SPM Maps of Relative Hypometabolism and Relatively Preserved Brain Regions

CSG PET workshop

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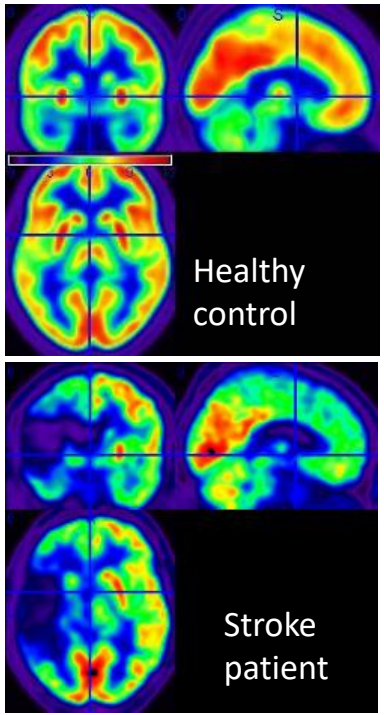
Voxel-level PET image analysis

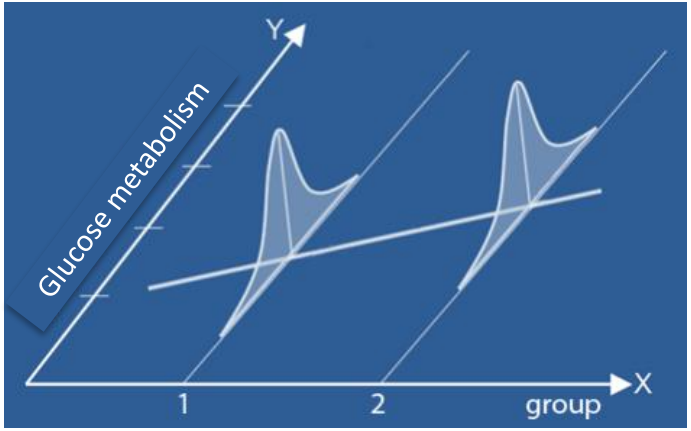


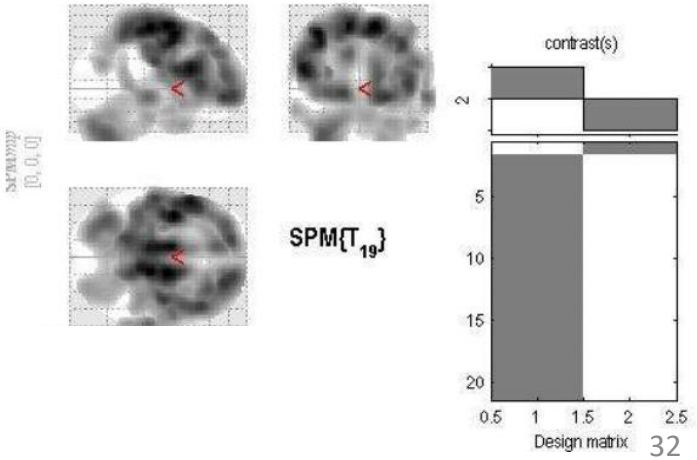
- 1) Spatial Registration, Normalization (or Warping) and Smoothing –> to put all the different images in the same "space", crucial for statistical comparisons
- 2) Creation of a Parametric Image (SUVRs, DVRs, BP…) -> to put all the different images in the same «scale»
- 3) Statistical Model -> to statistically compare images

Courtesy of Leonardo Iaccarino, PhD, UCSF

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)





Design Specification: two sample t-test

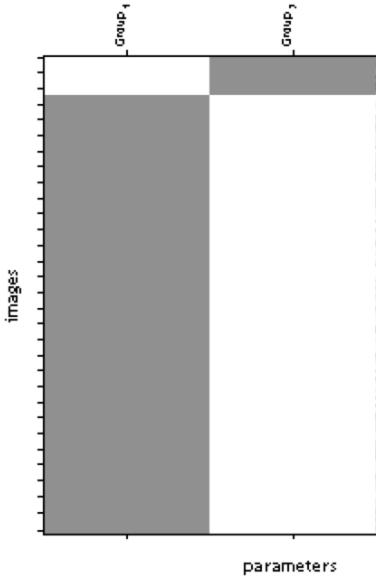
- Employs GLM, providing the residuals are normally distributed, **GLM: Y = Xβ + ε**
- **In the case of a two-sample t-test:**

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

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

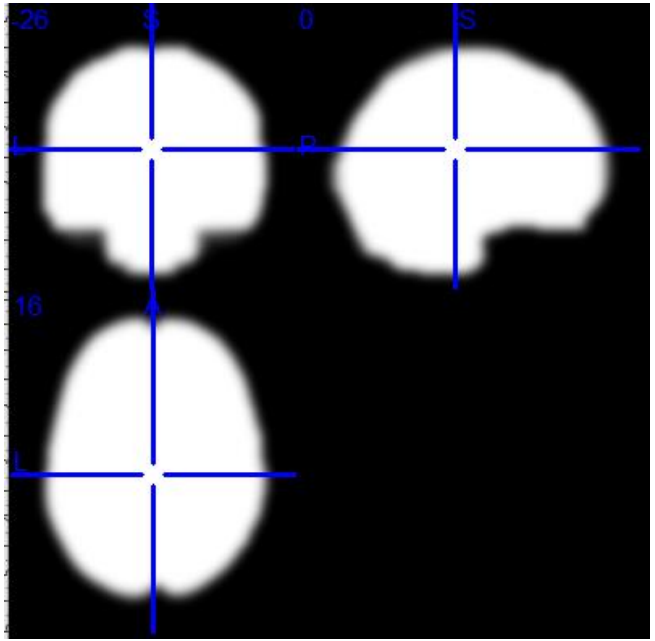
Comparison with healthy controls

Dataset	Subjects, N	Population	Age Range (y)	Tracer	Data Access
ADNI	1958	HC, SMC, MCI, ADD	55-98	FDG, Florbetapir, Florbetaben, Flortaucipir	Simple application
ADNI-ARG	56	HC, MCI, ADD		FDG, PiB	Simple application
AIVO	4339	HC, PD, obesity, schizophrenia, depression, other	18-90	FDG, H2O, PiB, Flutemetamol, DOPA, NNC112, Reclopride, FLB457, CFT, WAY-100635, MADAM, Carfentanil, PK11195, PBR28	Detailed application (incl. approval through ethical committe)
ALFA+ Study	361	HC, SCC - enriched for AD risk factors	45-65	Flutemetamol	Detailed application
Alzheimer´s Disease Repository without Borders (ARWIBO)	60	HC, SSC, MCI, ADD FTLD, PD, major depression	48-85	FDG	Detailed application
APOE E4 Arizona Dose Programme	447	HC - enriched for AD risk factors	20 - 87	FDG, PIB, Florbetapir, Flortaucipir,	Detailed application
Associazione Italiana Medicina Nucleare (AIMN)	155	HC	22-84	FDG	Simple application
Centro Nacional de Investigaciones Cardiovasculares (CNIC)	547	Asymptomatic middle-aged participants with evidence of subclinical atherosclerosis	41-58	FDG	Detailed application
DIAN (observational study)	556	HC, MCI, ADD (autosomal dominant)	18-69	FDG, PiB	Detailed application
DIAN-TU	249	HC, MCI, ADD (autosomal dominant)	21-72	FDG, PIB, Florbetapir, Flortaucipir	Detailed application
European Alzheimer's Disease Consortium (EADC)	1114	HC, SCC, MCI, pseudo-dementia, ADD, FTLD	41-91	FDG, Florbetapir, Florbetaben, Flutemetamol	Other (available to all EADC centers contributing a minimum dataset of relevant data)
Harvard Aging Brain Study (HABS)	290	HC	62-90	FDG, PiB, Flortaucipir	Detailed application
Hôpitaux Universitaires de Genève (HUG)	603	HC, SCD, MCI, Dementia	28-92	FDG, florbetapir, flutemetamol, flortaucipir	Detailed application
International Consortium for Brain Mapping (ICBM)	28	HC, MCI, ADD	29-92	FDG	Detailed application
J-ADNI	344	HC, MCI, ADD	60-85	FDG, PiB, BF227	Detailed application
KBASE	643	HC, MCI, ADD	25-90	FDG, PiB, Flortaucipir	Detailed application
Knight ADRC	1142	HC, MCI, ADD	34-100	FDG, PIB, Florbetapir, Flortaucipir	Detailed application
Mayo Clinical Study of Aging	2245	HC, MCI, dementia	30-90+	FDG, PiB, Flortaucipir	Detailed Application
Monash rsPET-MR	27	HC	18-21	FDG	Freely available
Monash vis-fPET-fMRI	10	HC	18-48	FDG	Freely available
OASIS-3	777	HC, SCC, MCI, ADD	42-95	FDG, PiB, Florbetapir	Simple application
The Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation-PD (ICICLE-PD)	99	HC, PD, PD-MCI	54-91	FDG	Detailed application
University Medical Centre - Ljubljana	159	HC, SCC, MCI, ADD	49-89	FDG, Florbetaben	Other (bilateral agreement)

Sala et al., in preparation

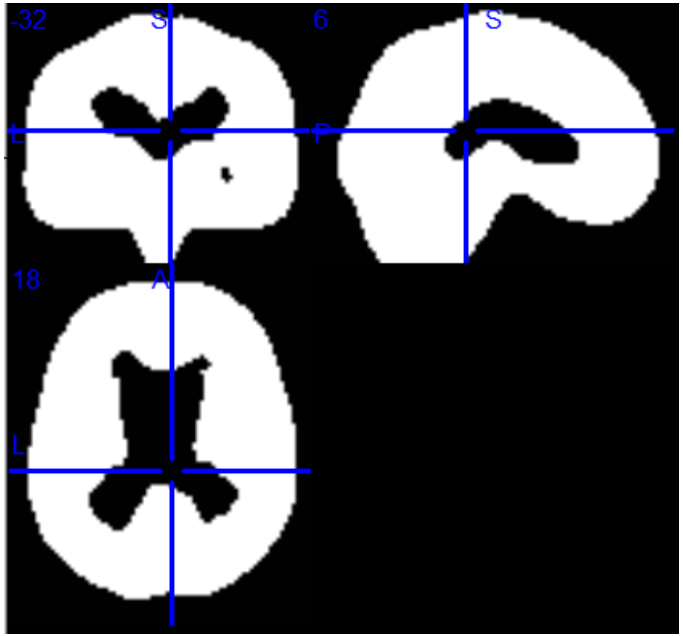
Masking

Explicit Mask



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

Relative Mask



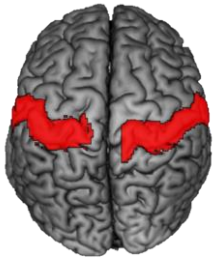
- Creates mask based on intensity values of the image
- Usual threshold set to **0.8** (exclude the voxels with intensity **>80%** of the mean global value, computed after excluding image voxels < mean global value/8)

Scaling

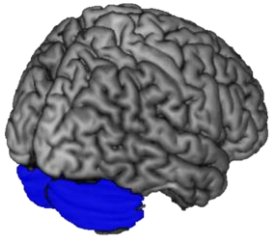
A reference region should be:

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

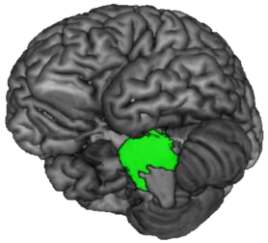
=> The delivery of the tracer in this region is similar across patients and healthy controls



Somatosensory Cortex



Whole Cerebellum (or only CER GM)

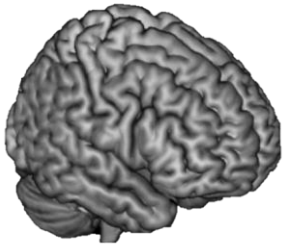


PONS

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, UCSF

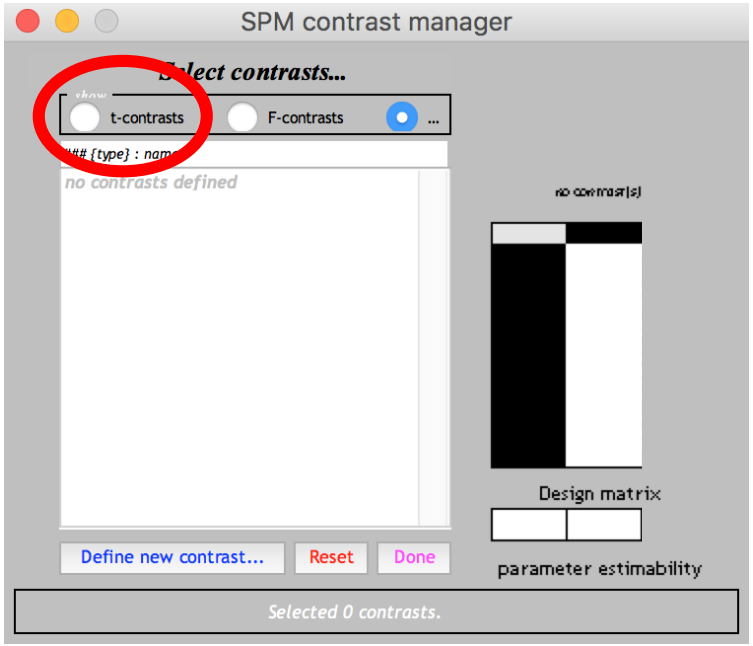
SPM standard approach considers a "Global Mean", which computes an average value from all the GM cortical regions.



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

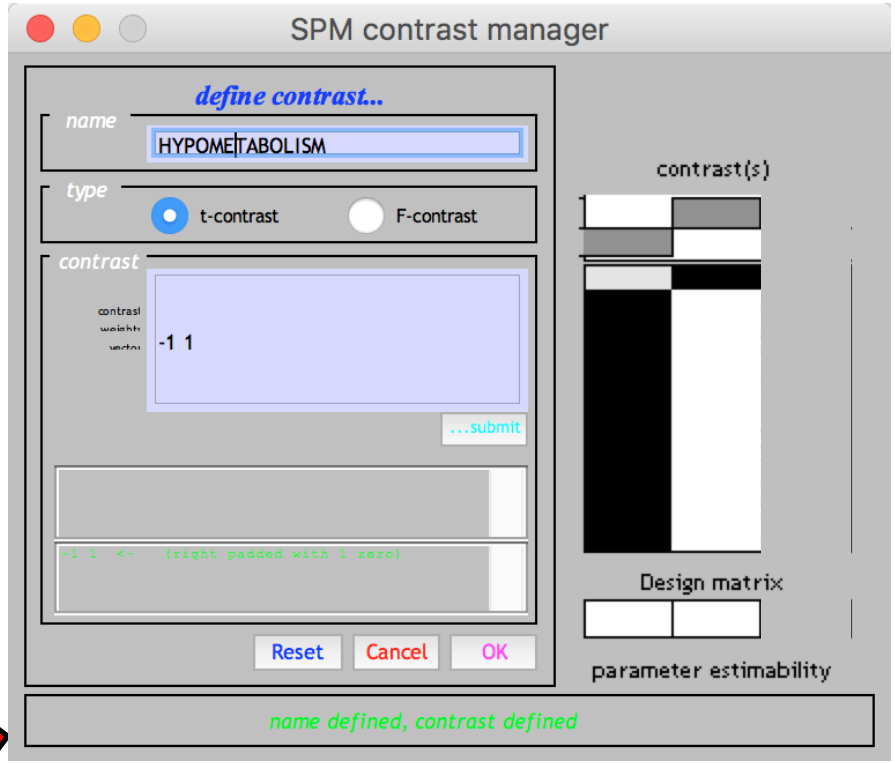
When comparing patient and controls we then obtain a *relative* measure of decreases and increases

Contrasts



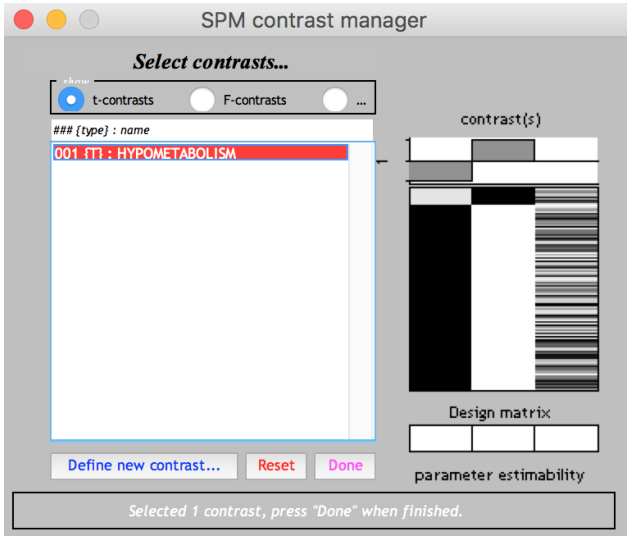
The contrast you specify relates to your question.

Contrast

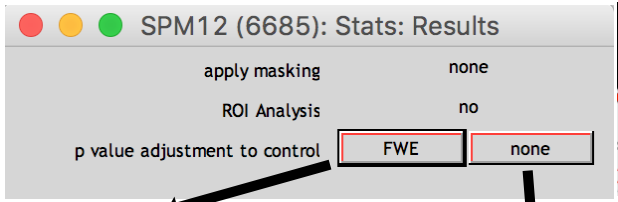


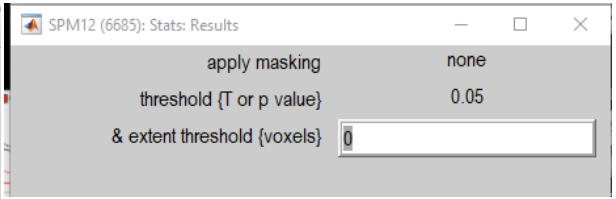
Courtesy of Leonardo Iaccarino, PhD, UCSF

Results



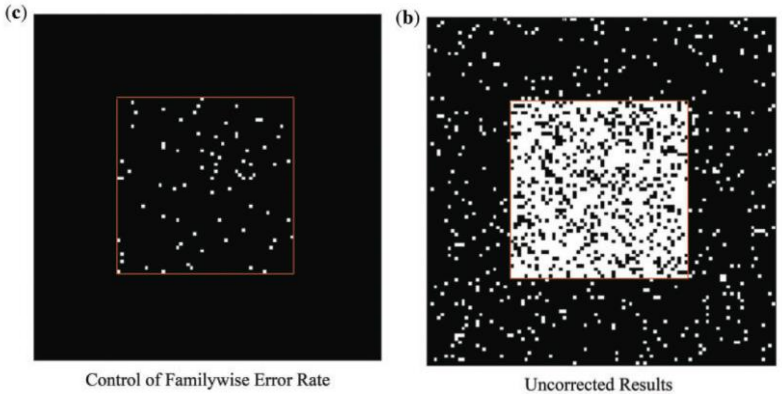
Statistical adjustments





FWE

Uncorrected



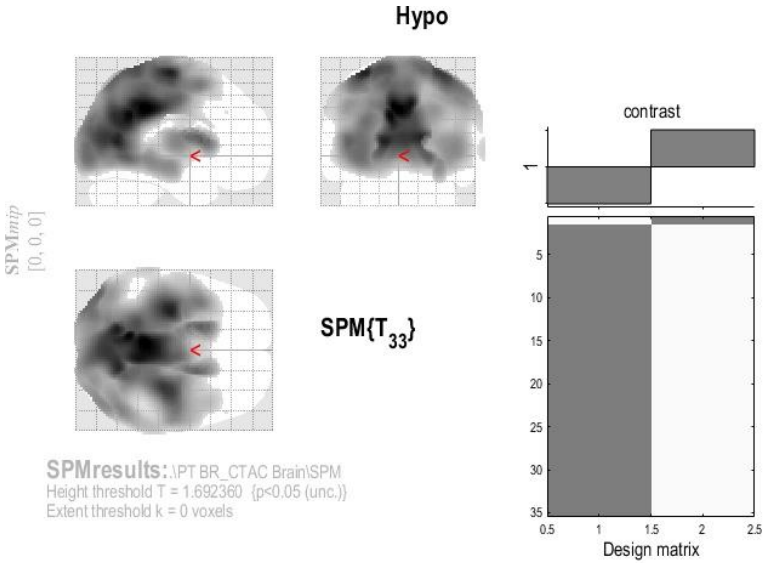
Courtesy of Leonardo Iaccarino, PhD, UCSF

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*	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	*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)