## A Bootstrap Method to Improve Brain Subcortical Network

# **Segregation in Resting-State FMRI Data**

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**Problematic – cortico-subcortical loops** 

II - Method

Connection between cortex and basal ganglia: controlling language, motor function, cognition...



#### **Motor loop**

Purves, Neuroscience, Sinauer Associates Inc., 2004



IV – Discussion

#### State of the art

Animal studies:

Cortico-subcortical loops were often studied in monkey brain, biological tracers used to reveal the links between the basal ganglia and the cortex\*.

II - Method

#### Post mortem human studies:

Remove the brain of the skull, cut into thin strips and use immunohistochemical markers to detect same kind of neurons.

III - Results



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IV – Discussion

\* Draganski et al., J. Neurosci., 2008 ; \*\* Damoiseaux et al., PNAS, 2006

#### State of the art

I - Context

Non invasive human studies:

Diffusion MRI: average diffusion of water molecules along the white matter fibers (axons)

II – Method

III - Results

Functional MRI: haemodynamics activity, signals synchronization, brain functional networks\*\*

non-stationarity

Aim of this work: provide a robust method to detect precisely subcortical components in the large-scale functional networks observed in resting state fMRI.





IV – Discussion

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l - Result

#### **Studied population**



For the resting-state scan, subjects were instructed to lie with their eyes closed think of nothing in particular and not fall asleep





Anatomical  $T_1$  sagittal slice

Individual fMRI dataset

**IV** – Discussion

# Methodology

Identification of functional cortico-subcortical group networks



Non stationarity

Signal inside the BG 5,35% lower than in the cortex,

standard deviation 11,81% higher than in the cortex

**Y** a T - by - N2 matrix

N = N1 + N2

## Identification of functional cortico-subcortical group networks

Hierarchical individual model:



 $\mathbf{X}=\mathbf{AS},$ 

Spatial components must be independent



- $\mathbf{Y}_i = \mathbf{A}_i \mathbf{B}_i + \varepsilon_i,$
- $\varepsilon_i$  is an independent and identically distributed (i. i. d.) gaussian noise

#### Identification of functional cortico-subcortical group networks

Individual model resolution:



Principal Component Analysis (obtained a number of components like we explain 99% of inertia),

Spatial Independent Component Analysis (sICA): 40 components per subjects  $\hat{S}$  and the associated time courses  $\hat{A}$  (obtained with the InfoMax algorithm\*)



General Linear Model (GLM), least square estimation

 $\hat{B} = (\mathbf{A}^T \mathbf{A})^{-1} \mathbf{A} \mathbf{Y}$ 

Identification of functional cortico-subcortical group networks Cortical group analysis

> For each subject, K= 40 spatial components Spatial normalization in a template space Hierarchical group analysis for the spatial cortical components





#### Identification of functional cortico-subcortical group networks subcortical group analysis

Statistical inference at the group level\*

For each network p:

- conventional parametric random effects analysis:

$$y_i = \hat{\beta}_i + e_i$$
$$\hat{\beta}_i = \hat{\beta}_{pop} + z_i$$

 $t_0$  value for all the  $\hat{\mathcal{B}}_p$  obtained with all subjects

- a set  $\widehat{\mathcal{B}}_p^*$  of S=100 surrogate data were then obtained by drawing randomly with replacement S times 40 maps from the initial  $\widehat{\mathcal{B}}_p$  set.

A student t\* value was computed for each sample  $\hat{\mathcal{B}}_p^*$ 

- Inference: achieved signifiance level (ASL)

$$ASL_{bootstrap} = \frac{\operatorname{card}\{t^* \ge t_0\}}{S}.$$

- We selected the ASLbootstrap < 0.01



## Summary

Identification of functional cortico-subcortical group networks



IV – Discussion

#### **Results**

10 networks (interesting components)...

II - Method



Motor network



Default mode network

#### **Results**

... and 30 noise components



Heartbeating noise







Immunohistochemical basal ganglia functional atlas

II – Method





Post mortem human atlas

III - Results

Immunohistochemical techniques

IV – Discussion

reconstruction

segment



D

Yelnik et al., 2007, Neuroimage

l – Context

III - Results

IV – Discussion

## Validation

 $\rightarrow$  Immunohistochemical functional atlas of subcortical structures

II - Method





Motor network and atlas motor shapes, for putamen and pulvinar structures

On the right hemisphere, we detect 89% of the sensorimotor putamen and 21% of the pulvinar and on the left, 52% of the sensorimotor putamen. <sup>15</sup> Yelnik et al., Neuroimage, 2007

#### **Discussion and conclusion**

Context

- The method extracts cortico-subcortical networks (GLM, sICA, bootstrap)

- Subcortical validation using an atlas\*: - qualitative

II – Method

- quantitative

III - Results

- Measures between BG and cortex (entropy, correlation...)\*\*

- Compare healthy subjects and patients with cortico-subcortical dysfunctions

**IV** - **Discussion** 

# **Thanks for your attention**

#### Thanks to the collaborators:

E. Bardinet	Engineer
A. Messé	Imagist
V. Perlbarg	Statistician
G. Marrelec	Statistician
M. Pélégrini-Issac	Engineer
J. Yelnik	Anatomist
S. Lehéricy	Neurologist
H. Benali	Imagist



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We only consider K = 40 << T components*
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The sICA model assumes statistical independance of the spatial components, which implies non-gaussiannity for the resulting time courses components <sup>19</sup> \* Perlbarg et al., Isbi 2008

#### **Discussion and conclusion**

The proposed method gives for the first time access to cortico-subcortical functional networks by using sICA, GLM at individual scale and boostrap group analysis

The subcortical segregation was qualitatively validated by using a functional atlas\*

A quantitative validation of the overlap between our results and the functional regions of the atlas is under investigation.

It will be interesting to quantify the functional interactions in terms of correlation or entropy measures between the BG and the cortex in a given network or between networks\*\*.

Another challenge would be to compare results obtained from healthy subjects with those obtained from patients with pathologies known to be associated with cortico-subcortical dysfunctions.

**Identification of functional cortico-subcortical group networks** Group cortical step:

We obtained a set of 40 spatial components per subject: {Kij}



- Data sets we have

Let  $Z = X \cup Y$  the whole data set of a subject with the cortical part (X) and Subcortical part (Y)

We assume X inter Y = ensemble vide

- X = T x N1 with T number of time samples, N1 number of voxels per acquired Volume in the cortical part
- $Y = T \times N2$  with N2 the number of voxels in subcortical part
- N = N1 + N2 total number of voxel per acquired volume.

- What we made

Cortical part: Individual sICA: X = A F, A: matrice de mélange (TxT) and F: spatial components Matrix (T x N1)

We assume indépendance des composantes spatiales => non gaussianité des Décours temporels associés

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We only take K = 40 << T composantes par sujets.
```

III - Result

IV – Discussion

## Methodology Identification of functional cortico-subcortical group networks



#### **Problematic – cortico-subcortical loops**

II - Method





Regions that operate simultaneously and are interconnected:

functional characteristics: connectivity networks

anatomical specifications: white matter fibers

## **Problematic – cortico-subcortical networks**

II – Method



Identification of functional cortico-subcortical group networks

For each subject:



I - Result

IV – Discussion

## **Studied population**

For the resting-state scan, subjects were ins<sup>-</sup> Think of nothing in particular and not fall asle



Anatomical sagittal slice





fMRI slice