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SPM Maps of Relative Hypometabolism and Relatively Preserved Brain Regions

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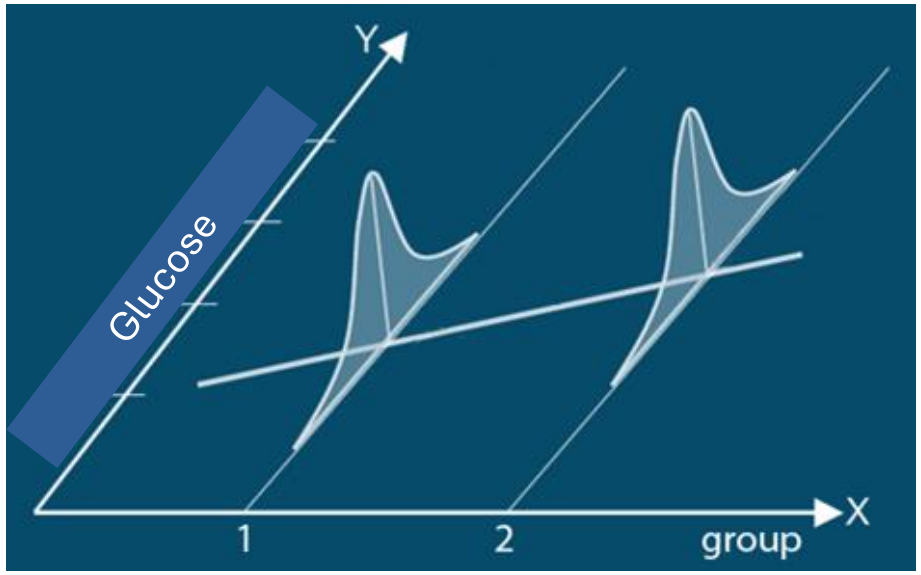
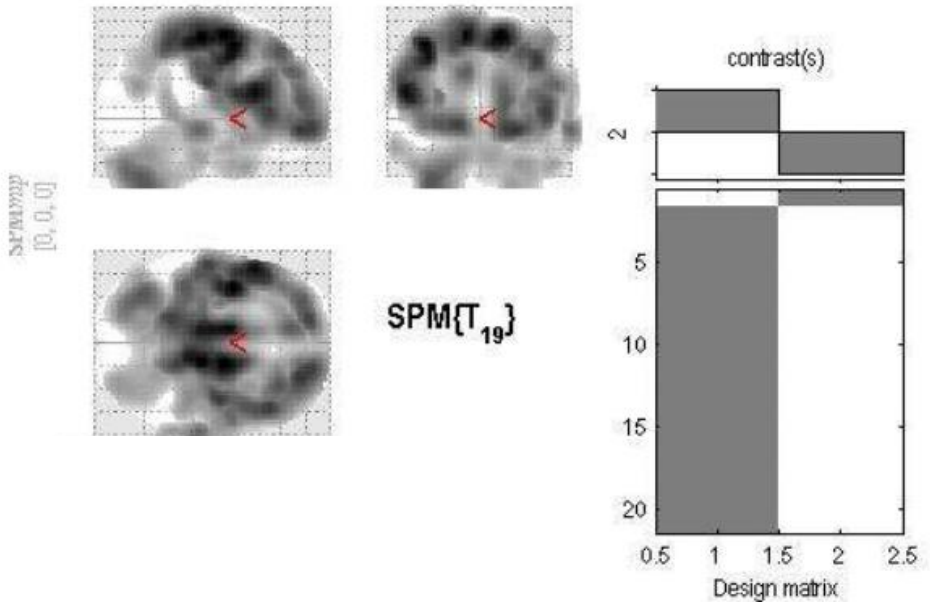
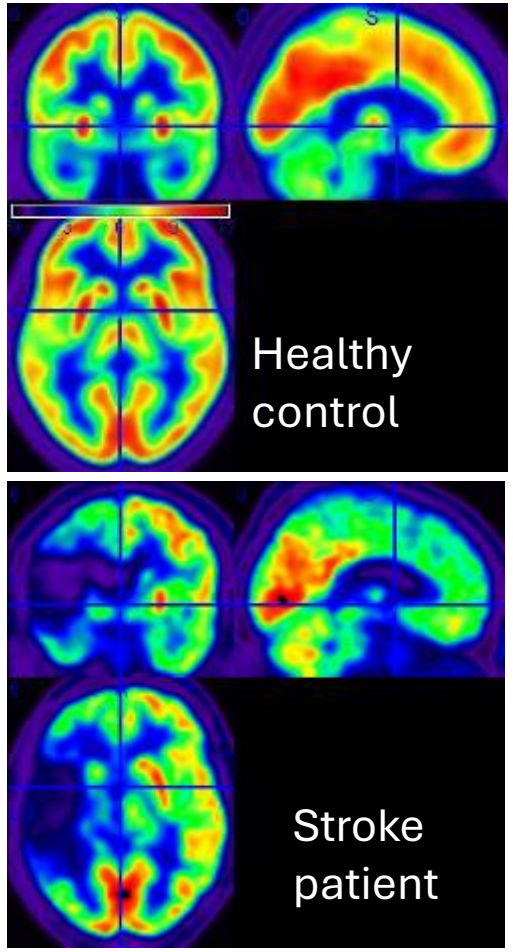
Outline

- Compare our patient to a reference group of healthy controls **(two-sample t-test)**
- **Voxel wise** (mass-univariate: independent statistical tests for every single voxel)
- Obtain a **statistical parametric map**, showing areas where there is a significant difference between patient and healthy controls (decreased or increased metabolism)





Voxel-level PET image analysis



- 1) Spatial Registration, Normalization (or Warping) and Smoothing –> to put all the different images in the same “space”, crucial for statistical comparisons

- 2) Creation of a Parametric Image (SUVRs, DVRs, BP…) -> to put all the different images in the same «scale»

- 3) Statistical Model -> to statistically compare images

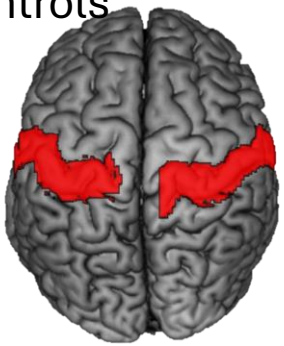
Courtesy of Leonardo Iaccarino, PhD, Eli

Scaling

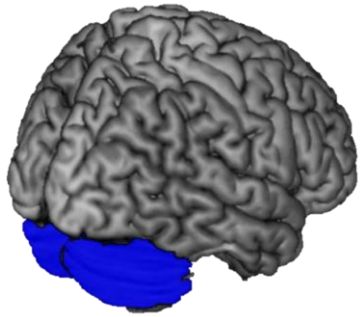
A reference region should be:

- Spared by the disease of interest
- Devoid of tracer specific uptake

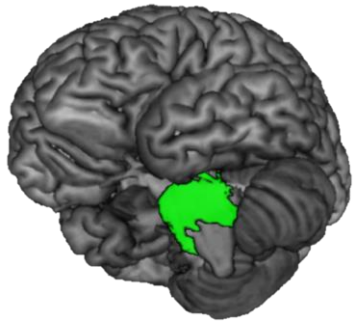
=> The delivery of the tracer in this region is similar across patients and healthy controls



Somatosensory Cortex



Whole Cerebellum (or only CER GM)



PONS

This allows us the compute a standardized uptake value ratio (comparable across subjects) that can be used for further analysis

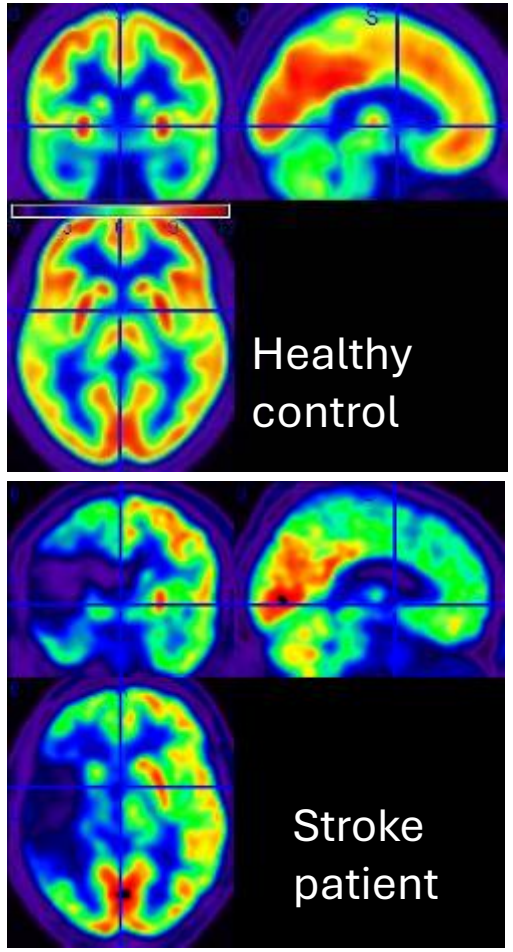
Courtesy of Leonardo Iaccarino, PhD, Eli Lilly

SPM standard approach considers a "Global Mean", which computes an average value from all the GM cortical regions.

Each image (patient and controls) is scaled to its global mean; this provides a relative, NOT absolute measure of metabolism!

When comparing patient and controls we then obtain a *relative* measure of decreases and increases

Voxel-level PET image analysis



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Courtesy of Leonardo Iaccarino, PhD, Eli

General linear model: two sample t-test

- Employs GLM, assuming the residuals are normally distributed, **GLM: Y = Xβ + ε**
- **In the case of a two-sample t-test:**

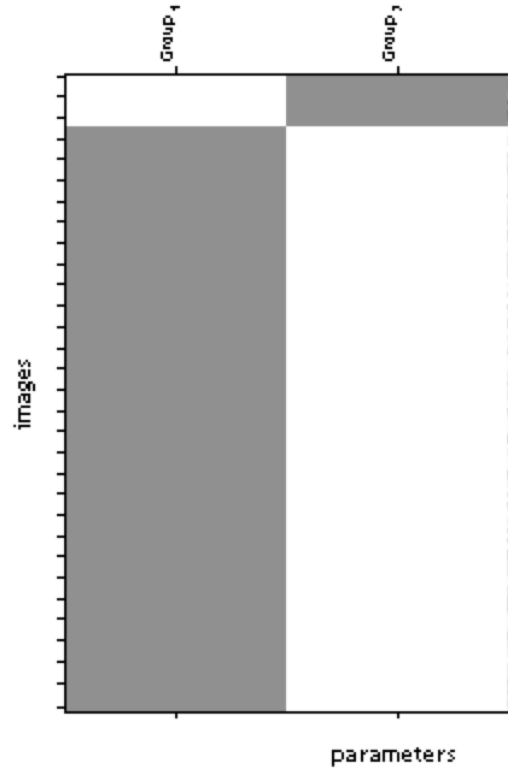
$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}$$

$$\begin{pmatrix} Y_1 \\ Y_1 \\ Y_1 \\ Y_1 \\ Y_1 \\ Y_2 \\ Y_2 \\ Y_2 \\ Y_2 \\ Y_2 \end{pmatrix} = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_2 \end{pmatrix} + \boldsymbol{\varepsilon}$$

Parameters

Voxel value *G1 G2*

SPM Study Design



Comparison with healthy controls

DATASET

FDG-PET/CT data of healthy volunteers and patients with disorders of consciousness

Annen, J.; Sala, A.; Bonin, E.A.C.; Sanz, L.R.D.; Barra, A.; Cecconi, B.; Vitello, M.; Szymkowicz, E.; Cardone, P.; Bernard, C.; Martial, C.; Laureys, S.; Gosseries, O.; Thibaut, A.

Download Dataset | Data-descriptor

https://object.cscs.ch/v1/AUTH_25b4e28a742d4987a7b6f84c0c36512e/hbp-d000052_FDG-PET-in-HC-and-DoC/EBRAINS-DataDescriptor_FDG-PET-in-HC-and-DoC.pdf

DOI: 10.25493/7TXP-WCF

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Custodians: Laureys, Steven

This dataset contains the cerebral 18F-Fluorodeoxyglucose PET-CT scans of 33 healthy volunteers and 2 patients with disorder of consciousness. The data of the healthy volunteers has been normalized to MNI space and smoothed, and can be used as control group for assessing regions with relative preserved or reduced glucose uptake in patients with disorders of consciousness after severe brain injury. The toolbox to do the analysis, based on SPM, is shared as well. Two datasets also contain the raw DICOM images of 2 patients with severe brain injury as example. For the interpretation of the glucose uptake maps and standardized uptake values we refer the user to the EBRAINS Collab

Annen, J. and Sala, A. contributed equally
Gosseries, O. and Thibaut, A. contributed equa

Modality:
- radiology
- multimodal approach
- anatomical approach

Preparation: In vivo

Methods:
Positron emission tomography/computed tomography (PET/CT)

Keywords:
glucose uptake

Scanner
Gemini TF PET-CT scanner
(Philips Medical Systems)

Files (247) | Related publications (4) | Subjects (2)

Name	Species	Sex	Age	Age category	Weight	Strain	Genotype	Samples
DoC (n = 2)	Homo sapiens	• Female • Male	-	Adult	-	-	-	-
healthy (n = 33)	Homo sapiens	• Female • Male	19 - 70 years	Adult	-	-	-	-

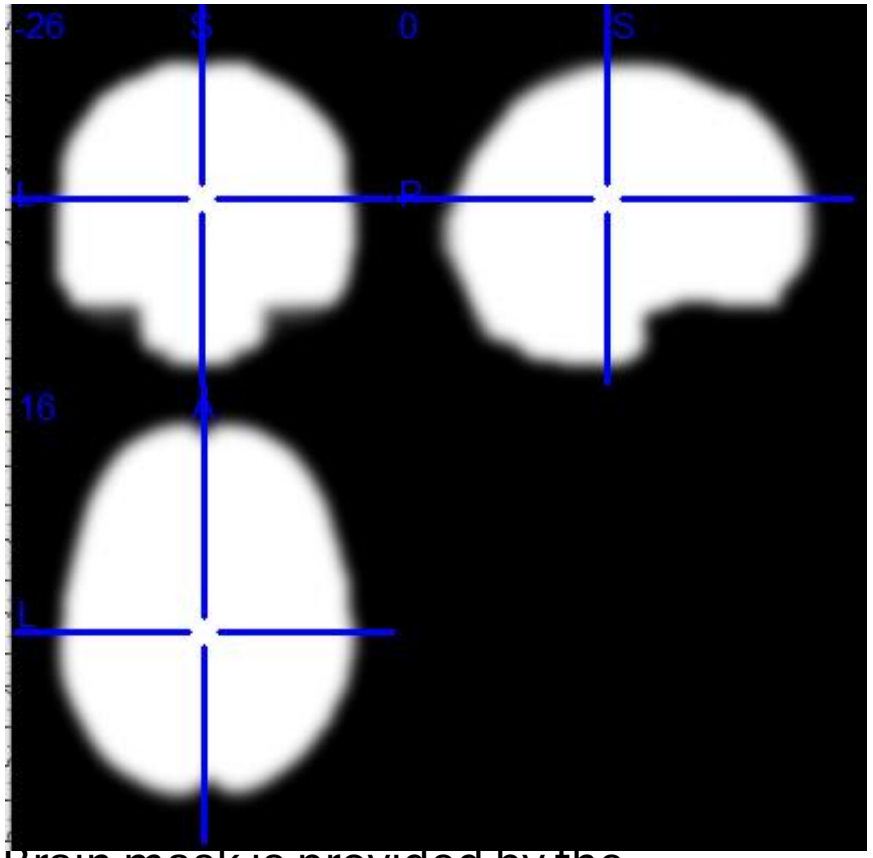
https://search.kg.ebrains.eu/instances/Dataset/68a61eab-7ba9-47cf-be78-b9addd64bb2f

Comparison with healthy controls

Dallas Lifespan Brain Study	147	HC	30-89	Amyloid burden	Florbetapir	BI	Static	x		
FDG-PET/CT data of healthy volunteers and patients with disorders of consciousness	35	HC, DoC	19-70	Glucose metabolism	FDG	BI	Static			
Mesolimbic dopamine D2 receptors and neural representations of subjective value	25	HC	18-24	D2 receptors	Fallypride	BI	Dynamic	x		
Monash DaCRA fPET-fMRI	15	HC	18-20	Glucose meatabolism	FDG	BI, CI, BI+CI	Dynamic	x		
Monash rsPET-MR	27	HC	18-21	Glucose meatabolism	FDG	CI	Dynamic	x		
Monash vis-fPET-fMRI	10	HC	18-48	Glucose meatabolism	FDG	CI	Dynamic			

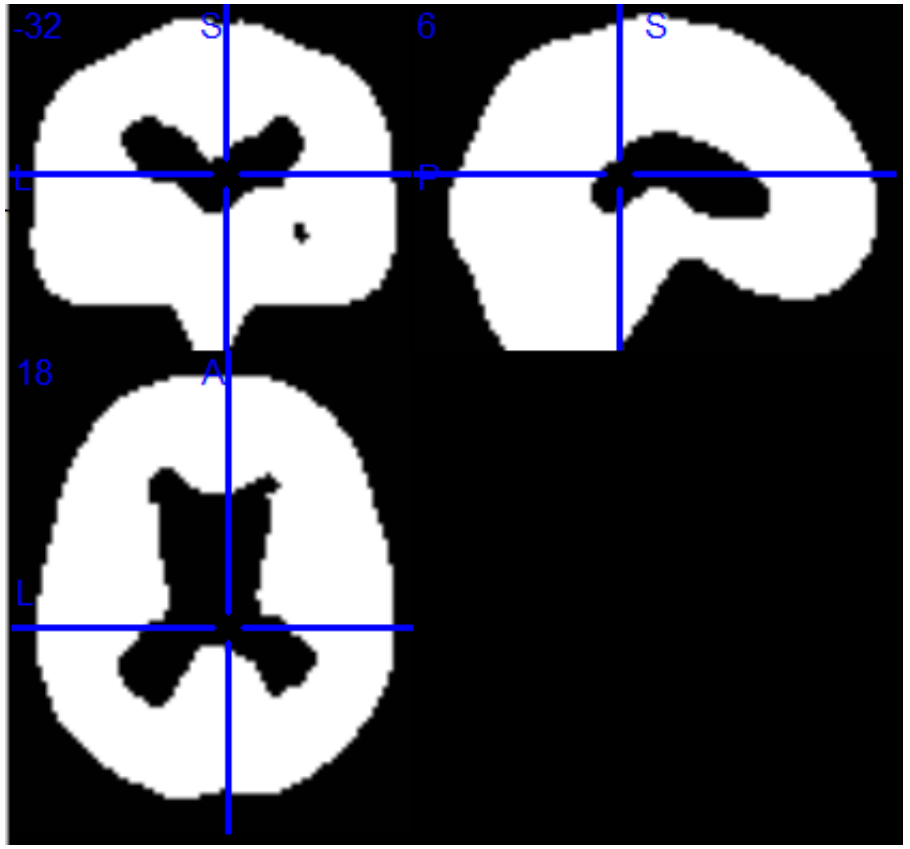
Masking

Explicit Mask



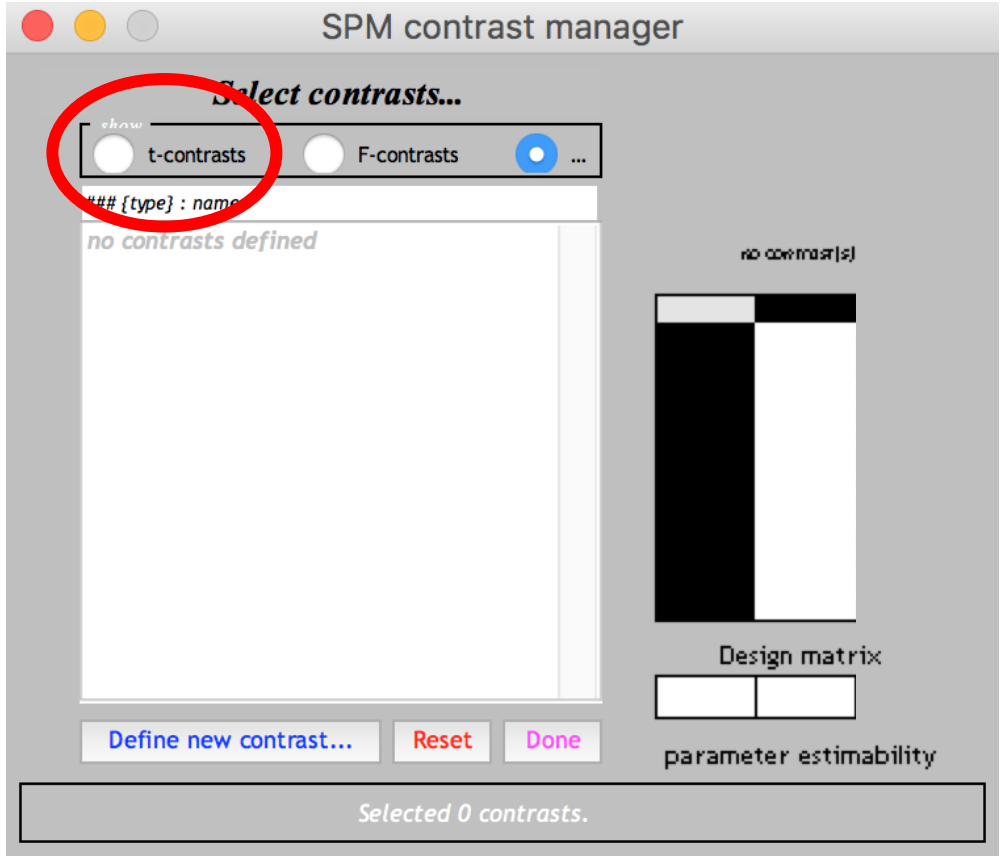
- Brain mask is provided by the experimenter (default brain mask provided in SPM fieldmap toolbox used in our case)

Relative Mask



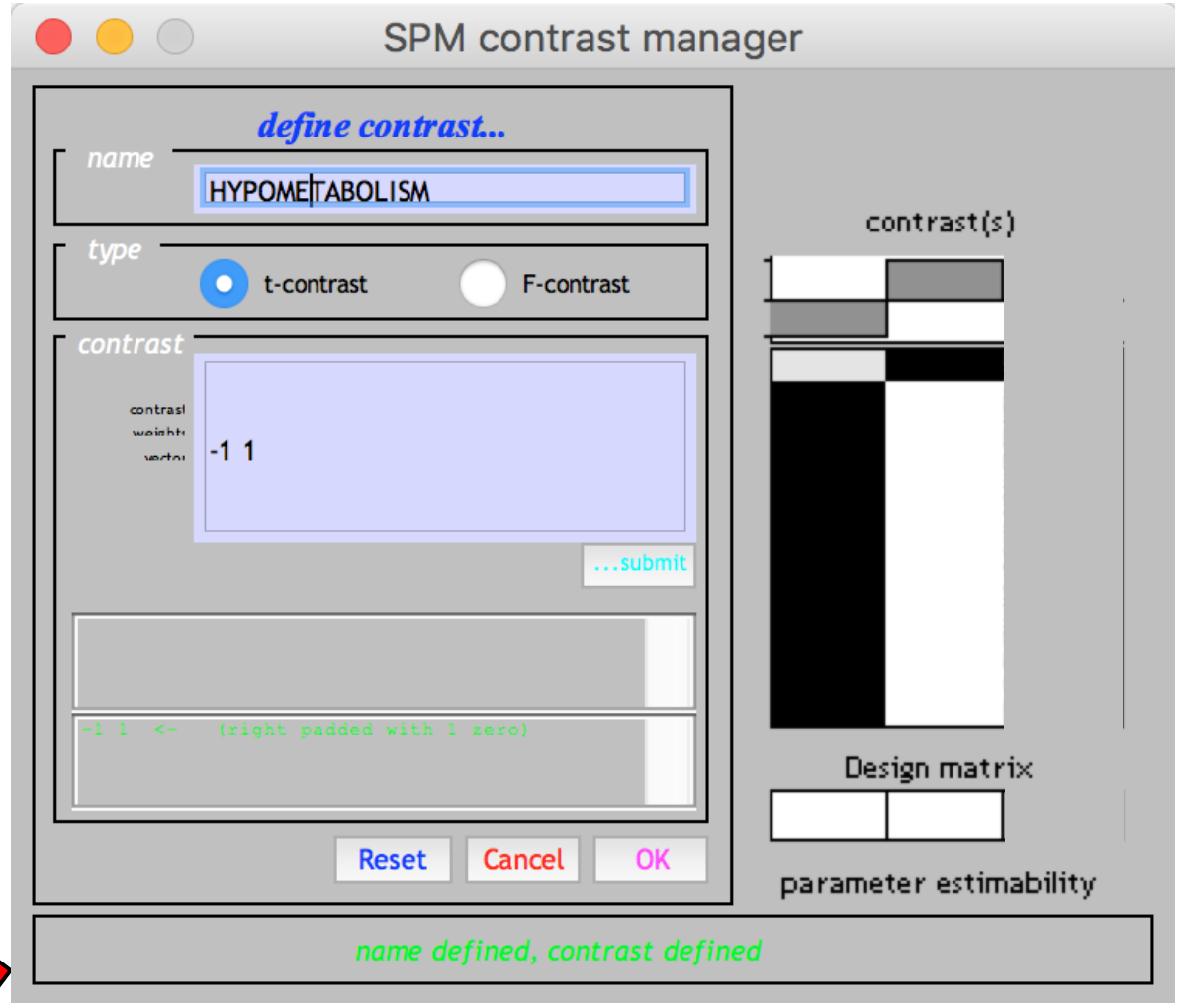
- Creates mask based on intensity values of the image
- Usual threshold set to **0.8** (exclude the voxels with intensity **>80%** of the mean global value, computed after excluding image voxels < mean global value/8)

Contrasts



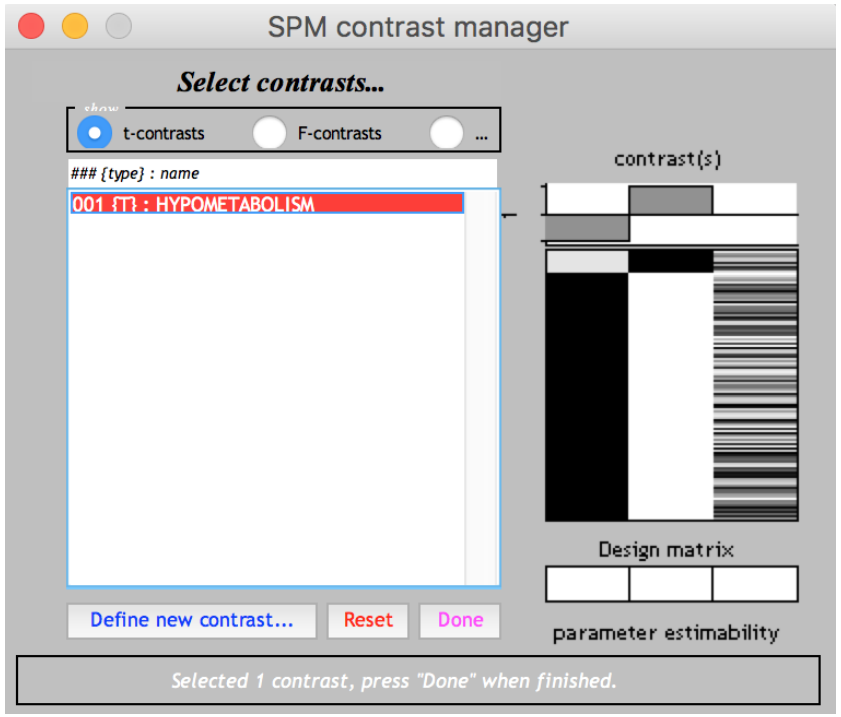
The contrast you specify relates to your question.

Contrast

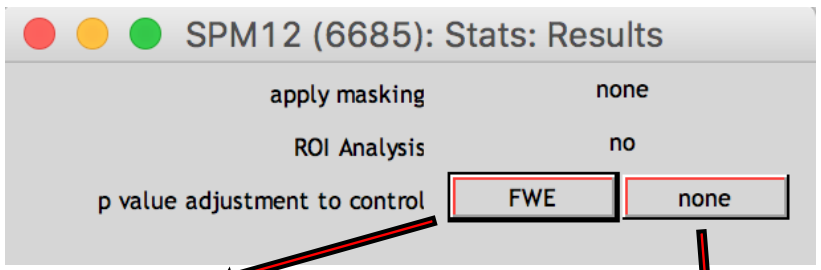


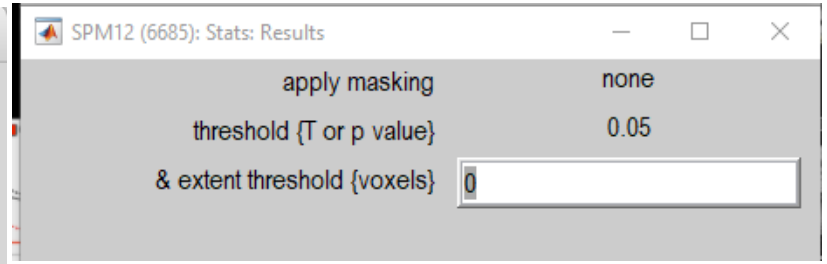
Courtesy of Leonardo Iaccarino, PhD, UC

Results



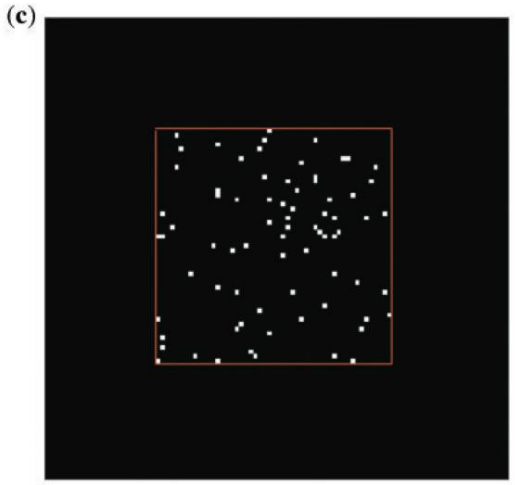
Statistical adjustments



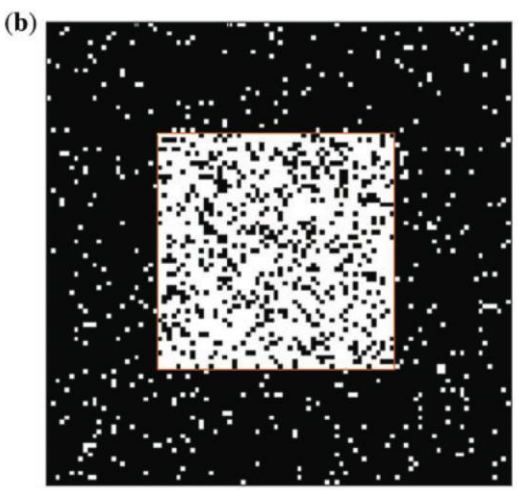


FWE

Uncorrected



Control of Familywise Error Rate



Uncorrected Results

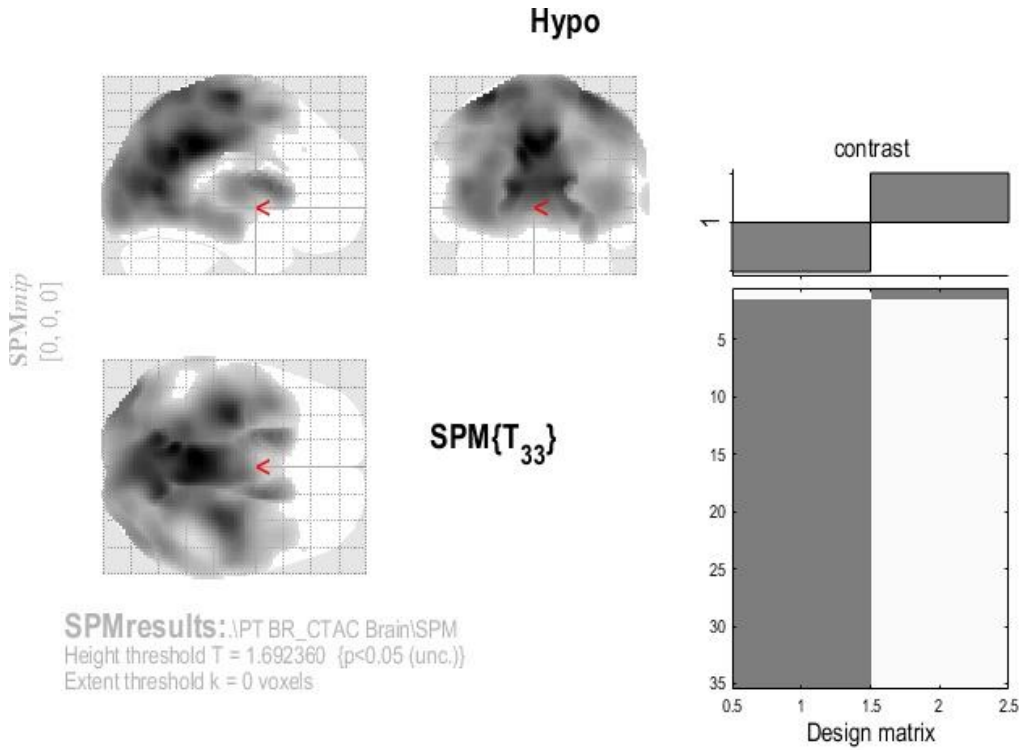
Courtesy of Leonardo Iaccarino, PhD, Eli

Bennet et al 2009

SPM maps

Significant areas

Details, t-val and p-val, peak coordinates



Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm		
p	c	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	k_E	p_{uncorr}	$p_{FWE\text{-}corr}$	$q_{FDR\text{-}corr}$	T	$(Z_{=})$	p_{uncorr}			
1.000	4	0.000		62299	0.000	0.000	0.000	11.59	7.27	0.000	-4	-42	38
						0.000	0.000	11.03	7.09	0.000	-10	-54	32
						0.000	0.000	10.64	6.96	0.000	8	-46	42
		1.000		124	0.778	1.000	0.048	2.34	2.24	0.013	72	-32	4
		1.000		1	0.990	1.000	0.156	1.71	1.67	0.047	54	30	34
		1.000		2	0.984	1.000	0.157	1.71	1.67	0.047	-28	-14	-2

table shows 3 local maxima more than 8.0mm apart

Height threshold: T = 1.69, p = 0.049 (1.000)
Extent threshold: k = 0 voxels
Expected voxels per cluster, <k> = 1307.636
Expected number of clusters, <c> = 18.33
FWEp: 5.042, FDRp: 2.325, FWEc: 62299

Degrees of freedom = [1.0, 33.0]
FWHM = 22.1 24.2 21.4 mm mm mm; 11.1 12.1 10.7 {voxels}
Volume: 1610344 = 201293 voxels = 127.9 resels
Voxel size: 2.0 2.0 2.0 mm mm mm; (resel = 1435.20 voxels)