

Analisi semi-quantitativa di immagini cerebrali

# IMMAGINE:

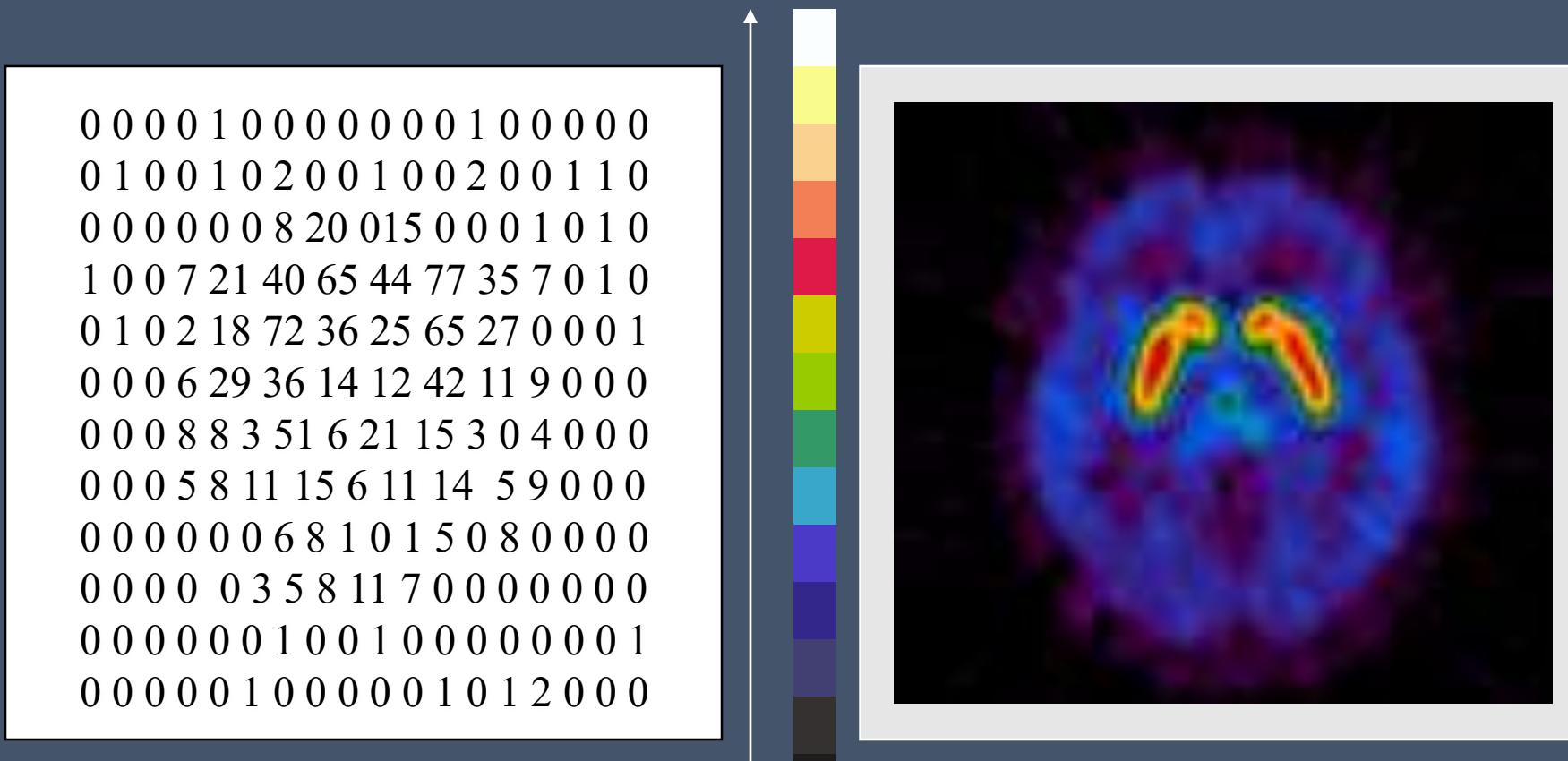
rappresentazione digitale su scala colorimetrica  
di una matrice di valori numerici di intensità nota

0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
0	0	0	1	0	0	1	0	2	0	0	1	0	0	2	0
0	1	1	0	0	0	0	0	0	8	20	0	15	0		
0	0	1	0	1	0	1	0	7	0	0	4	0	0		
0	77	35	7	0	1	0	0	1	0	2	18	0			
72	36	25	65	27	31	0	0	1	0	0	0	0	0	0	0
6	29	36	14	12	42	11	9	0	0	0	0	0	0	0	0
0	0	8	8	3	51	6	21	15	3	0	4	0	0		
0	0	0	3	5	8	11	15	6	11	14	5	9			
0	0	0	0	21	34	0	68	0	6	8	1	0	1		
5	0	8	0	0	22	0	0	0	0	0	3	5	8		
11	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0
0	1	0	0	0	0	1	0	1	2	0	0	0	23	0	



# IMMAGINE CEREBRALE:

rappresentazione digitale su scala colorimetrica  
di una matrice di misura del cervello

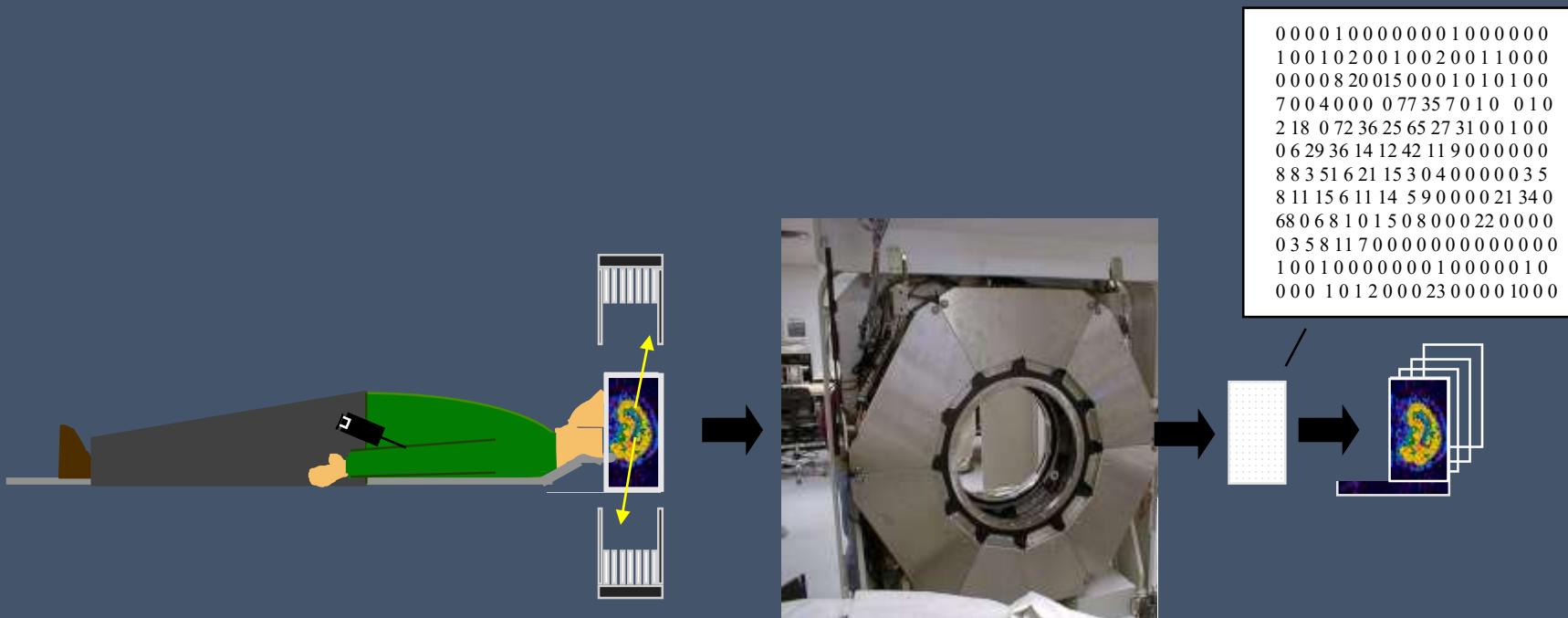


# MISURA DEL CERVELLO:

- Come misuriamo
- Cosa misuriamo
- Come analizziamo

# COME MISURIAMO:

Tecniche tomografiche ad emissione: SPET, PET



## **SPET**

**Risoluzione: 8 – 15 mm**

**Tempo di acquisizione: 45 min**

**Rumore: alto (radiazione diffusa e attenuazione)**

## **PET**

**Risoluzione: 4 – 6 mm**

**Tempo di acquisizione: 10 min**

**Rumore: basso (radiazione diffusa e attenuazione corrette)**

# COSA MISURIAMO:

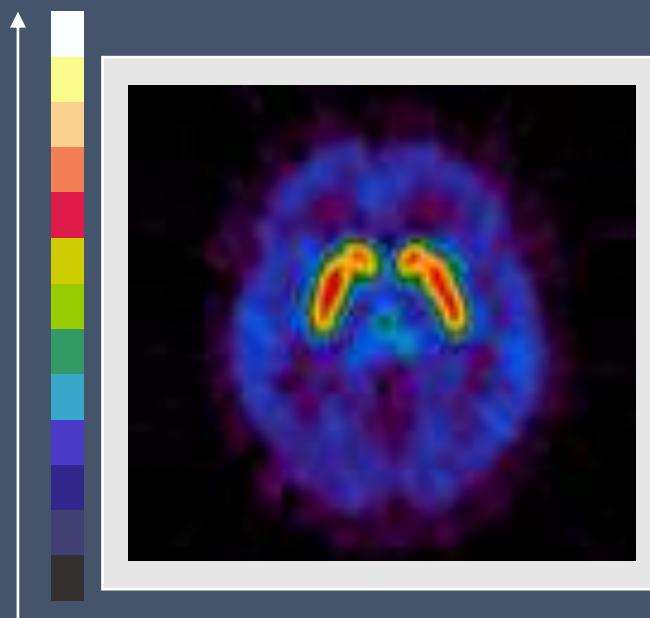
- Flusso
- Metabolismo
- Densità recettoriale

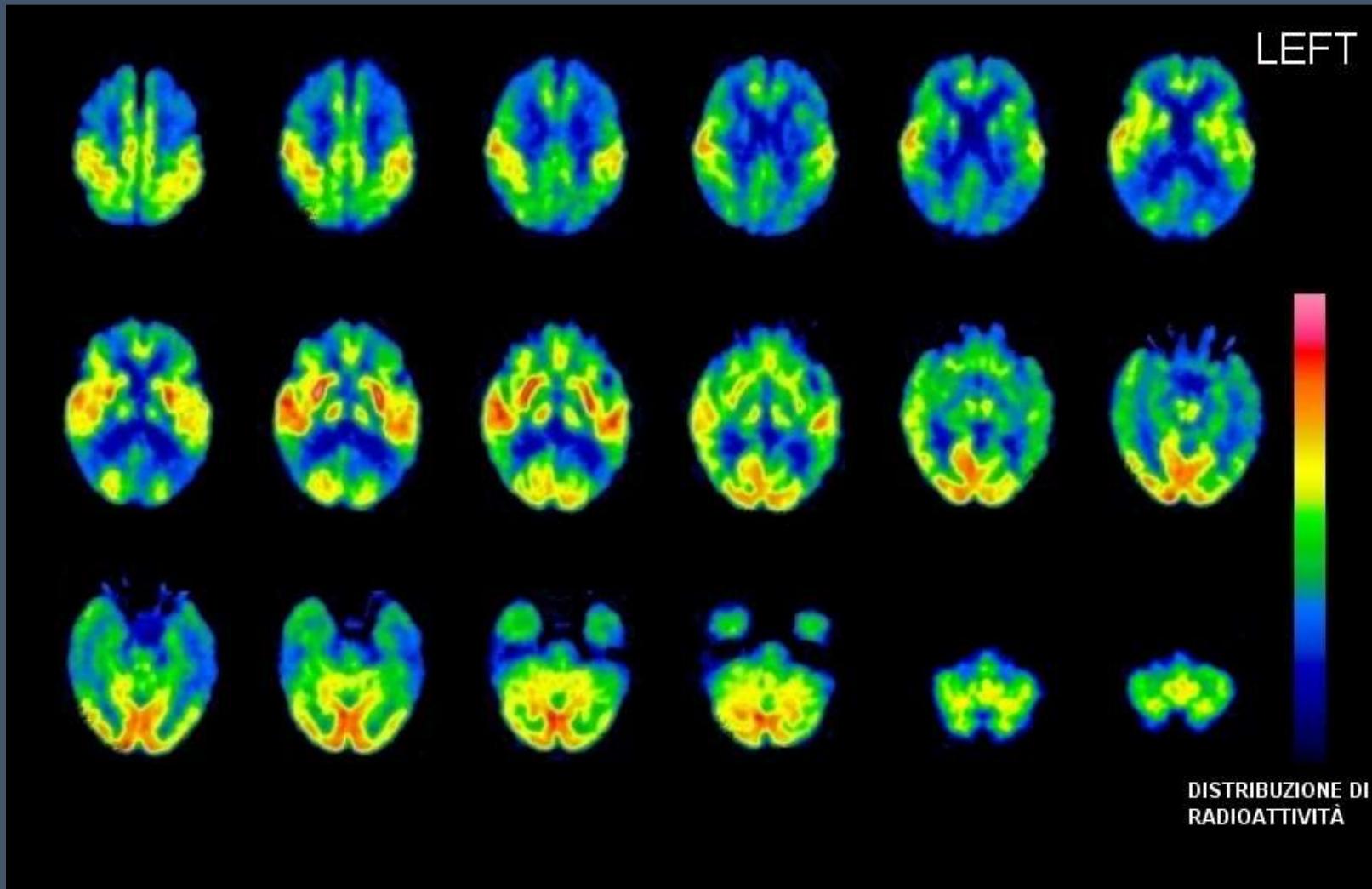
# **ANALISI DATI:**

- Qualitativa
- Quantitativa
- Semi-quantitativa

# **ANALISI QUALITATIVA:**

**Osservazione delle immagini e valutazione sulla base  
di differenze macroscopiche dei valori misurati**





Studio  $^{18}\text{F}$ -FDG PET. Paziente con AD in fase avanzata. Oltre alla tipica riduzione di metabolismo temporo-parietale si osserva una estensione dell'ipometabolismo anche alle regioni frontali.

# Refertazione convenzionale: analisi qualitativa immagini di flusso

## F18-FDG

L'analisi qualitativa delle immagini **non evidenzia anomalie della distribuzione del tracciante** nelle regioni corticali, sottocorticali e cerebellari. Studio metabolico nei limiti della norma.

L'analisi qualitativa delle immagini **evidenzia riduzione dell'accumulo** di tracciante in corrispondenza del lobo parietale inferiore, bilateralmente, maggiore a destra. Ipometabolismo nelle regioni sovradescritte

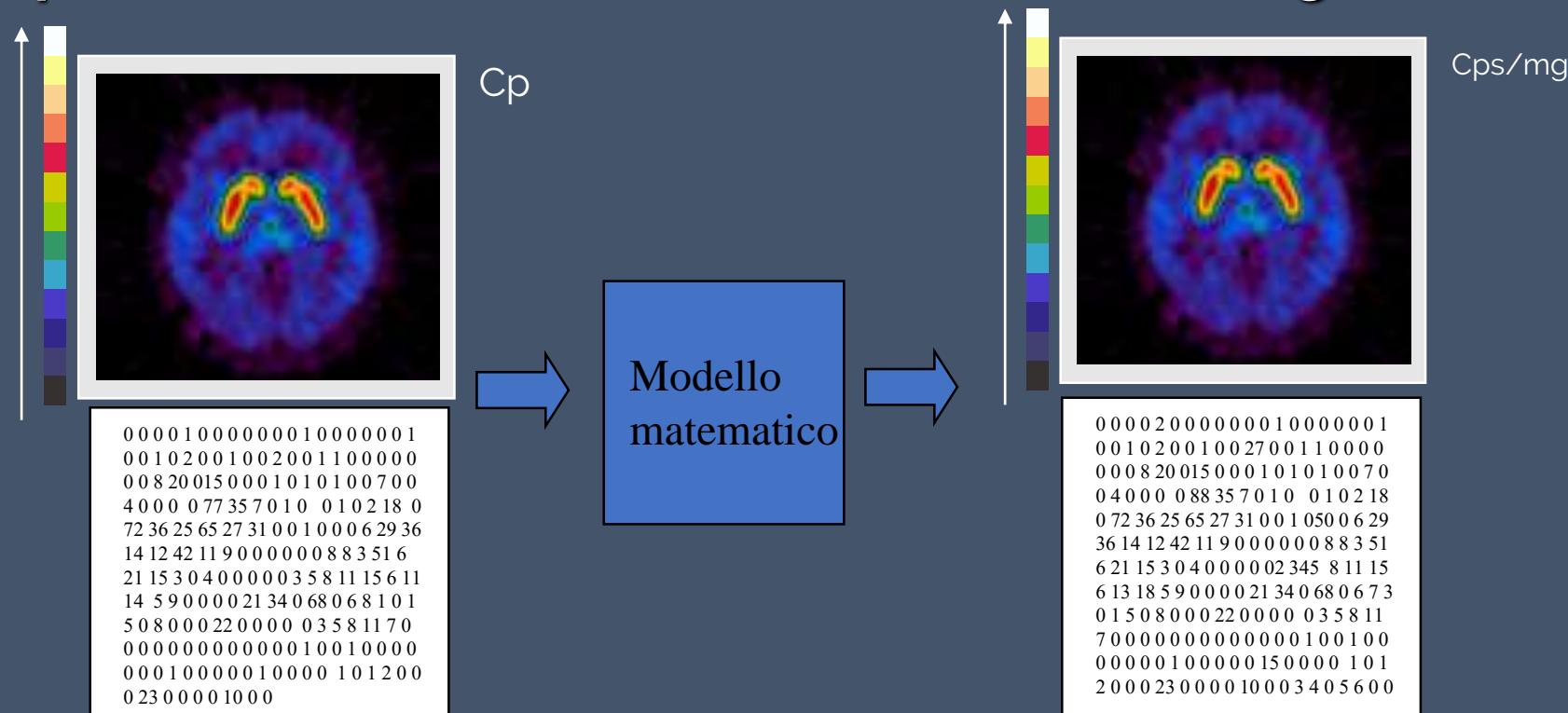
## Tc99-ECD

L'analisi qualitativa delle immagini **non evidenzia anomalie della distribuzione del tracciante** nelle regioni corticali, sottocorticali e cerebellari. Studio di flusso nei limiti della norma.

L'analisi qualitativa delle immagini **evidenzia riduzione dell'accumulo** di tracciante in corrispondenza del lobo parietale inferiore, bilateralmente, maggiore a destra. ipoperfusione parietale

# MISURA QUANTITATIVA:

**Valutazione di parametri numerici (es. parametri di flusso, metabolismo, densità recettoriale) misurati dopo l'applicazione di modelli matematici che simulano il comportamento del tracciante all'interno dell'organismo**



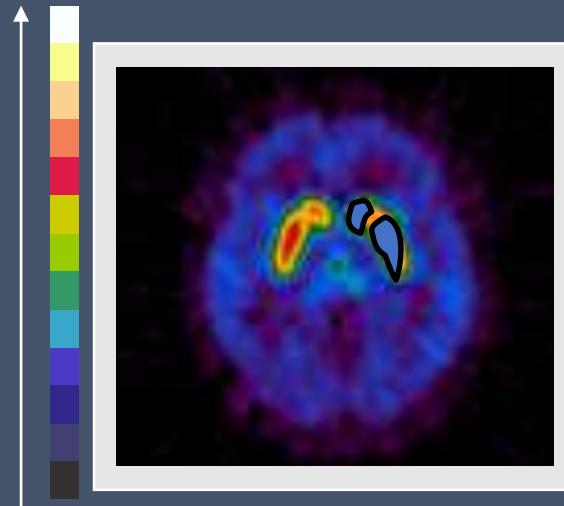
## **MISURA SEMI-QUANTITATIVA:**

**Valutazione di valori numerici che esprimono la distribuzione di radioattività all'interno di organi di interesse**

analisi semi-quantitativa  
mediante regioni di  
interesse sulle immagini



ROI analysis



Confronto intra soggetto

Confronto inter soggetto

analisi semi-quantitativa  
mediante confronto  
statistico di immagini di  
flusso con gruppo di  
controllo (soggetti  
normali)



Statistical Parameter Mapping (SPM)

## Programma Statistical Parametric Mapping (SPM)

Vantaggi

- free download
- Compatibilità con sistemi UNIX e Windows

Constraints

- Protocolli di acquisizione rigidi
- Hardware: spazio disco 1 Gbyte
- Software:

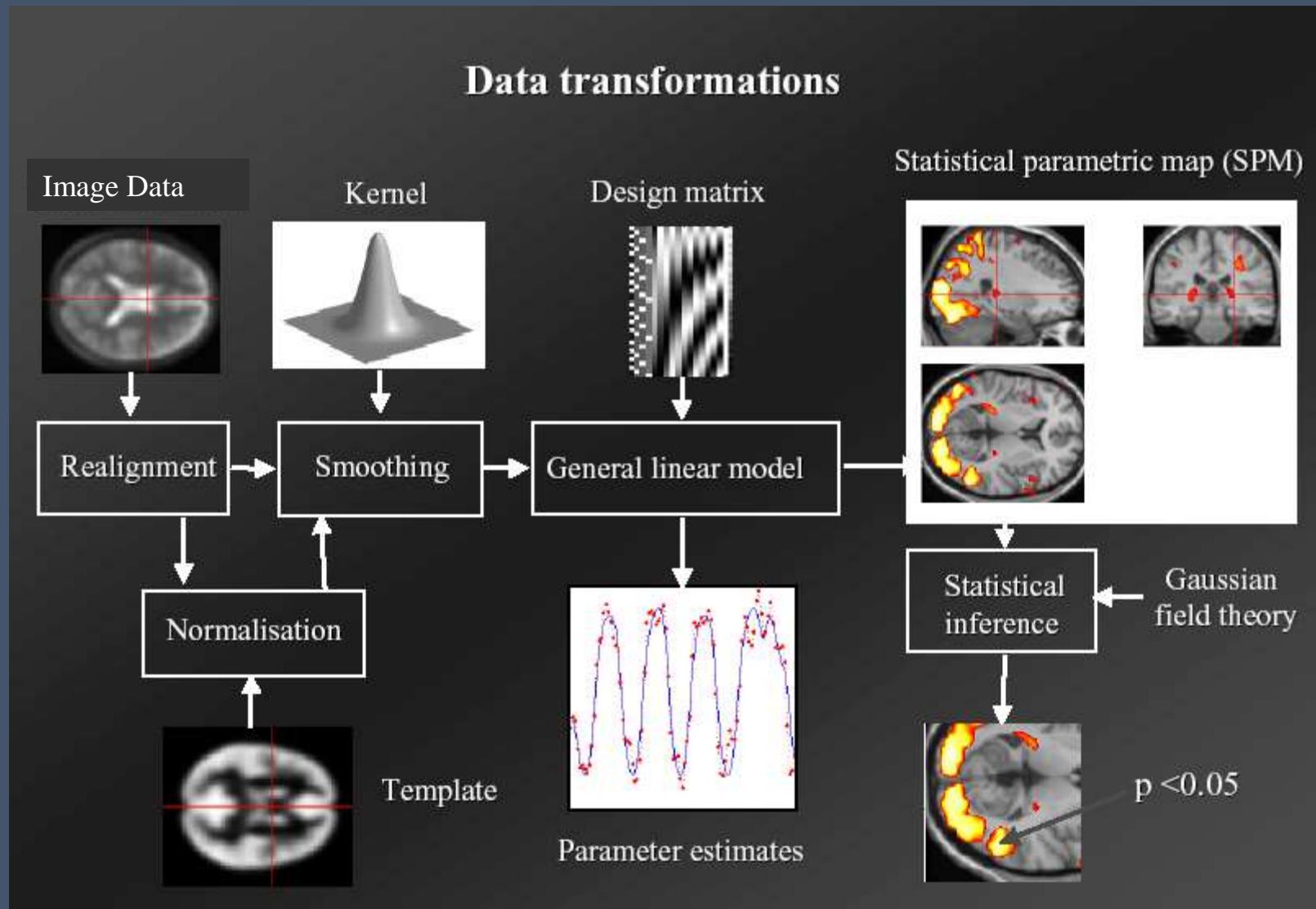
Formato Analyze (int 8 bit)

Matlab: versioni superiori alla 5



- Sviluppo di procedure per l'estrazione dei dati dai tomografi
- Sviluppo di programmi per la conversione dei dati

## Data transformations



## Spatial normalisation

- Inter-subject averaging
  - extrapolate findings to the population as a whole
  - increase activation signal above that obtained from single subject
  - increase number of possible degrees of freedom allowed in statistical model
- Enable reporting of activations as co-ordinates within a known standard space
  - e.g. the space described by Talairach & Tournoux
- Warp the images such that functionally homologous regions from the different subjects are as close together as possible
  - Problems:
    - no exact match between structure and function
    - different brains are organised differently
    - computational problems (local minima, not enough information in the images, computationally expensive)
  - Compromise by correcting for gross differences followed by smoothing of normalised images

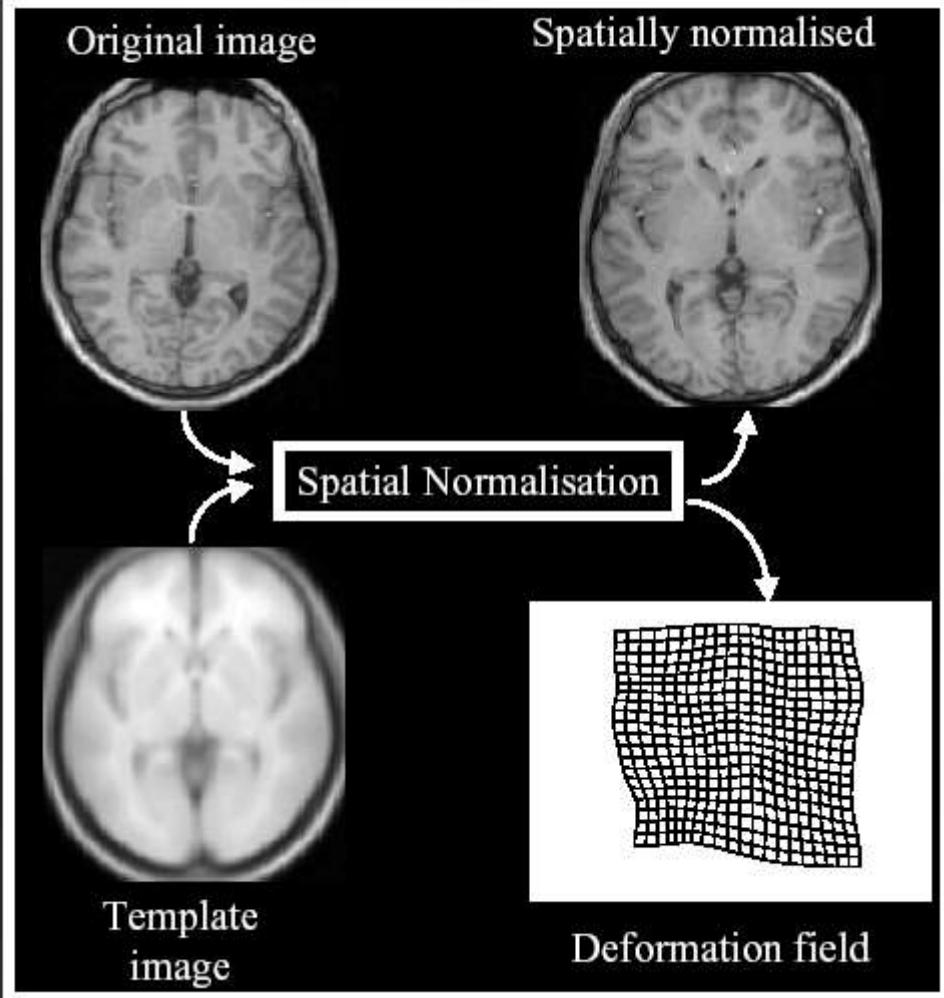
## Spatial Normalisation

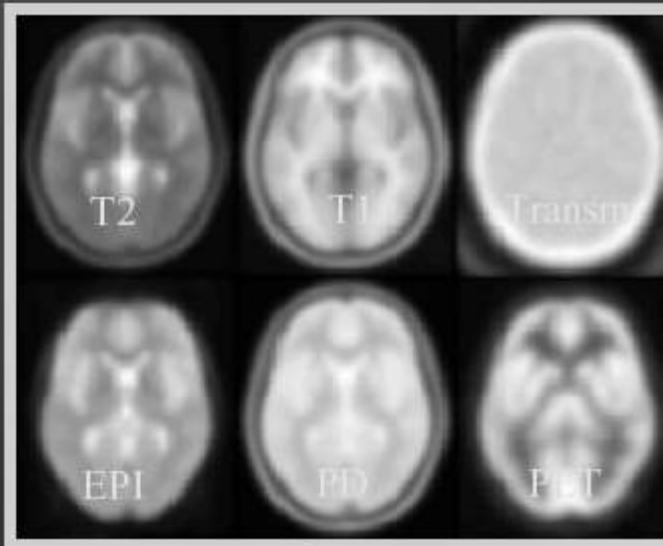
Determine the spatial transformation that minimises the sum of squared difference between an image and a linear combination of one or more templates.

Begins with an affine registration to match the size and position of the image.

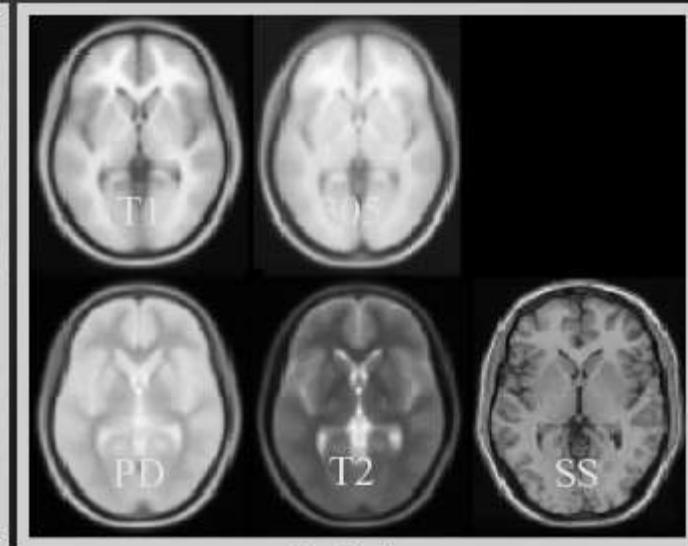
Followed by a global non-linear warping to match the overall brain shape.

Uses a Bayesian framework to simultaneously maximise the smoothness of the warps.

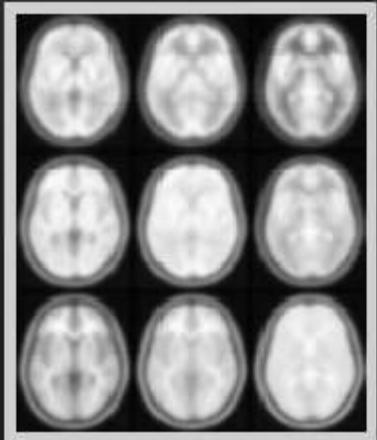




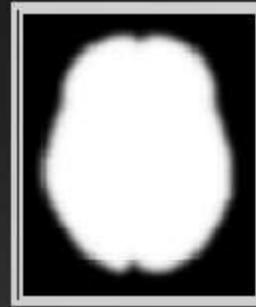
Template Images



“Canonical” images



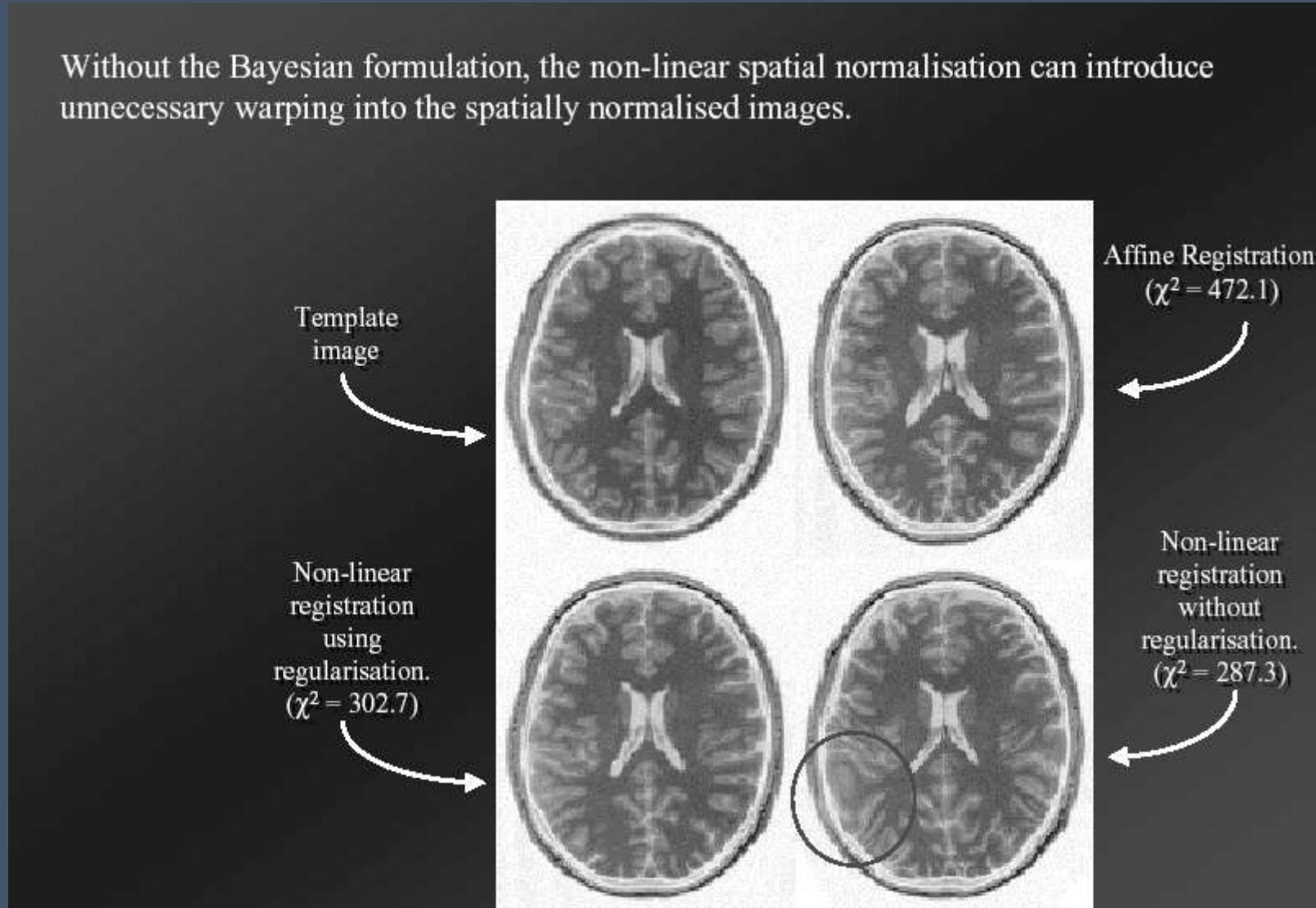
A wider range of different contrasts can be normalised by registering to a linear combination of template images.

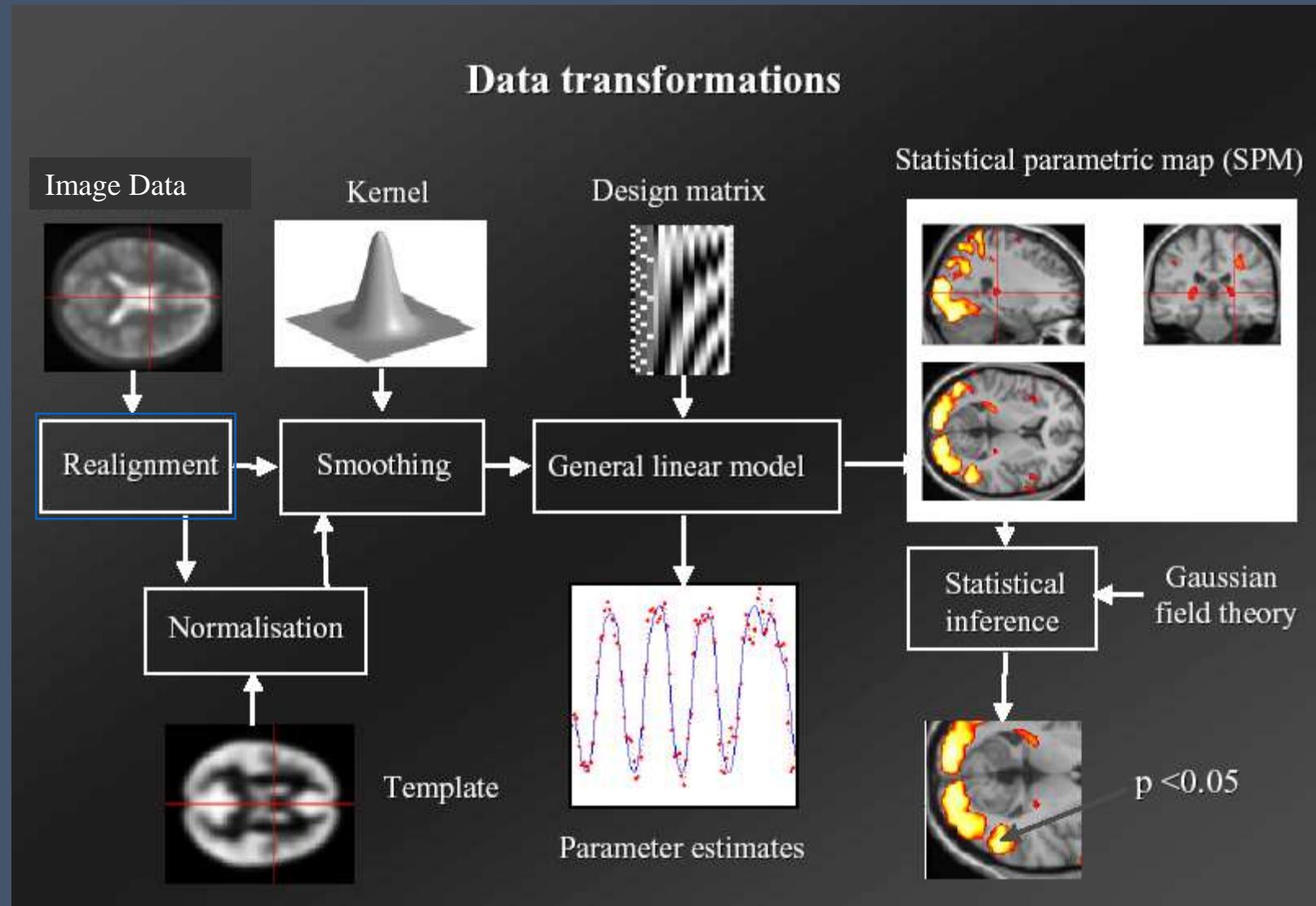


Spatial normalisation can be weighted so that non-brain voxels do not influence the result.

Similar weighting masks can be used for normalising lesioned brains. (Mask)

Without the Bayesian formulation, the non-linear spatial normalisation can introduce unnecessary warping into the spatially normalised images.

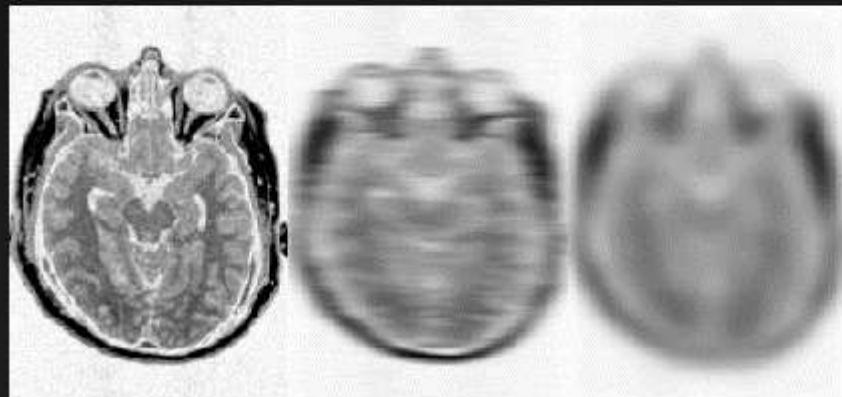




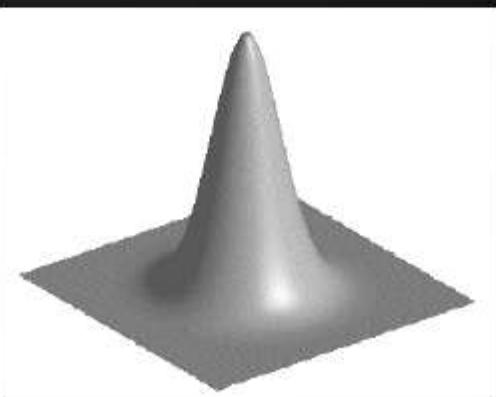
## Smoothing

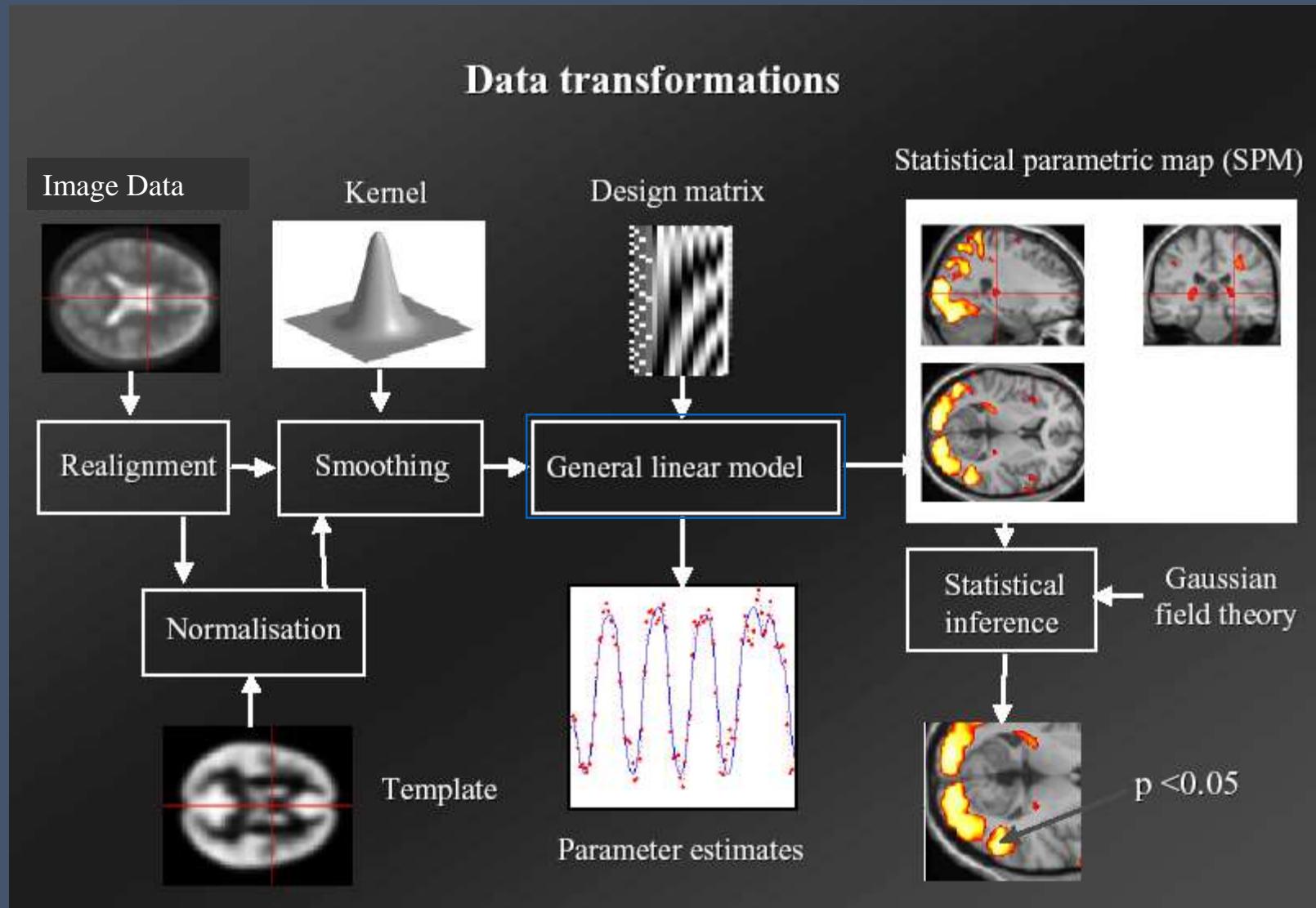
- Why Smooth?
  - Potentially increase signal to noise.
  - Inter-subject averaging.
  - Increase validity of SPM.
- In SPM, smoothing is a convolution with a Gaussian kernel.
- Kernel defined in terms of FWHM (full width at half maximum). (e.g. 8, 8, 8 mm)

Gaussian convolution is separable



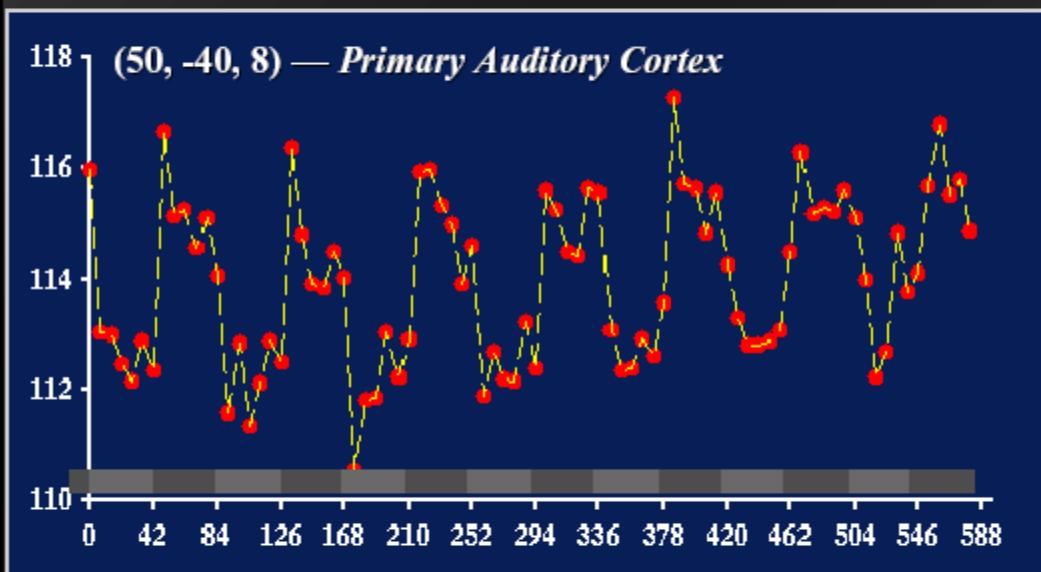
Gaussian smoothing kernel



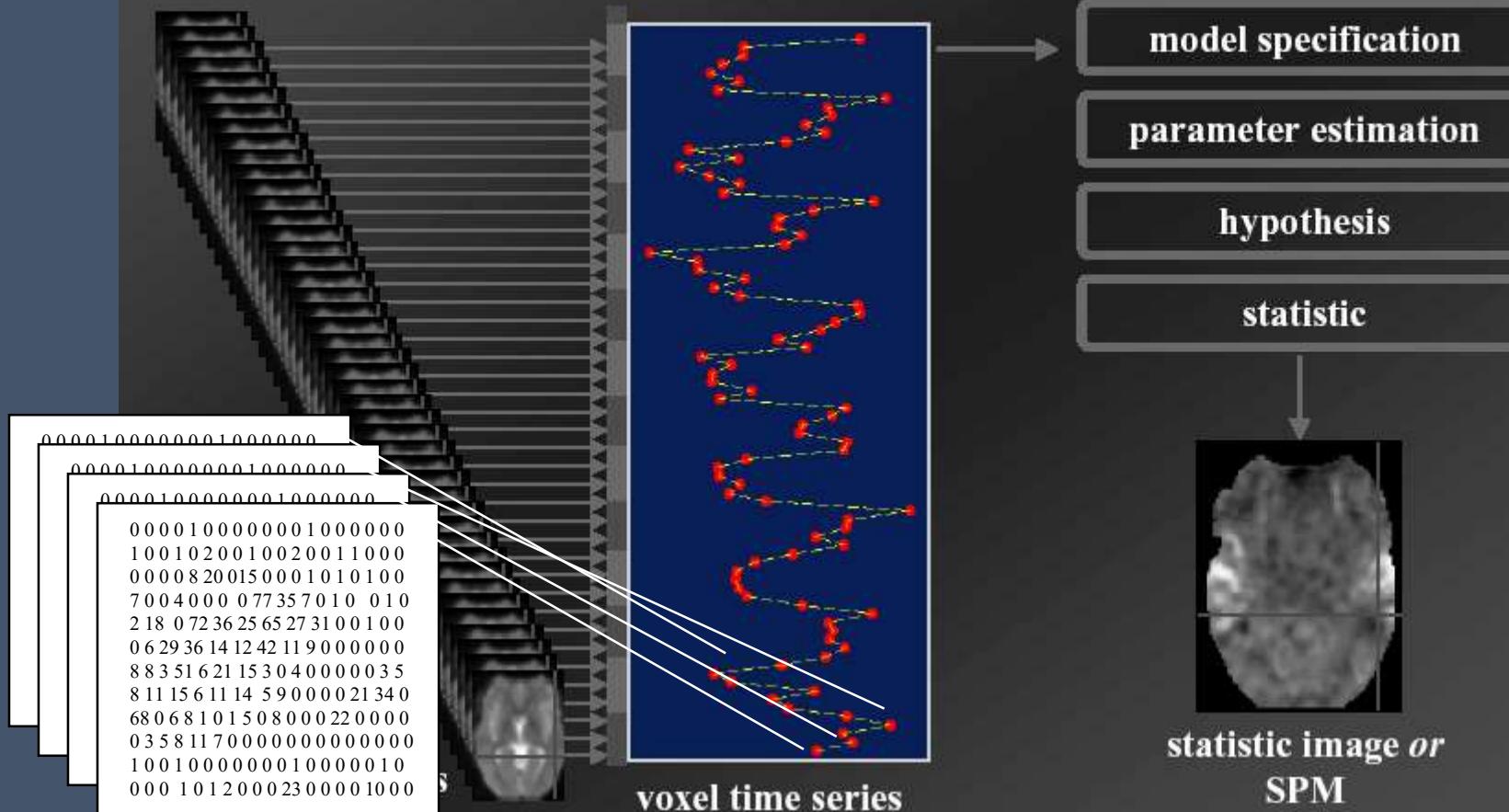


## Example epoch fMRI activation dataset: Auditory stimulation

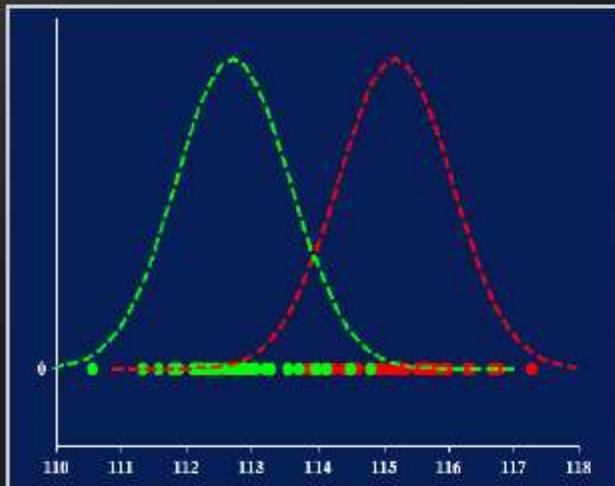
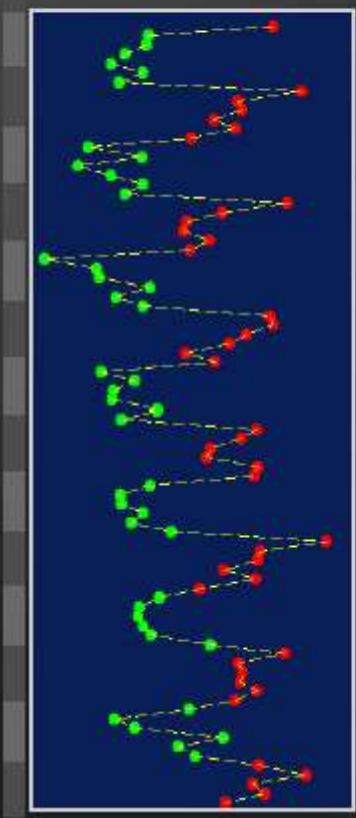
- Single subject
    - RH male
  - Conditions
    - Passive word listening
    - Bisyllabic nouns
    - 60wpm
    - against rest
  - Epoch fMRI
    - rest & words
    - epochs of 6 scans
    - ⇒ 42 second epochs
    - 7 BA cycles
- experiment was 8 cycles:  
first pair of blocks dropped  
→BABABABABABA  
⇒last 84 scans of experiment  
images 16–99  
→~10 minutes scanning time*



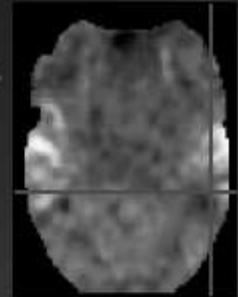
# Voxel by voxel statistics...



...e.g. two-sample *t*-test?



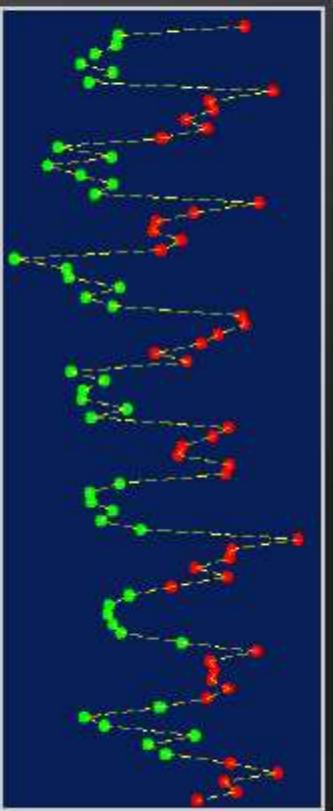
$$t = \frac{\bar{Y}_{1*} - \bar{Y}_{0*}}{\sqrt{\hat{\sigma}^2(\gamma_{n_1} + \gamma_{n_0})}}$$



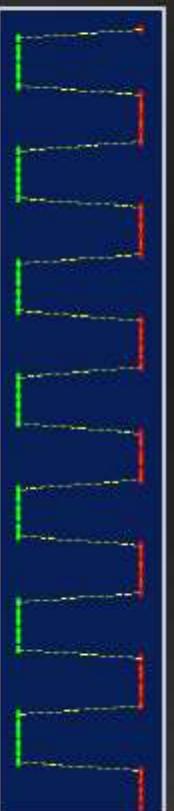
*t*-statistic image  
 $SPM\{t\}$   
compares size of effect  
to error variance

? standard *t*-test assumes independence  
⇒ ignores temporal autocorrelation!

## Regression example...



voxel time series



$$= \mu + \alpha$$

box-car reference function

$$Y_s = \mu + \alpha f(t_s) + \varepsilon_s$$

$$f(t_s) = 0 \text{ or } 1$$

$$\varepsilon_s \sim N(0, \sigma^2)$$

+ error  $\rightarrow t\text{-statistic for } H_0: \alpha > 0$

\* correlation:

test  $H_0: \rho = 0$  equivalent to  
test  $H_0: \alpha = 0$

\* two-sample  $t$ -test:

test  $H_0: \mu_0 = \mu_1$  equivalent to  
test  $H_0: \alpha = 0$

✓ can extend to account for  
temporal autocorrelation!

...revisited

$$Y_s = \mu \times 1 + \alpha \times f(t_s) + \varepsilon_s$$

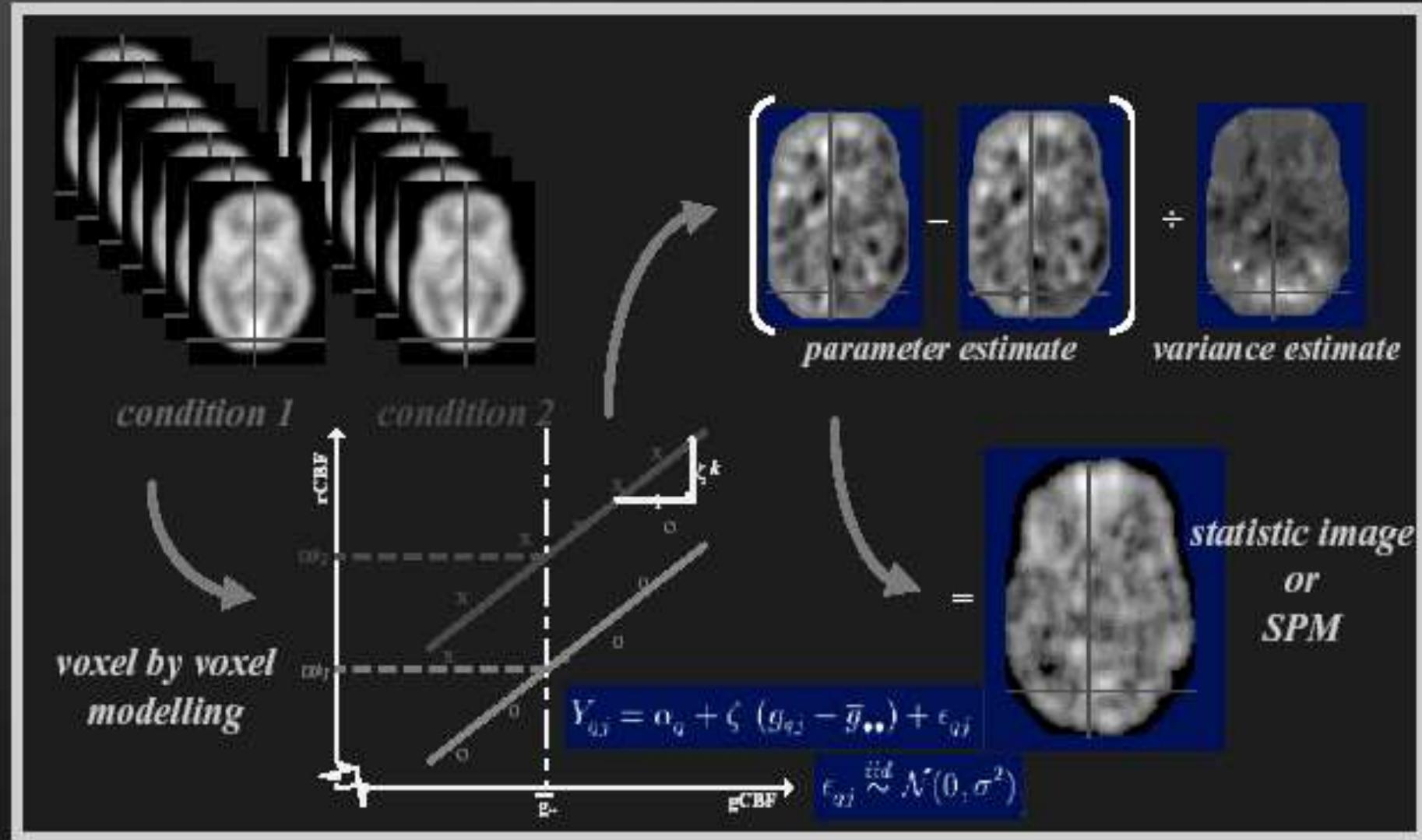
## fMRI box car example...

$$Y = X\beta + \varepsilon$$

Diagram illustrating the linear model components:

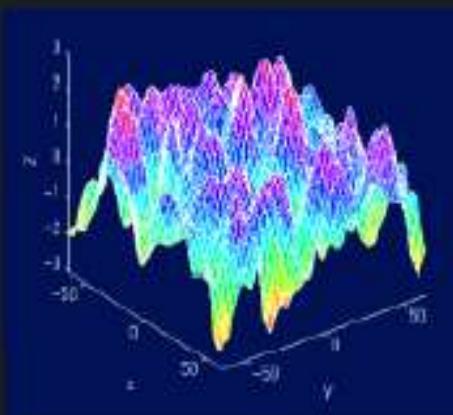
- data vector**:  $Y$  (vertical stack of fMRI time series)
- design matrix**:  $X$  (matrix of boxcar functions)
- parameters**:  $\beta$  (vector of regression coefficients:  $\alpha, \mu, \beta_3, \beta_4, \beta_5, \beta_6, \beta_7, \beta_8, \beta_9$ )
- error vector**:  $\varepsilon$  (vertical stack of error terms)

# Statistical Parametric Mapping...

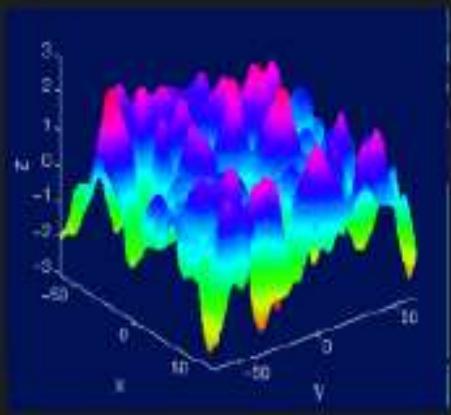


## SPM approach: Random fields...

- Consider statistic image as lattice representation of a continuous random field
- Use results from continuous random field theory

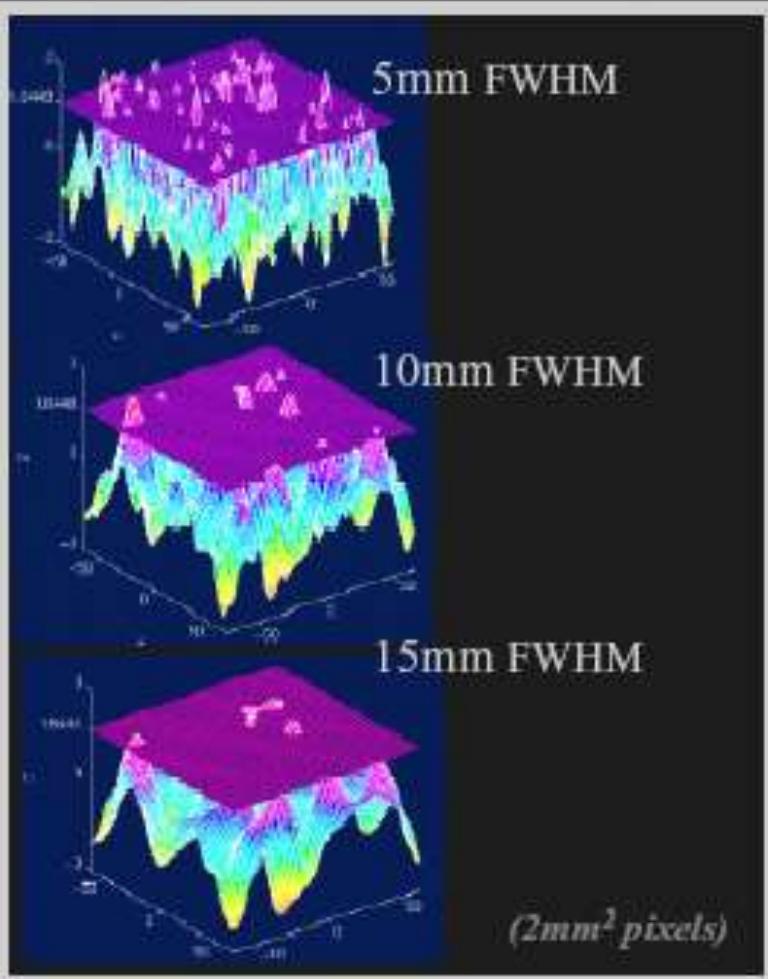


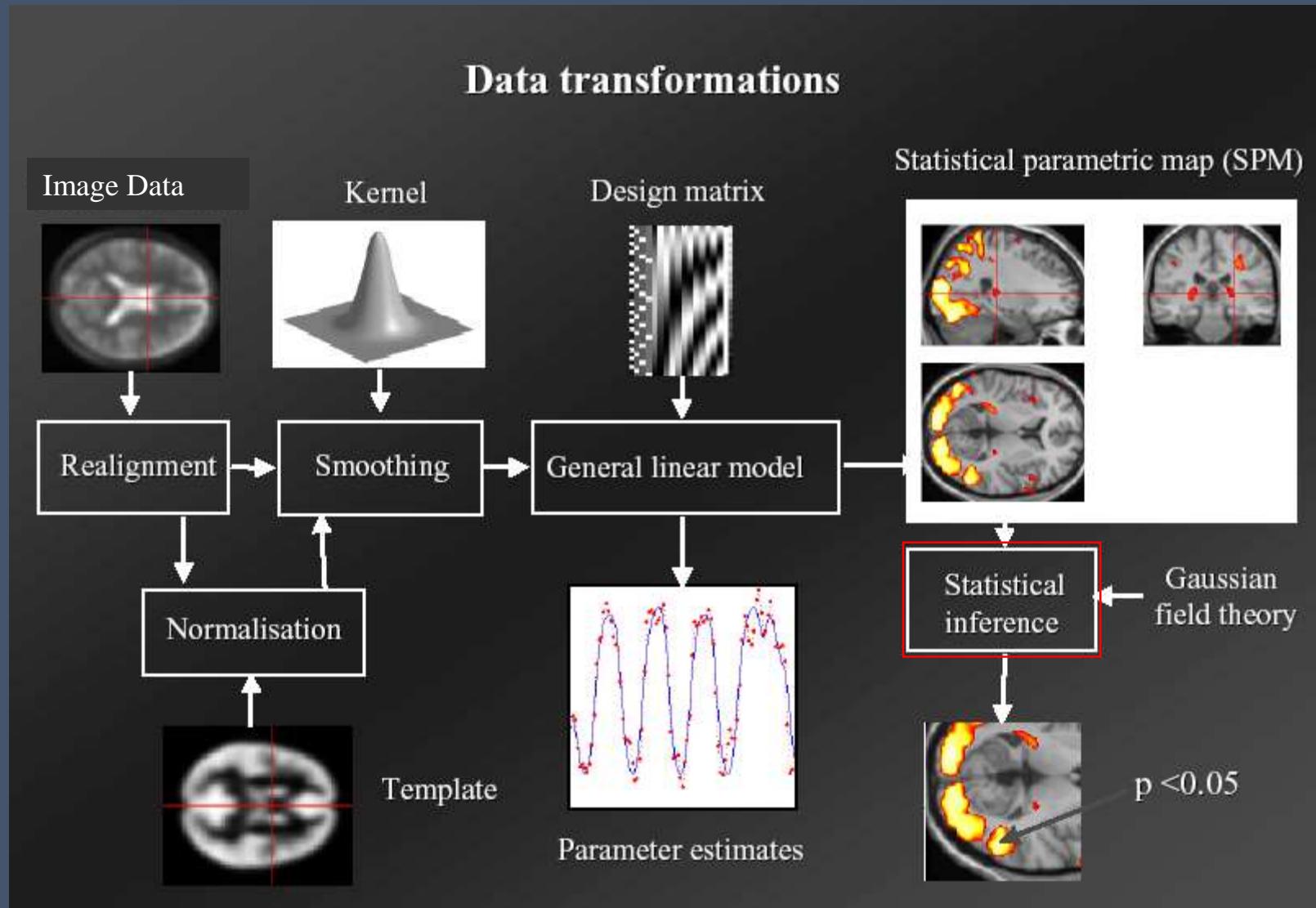
*lattice representation*



# Suprathreshold cluster tests...

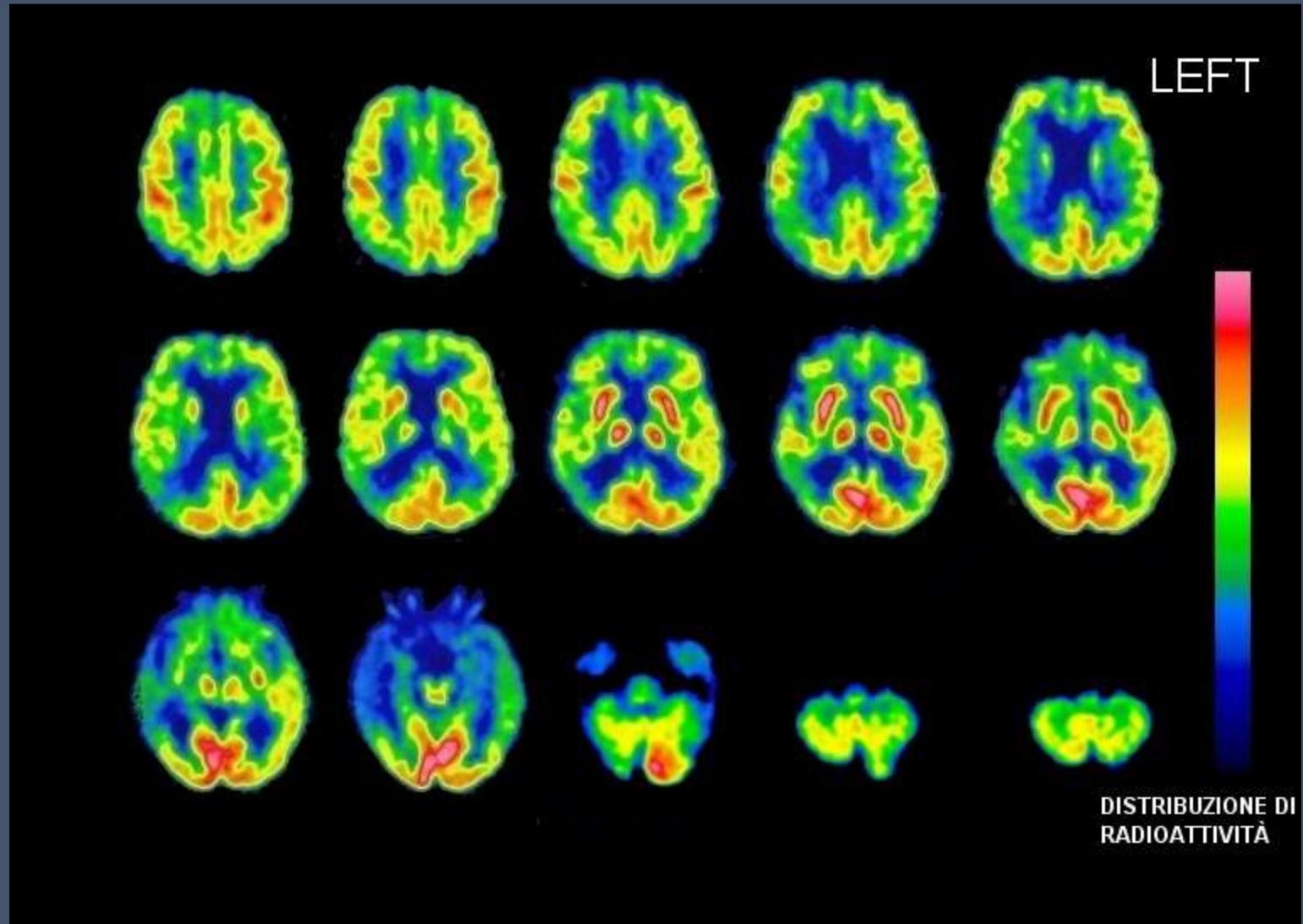
- Primary threshold  $\alpha$ 
  - examine connected components of excursion set
  - *Suprathreshold clusters*
  - Reject  $H^W$  for clusters of voxels  $W$  of size  $S > s_\alpha$
- Localisation (Strong control)
  - at cluster level
  - increased power
  - esp. high resolutions (*fMRI*)
- Thresholds,  $p$ -values
  - $\Pr(S_{\max}^\Omega > s_\alpha \mid H^\Omega) \leq \alpha$   
*Nosko, Friston, (Worsley)*
  - Poisson occurrence (*Adler*)
  - Assume form for  $\Pr(S=s \mid S>0)$



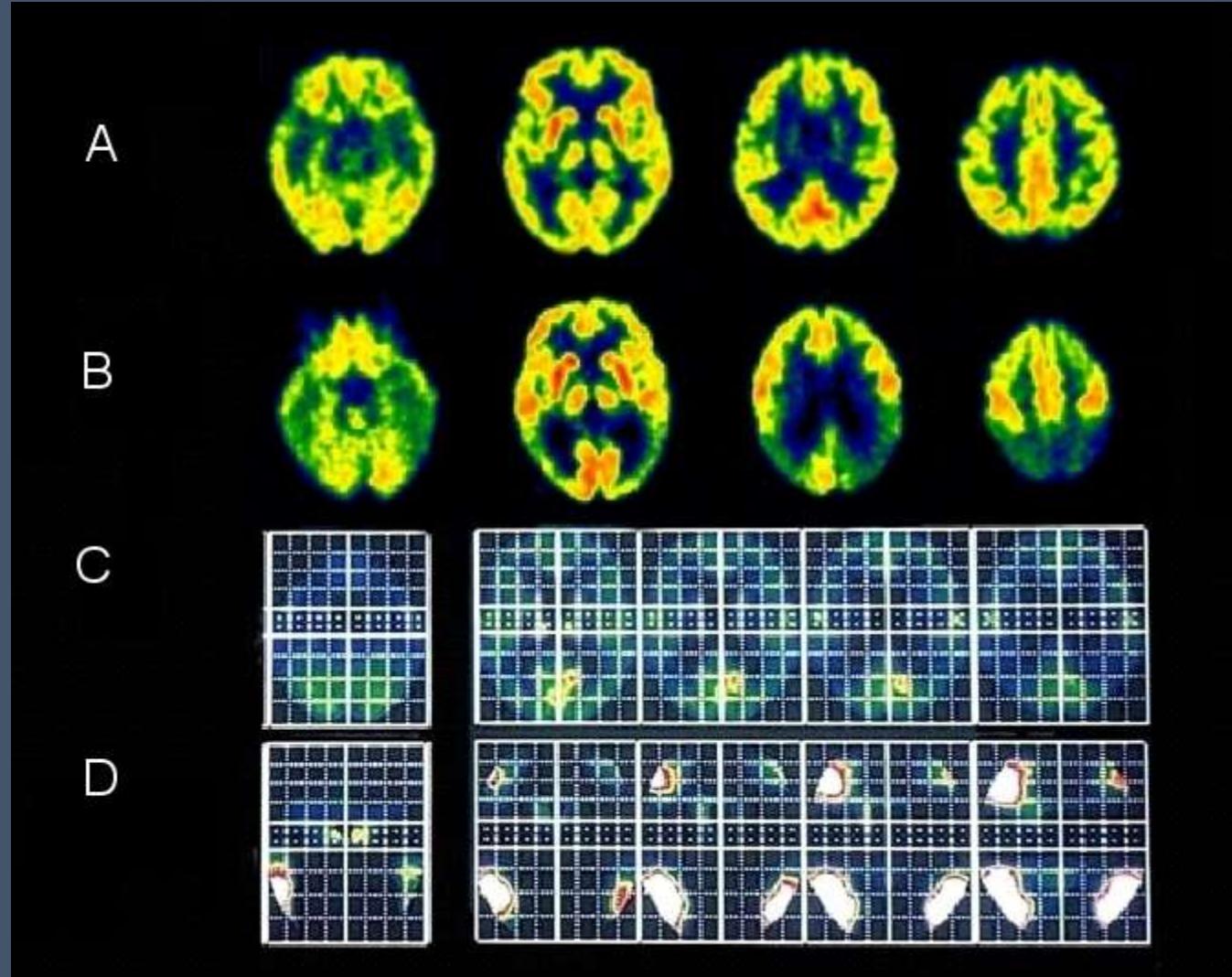


## **Principali applicazioni cliniche di SPM in Neurologia PET**

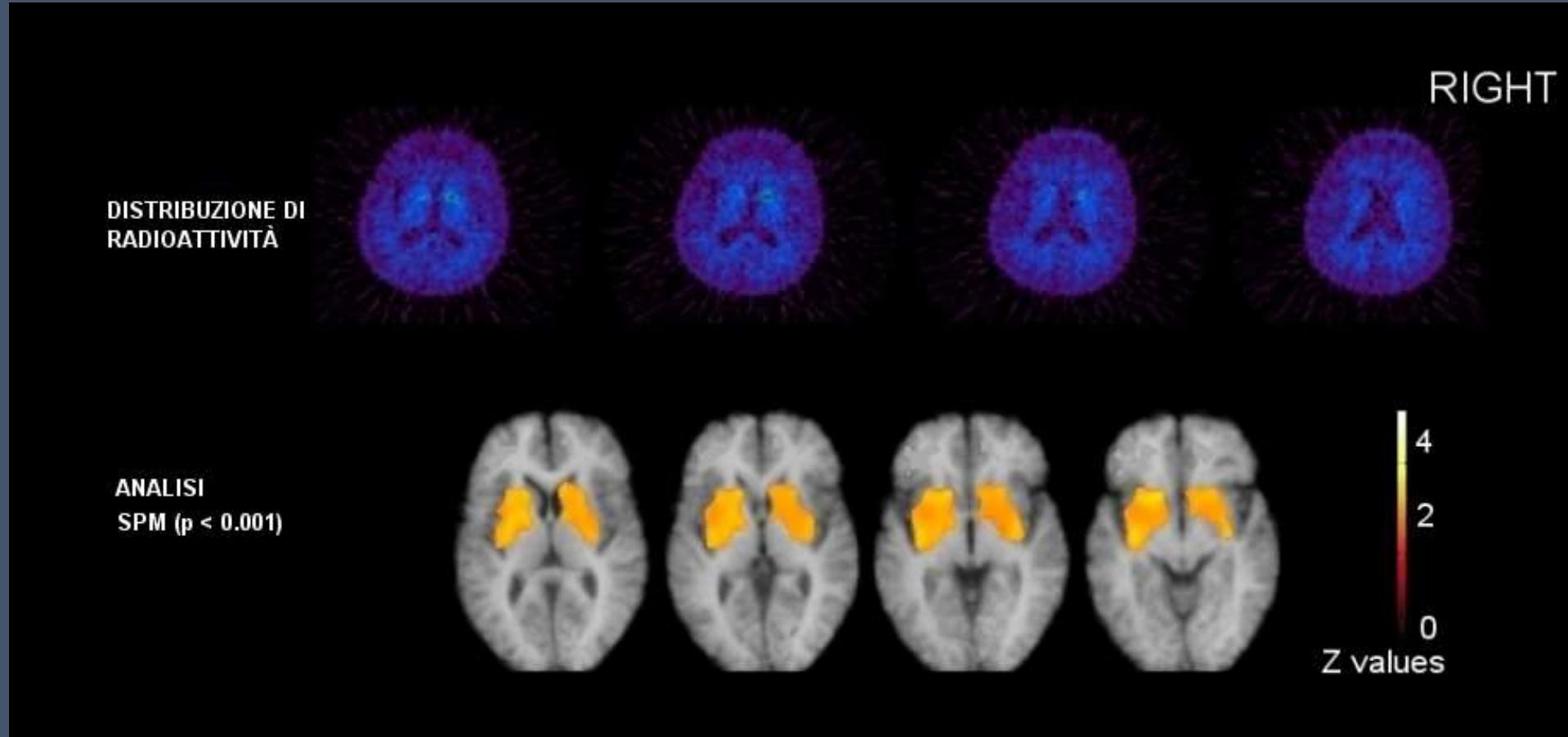
- Valutazione delle demenze e diagnosi precoce di AD
- Valutazione diagnostica e follow-up dei disordini del movimento
- Localizzazione del focolaio epilettogeno
- Etc.



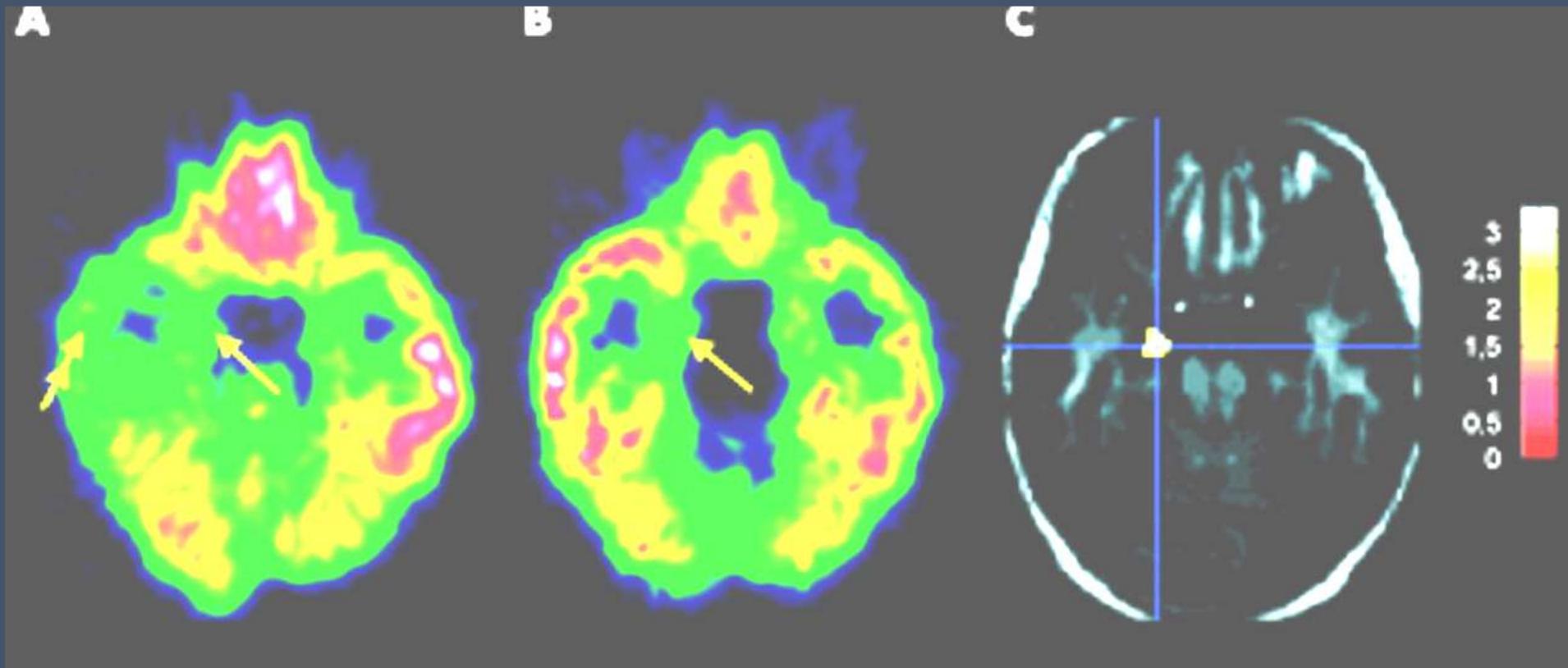
Studio  $^{18}\text{F}$ -FDG PET in un caso di AD che presenta prevalenti disturbi visuospatiali. L'ipometabolismo è asimmetrico con prevalente compromissione emisferica destra.



SPM. I confronti statistici tra immagini normalizzate consentono di identificare le regioni in cui il metabolismo glucidico e' inferiore in modo statisticamente significativo rispetto ai valori di un gruppo controllo.



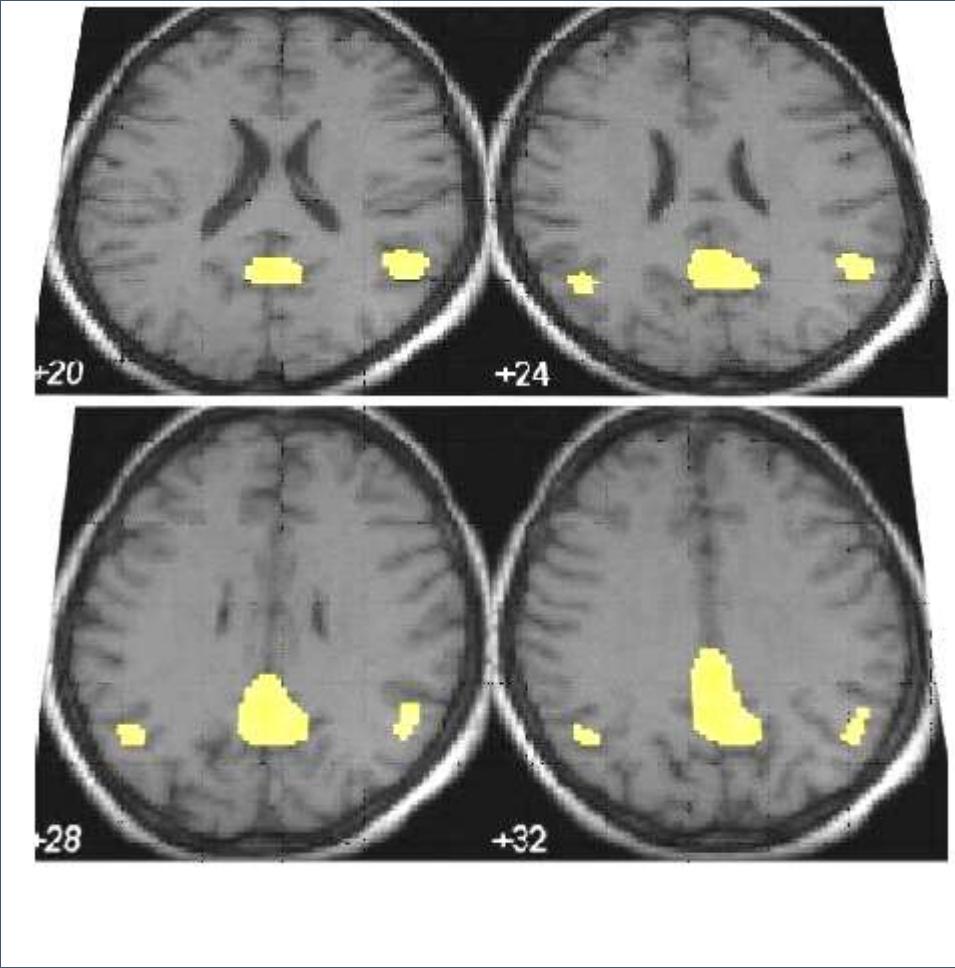
Studio PET con  $^{11}\text{C}$ -beta-CIT-FE in un paziente con demenza a corpi di Lewy. L'analisi qualitativa e statistica delle immagini evidenzia riduzione bilaterale della captazione del radiotracchiatore a livello dei gangli della base, estesa a tutto lo striato.



28 year-old patient with complex partial seizure

- A)  $^{18}\text{F}$ -FDG-PET
- B)  $^{11}\text{C}$ -FMZ-PET
- C) SPM : significant decrease of FMZ VD in the left anterior hippocampus compared with 21 controls. Statistical map is overlaid on the patient's own MRI.

(from Tai & Piccini, JNNP, 2004)



Studio  $^{18}\text{F}$ -FDG PET in soggetti con Mild Cognitive Impairment (MCI) che hanno successivamente dimostrato una progressione ad AD nel corso di un anno. In giallo aree ipometaboliche: corteccia retrospleniale e corteccia temporo-parietale bilaterale ( $p < 0.001$ ).