Brain connectivity in MRI: Methods, Interpretation & Needs

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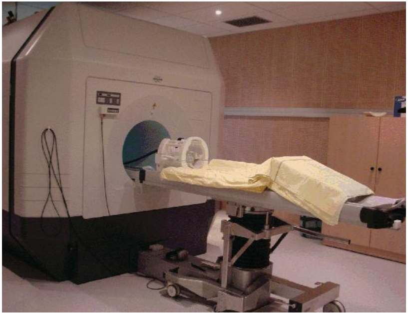
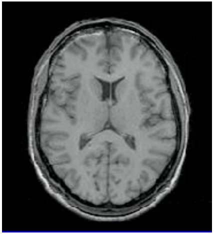
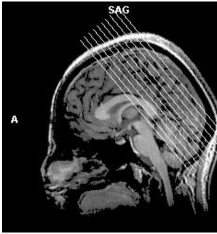
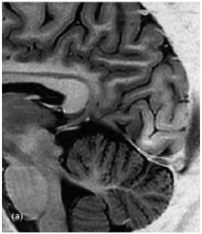
Anatomical acquisition

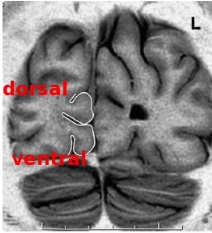




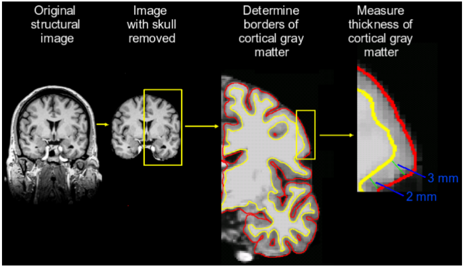


Anatomy





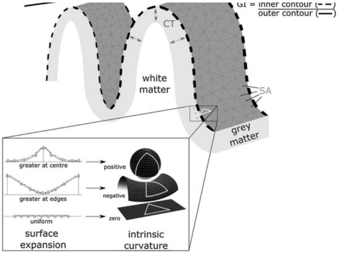
Anatomical information



Forde etal (2017), DOI: 10.1007/s00429-017-1424-0

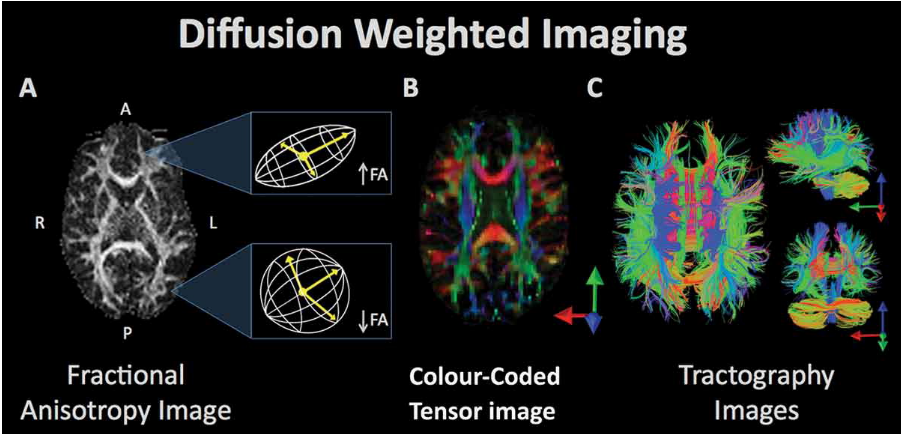
After pre-processing
Segmentation GM,WM,CSF
Extract various scores

Thickness
Curvature
Volumes...



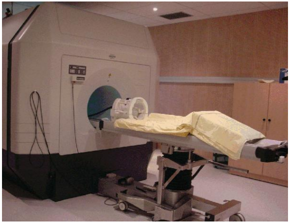
www.nmr.mgh.harvard.edu/neurorecovery/technology.htm

Diffusion tensor imaging and fiber tractography

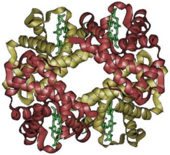


from Salat etal (2017), DOI:10.1080/02699052.2017.1327672

MRI machine



Hemoglobine



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Hb = deoxy-hemoglobine (paramagnetic)

Rest : blood : 60% $Hb\text{-}O_2$ and 40% Hb
Activation : blood : 63% $Hb\text{-}O_2$ and 37% Hb

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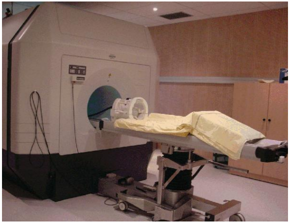

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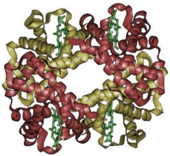

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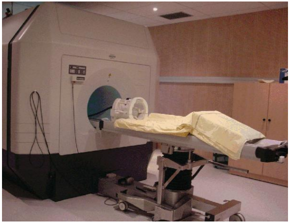
If Neural activity

$\searrow$ Hb

$\rightarrow$ Local magnetic perturbation

$\nearrow$ RMN signal (bold)

MRI machine



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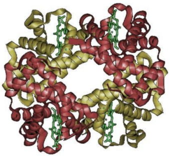

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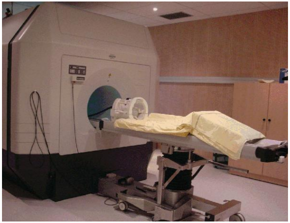

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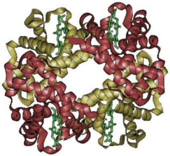

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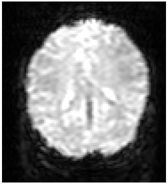

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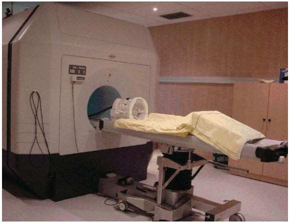

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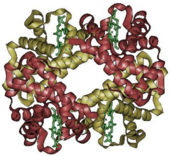

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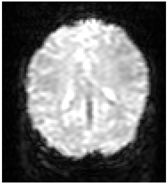


Localisationism

<u>Idea:</u> Function are localized in anatomic cortical regions
$\Longrightarrow$ Damage to a region results in loss of function

$\Downarrow$

Functional Segregation

Functions are carried out by specific areas in the cortex that can be anatomically separated

Functional Segregation
Different brain areas are specialized for different functions

Globalism

<u>Idea:</u> The brain works as a whole.

$\Longrightarrow$ Extent of brain damage is more important than its location

$\Downarrow$

Functional Integration

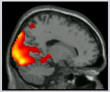
Networks of simple connected units

Functional Integration
Networks of interactions among specialised areas

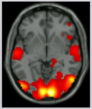
Functional neuroimaging analysis

Functional Segregation
Specialised areas in the cortex

- Analysis of regionally specific effects
- Identification of regions specialized for a particular task
- Univariate analysis



SPM Analysis



Functional Integration
Networks of interactions among specialised areas

- Analysis of how different regions in a neuronal system interact (coupling)
- Determines how an experimental manipulation affects coupling between regions
- Univariate & Multivariate analysis

Functional Connectivity

Effective Connectivity

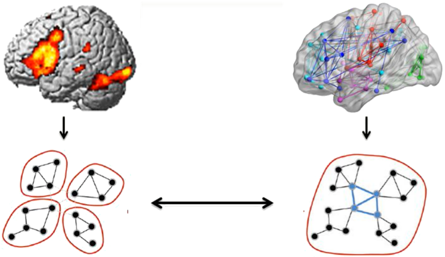
Functional neuroimaging analysis : Resume

Functional Segregation

A given cortical area is specialized for some aspects of perceptual, motor or cognitive processing

Functional Integration

Refers to the interactions among specialised neuronal populations and how these interactions depend upon the sensorimotor or cognitive context



from https://slideplayer.com/slide/5843319/

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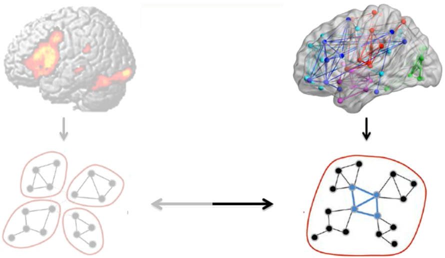

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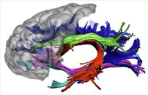
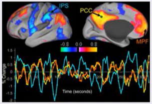
Structural Connectivity = presence of axonal connections



Large-scale anatomical infrastructures that support effective connections for coupling

Example: tracing technique, DTI...

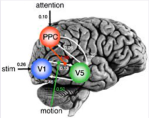
Functional Connectivity = statistical dependencies between regional t-s



Simple temporal correlation between activation of remote neural areas

Example: seed voxel, ICA, PCA...

Effective Connectivity = causal (directed) influences between neurons



The influence that one neuronal system exerts over another

Example: Static model (PPI, SEM), Dynamic model (DCM)

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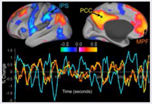

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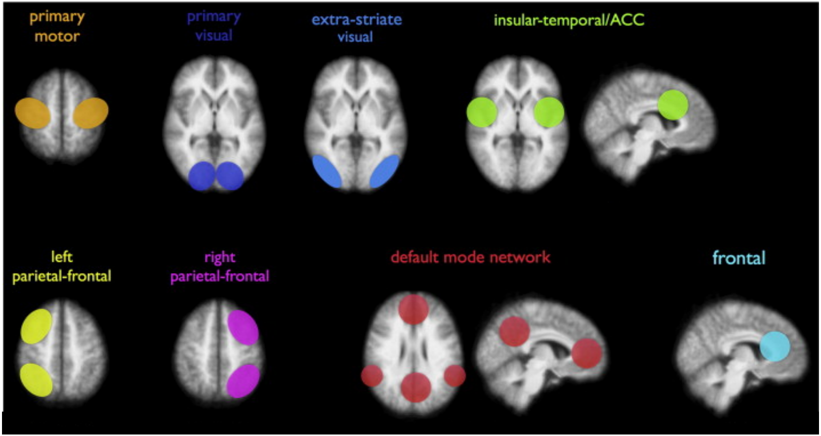
Spontaneous BOLD activity

The brain is always active, even in the absence of explicit input or output

Neuroscientists are studying this spontaneous BOLD signal and its correlation between brain regions in order to learn about the intrinsic functional connectivity of the brain resting-state networks.

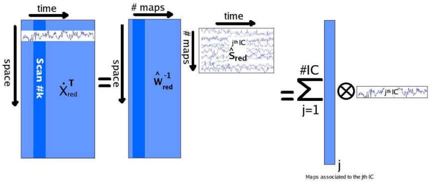
Resting-state networks



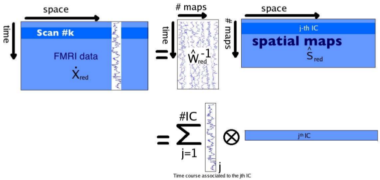
Demoiseau etal. (2006): 10.18637/jss.v044.i09

ICA temporal or spatial?

Temporal ICA decomposition TICA



Spatial ICA decomposition SICA



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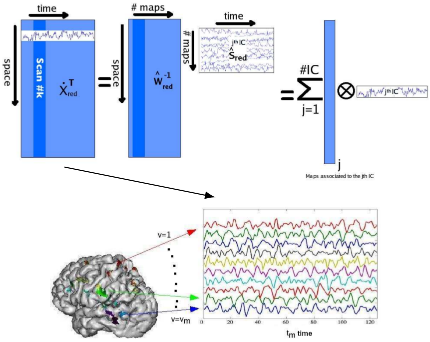

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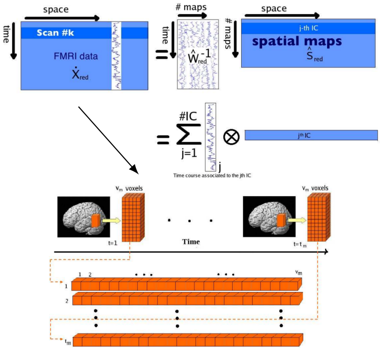

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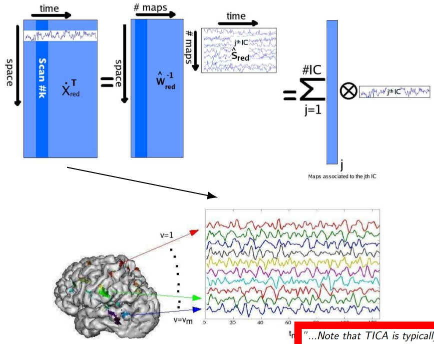

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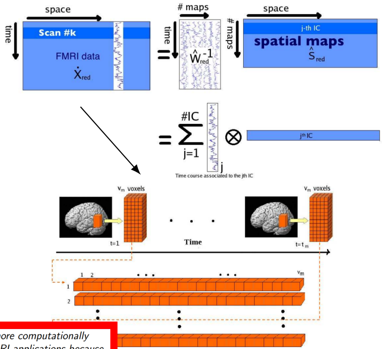

"...Note that TICA is typically much more computationally demanding than SICA for functional MRI applications because of a higher spatial than temporal dimension and can grow quickly beyond practical feasibility. Thus a covariance matrix on the order of N^2 (where N is the number of spatial voxels of interests) must be calculated. A combination of increased hardware capacity as well as more advanced methods for calculating and storing the covariance matrix may provide a solution in the future ..."

Calhoun, Human Brain Mapping, 2001

Bordier etal. (2011): 10.18637/jss.v044.i09 ; Calhoun etal. (2001), DOI: 10.1002/hbm.1024

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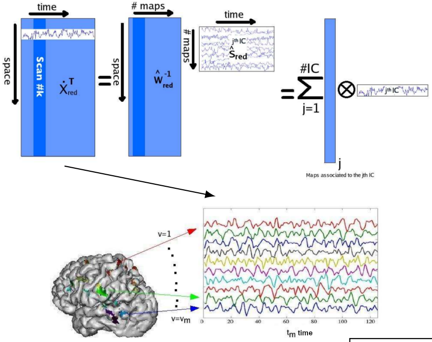

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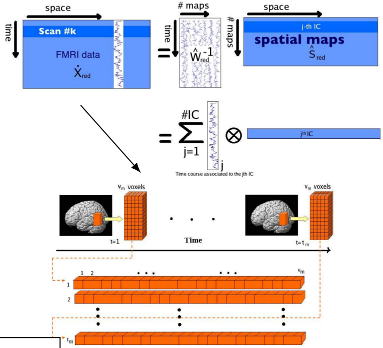

Volume:
128x128x30vx
Time: 240 vol.

Bordier etal. (2011): 10.18637/jss.v044.i09 ; Calhoun etal. (2001), DOI: 10.1002/hbm.1024

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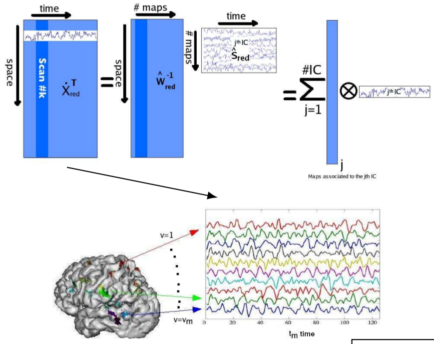
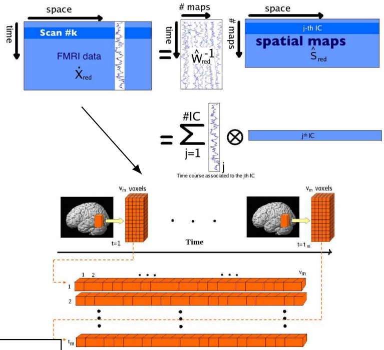


TICA covariance matrix: $500000^2 \approx 25x10^{11}$

Spatial ICA decomposition SICA



SICA covariance matrix: $240^2 = 57600$

Volume: 128x128x30vx

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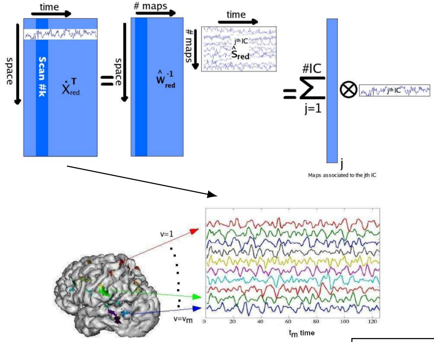

TICA covariance matrix: $500000^2 \approx 25x10^{11}$

With the singular value decomposition (svd) ➡ Possible!

Volume: 128x128x30vx

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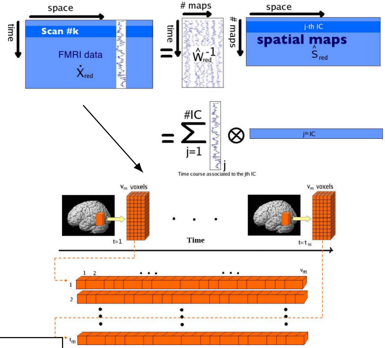
Spatial ICA decomposition SICA



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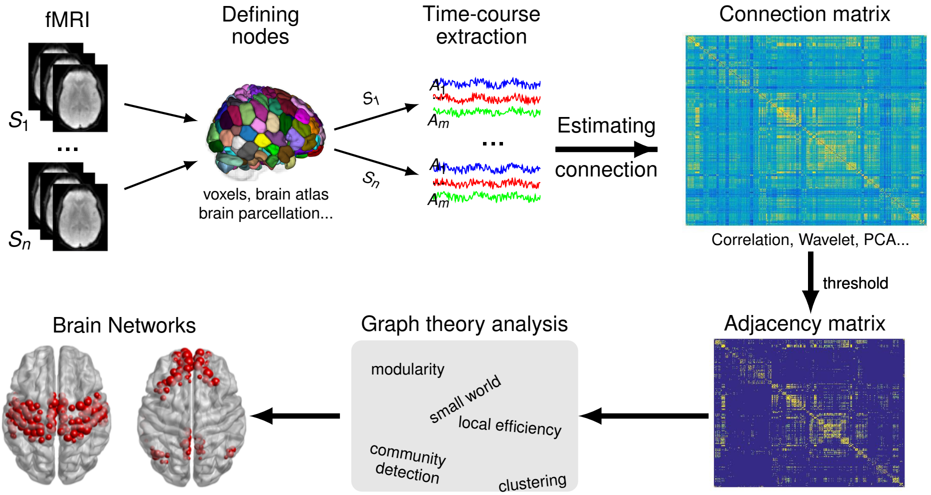
Tools

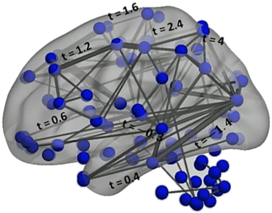
Network Based analysis (NBS), statistics at the edges level: to know edges which are significantly different between subjects.

Community detection: to know the organization of functional connectivity in modules

General Pipeline



NBS: problems



inspired by Zalesky's presentations

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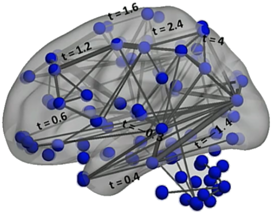

Mass univariate hypothesis testing

inspired by Zalesky's presentations

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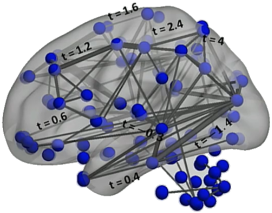

Mass univariate hypothesis testing

↓

Independently test the same hypothesis for each connection

inspired by Zalesky's presentations

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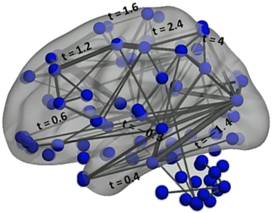

Mass univariate hypothesis testing

⬇

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⬇

Fit GLM on each connection

$$Y = X\beta + \epsilon$$

inspired by Zalesky's presentations

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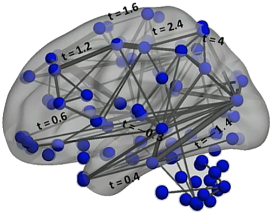

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⬇

Apply test: t-test, f-test, anova,ancova, regression ...

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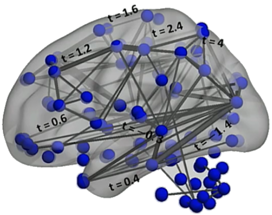
NBS: problems



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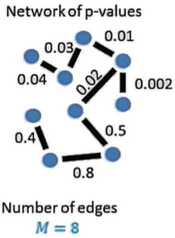

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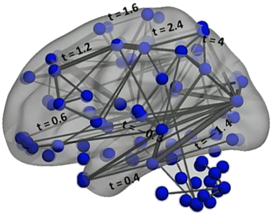

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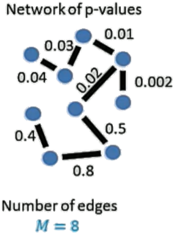

Statistics Correction:

$$FDR = \frac{Nb\ \ of\ \ false\ \ discoveries}{Total\ \ nb\ \ of\ \ discoveries}$$

- 1st step: rank p-value from smallest to largest
- 2nd step: identify largest j(rank) such that $p_j \leq \frac{j x 0.05}{M}$
- 3rd step: declare the tests of rank 1, 2, ... , j as significant!

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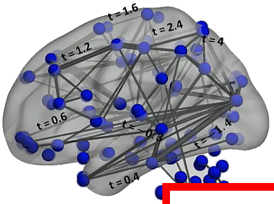
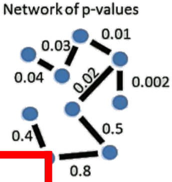
NBS: problems





of edges

= 8

Mass univariate hyp

Independently test

pothesis for each connection

Fit GLM on each connection

$$Y = X\beta + \epsilon$$

Apply test: t-test, f-test, anova,ancova, regression ...

Generic methods ignore the topological configuration!

cs Correction:

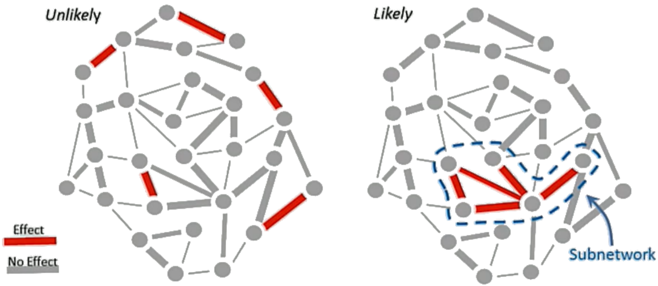
$\frac{Nb\ of\ false\ discoveries}{Total\ nb\ of\ discoveries}$

- 1st step: rank p-value from smallest to largest
- 2nd step: identify largest j(rank) such that $p_j \leq \frac{j x 0.05}{M}$
- 3rd step: declare the tests of rank 1, 2, ... , j as significant!

inspired by Zalesky's presentations

NBS: idea

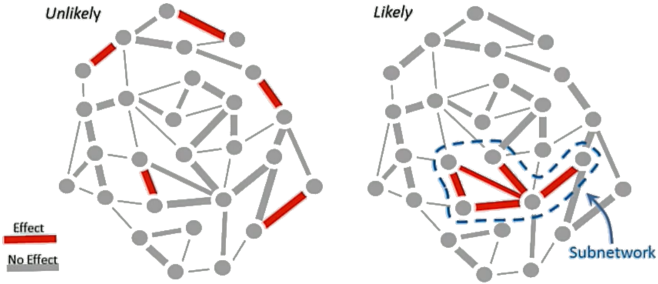
Effects of interest in connectomes are seldom confined to sigle locus. They are likely to encompass multiple connections and nodes, which form **interconnected subnetworks**



from Zalesky's presentations

NBS: idea

Effects of interest in connectomes are seldom confined to sigle locus. They are likely to encompass multiple connections and nodes, which form **interconnected subnetworks**

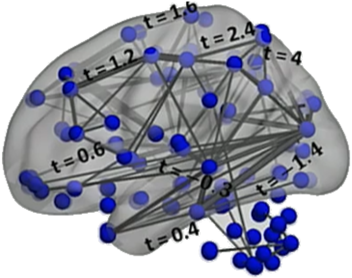


Statistical power can be improved by seeking to reject null hypothesis at the level of subnetworks, rather than for individual connections

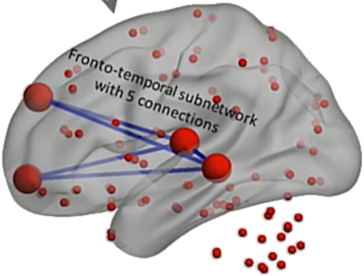
from Zalesky's presentations

NBS: step 1

Threshold and identify subnetworks



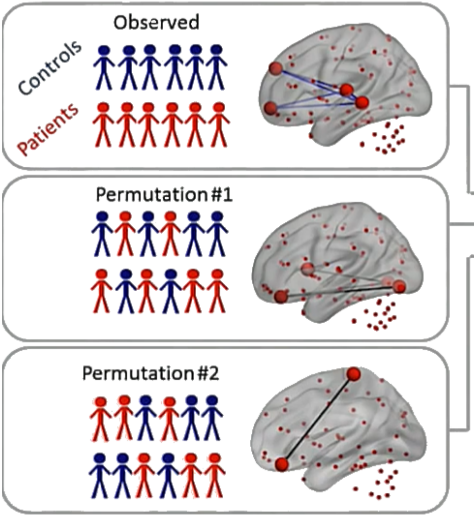
Eliminate connections with a test statistic or effect size below a desired threshold



Thresholded network: edges below a minimum meaningful effect size eliminated

from Zalesky's presentations

NBS: step 2



Permutation	*Max subnetwork size (edges)*
Observed	5
Permutation #1	3
Permutation #2	1
Permutation #3	**10**
Permutation #4	2
Permutation #5	3

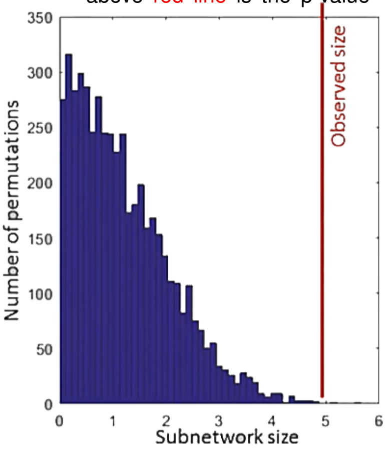
from Zalesky's presentations

NBS: step 3

After many permutaion

Permutation	*Max subnetwork size (edges)*
Observed	5
Permutation #1	3
Permutation #2	1
Permutation #3	**10**
Permutation #4	2
Permutation #5	3
Permutation #6	3
Permutation #7	4
Permutation #8	1
Permutation #9	4
Permutation #10	2

Proportion of permutation above red line is the p-value



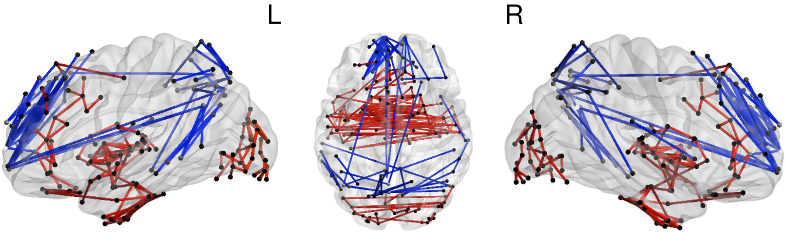
one-sided p-value: $p\text{-}value = \frac{nb\ of\ permutation\ with\ t\text{-}stat \leq 5}{nb\ of\ permutation}$

from Zalesky's presentations

NBS: results

Populations:

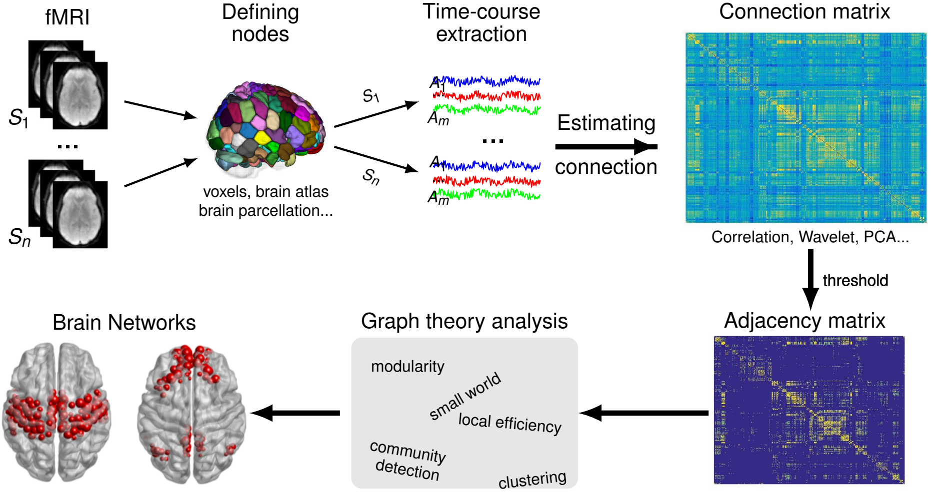
- 61 stroke patients with minor or nonexistent cognitive impairment scanned at 3 time points (6, 36 and 60 months)
- 61 control subjects matched in age and gender



In blue common significant links for *Control* $<$ *Patient* at each time acquisition. In red common significant links for *Control* $>$ *Patient* at each time acquisition (statistical comparison p<0.05 FWE corrected) .

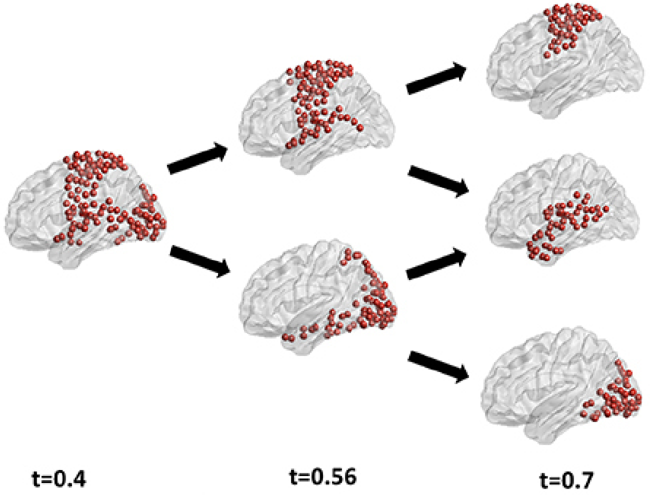
Bordier etal. (in review)

General Pipeline



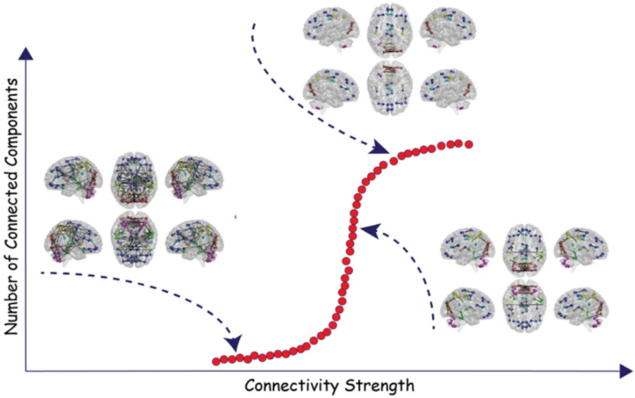
Threshold

Very often in the litterature: many thresholding!



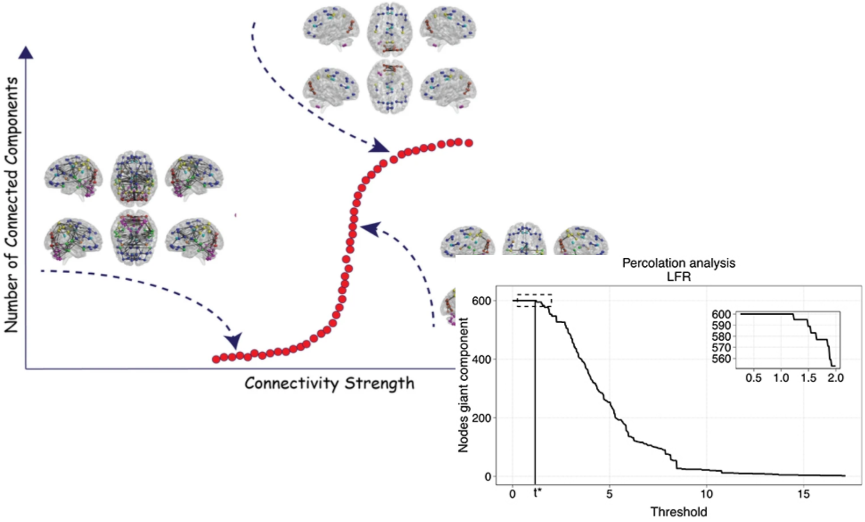
Bordier etal. (2017)

Threshold



Mastrandrea etal. (2021) ; Bordier etal. (2017)

Threshold



Mastrandrea etal. (2021) ; Bordier etal. (2017)

Methods

Louvain Community Detection (Newman (2006), Blondel etal. (2008)), based on modularity, which tries to maximize the difference between the actual number of edges in a community and the expected number of edges in the community.

InfoMap Community Detection (Rosvall etal.(2008)) based on the minimization of the description length (Rissanen, 1978) of a random walker defined on the network through a set of heuristics.

Surprise Community Detection (Nicolini (2016 & 2017)) based on classical probabilities known as Surprise. It has been introduced to evaluate the quality of a partition of a network into communities.

The goal

- Finding connectivity differences: hypo or hyper connectivity
  - between groups : control vs patient
  - over time : at Year 0 and Year N to mmonitor the illness evolution

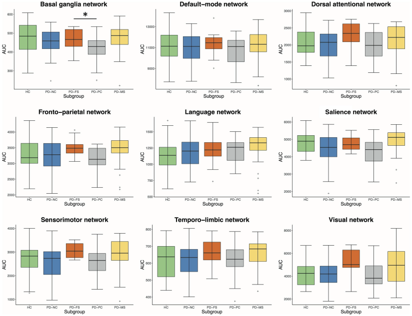
- Finding community difference: breaking or joining
  - between groups : control vs patient
  - over time : at Year 0 and Year N to mmonitor the illness evolution

Connectivity on Parkinson patients

- Material
  - 24 controls (HC) and 95 patients parkinson (PD):
    - 31 normal cognition (NC)
    - 14 with attentional and executive deficits (FS)
    - 20 with visuospatial, memory and language deficits (PC)
    - 30 (mixed) with all previous deficits (MS)
- Question:
  What are the connectivity differences between different type of parkinson? Can we predict from which subtype parkinson ar coming the mixed subgroup?
- Methods:
  - ICA to extract the resting state network of our groups
  - NBS to find significant difference between groups in intra or inter networks

Devignes etal. (2022)

Intra Connectivity



HC: healthy control; PD-NC: normal cognition; PD-FS: attention/exceutive deficits; PD-PC: vosuospatial/memory/language deficits; PD-MS: mixed subtype

Devignes etal. (2022)

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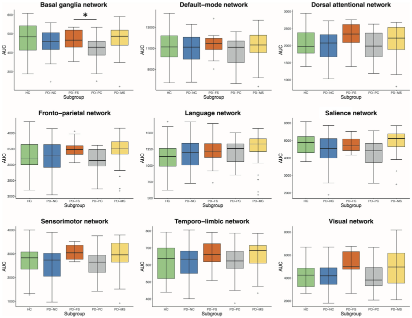
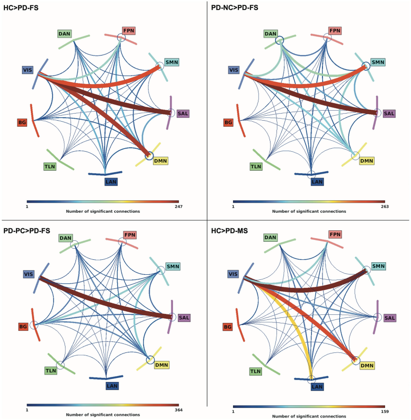


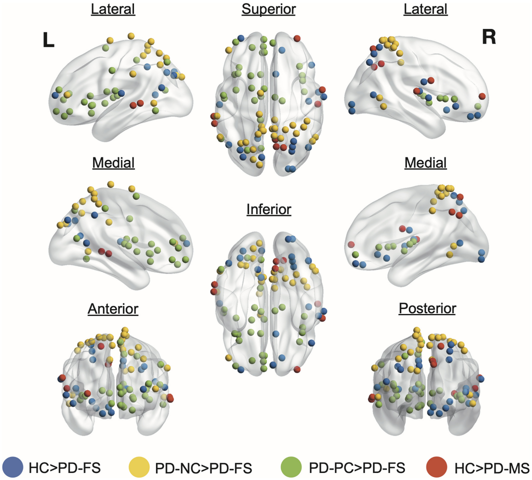
Inter connectivity



HC: healthy control; PD-NC: normal cognition; PD-FS: attention/exceutive deficits; PD-PC: vosuospatial/memory/language deficits; PD-MS: mixed subtype

Devignes etal. (2022)

Spatial location of brain regions for each significant comparison (region with at least 25 significant connections)



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Devignes etal. (2022)

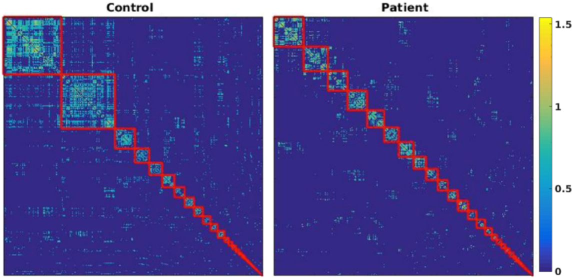
Connectivity on Schizophrenia patients

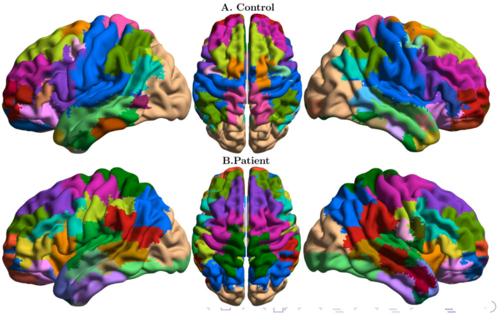
- Hypothesis:

  Aberrant brain functional connectivity in the brain of schizophrenia patients affects its modular organization

- Materials
  - 78 schizophrenia patients (from DSM IV)
  - 91 healthy controls
- Methods
  - Community detection : Asymptotical surprise with percolation threshold
  - Comparison and statistics: NMI, participation coefficient...

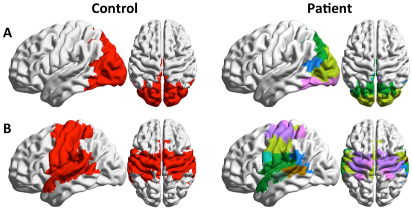
Connectivity on Schizophrenia patients





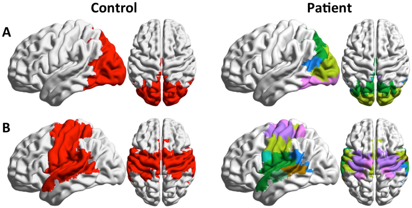
Bordier etal. (2018)

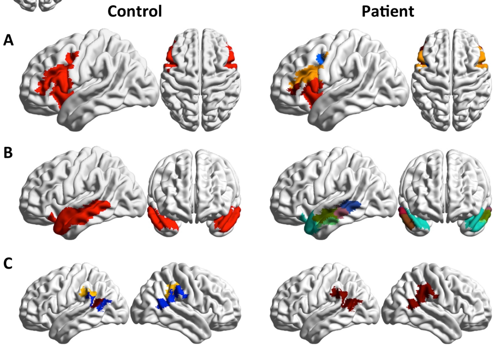
Connectivity on Schizophrenia patients



Bordier etal. (2018)

Connectivity on Schizophrenia patients





Bordier etal. (2018)

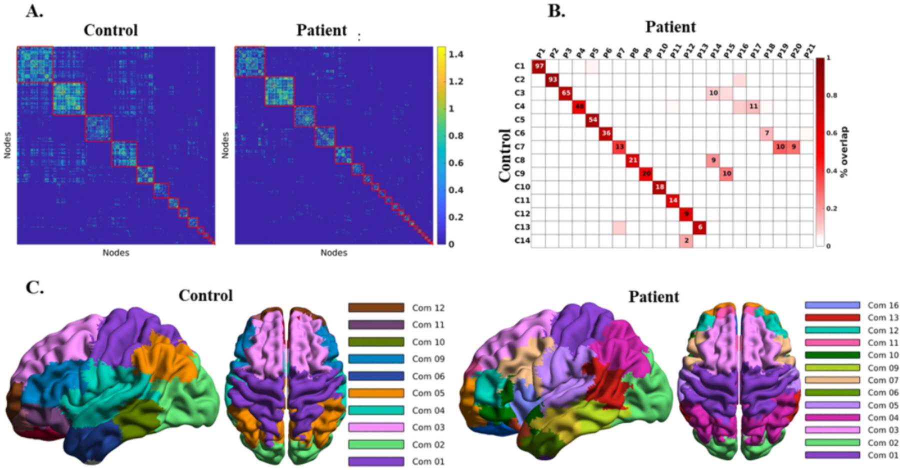
Connectivity on Alcoholic patients

- Hypothesis:

  Brain functional connectivity comparison between
  1) Control and Patient
  2) before and after treatment in alcoholic patients

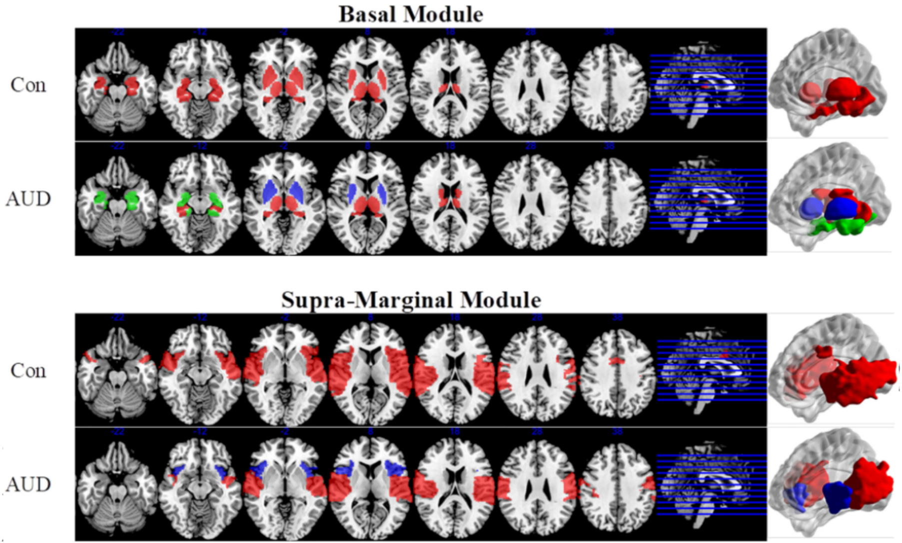
- Materials
  - 35 recently desintoxified alcohol dependent patients
    - 12 intensive withdrawal treatment(IWT)
    - 17 naltrexone(NTX) + intensive widthdrawal treatment
  - 34 healthy controls
- Methods
  - Community detection : consensus infomap (percolation threshold)
  - Comparison and statistics: NMI, participation coefficient...

Connectivity on Alcoholic patients



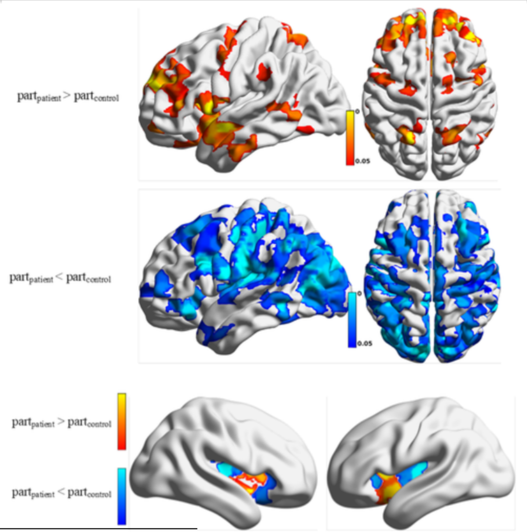
Bordier etal. (2021)

Connectivity on Alcoholic patients



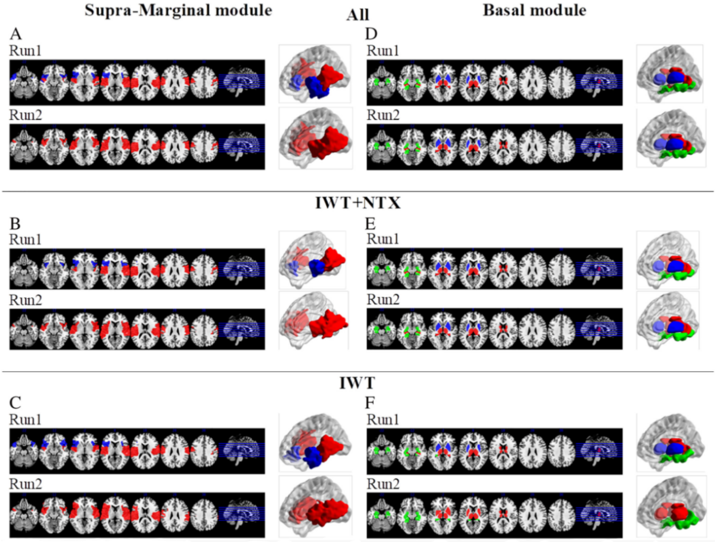
Bordier etal. (2021)

Connectivity on Alcoholic patients: participation coefficient



Bordier etal. (2021)

Connectivity on Alcoholic patients



Bordier etal. (2021)

Conclusion

- Functional connectivity is still at its beginning and there is still a lot to do
- New methods and community detection are getting out every 3-6 months

- Application on other dataset such as PET, structural (T1 or DTI) or iron maps!

Needs

- Reliable tool to make statistics and compare communities
- Optimization of the speed and computer power (passing from region to vx)
- Method for simultaneous parallele dynamic spatial and temporal connectivity (let s be crazy!)
- Graph theory adapted on multi modal data
- Deep learning on graph or on different MRI modalities

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but also ... the majority of idea that you can find in the perspective of connectivity papers

Thank you for your attention...

and thanks to ...

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