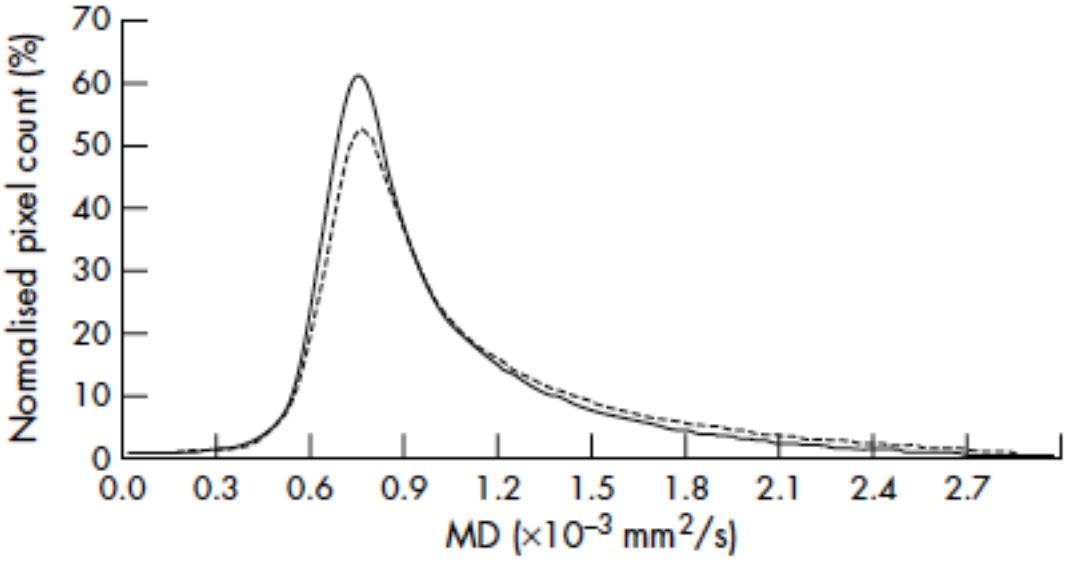
Lutz J et al. Arthritis & Rheumatism 2008

# Diffusione tensoriale

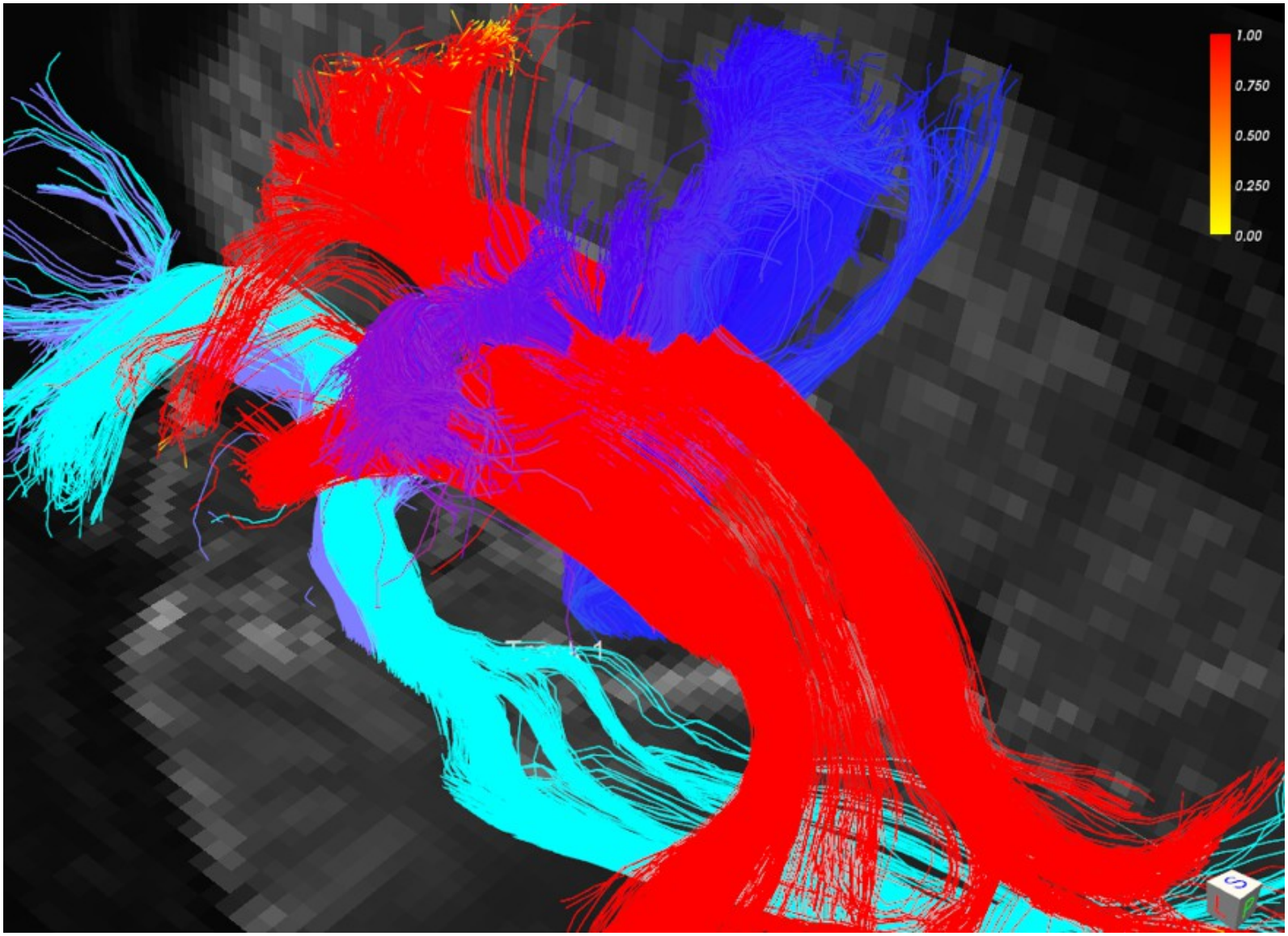
## Diffusion tensor magnetic resonance imaging at 3.0 tesla shows subtle cerebral grey matter abnormalities in patients with migraine

**M A Rocca, A Ceccarelli, A Falini, P Tortorella, B Colombo, E Pagani, G Comi, G Scotti, M Filippi**

*J Neurol Neurosurg Psychiatry* 2006;77:686–689. doi: 10.1136/jnnp.2005.080002



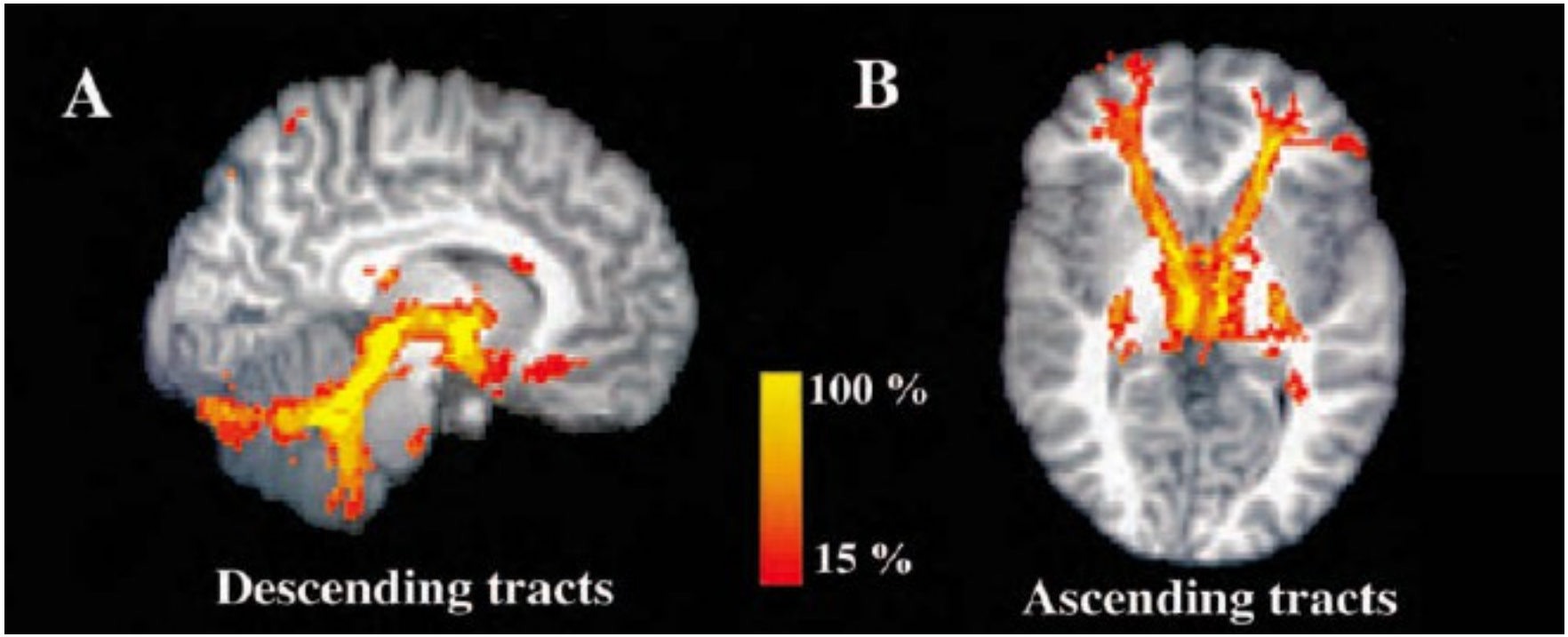
# Diffusione tensoriale: Trattografia



# Diffusione tensoriale: Trattografia

Connectivity of the human periventricular–periaqueductal gray region

**J Neurosurg 103**:1030–1034, 2005

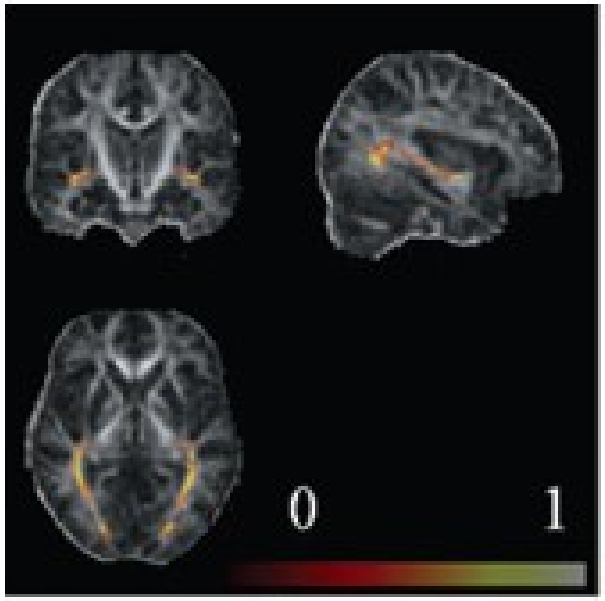


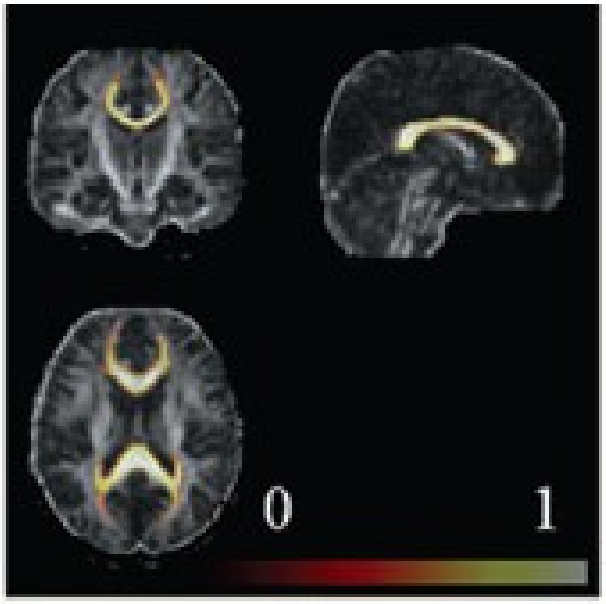
# Diffusione tensoriale: Trattografia

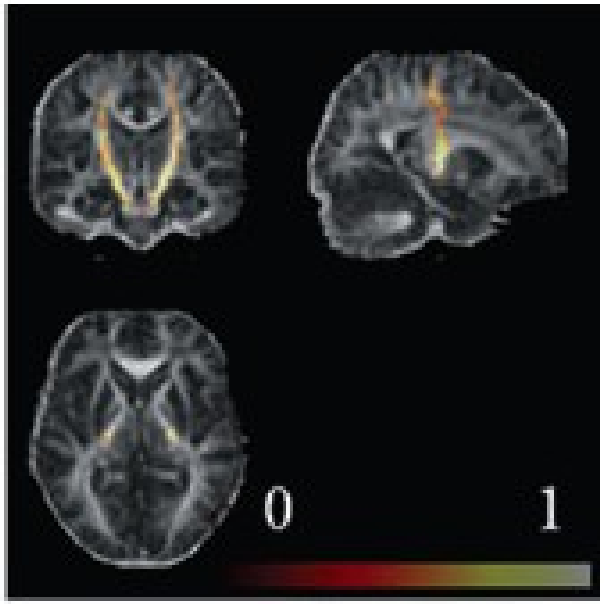
Selective diffusion changes of the visual pathways in patients with migraine: a 3-T tractography study

MA Rocca[1,2,3], E Pagani[1], B Colombo[3], P Tortorella[1], A Falini[2,4], G Comi[3] & M Filippi[1,2,3]

*Cephalalgia*, 2008, **28**, 1061–1068

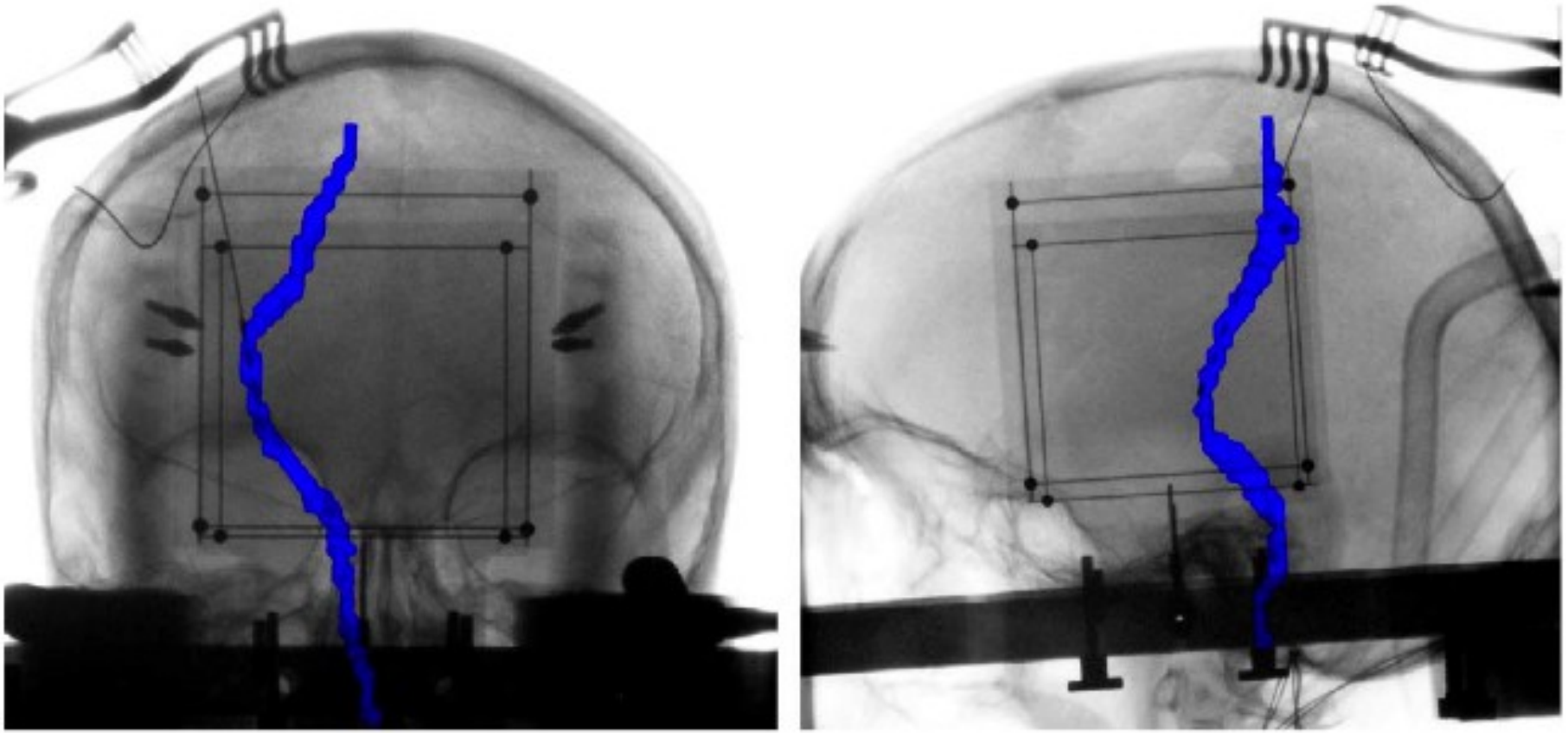


# Diffusione tensoriale: Trattografia

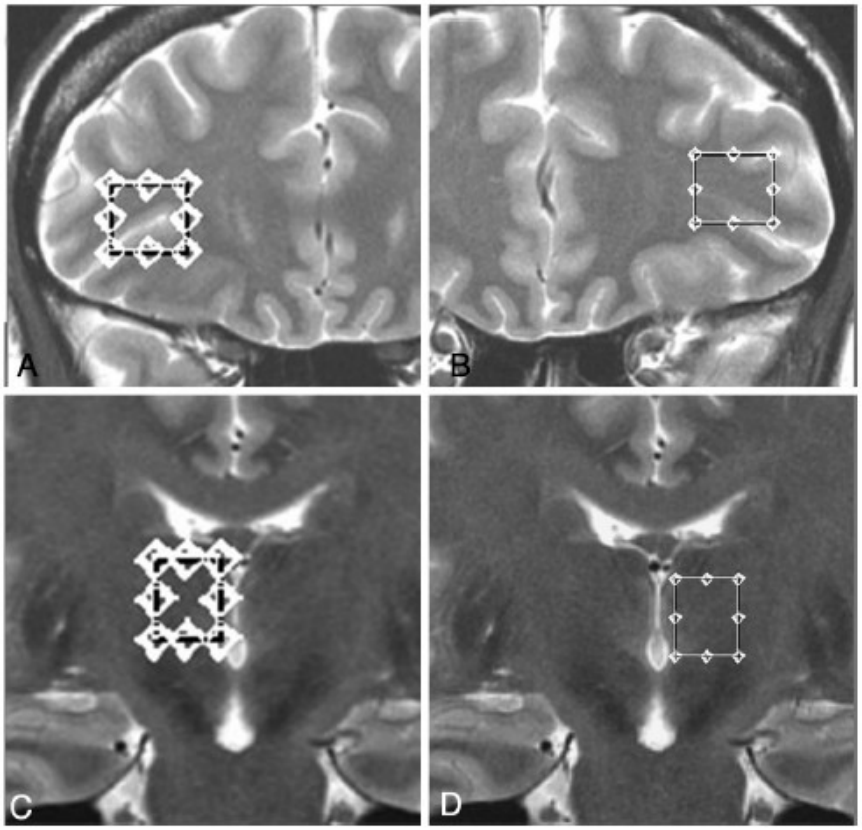
**Tractography-Guided Stimulation of Somatosensory Fibers for Thalamic Pain Relief**



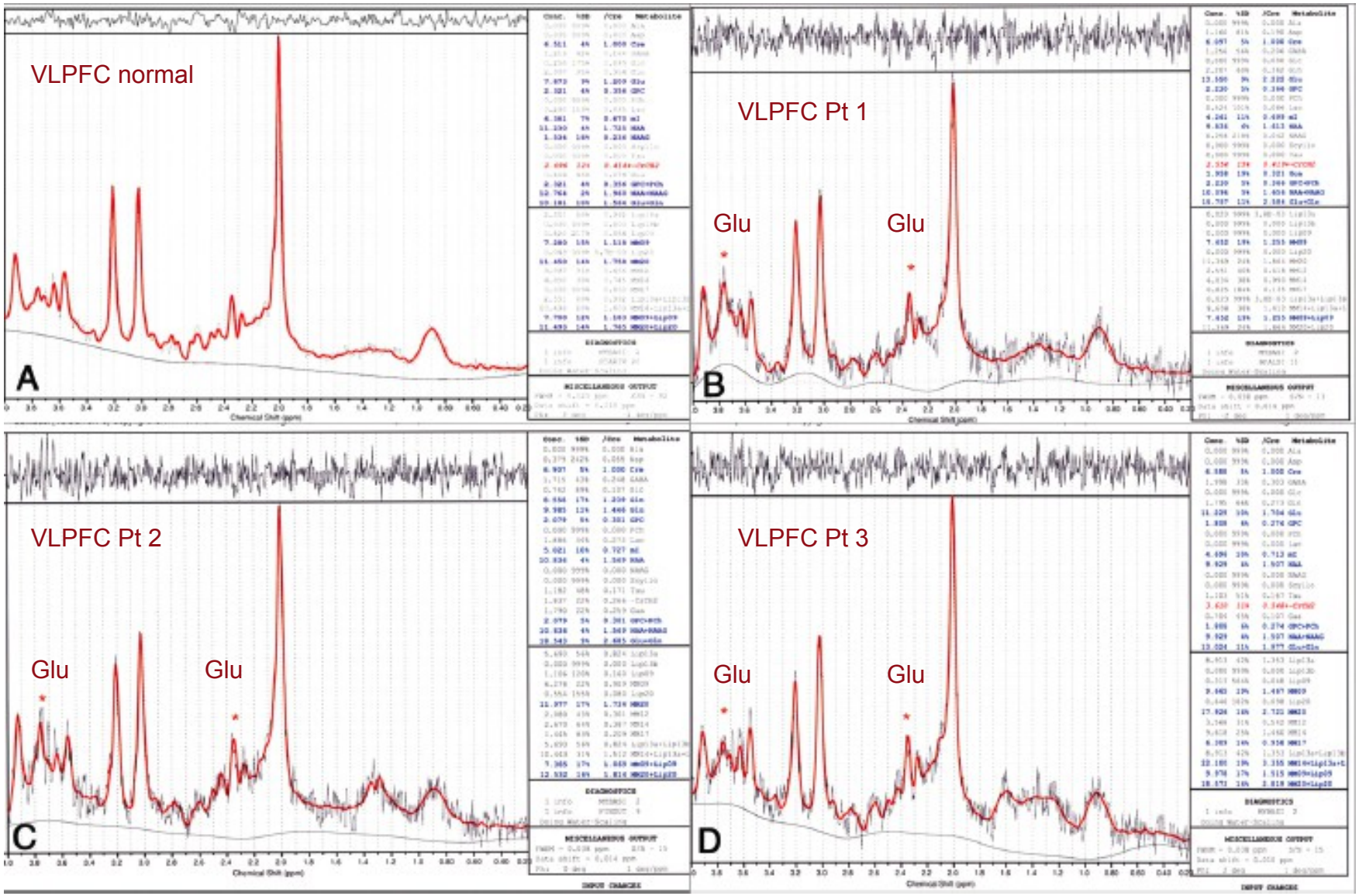
# Spettroscopia

## Metabolic Abnormalities in Pain-Processing Regions of Patients with Fibromyalgia: A 3T MR Spectroscopy Study

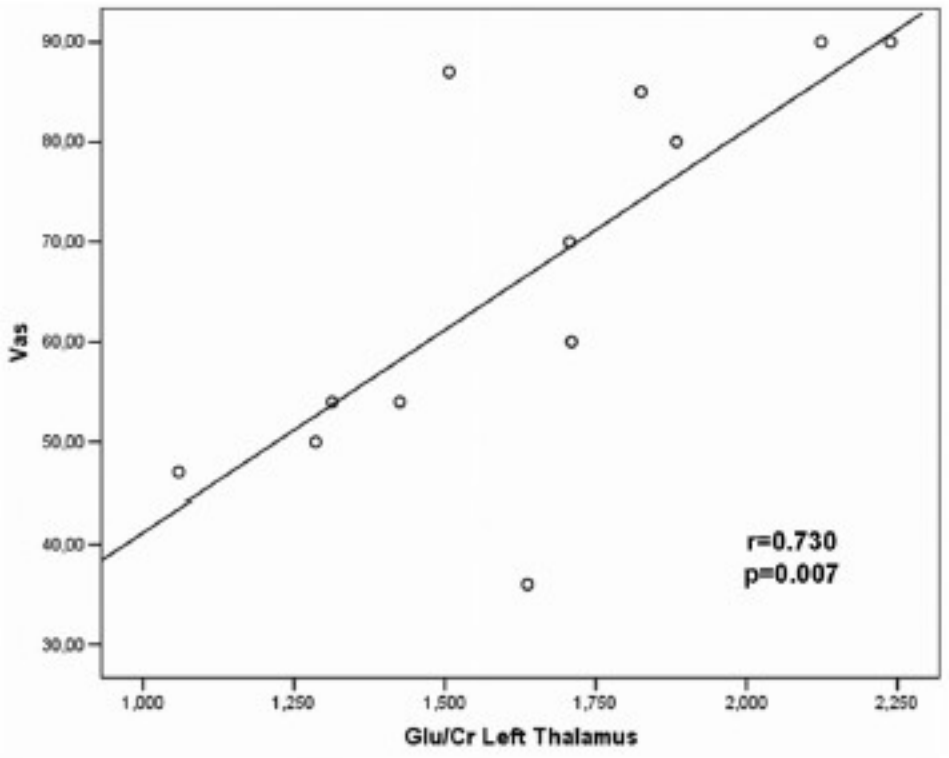
AJNR Am J Neuroradiol 32:1585–90 | Oct 2011 |



# Spettroscopia



# Spettroscopia



# Spettroscopia

## Hippocampus Dysfunction May Explain Symptoms of Fibromyalgia Syndrome. A Study with Single-Voxel Magnetic Resonance Spectroscopy

YASSER EMAD, YASSER RAGAB, FATMA ZEINHOM, GHADA EL-KHOULY, ALAA ABOU-ZEID, and JOHANNES J. RASKER

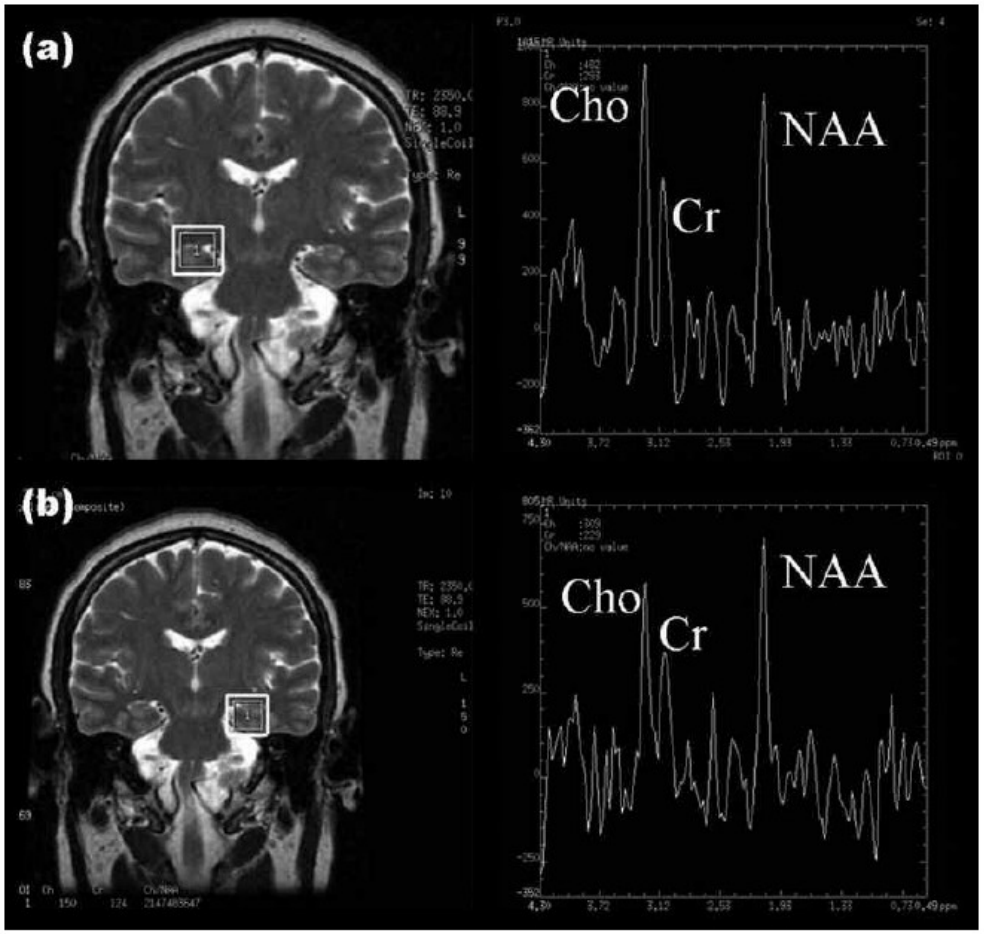
*The Journal of Rheumatology 2008; 35:7*

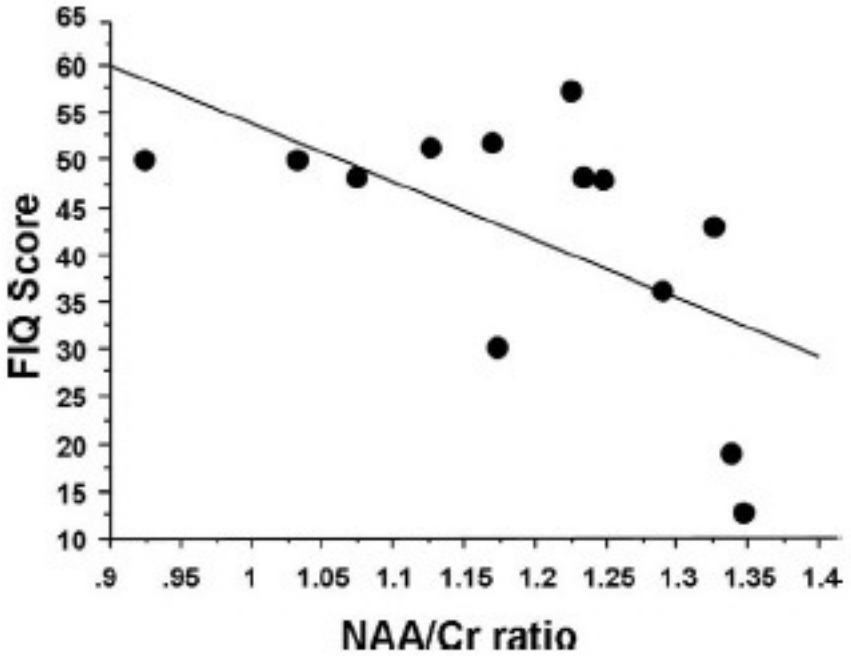
## Hippocampal Metabolite Abnormalities in Fibromyalgia: Correlation With Clinical Features

Patrick B. Wood,* Christina R. Ledbetter,† Michael F. Glabus,‡,# Larry K. Broadwell,§ and James C. Patterson 2nd‖,¶

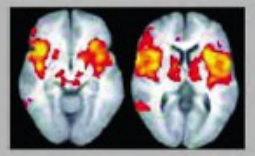
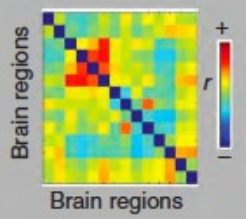
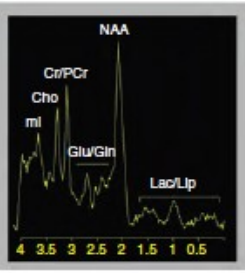
**The Journal of Pain. Vol 10. No 1 (January). 2009: pp 47-52**

# Spettroscopia



# Conclusioni

| MRI-modality | Physiological measure | |
|---|---|---|
| **Neurovascular** | | |
| *FMRI–BOLD* stimulus-evoked pain | |  |
| | **Activation maps** *Which brains regions show increased activity?* |  |
| | **Functional connectivity** *Which brain regions show closely correlated activity?* |   |
| *ASL* Spontaneous, ongoing pain | |  |
| **Anatomical** *Structural* *Diffusion weighted* | | |
| | **Grey matter** *Where are grey matter densities or cortical thickness altered?* |  |
| | **White matter tracts** *Is anatomical connectivity altered ?* |  |
| **Neurochemical** *MRS* | | |
| | **Brain metabolites** |    |

# Grazie per l’attenzione