Linear parametric neurotransmitter PET model (lp-ntPET)
Modeling dopamine variations across time

2012

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NeuroImage
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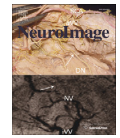

A linear model for estimation of neurotransmitter response profiles from dynamic PET data

CrossMark

→ Region-of-Interest

2013

jove Journal of Visualized Experiments www.jove.com

Video Article

Creating Dynamic Images of Short-lived Dopamine Fluctuations with lp-ntPET: Dopamine Movies of Cigarette Smoking

Evan D. Morris[1,2,3,4], Su Jin Kim[1,3], Jenna M. Sullivan[1,3,4], Shuo Wang[3,4], Marc D. Normandin[5], Cristian C. Constantinescu[6], Kelly P. Cosgrove[1,2,3]

→ Voxel-based

DA movie

2014

Voxelwise lp-ntPET for Detecting Localized, Transient Dopamine Release of Unknown Timing: Sensitivity Analysis and Application to Cigarette Smoking in the PET Scanner

Su Jin Kim,[1,2] Jenna M. Sullivan,[1,3] Shuo Wang,[1,3] Kelly P. Cosgrove,[1,2,4] and

2016

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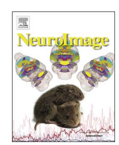


→ Optimization

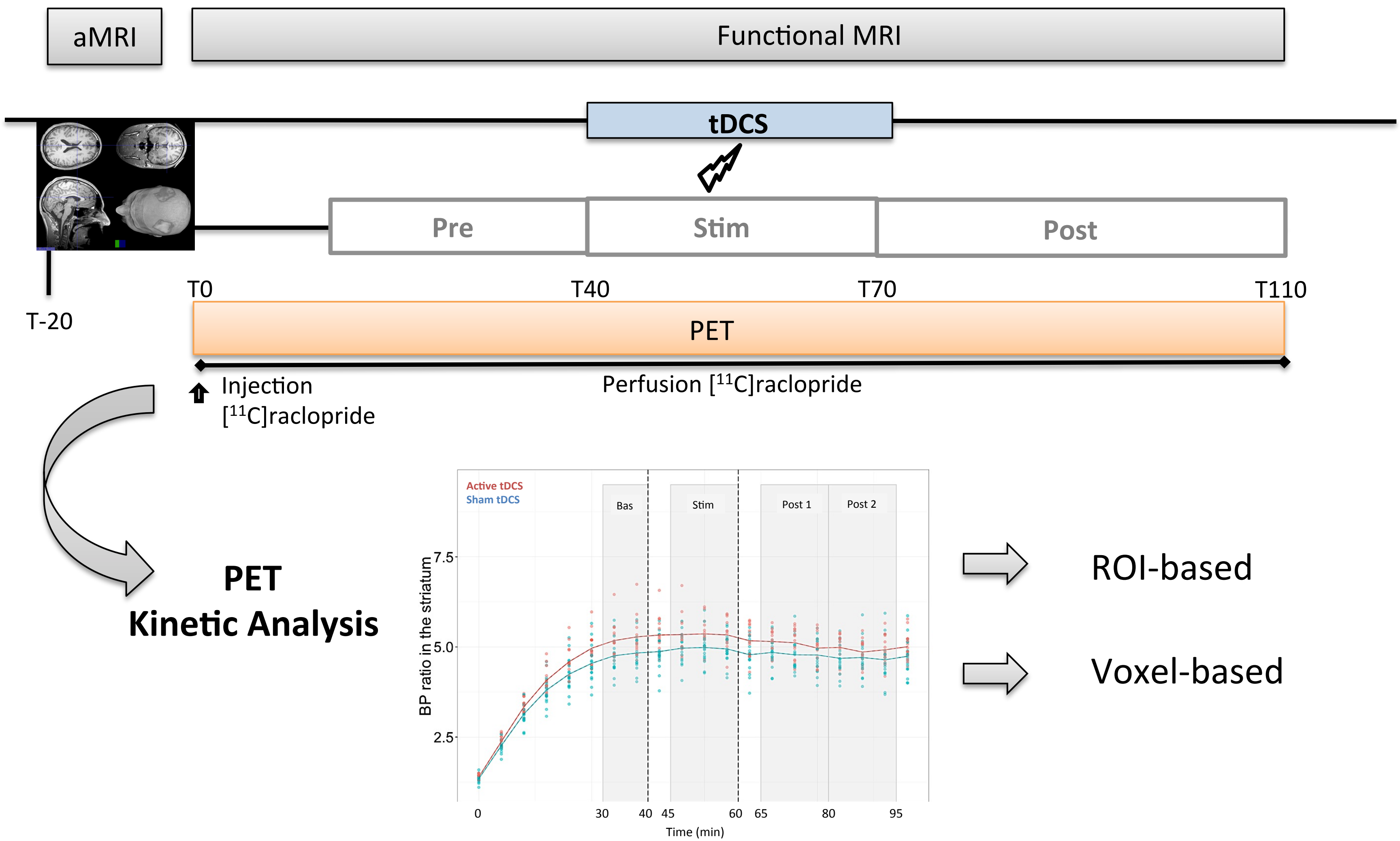
A framework for designing dynamic lp-ntPET studies to maximize the sensitivity to transient neurotransmitter responses to drugs: Application to dopamine and smoking

Shuo Wang[a,b], Sujin Kim[a,c], Kelly P. Cosgrove[a,c,d], Evan D. Morris[a,b,c,d,*]

[a] Yale PET Center, Yale University, New Haven, CT, USA
[b] Department of Biomedical Engineering, Yale University, New Haven, CT, USA
[c] Department of Radiology and Biomedical Imaging, Yale University, New Haven, CT, USA
[d] Department of Psychiatry, Yale University, New Haven, CT, USA

Clara Fonteneau
Journal Club CERMEP
23 Mars 2017
clara.fonteneau@ch-le-vinatier.fr

Neurophysiological impact of a fronto-temporal transcranial direct current stimulation in healthy subjects



Region-of-Interest lp-ntPET

2012

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A linear model for estimation of neurotransmitter response profiles from dynamic PET data

Marc D. Normandin [a,b,1], Wynne K. Schiffer [c,2], Evan D. Morris [a,b,d,*,3]

[a] Weldon School of Biomedical Engineering, Purdue University, West Lafayette, IN, USA
[b] Department of Radiology, Indiana University School of Medicine, Indianapolis, IN, USA
[c] Medical Department, Brookhaven National Laboratory, Upton, NY, USA
[d] Department of Biomedical Engineering, Indiana University-Purdue University at Indianapolis, Indianapolis, IN, USA

Présentation N. Costes

Journal Club CERMEP

Janvier 2016

MRTM (Ichise et al, 2003)

$$C_T(t)=R_1 C_R(t)+k_2\int_0^t C_R(u)du-k_{2a}\int_0^t C_T(u)du$$

LSSRM (Alpert et al, 2003)

$$C_{\boldsymbol{T}}(t) = R_1 C_{\boldsymbol{R}}(t) + k_2\int_0^t C_{\boldsymbol{R}}(u)du - k_{2a}\int_0^t C_{\boldsymbol{T}}(u)du - \gamma\int_0^t C_{\boldsymbol{T}}(u)h(u)du$$

Time varying dopamine

(**Fonction fixe**)

lp-ntPET (Normandin et al, 2012)

$$C_T(t)=R_1 C_R(t)+k_2\int_0^t C_R(u)du-k_{2a}\int_0^t C_T(u)du-\gamma\int_0^t C_T(u)\boxed{h_i}(u)du$$

Fonctions de réponses **flexibles**

Region-of-Interest lp-ntPET

> Fonctions de réponses **flexibles**

$$h_i(t) = \left(\frac{t - t_D}{t_P - t_D}\right)^{\alpha} exp\left(\alpha\left[1 - \frac{t - t_D}{t_P - t_D}\right]\right)u(t - t_D)$$

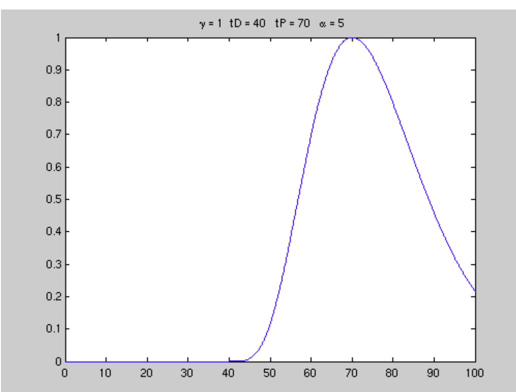
QUESTION 1 – CHOIX DES FONCTIONS

$$h_i(t) = exp(\beta(t - t_D))u(t - t_D)$$

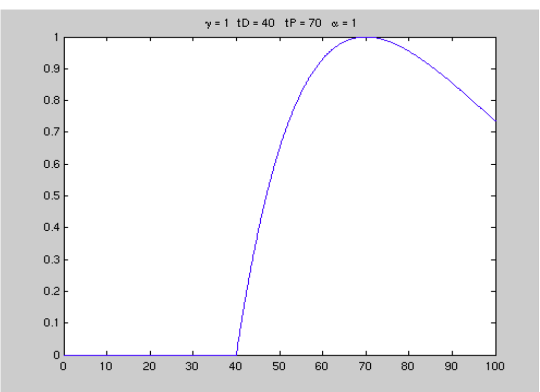
<ins>Modèles dépendants des entrées :</ins>

- tD : intervalle attendu des variations dopaminergiques
- tP : peak de la réponse
- Alpha : Sharpness (formes de la décharge attendue)

tD=40; tP=70



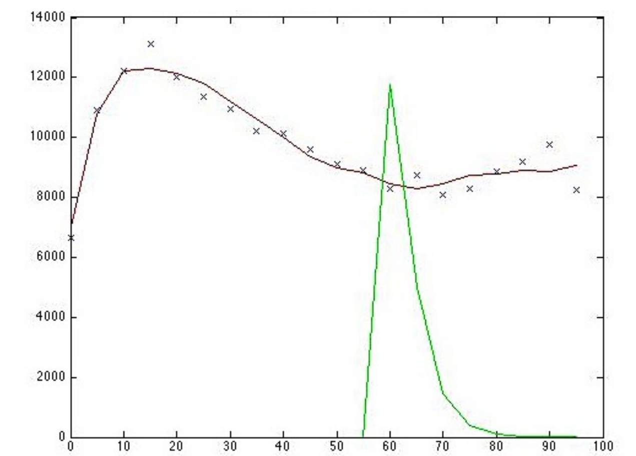
Alpha = 5



Alpha = 1

Ex : Caudate L

Gamma=0.012 / tD =56 / tP=59 / Alpha =1



Voxel-based-Analysis lp-ntPET

2013

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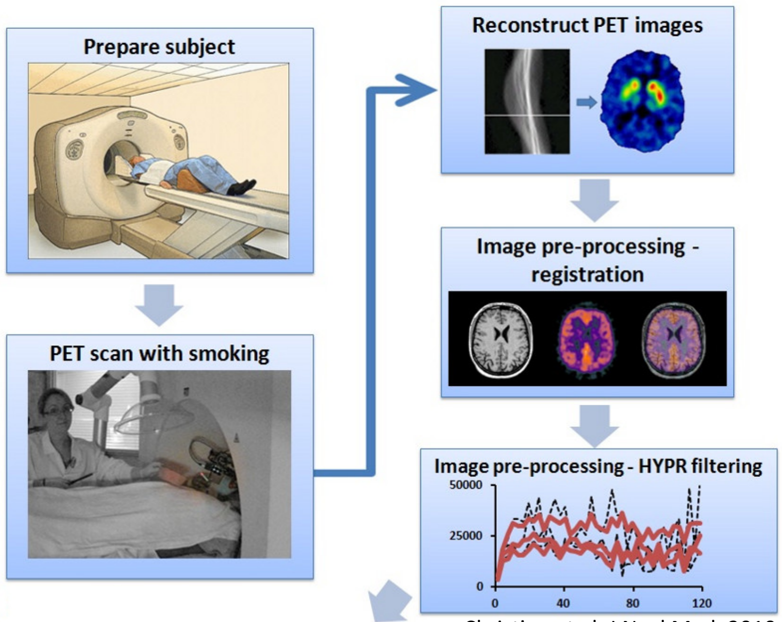
[1]*Yale PET Center, Yale University, New Haven, Connecticut*
[2]*Department of Diagnostic Radiology, Yale University, New Haven, Connecticut*
[3]*Department of Biomedical Engineering, Yale University, New Haven, Connecticut*
[4]*Department of Psychiatry, Yale University, New Haven, Connecticut*

→ DA movie!!!!

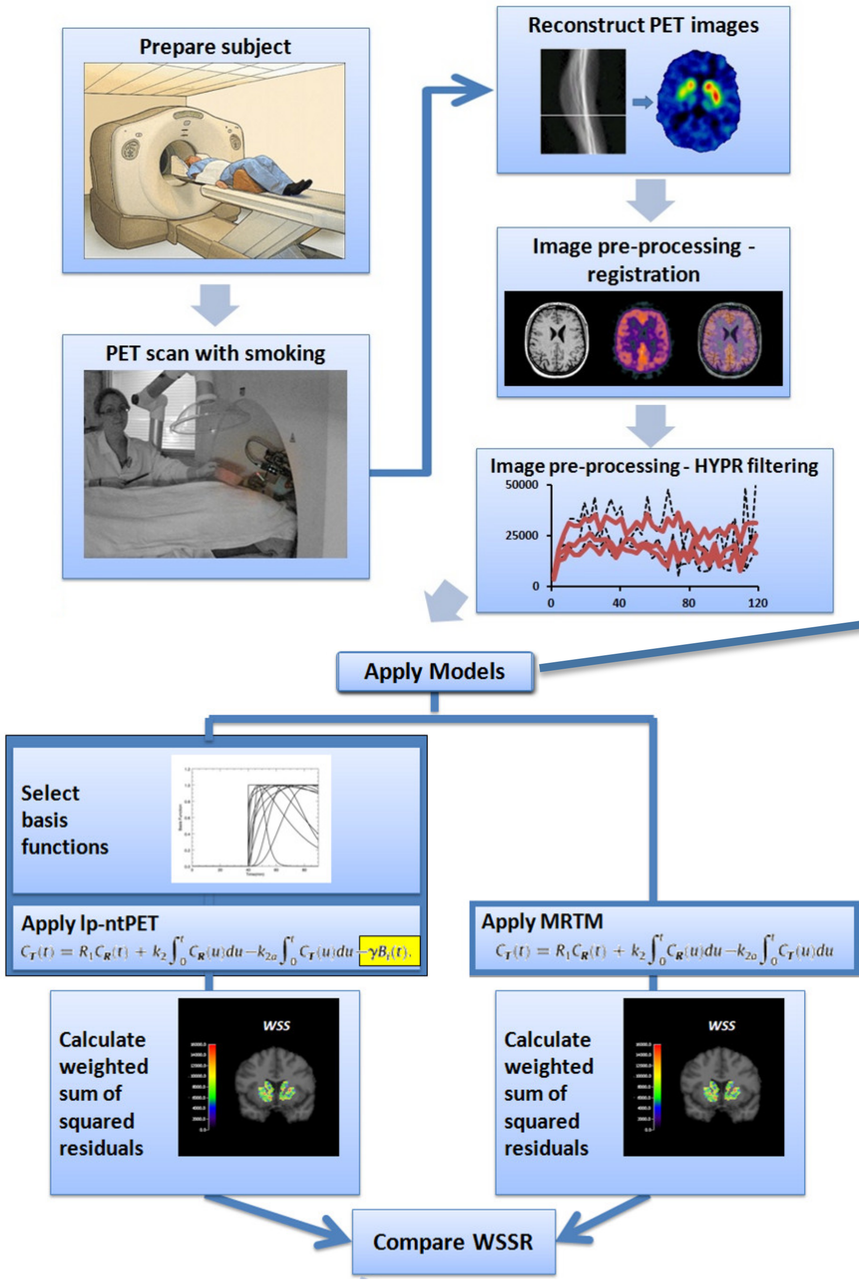
Voxel-based-Analysis lp-ntPET



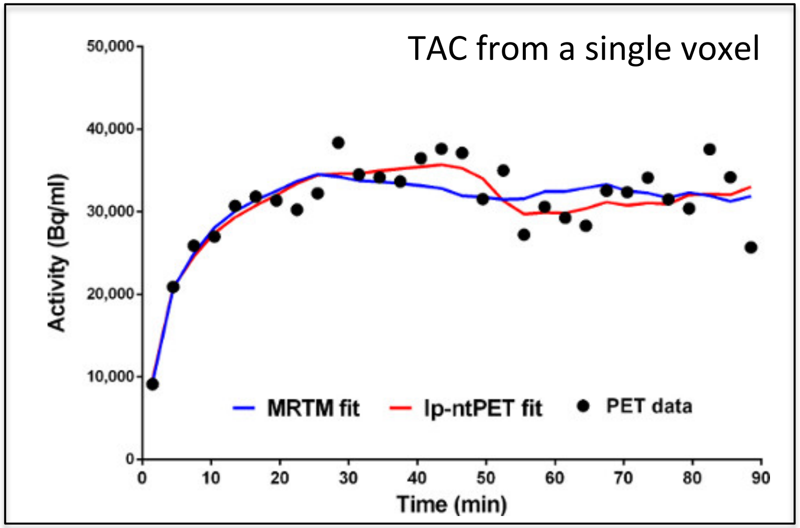
Christian et al, J Nucl Med, 2010

Pipeline for each subject

Voxel-based-Analysis lp-ntPET

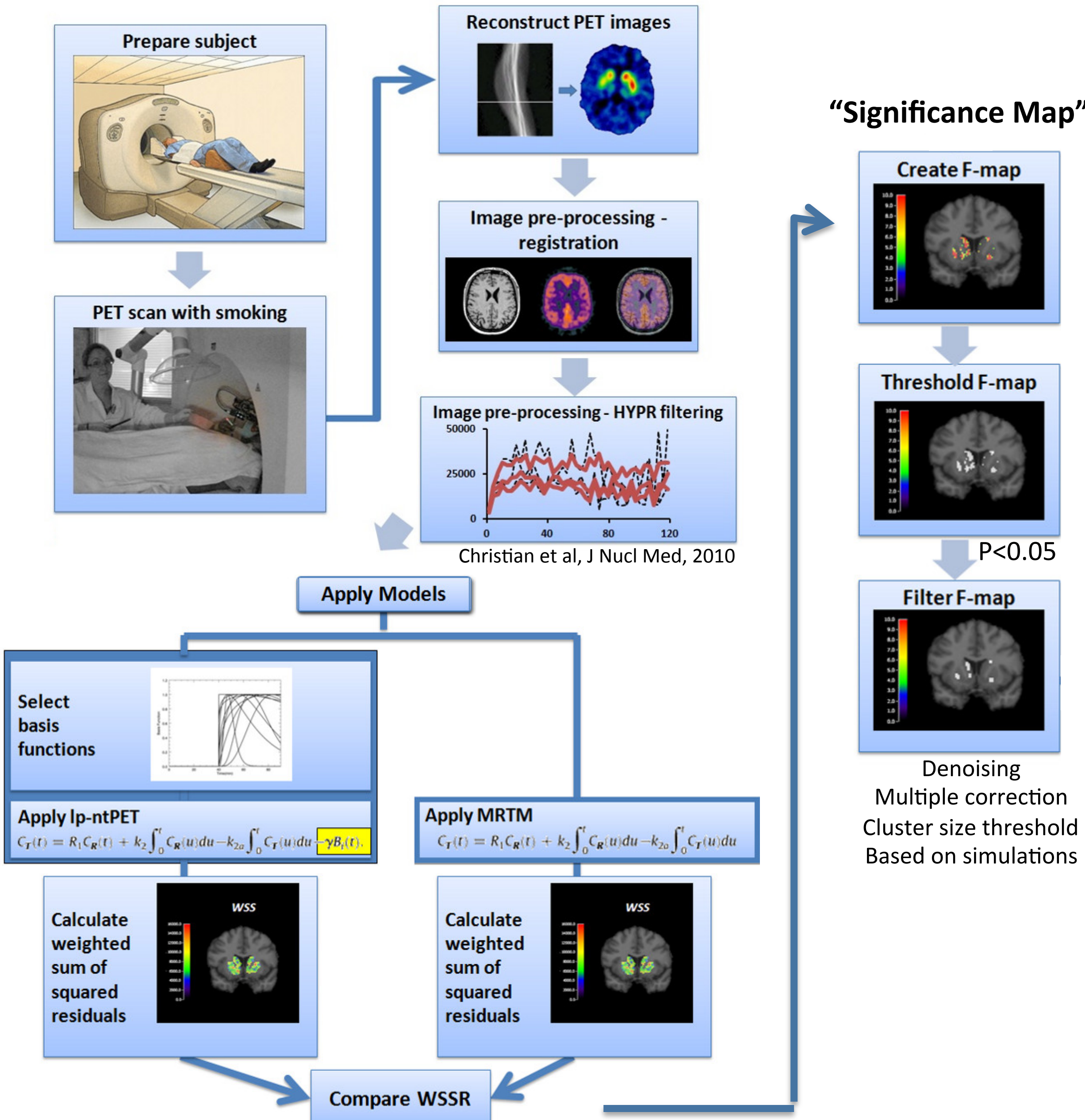


Model Fit



Pipeline for each subject

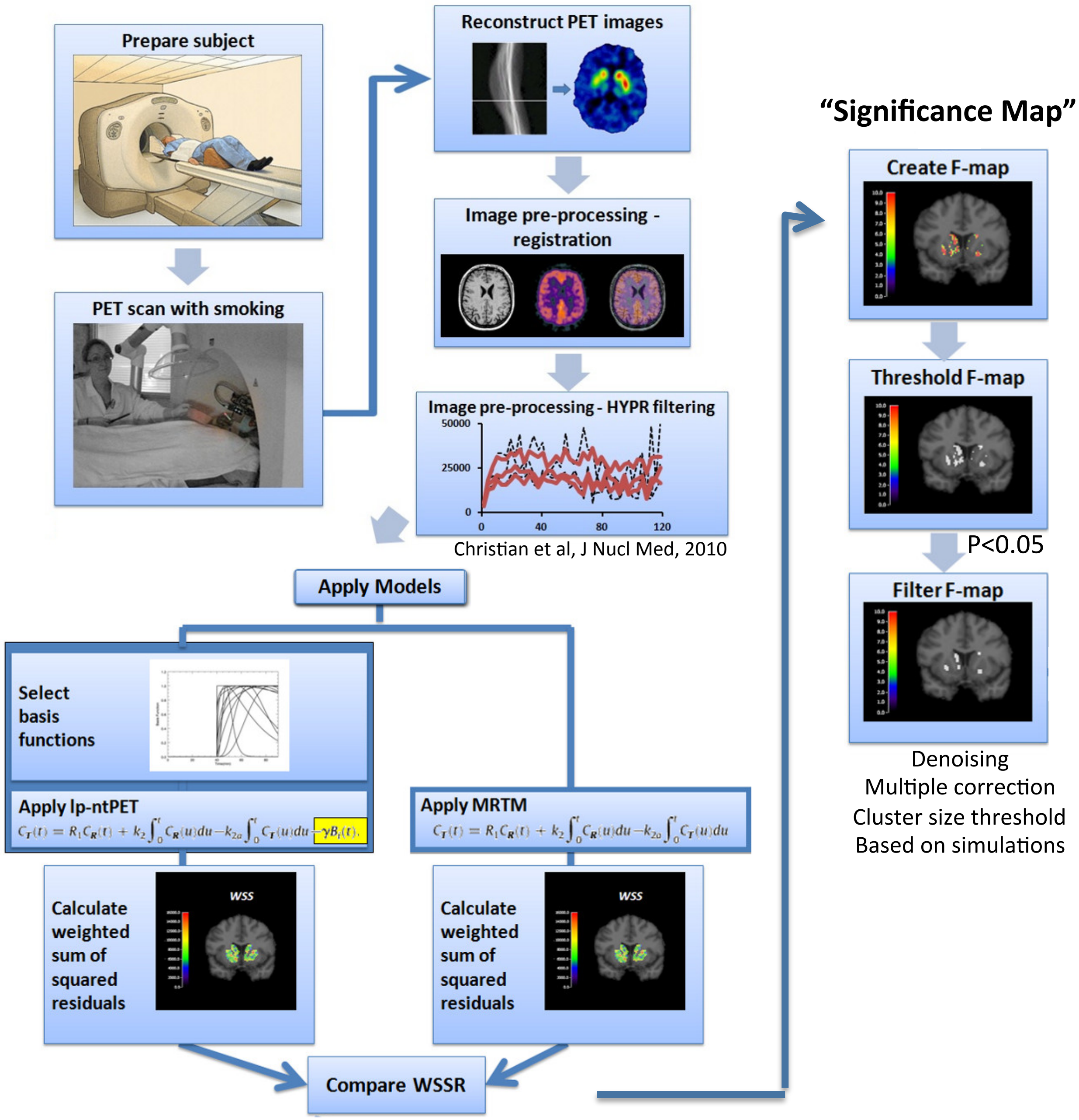
Voxel-based-Analysis lp-ntPET

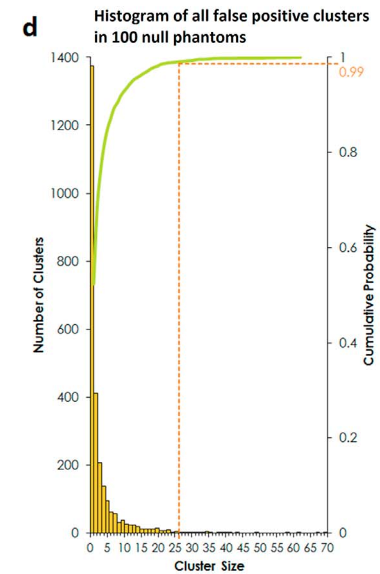


$$F = \frac{\left(\dfrac{WRSS_{MRTM} - WRSS_{lp-ntPET}}{p_{lp-ntPET} - p_{MRTM}}\right)}{\left(\dfrac{WRSS_{lp-ntPET}}{n - p_{lp-ntPET}}\right)}$$

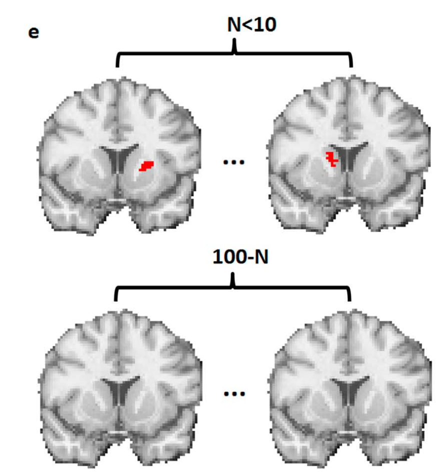
Pipeline for each subject

Voxel-based-Analysis lp-ntPET



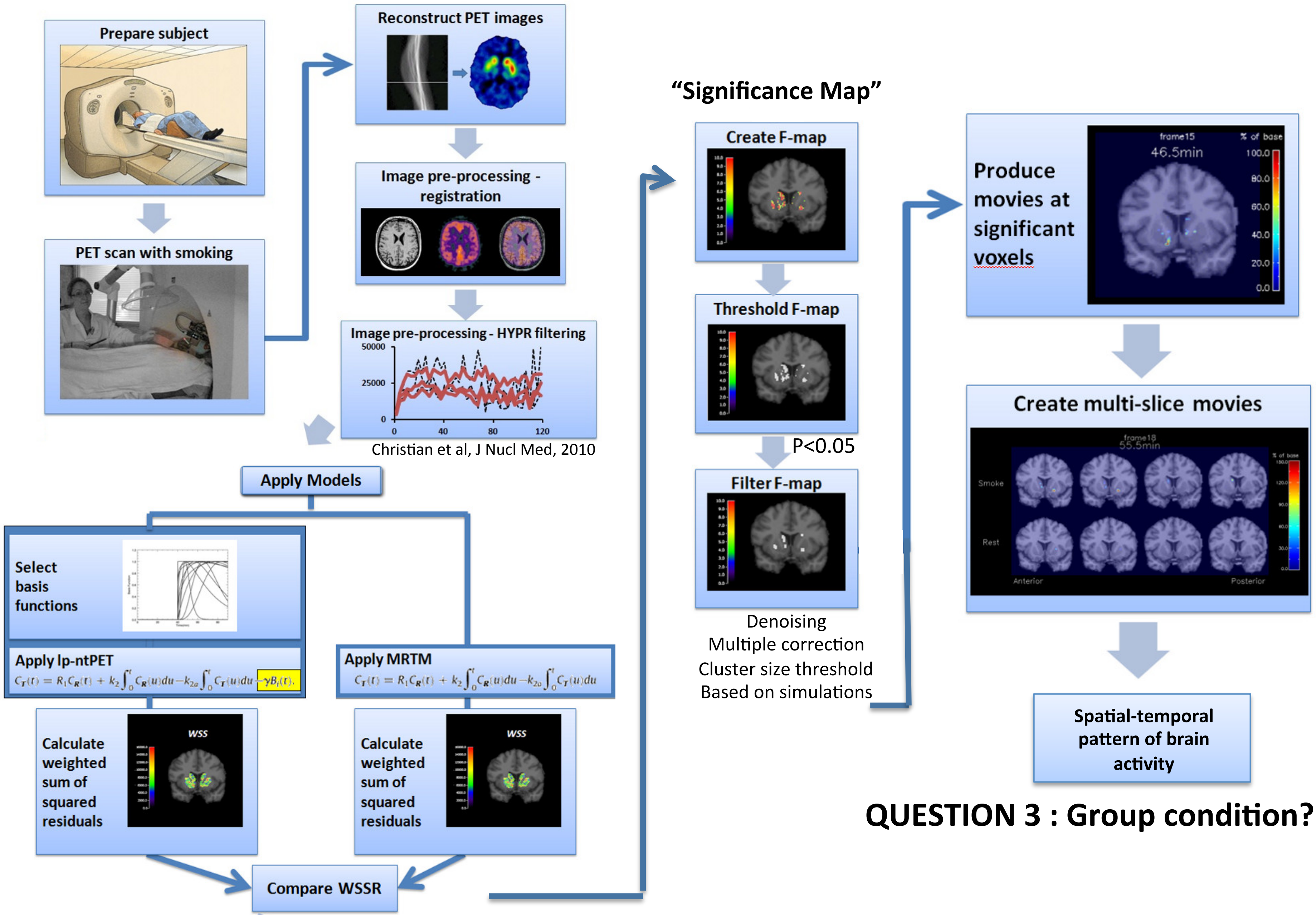


QUESTION 2 – CLUSTER SIZE THRESHOLDING



Pipeline for each subject

Voxel-based-Analysis lp-ntPET



Pipeline for each subject

Voxel-based-Analysis lp-ntPET

Movie 11:15 – 11:40

QUESTION 3 : Group condition?

Voxel-based-Analysis lp-ntPET

2016

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[d] Department of Psychiatry, Yale University, New Haven, CT, USA

Optimisation

Simulation study

Challenges :

- Sufficient radioactivity dose
- High noise level of voxel-by-voxel analysis

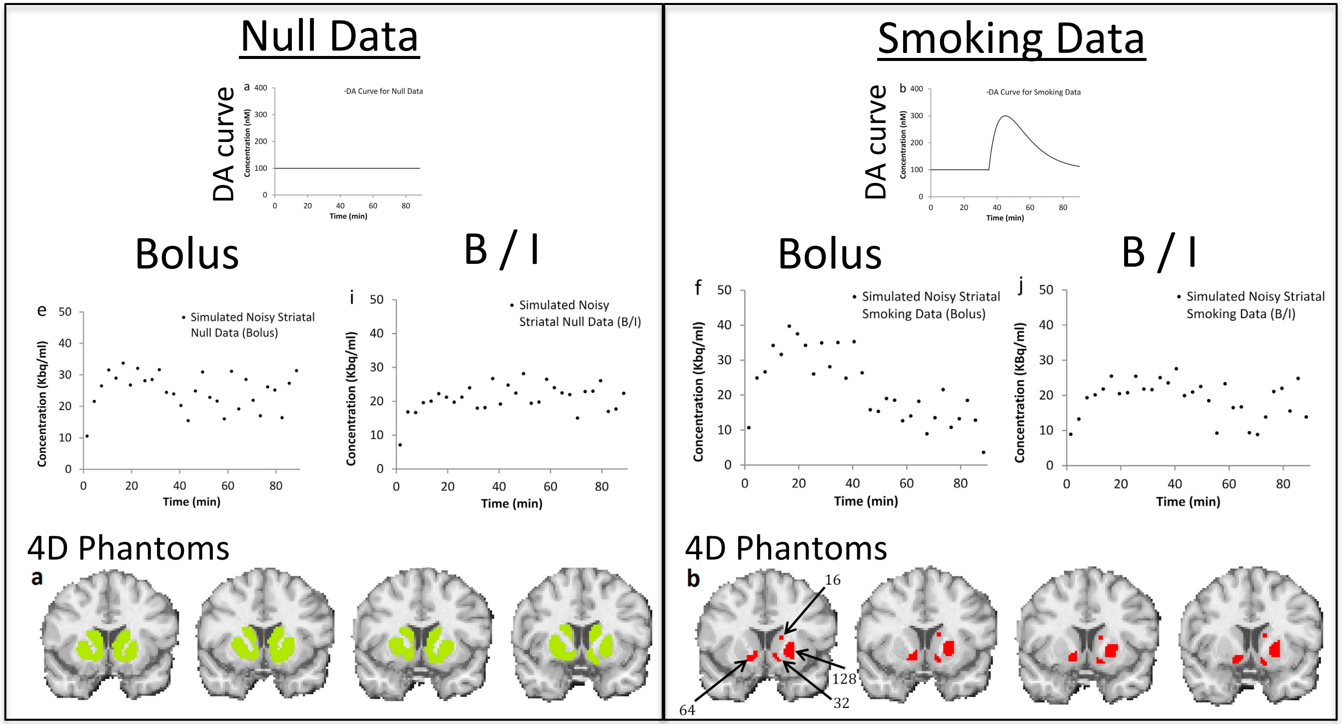
5 factors influencing sensitivity of lp-ntPET

- Tracer delivery protocol
- Preprocessing (image denoising)
- Timing of the challenge/task
- Duration of the PET scan
- Dose of the radiotracer

Data acquisition

Voxel-based-Analysis lp-ntPET

Simulated striatal data



HYPR Filtering

Apply Models

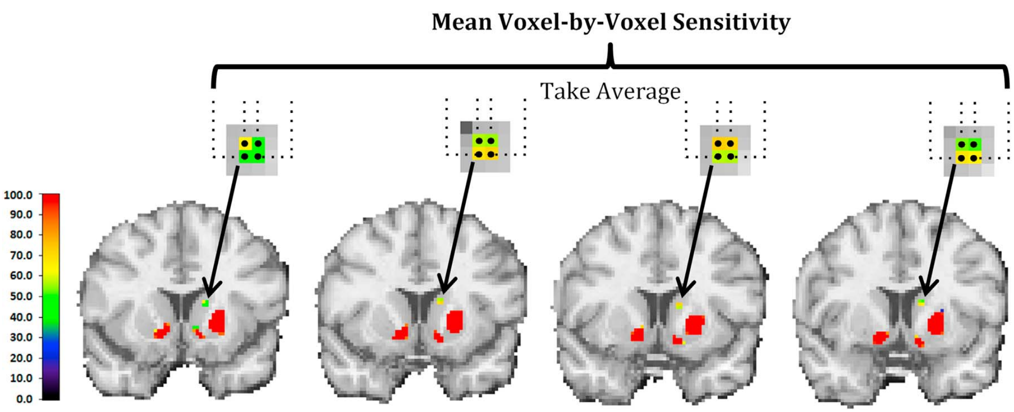
lp-ntPET *MRTM*

tD = [35 : 1.5 : 55]
alpha = [0,25 : 1 : 4]
tP = [tD + 1.5min : 1.5 : total scan time − 5min]

Voxel-based-Analysis lp-ntPET

2 METHODS

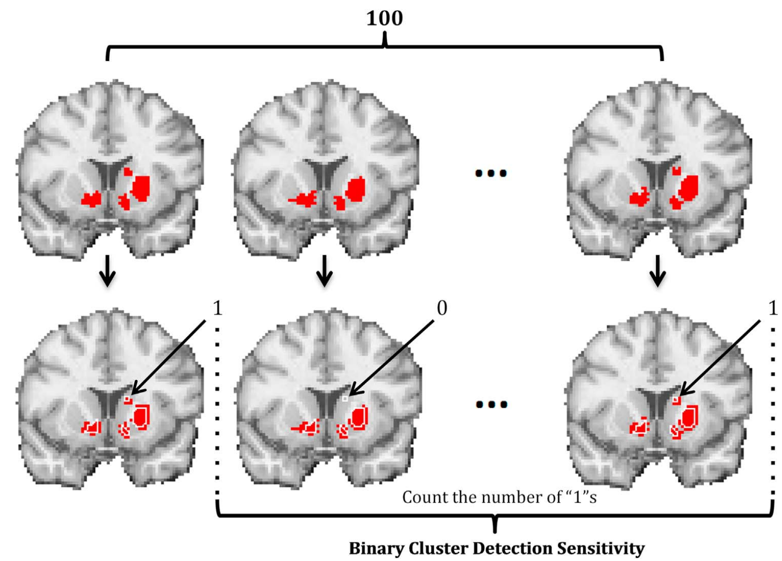
1) Mean voxel-by-voxel sensitivity



$$Mean\ Sensitivity = \frac{\sum_{i=1}^{N_{Voxels}} \frac{1}{100}\left(\sum_{j=1}^{100} I_{Voxel\ i,\ Phantom\ j}\right)}{N_{Voxels}}$$

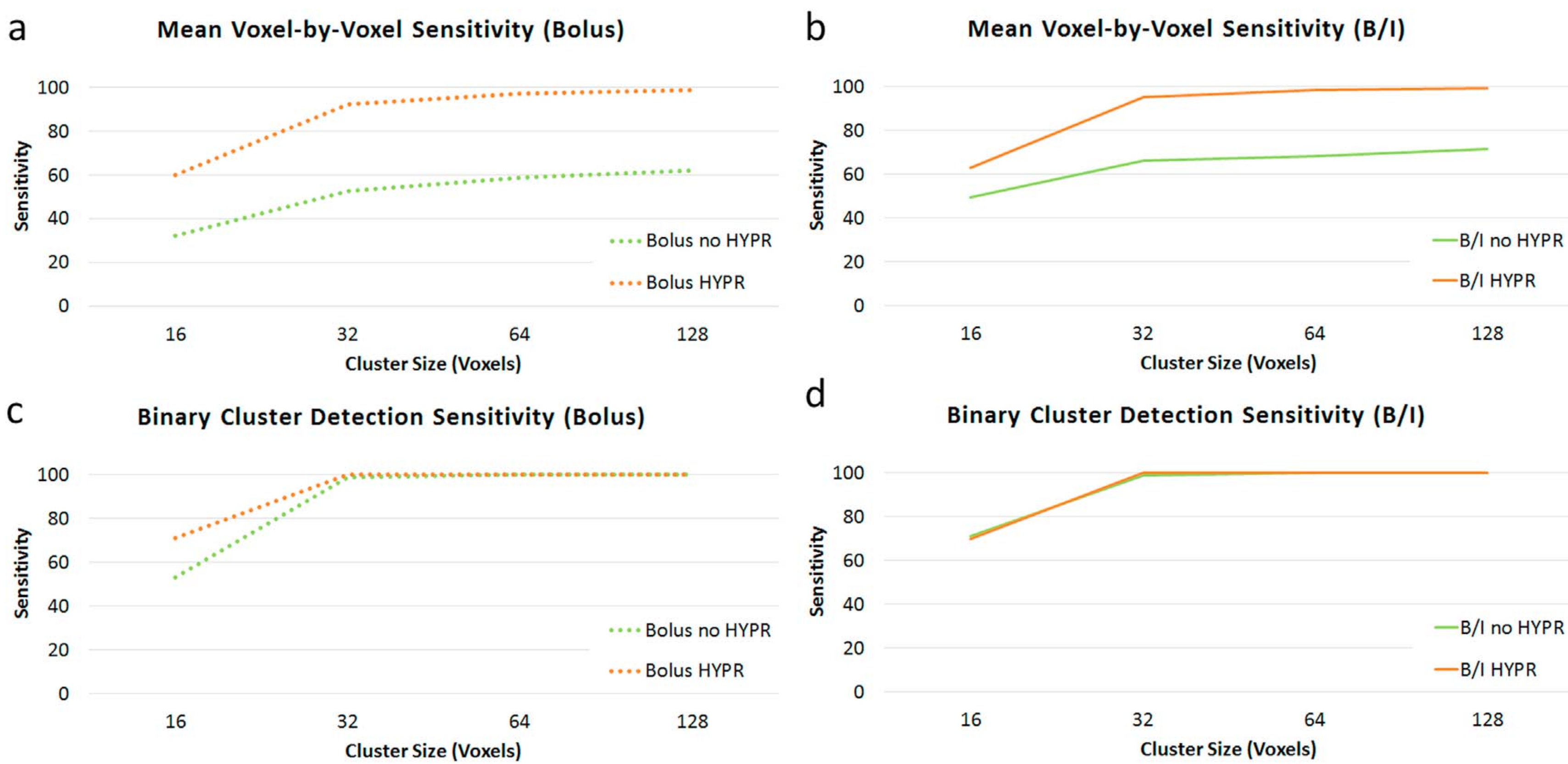
Mean Percent of Spatial Extent

2) Binary cluster detection sensitivity



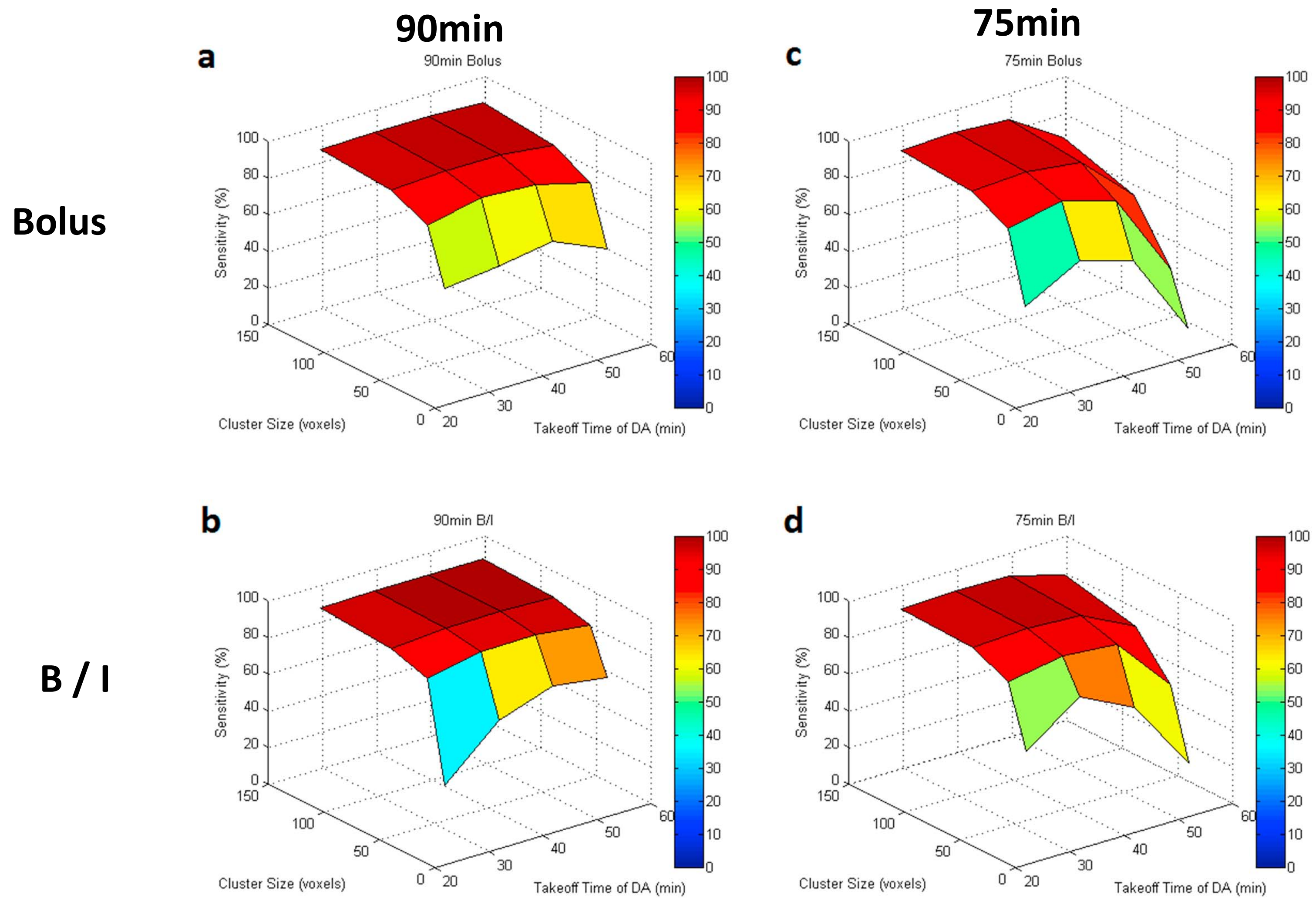
Partial overlap

Voxel-based-Analysis lp-ntPET



- Equivalent sensitivity for bolus and for B/I if HYPR is applied
- Lower spatial resolution with spatially smoothed PET frames compared to HYPR (Supplementary data)

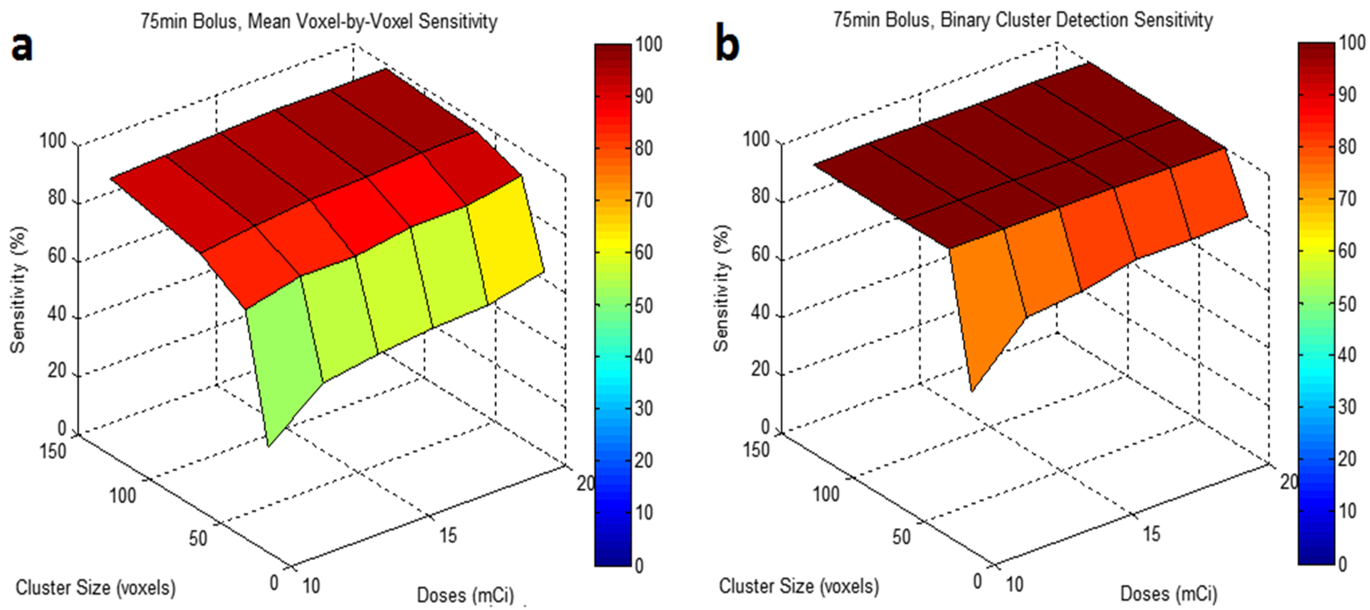
Voxel-based-Analysis lp-ntPET



- For 90min scan : Optimal timing after 45min
- For 75min scan : Optimal timing after 35min

Voxel-based-Analysis lp-ntPET

75min Bolus paradigm



- ➢ For 75min bolus scan : Minimum of 16mCi

Voxel-based-Analysis lp-ntPET

2016

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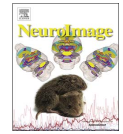

→ **Optimisation**

Simulation study

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[c] Department of Radiology and Biomedical Imaging, Yale University, New Haven, CT, USA
[d] Department of Psychiatry, Yale University, New Haven, CT, USA

5 factors influencing sensitivity of lp-ntPET

- Tracer delivery protocol : **B/I or Bolus**
- Preprocessing (image denoising) : **HYPR**
- Timing of the challenge/task : **35min – 45min (depending on scan duration)**
- Duration of the PET scan : **equivalent sensitivity**
- Dose of the radiotracer : **at least 16mCi**

Linear parametric neurotransmitter PET model (lp-ntPET)
Modeling dopamine variations across time

QUESTIONS

QUESTION 1 – **CHOIX DES FONCTIONS**

Effet de la stimulation attendue

- Si soutenue?
- Paramètre Beta

$$h_i(t) = \left(\frac{t - t_D}{t_P - t_D}\right)^{\alpha} exp\left(\alpha\left[1 - \frac{t - t_D}{t_P - t_D}\right]\right) u(t - t_D)$$

$$h_i(t) = exp(\beta(t - t_D))u(t - t_D)$$

QUESTION 2 – **CLUSTER SIZE THRESHOLDING**

Toujours avec des simulations ou 10% clusters ?

QUESTION 3 - **Group condition?**

Summing the significance mask by group and dividing by number of group members then permutation tests and 2-sample t-test in SPM (Cosgrove et al, 2014)

- Magnitude of peak DA activation (gamma)
- "Peak Height" of DA curves [gamma * peak (*h*(*t*))]
- "Rise Time" (*tP-tD*)
- "Recovery Time" $\left(\frac{(t_P - t_D)ln2}{\alpha}\right)$