

# **Nuclear neurology**



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# To refresh your memory

- Brain has a **high rate of oxidative metabolism**. It has **no reserves** either of **oxygen** or of **glucose** and has a very limited capacity for anaerobic metabolism. Therefore normal **brain function** is critically **dependent on** maintenance of an adequate **blood supply**. There is a linear association between glucose metabolism and functional activity of the brain.
- Normal cerebral blood perfusion: 50-60 ml/min/100g
- Cortex: 65-85 ml/min/100g
- White matter: 25-35 ml/min/100g
- **No EEG activity: below 17 ml**
- **Failure of Na/K ATP-ase: below 10 ml**

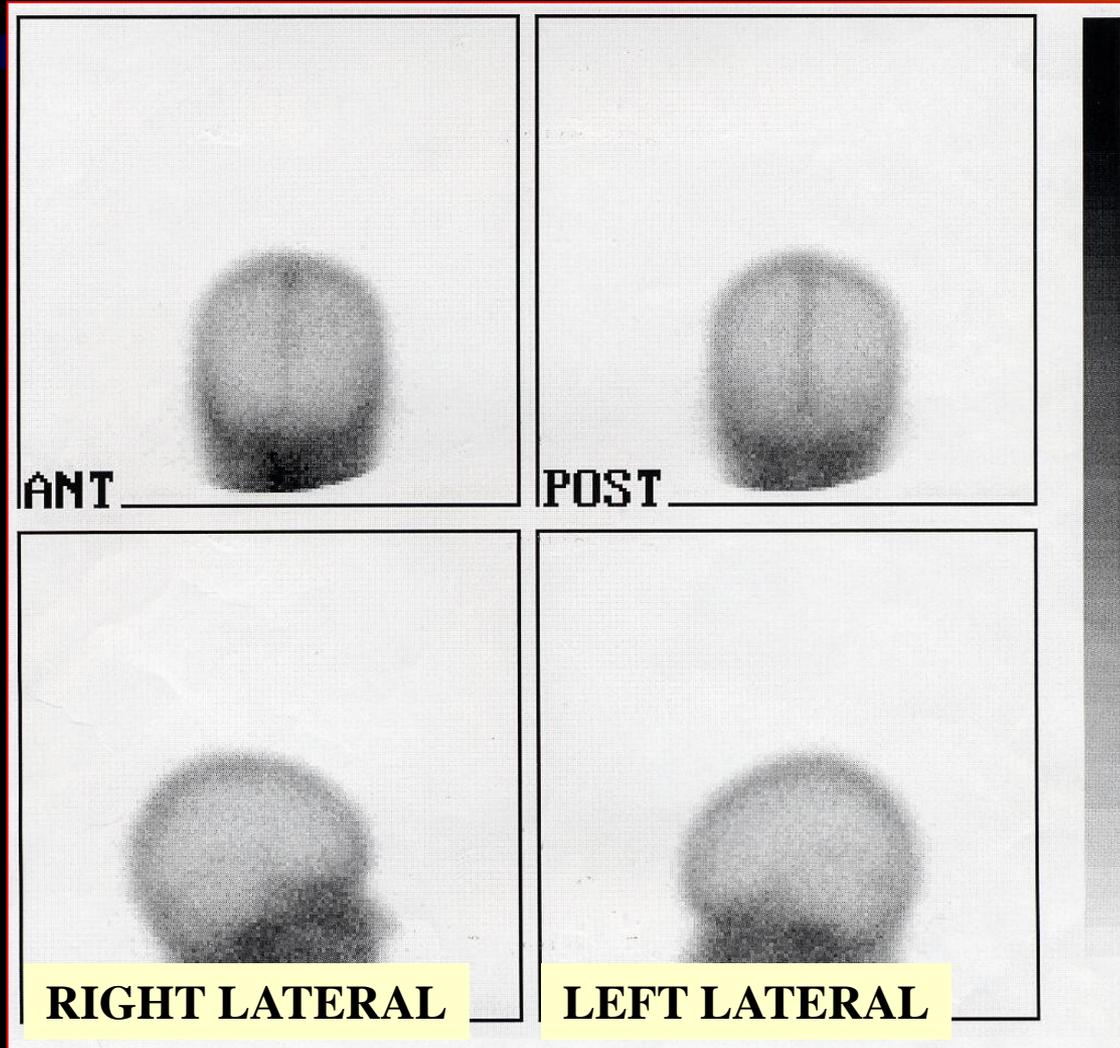
# Methods

- **Brain scintigraphy** - damaged blood-brain barrier (BBB)
- **Brain perfusion study** - vascular lesions (SPECT/CT)
- **Examination of cerebrospinal fluid (CSF)** - (dynamics, liquorrhoea)
- **Receptor studies** - gamma or positron emitting isotopes (SPECT/CT, PET/CT)
- **Glucose-, aminoacid metabolism, quantitative CBF examination** (PET/CT)

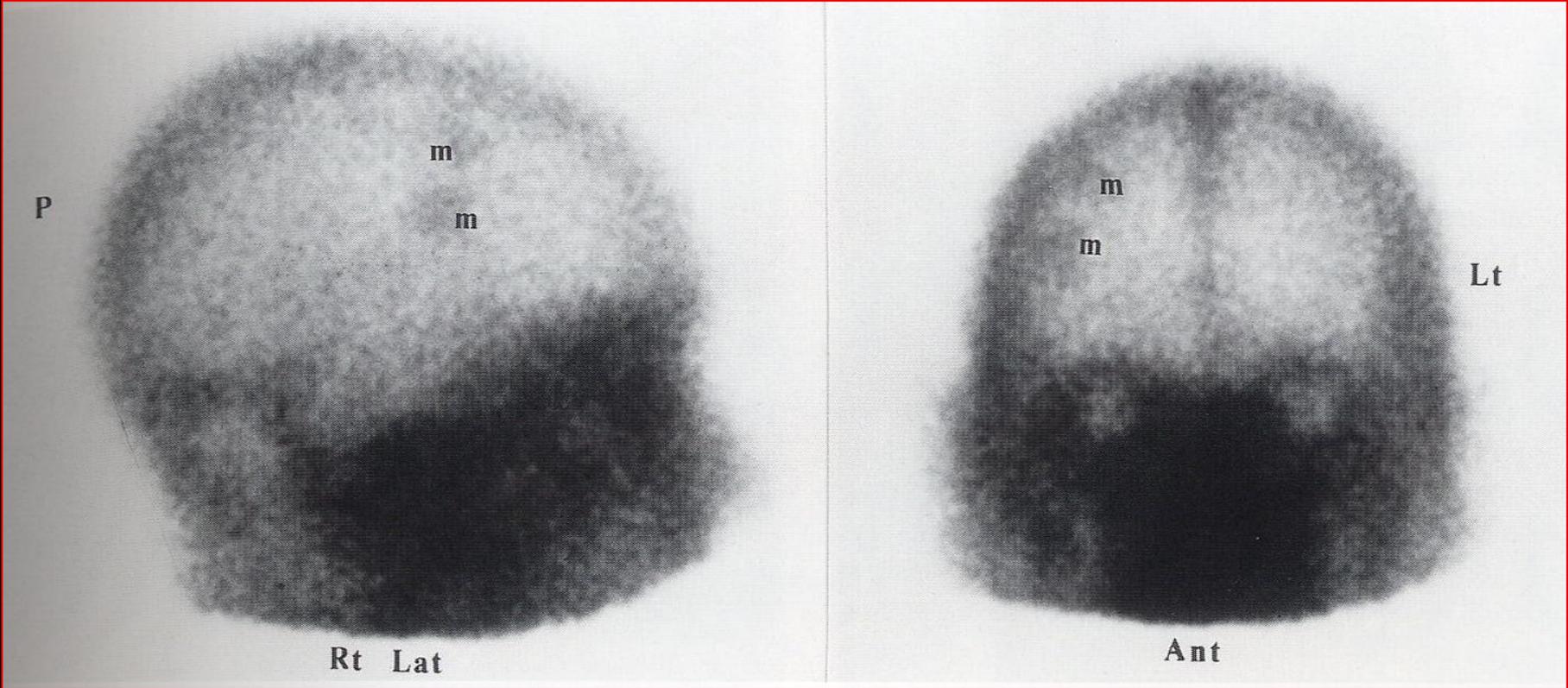
# Brain scintigraphy

- **Blood-brain barrier (BBB):** lipid-protein double layer  
- protective function
- **Radiopharmaceutical:** 500-750 MBq  $^{99m}\text{Tc}$ -DTPA  
i.v., 40 min. waiting
- 4 projection - static scans (A, P, right, left) + combined with SPECT or SPECT/CT scan (dual-head SPECT)
- **Abnormalities of permeability** indicate disruption of BBB (tumor, vasculare lesion), but CT and MR with contrast show more detailed anatomical correlations
- **Historical role:** confirmation of brain death

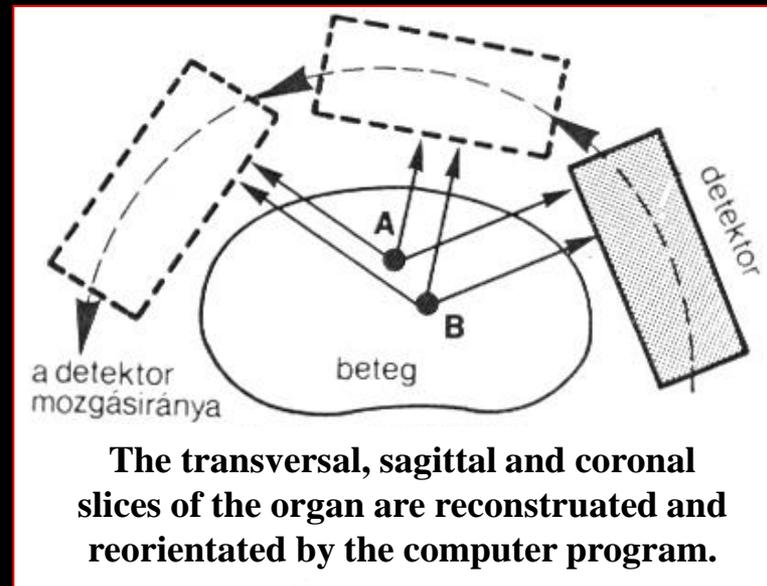
# Normal brain scintigraphy



# Cerebral metastases in the right hemisphere



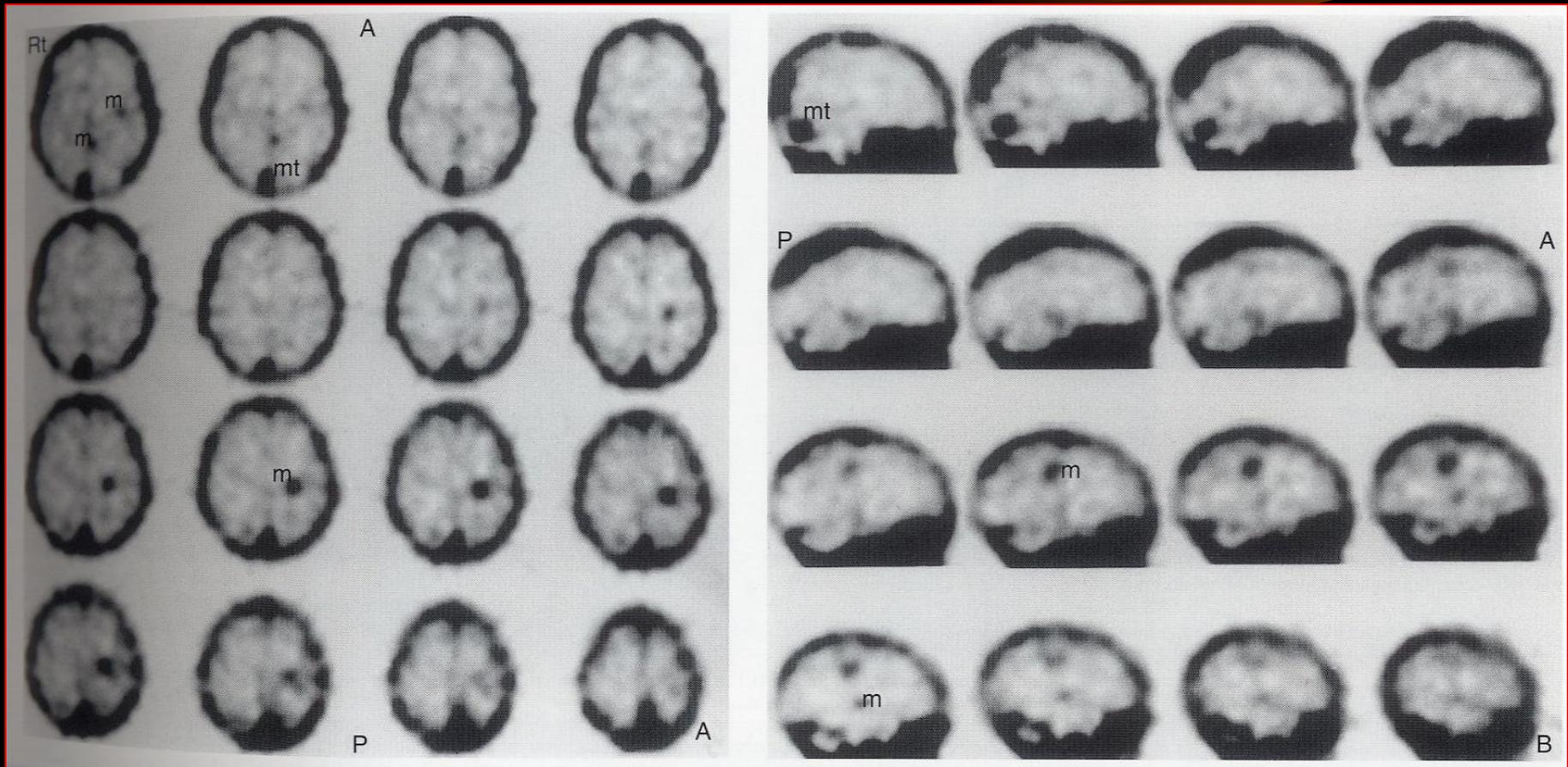
# SPECT (Single Photon Emission Computer Tomograph)



**The transversal, sagittal and coronal slices of the organ are reconstructed and reorientated by the computer program.**

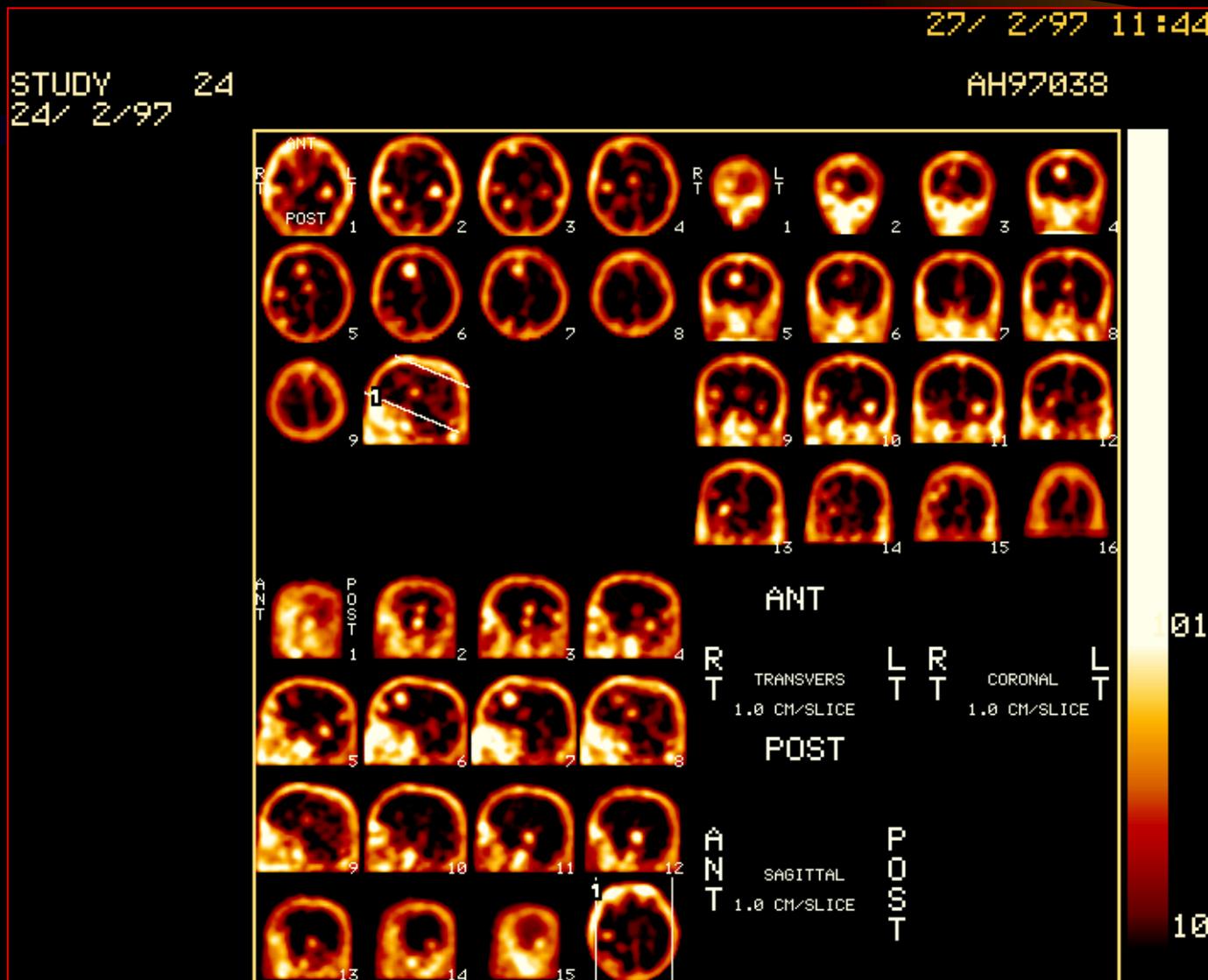
# Multiple metastatic lesion in the left hemisphere of the brain

## SPECT scan

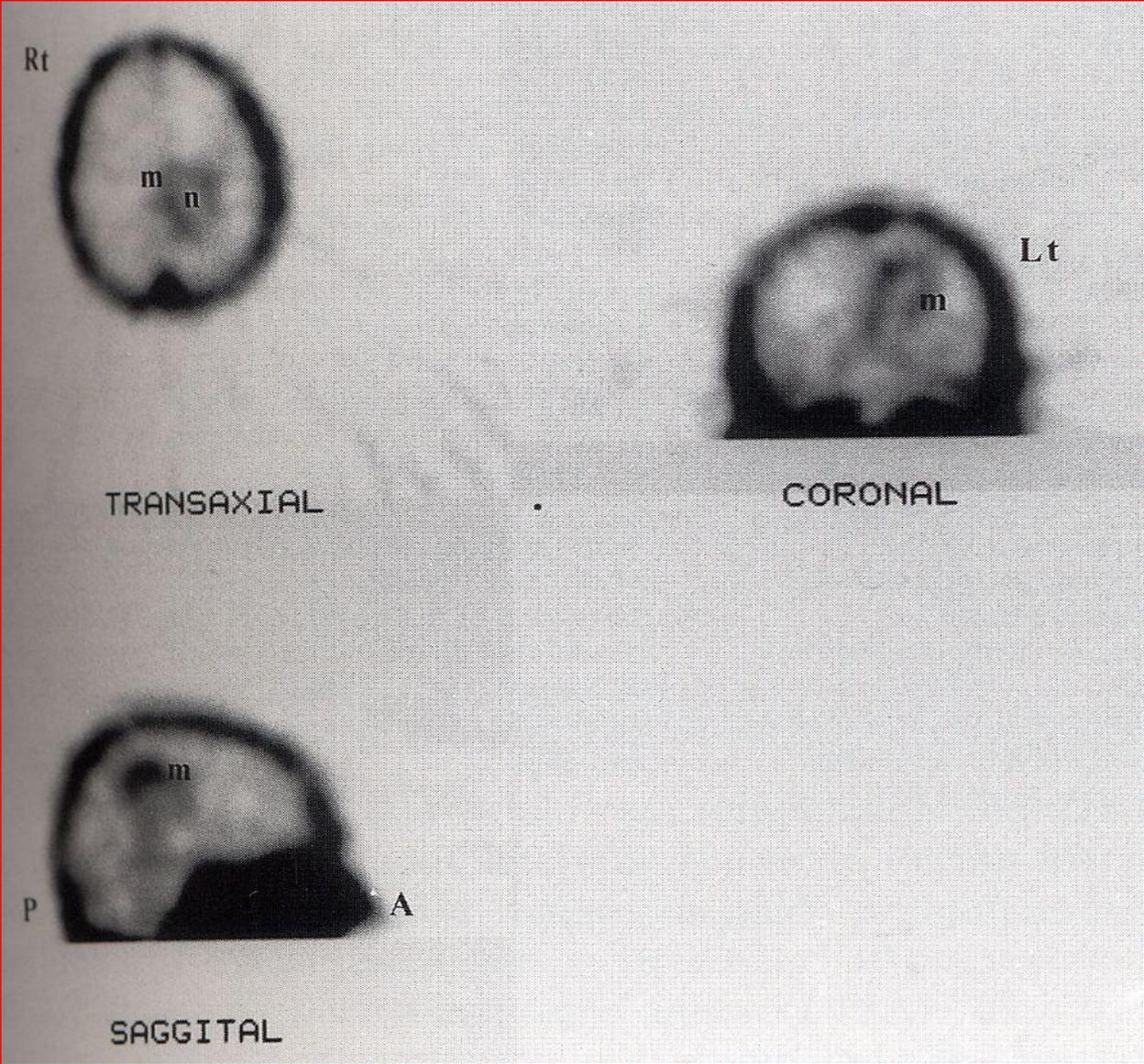


# Multiplex brain metastases in melanoma malignum

## SPECT imaging



# Cerebral embolisation in the left hemisphere



**SPECT  
scan**

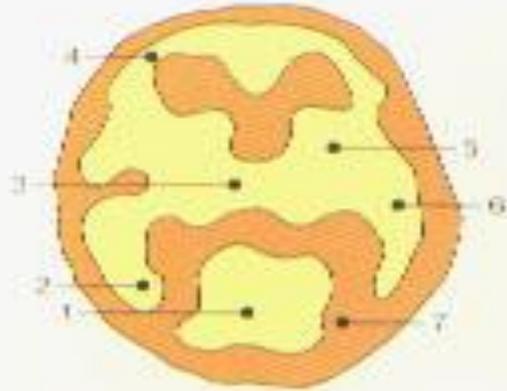
# Cerebral blood flow and perfusion

- Lipophilic tracer is enriched in the gray matter (800 MBq  $^{99m}\text{Tc}$ -HM-PAO – hexamethylpropylene amine oxime)
- Advantage of dual-head SPECT = faster acquisition
- Reconstructed and reorientated transversal, sagittal and coronal slices are made
- Decreased/absent activity indicates the perfusion abnormalities

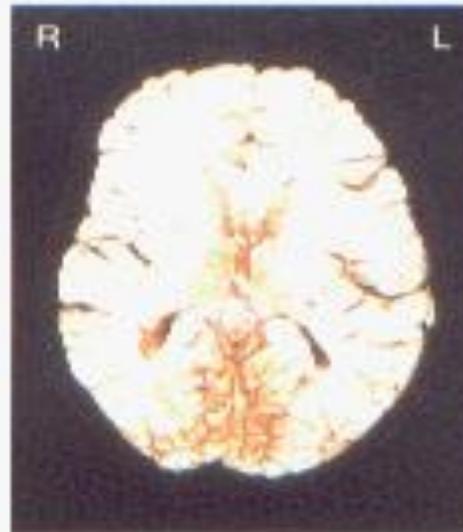
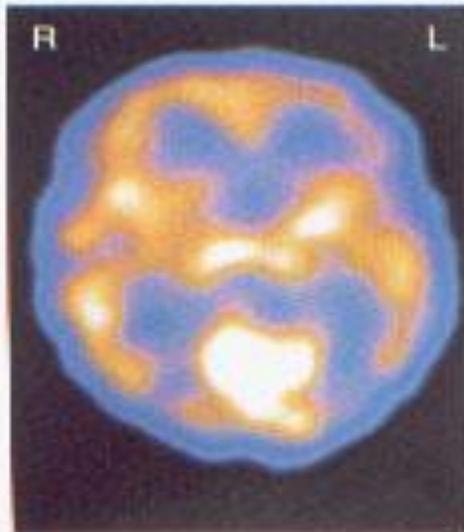
# Indications of CBF SPECT

- **Evaluation of cerebrovascular disease (TIA, stroke, AVM, migraine)**
- **Dementias (Alzheimer, Pick)**
- **Preoperative detection of seizure focus in epilepsy**
- **Suspected brain trauma**
- **Substance abuse**
- **Inflammations, infections**
- **Diagnosis of brain death**

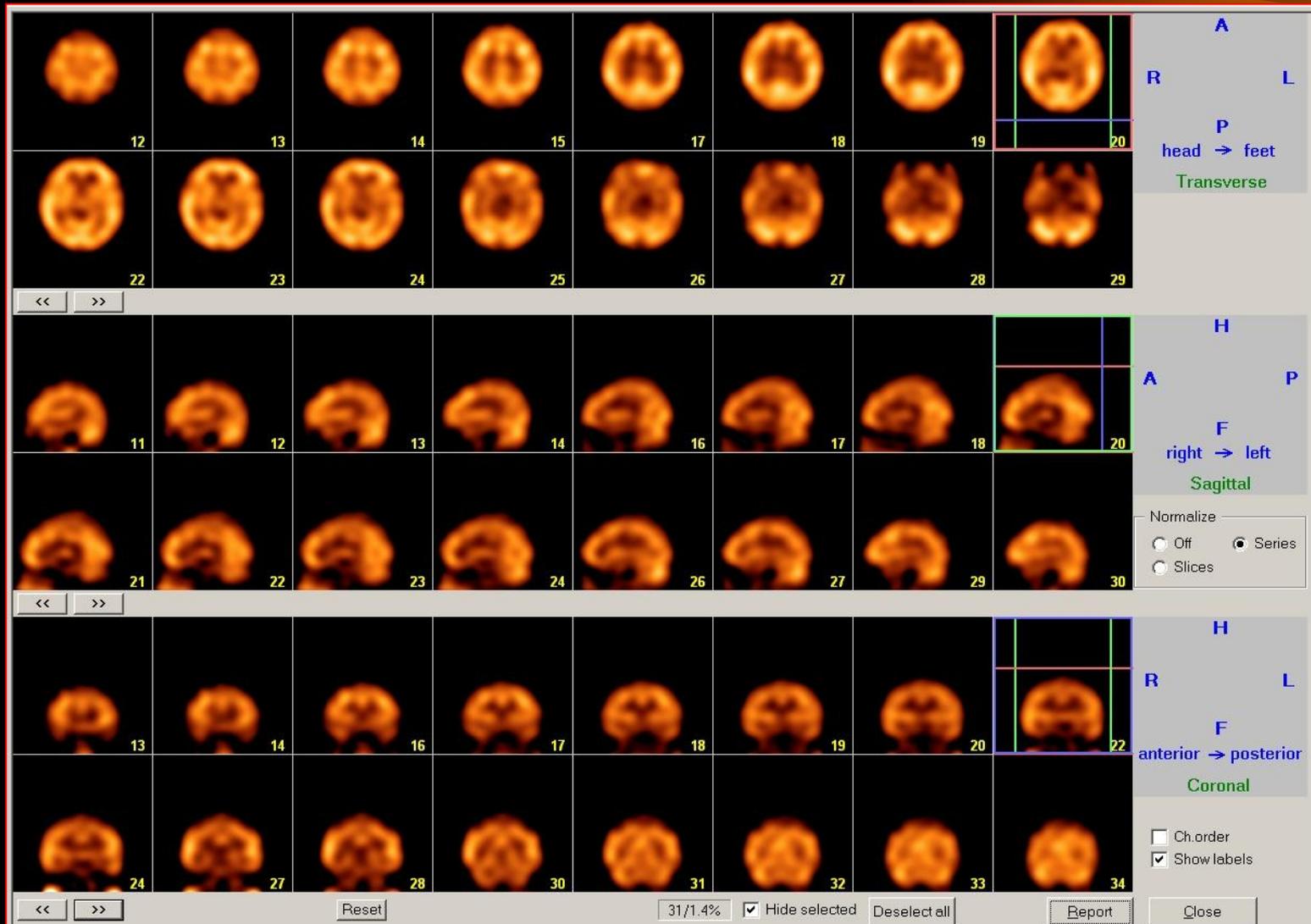
# Transversal section of the human brain



1. Visual cortex
2. Occipital lobe
3. Thalamus
4. Frontal lobe
5. N. caudatus
6. Temporal lobe
7. Lateral ventricle

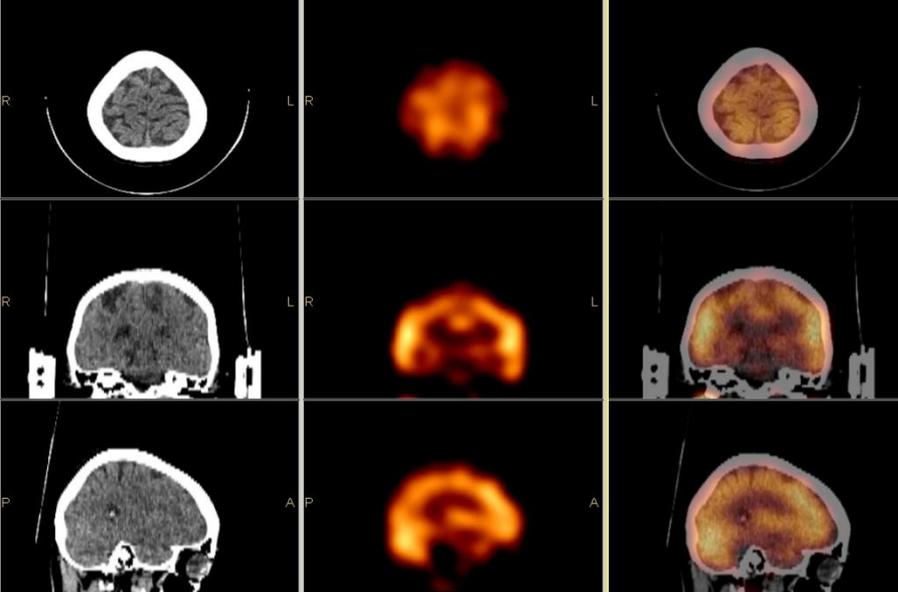


# Transversal, sagittal and coronal slices of the normal brain by SPECT

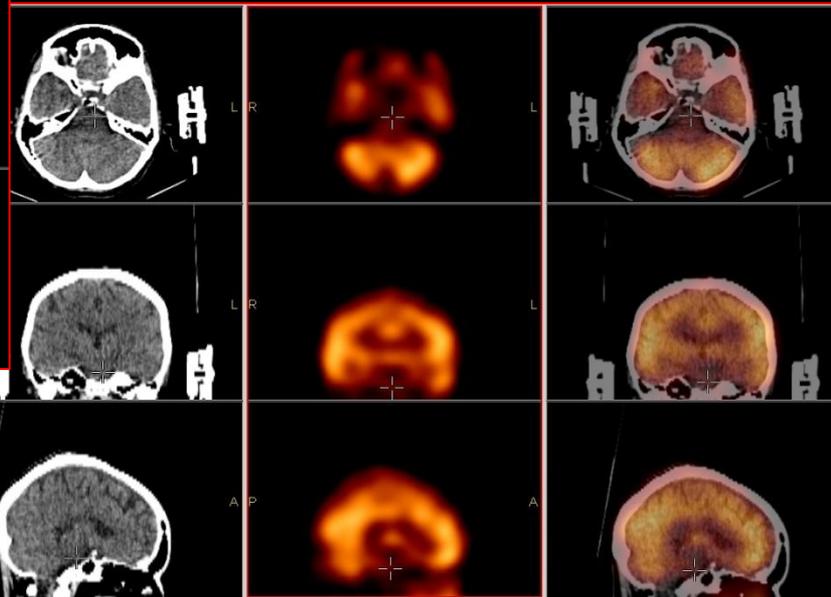
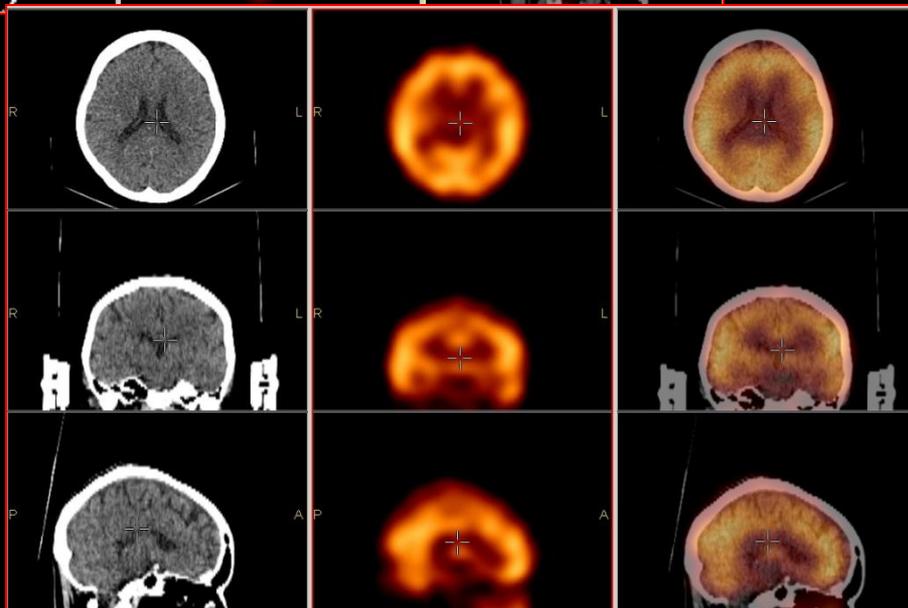


# SPECT/CT (Multimodality!)

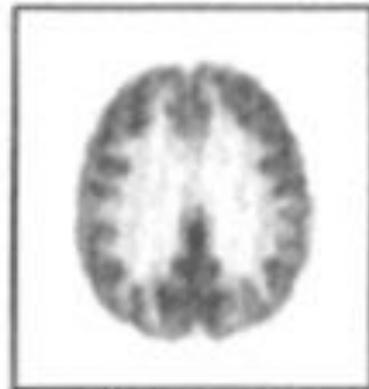




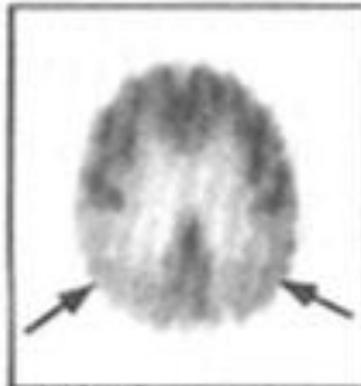
# Different slices of the brain by SPECT/CT



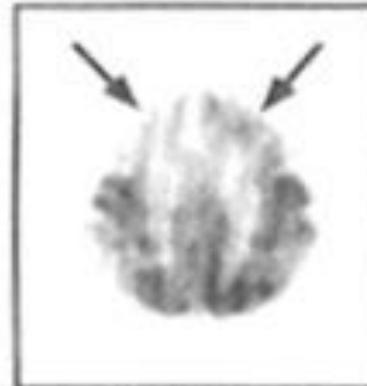
# Perfusion abnormalities in different brain disorders



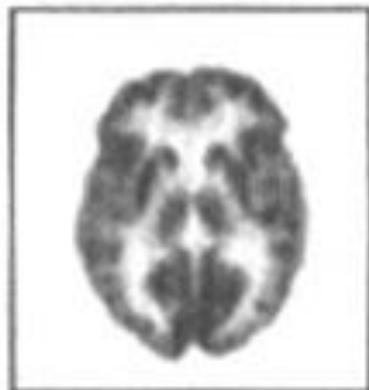
Normal



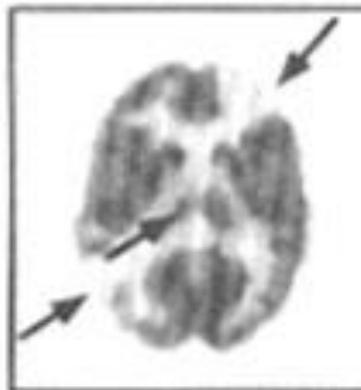
Alzheimer's



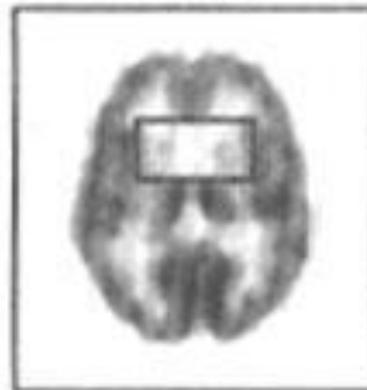
Pick's



Normal

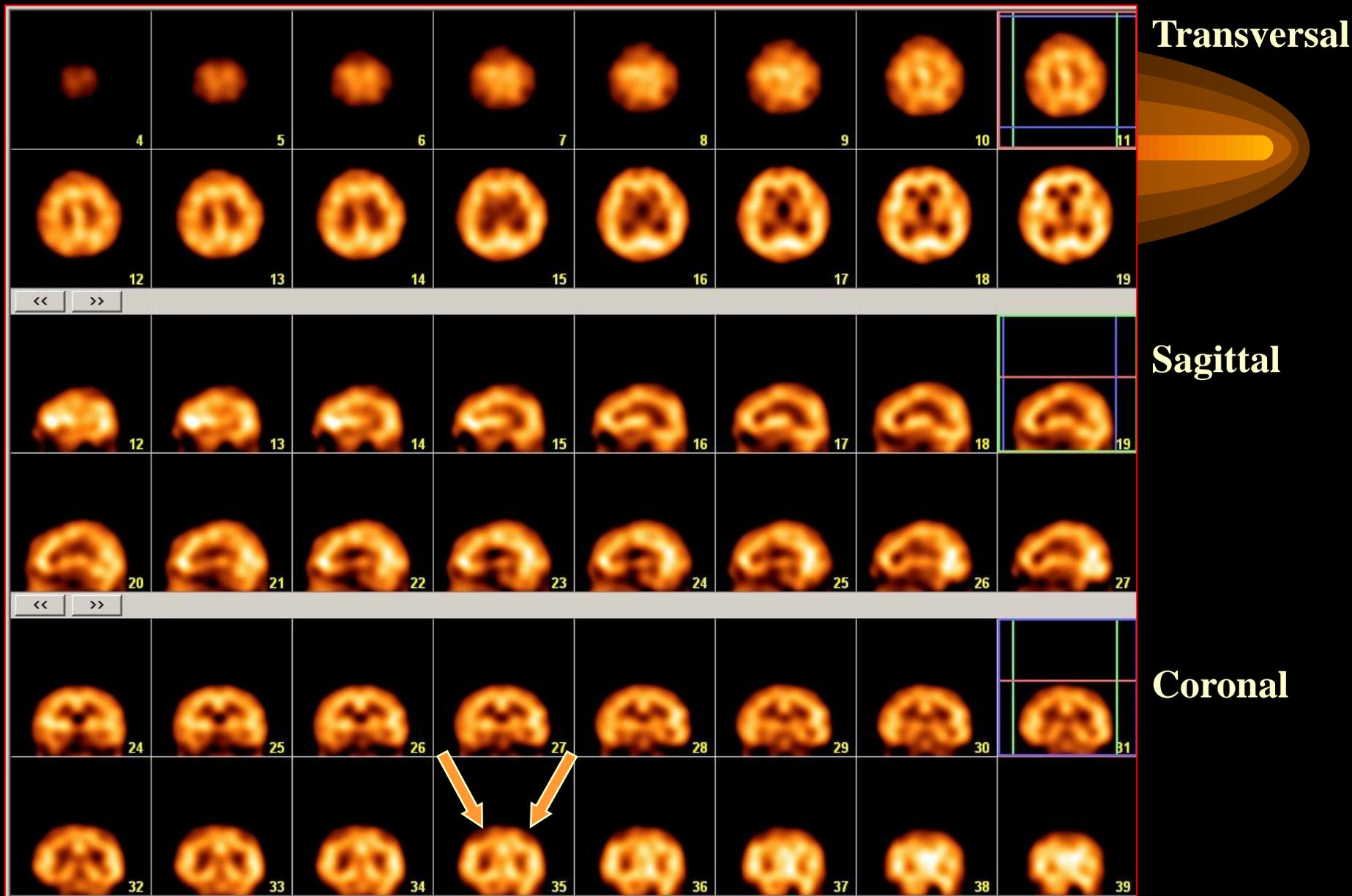


Multiple Infarct  
Dementia

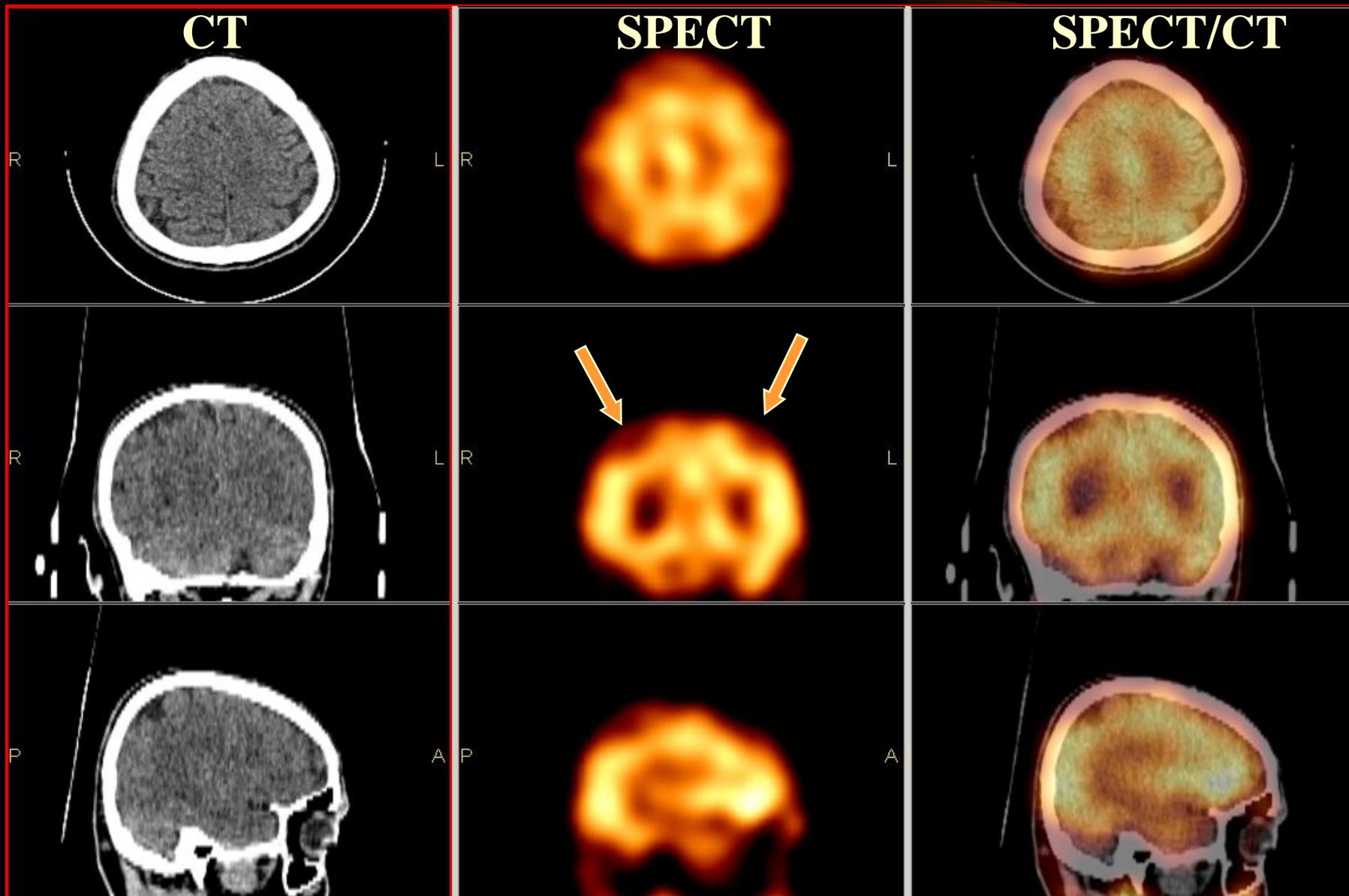


Huntington's

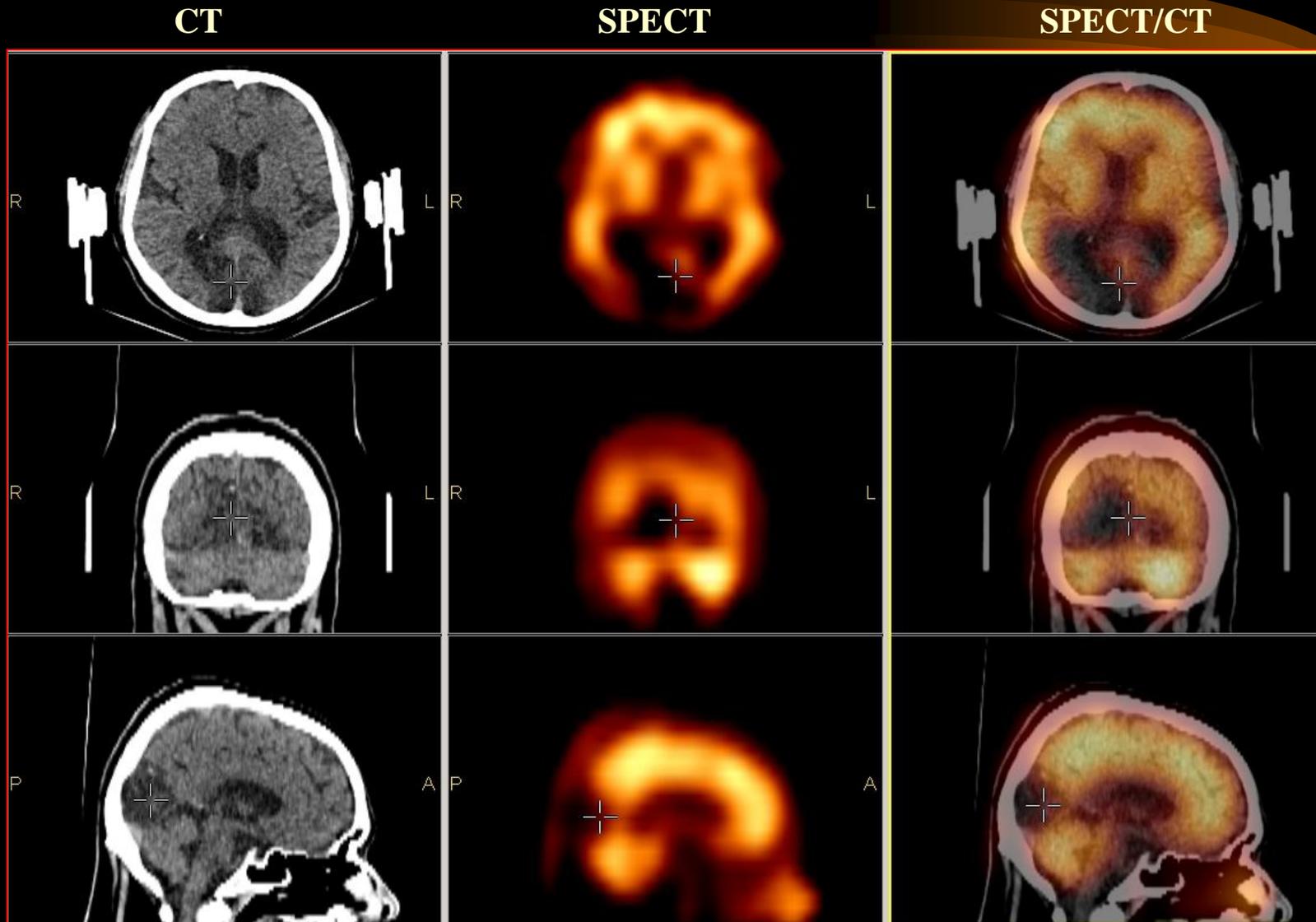
# Bilateral parieto-occipital hypoperfusion



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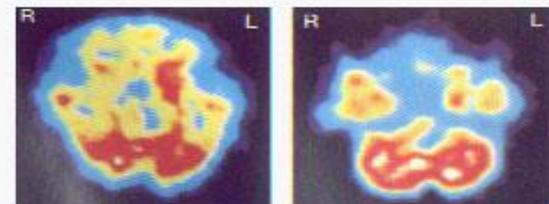
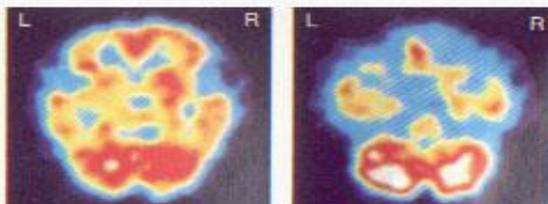
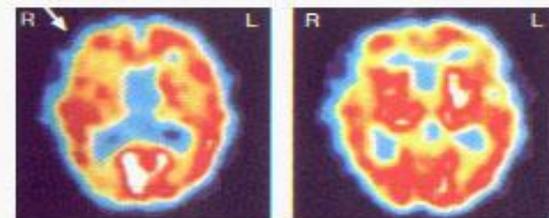
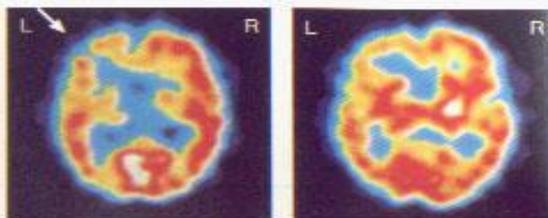
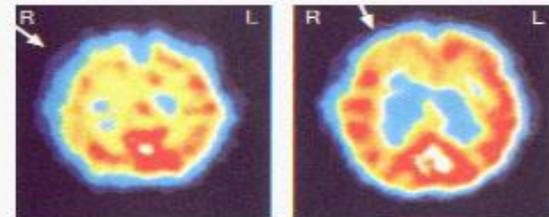
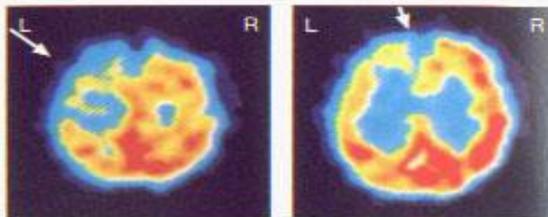
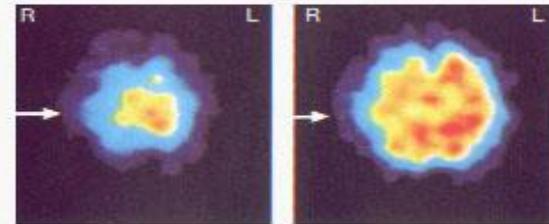
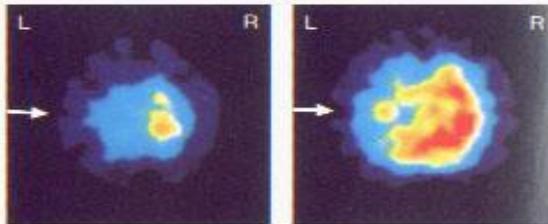
# Perfusion defect (stroke) in the right occipital region



# Occlusion of the right carotid artery

Pre-operative

Post-operative



# Dementia: Pick disease

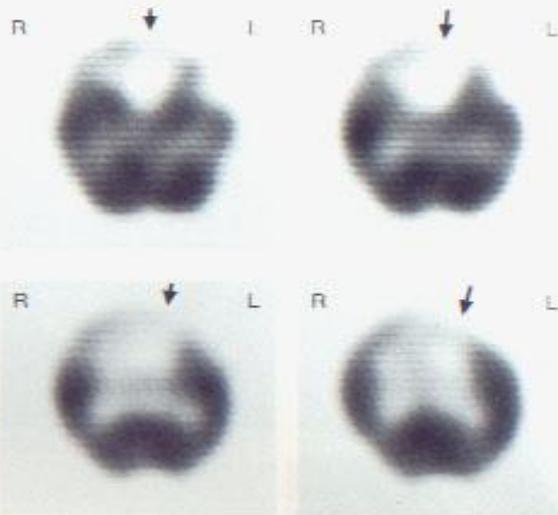
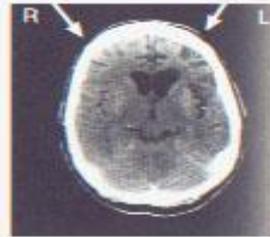


Figure 2a



Figure 2b

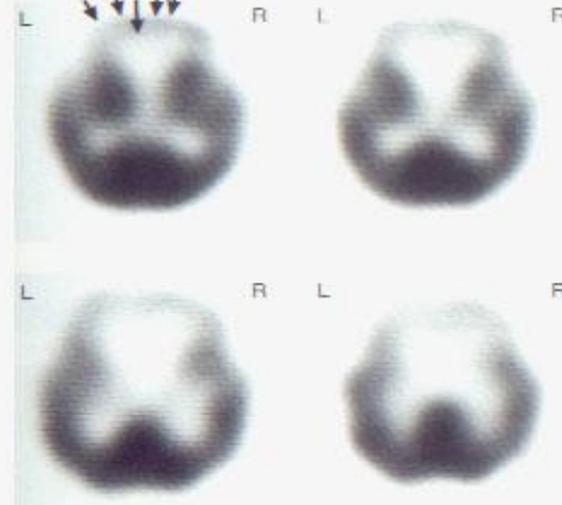


Figure 1a

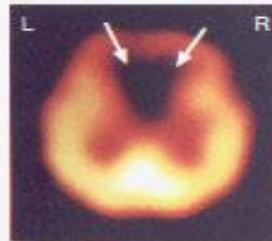


Figure 1b

# Hyperperfusion

# Migraine

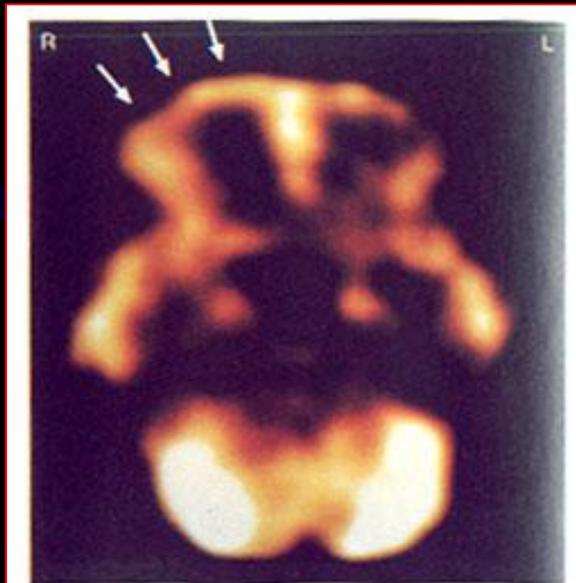


Figure 1

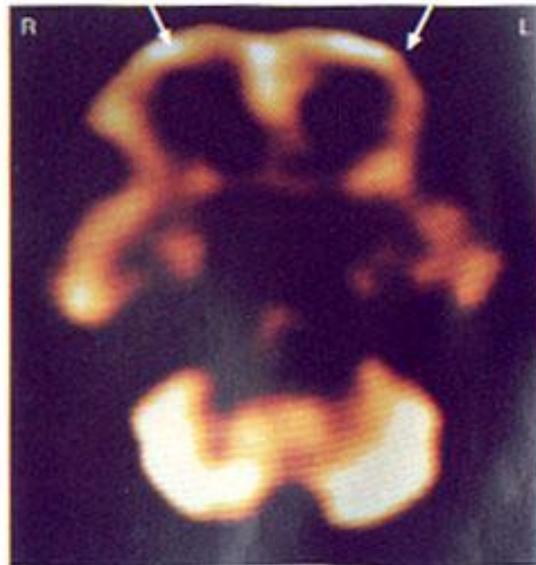
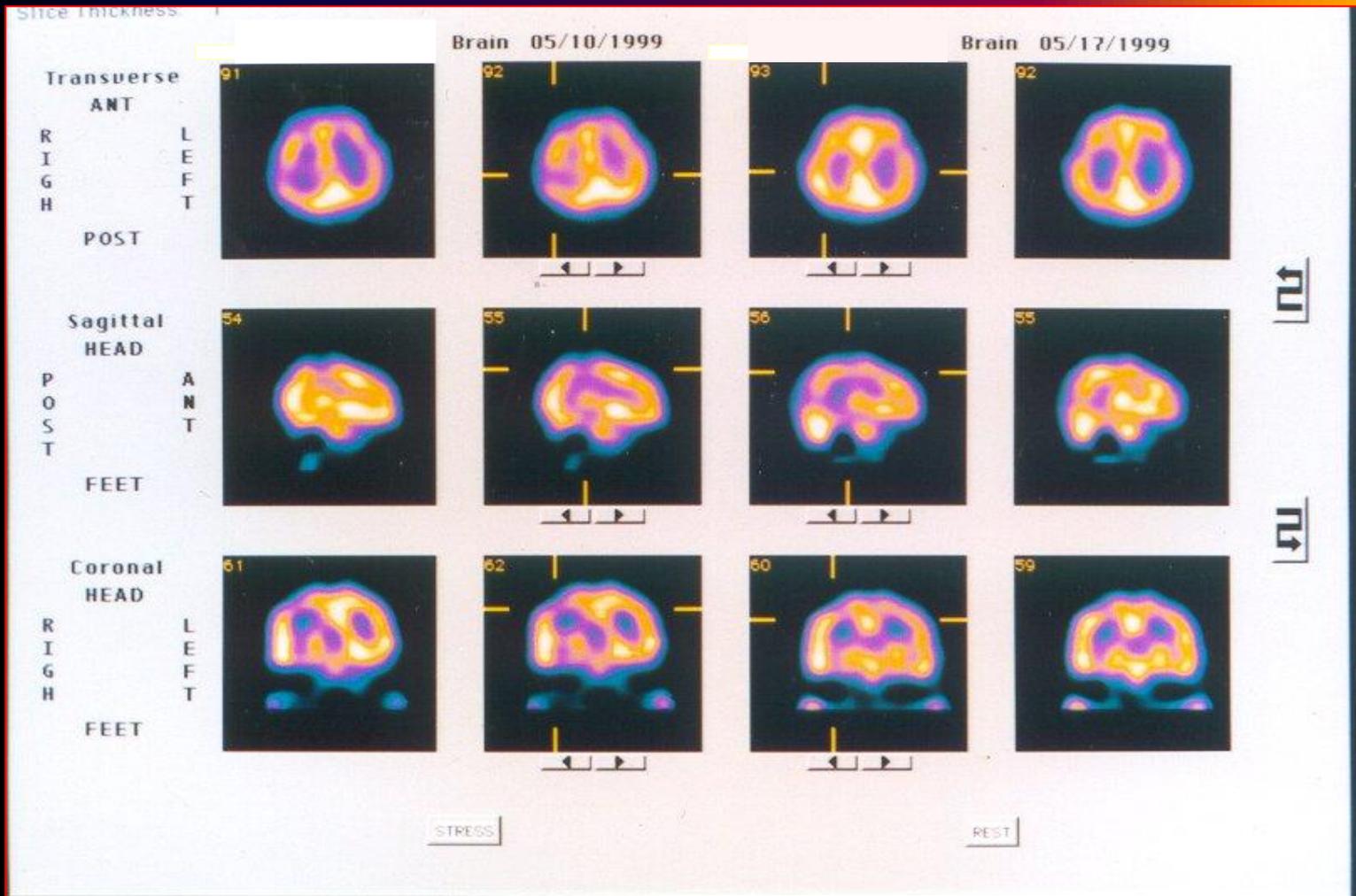


Figure 2

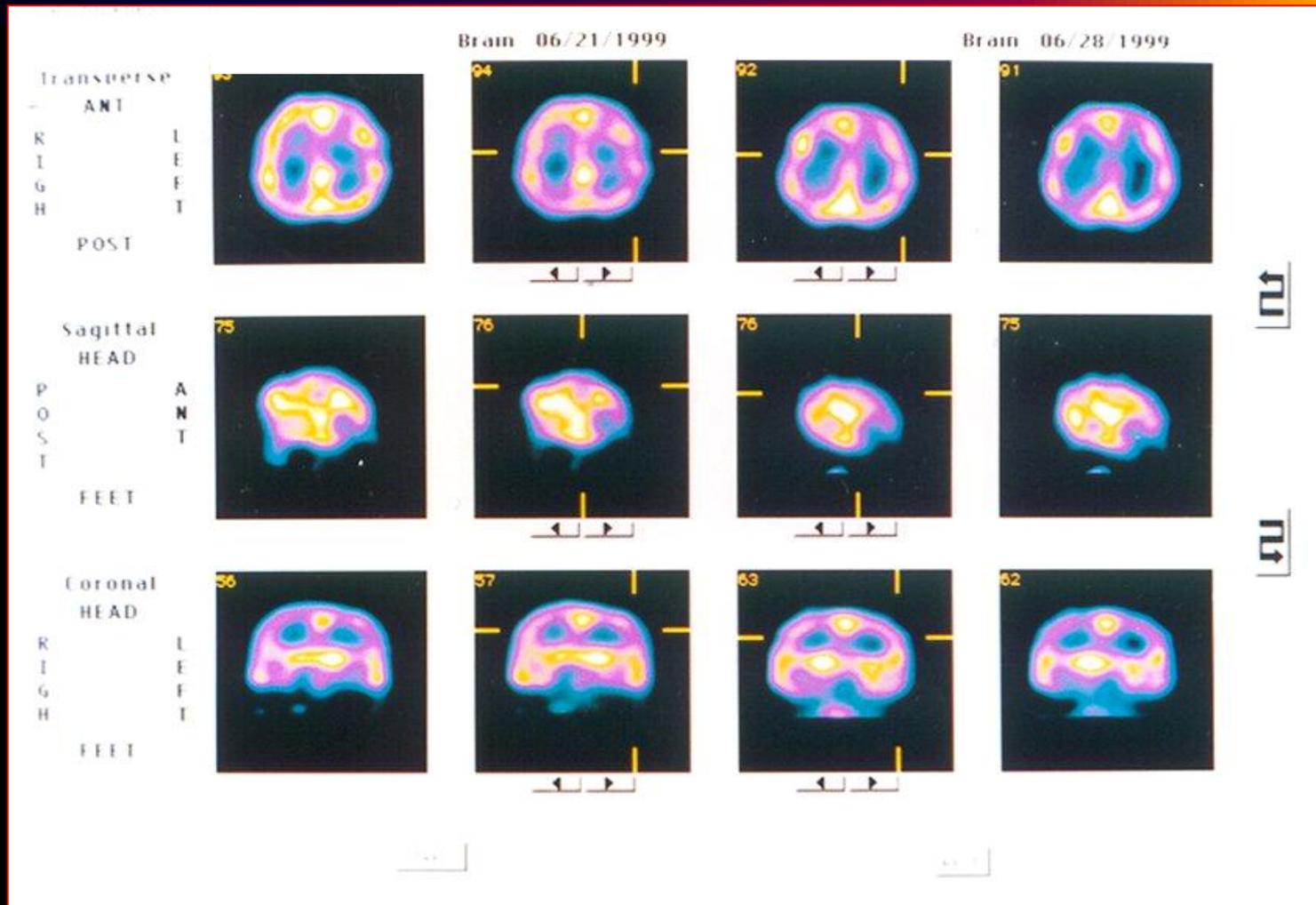
Before treatment

After treatment

**51 y., female patient. Complain: numbness of the left arm. Examination: facio-brachial hypalgesia on the left side, accentuated deep tendon reflexes, mild dysmetry, pronation in Barre position (two columns from left: after DP stress)**



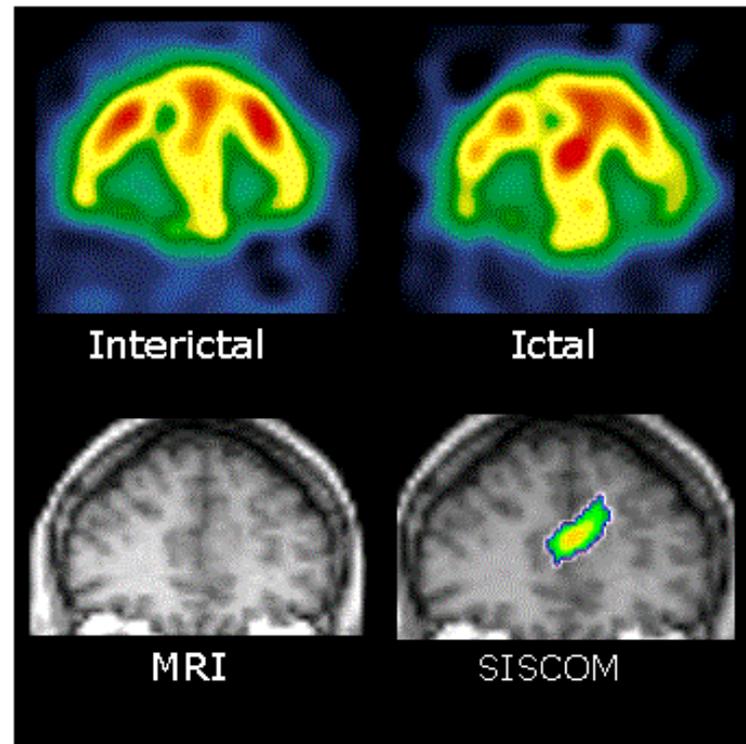
**42 y., female patient. Examination: right-sided hemihypalgesia, latent paresis, accentuated deep tendon reflexes, mild dysmetria and dysdiadochokinesis (two column from left: after DP stress)**



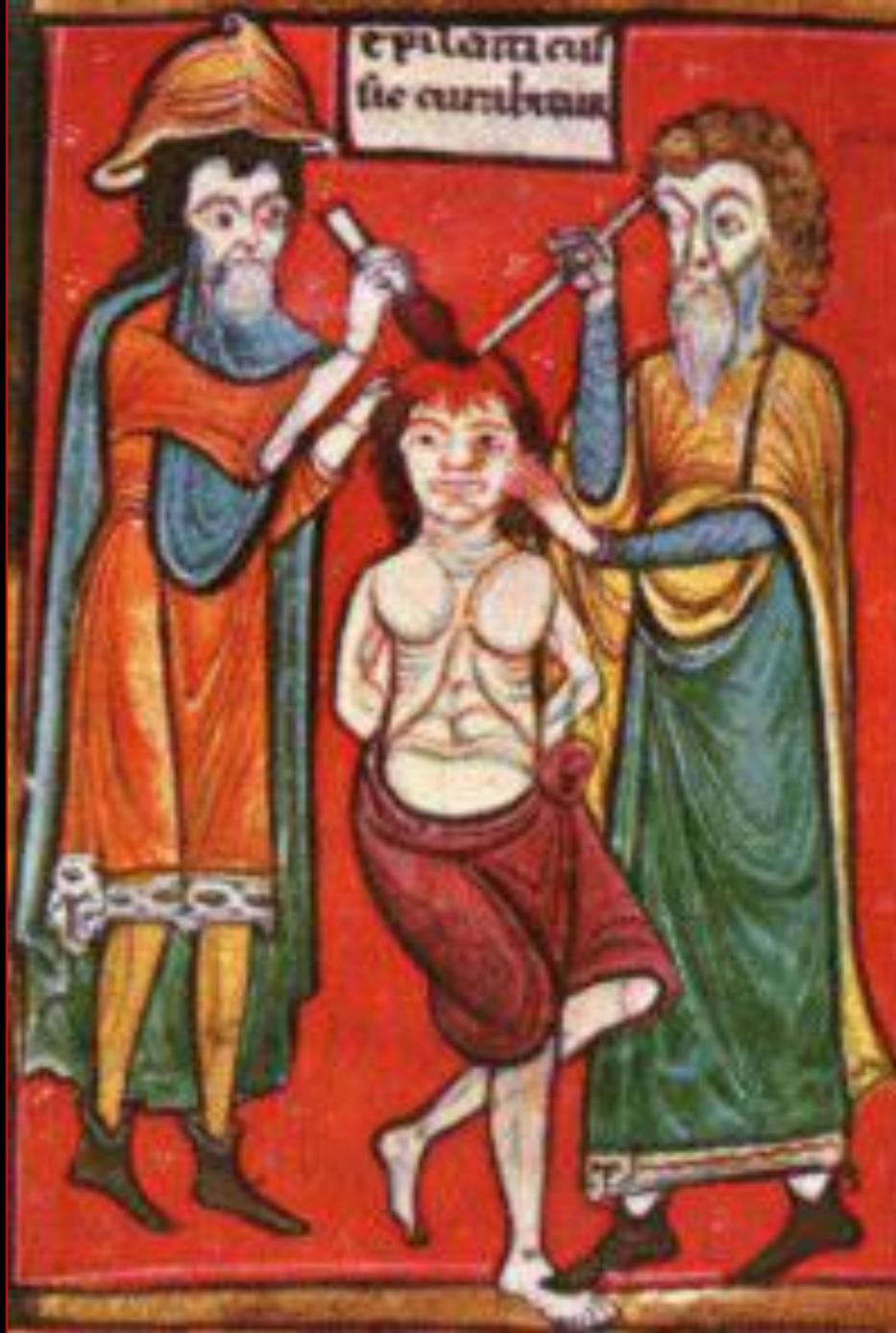
# Epilepsy

## Methods to process and analyse SPECT images - SISCOM

- Interictal and ictal SPECT images
- Coregistration of interictal and ictal SPECT scans
- Normalisation
- SPECT subtraction
- Thresholding of difference image
- Subtraction SPECT to MRI-coregistration
  - Localization<sup>1,2</sup>:
    - SISCOM: 88%
    - Side-by-side visual inspection: 39%



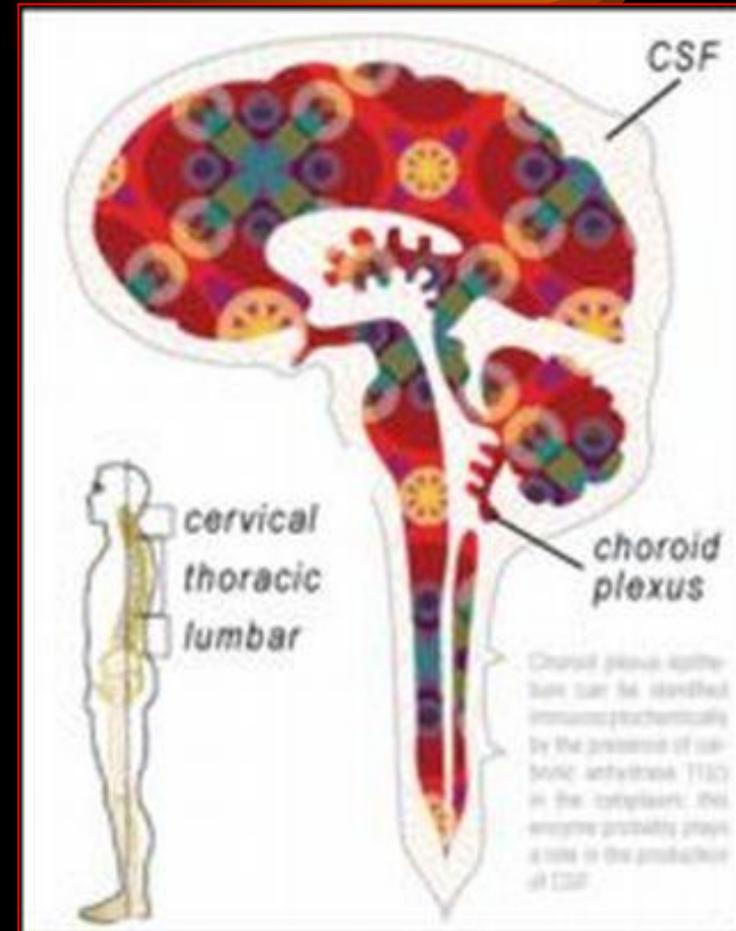
<sup>1</sup>O'Brien TJ et al, Neurology 1998; 50: 445-454. <sup>2</sup>Lewis PJ et al, J Nucl Med 2000; 41: 1619-1626



## Therapy of epilepsy in the XII. Century

# Circulation of the cerebrospinal fluid (CSF)

It is produced in the brain by modified ependymal cells in the choroid plexus. It circulates from the choroid plexus through the interventricular foramina (foramen of Monro) into the third ventricle, and then through the mesencephalic duct (cerebral aqueduct) into the fourth ventricle, where it exits through two lateral apertures (foramina of Luschka) and one median aperture (foramen of Magendie). It then flows through the cerebromedullary cistern down the spinal cord and over the cerebral hemispheres.



# Examination of CSF

- **Radiopharmaceutical: 500 MBq  $^{99m}\text{Tc}$ -DTPA** via intrathecal route (lumbal or cisternal)
- Whole body scan + static lateral scans  
**1, 3, 6, 24 hours after administration**
- **Normal dynamic:** cisterna magna-3 hours later, flow to the convexity-6 hours later, predominantly the convexity is shown-24 hours later, no activity in the lateral ventricles!
- **Abnormal:** - slow dynamic (spinal tumor)
  - hydrocephalus: reflux – only lateral ventricles

# Liquor dynamic investigation in a patient with reflux (lumbar administration)

1 hour

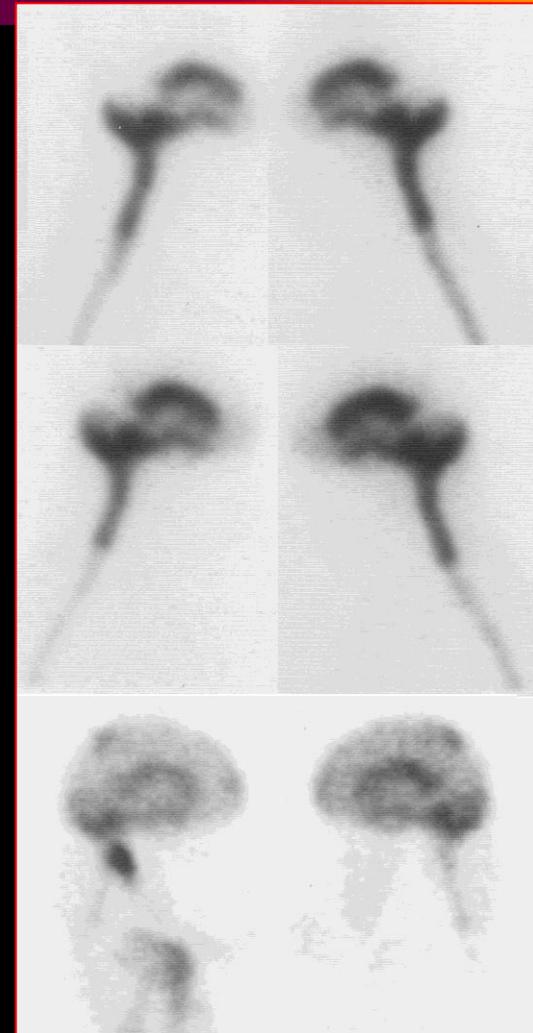
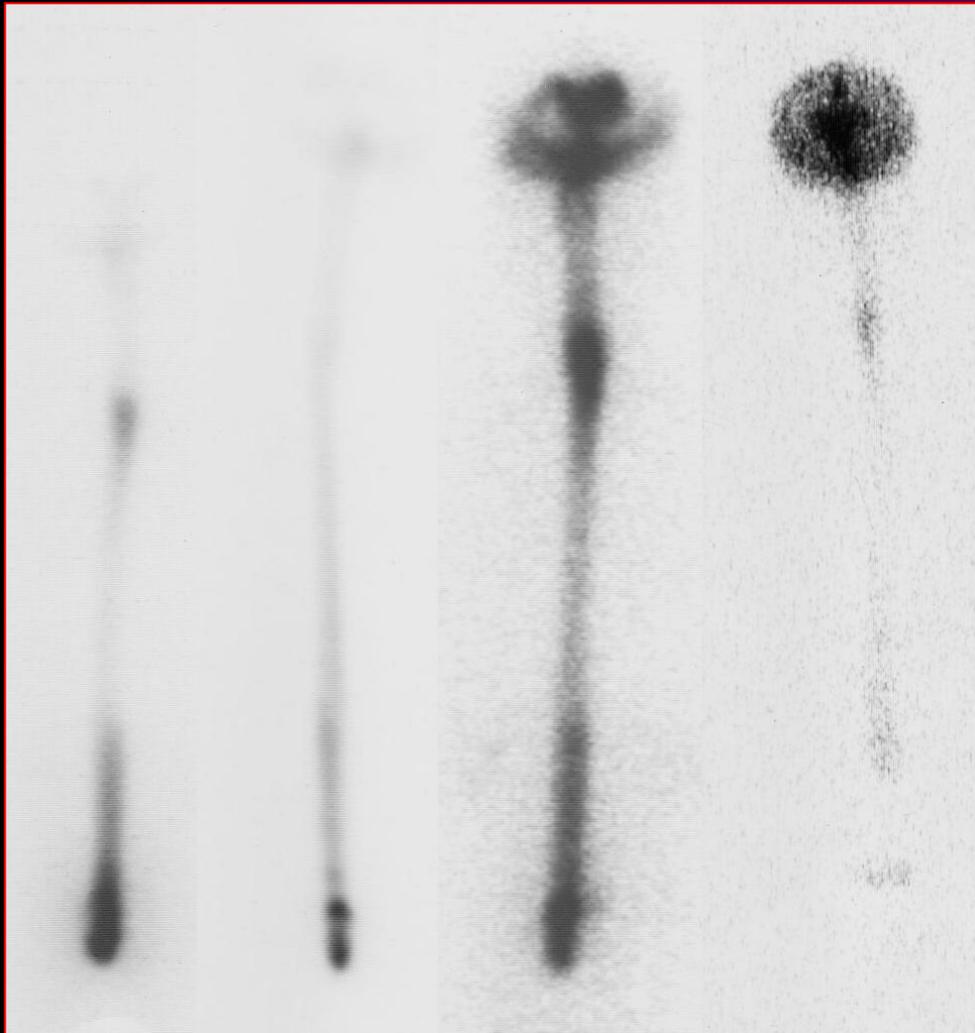
3 hrs

6 hrs

24 hrs

right

left

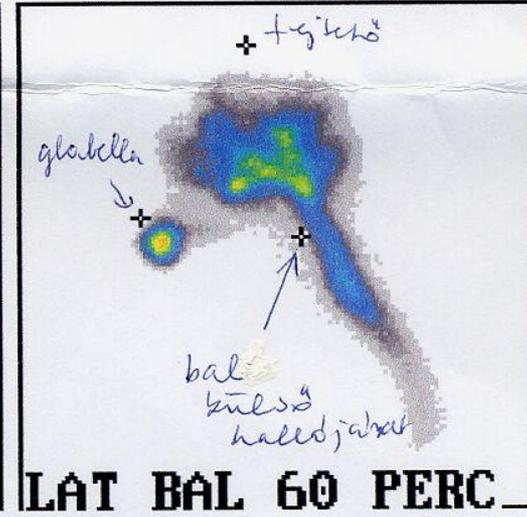
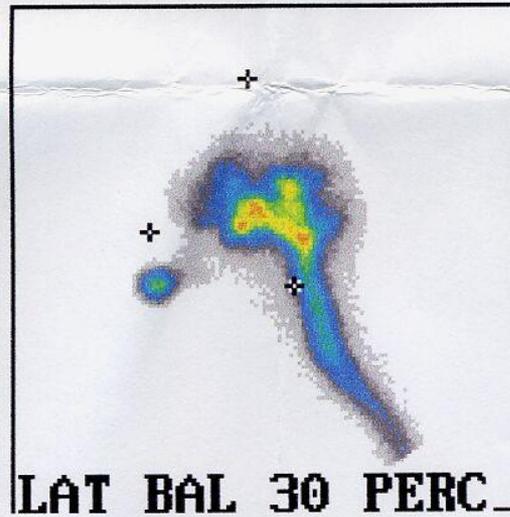
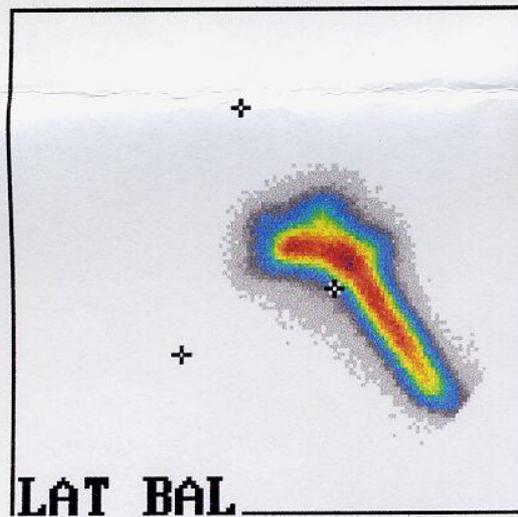
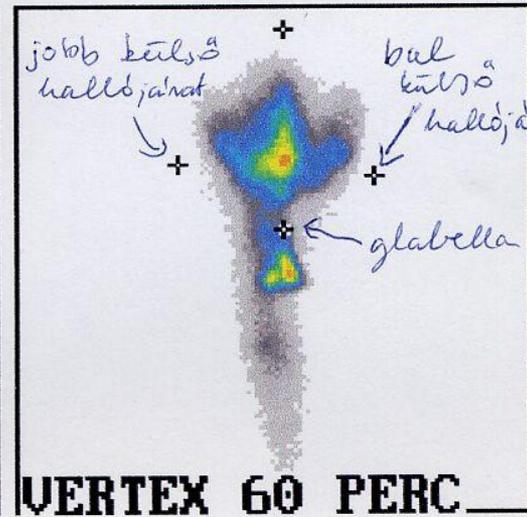
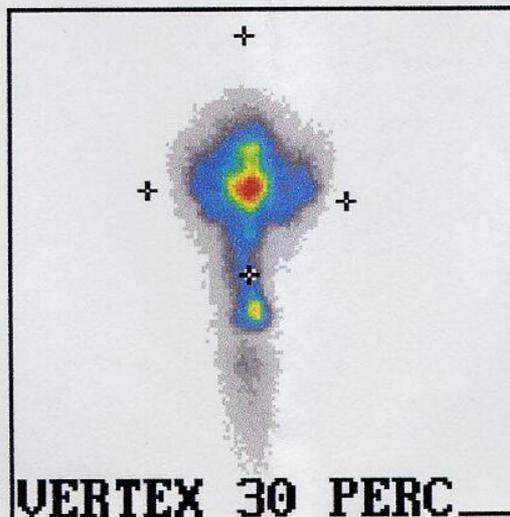
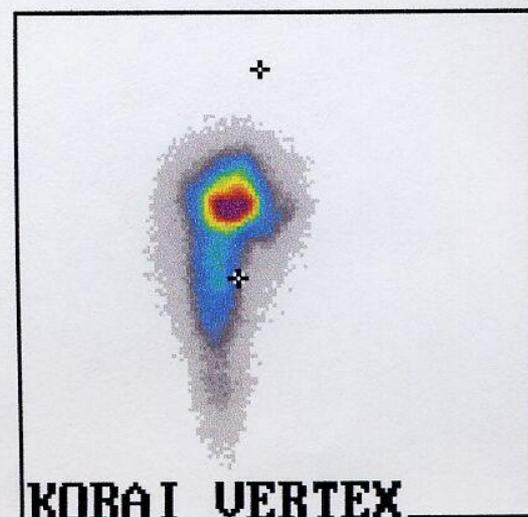


3 hrs

6 hrs

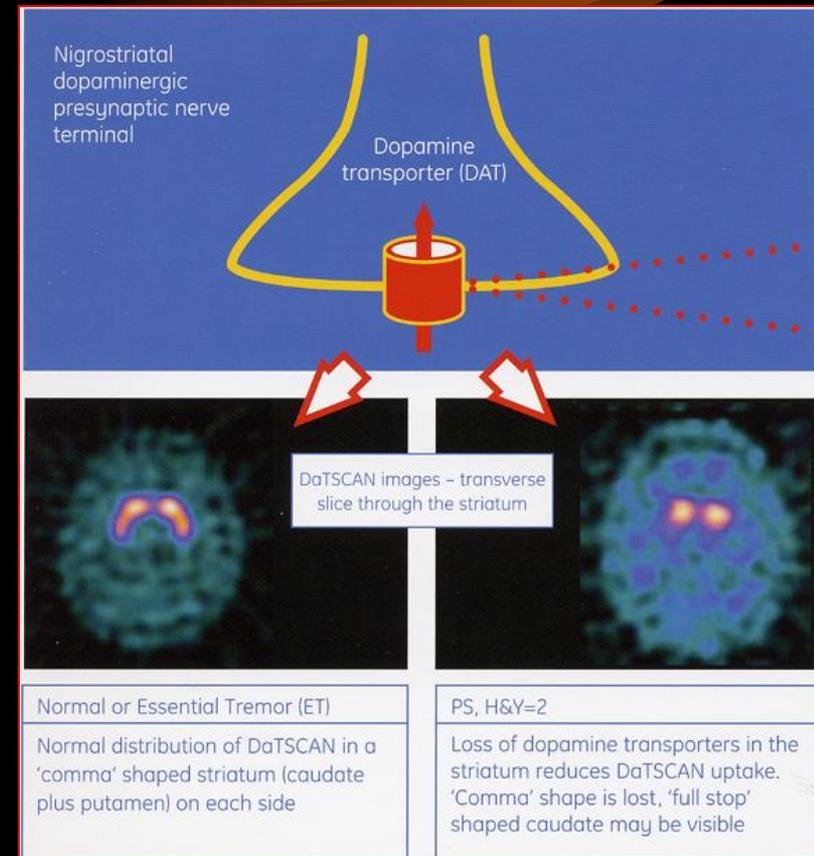
24 hrs

# Investigation of liquorrohea (cisternal administration)



# Theory of presynaptic dopamine receptor scintigraphy

- **DATSCAN™ binds to the dopamine transporters (DAT),** which are on the neurons in specific areas of the brain. When neuronal degeneration is present, the number of DAT are **significantly reduced** (for example in patients with **Parkinson's disease**).
- By detecting the binding of **DATSCAN™** to the dopamine transporters will be a clear visualisation of dopamine transporter integrity and consequently an **accurate diagnosis** of disease.

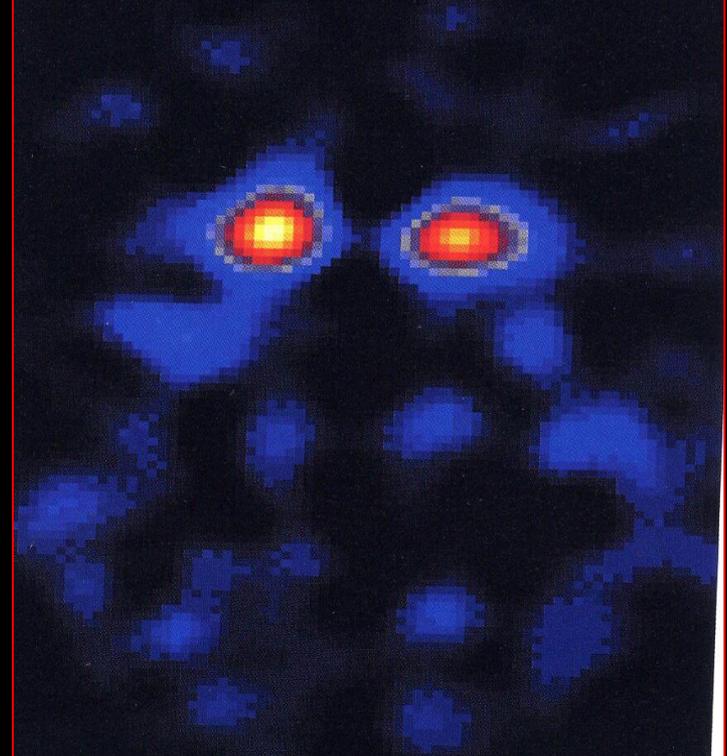


# Dopamin receptor examination (DATSCAN™) in a patient with Parkinson's disease

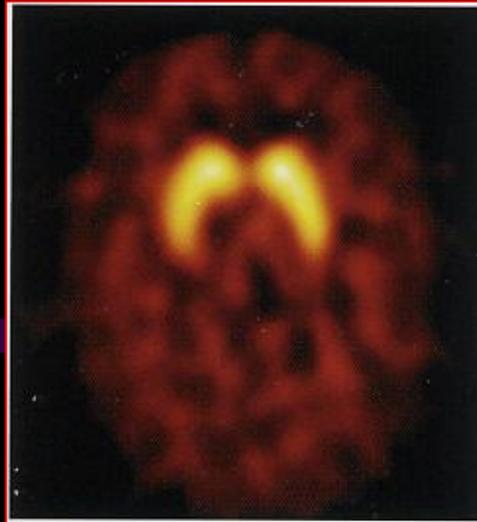
**Normal distribution**



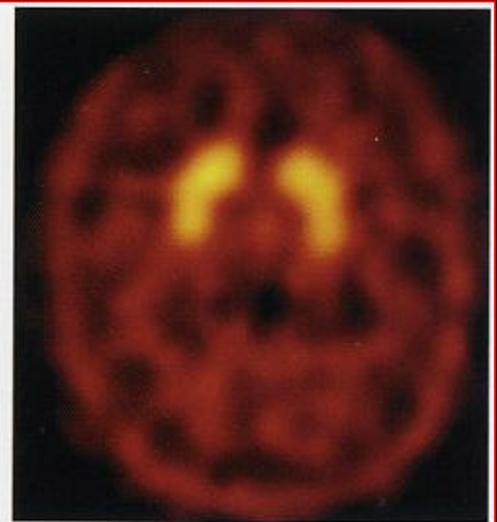
**Absence of receptors**



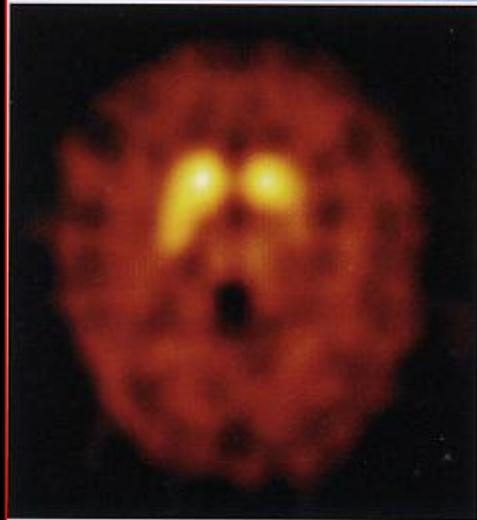
# Presynaptic dopamin receptor examination in different disorders



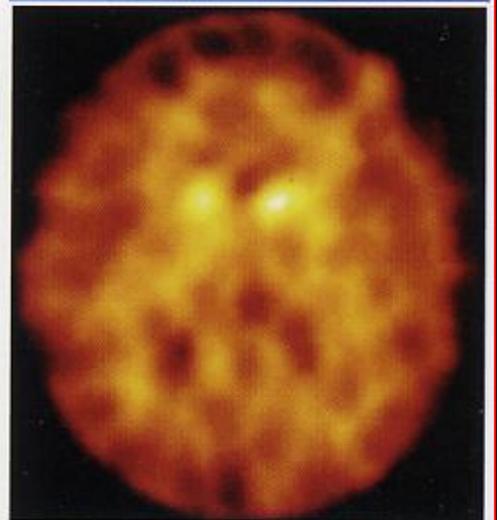
Healthy control



ET



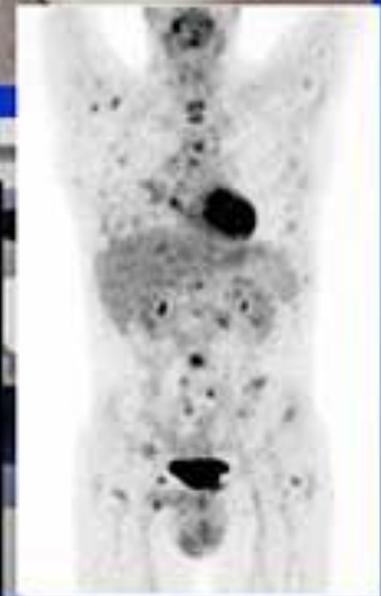
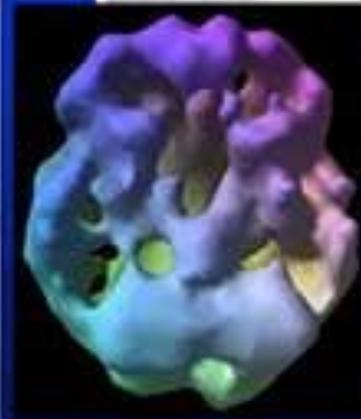
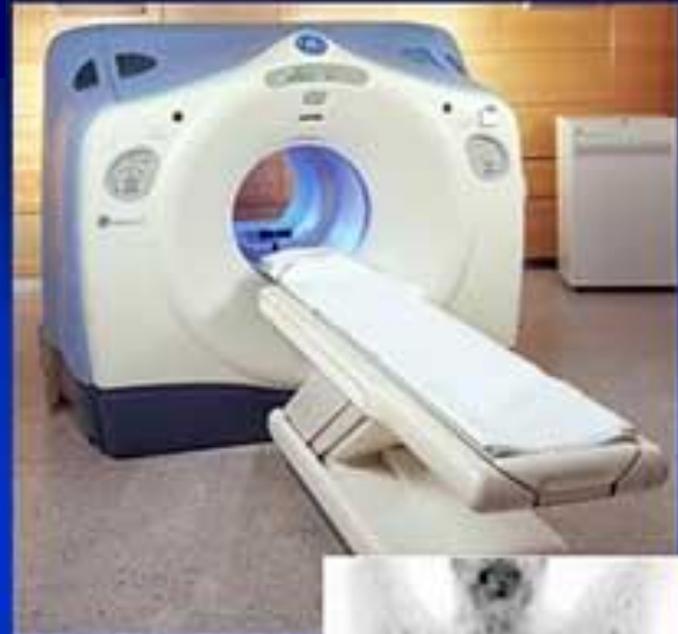
Early stage PD, H&Y=1



Advanced stage PD,  
H&Y=4

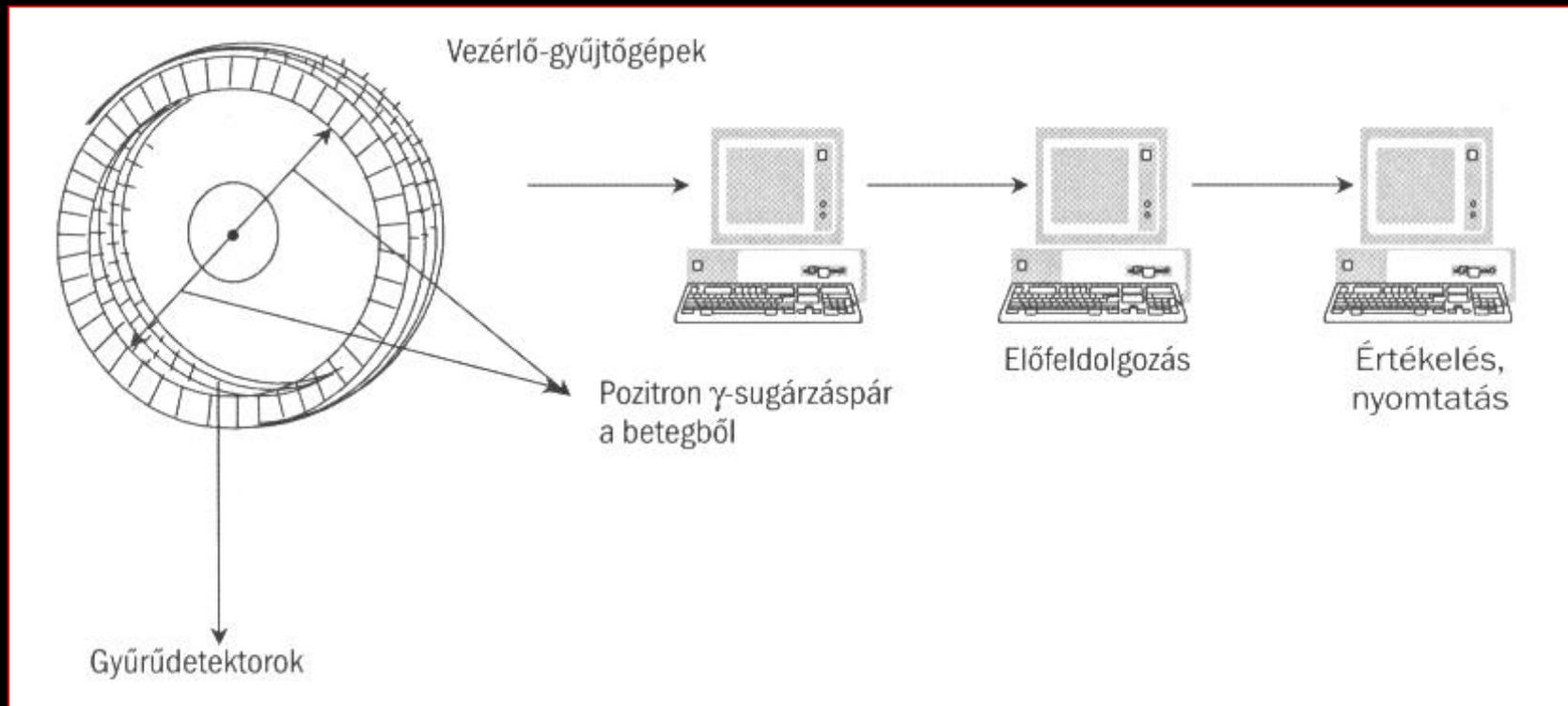
# PET/CT (positron emission tomograph)

This is the „today's” method

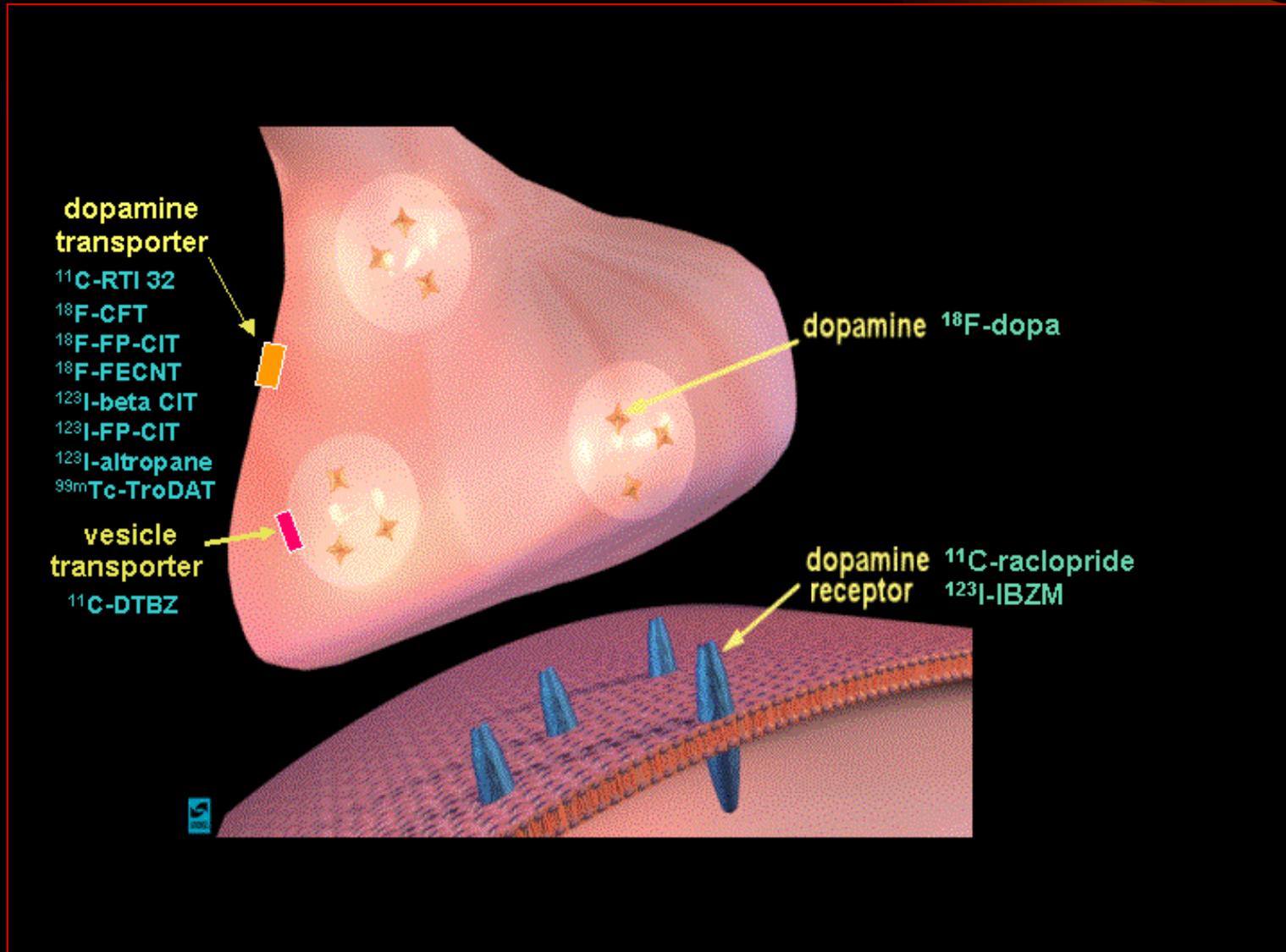


# How the PET works:

- The injected radiopharmaceutical is a **positron emitted** substance, the equipment is capable to detect the annihilation-rays (**two gamma-photons with 511 keV**)
- Usage of isotopes with ultrashort half-life ( $^{11}\text{C}$ ,  $^{15}\text{O}$ ,  $^{13}\text{N}$ ,  $^{18}\text{F}$ ), which are suitable for measurement of metabolic processes



# Neuroreceptor studies



$^{11}\text{C}$ -RTI 32

$^{123}\text{I}$ -FP-CIT

$^{11}\text{C}$ -DTBZ

$^{18}\text{F}$ -dopa

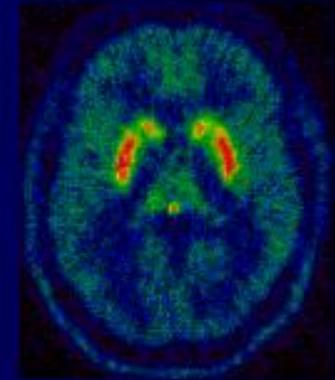
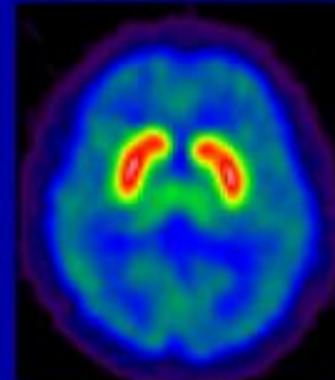
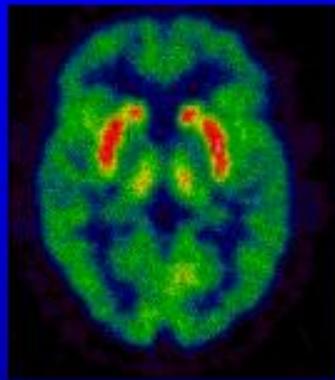
DAT

DAT

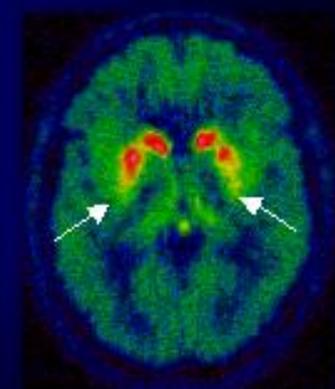
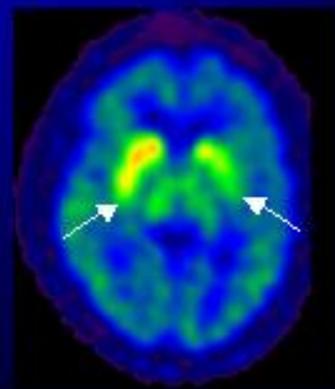
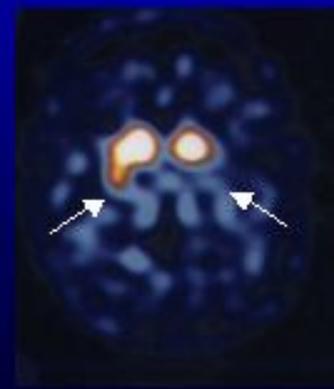
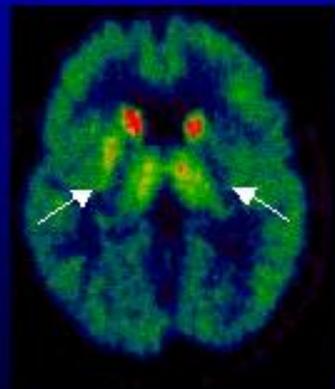
VMAT2

DDC

Healthy

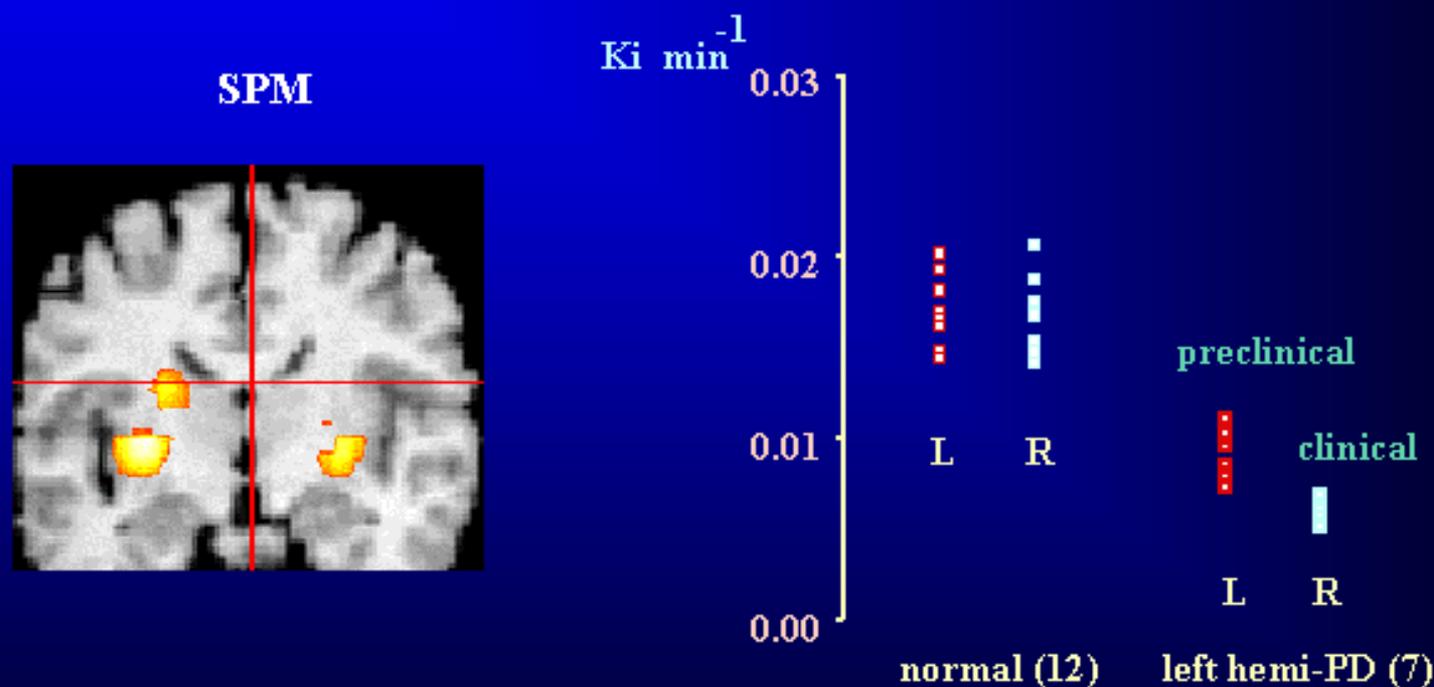


PD



# *<sup>18</sup>F-dopa PET*

## Putamen uptake in early hemi-PD



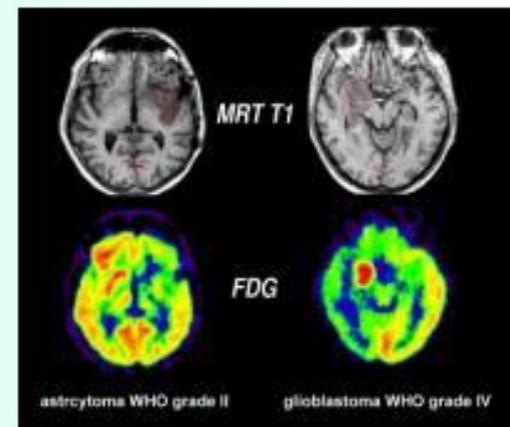
# Indications of PET/CT

- **Differential diagnosis of Parkinson's disease**
- **Dementia**
- **Tumors**
- **Presurgical localization of epileptic foci**
- **Therapy monitoring**
- **Neuroreceptor imaging**
- **Task-related mapping of the human cortex**



# Is it a malignant tumour

- **FDG uptake is related to histological tumor grade (Di Chiro et al. 1982; Alavi et al. 1988)**
- **FDG uptake in low-grade gliomas is usually close to that of normal white matter,**
- **grade 3 gliomas have FDG uptake similar to or even exceeding that of normal grey matter.**
- **glioblastomas usually also show high uptake, which may be inhomogeneous due to microscopic and macroscopic necroses that are typical for this tumor type**





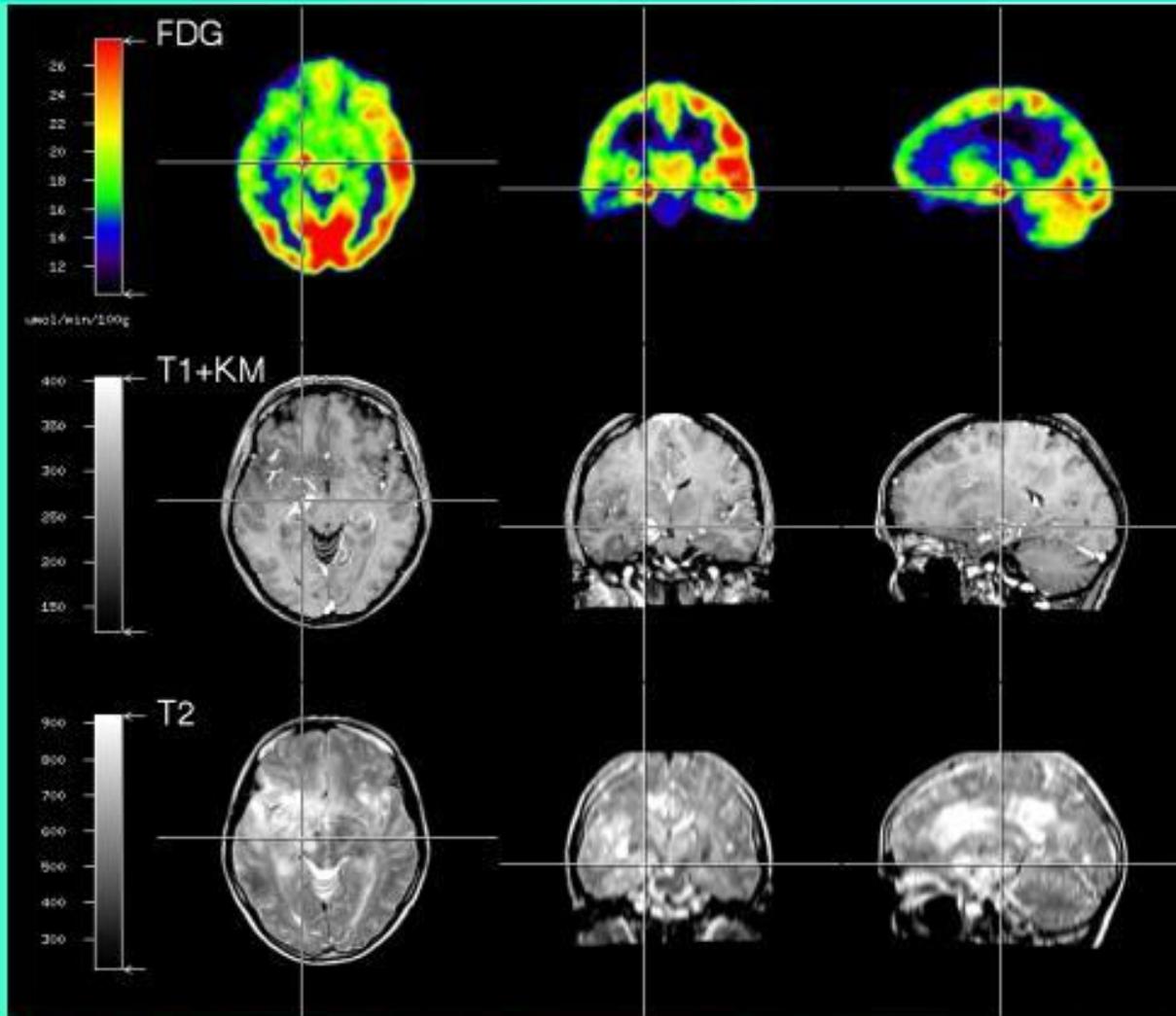
# Target for biopsy ?

Stereotactic biopsy offers a possibility to obtain a histological diagnosis in lesions of unknown dignity but may sample material that does not represent the most malignant part of the tumor (Jackson et al. 2001)

It has been demonstrated that the most metabolically active tumor part on **FDG-PET indicates the most informative location for taking a biopsy (Levivier et al. 1995)**



# Target for biopsy ?

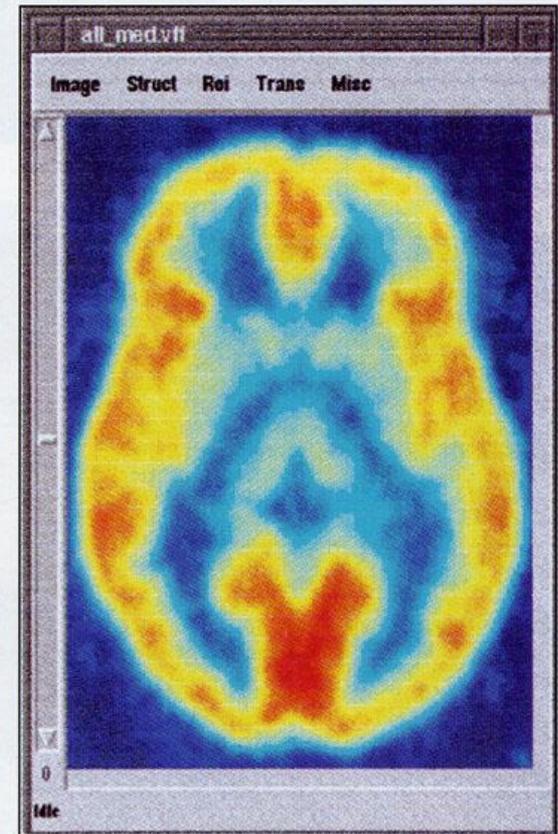
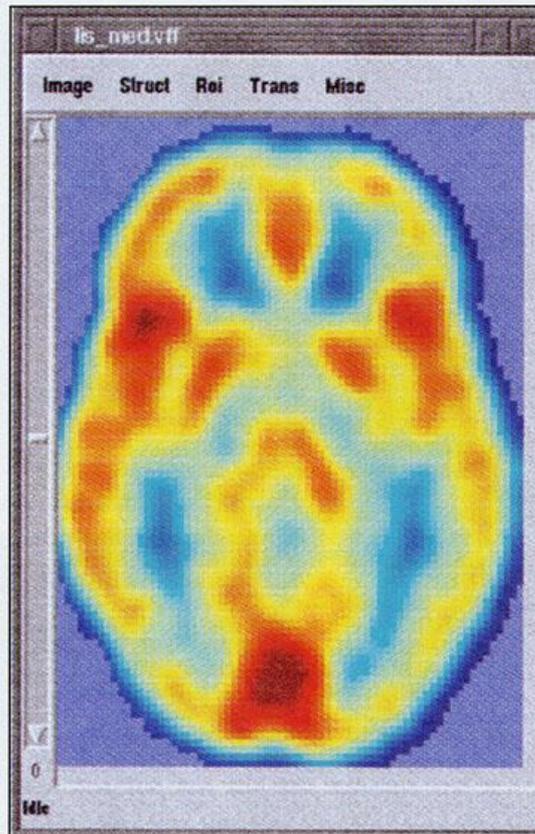
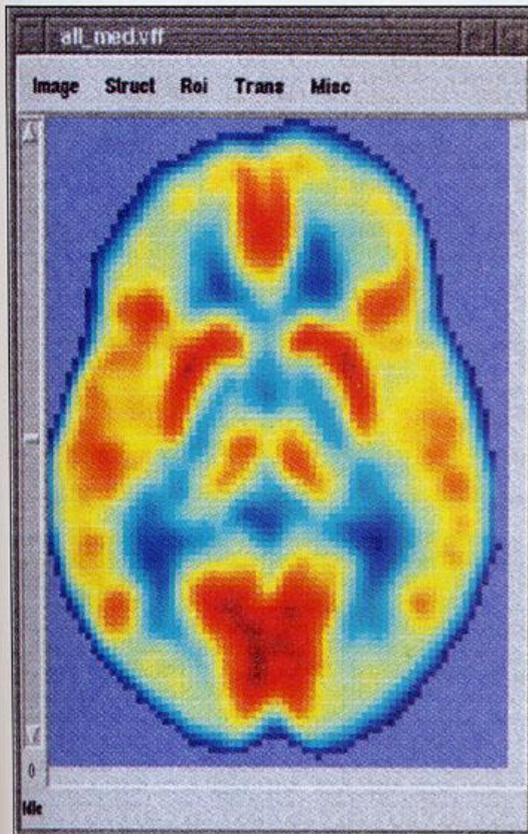


# Brain PET with different ligands (normal uptake and distribution)

**18F-FDG**

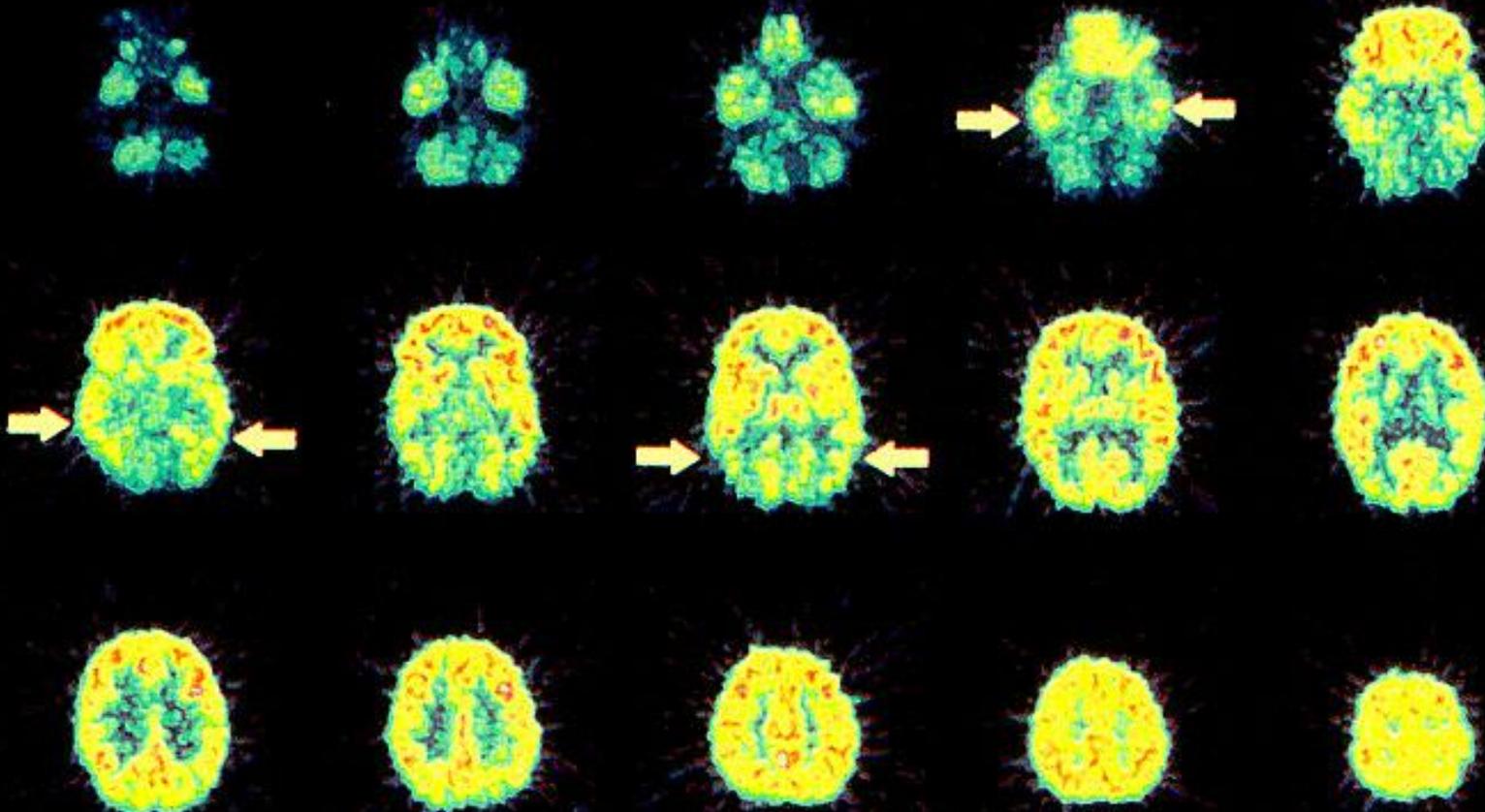
**15O-butanol**

**11C-flumazenil**



# Alzheimer disease: decreased bilateral temporal glucose metabolism

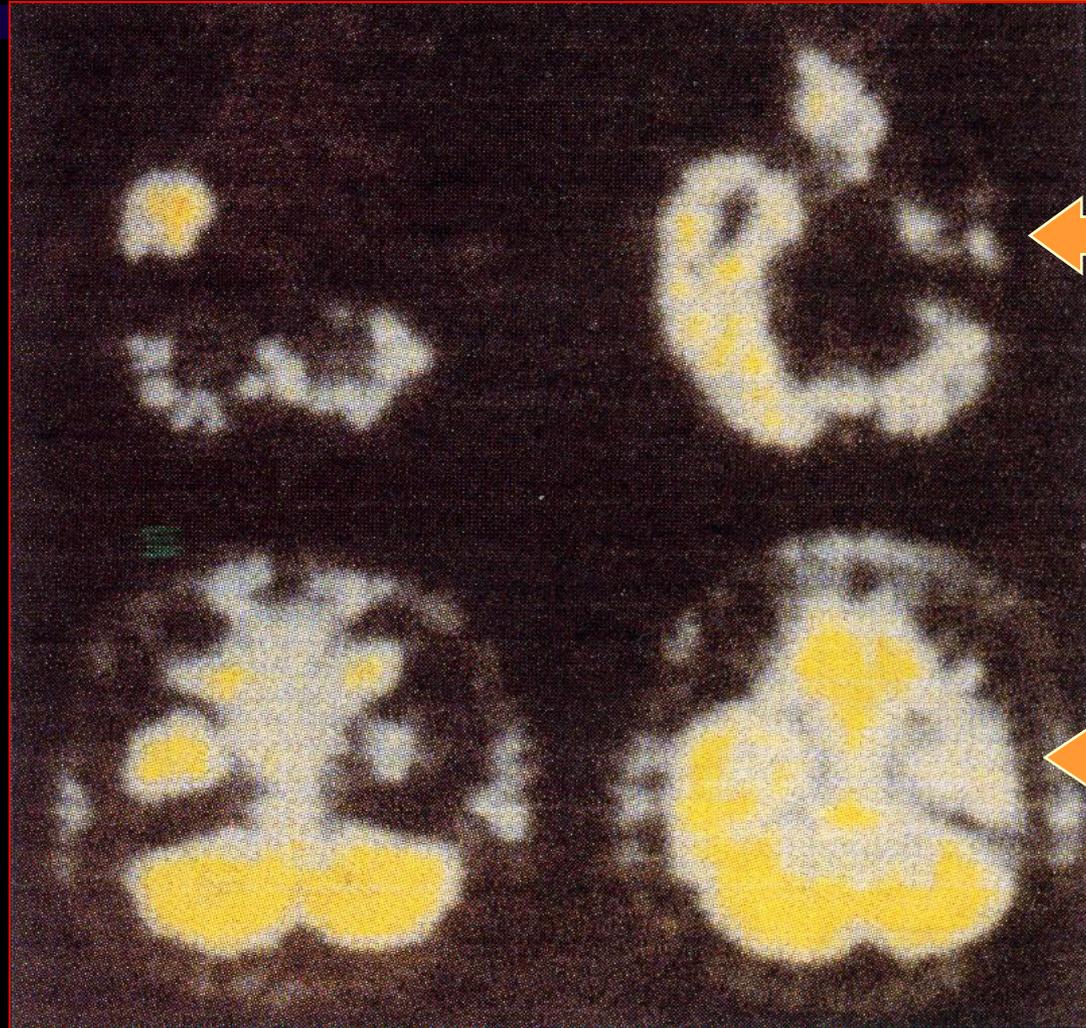
## $^{18}\text{F}$ -FDG PET



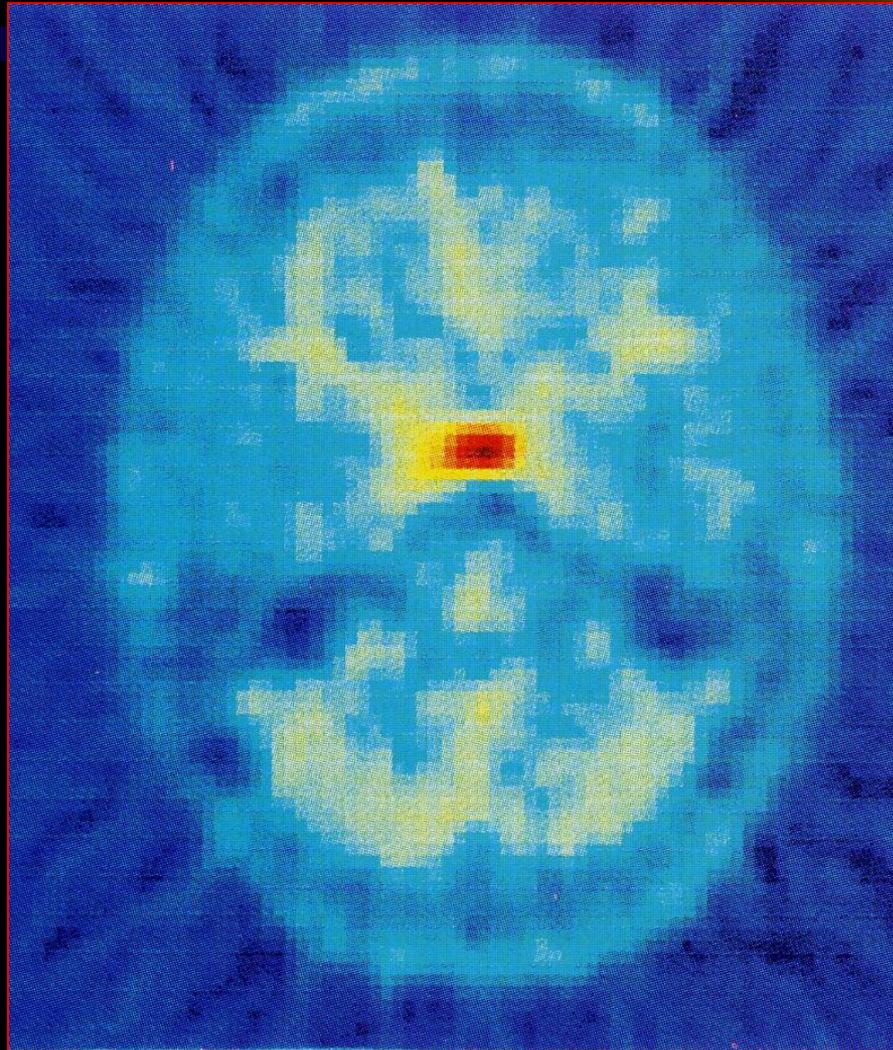
# Epileptic focus: decreased activity

**$^{11}\text{C}$ -flumazenil**

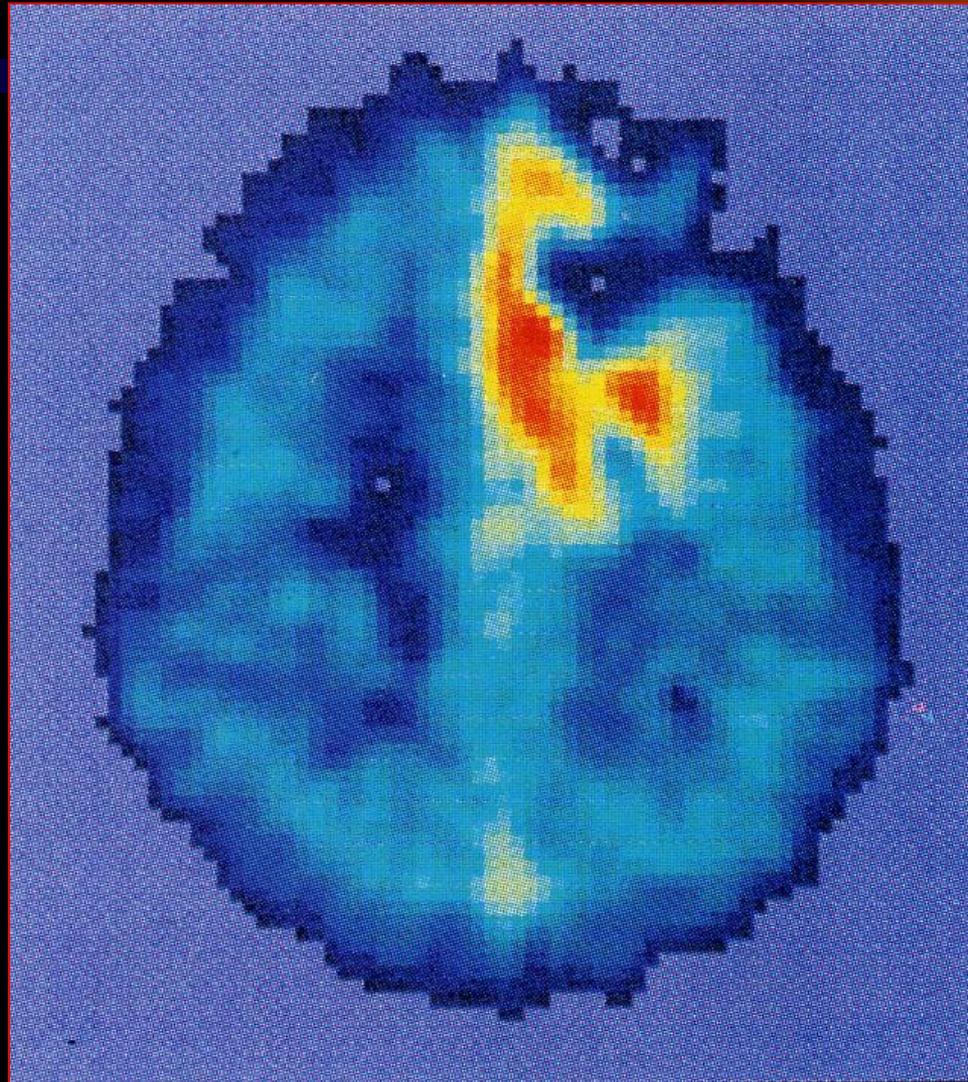
**$^{18}\text{F}$ -FDG**



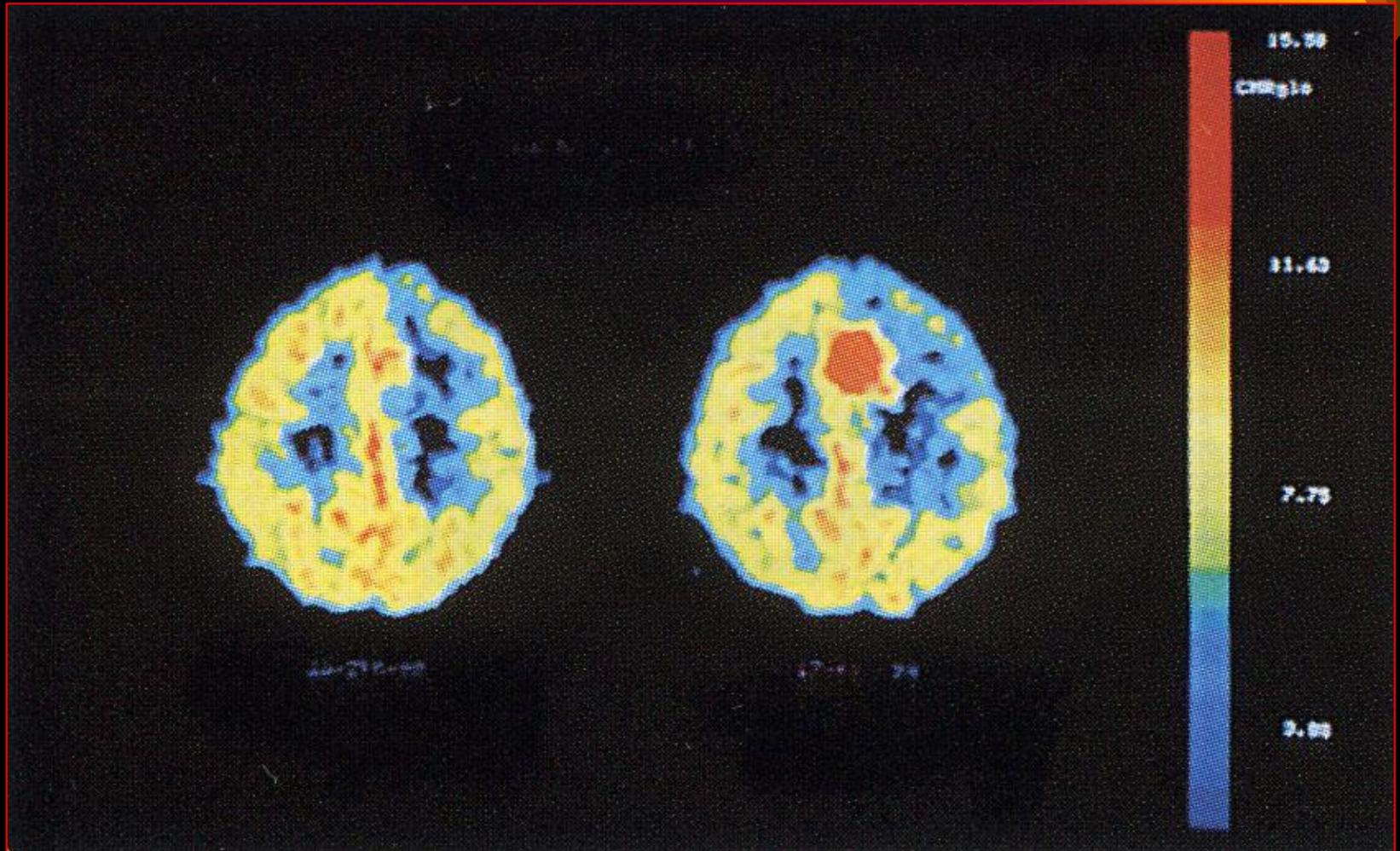
# **$^{11}\text{C}$ -methionin uptake: microadenoma**



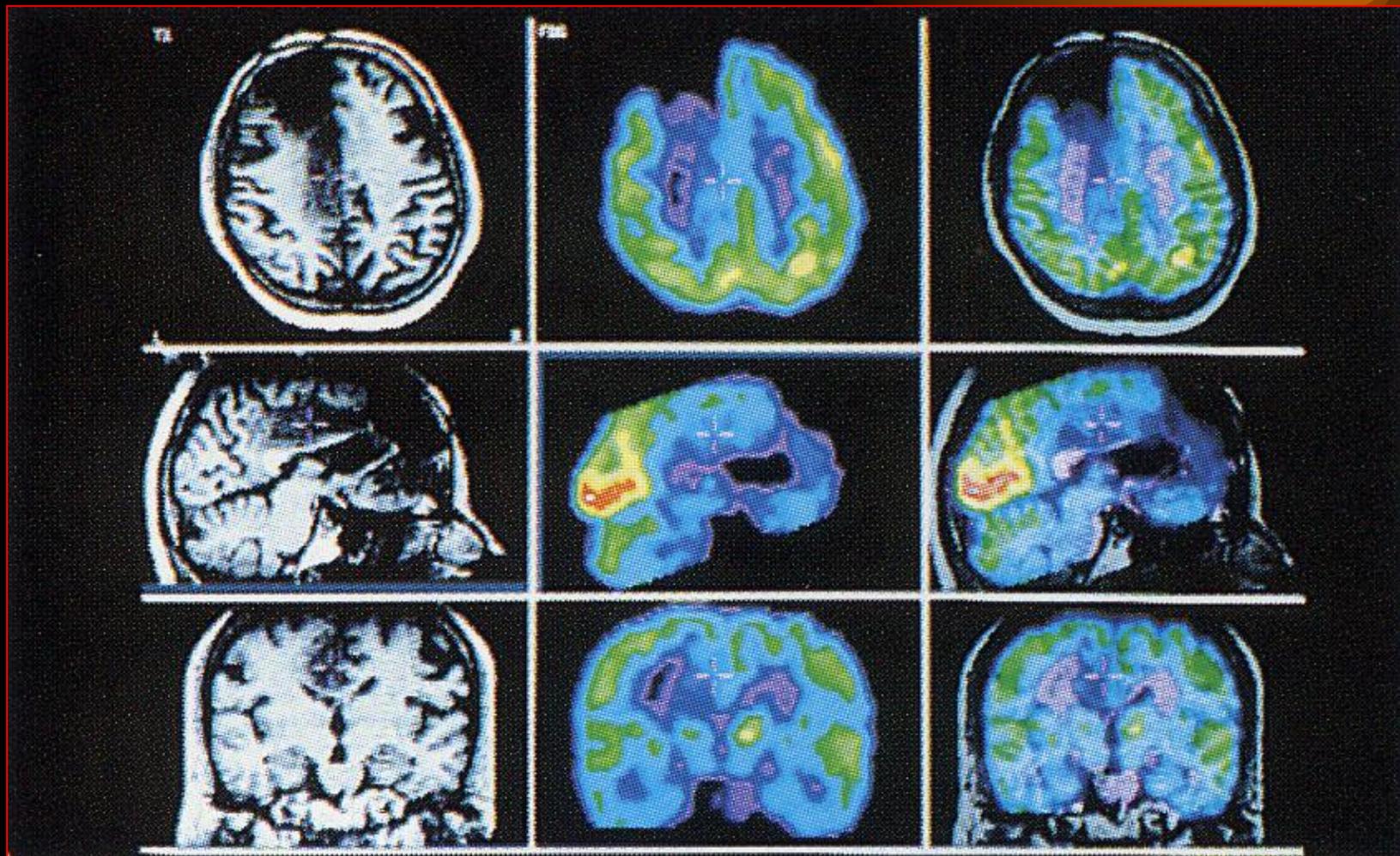
# 18F-FDG uptake after surgery of a recurrent tumor



# Revealing of recurrence of a parasagittal meningioma by $^{18}\text{F}$ -FDG



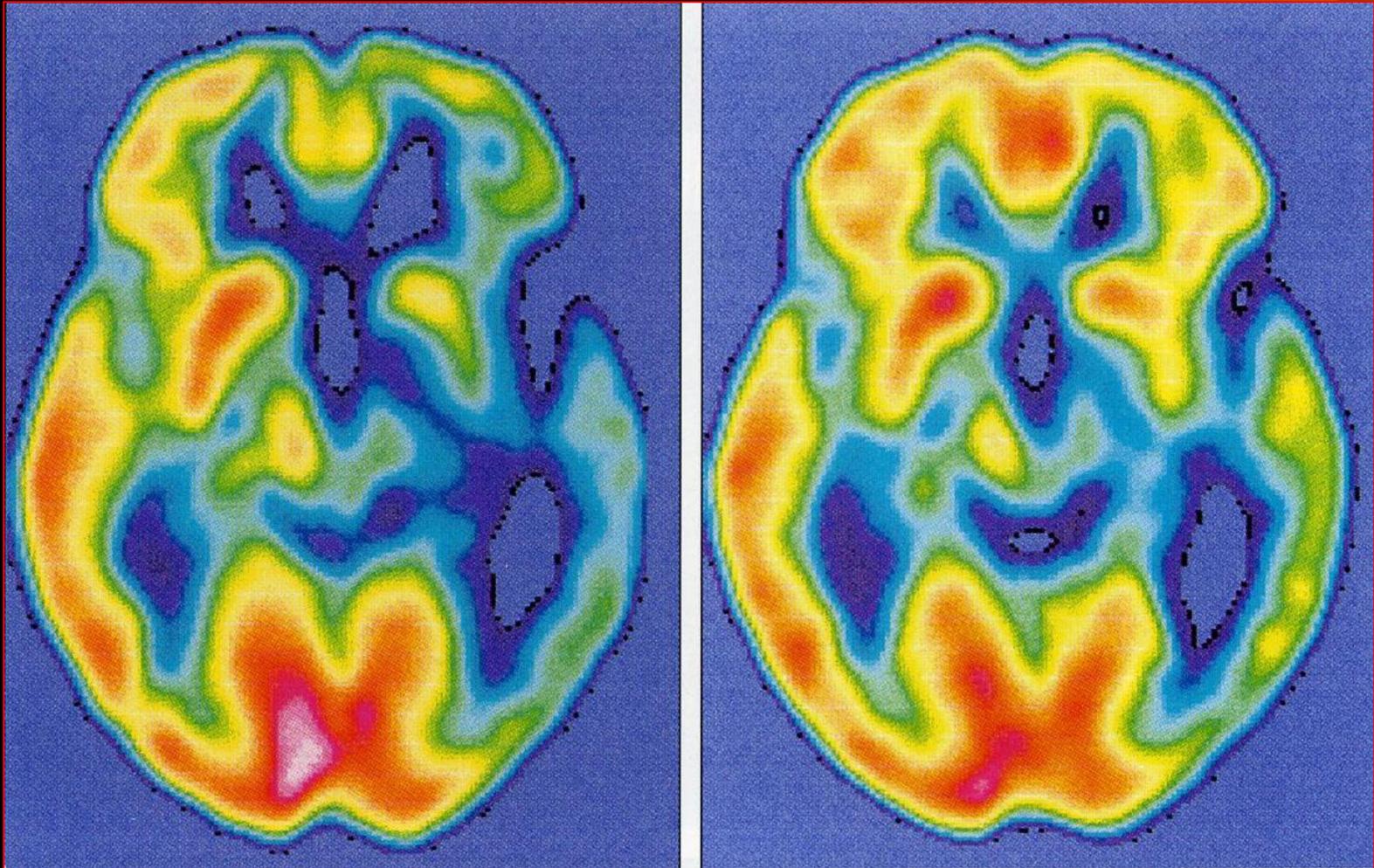
# 18F-FDG PET-MR fused scan of a glioma's recurrence after surgery



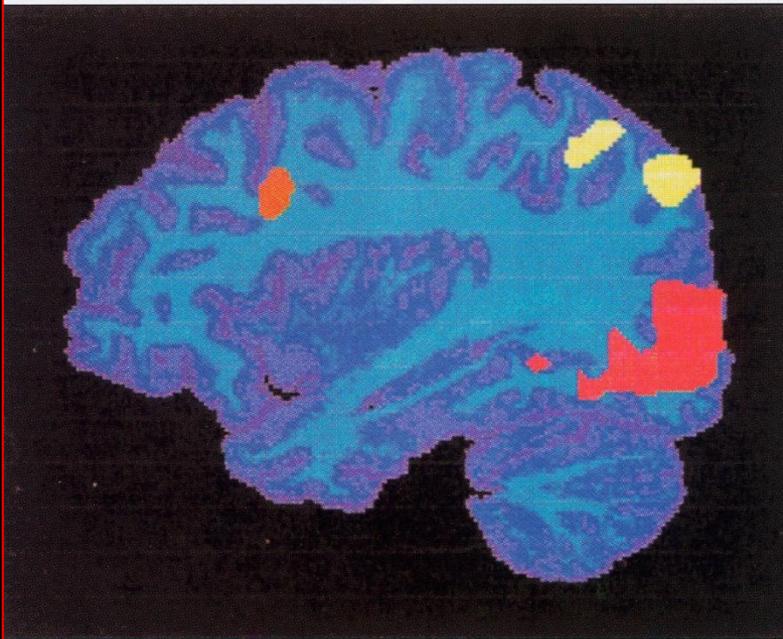
# Evaluation of therapeutic effects by $^{18}\text{F}$ -FDG

Stroke

after vinpocetin infusion  
(2 weeks later)

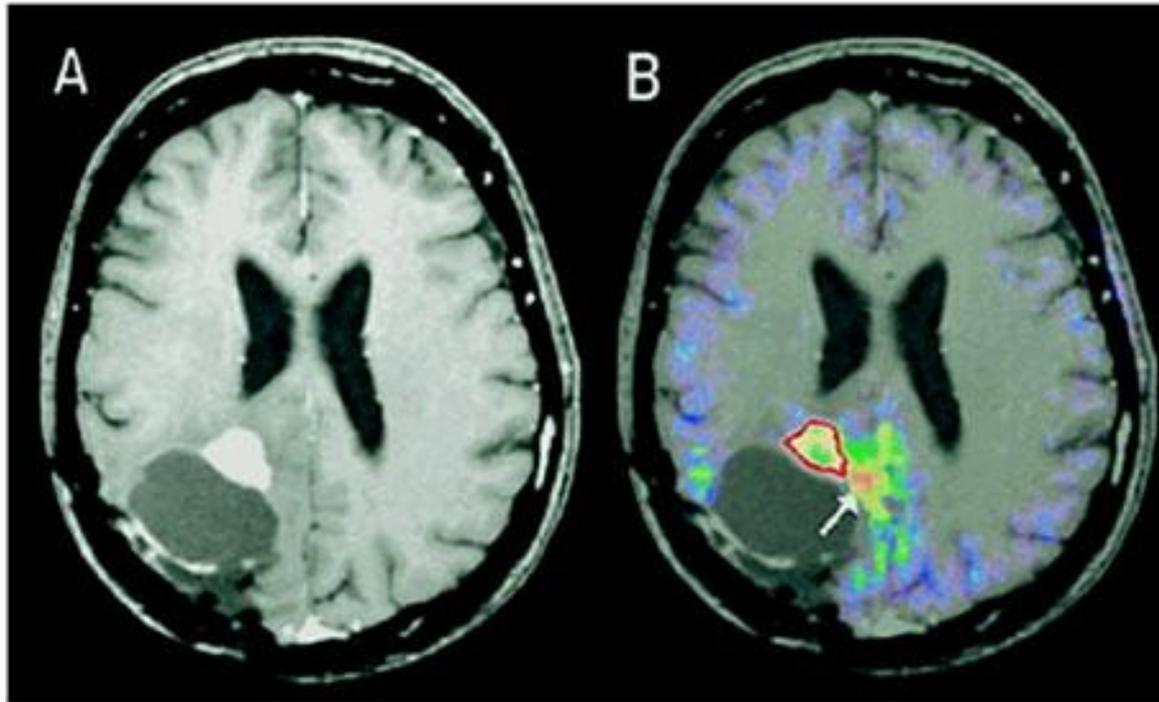


# Mapping of brain function

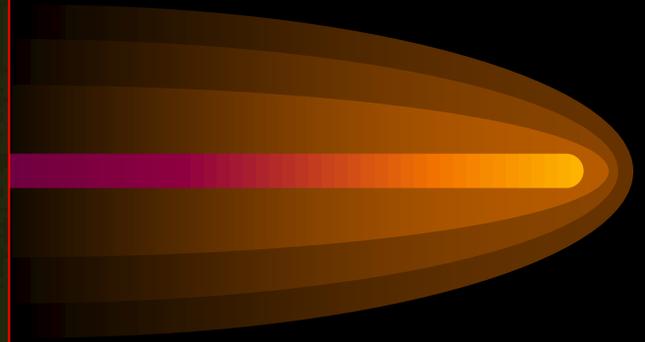


**Task-related functional  
PET investigations**

# Methionin PET and MRI fused imaging: size of recurrent tumor after surgery



A, T1-weighted MRI scan with gadolinium-diethylenetriamine penta-acetic acid shows contrast enhancement of the suspected lesion at the mesial wall of the cavity where the tumor was removed. B, fusion of coregistered [11C]methionine PET and MRI shows increased tracer uptake (arrow) outside the contrast-enhancing area (red contour in B corresponds to contrast enhancement in A).



*Thank you  
for  
your attention!*

**Loris Marazzi:  
Your brain is your power**