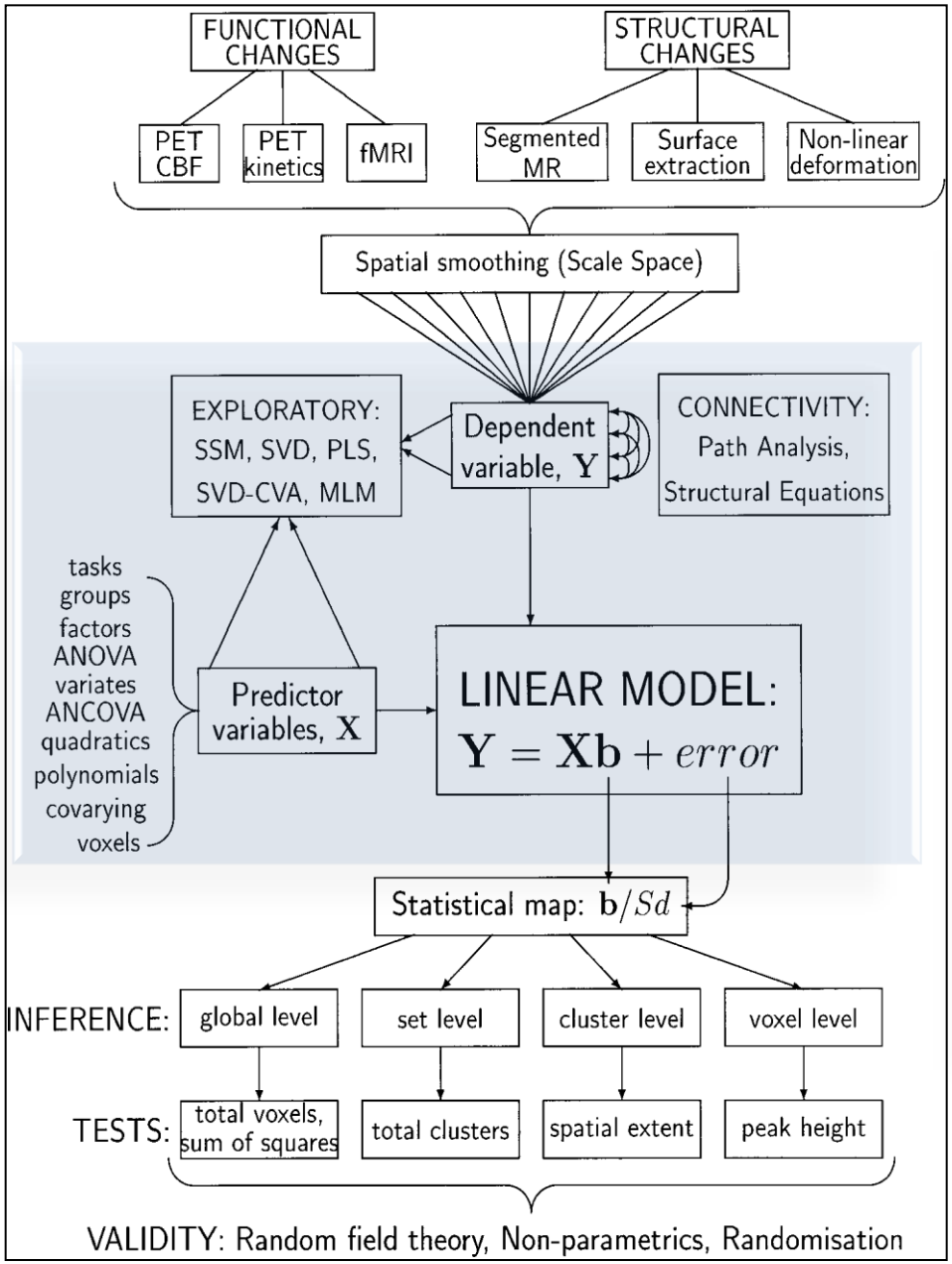
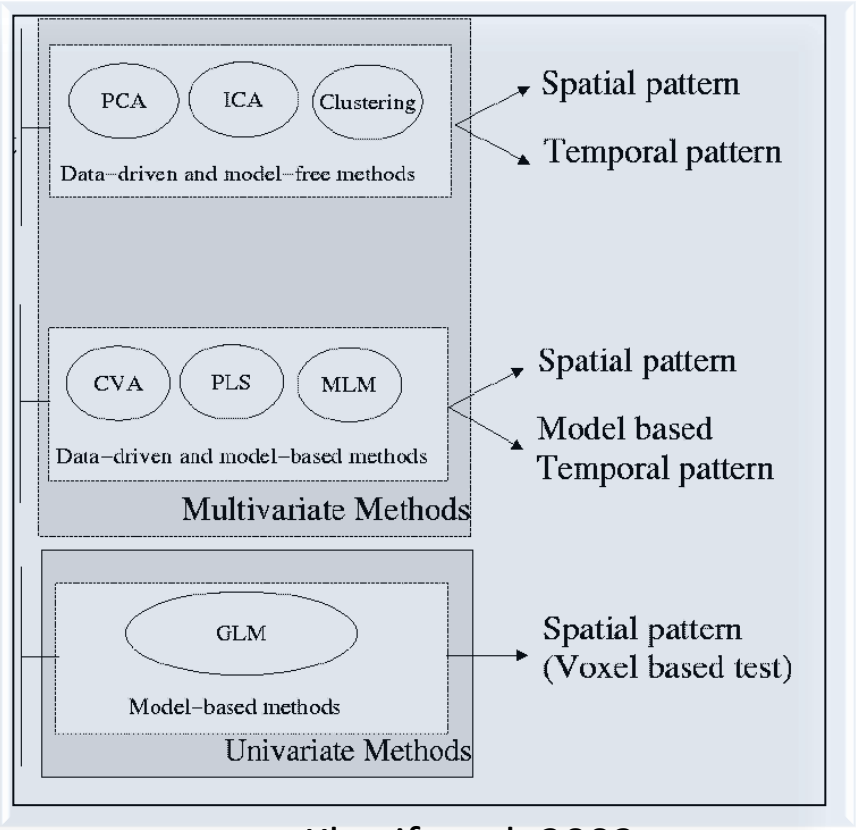
Multivariate Methods
Some applications

Ferath Kherif

Multivariate methods





Kherif et al, 2003

From K Worsley, 2001

Multivariate methods

- **Encoding** model : **generative model** relates context (independent variable) to brain observation(dependent variable).

$$X \longrightarrow Y$$

- **Decoding** model : **recognition model** relates brain outcome (independent variable) to context (dependent variable).

$$Y \longrightarrow X$$

- **Integration** model : **calibration model** relates brain activity to other exogenous variables.

$$Y \longleftrightarrow X$$

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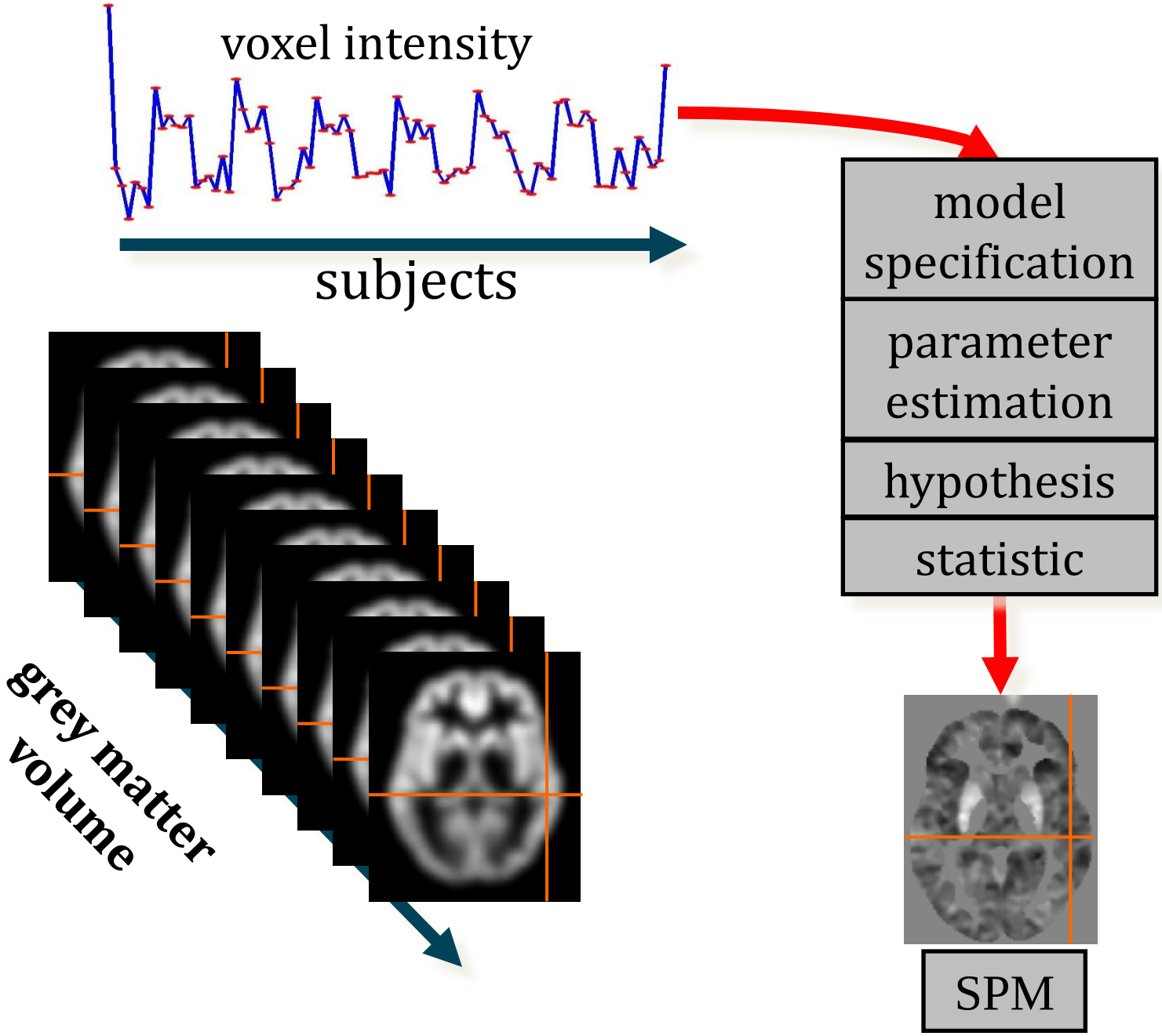
Voxel-Based Morphometry - SPM



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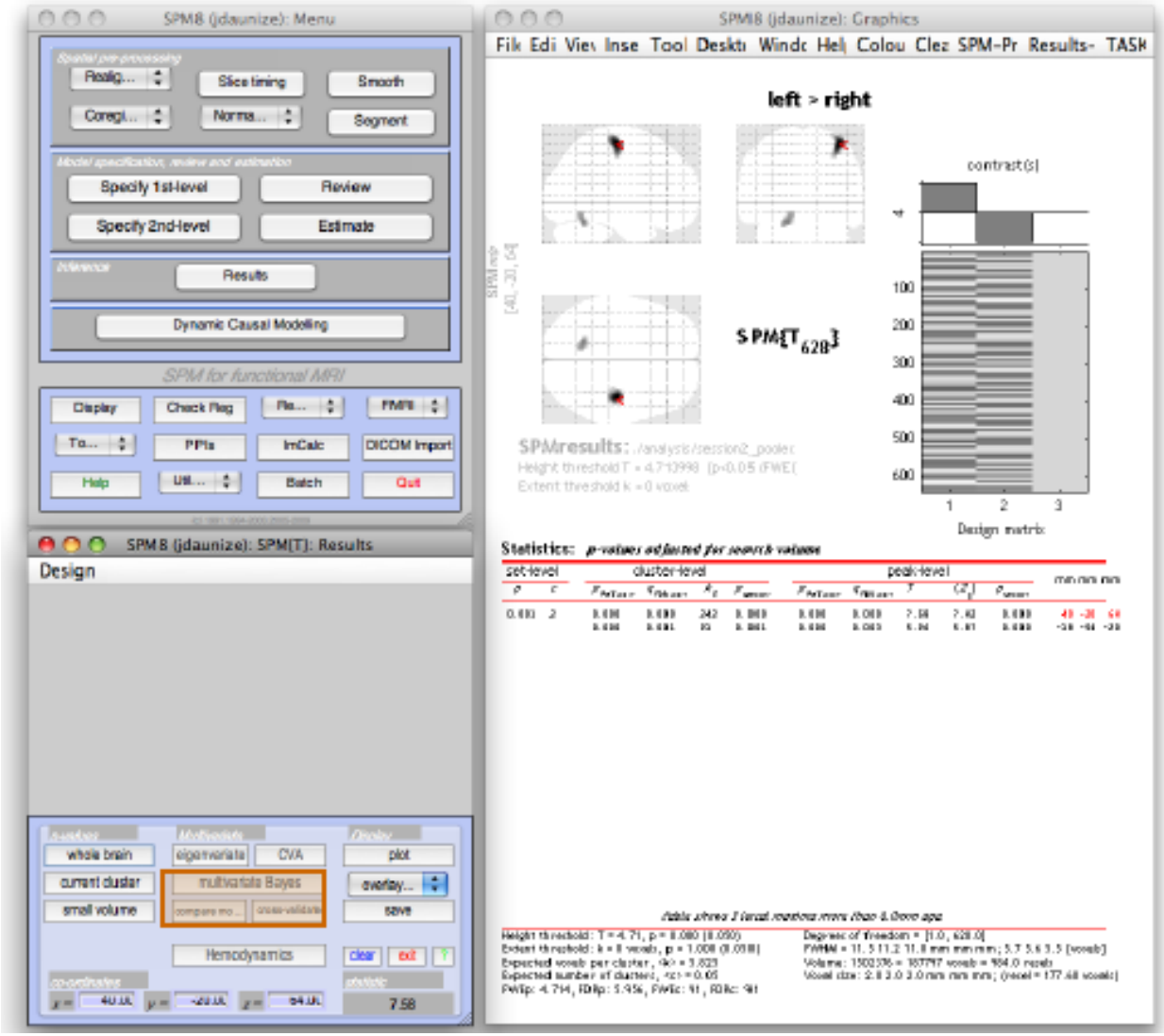


- target:

$$TX = \mathbf{X}c$$

design matrix

contrast

- confounds:

$$G = \mathbf{X}\left(I - cc^{-}\right)$$

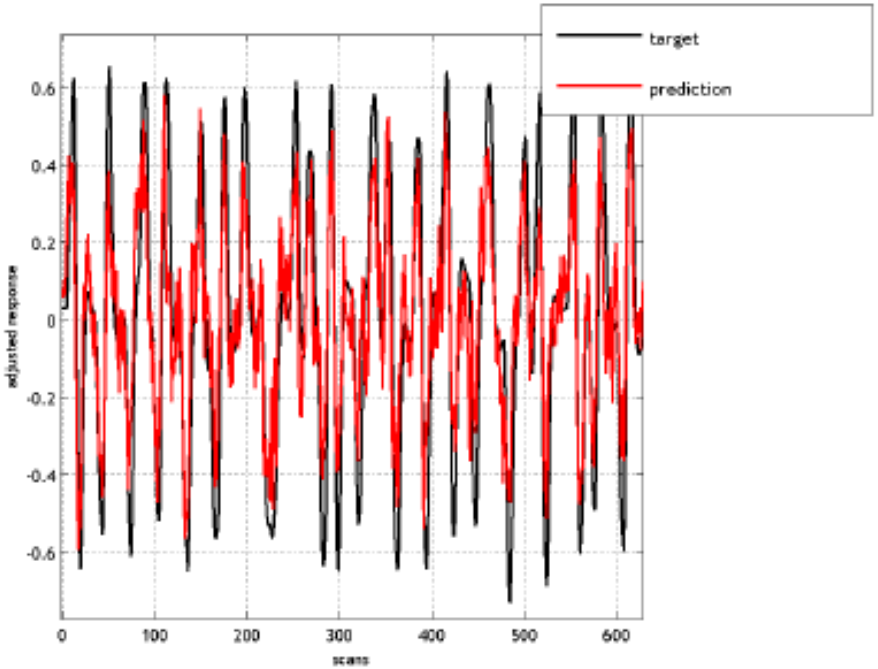
$$\Rightarrow Gc = 0$$

Example

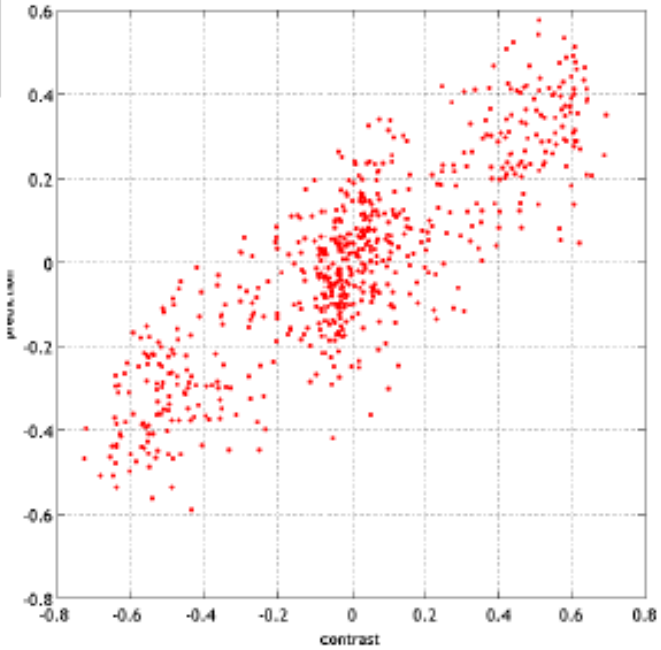
predicted responses from left & right motor cortices

- MVB-based predictions closely match the observed responses. But crucially, they don't perfectly match them. Perfect match would indicate overfitting.

target and (MVB) predicted responses over scans



target versus (MVB) predicted responses

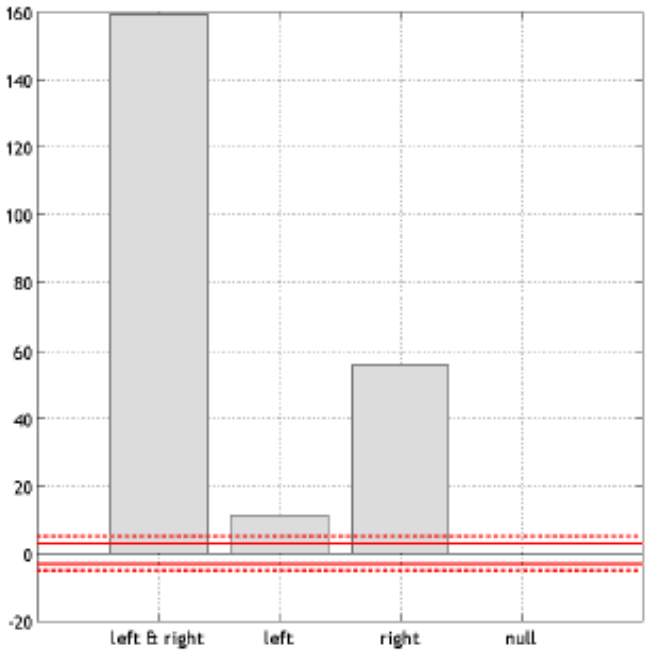


Example

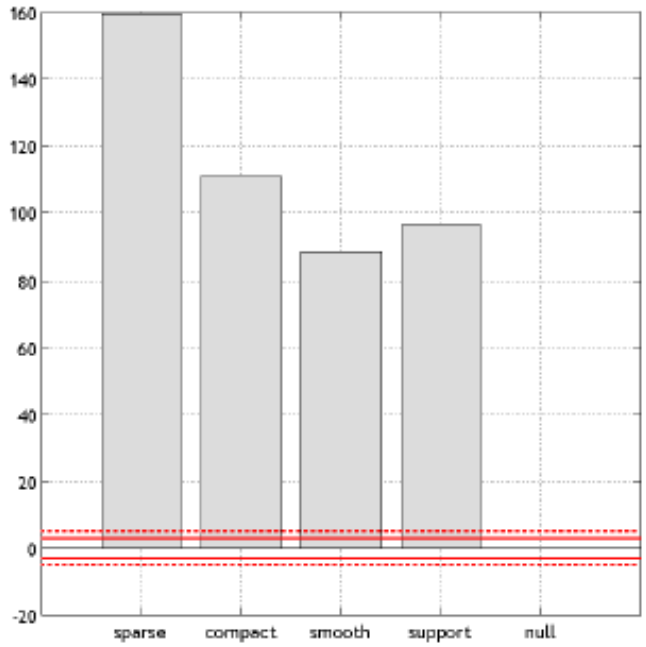
model comparison illustration

- The best model corresponds to a sparse representation of motion ; as one would expect from functional segregation.

log-evidence of X-Y sparse mappings:
effect of lateralization



log-evidence of X-Y bilateral mappings:
effect of spatial deployment



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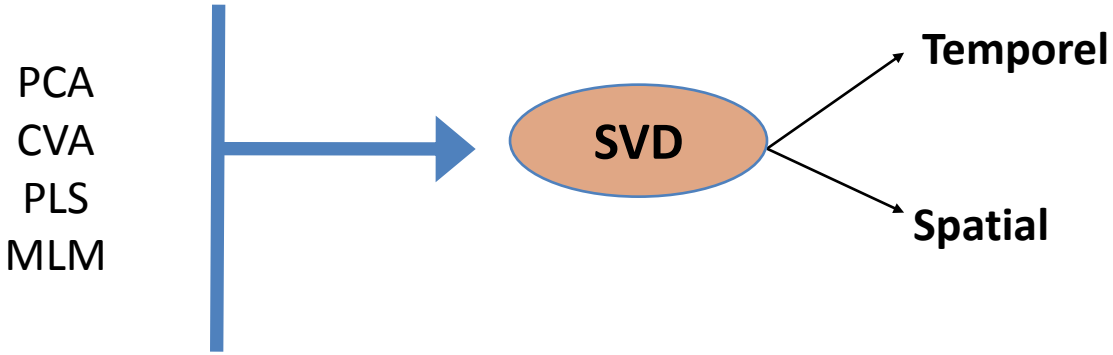
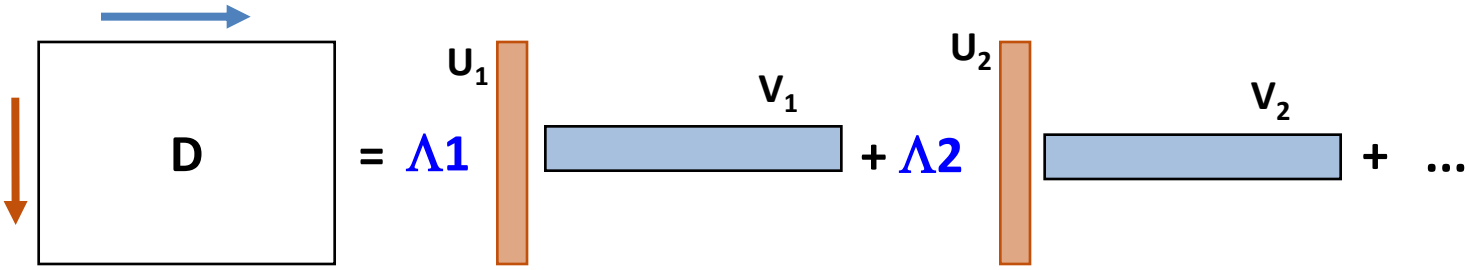
Singular value decomposition : SVD





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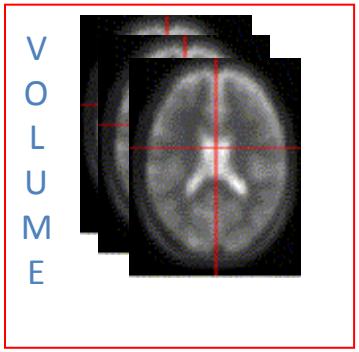
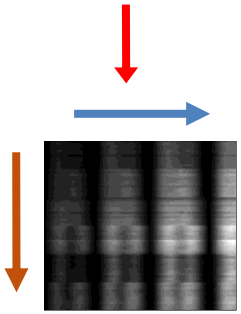


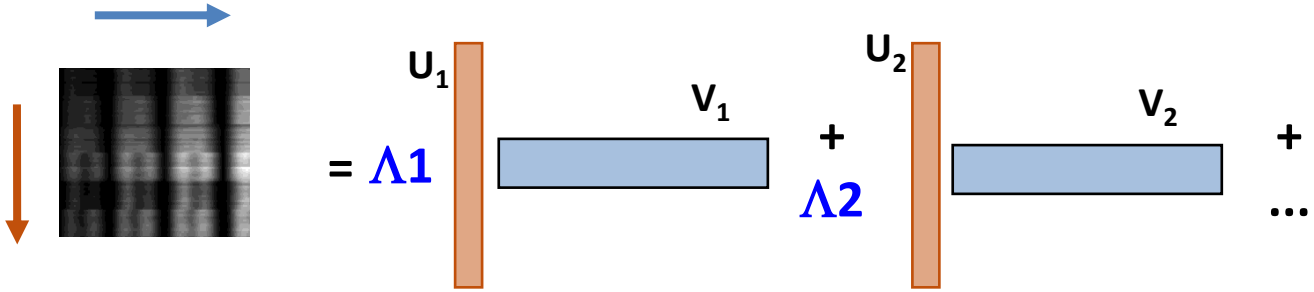


- **PCA : Y (time x voxels)**

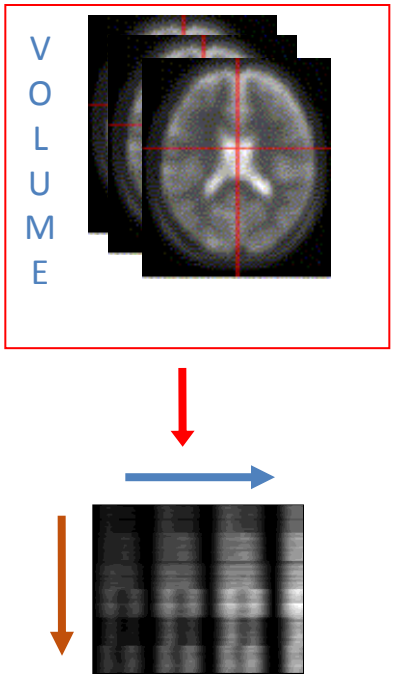
PLS : X'Y (param x voxels)

CVA : $(X'X)^{-1/2} X'Y (R)^{-1/2}$ (param x voxels)

MLM : $(X'VX)^{-1/2} X'Y (R^*)^{-1/2}$ (param x voxels)



Multivariate methods



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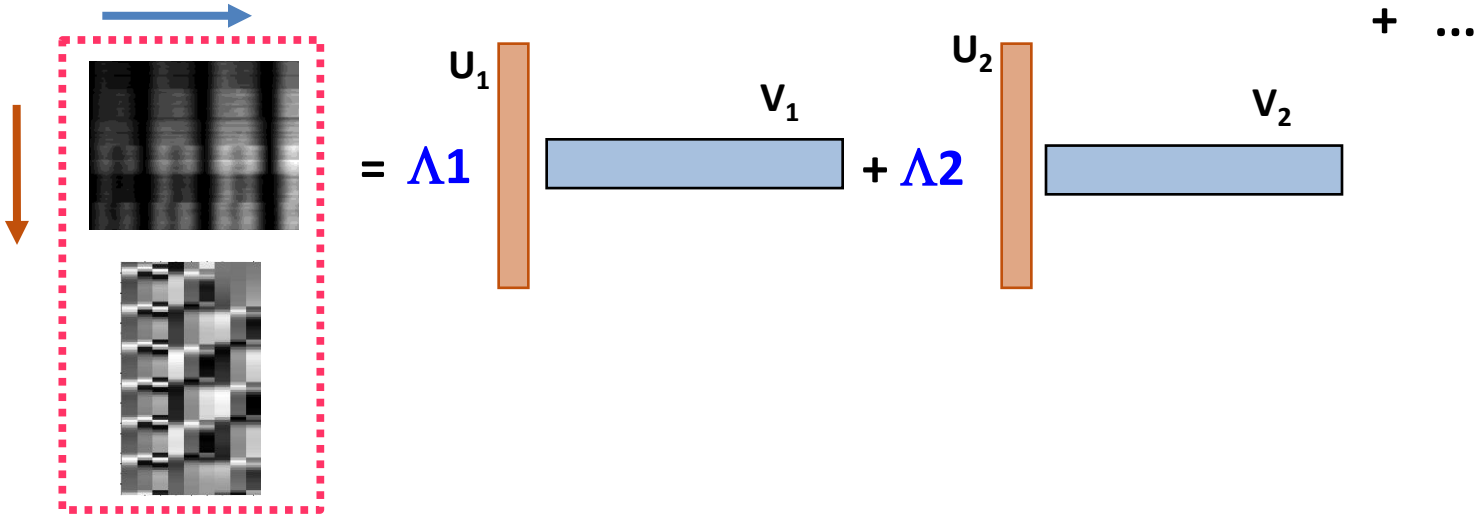

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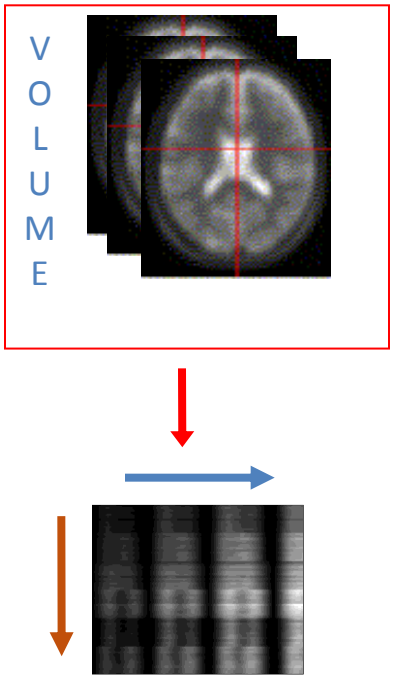

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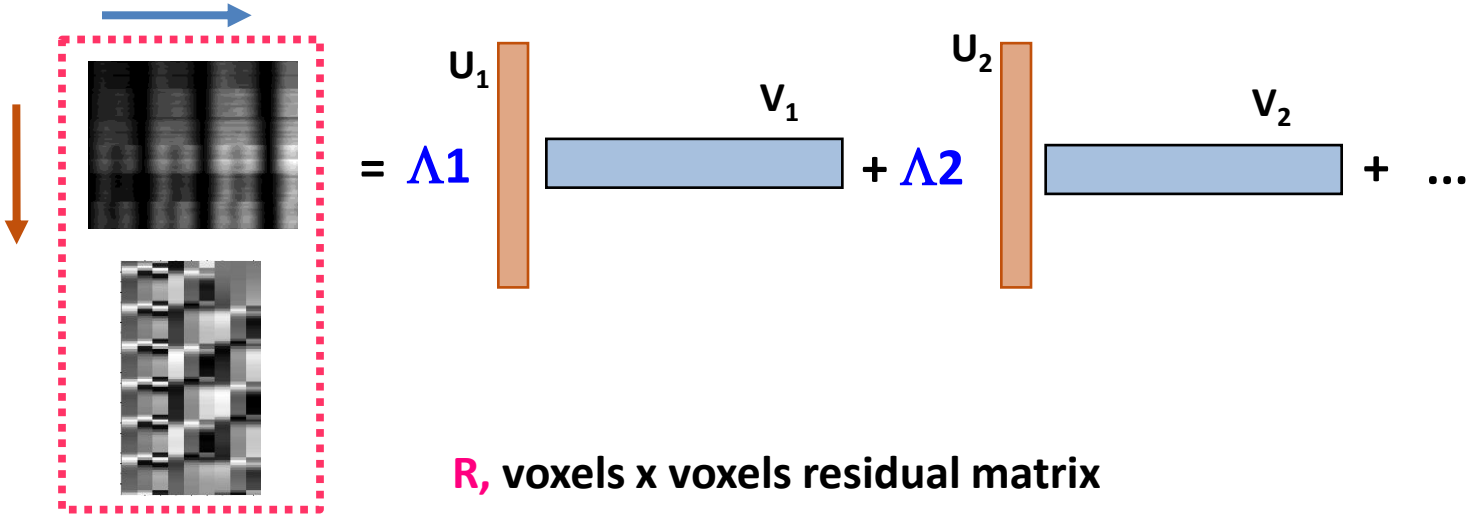
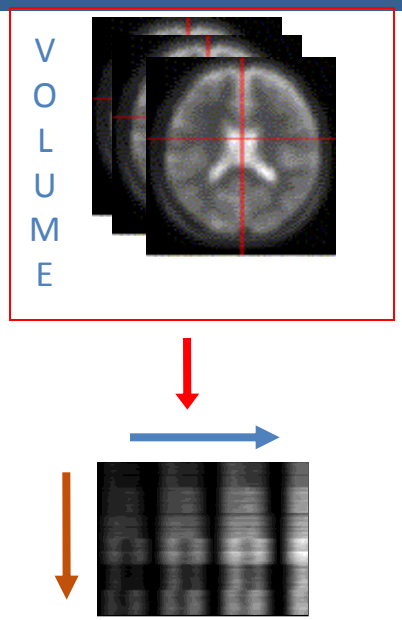


R, voxels x voxels residual matrix

Multivariate methods



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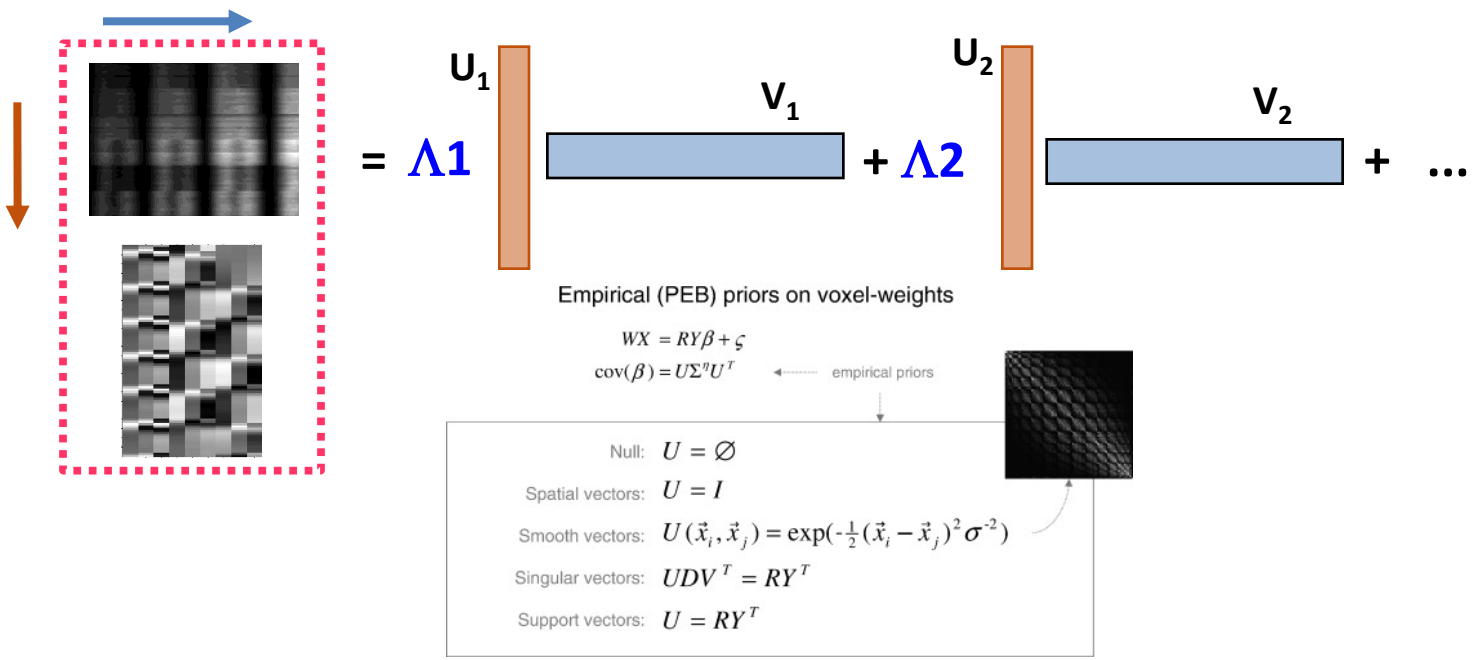

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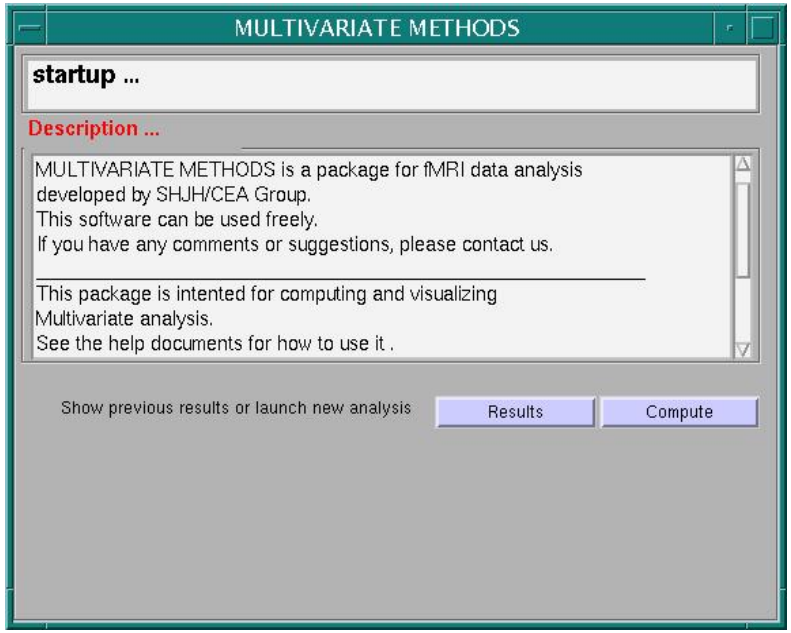
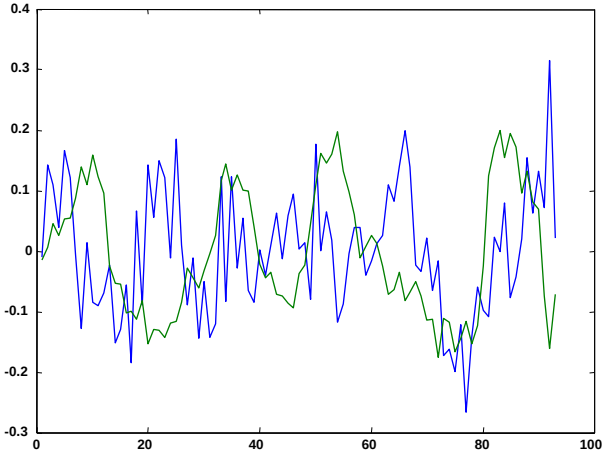
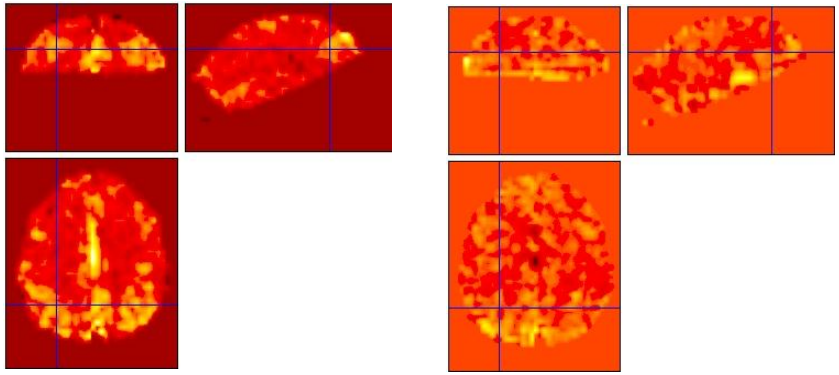


$$Y = XB + E$$

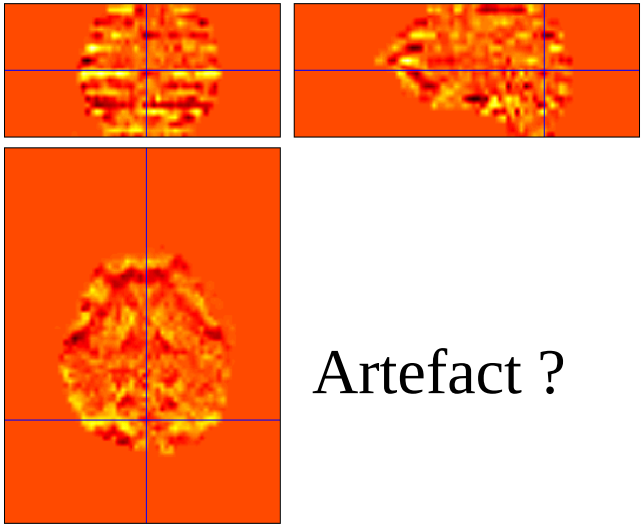
Y	XB	E
Data exploration	Model exploration	Model diagnosis
PCA	PLS CVA MLM	PCA on the residiual

Multivariate methods

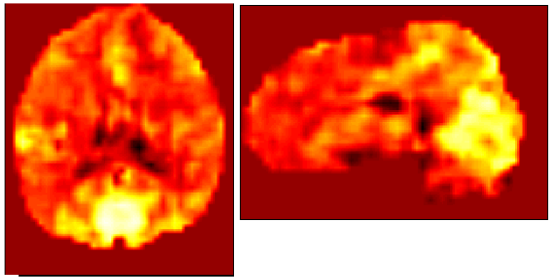




activation

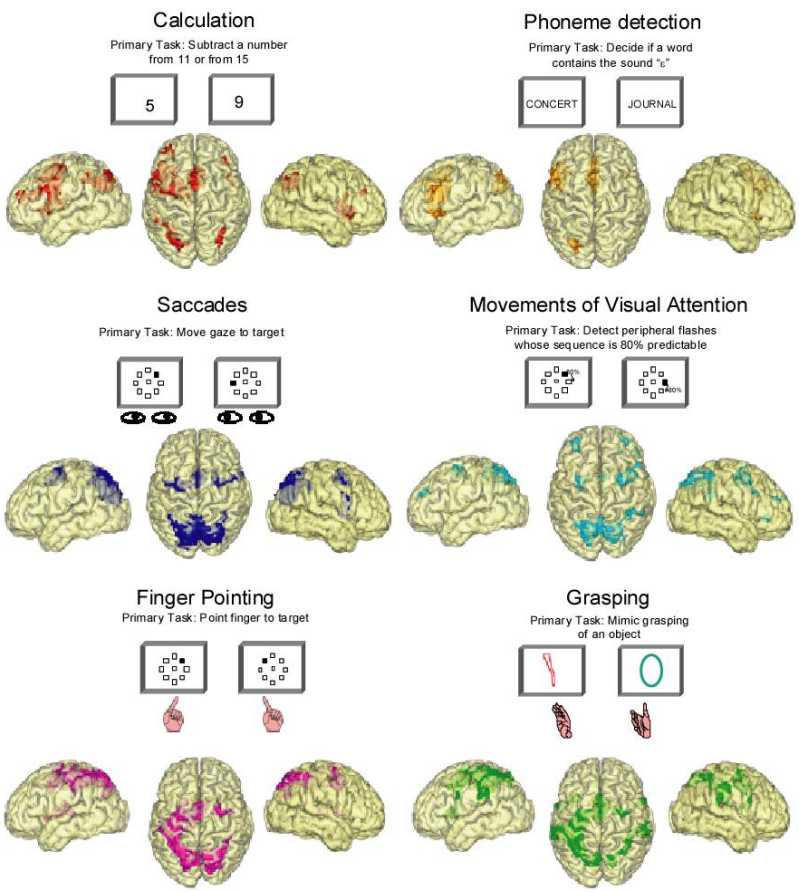


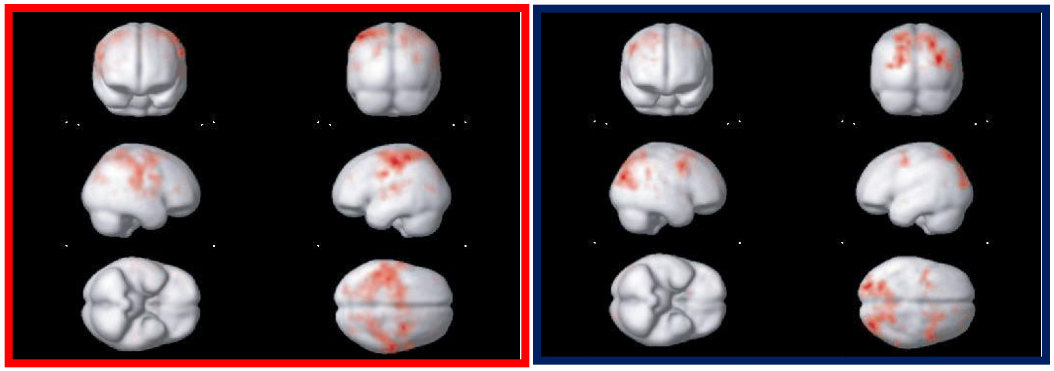
Artefact ?

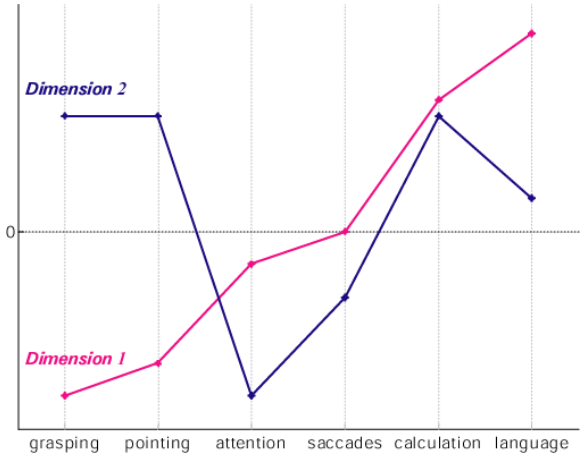


Activation, resting state?

Multivariate methods



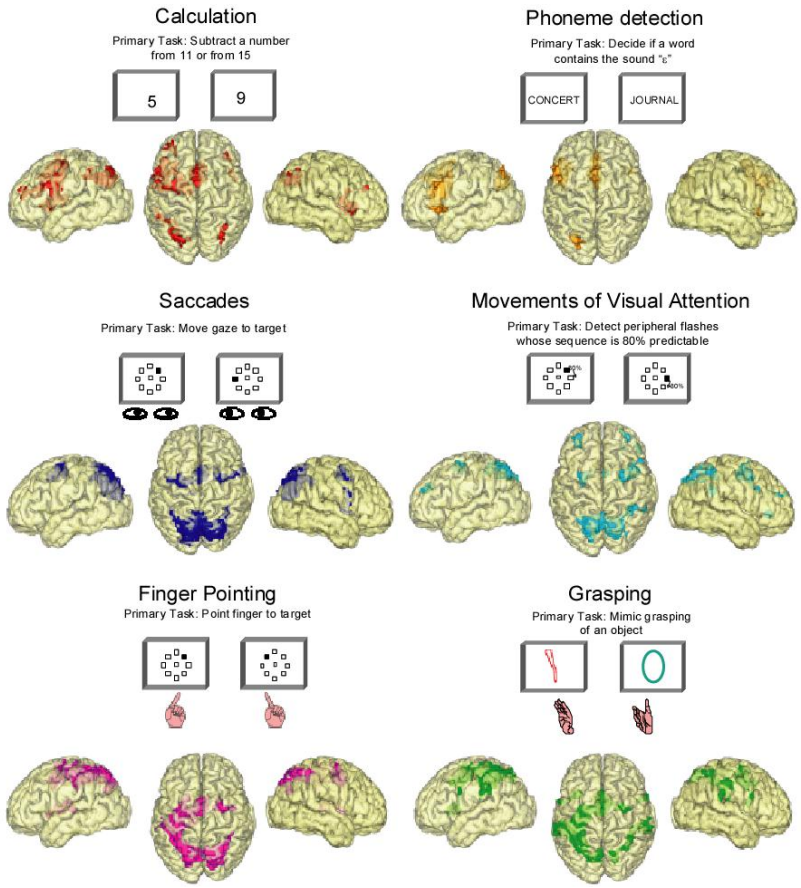




SPM analyses

Networks

Multivariate methods



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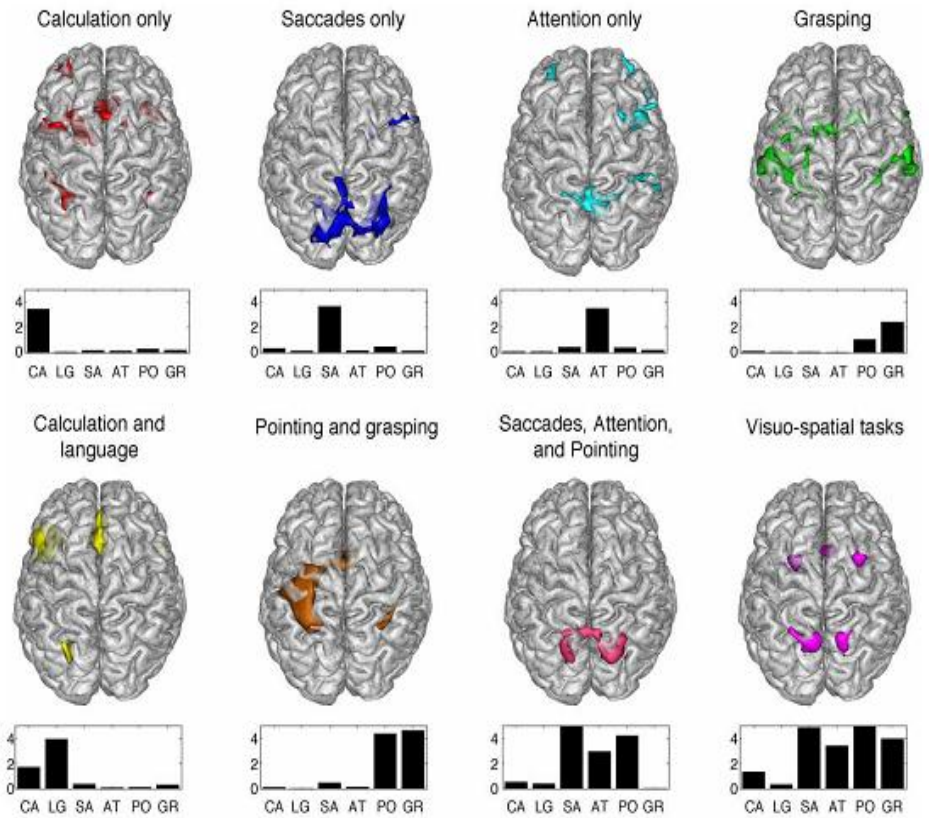
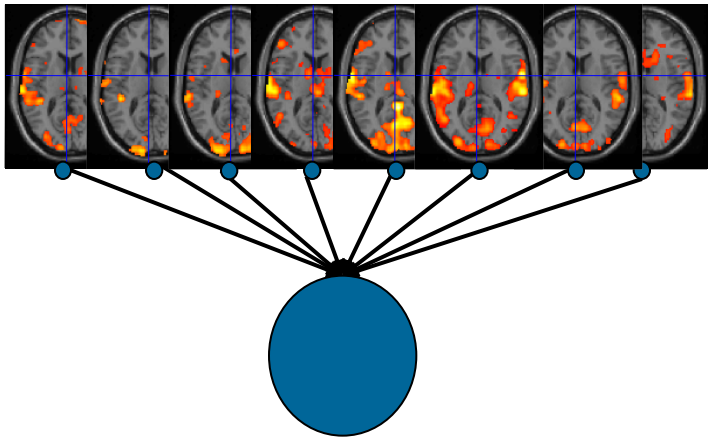


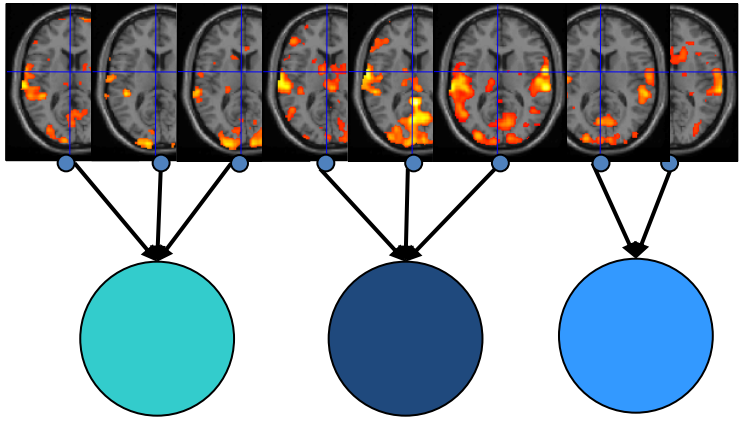
Spatial clustering

Model of language recovery



Typical Group Analysis

Assumes that subjects are drawn from the *same and unique population.*



Individual difference Models:

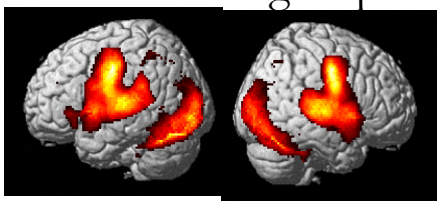
Assume that subjects are drawn from a *multimodal population*.

1) *Apriori* comparisons: to look for expected differences.

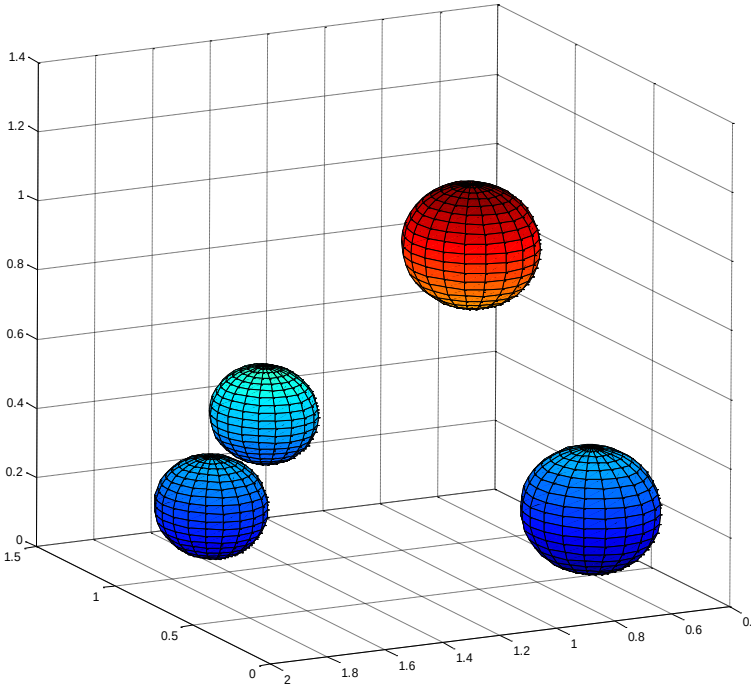
2) Unbiased classification: to reveal hidden (unexpected) differences

Variability in language system

Common to all 4 groups



Pars Orbitalis (Group 4 > others)
Dorsal Premotor (Group 3 > others);
Pars Opercularis (Group 2 > others);



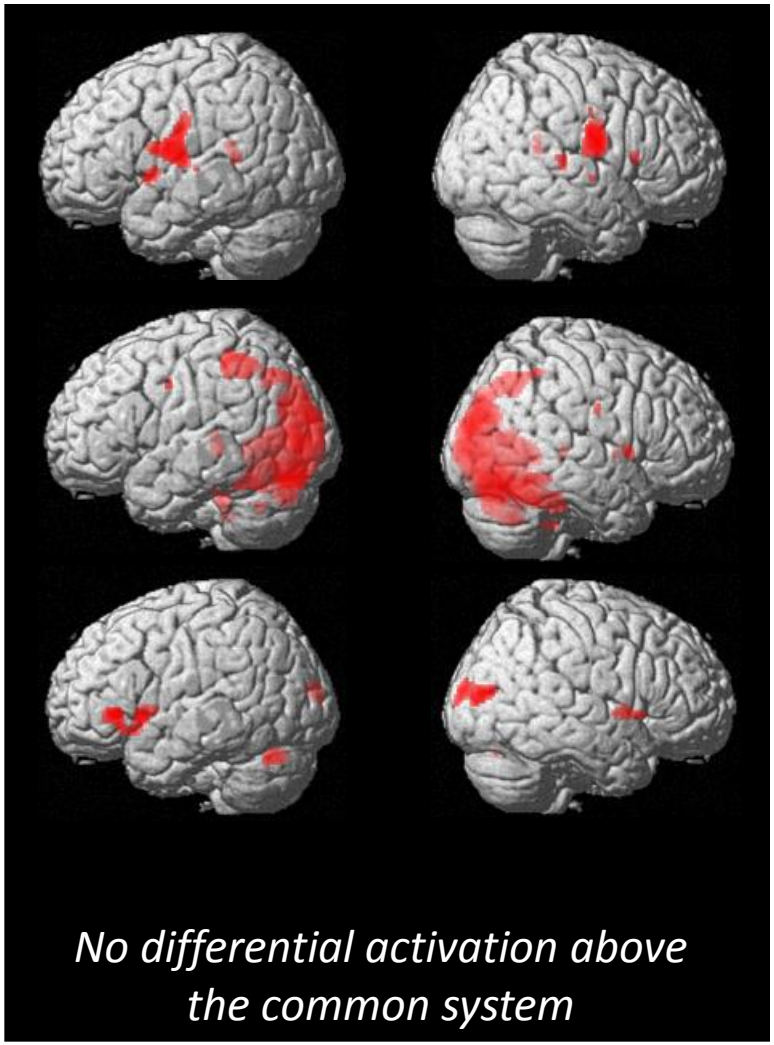
Group 2 >others

Group 3 >others

Group 4 >others

Group 1 > others

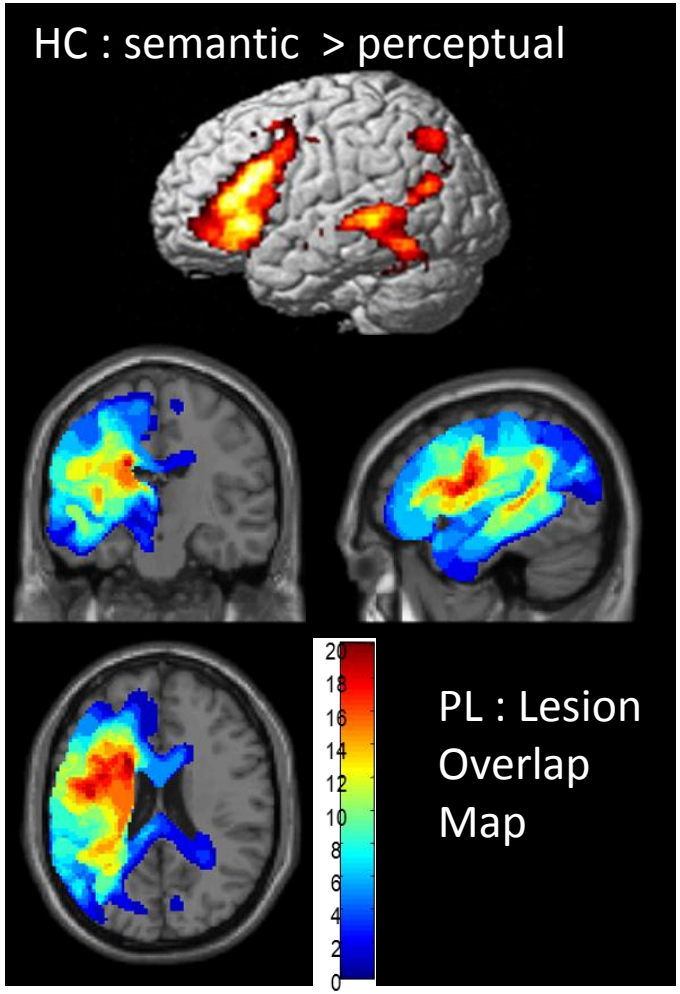
Group Differences



Kherif et al., 2009 *JCogNeurosci*

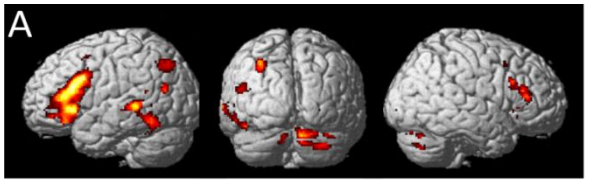
Model of language recovery

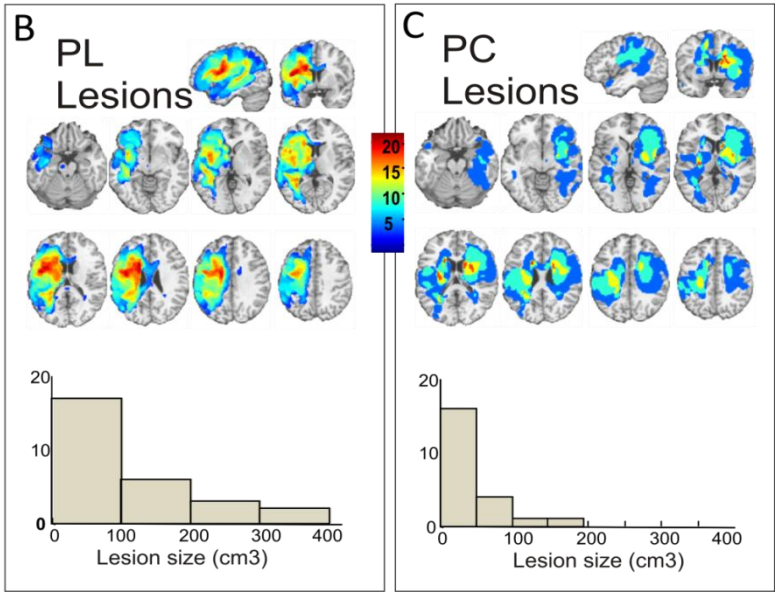
The healthy controls (HC) varied in term of age, gender and handedness
The patients were divided in two groups (PL, PC) depending on whether their lesion damaged an area that was activated in the healthy control group.



- 80 healthy controls (HC)
- The 50 patients were divided in two groups :
- PC : 22 Patients Controls with no damage to the “semantic areas”
- PL : 28 patients with Lesions in the “semantic areas” :
  - frontal (n=11),
  - posterior temporal (n=7),
  - subcortical (n= 5)
  - or premotor areas (n=5).

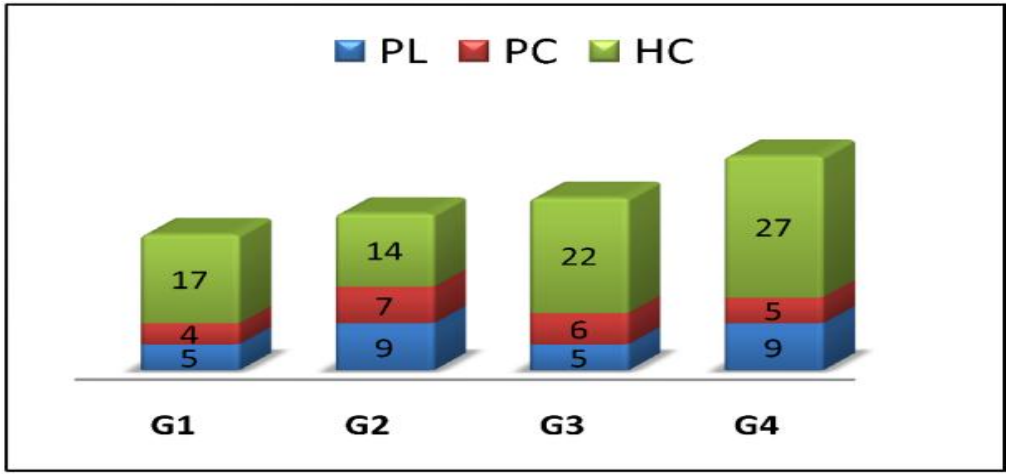
Model of language recovery





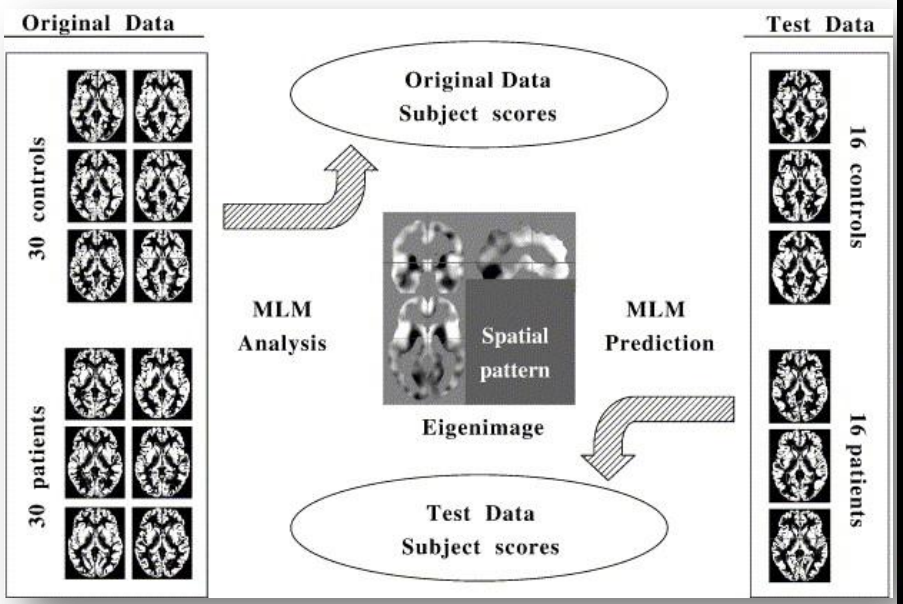
Remarkably, the subgroups had an equivalent mix of patients and controls and an equivalent mix of PL-patients and PC-patients.

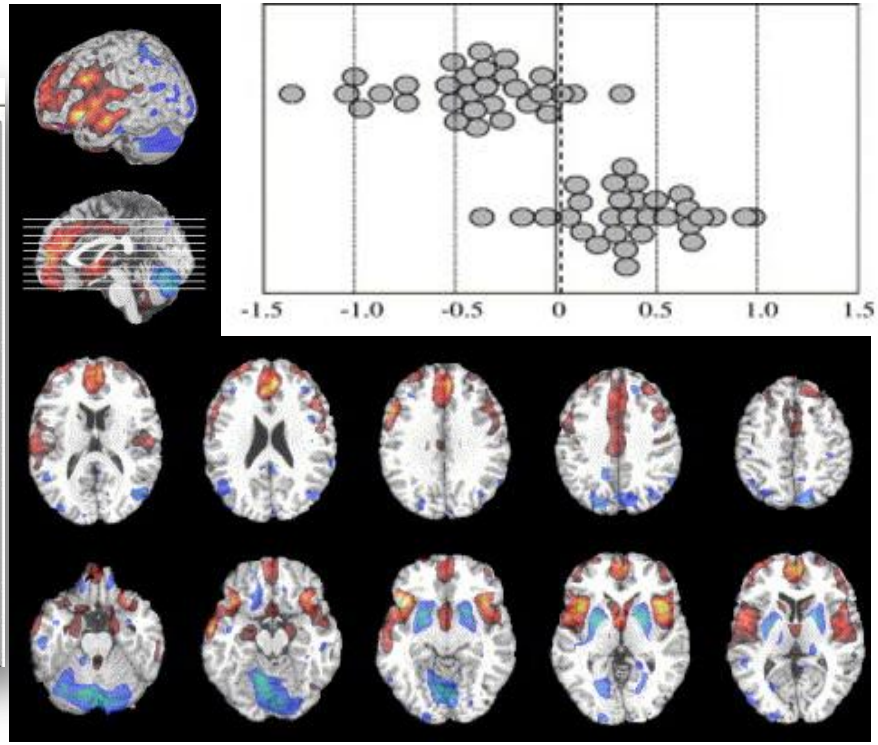
GMM-group 1: 5 PL ; 4 PC; 17 HC .
GMM-group 2: 9 PL; 7 PC; 14 HC.
GMM-group 3: 5 PL; 6 PC; 22 HC.
GMM-group 4: 9 PL; 5 PC; 27 HC.



VBM Schizophrenia

Multivariate VBM successfully differentiates schizophrenia patients from healthy controls





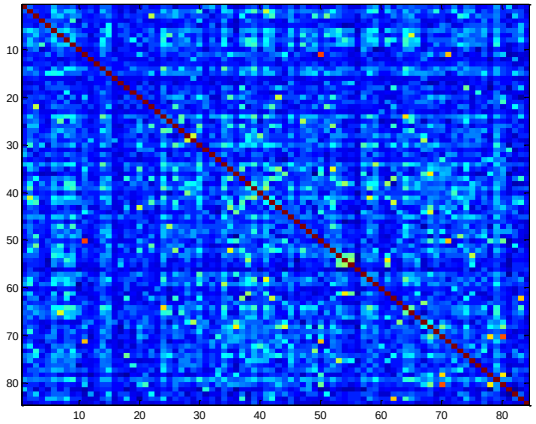
Kawasaki et al., 2007 *Neuroimage*

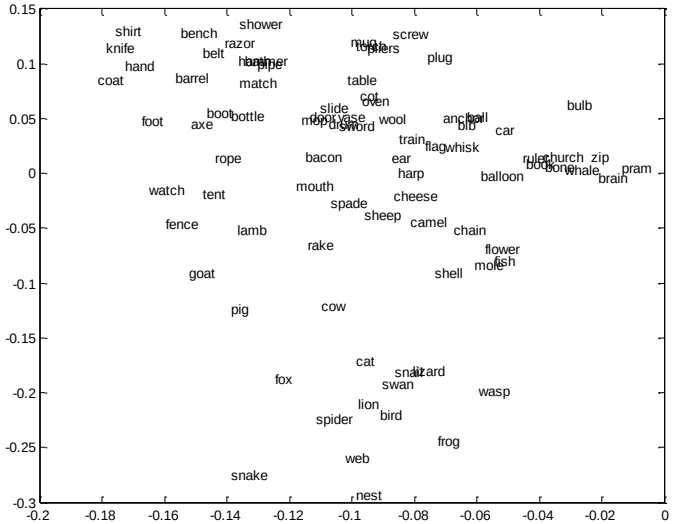
Question: how Concepts are represented in the brain
Comparing words and picture allow to answer this question

'anchor' 'bench' 'bulb' 'cot' 'flower' 'knife' 'mug'
'axe' 'bib' 'camel' 'cow' 'foot' 'lamb' 'nest'
'bacon' 'bird' 'car' 'door' 'fox' 'lion' 'oven'
'ball' 'bone' 'cat' 'drum' 'frog' 'lizard' 'pig'
'balloon' 'book' 'chain' 'ear' 'goat' 'match' 'pipe'
'barrel' 'boot' 'cheese' 'fence' 'hammer' 'mole' 'pliers'
'bath' 'bottle' 'church' 'fish' 'hand' 'mop' 'plug'
'belt' 'brain' 'coat' 'flag' 'harp' 'mouth' 'pram'

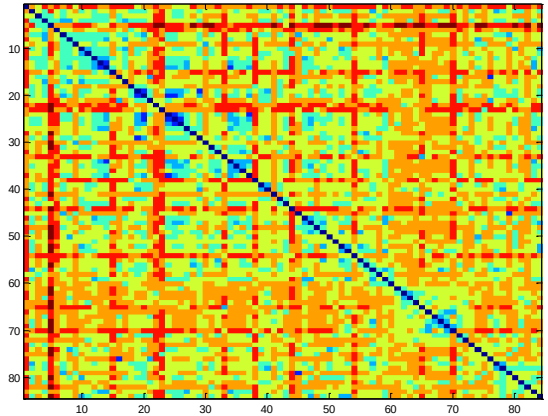
'rake' 'shower' 'table'
'razor' 'slide' 'tent'
'rope' 'snail' 'torch'
'ruler' 'snake' 'train'
'screw' 'spade' 'vase'
'sheep' 'spider' 'wasp'
'shell' 'swan' 'watch'
'shirt' 'sword' 'web'

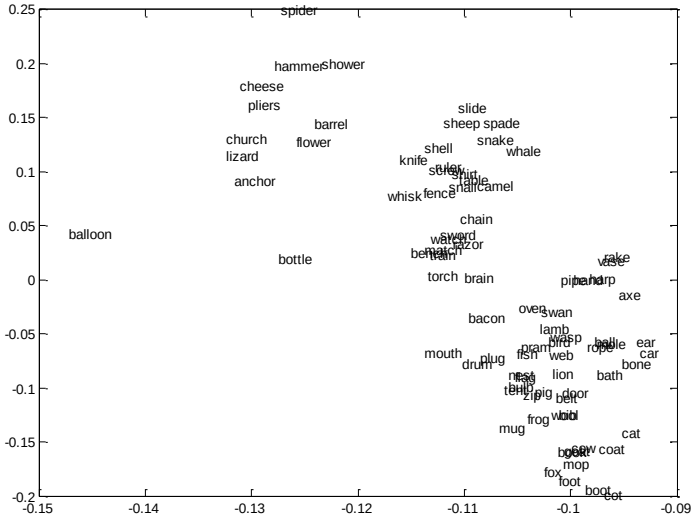
Semantic association LSA





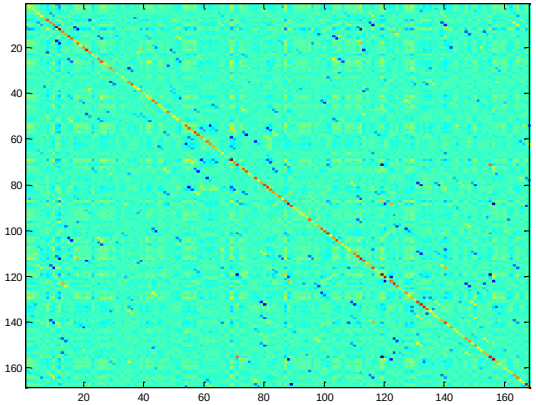
Orthographic (spelling) distance

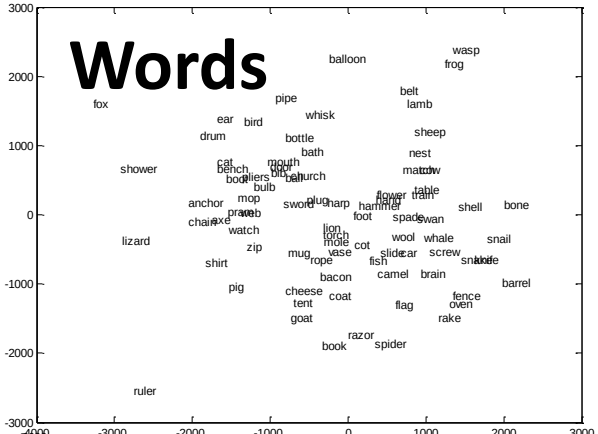


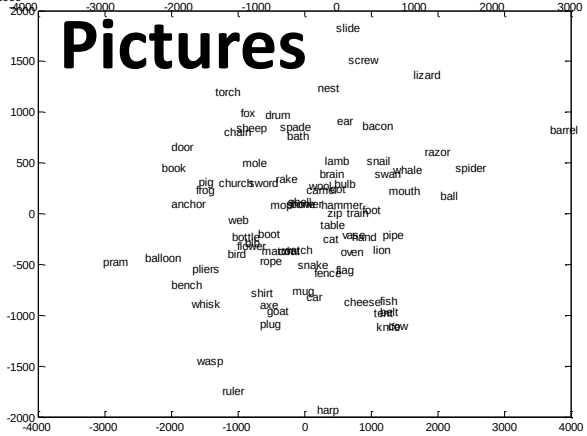


Similarity based on brain activation

For each subject : Estimate the contrast image corresponding to one word or picture
With our dataset 84 images for the word set and 84 images for the picture set.







Correlation between the similarity measures

	Phi Words	Phi Pictures
Sim Semanctic	0.4	0.4
Sim Orthographic	0.4	0.2
Phi words		0.49

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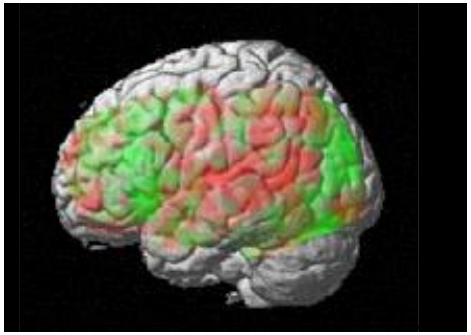
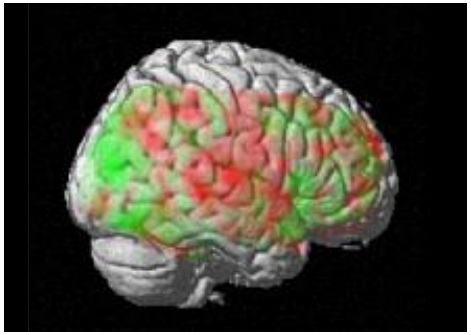
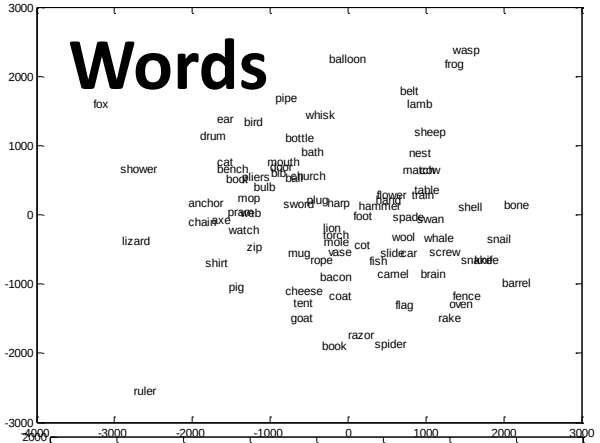
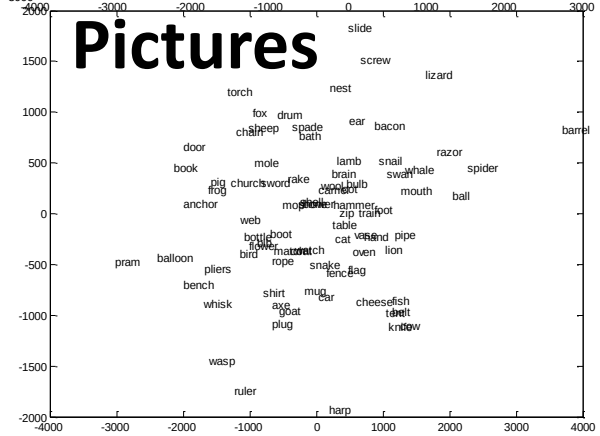
For each subject : Estimate the contrast image corresponding to one word or picture
With our dataset 84 images for the word set and 84 images for the picture set.



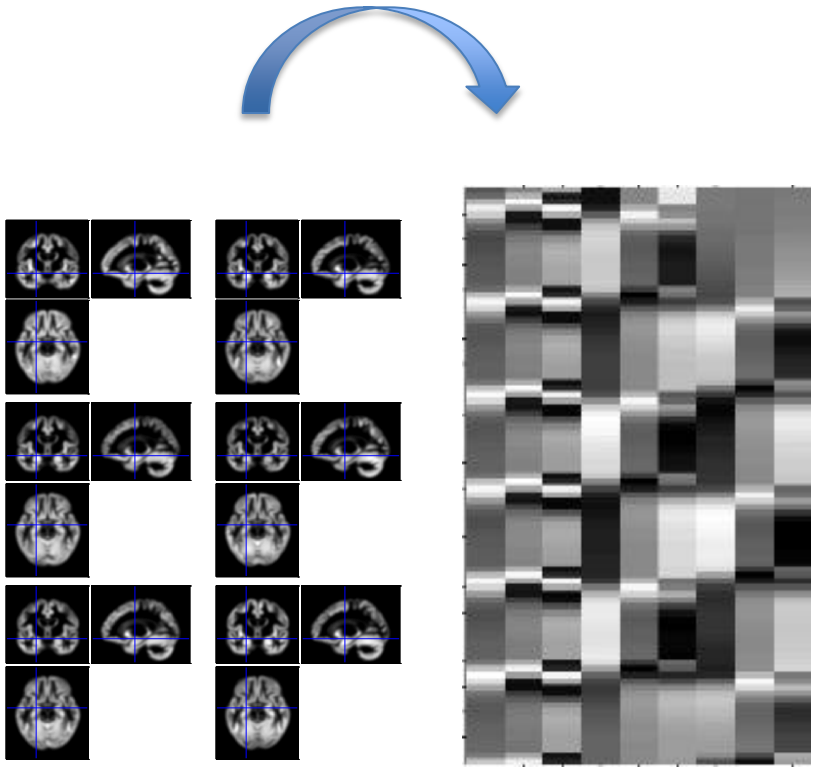




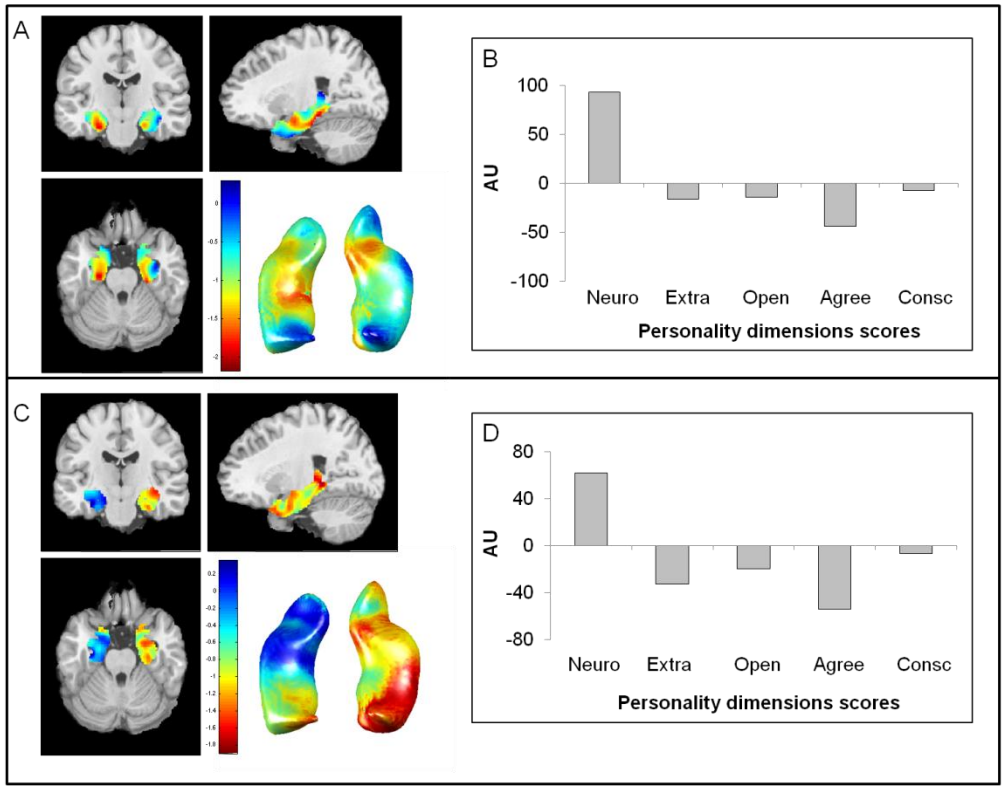


- The predictive MM model achieved 64% of accuracy for detecting the concept
- And 90 % accuracy for detecting the modality

Combining clinical and structural information



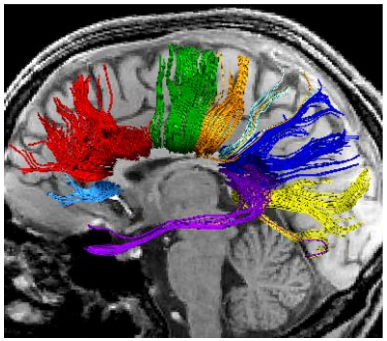
Test battery



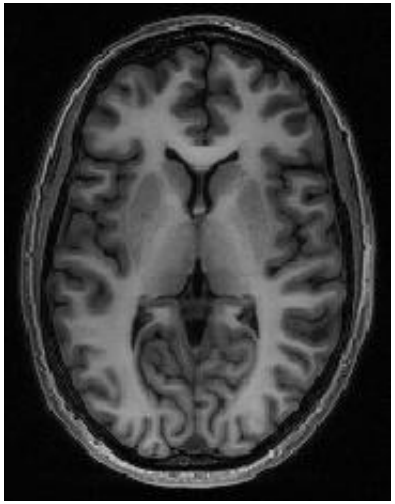
Zufferey et al in preparation

Multi-spectral structural imaging

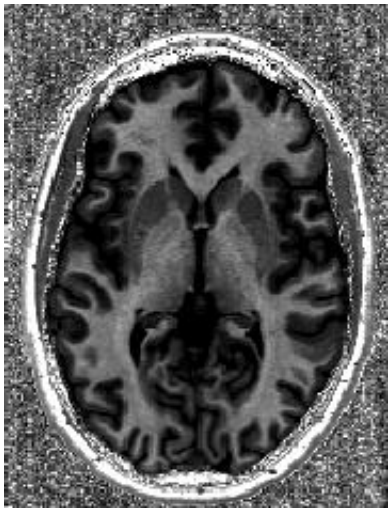
- Clinically feasible (off-the-shelf sequences, 18min. duration)
  - Combination of T1, MT & PD sequences – resolution 1mm^3
  - Quantitative maps
  - Post hoc – T1, MT, R2* synthetic maps



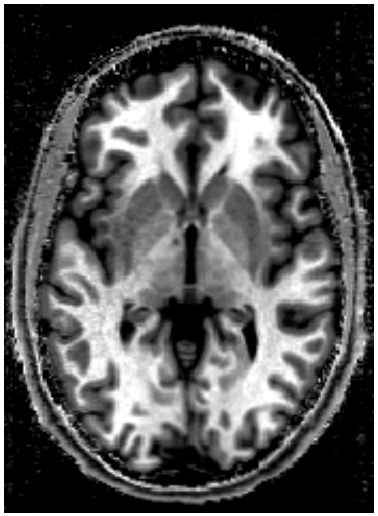
DW



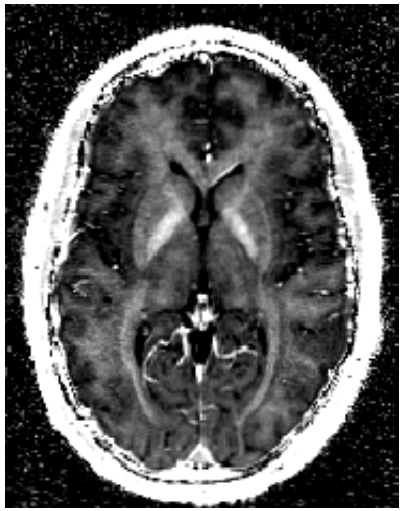
T1w



T1



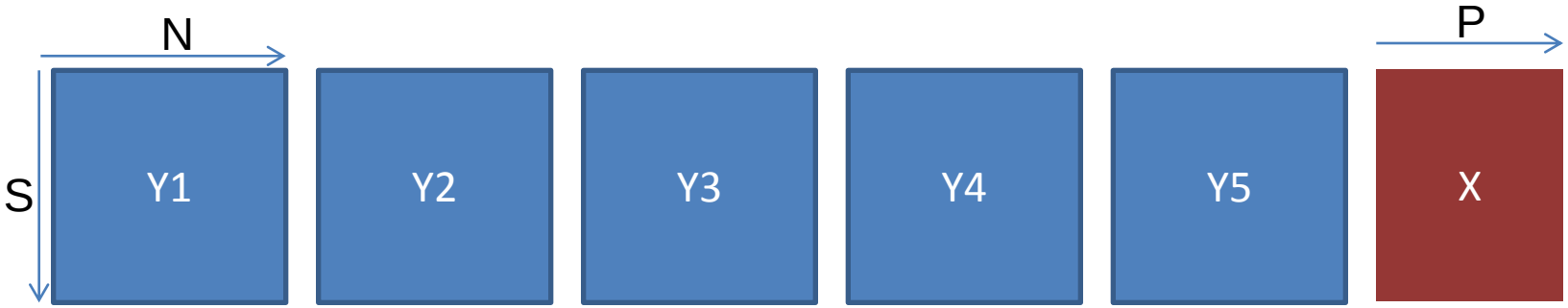
MT



R2*

possible MV extensions

- Voxelwise multivariate
- Whole brain Multivariate

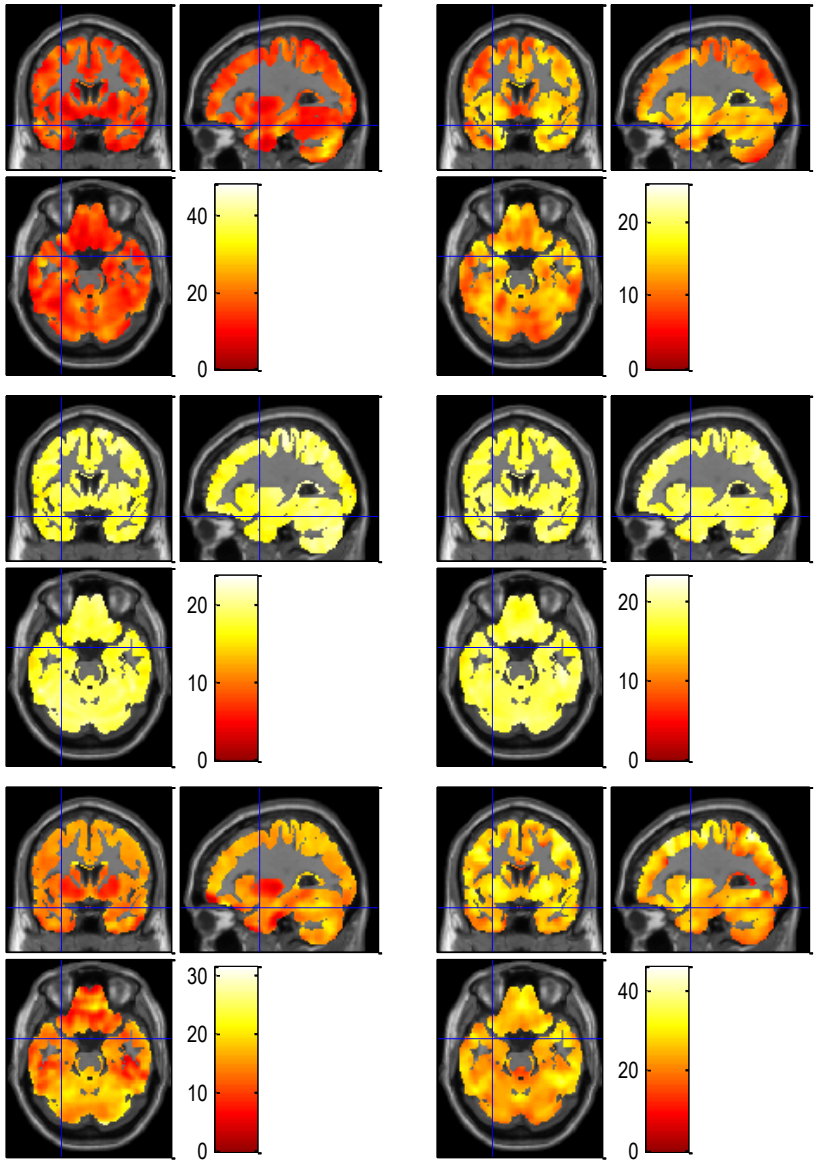


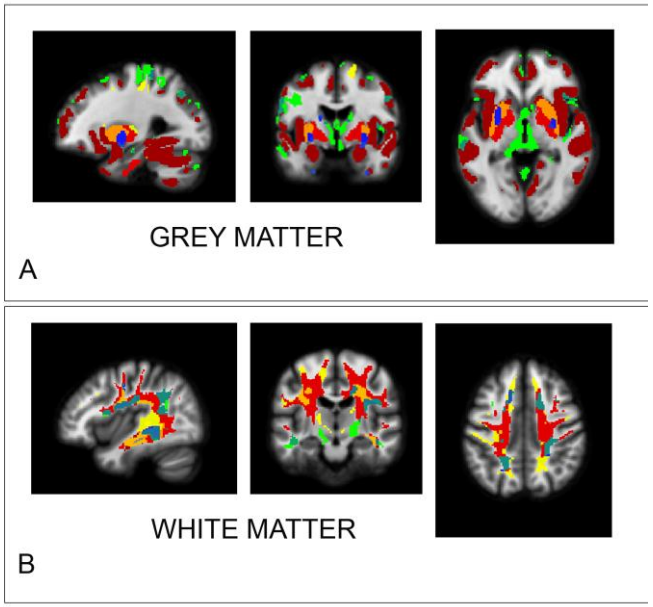
- Voxelwise covariate
- Causal model (SEM)

Voxelwise multivariate

• Single variable at each voxel • Univariate ANOVA • Separate analyses • sphericity assumption (?). • Can be powerfull ()	• Multiple variables at each voxel • Multivariate T^2 : MANOVA profile analyses • sphericity assumption (not required). • More powerfull (n should be big)

Univariate ANOVAs





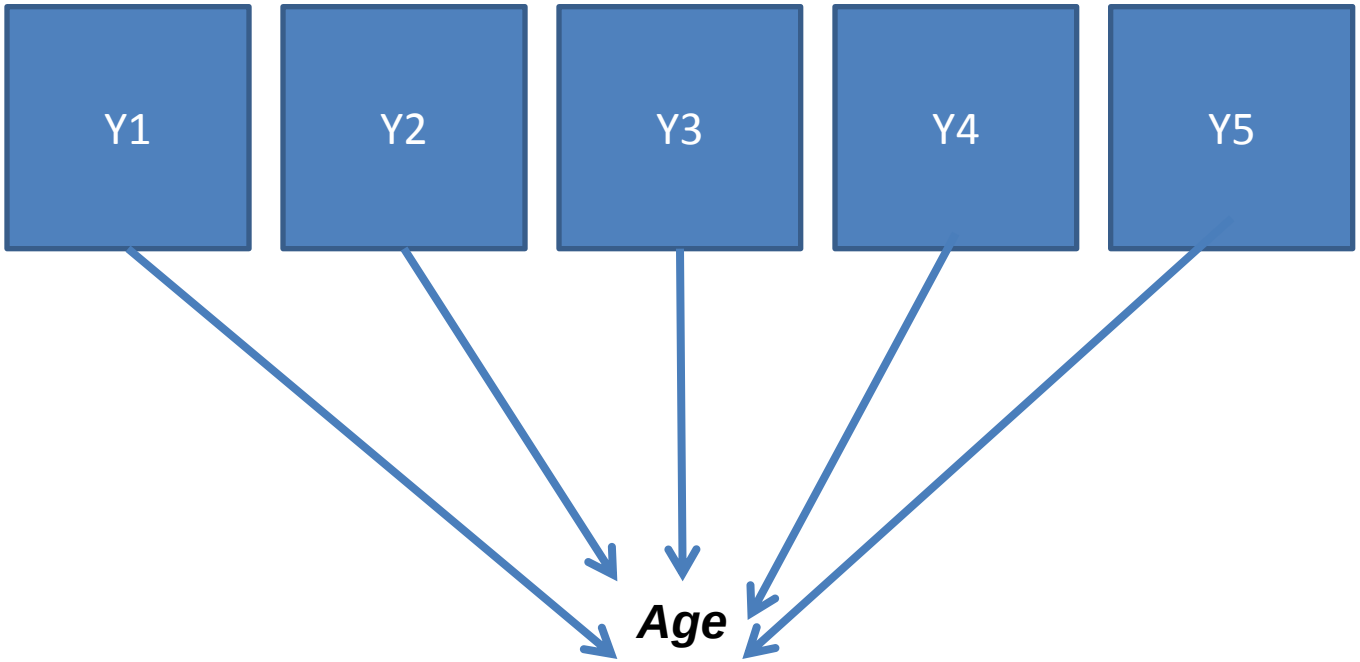
Fingerprint of tissue properties

	FA	MD	MT	R2*	VBM
					-
				+	-
				+	
	-			+	-
			-		
		+			
		+	-		

	FA	MD	MT	R1	R2*
					-
			-	-	
			-		
	-	+	-		
		+			
	-				
	-		-		

Whole brain Multivariate
Predicting age using multiple sources

20	26.0701
24	43.6065
24	27.6333
25	30.7243
25	33.3435
25	36.2153
26	33.0484
27	39.9625
27	45.7347
28	36.5503
29	38.6941
30	40.2426
30	36.8966
32	35.1314
34	28.7709
35	40.5643
38	44.8832
39	34.9653
45	38.6204
54	38.9066
61	44.1481
66	48.5588
69	45.8561
75	44.3738
77	47.3703
87	48.0909



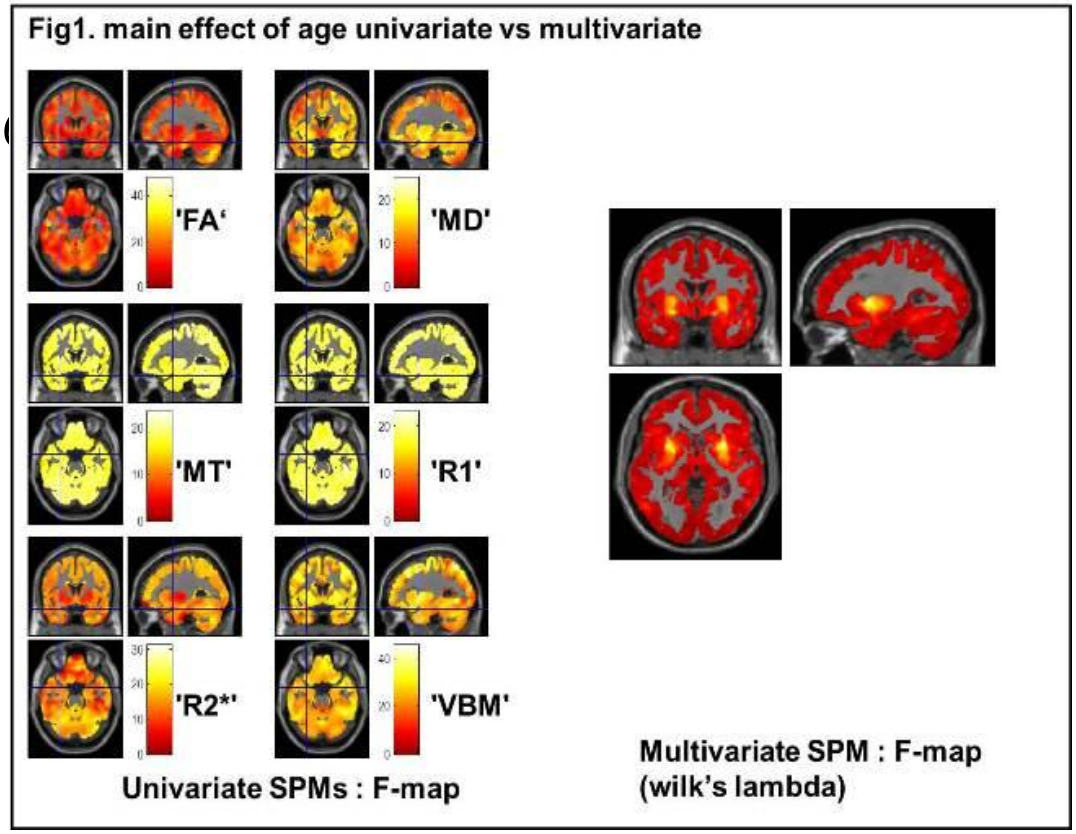
$$Y = XB + E$$

Multivariate inference – age prediction

- Voxel-based MANOVA/MANCOVA using parameter maps as dependent variables

- advantage - error Type I protection and better sensitivity

- output - multivariate F-statistic (Wilks' lambda)



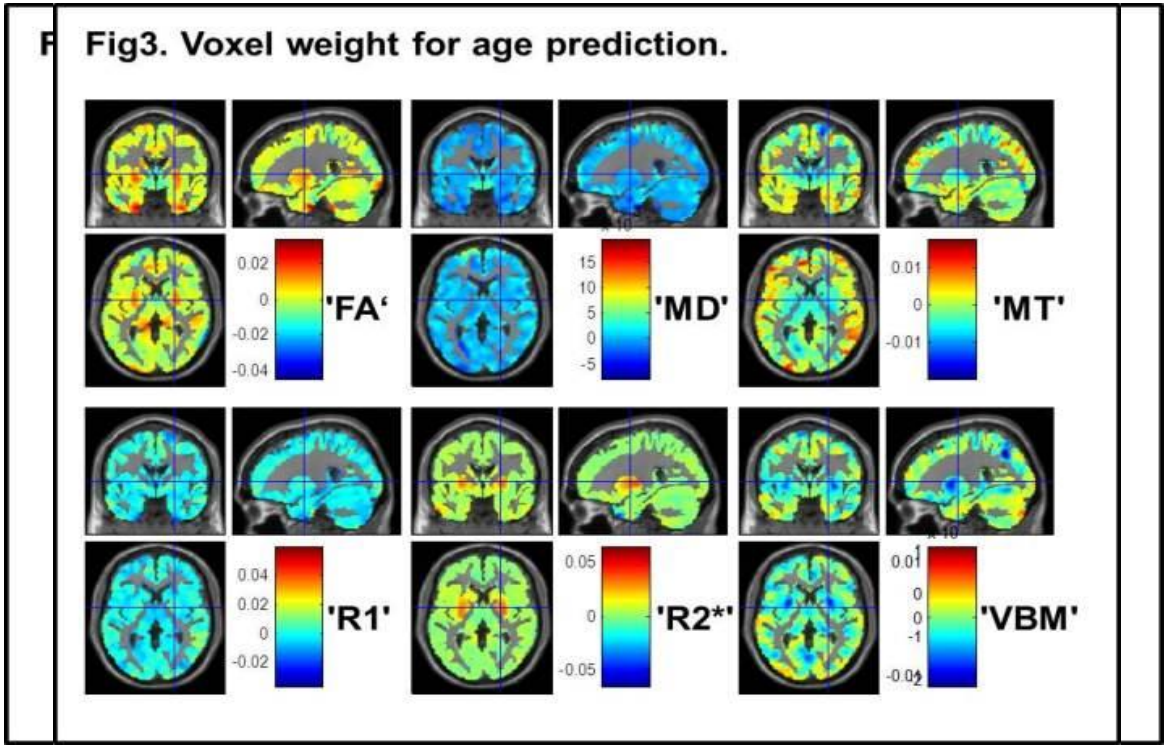
Multivariate inference – age prediction

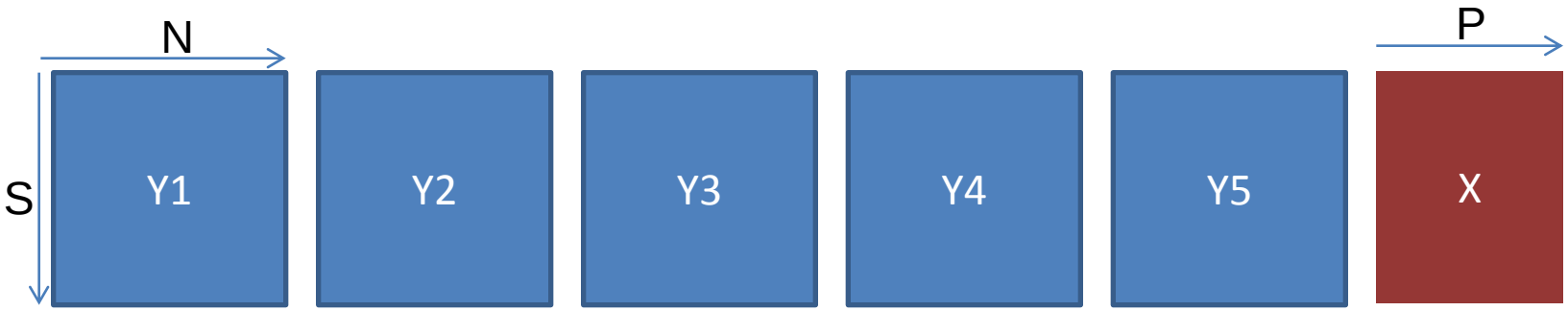
- Multivariate calibration analysis using partial least square regression (PLSR)

- leave-one-out cross-validation - Mean Error in prediction:

12.75y - FA, 11.8y - MD, 12.4y - MT, 12.6y - R1, 9.7y - R2* and 9.4y - VBM.

COMBINED Mean Error in prediction - 7.8 years





Voxelwise covariate : adjustement

$$Y_1 = X\beta + Y_2\delta + \epsilon$$

Causal inference (SEM)