

V CORSO

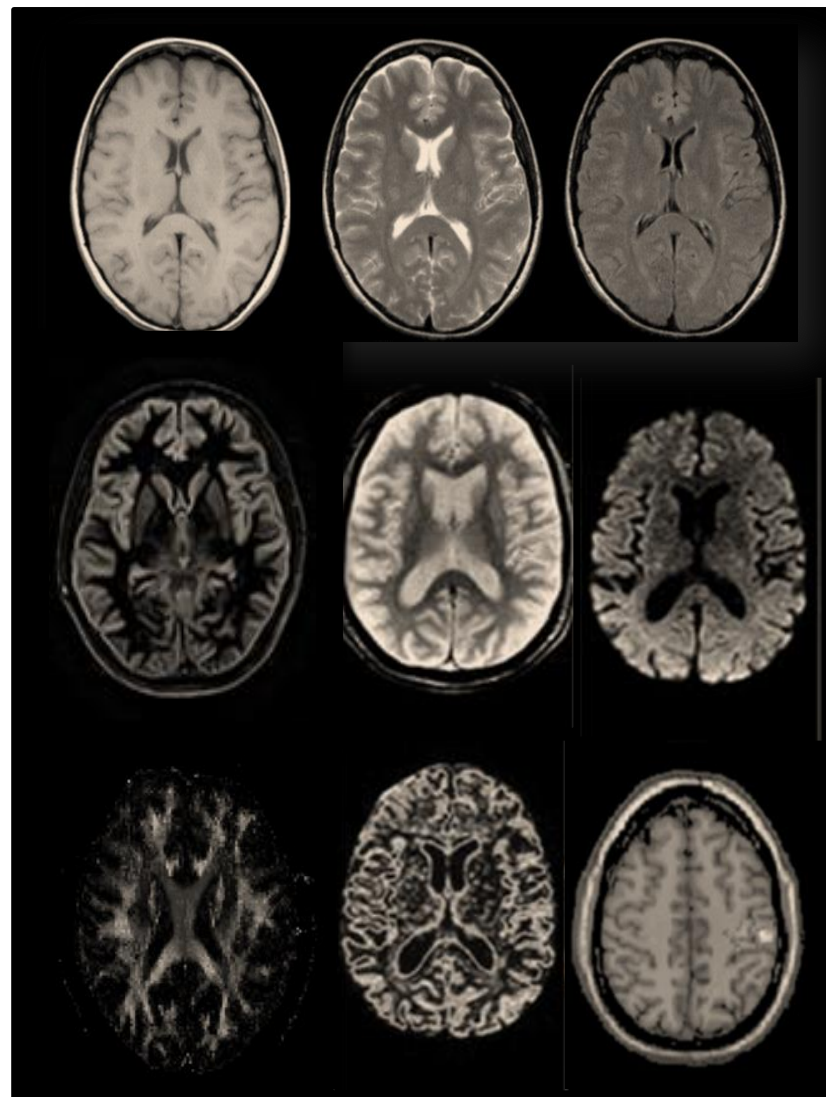
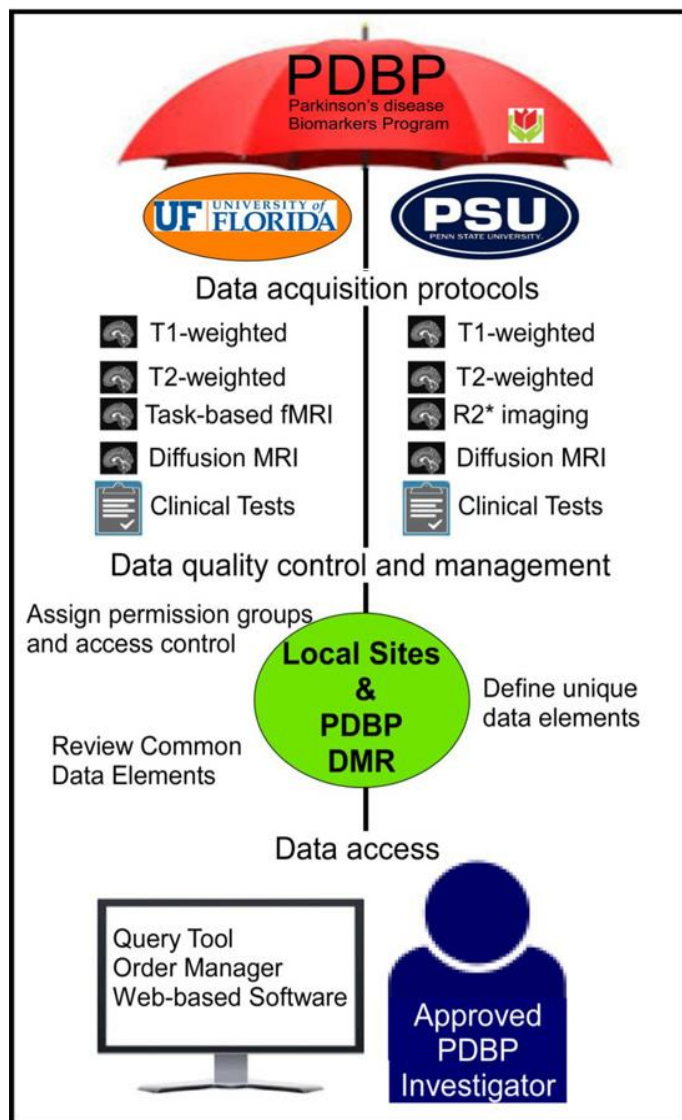
Neuroimmagini nella Malattia di Parkinson e Parkinsonismi



Task-based fMRI in Parkinson's disease

Umberto Sabatini
Università Magna Graecia

Multimodal MRI in Parkinson's disease

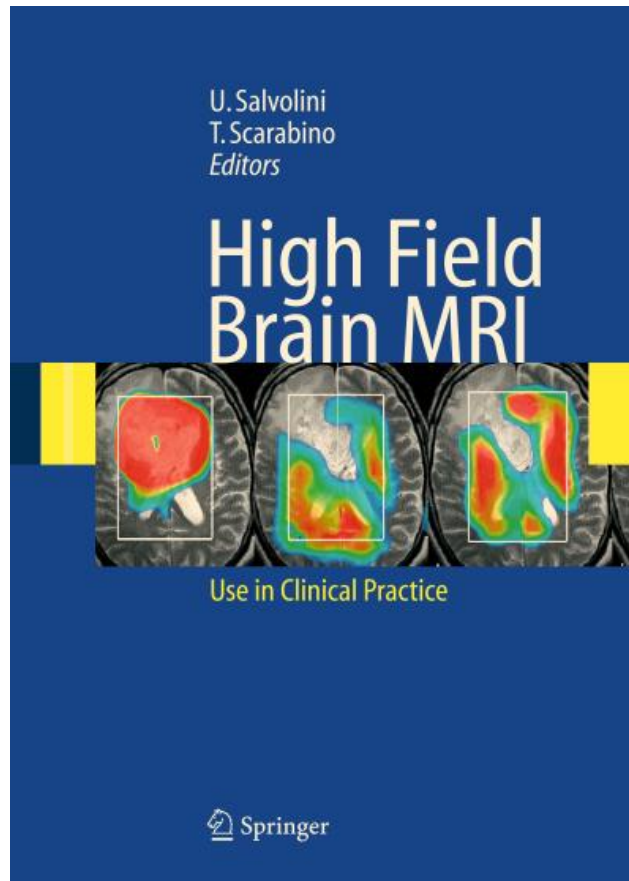


Individual/group profile

High-Field Neuroimaging in Parkinson's Disease

P. PÉRAN, G. LUCCICHENTI, A. CHERUBINI, G. E. HAGBERG, U. SABATINI

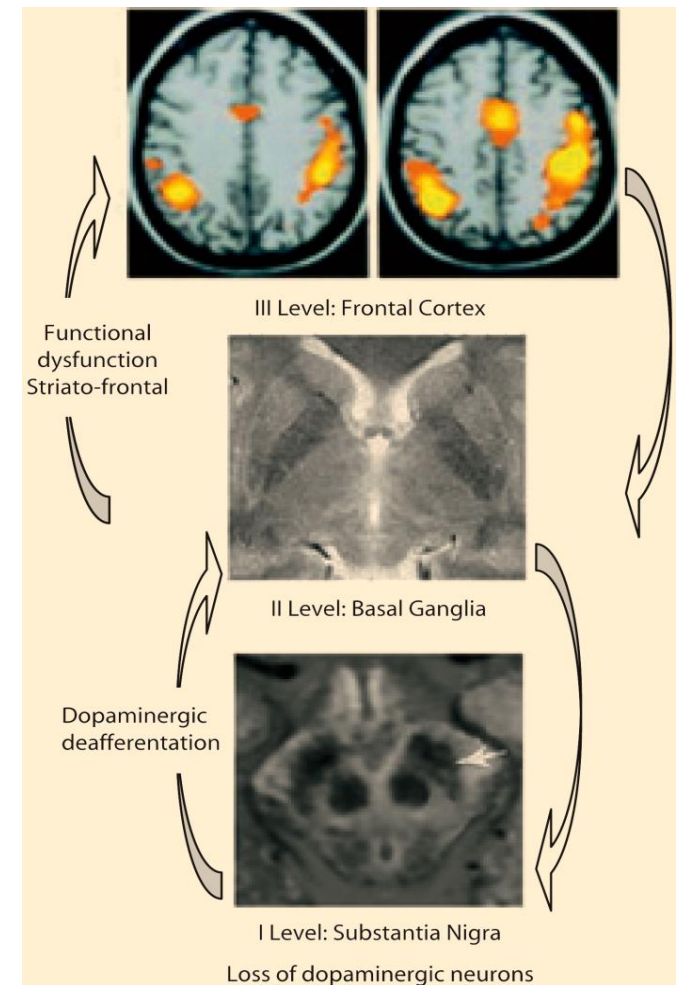
2006/2017



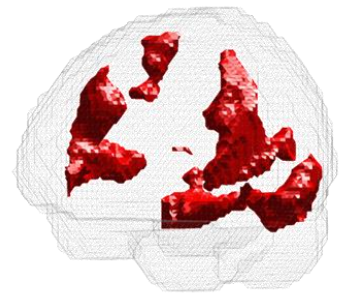
Functional MRI



Structural MRI



Teaching course: 4 key points



-  1 - Parkinson's disease: rationale
Going to pathophysiology at functional imaging
-  2 - Functional MRI: BOLD signal, methodology
task-based, maps
-  3 - Task-based functional imaging:
exploring the motor system
-  4 - Parkinson's disease:
A model of plasticity of the motor system



1 - Parkinson's disease: rationale

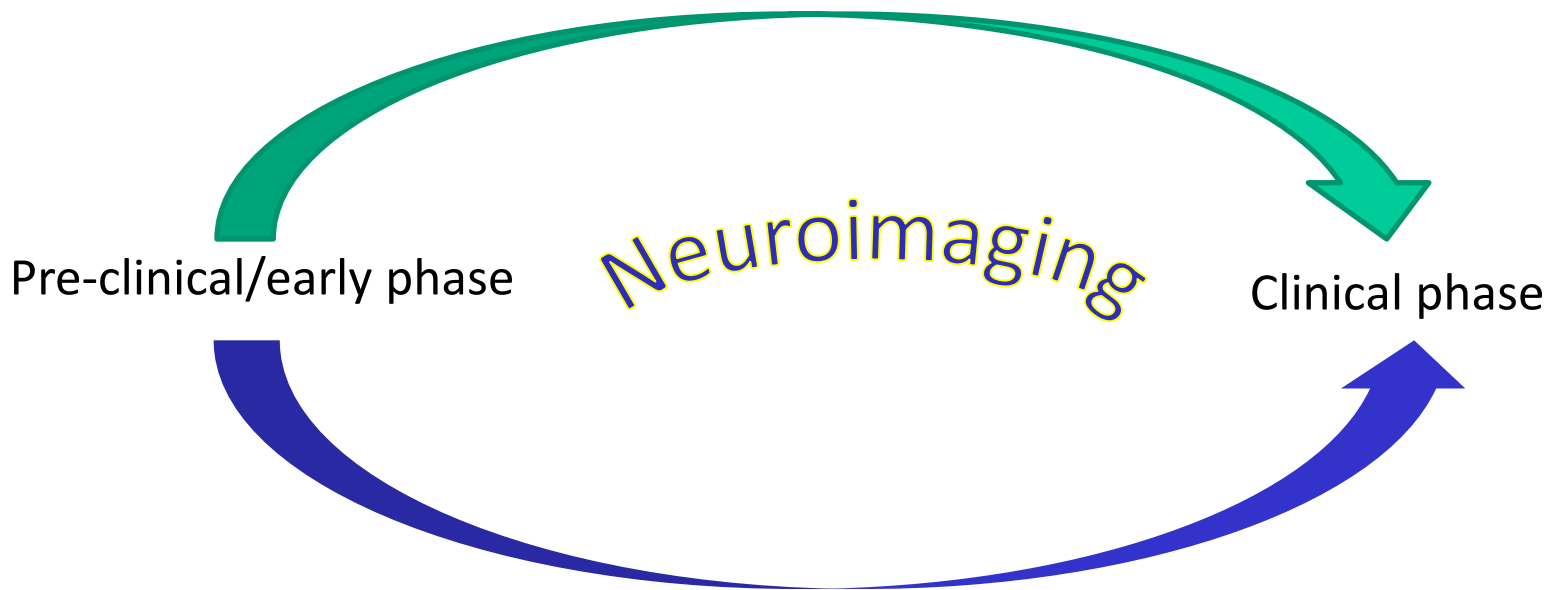
Going to pathophysiology at functional imaging

1 – starts many years before the symptoms

(**progressive system dysfunction**)

2 – induces progressive structural/**functional changes**

3 – is associated to a **reorganisation**



Going to physiopathology at functional imaging

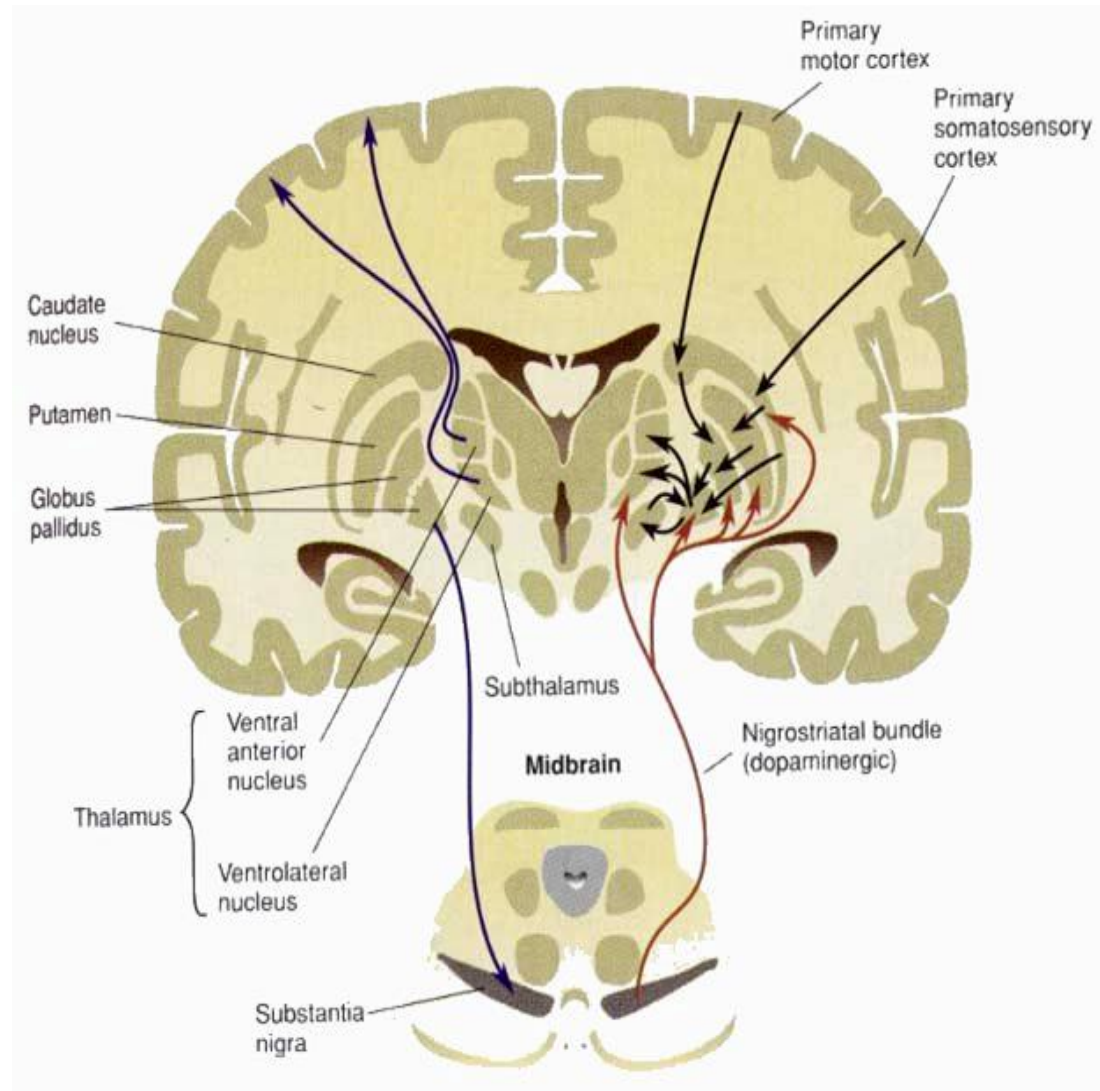
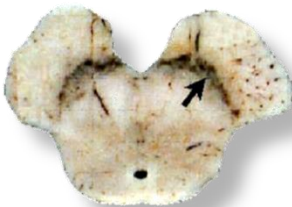
Cortical deafferentation



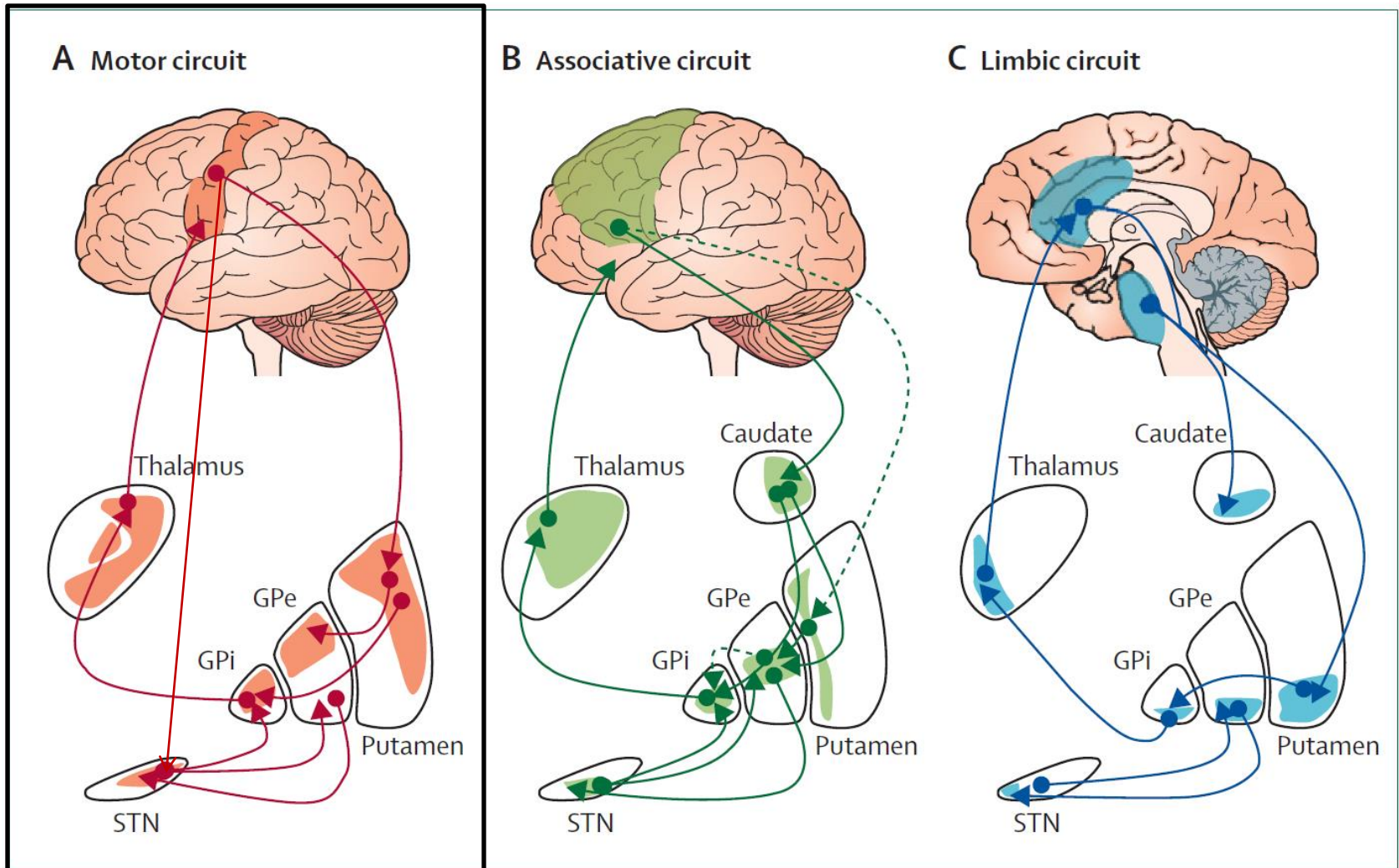
Nigro-striatal axon degeneration
Dopaminergic deafferentation



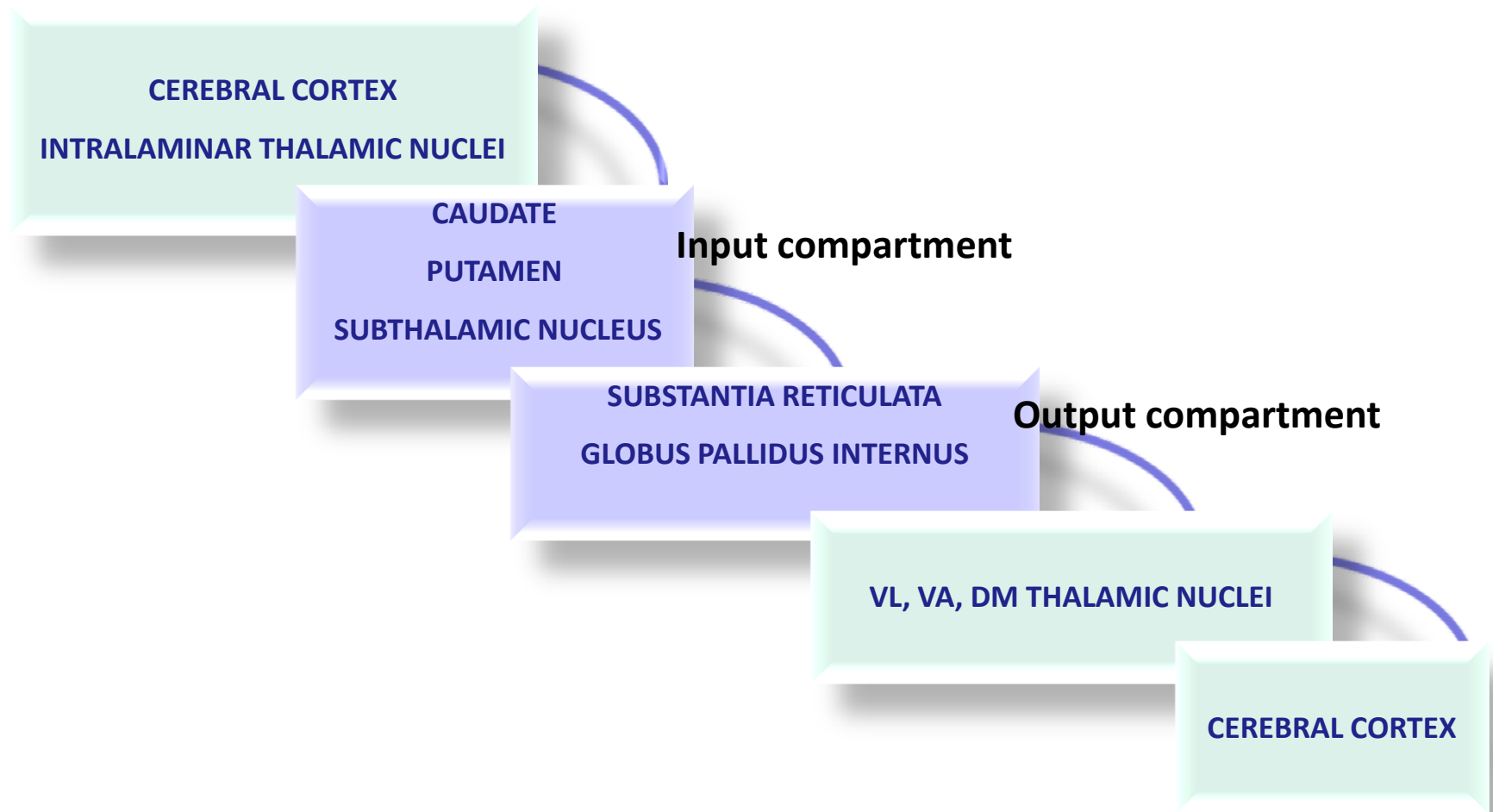
Loss of dopaminergic neurons



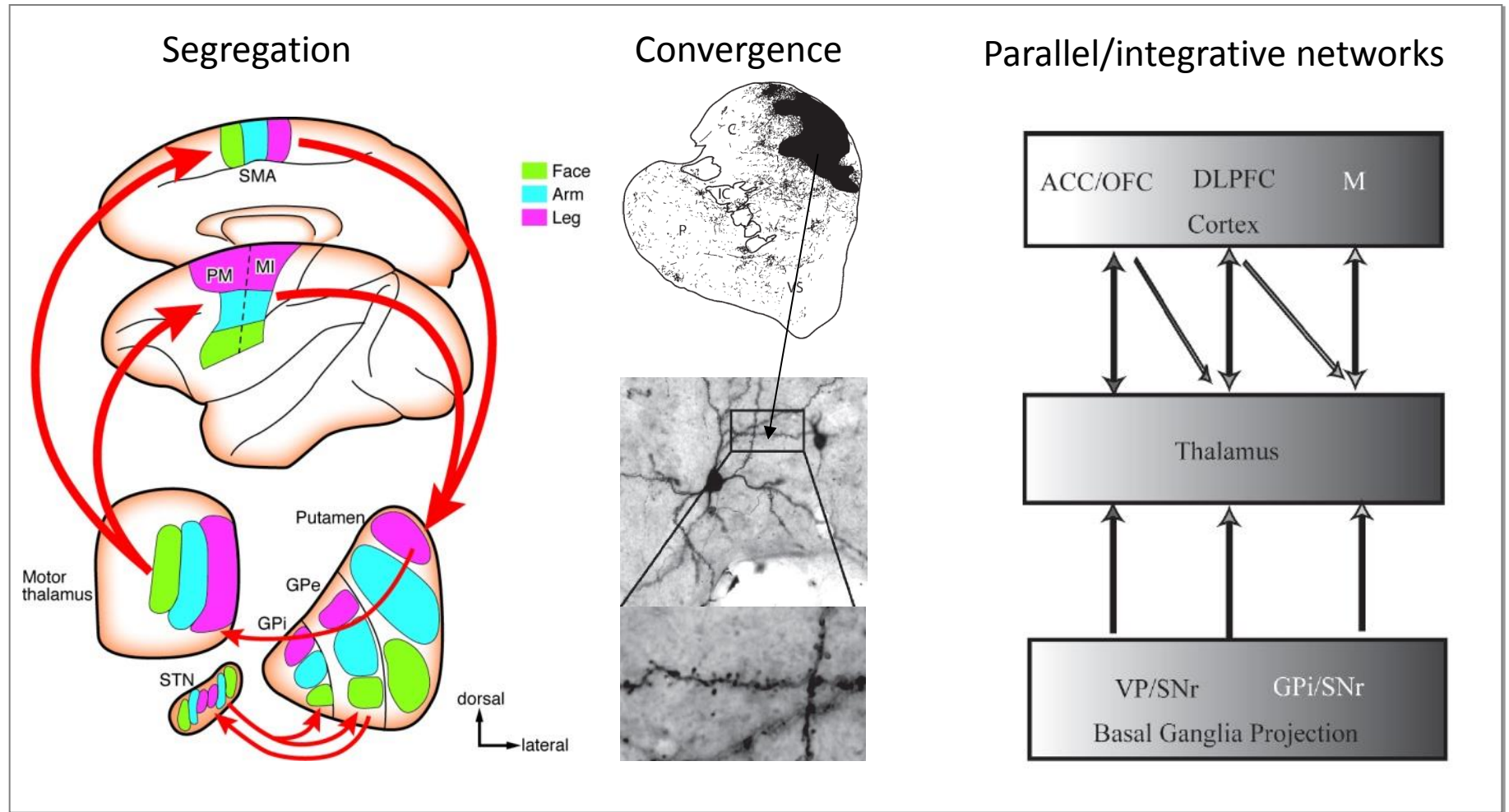
3 main circuits



Basal Ganglia functional outflow: 2 main compartments

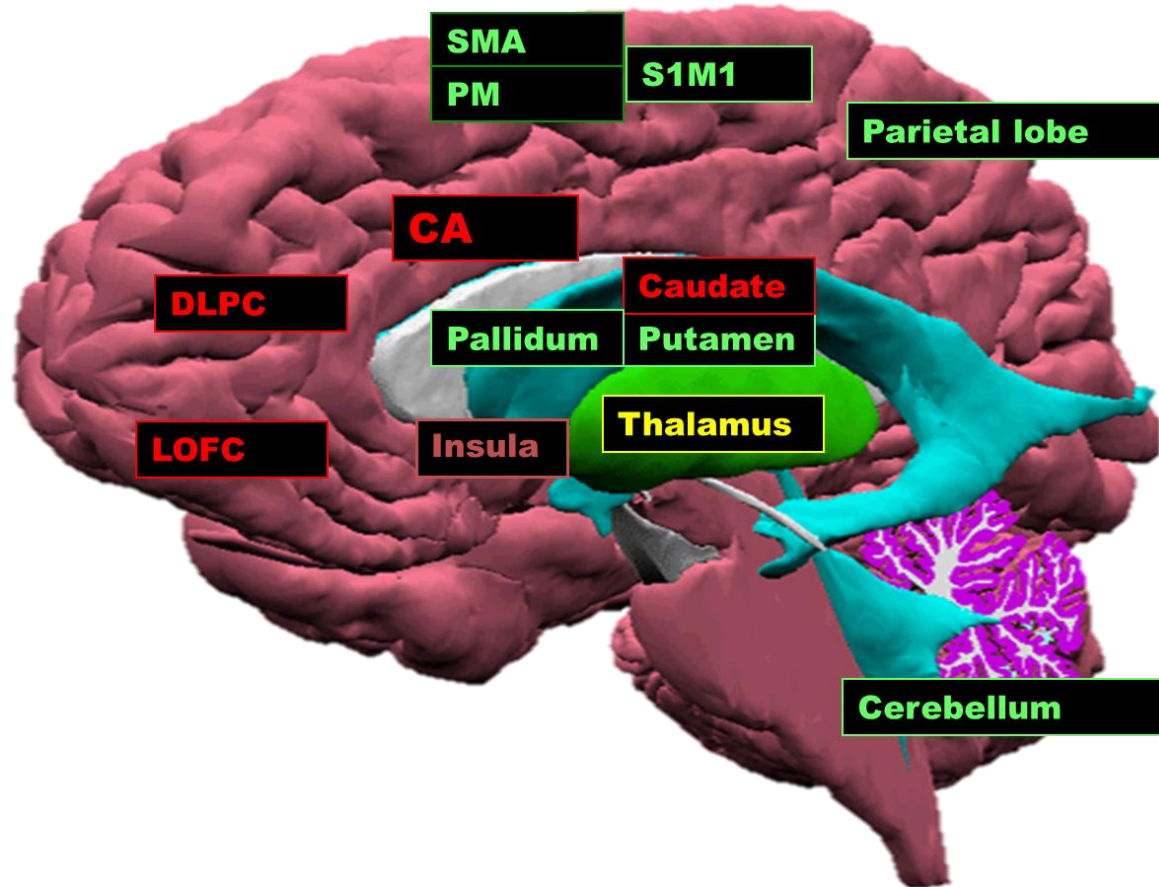


Basal Ganglia Connectivity: 3 main Functions



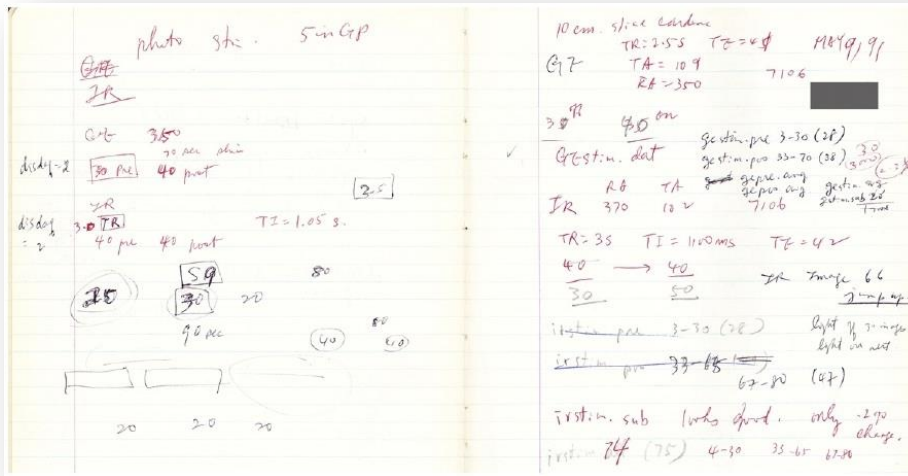
Global view: parallel/integrative system, segregated/flexible

Exploring the motor system by functional imaging



Key point 2

2 – Functional MRI: BOLD signal methodology, task based, maps



Kwong's log book pages recording the fMRI experiment (May 9, 1991)



Belliveau et al, 1991



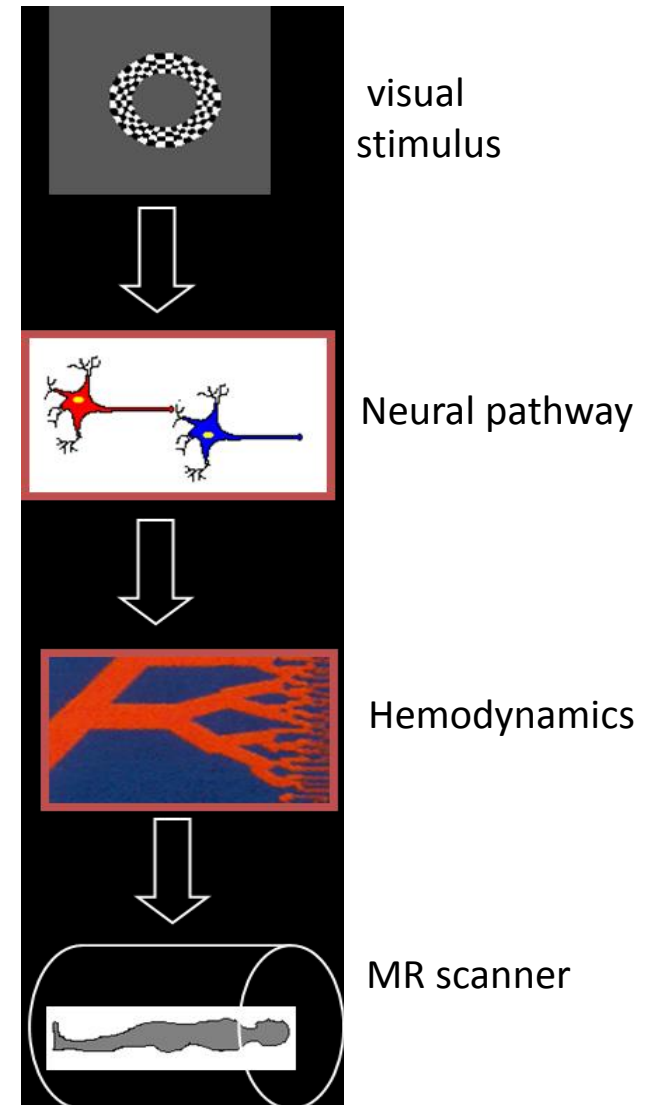
BOLD signal: changes in O₂ ratios in blood

When the **neuronal activity** in an area of the brain increases, that area consumes **more energy**

The **neuronal tissue** gets its energy from **oxygenated hemoglobin** in the blood

Within about 2 seconds the blood flow and the concentration of oxygenated hemoglobin in the blood locally increases in that area (on the scale of 1-2 mm). This is the **hemodynamic response**

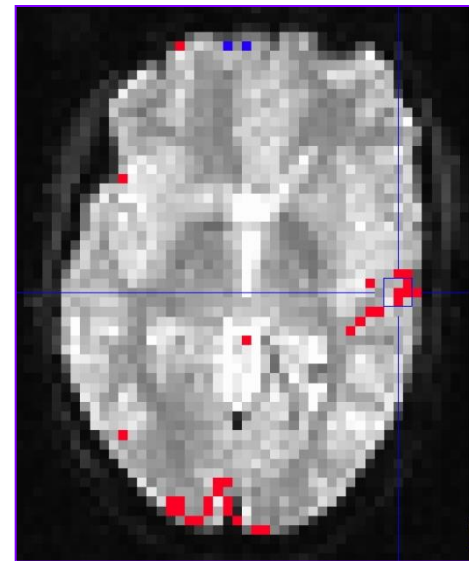
The hemodynamic response can be imaged with **functional MRI by changes in the BOLD** (Blood oxygenation dependent level) signal



fMRI methodology

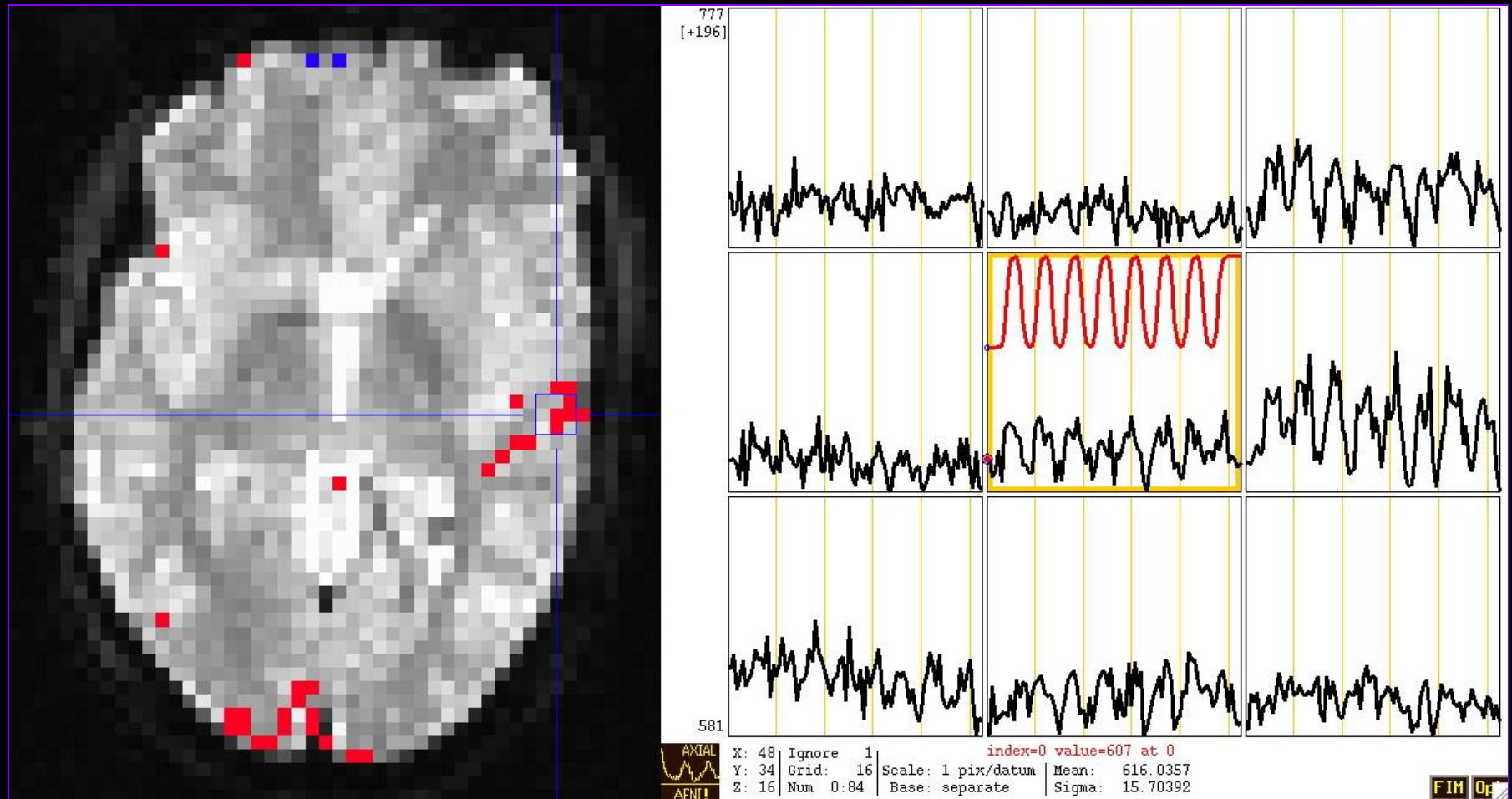
Scan brain with T2*-weighted sequence every 2-3 seconds

- Subject performs **task in an on/off fashion**, (visual, auditory, tactile, ...)
- Usually gather about **1000 brain volumes at low spatial resolution**
- Images look **bad in space**, but are designed to provide useful information through **time**
- Analyze data time series to look for **up-and-down signals** that match the stimulus time series



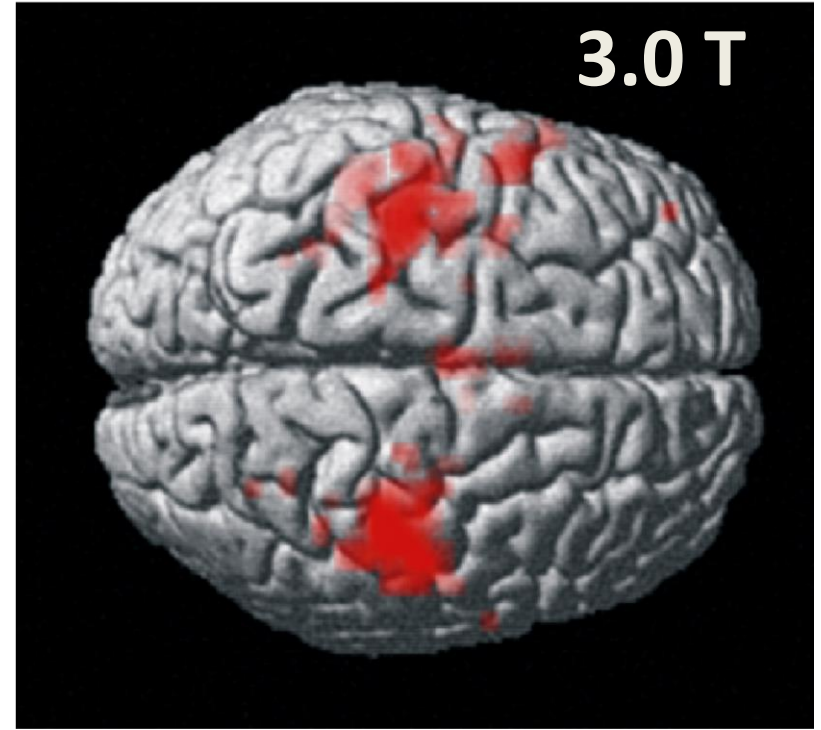
A single fast (100 ms) 2D image

fMRI methodology



One fast image *and* a 3×3 grid of voxel time series

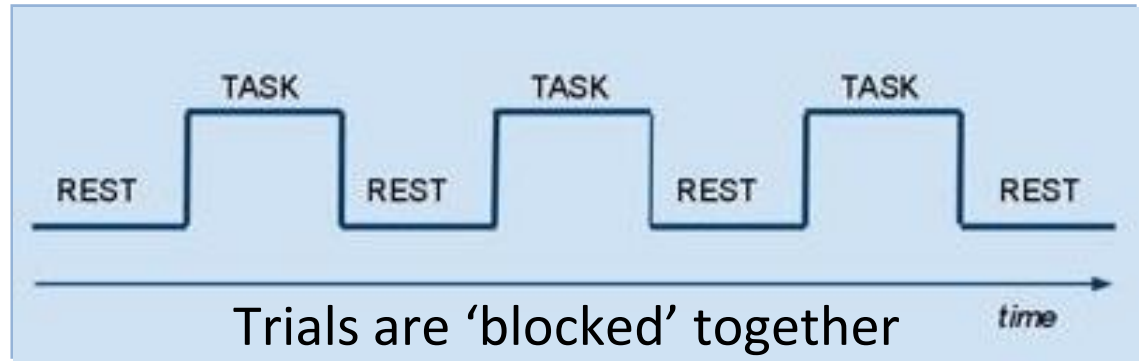
Going from 1.5T to 3T



T2* sensitivity is increased at 3T

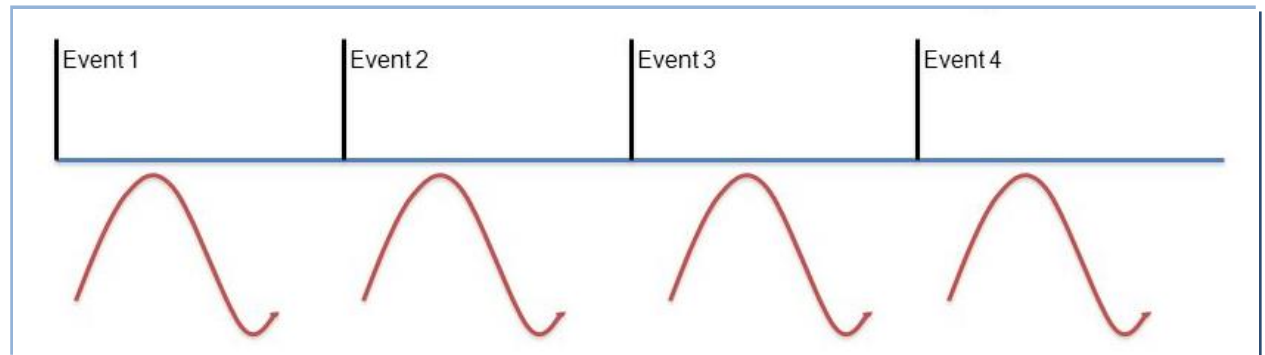
Task-based designs

- **Blocked design**



Powerful for detecting activation. Useful for examining state changes

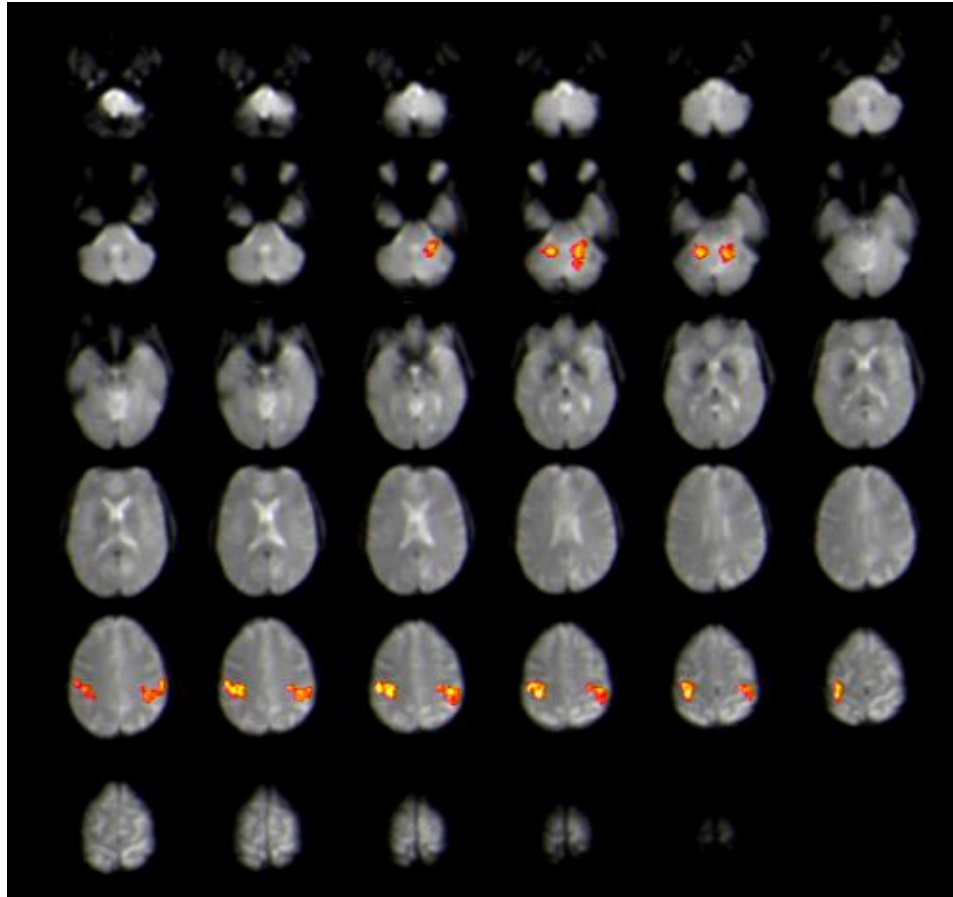
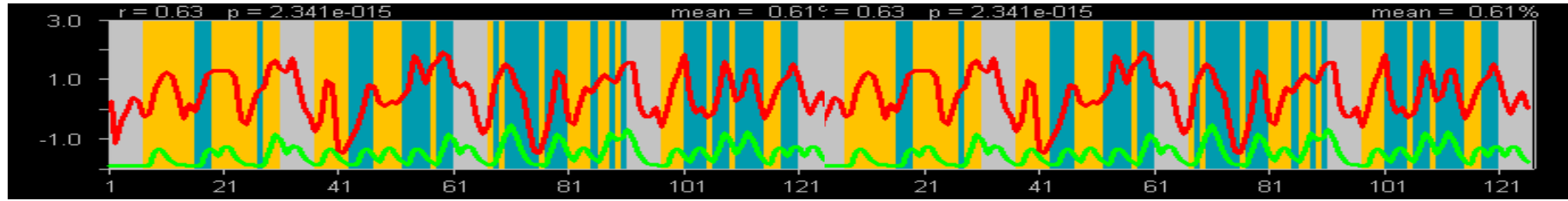
- **Event related design**



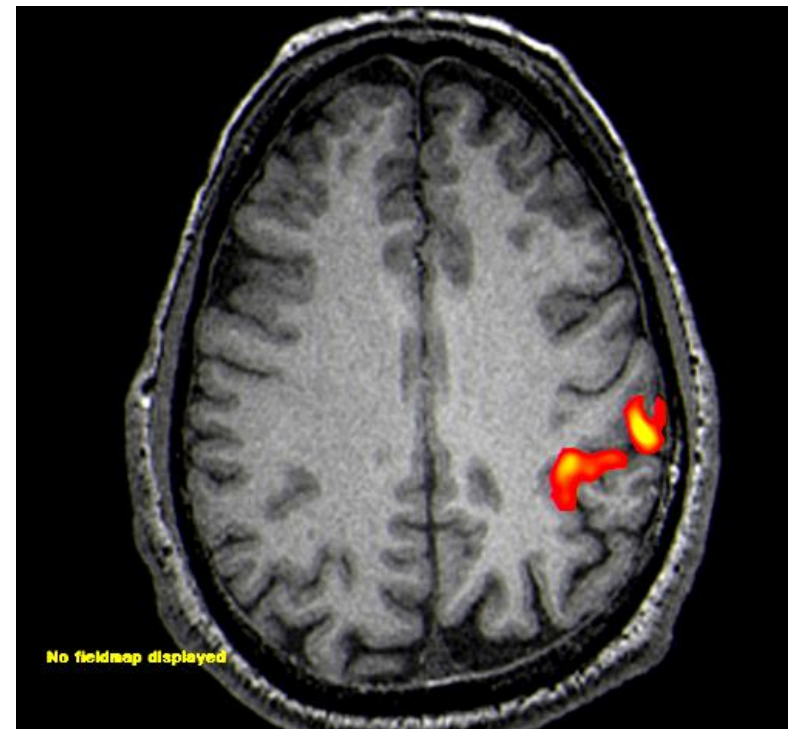
Each trial is modelled separately as an 'event'

Powerful for estimating time course of activity

Motor task



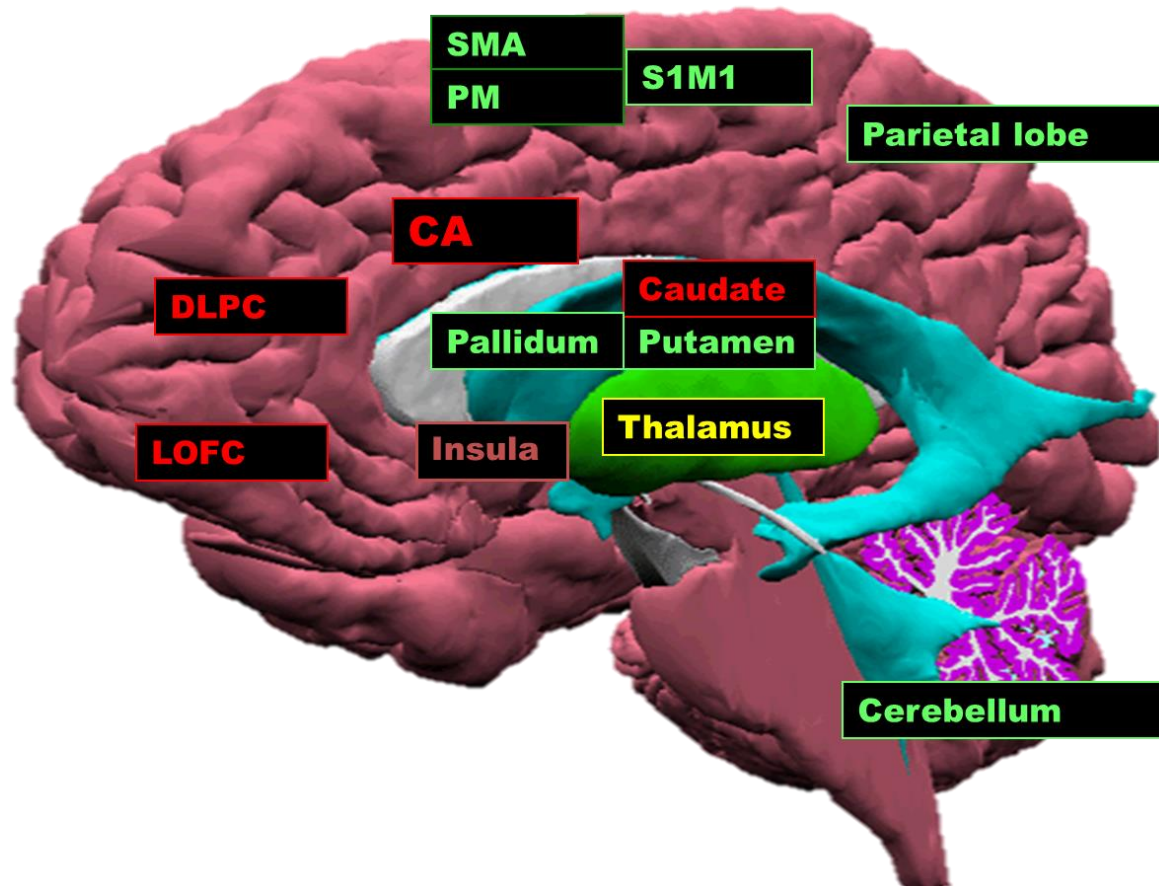
3D real-time processing



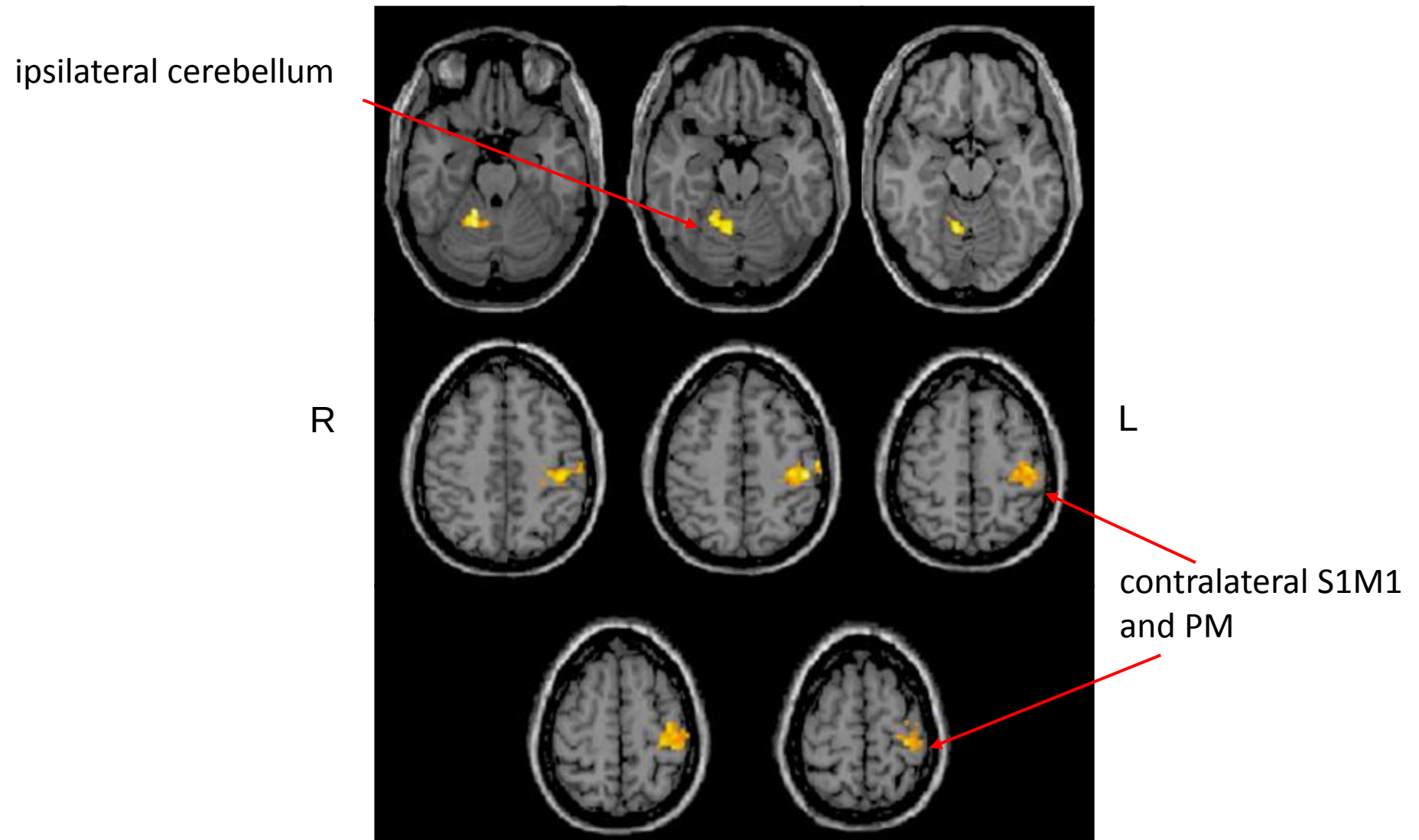
overlay onto anatomical data

Key point 3

- 3 - Task-based functional imaging: exploring the motor system



BOLD-activation Finger tapping Right hand (internal cue)



BOLD-activated areas are UNILATERAL

BOLD-activation Finger tapping right hand by simple acoustic stimulus (external cue)

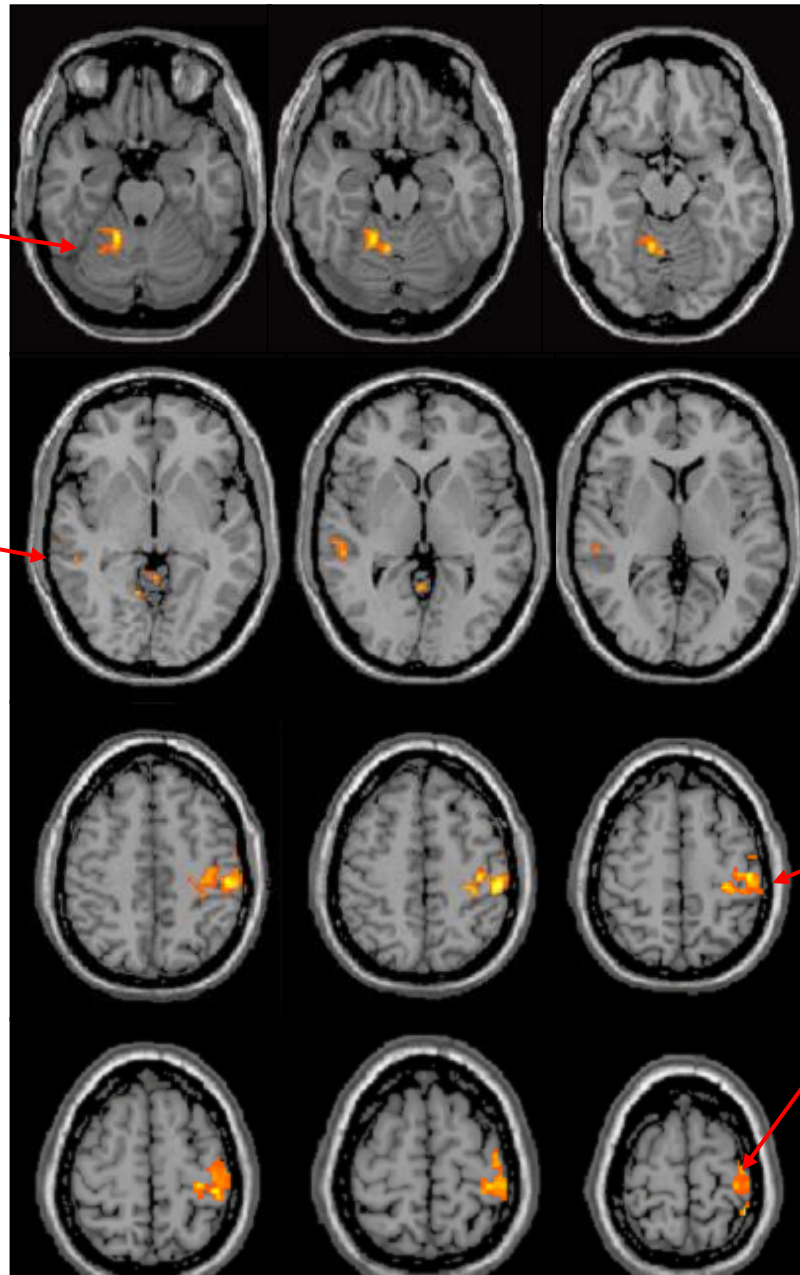
ipsilateral cerebellum

ipsilateral STG

R

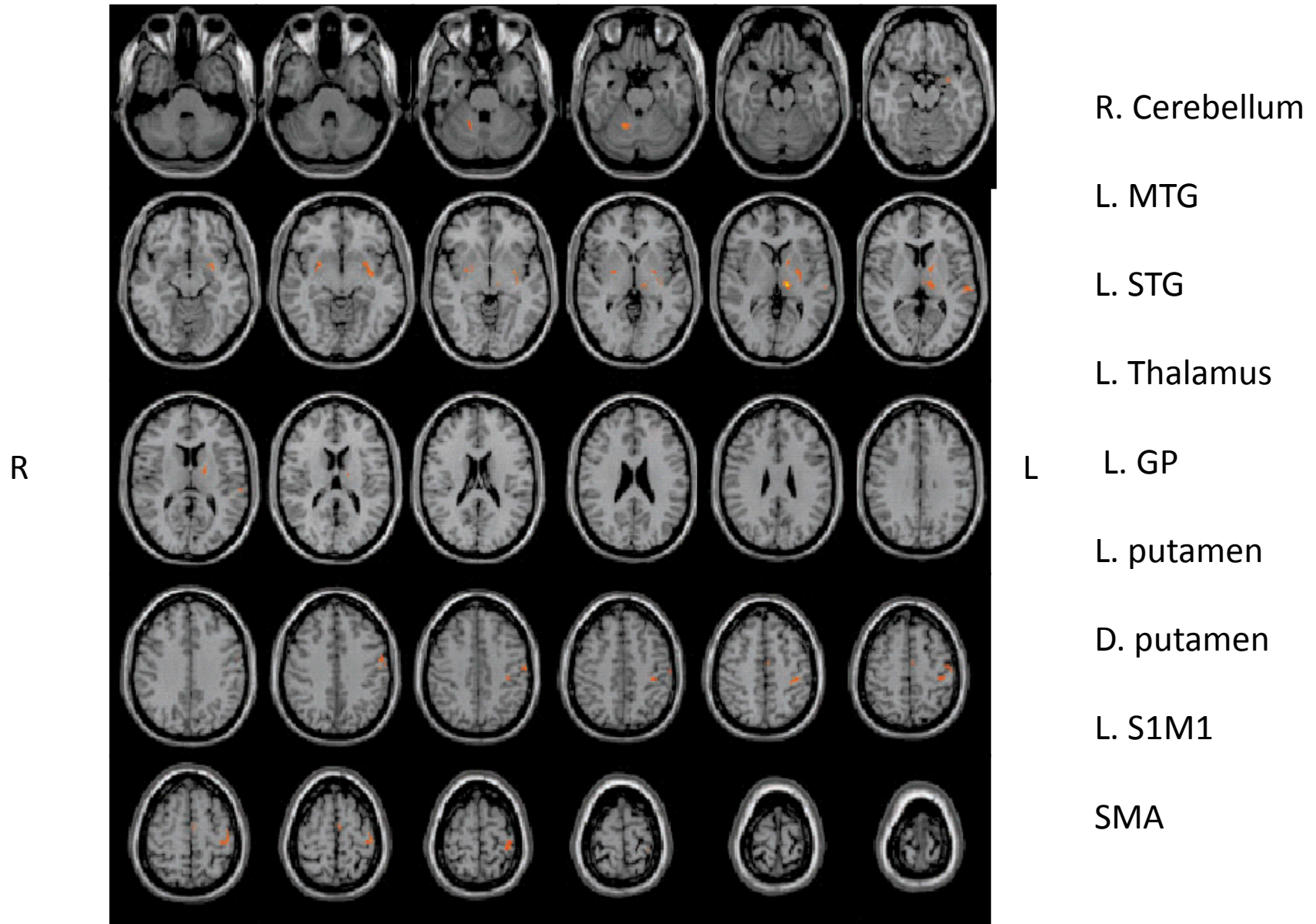
L

contralateral S1M1
and PM

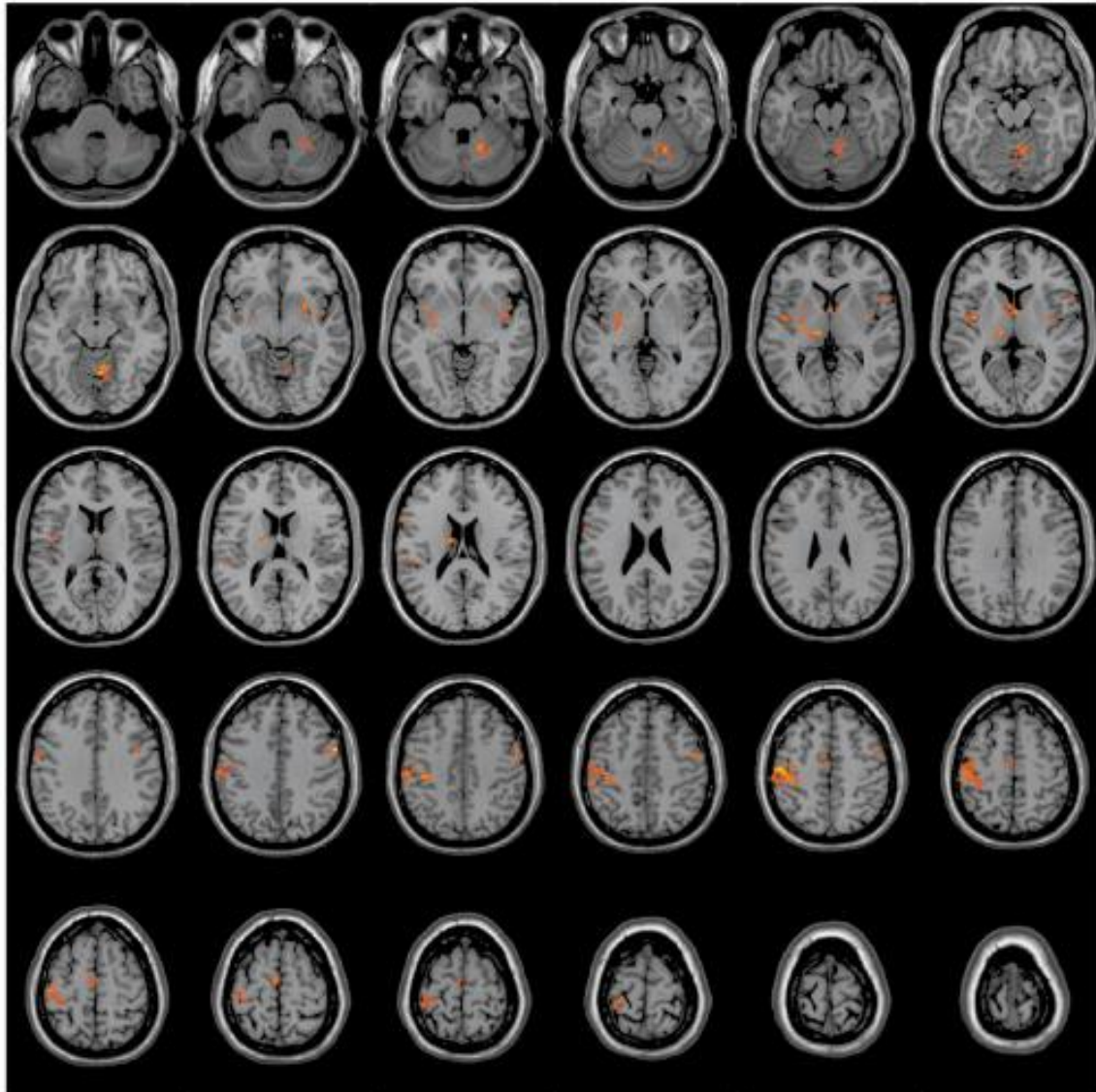


Cerasa et al, 2006

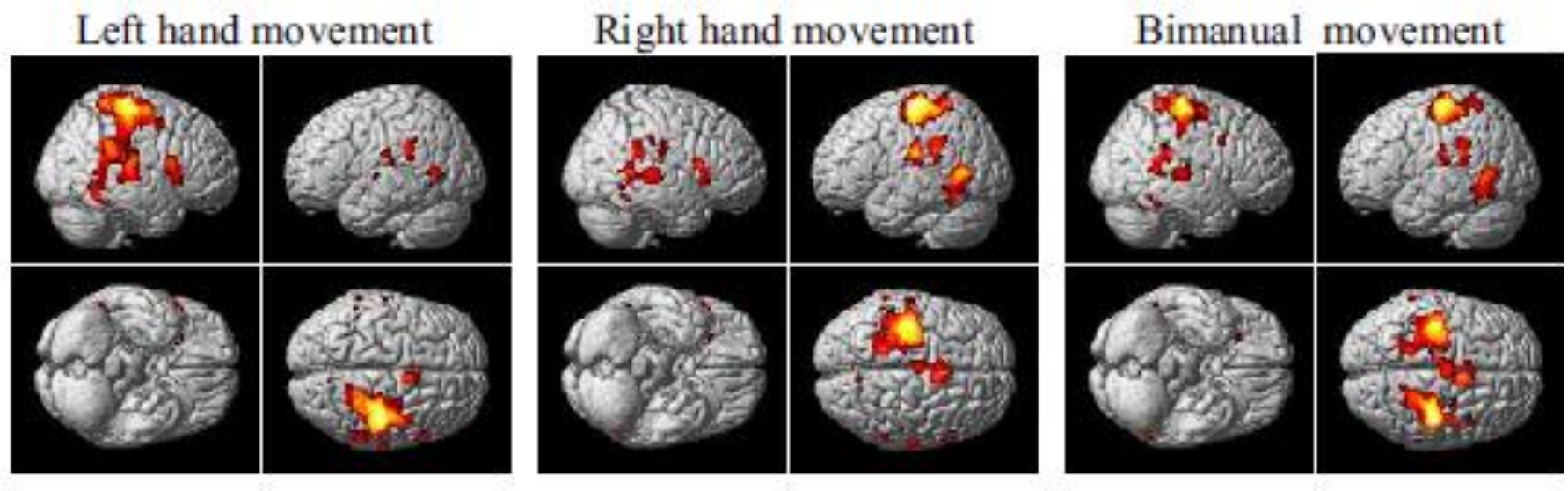
BOLD-activation Finger tapping Right hand complex acoustic stimulus (external cue)



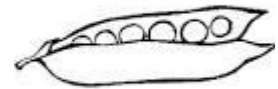
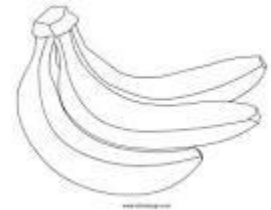
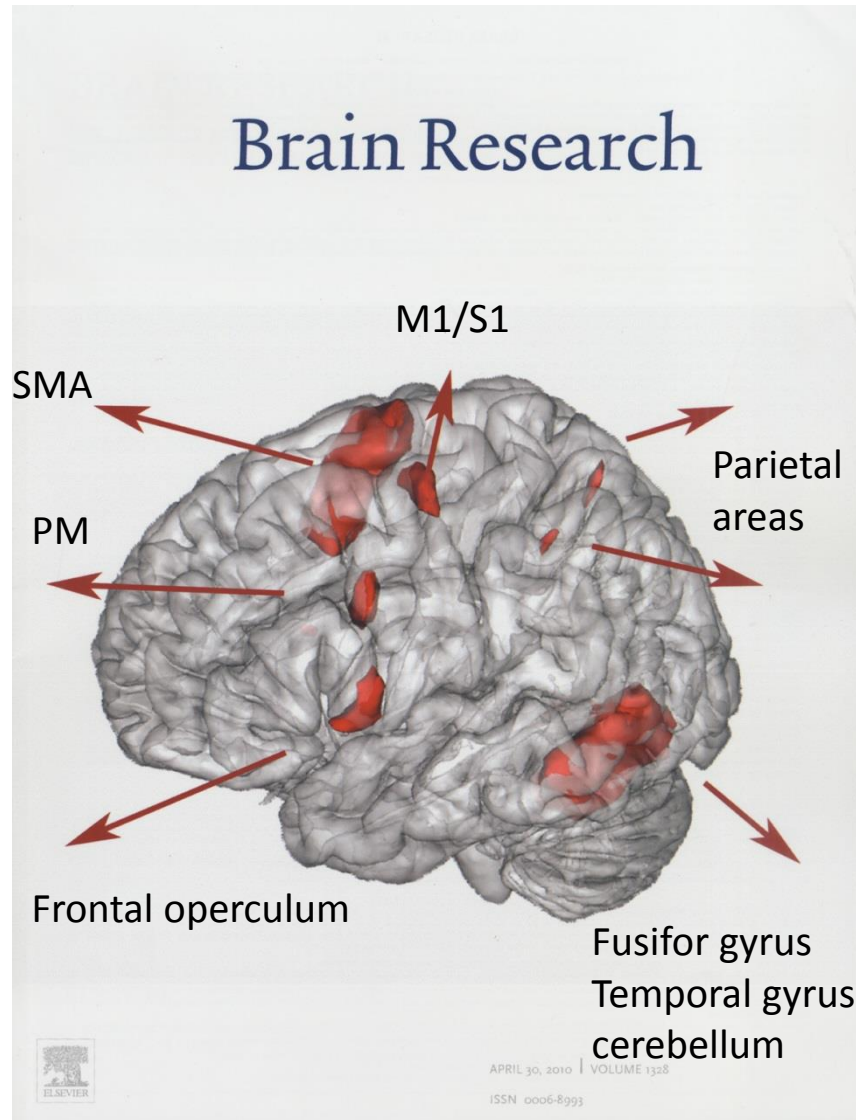
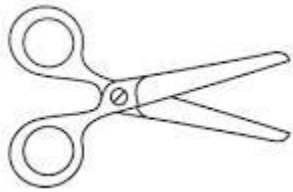
BOLD-activation Finger tapping Left hand simple visual stimulus (external cue)



BOLD-activation Finger tapping Left, Right hand, both hands,
induced by simple acoustic stimulus (external cue)



BOLD-activation induced by mental representation of action





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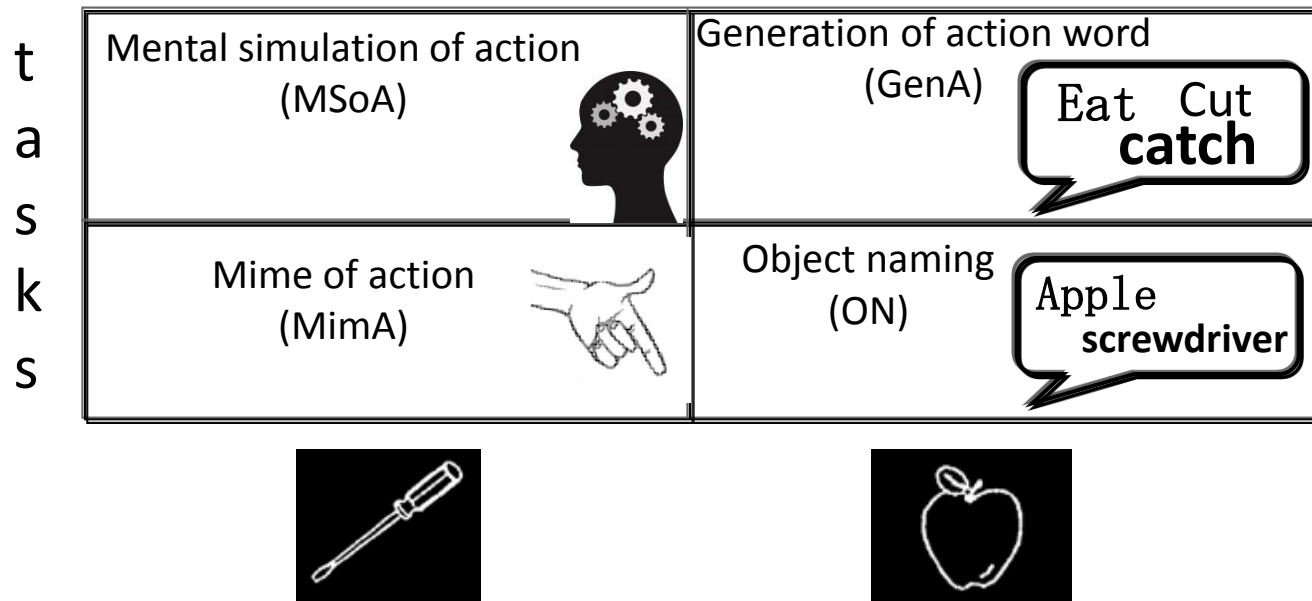
www.elsevier.com/locate/brainres

BRAIN
RESEARCH

Research Report

Mental representations of action: The neural correlates of the verbal and motor components

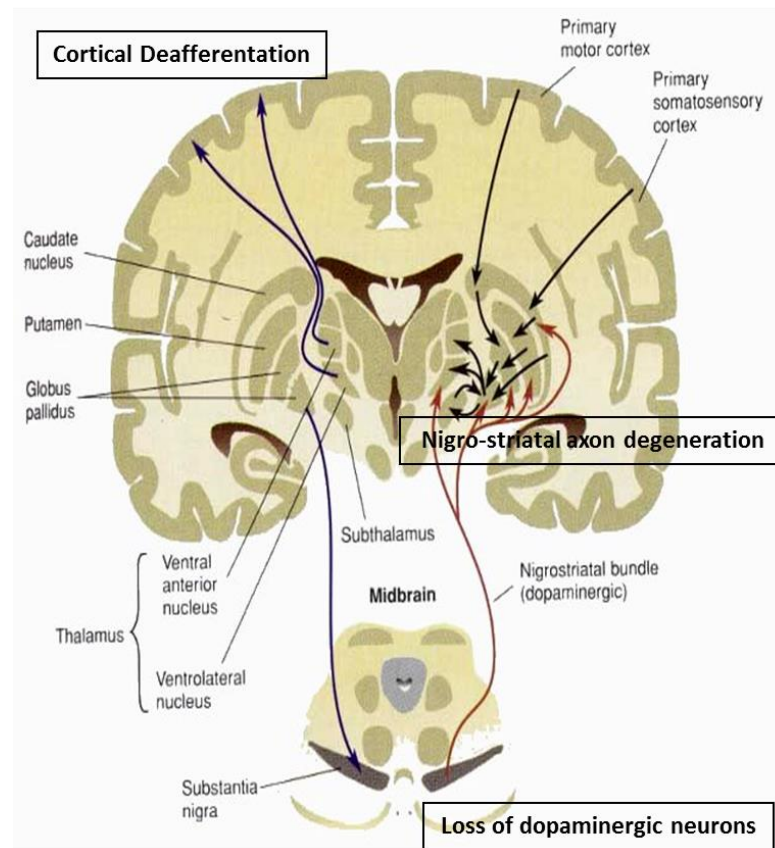
Patrice Péran^{a,b,*}, Jean-François Démonet^b, Andrea Cherubini^a, Dominique Carbebat^b, Carlo Caltagirone^{c,d}, Umberto Sabatini^a



Key point 4

- Parkinson's disease: a model of plasticity of the motor system

Idiopathic Parkinson



Supplementary and Primary Sensory Motor Area Activity in Parkinson's Disease

Regional Cerebral Blood Flow Changes During Finger Movements and Effects of Apomorphine

Olivier Rascol, MD; Umberto Sabatini, MD; François Chollet, MD; Pierre Celsis, MD; Jean-Louis Montastruc, MD, PhD; Jean-Pierre Marc-Vergnes, MD, PhD; André Rascol

Ann Neurol 1992 Aug;32(2):151-61

Impaired mesial frontal and putamen activation in Parkinson's disease: a positron emission tomography study

Playford ED, Jenkins IH, Passingham RE, Nutt J, Frackowiak RS, Brooks DJ

Ann Neurol 1992 Dec;32(6):749-57

Impaired activation of the supplementary motor area in Parkinson's disease is reversed when akinesia is treated with apomorphine

Jenkins IH, Fernandez W, Playford ED, Lees AJ, Frackowiak RS, Passingham RE

Adv Neurol 1993;60:419-21

Impaired Activity of the Supplementary Motor Area in Akinetic Patients with Parkinson's Disease Improvement by the Dopamine Agonist Apomorphine

O. J. Rascol, U. Sabatini^{*†}, F. Chollet^{*‡}, J. L. Montastruc, J. P. Marc-Vergnes^{*}, and A. Rascol^{*‡}

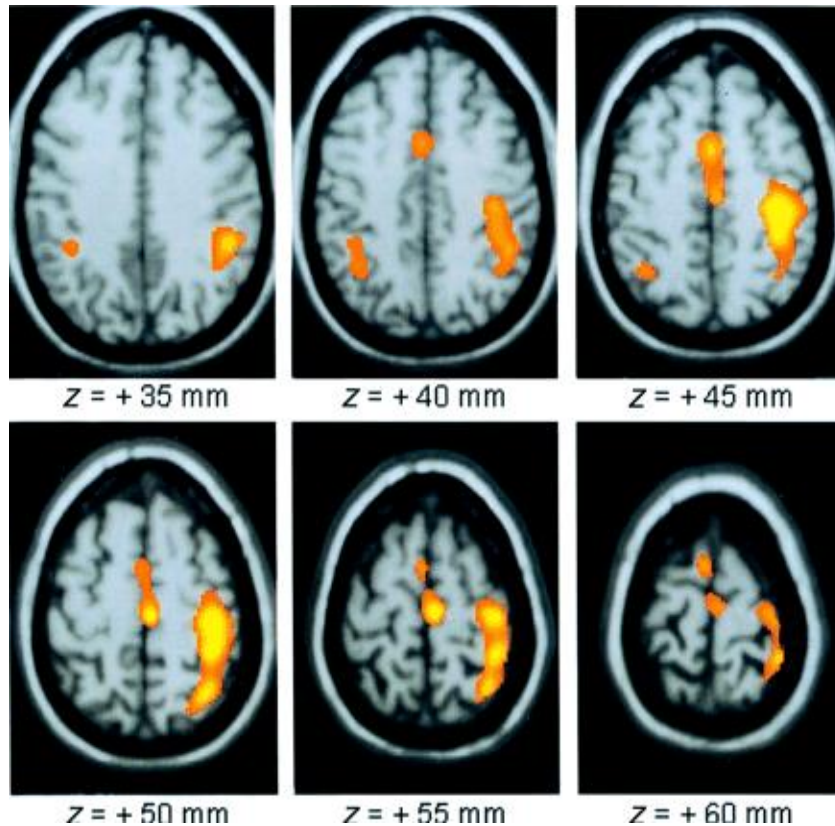
Journal of Neurology, Neurosurgery, and Psychiatry 1994;57:567-571

Normal activation of the supplementary motor area in patients with Parkinson's disease undergoing long-term treatment with levodopa

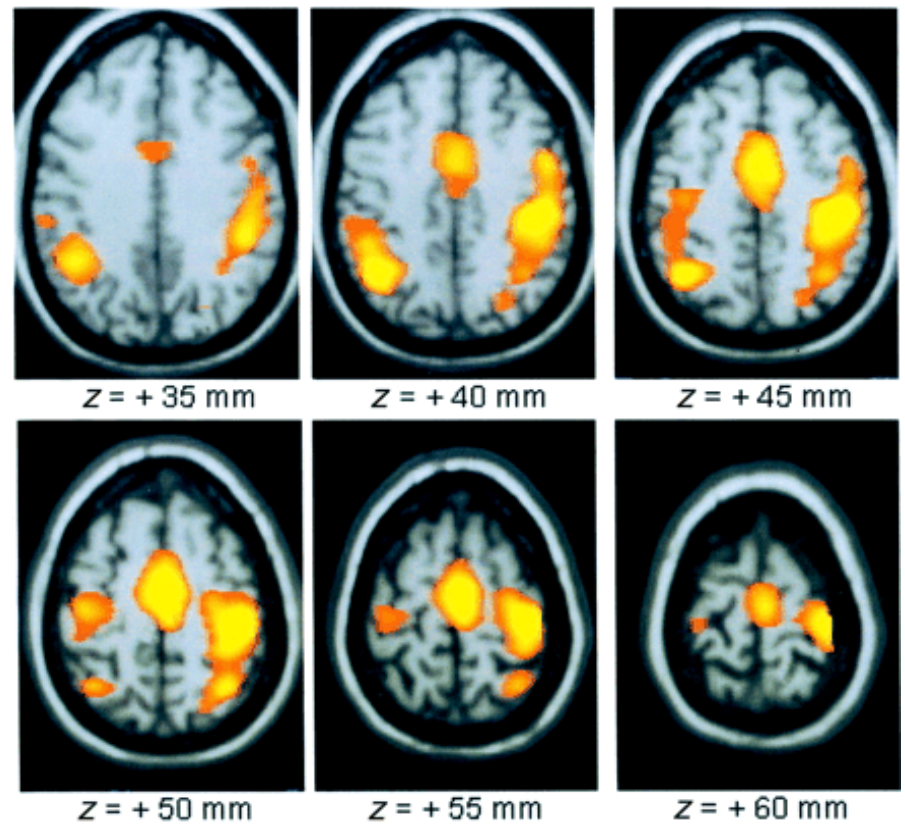
O Rascol, U Sabatini, F Chollet, N Fabre, J M Senard, J L Montastruc, P Celsis, J P Marc-Vergnes, A Rascol

BOLD-activation Finger tapping Right hand (internal cue)*

Normals



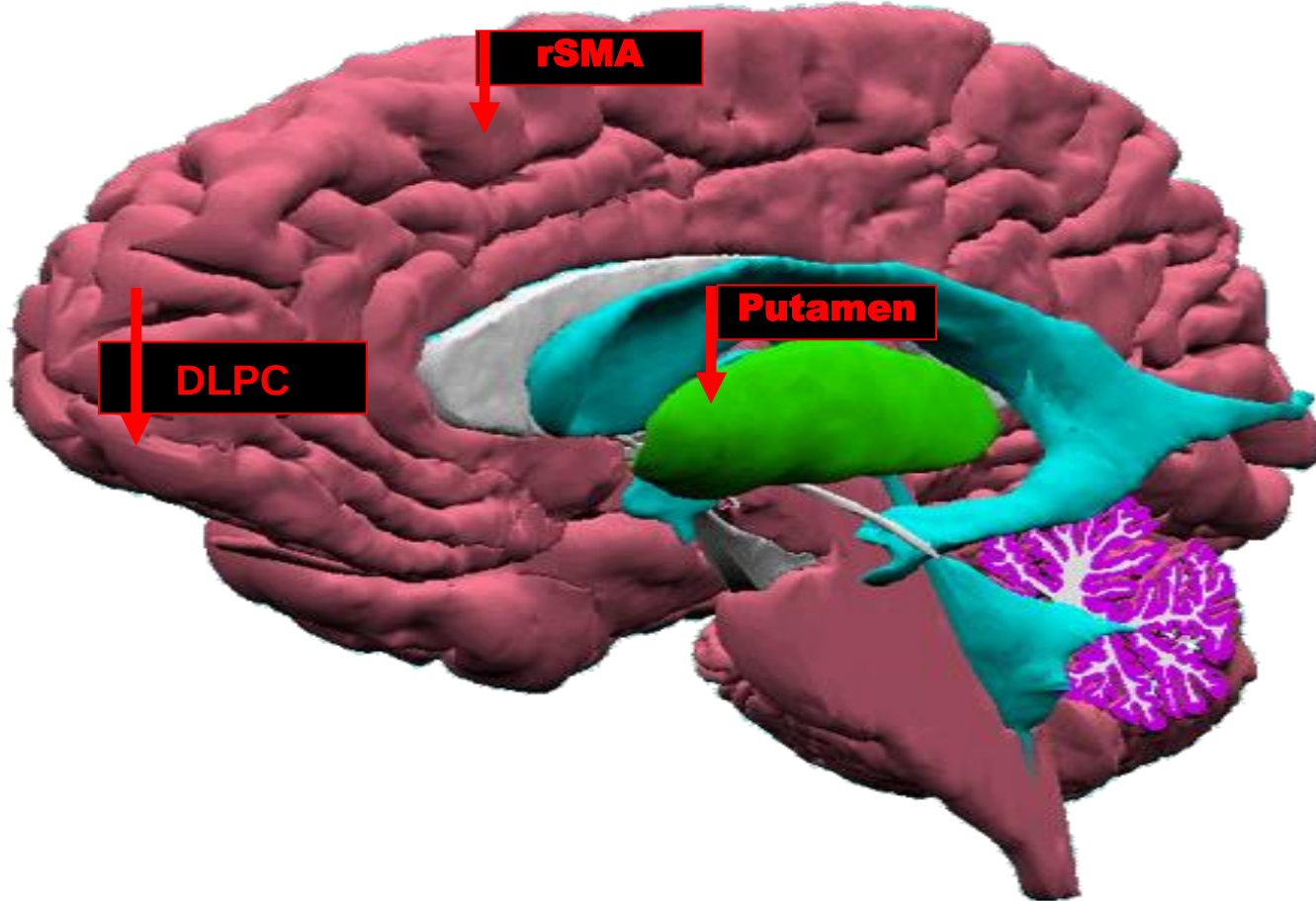
Parkinson Disease



(DD 5 years, UPDRS off 16, Hoehn Yahr 2.7)

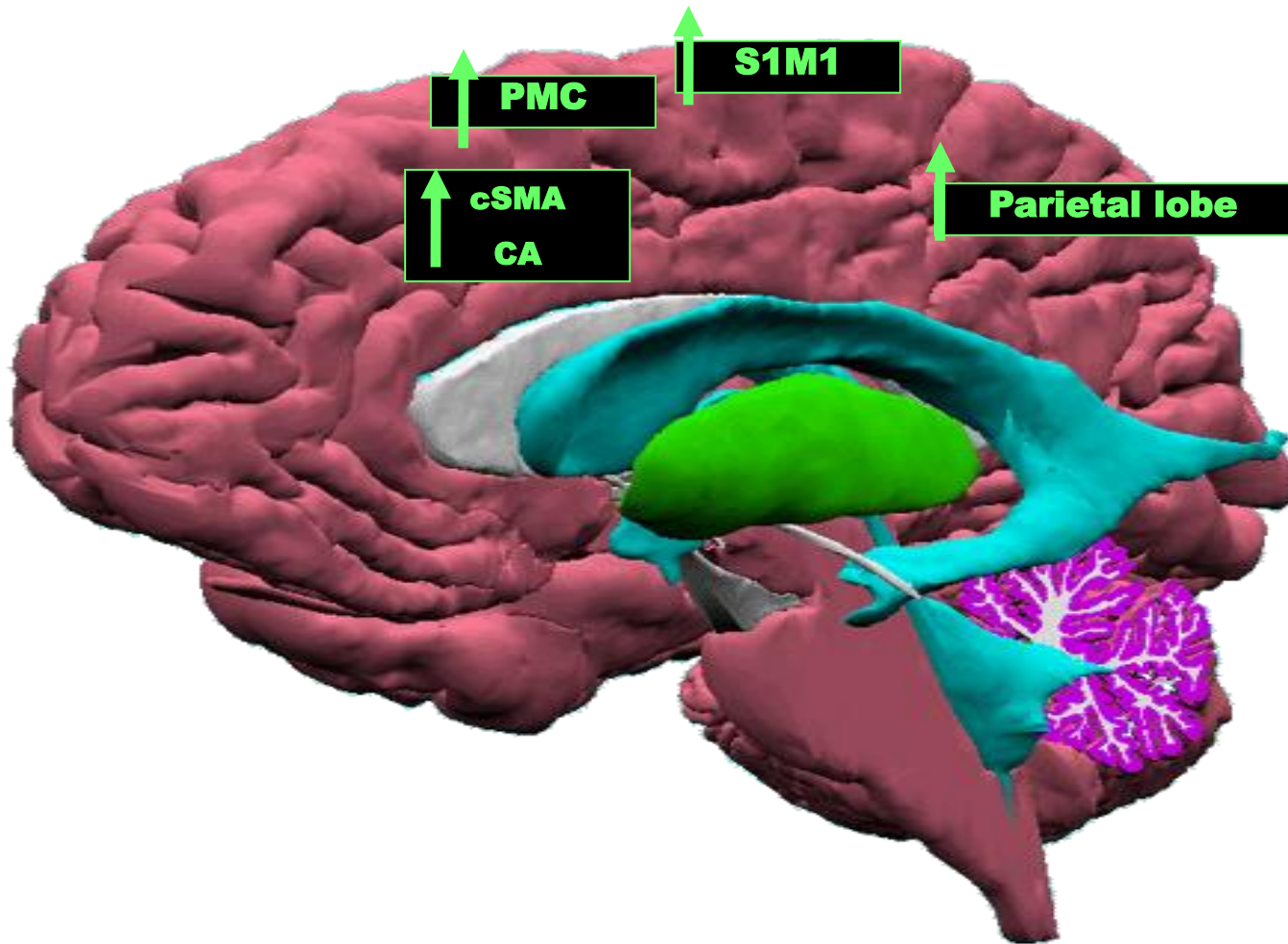
* M-task: finger to thumb oppositions, fist twice, finger to thumb oppositions

Functional mapping of the motor system in PD



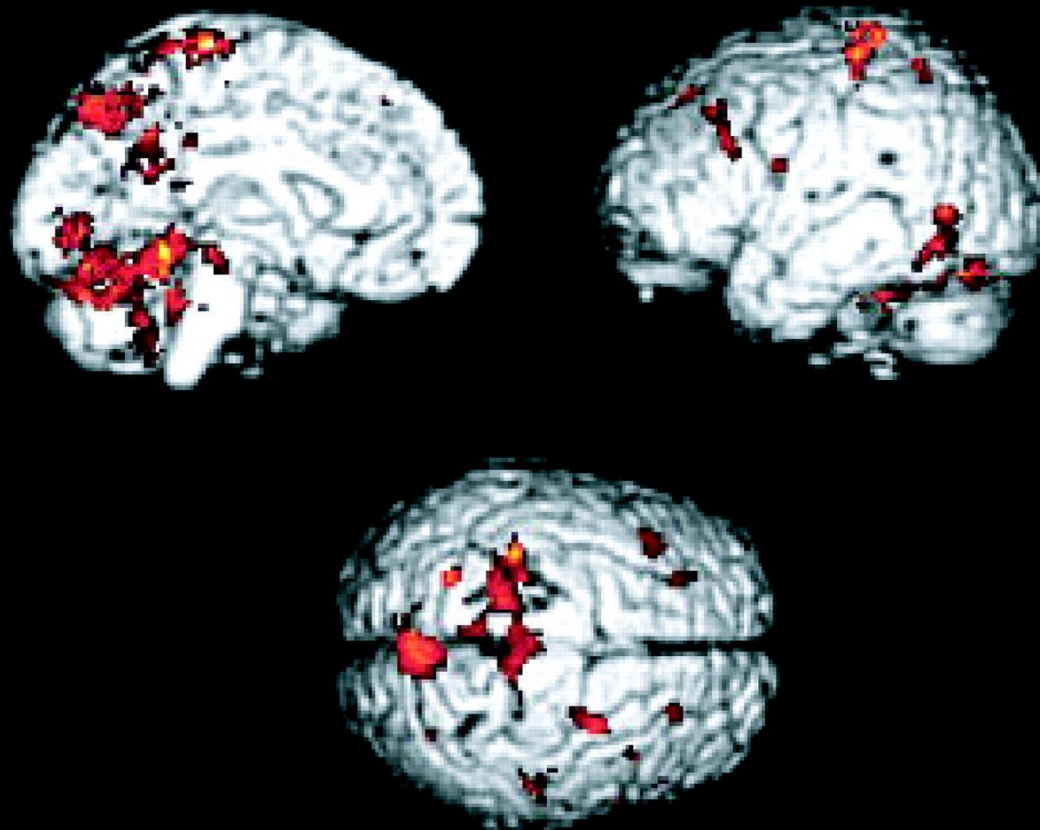
SMA contributes to the preparation/execution of learned motor sequences. Its decreased activation contributes to the lack of readiness and to the difficulty in initiating voluntary movements in PD

Functional mapping of the motor system in PD



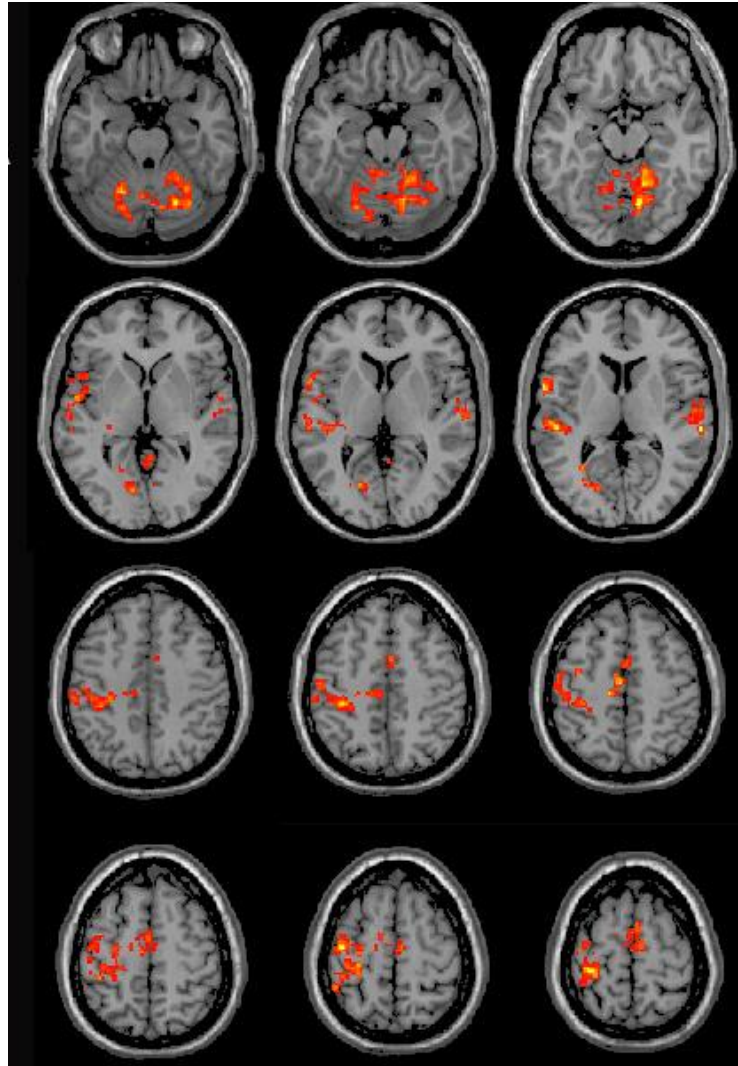
Hyperactivation of cortical areas may reflect a functional compensation for the defective basal ganglia. PD patients need compensatory activity of other motor circuits to overcome their difficulty in performing self-initiated movements

A functional MRI study of automatic movements in patients with Parkinson's disease



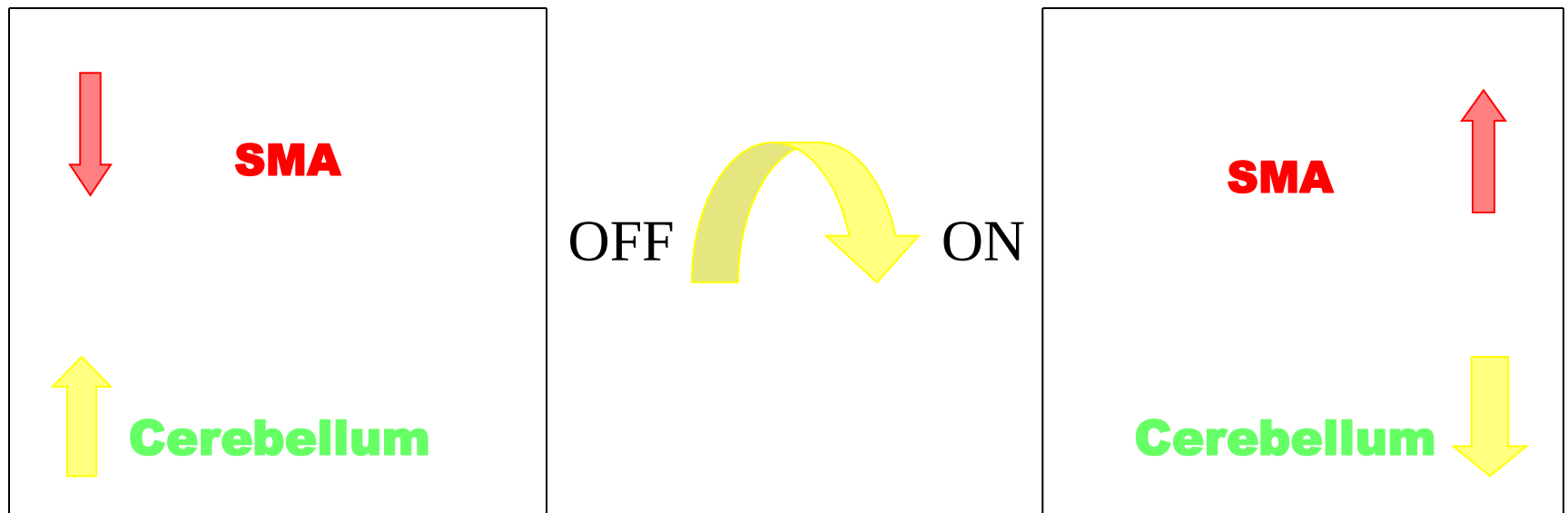
Brain areas more activated in PD patients than in normal subjects during automatic execution of motor sequence

BOLD-activation Finger tapping left hand
induced by simple visual stimulus (external cue)

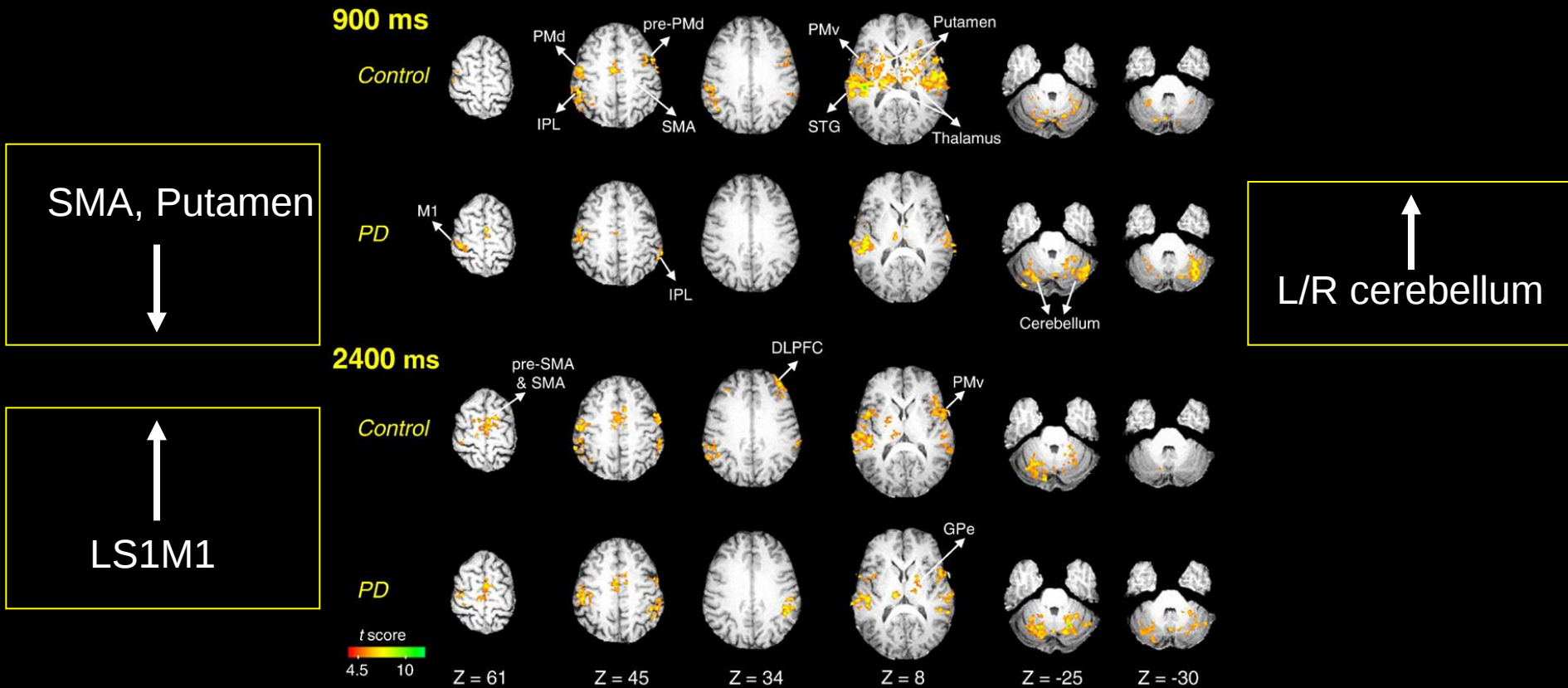


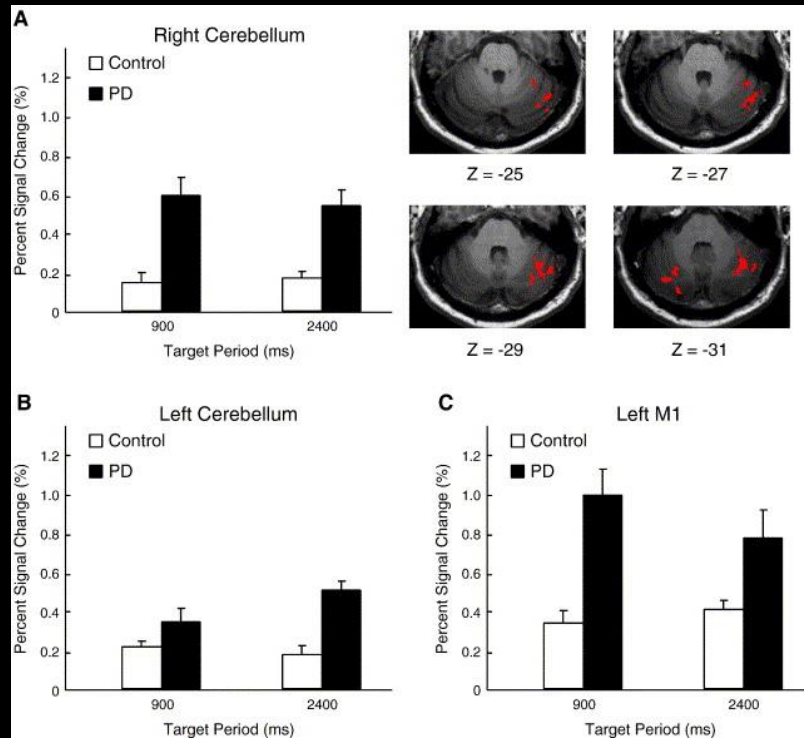
Parkinson disease

The ipsilateral cerebellar hemisphere is overactive during hand movements in akinetic parkinsonian patients



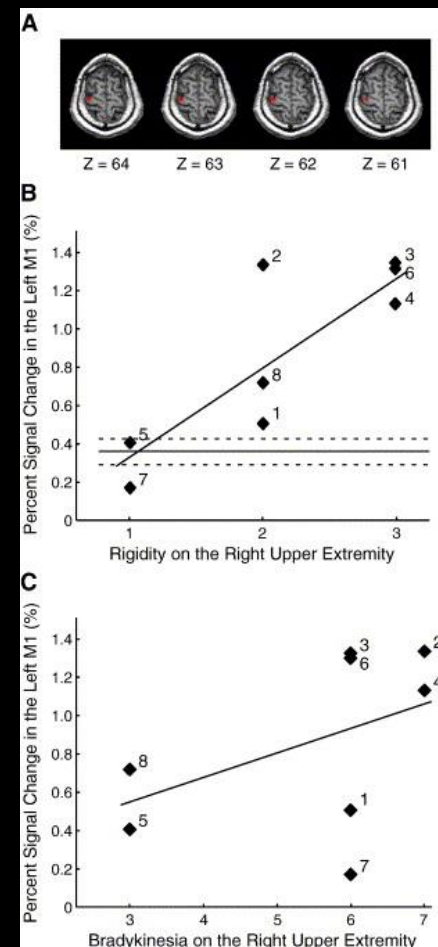
Role of hyperactive cerebellum and motor cortex in Parkinson's disease





cerebellar hyperactivation is a compensatory mechanism for the defective basal ganglia

S1/M1 hyperactivation is not only a compensatory response but is related to upper limb rigidity



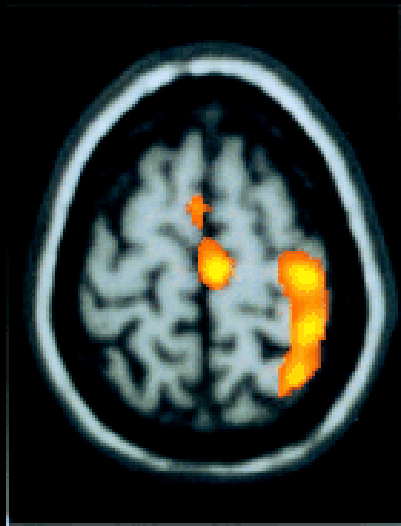
PD – OFF phase



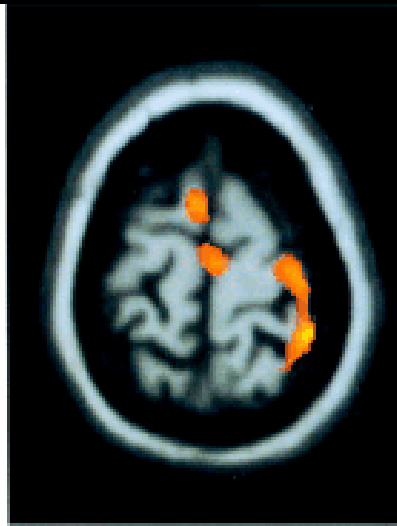
Motor activation



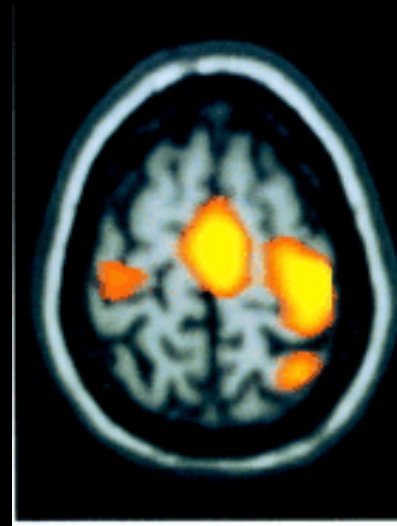
↓ Activity of rostral SMA



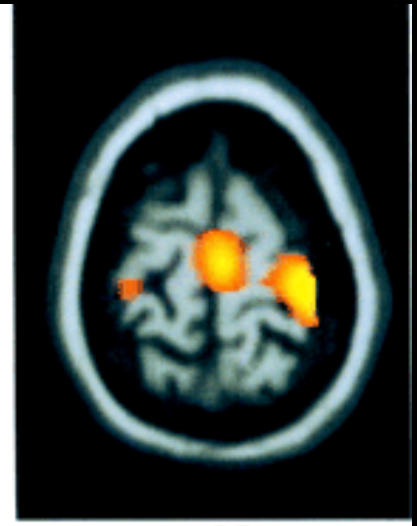
Z = +55 mm



Z = +60 mm



Z = +55 mm

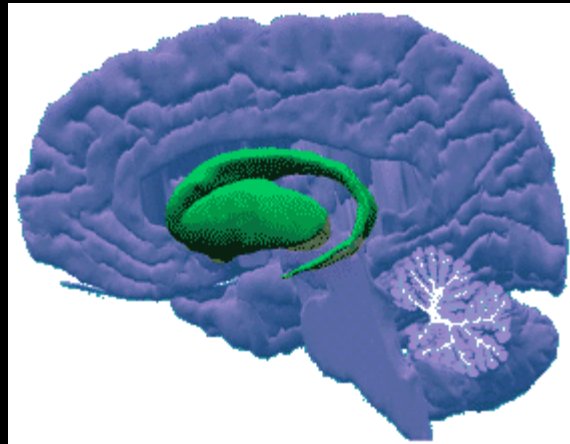
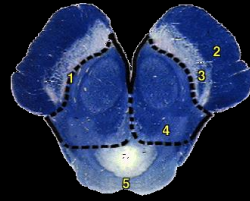


Z = +60 mm



ON - PHASE

Reversible after dopaminergic therapy



Dopaminergic agonist

surgery



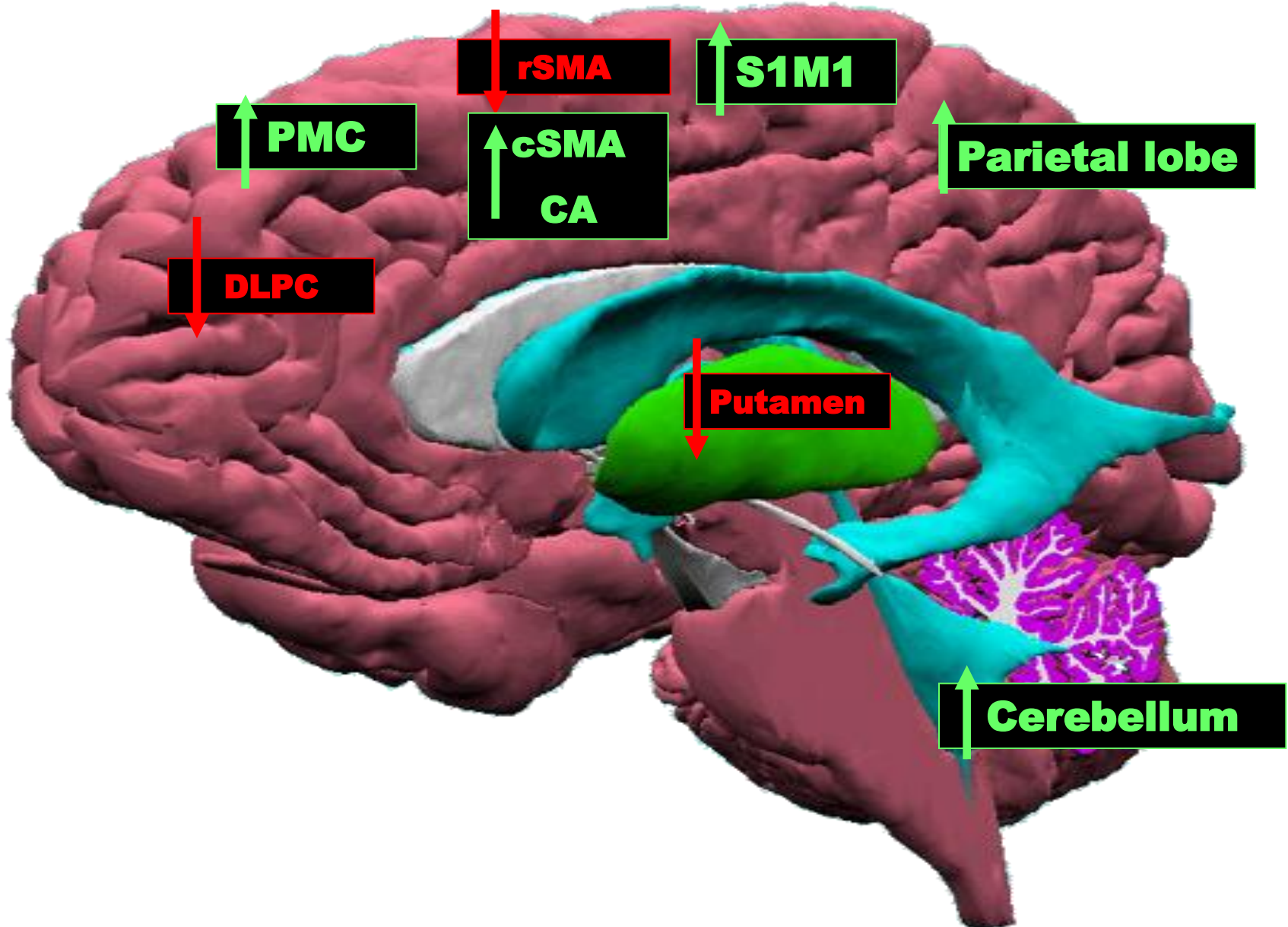
Functional deafferentation

M1, SMA, PM



Brain plasticity

Functional remapping of the motor system in PD



BOLD fMRI Hypoactivation in de novo PD during Motor Tasks

Grip Force Transducer



Fiber Optic Interrogator



Visual Displays

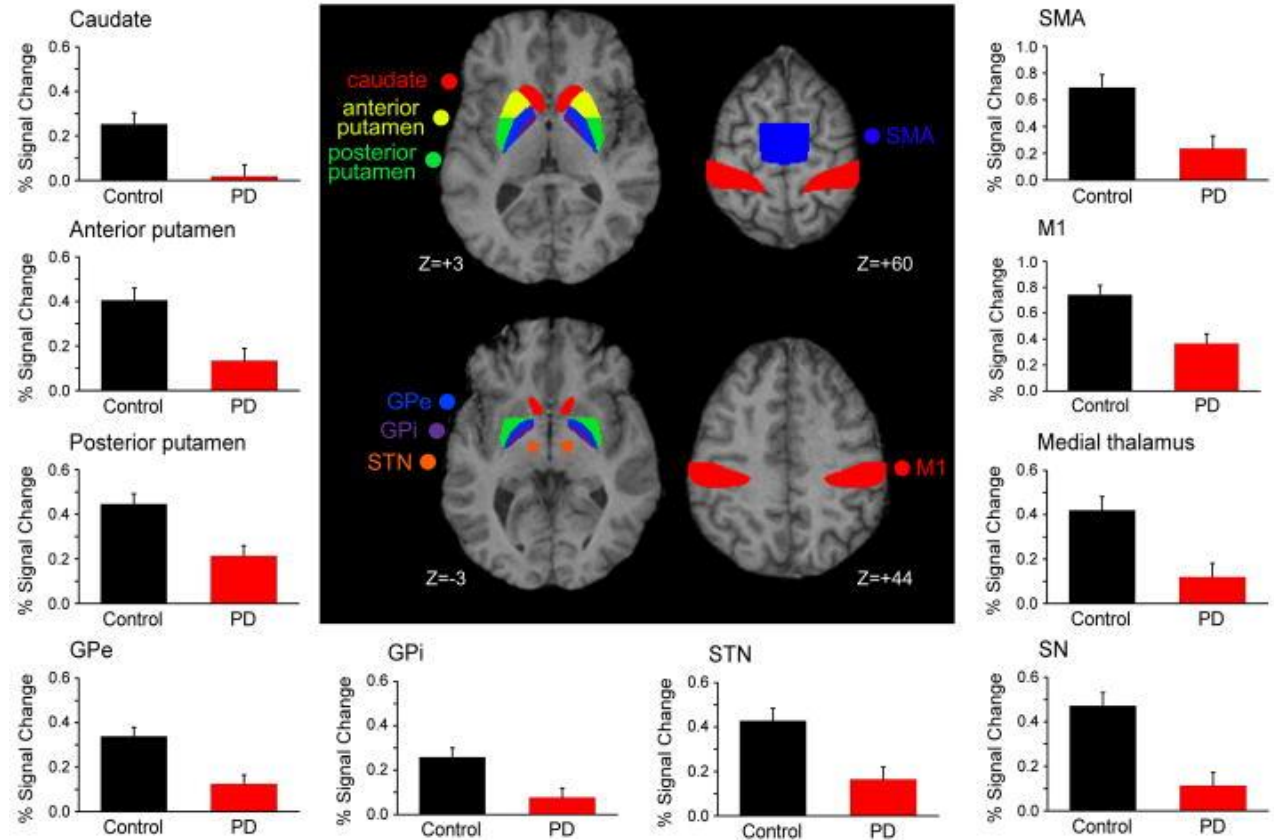
Rest



Force



Visually guided M-task





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journal homepage: www.elsevier.com/locate/cortex



Special issue: Original article

Object naming and action-verb generation in Parkinson's disease: A fMRI study

Patrice Péran^{a,b,*}, Dominique Cardebat^b, Andrea Cherubini^a, Fabrizio Piras^{c,d},
Giacomo Luccichenti^a, Antonella Peppe^e, Carlo Caltagirone^{e,f}, Olivier Rascol^b,
Jean-François Démonet^b and Umberto Sabatini^a

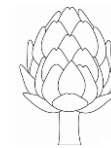
t
a
s
k
s

Object naming
(ON)

Apple pen
screwdriver

Generation of action word
(GenA)

Eat Cut
catch



.....

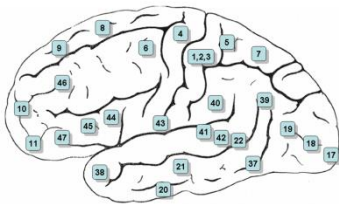
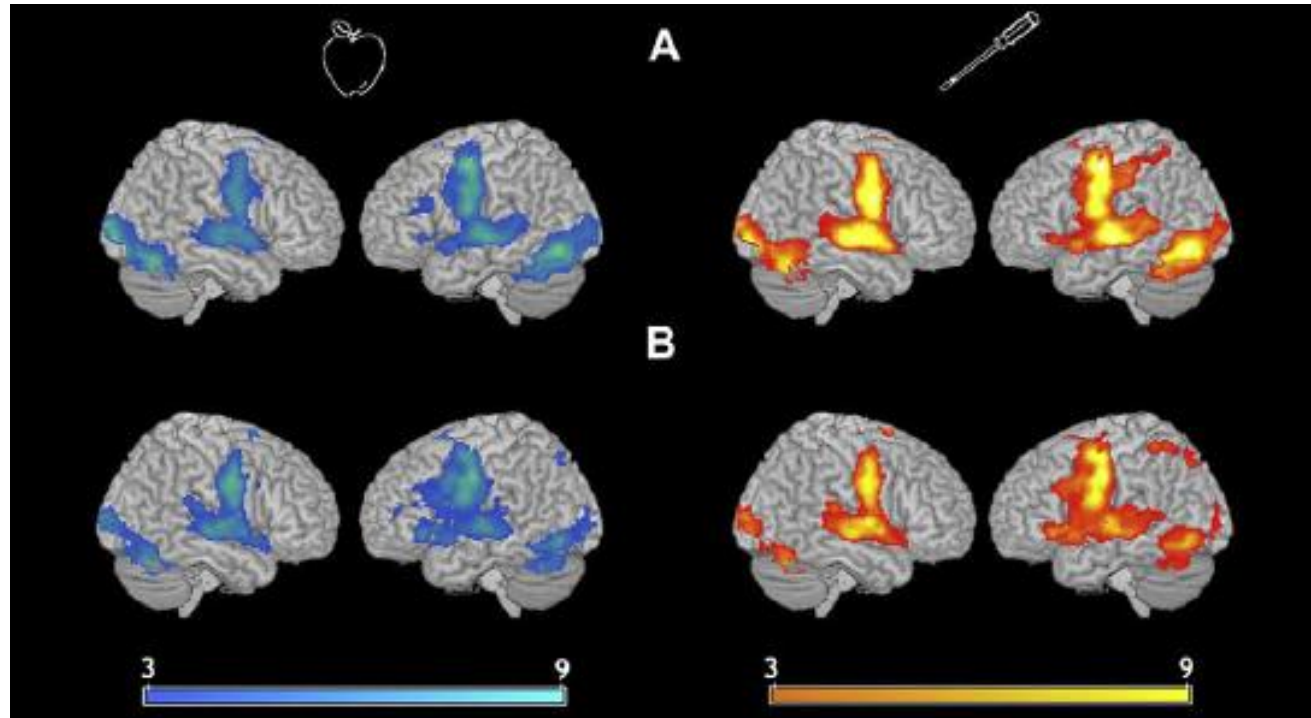
Common neural network for object naming and generation action word

Object naming
(ON)

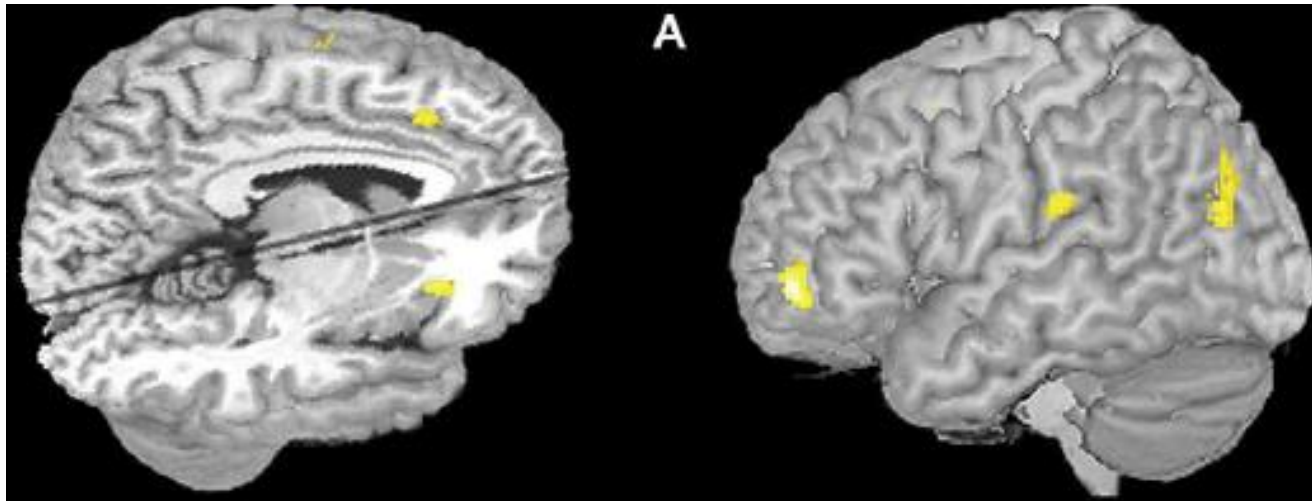
Apple
screwdriver

Generation of action word
(GenA)

Eat Cut
catch



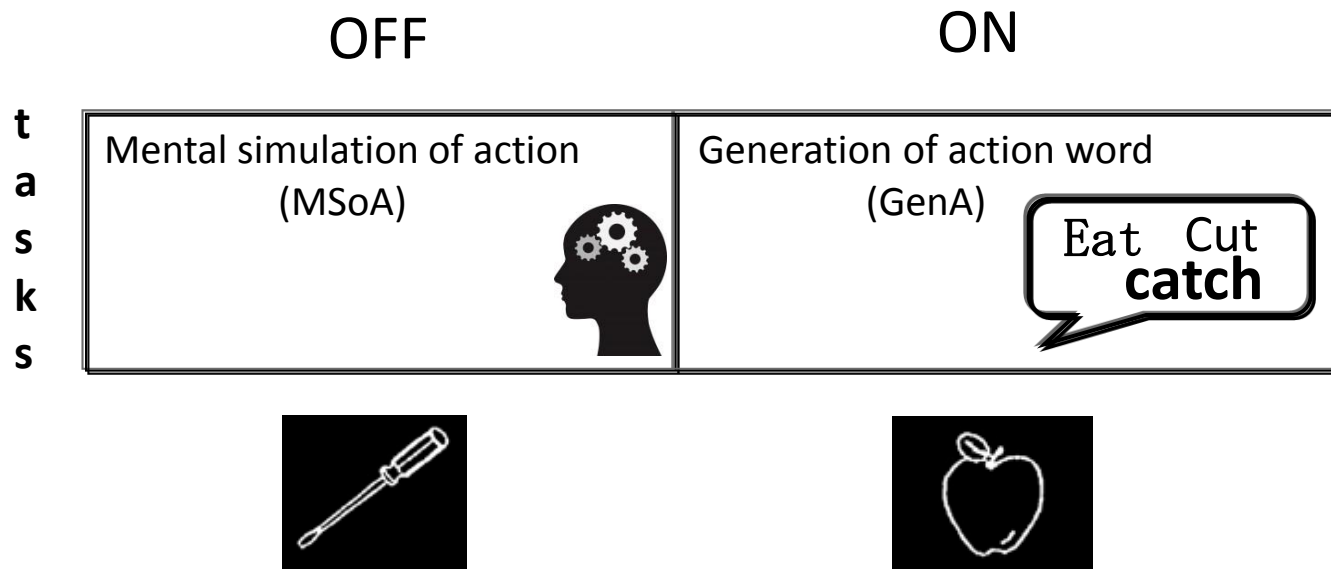
Bilateral activations in the frontal (4, 6, 43, 44) and superior temporal (22, 41, 42), insula, occipital cortices (18, 19, 37), SMA and Cingulate (6, 32, 24), cerebellum



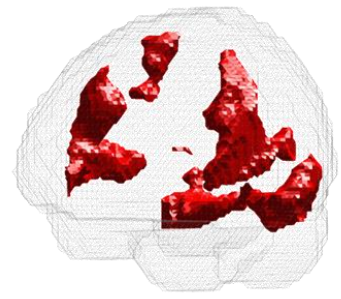
GenA: greater extent of activations in both prefrontal cortices, left middle frontal cortex, left supramarginal gyrus, anterior cingulate, left middle occipital cortex, additionally cluster in the left parietal cortex

Effect of levodopa on both verbal and motor representations of action in Parkinson's disease: A fMRI study

P. Péran^{a,b,c,*}, F. Nemmi^c, D. Méligne^{a,b}, D. Cardebat^{a,b}, A. Peppe^d, O. Rascol^{a,b,e}, C. Caltagirone^{d,f}, J.F. Demonet^g, U. Sabatini^c



Take home messages



- Functional imaging and PD:
 - how PD brain works
 - Pathophysiological mechanisms of PD
- Task-based functional imaging:
 - exploring the motor system of PD
- Motor system and Parkinson's disease:
 - Defective and compensatory mechanisms
 - Plasticity of the motor system



Questo viaggio
non è per i piedi

Plotino

Grazie