Brain Connectivity through Graph Theory: SPIDER-NET a New Tool to Explore Sub-Networks

Davide Coluzzi

About myself

- PhD student in Bioengineering
- Dipartimento di Elettronica, Informazione e Bioingegneria at Politecnico di Milano
- Brain connectivity, MRI/f-MRI, biomedical/sensor signal processing and applied machine/deep learning
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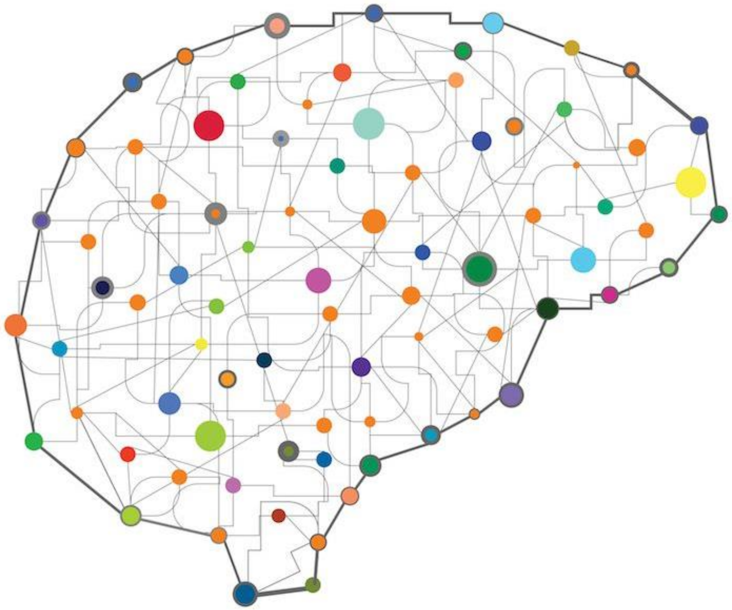
Omics and big data

- Development of OMICS disciplines integrating **large amount of data** with the aim of mapping complex systems;

- Connectomics development thanks to the advanced MRI sequences providing data on brain **structure** and **function**

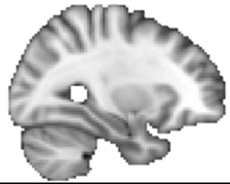
- The brain is depicted in term of fondamental **units** and their pairwise **connections**, forming a **graph**

- Brain regions are strongly connected, determining a **complex system**



Brain connectomics: a frontier problem

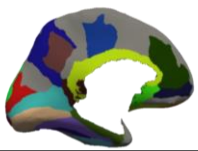
Raw data: MRI acquisition

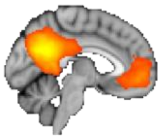


Preprocessing and normalization

Atlas-based Parcellation → **NODE** DEFINITION

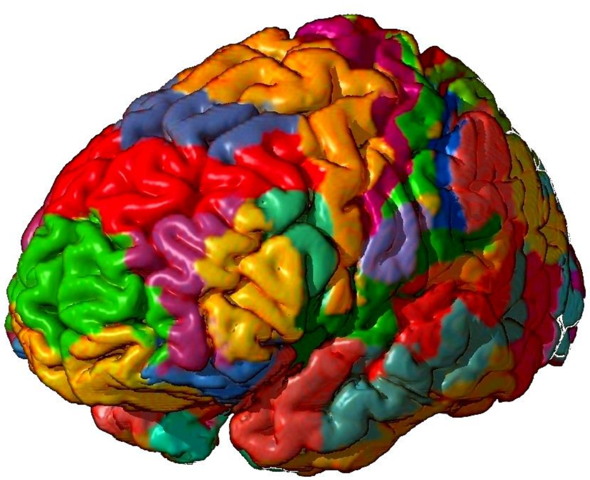
Anatomical Parcellation (e.g. Destrieux)





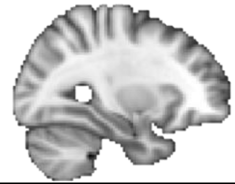
Functional Parcellation (e.g. Smith)

- Since Broadmann we know that brain is organized in specialized areas
- Neurology focused the main “circuits”, alias sub-networks: speech, sensorimotor, visual etc.
- The whole connectomics integration is still a question mark. E.g.: How is our consciousness generated?



Connectomics: brain as a complex network

Raw data: MRI acquisition



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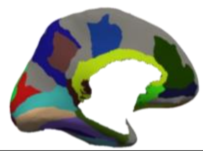
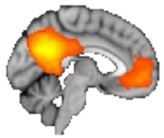
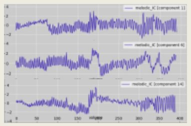




Functional Parcellation (e.g. Smith)

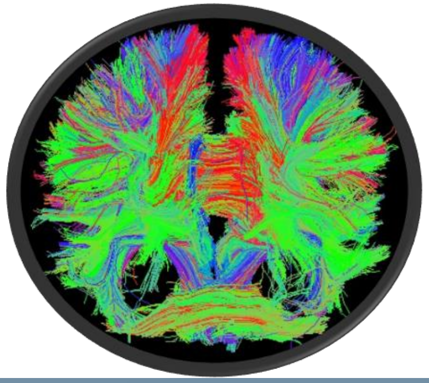
Extraction of connectivity measures → **EDGE** DEFINITION

Mapping of Anatomical Connections



Time Series Extraction

NF, FA etc. from Diffusion Tensor Imaging



Pairwise Pearson's correlation of BOLD signals

Connectomics: brain as a complex network

Raw data: MRI acquisition

Preprocessing and normalization

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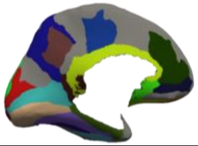
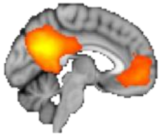
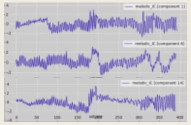




Functional Parcellation (e.g. Smith)

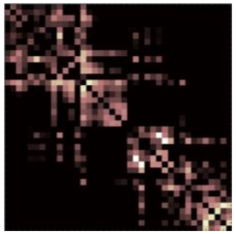
Extraction of connectivity measures → **EDGE** DEFINITION

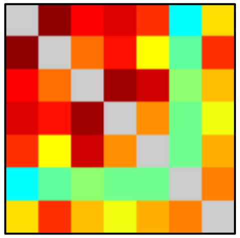
Mapping of Anatomical Connections



Time Series Extraction

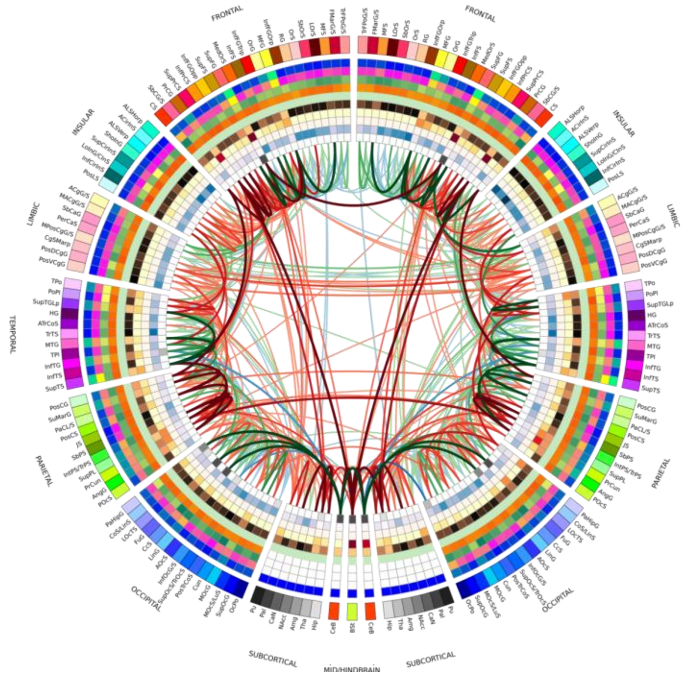
NUMERICAL MATRICES





The connectogram

- Method of connectome mapping and visualization *[Irimia et al., 2012]*
  - Circular graphs where all nodes are represented along the perimeter of the circle, while the edges are shown as arcs connecting pairs of nodes
  - “The **connectogram**” – bridge the gap between quantitative connectivity analyses and intuitive visualization of the results
    - Although connectograms with high number of nodes and connections may be anyway difficult to be analyzed



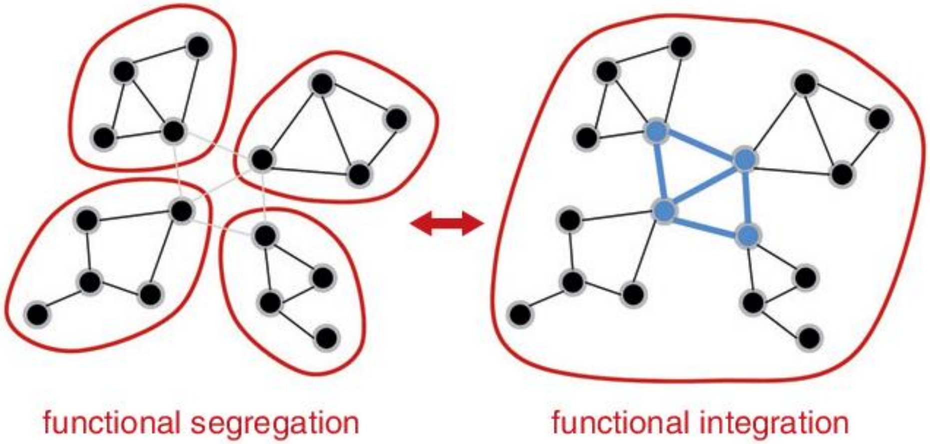
Connectogram of a normal brain

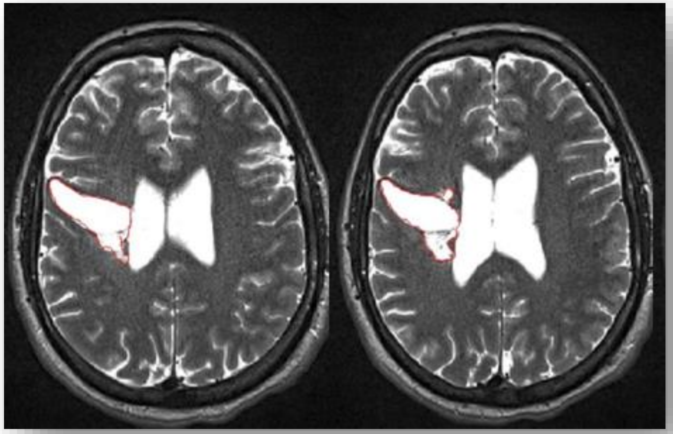
Investigation of connectivity pattern

- Investigation of human brain networks and sub-networks can provide insight of functioning in physiological and pathological conditions

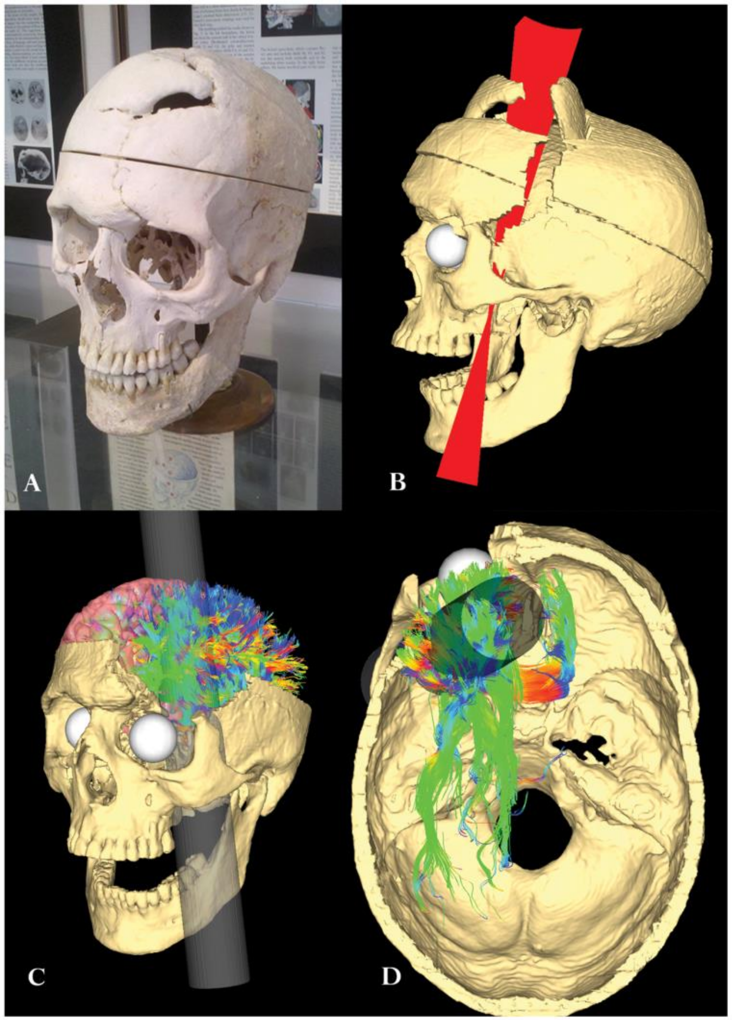
- Segregation/Integration balance for information processing
  - Synchronous and asynchronous activity of specific brain regions (**specialized circuits**) allows for complex cognitive functions

- **Focal lesions**

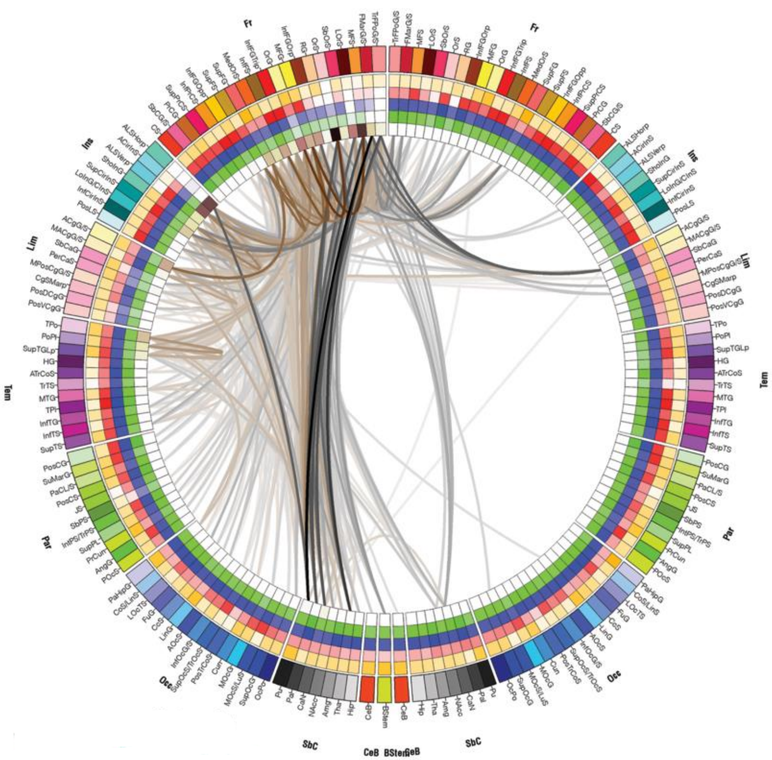




Phineas Gage's estimated connectogram



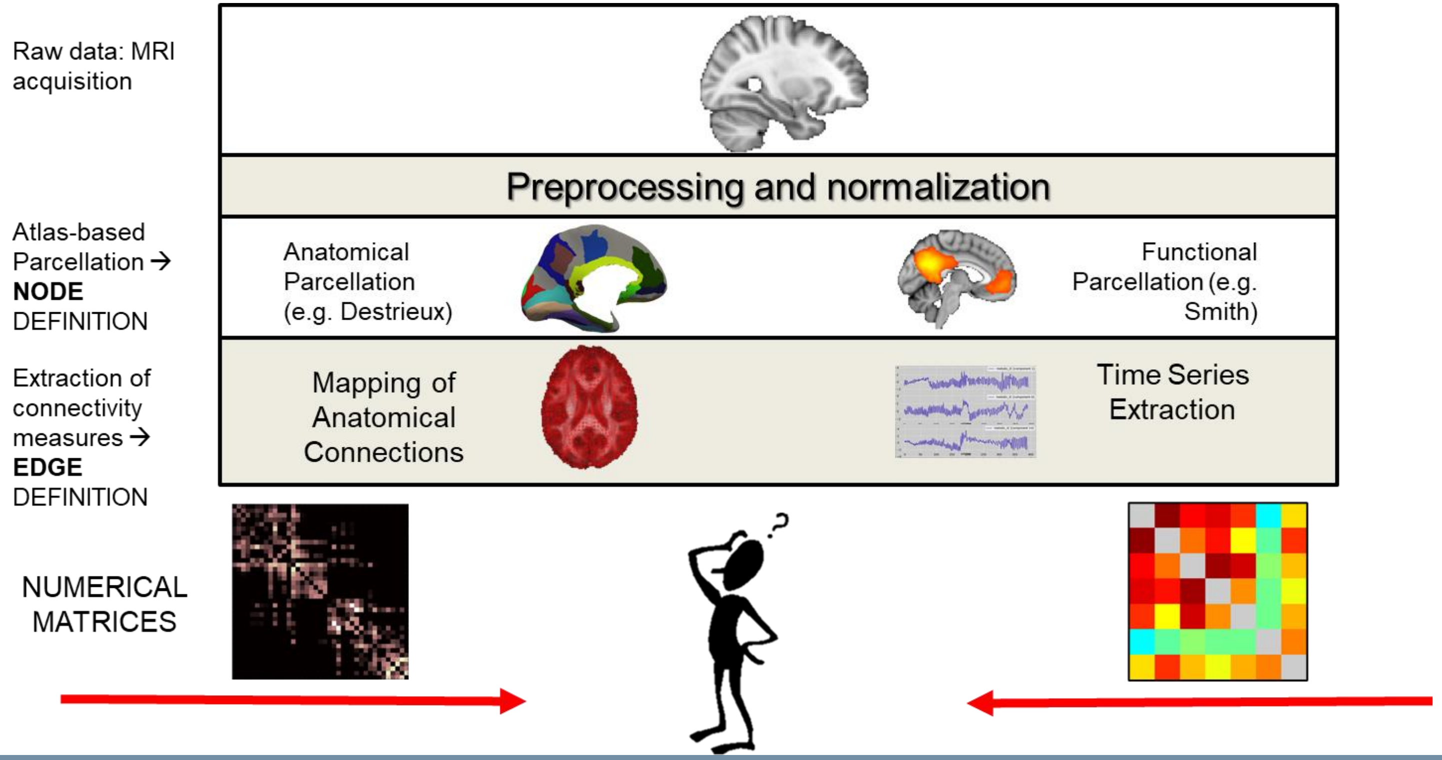
- One of the most notable clinical neuroanatomy case
- Widely discussed for prefrontal function and its relation to personality and behaviour



[Van Horn, et al., 2012]

Open issues

1. Difficulty in interpretation of large amounts of data
2. Brain sub-network extraction and analysis
3. Quality check of processing pipelines



SPIDER-NET (Software Package Ideal for Deriving Enhanced Representations of brain NETworks)

Raw data: MRI acquisition

Atlas-based Parcellation → **NODE** DEFINITION

Extraction of connectivity measures → **EDGE** DEFINITION

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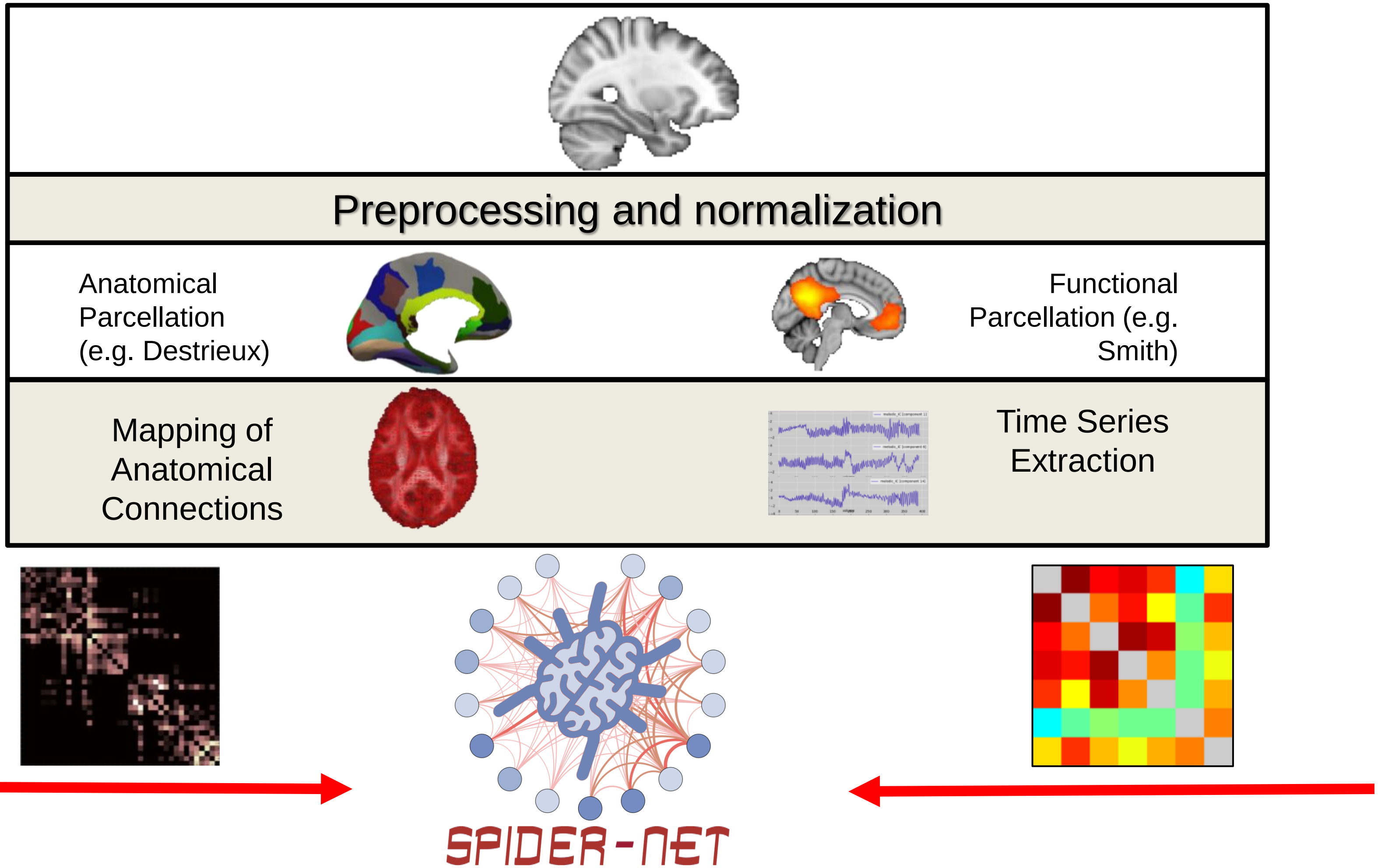


SPIDER-NET (Software Package Ideal for Deriving Enhanced Representations of brain NETworks)

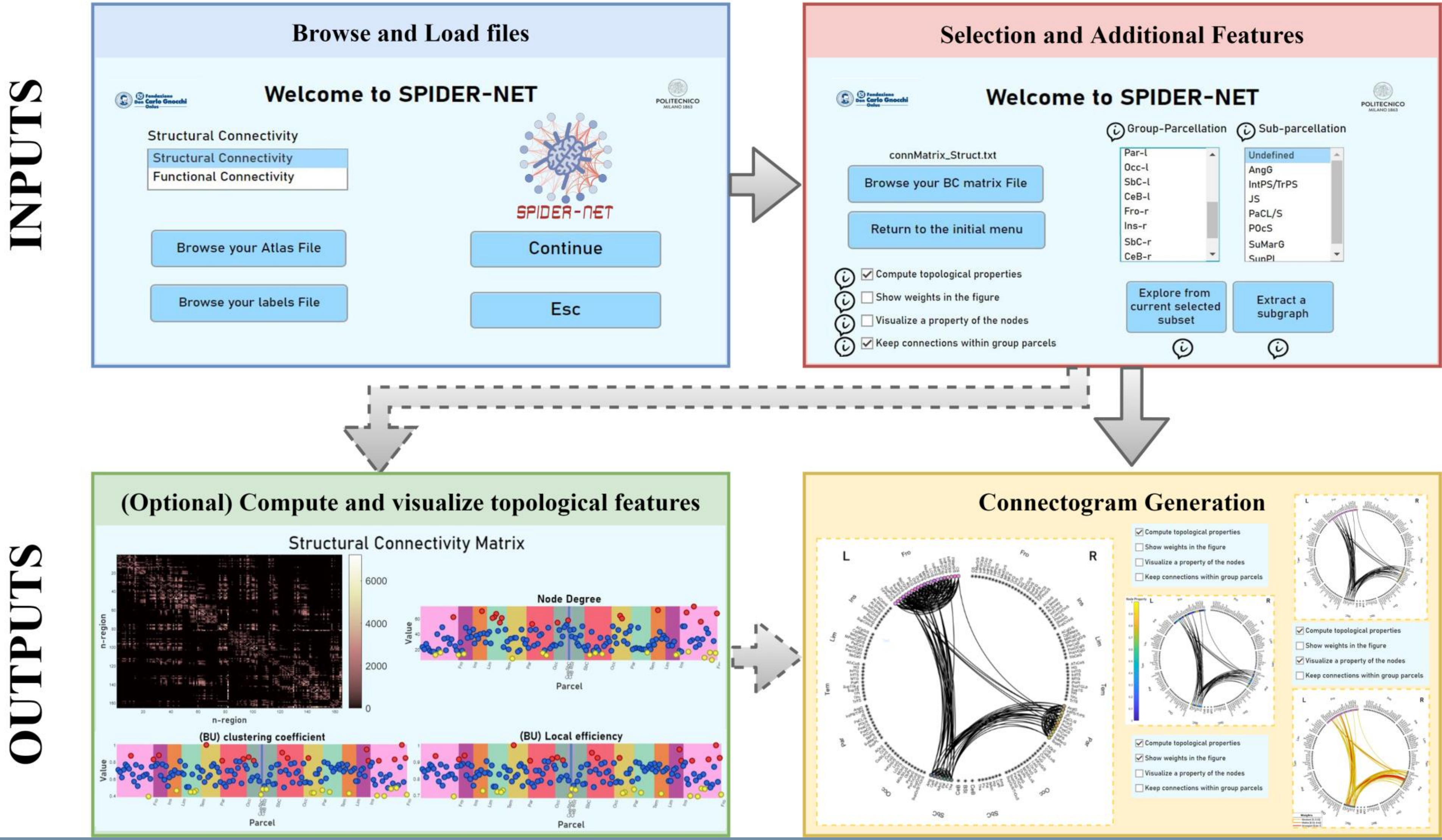
- Motivations:
    1. Qualitative analysis of **connectograms** revealed valuable indications of focal lesions
    2. Quantitative analysis of the connectivity revelead significant changes of **topological properties** in brain disorders
    3. Complete brain network is made of thousands of links and softwares for connectivity pattern visualization do not allow selections and **sub-network extraction**, although the great interest
    4. Softwares for connectogram generation have **no interface** and are **noninteractive**

❑ SPIDER-NET: Interactive visualization based on the selection of anatomical areas, functional networks and/or attributes for an easier interpretation of the maps

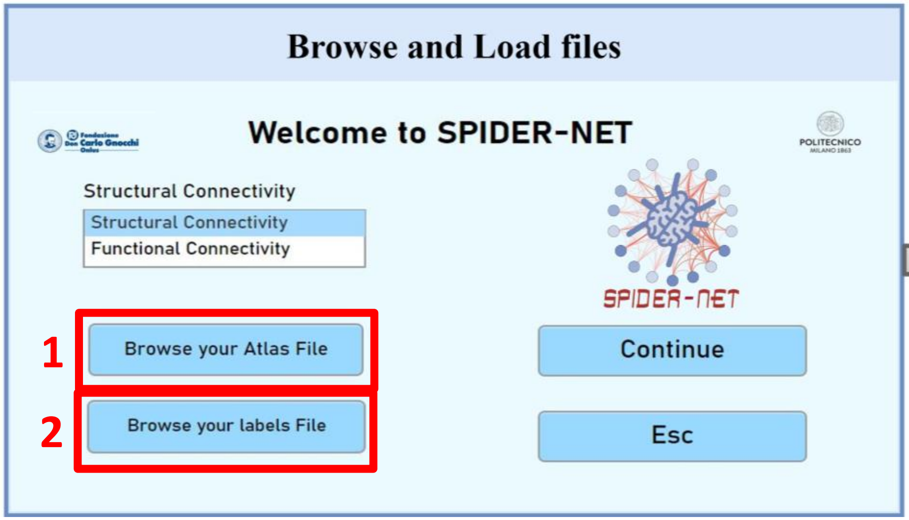
SPIDER-NET

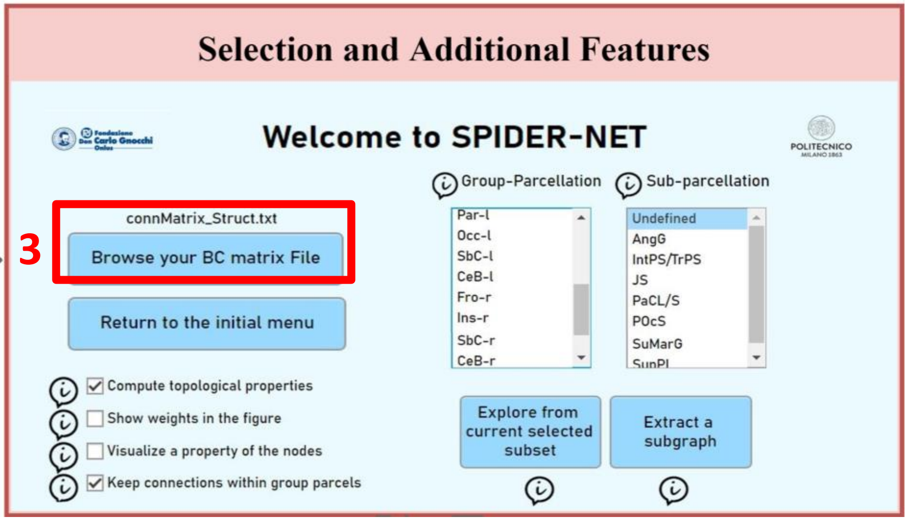
Fondazione Don Carlo Gnocchi Onlus

SPIDER-NET Workflow



SPIDER-NET input





	A	B	C	D	E	F	G
1	PARCELLATION	DESCRIPTION	GROUP-PARCELLATION	ATTRIBUTE	ATTRIBUTE	ATTRIBUTE	ATTRIBUTE
2	BSt	Brain stem	BSt	Attr1			
3	CS	Central sulcus (Rolando's fissure)	Fro	Attr2	Attr1		
4	FMarG/S	Fronto-marginal gyrus (of Wernicke) and sulcus	Fro	Attr2	Attr1		
5	InfFGOpp	Opercular part of the inferior frontal gyrus	Fro	Attr2	Attr1		
6	InfFGOrp	Orbital part of the inferior frontal gyrus	Fro	Attr2	Attr1		
7	InfFGTrip	Triangular part of the inferior frontal gyrus	Fro	Attr2	Attr1		
8	InfFS	Inferior frontal sulcus	Fro	Attr2	Attr1		
9	InfPrCS	Inferior part of the precentral sulcus	Fro	Attr2	Attr1		
10	LOrS	Lateral orbital sulcus	Fro	Attr2	Attr1		
11	MedOrS	Medial orbital sulcus (olfactory sulcus)	Fro	Attr2	Attr1		
12	MFG	Middle frontal gyrus	Fro	Attr2	Attr1		
13	MFS	Middle frontal sulcus	Fro	Attr2	Attr3	Attr1	
14	OrG	Orbital gyri	Fro	Attr2	Attr3	Attr1	
15	OrS	Orbital sulci (H-shaped sulci)	Fro	Attr2	Attr3	Attr1	

1

```
69 lh.PosTrCoS
70 lh.Cun
71 lh.MOcG
72 lh.MOcS/LuS
73 lh.SupOcG
74 lh.OcPo
75 lh.Amg
76 lh.CaN
77 lh.Hip
78 lh.NAcc
79 lh.Pal
80 lh.Pu
81 lh.Tha
82 lh.CeB
83 BSt
84 rh.TrFPoG/S
85 rh.FMarG/S
86 rh.MFS
87 rh.LOrS
88 rh.SbOrS
89 rh.OrS
90 rh.RG
91 rh.InfFGOrp
92 rh.MFG
93 rh.OrG
94 rh.InfFGTrip
95 rh.InfFS
96 rh.MedOrS
97 rh.SupFG
98 rh.SupFS
99 rh.InfFGOpp
100 rh.InfPrCS
101 rh.SupPrCS
102 rh.PrCG
103 rh.SbCG/S
```

2

```
0,717,118,0,
717,0,656,67,
118,656,0,622,
0, 67, 622, 0,
```

3

Atlases construction

	A	B	C	D	E	F	G
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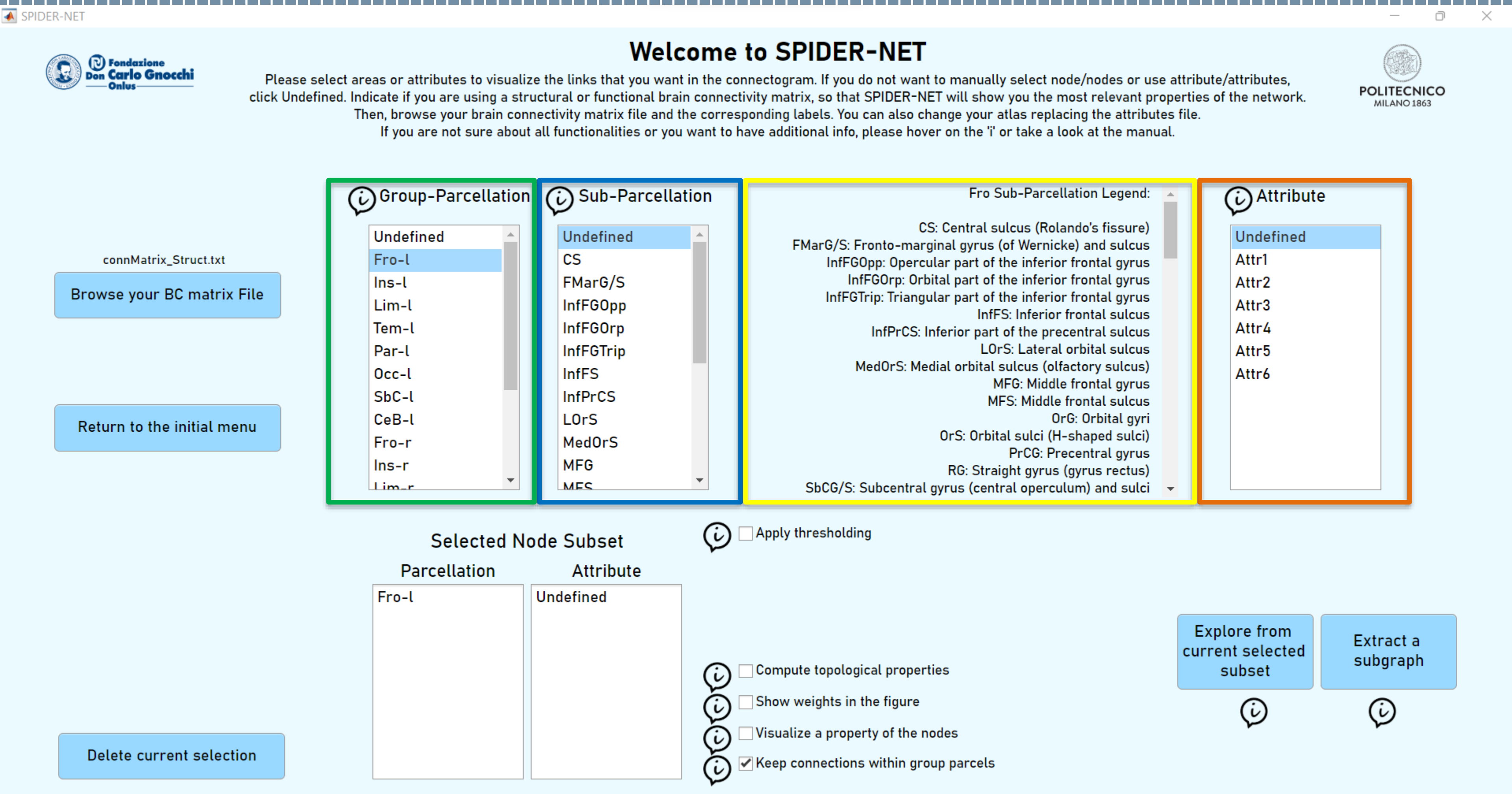
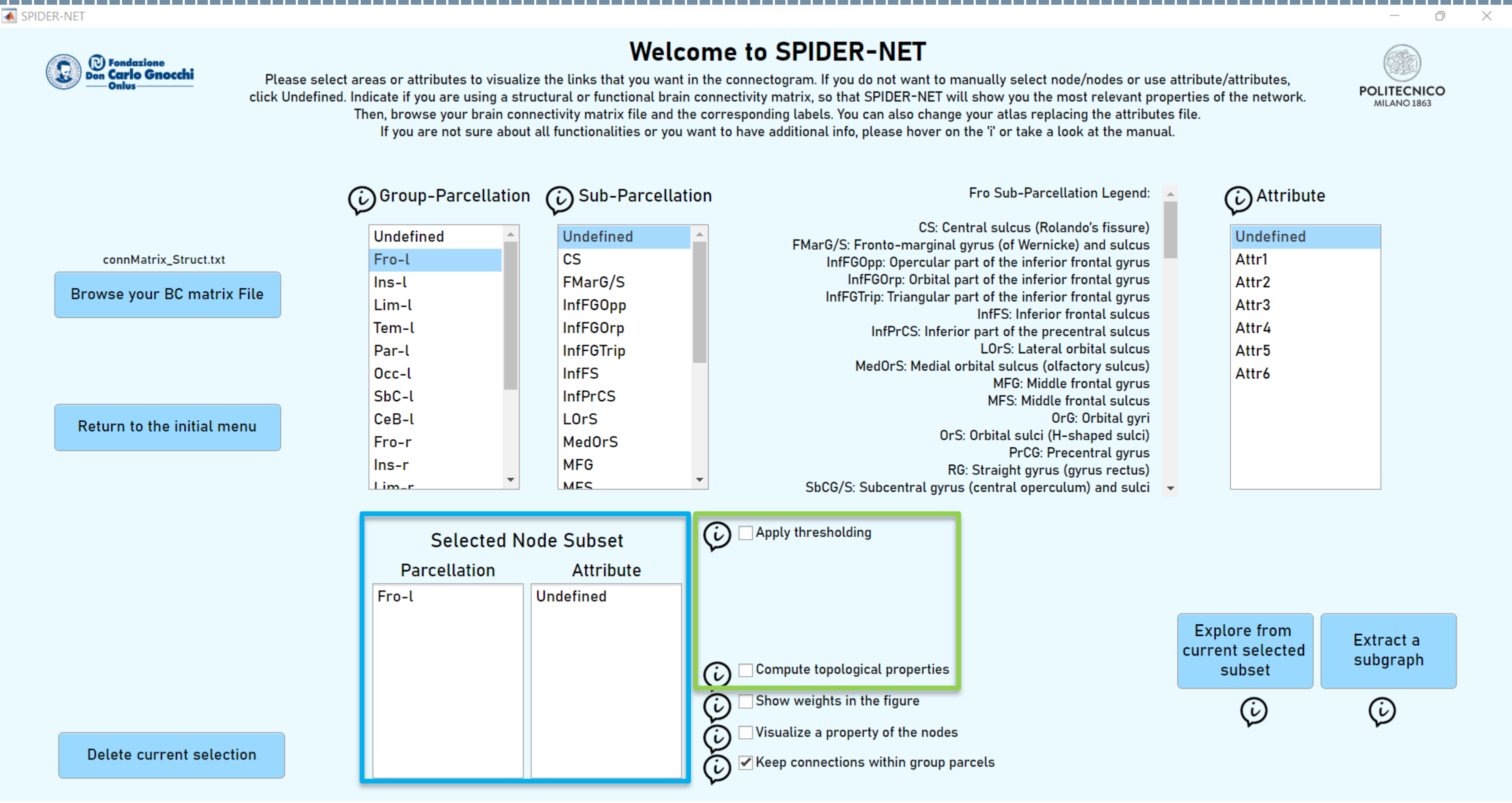
14	OrG	Orbital gyri	Fro	Attr2	Attr3	Attr1	
15	OrS	Orbital sulci (H-shaped sulci)	Fro	Attr2	Attr3	Attr1	

- Flexible sub-network extraction according to brain structure and/or function
    - Selection of anatomical areas, functional networks or attributes

Atlases construction and guided GUI

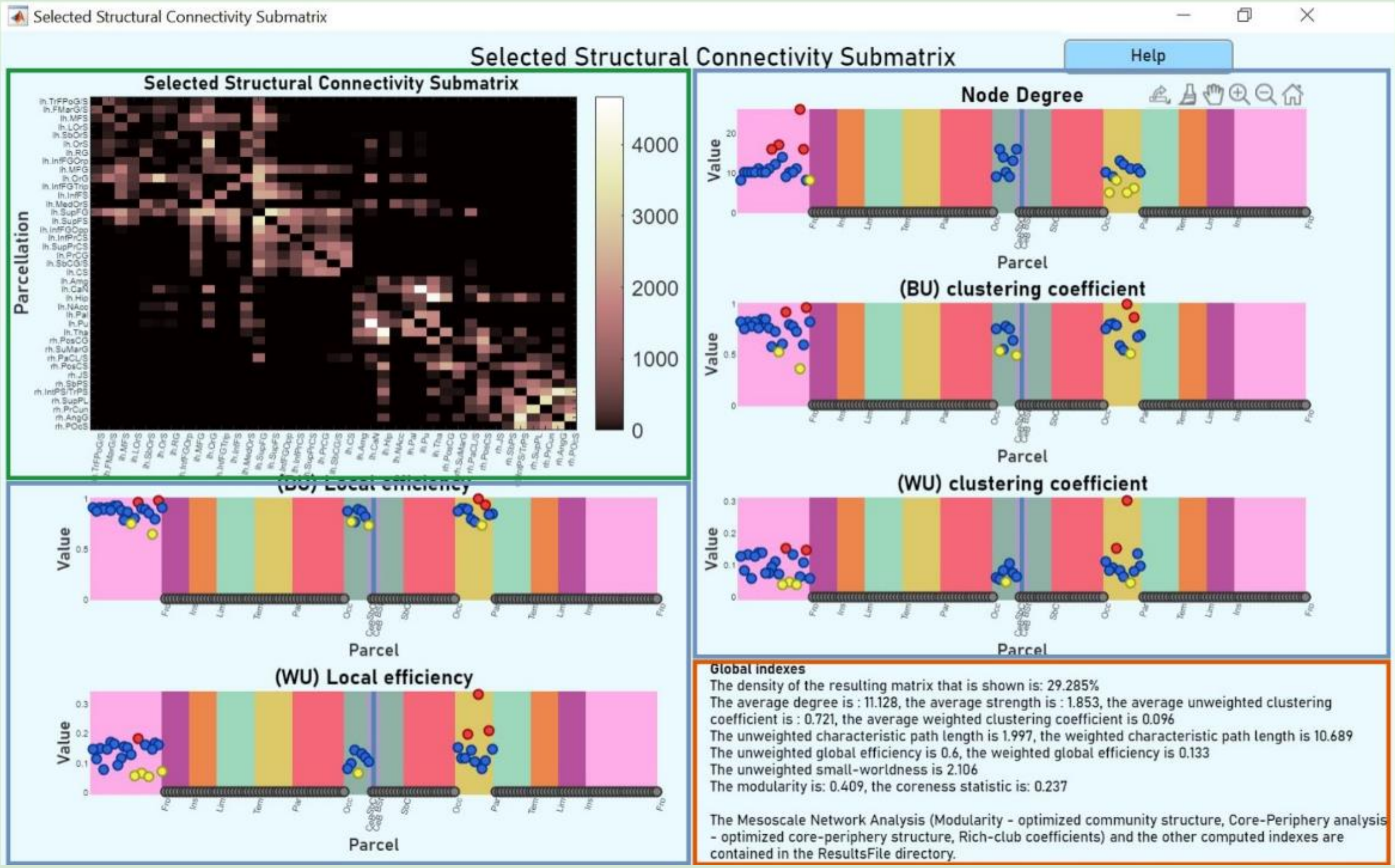


Guided GUI – Selection and additional options

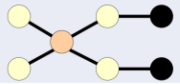
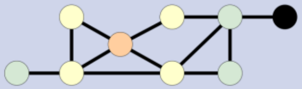
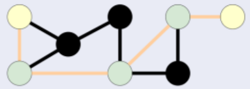
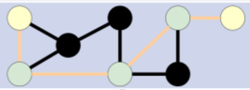
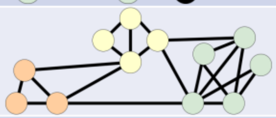
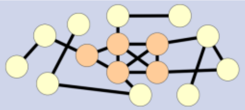
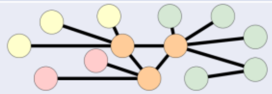
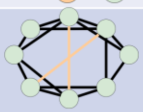


SPIDER-NET output

(Optional) computation and visualization of topological features

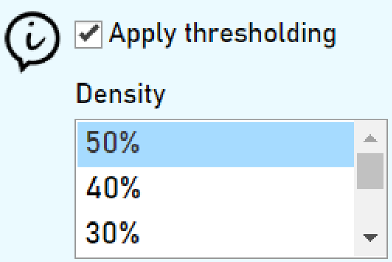


Topological properties and thresholding method

Graph-Based Index	Graphical Representation	Mathematical Expression
Density		$D = \frac{X}{(n^2 - n)/2}$
Degree Strength		$k = avg(\sum_j a_{ij})$; $k^w = avg(\sum_j w_{ij})$
Average clustering coefficient (binary and weighted)		$C = \frac{1}{n}\sum_{i\in N}\frac{2t_i}{k_i(k_i-1)}$; $C^w = \frac{1}{n}\sum_{i\in N}\frac{2t_i^w}{k_i(k_i-1)}$
Characteristic path length (binary and weighted)		$L = \frac{1}{n}\sum_{i\in N}\frac{\sum_{j\in N, j\neq i} d_{ij}}{n-1}$; $L^w = \frac{1}{n}\sum_{i\in N}\frac{\sum_{j\in N, j\neq i} d_{ij}^w}{n-1}$
Global Efficiency (binary and weighted)		$E = \frac{1}{n}\sum_{i\in N}\frac{\sum_{j\in N, j\neq i}(d_{ij})^{-1}}{n-1}$; $E^w = \frac{1}{n}\sum_{i\in N}\frac{\sum_{j\in N, j\neq i}(d_{ij}^w)^{-1}}{n-1}$
Modularity		$Q = \frac{1}{2m}\sum_{C_h}\sum_{i,j\in C_h}\left[a_{ij} - \frac{k_i k_j}{2m}\right]$ where m is the total number of edges in the network and C_h are the communities
Coreness statistics		$N = \frac{1}{v_S}\left(\sum_{i,j\in V_C}(w_{ij} - \bar{w}) - \sum_{i,j\in V_P}(w_{ij} - \bar{w})\right)$ where V_c, V_p are sets of all nodes in the core, periphery, $\bar{w}$ is the average edge weight and v_S is a normalization constant
Rich-club coefficients		$R_k = \frac{2o_{>k}}{m_{>k}(m_{>k}-1)} = \frac{n.\ edge\ linking\ nodes > k}{max\ n.\ edge\ linking\ nodes > k}$
Small-worldness		$S = \frac{C/C_{rand}}{L/L_{rand}}$ where rand refers to measures of random network

- Network indexes pointing out significant organizational changes in a number of brain disorders:
  - Alzheimer's Disease *[Daianu et al., 2013]*
  - Mild Cognitive Impairment *[Baggio et al., 2014]*
  - Parkinson's Disease *[Göttlich et al., 2013]*
  - Epilepsy *[Ji et al., 2017]*
  - Autism *[Barttfeld et al., 2012]*

- Density thresholding

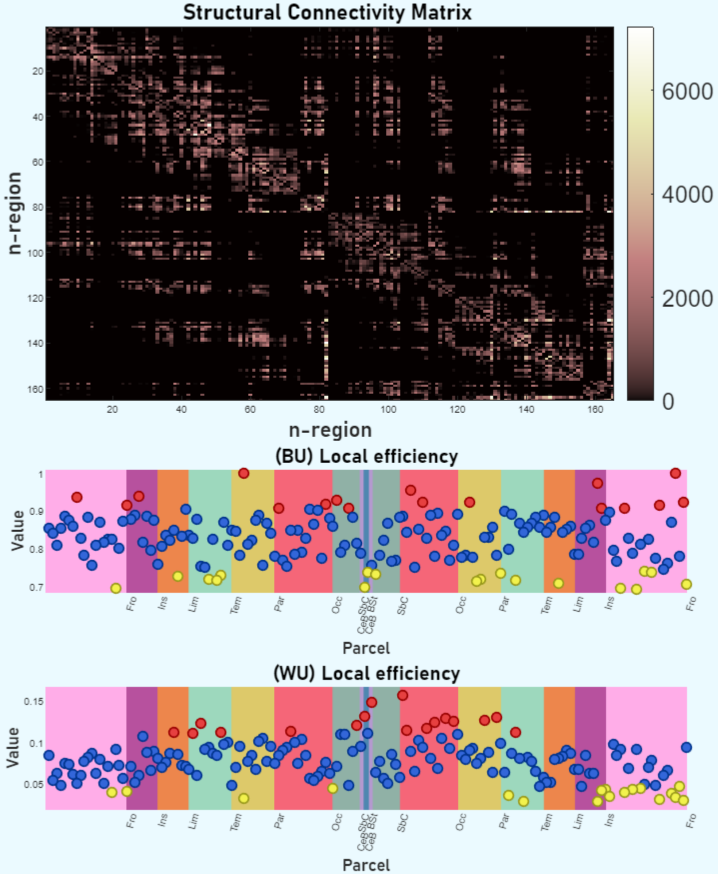


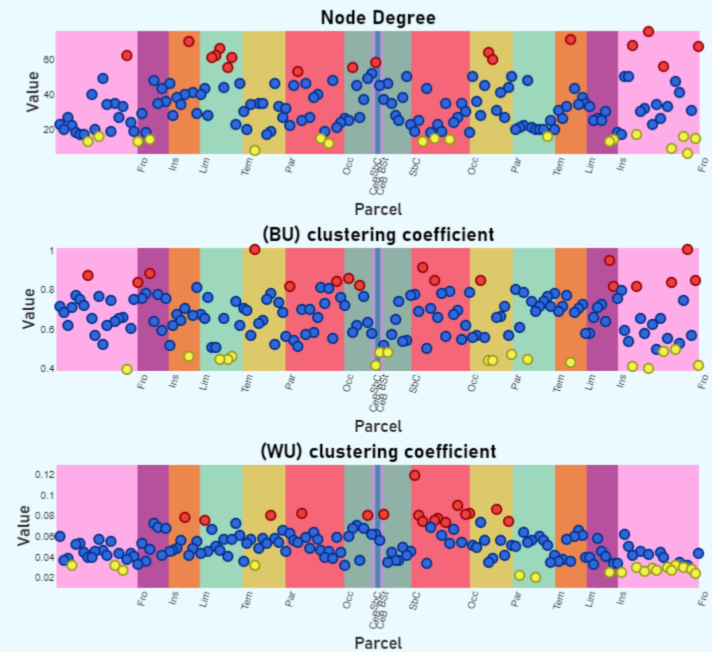
Topological properties – Whole-brain network

Structural Connectivity Matrix

Structural Connectivity Matrix

Help



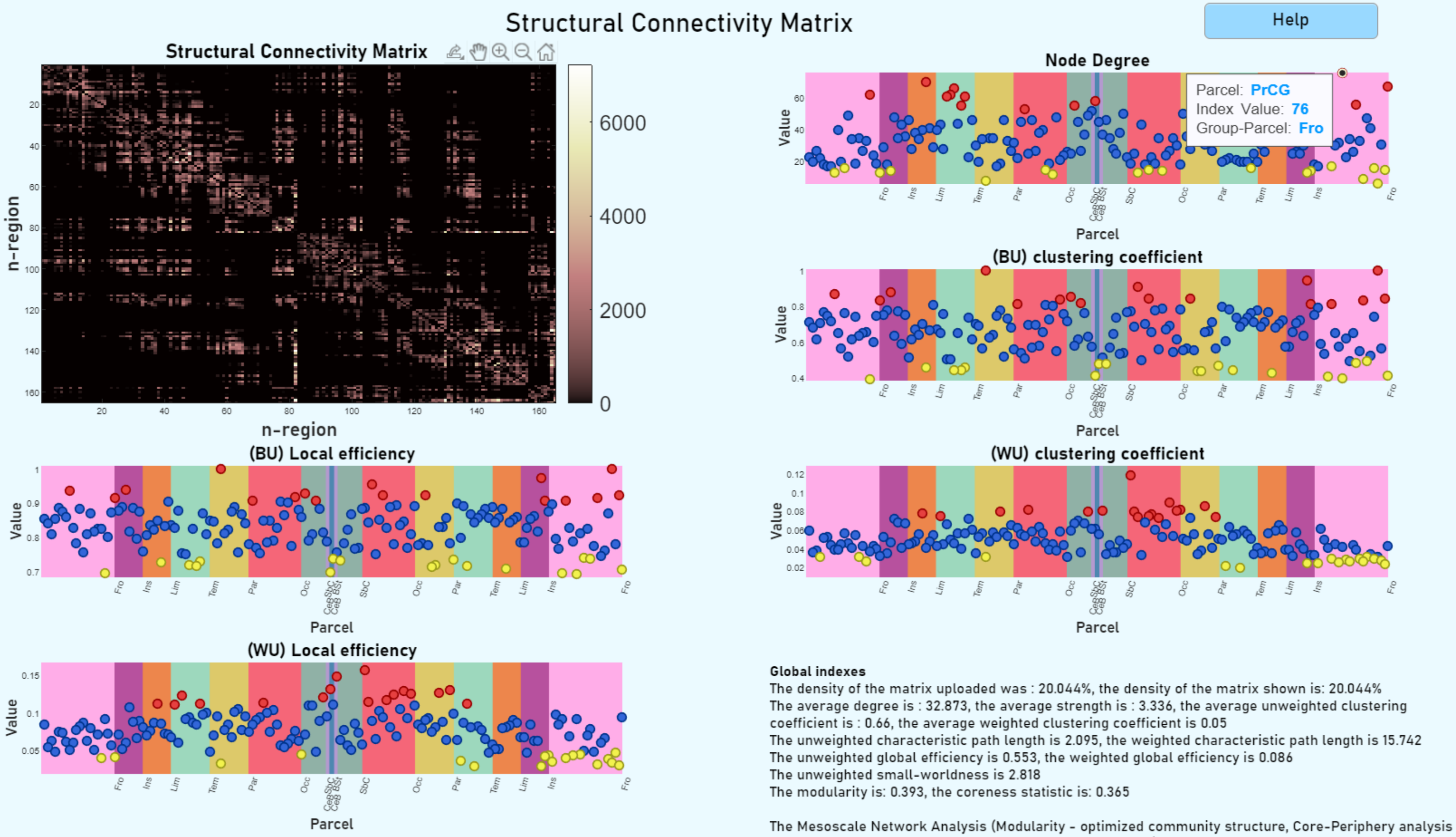


Global indexes
The density of the matrix uploaded was : 20.044%, the density of the matrix shown is: 20.044%
The average degree is : 32.873, the average strength is : 3.336, the average unweighted clustering coefficient is : 0.66, the average weighted clustering coefficient is 0.05
The unweighted characteristic path length is 2.095, the weighted characteristic path length is 15.742
The unweighted global efficiency is 0.553, the weighted global efficiency is 0.086
The unweighted small-worldness is 2.818
The modularity is: 0.393, the coreness statistic is: 0.365

The Mesoscale Network Analysis (Modularity - optimized community structure, Core-Periphery analysis - optimized core-periphery structure, Rich-club coefficients) and the other computed indexes are contained in the ResultsFile directory.

Topological properties – Whole-brain network – Interactivity

Structural Connectivity Matrix



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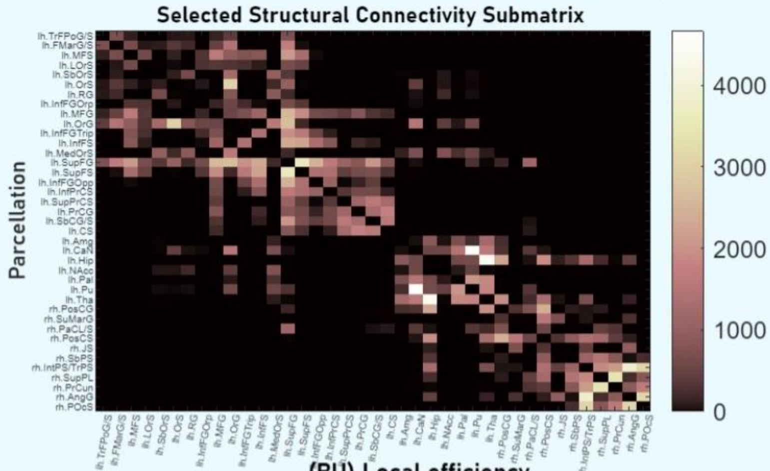
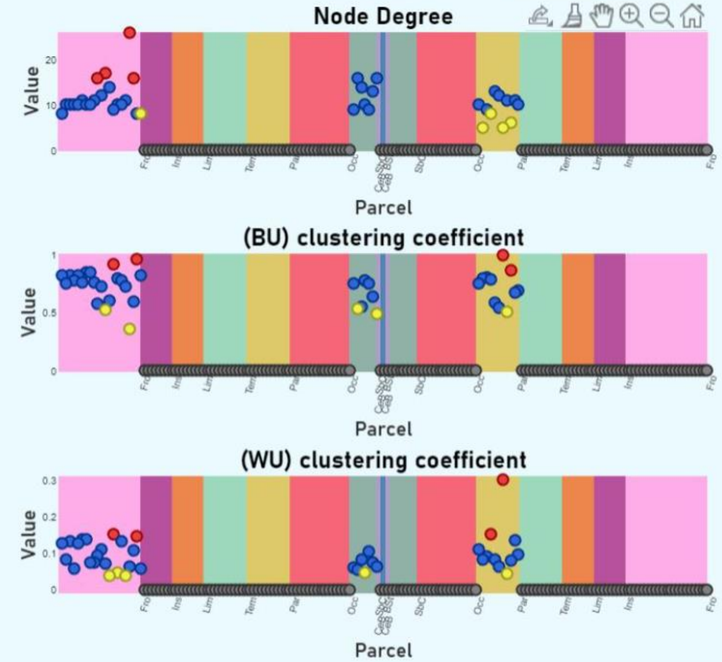
Topological properties – Selected sub-network

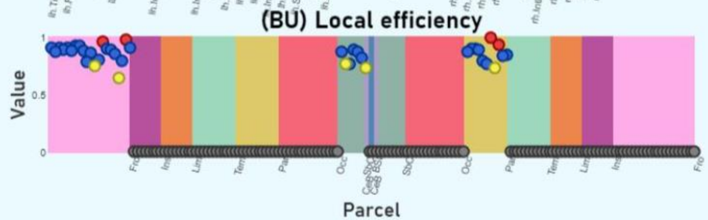
Selected Structural Connectivity Submatrix

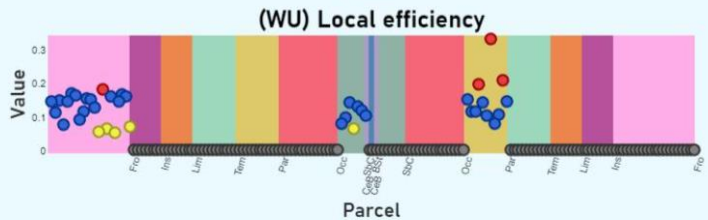
Selected Structural Connectivity Submatrix

Help









Global indexes

The density of the resulting matrix that is shown is: 29.285%
The average degree is : 11.128, the average strength is : 1.853, the average unweighted clustering coefficient is : 0.721, the average weighted clustering coefficient is 0.096
The unweighted characteristic path length is 1.997, the weighted characteristic path length is 10.689
The unweighted global efficiency is 0.6, the weighted global efficiency is 0.133
The unweighted small-worldness is 2.106
The modularity is: 0.409, the coreness statistic is: 0.237

The Mesoscale Network Analysis (Modularity - optimized community structure, Core-Periphery analysis - optimized core-periphery structure, Rich-club coefficients) and the other computed indexes are contained in the ResultsFile directory.

SPIDER-NET output

Connectogram generation

Extract a subgraph

Selected node subset

Parcellation	Attribute
Fro-l SbC-l Par-r	Undefined

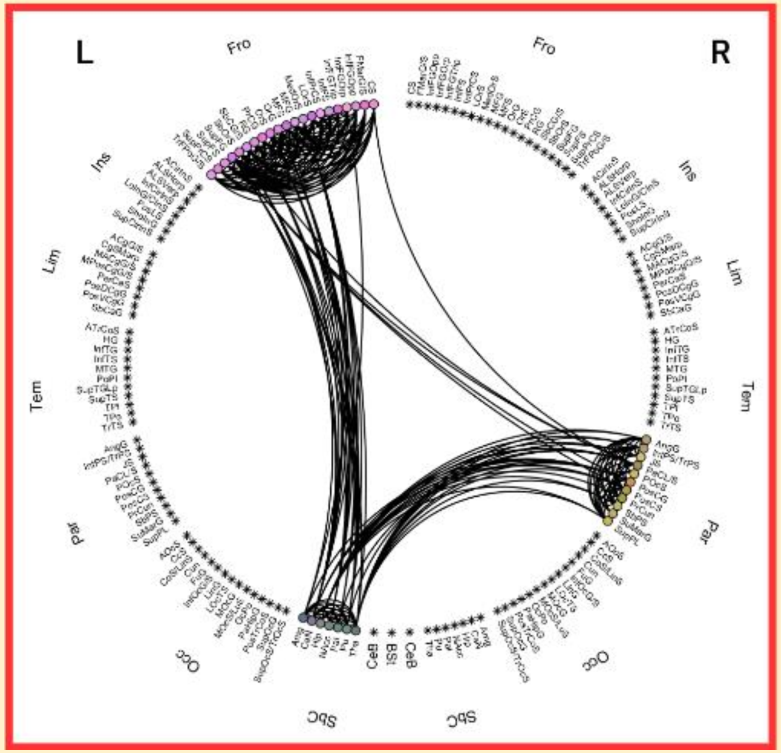
Explore from current selected subset

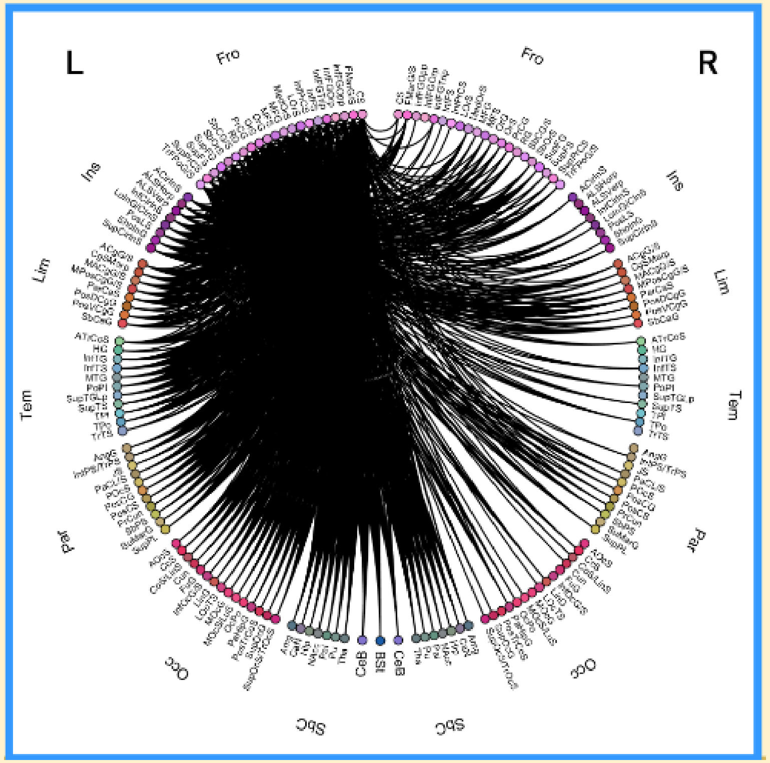
Exploration source

Parcellation	Attribute
Fro-l	Undefined

Selected Node Subset

Parcellation	Attribute
Undefined	Undefined





SPIDER-NET output

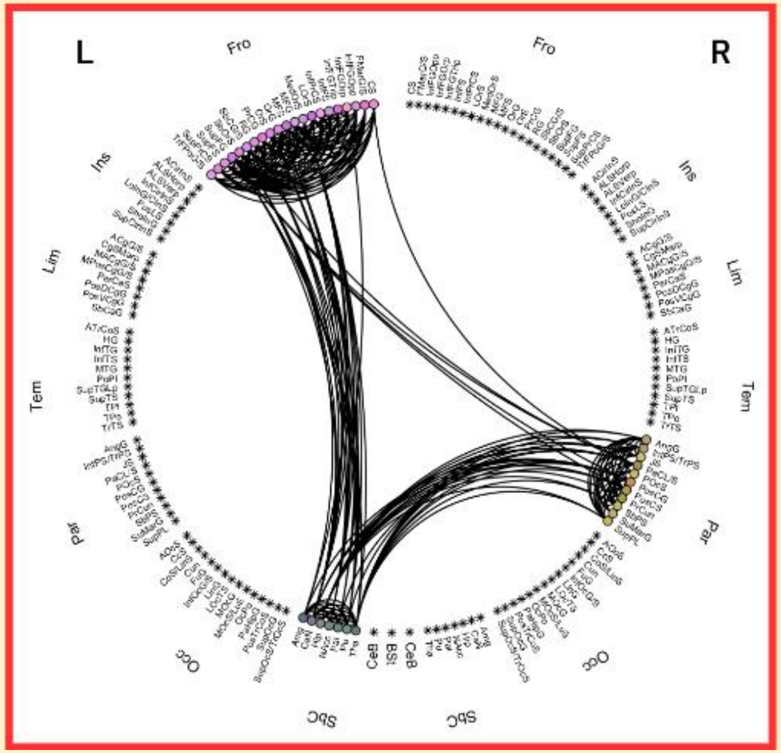
Connectogram generation

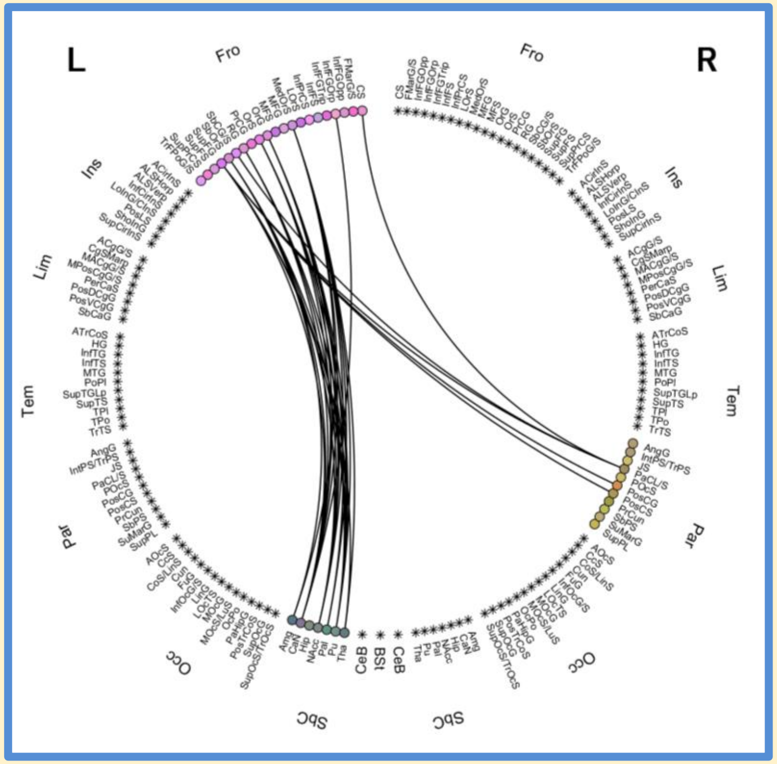
Extract a subgraph

Selected node subset	
Parcellation	Attribute
Fro-l SbC-l Par-r	Undefined

Explore from current selected subset

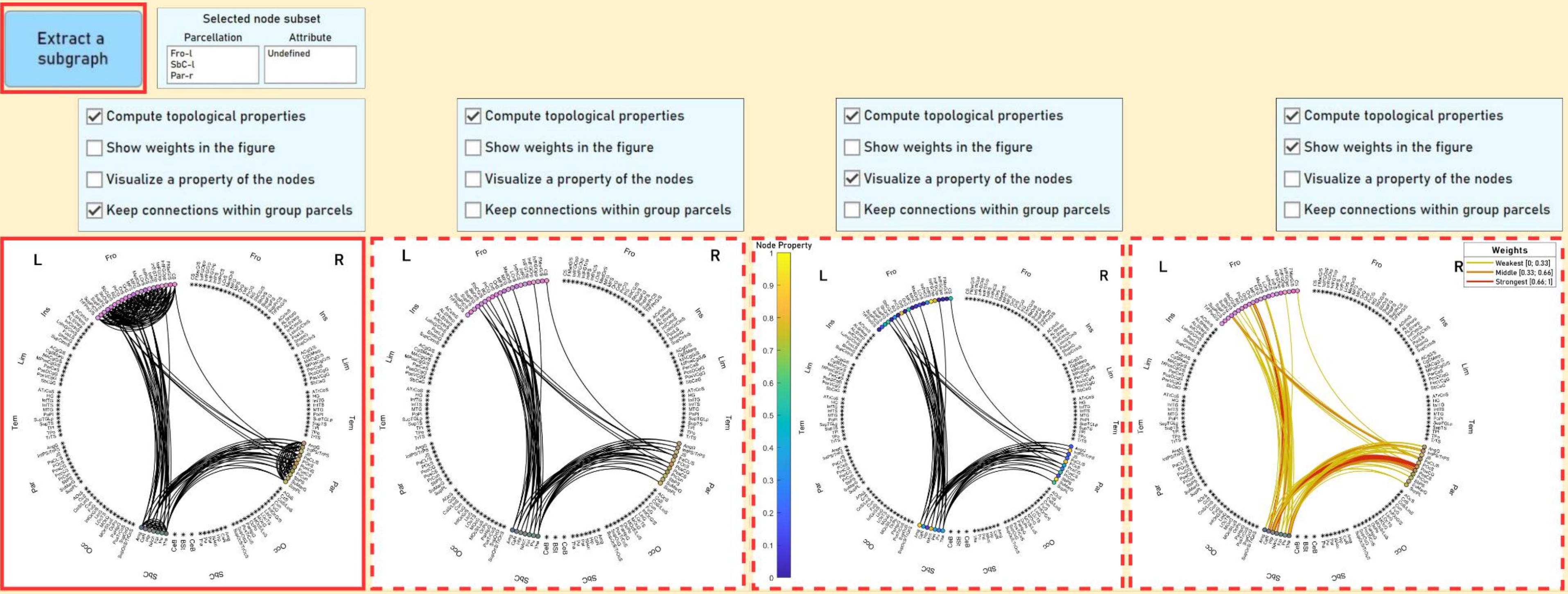
Exploration source	
Parcellation	Attribute
Fro-l	Undefined
Selected Node Subset	
Parcellation	Attribute
SbC-l Par-r	Undefined





SPIDER-NET output

Connectogram generation

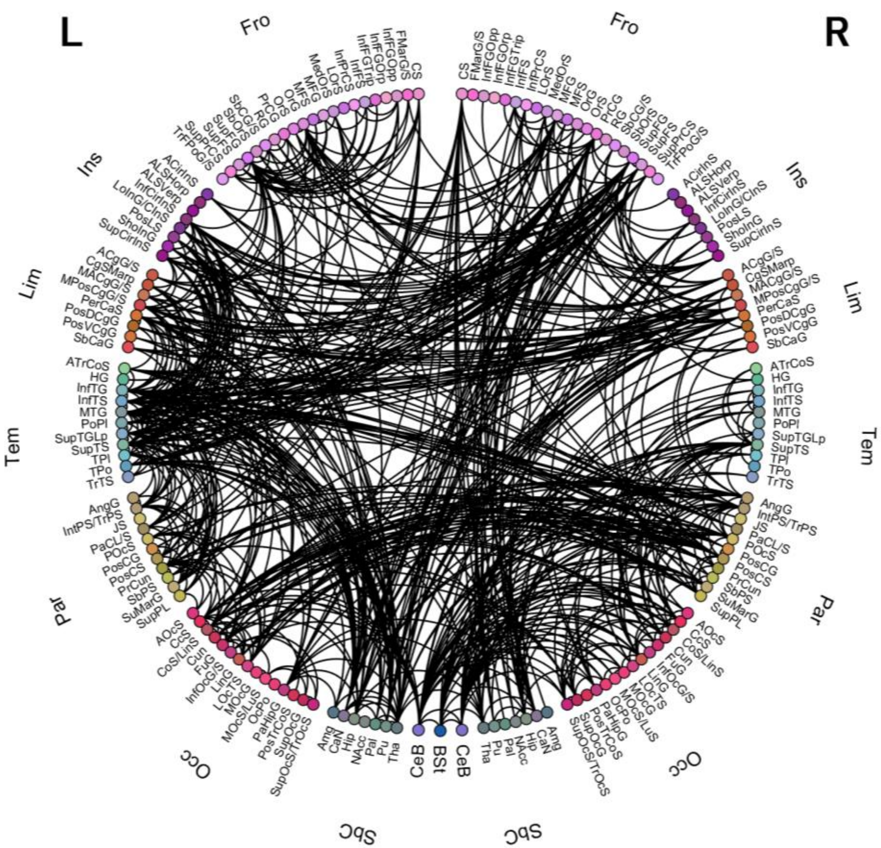


Davide Coluzzi, PhD candidate, DEIB.

Going into connectograms - Examples

- **Destrieux** 150 cortical atlas *[Destrieux et al., 2010]*
- 7 subcortical ROIs per hemisphere and the brainstem were also segmented using the FreeSurfer automatic labeling process *[Fischl et al., 2002]* for a total of 165 parcels

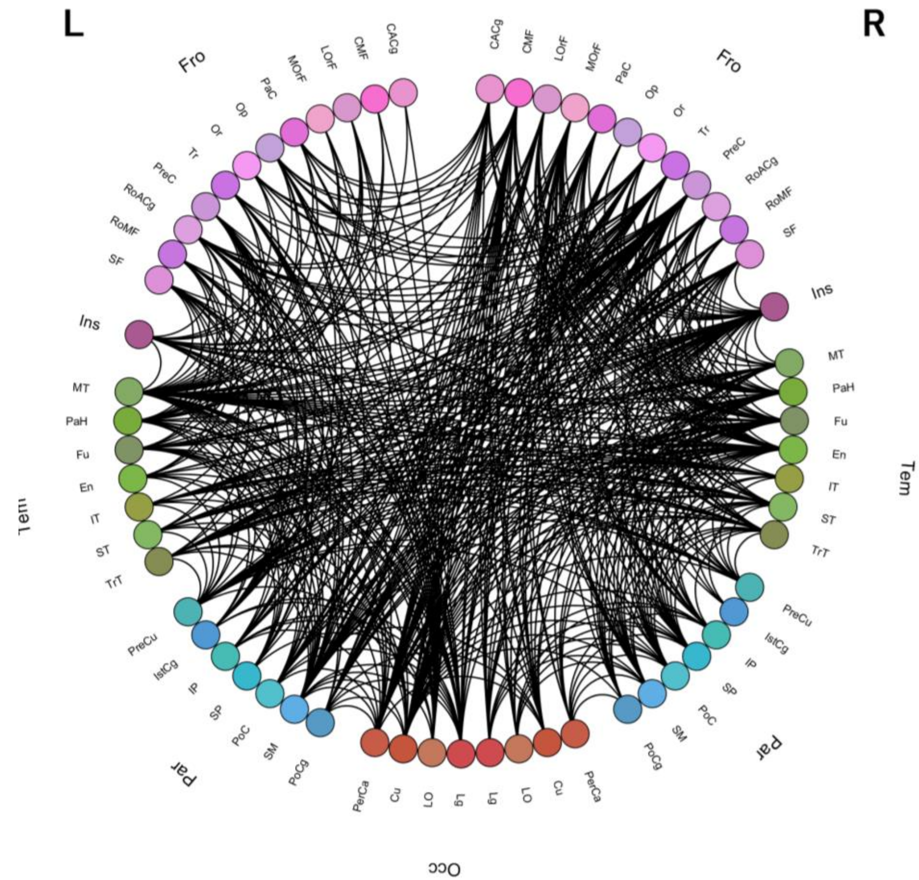
1	PARCELLATION	DESCRIPTION	GROUP-PARCELLATION
2	CS	Central sulcus (Rolando's fissure)	Fro
3	FMarG/S	Fronto-marginal gyrus (of Wernicke) and sulcus	Fro
4	InfFGOpp	Opercular part of the inferior frontal gyrus	Fro
5	InfFGOrp	Orbital part of the inferior frontal gyrus	Fro
6	InfFGTrip	Triangular part of the inferior frontal gyrus	Fro
7	InfFS	Inferior frontal sulcus	Fro
8	InfPrCS	Inferior part of the precentral sulcus	Fro
9	LOrS	Lateral orbital sulcus	Fro
10	MedOrS	Medial orbital sulcus (olfactory sulcus)	Fro
11	MFG	Middle frontal gyrus	Fro
12	MFS	Middle frontal sulcus	Fro
13	OrG	Orbital gyri	Fro
14	OrS	Orbital sulci (H-shaped sulci)	Fro
15	PrCG	Precentral gyrus	Fro



Going into connectograms - Examples

- **Desikan-Killiany-Tourville (DKT)** cortical atlas *[Desikan et al., 2006]*

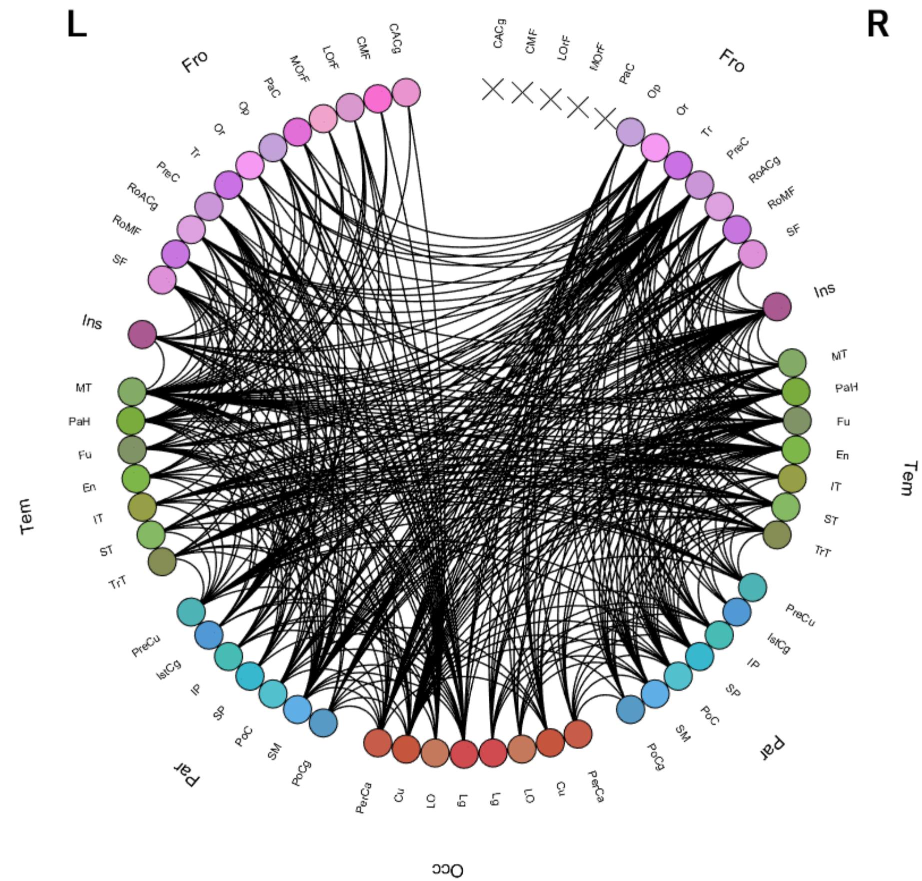
- 62 ROIs divided into the two hemispheres and 4 lobes



1	PARCELLATION	DESCRIPTION	GROUP-PARCELLATION
2	CACg	caudal anterior cingulate	Fro
3	CMF	caudal middle frontal gyrus	Fro
4	LOrF	lateral orbitofrontal cortex	Fro
5	MOrF	medial orbitofrontal cortex	Fro
6	PaC	paracentral lobule	Fro
7	Op	pars opercularis	Fro
8	Or	pars orbitalis	Fro
9	Tr	pars triangularis	Fro
10	PreC	precentral gyrus	Fro
11	RoACg	rostral anterior cingulate	Fro
12	RoMF	rostral middle frontal gyrus	Fro
13	SF	superior frontal gyrus	Fro
14	Ins	insula	Ins
15	MT	middle temporal gyrus	Tem

Going into connectograms - Examples - Interactivity

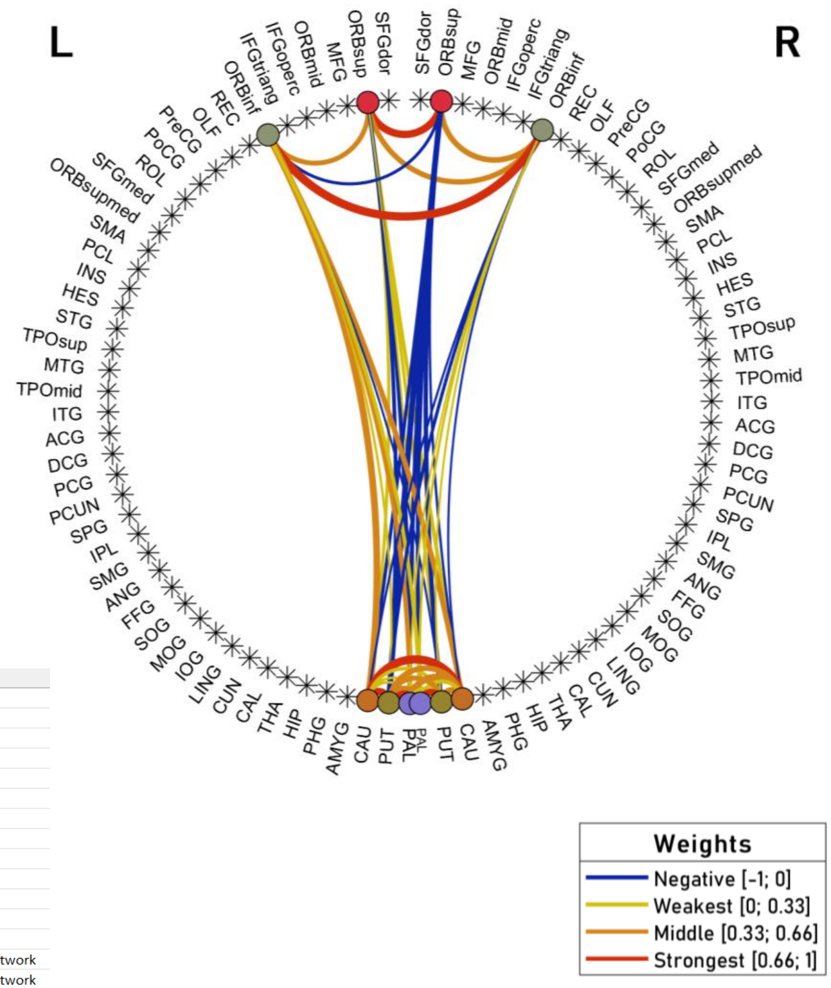
- **Desikan-Killiany-Tourville (DKT)** cortical atlas *[Desikan et al., 2006]*
- 62 ROIs divided into the two hemispheres and 4 lobes



1	PARCELLATION	DESCRIPTION	GROUP-PARCELLATION
2	CACg	caudal anterior cingulate	Fro
3	CMF	caudal middle frontal gyrus	Fro
4	LOrF	lateral orbitofrontal cortex	Fro
5	MOrF	medial orbitofrontal cortex	Fro
6	PaC	paracentral lobule	Fro
7	Op	pars opercularis	Fro
8	Or	pars orbitalis	Fro
9	Tr	pars triangularis	Fro
10	PreC	precentral gyrus	Fro
11	RoACg	rostral anterior cingulate	Fro
12	RoMF	rostral middle frontal gyrus	Fro
13	SF	superior frontal gyrus	Fro
14	Ins	insula	Ins
15	MT	middle temporal gyrus	Tem

Going into connectograms - Examples

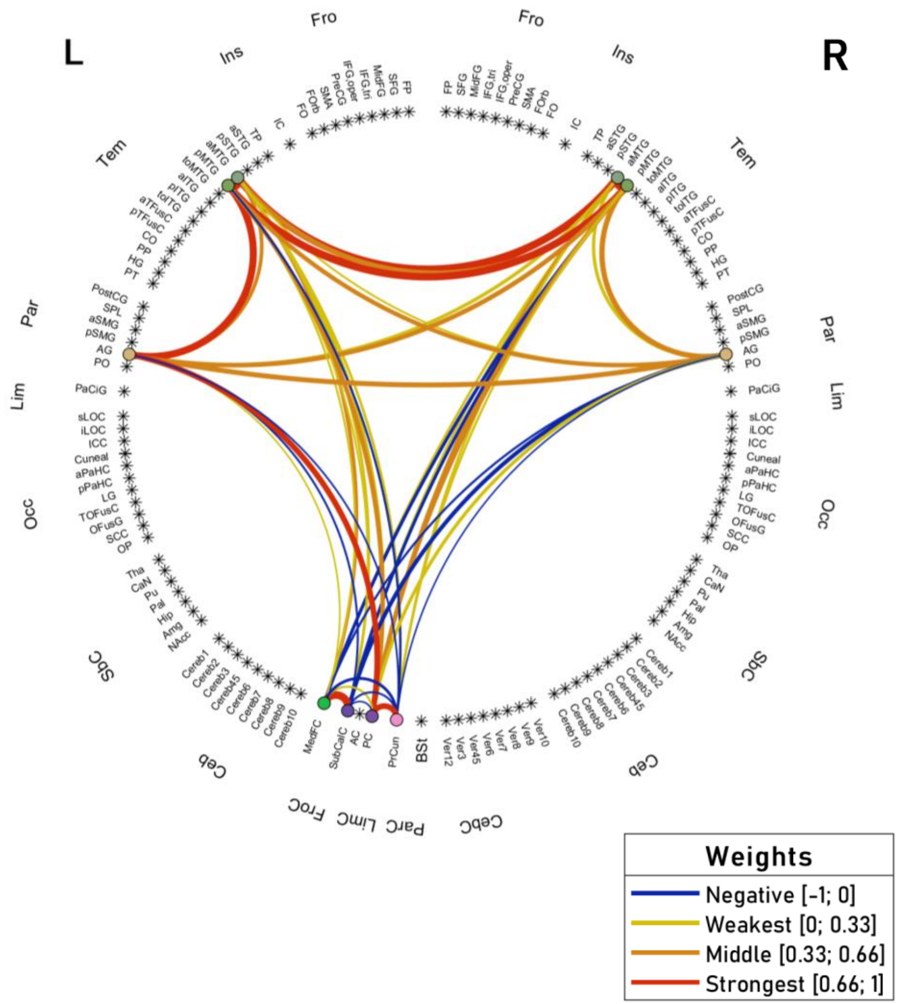
- **Automated Anatomical Labeling (AAL)** atlas *[Tzourio-Mazoyer et al., 2002]*
- 90 ROIs: 85 cortical and 5 subcortical ROIs
- Associated functional networks: Language, SensoriMotor, Default-Mode, Salience, VisuoSpatial, FrontoParietal or Visual Networks *[Smitha et al., 2017]*



	A	B	C	D	E	F
1	PARCELLATION	DESCRIPTION	ATTRIBUTE	ATTRIBUTE	ATTRIBUTE	ATTRIBUTE
2	SFGdor	Superior frontal gyrus, dorsolateral	Visuospatial Network	Language Network	Salience Network	
3	ORBsup	Superior frontal gyrus, orbital part	Visuospatial Network	Language Network		
4	MFG	Middle frontal gyrus	FPN/Executive Network	Visuospatial Network	Language Network	Salience Network
5	ORBmid	Middle frontal gyrus, orbital part	Visuospatial Network	Language Network		
6	IFGoperc	Inferior frontal gyrus, opercular part	FPN/Executive Network	Language Network	Salience Network	
7	IFGtriang	Inferior frontal gyrus, triangular part	FPN/Executive Network	Language Network	Salience Network	
8	ORBinf	Inferior frontal gyrus, orbital part	Language Network	FPN/Executive Network	Salience Network	
9	REC	Gyrus rectus	Sensorimotor Network			
10	OLF	Olfactory cortex	Language Network	Sensorimotor Network		
11	PreCG	Precental gyrus	Language Network	Sensorimotor Network	Salience Network	
12	PoCG	Postcentral gyrus	Sensorimotor Network	FPN/Executive Network	Salience Network	
13	ROL	Rolandic operculum	Language Network	Sensorimotor Network		
14	SFGmed	Superior frontal gyrus, medial	DMN	Visuospatial Network	Language Network	FPN/Executive Network
15	ORBsupmed	Superior frontal gyrus, medial orbital	Visuospatial Network	Language Network	Salience Network	FPN/Executive Network

Going into connectograms - Examples

- **FSL Harvard-Oxford** atlas cortical & subcortical areas and **AAL** atlas cerebellar areas *[Desikan et al. 2006, Tzourio-Mazoyer et al., 2002]*
- 132 ROIs: 91 cortical and 15 subcortical ROIs from the FSL maximum likelihood cortical and subcortical atlas, and 26 cerebellar ROIs from the AAL atlas

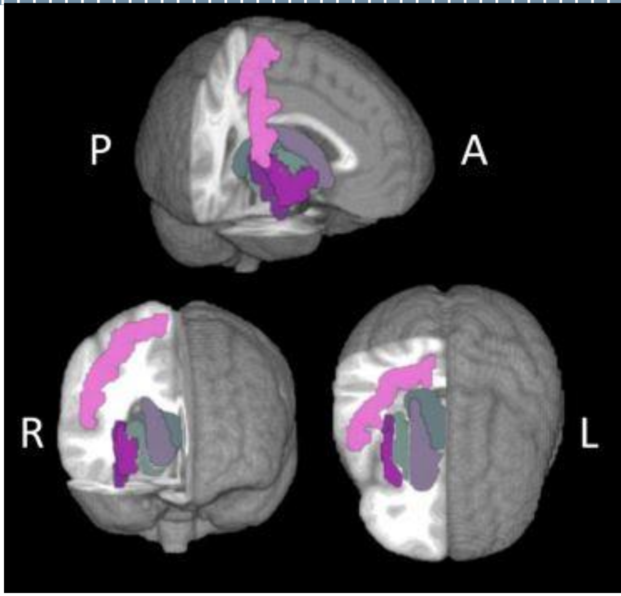


	A	B	C	D	E
1	PARCELLATION	DESCRIPTION	GROUP-PARCELLATION	ATTRIBUTE	ATTRIBUTE
2	FP	Frontal Pole	Fro	FPN	Lang
3	SFG	Superior Frontal Gyrus	Fro	FPN	Lang
4	MidFG	Middle Frontal Gyrus	Fro	FPN	Lang
5	IFG_tri	Inferior Frontal Gyrus, pars triangularis	Fro	ITG	FPN
6	IFG_oper	Inferior Frontal Gyrus, pars opercularis	Fro	Lang	FPN
7	PreCG	Precentral Gyrus	Fro	Motor	
8	SMA	Juxtapositional Lobule Cortex -formerly Supplementary Motor Corte	Fro	Auditory	
9	FOrb	Frontal Orbital Cortex	Fro	ITG	
10	FO	Frontal Operculum Cortex	Fro	Salience	
11	IC	Insular Cortex	Ins	Auditory	
12	TP	Temporal Pole	Tem	STG	
13	aSTG	Superior Temporal Gyrus, anterior division	Tem	STG	
14	pSTG	Superior Temporal Gyrus, posterior division	Tem	STG	
15	aMTG	Middle Temporal Gyrus, anterior division	Tem	aDMN	

Stroke case study application

Study population: The dataset consists of 17 healthy control (HC) subjects (7 males and 10 females; mean age ± SD : 52.5 ± 8.3 years) and two stroke patients (males, age 44 – case study 1 and 37 – case study 2).

MRI acquisition: All the participants underwent an MRI examination performed on a 1.5 T Siemens Magnetom Avanto scanner equipped with a 12-channels head coil

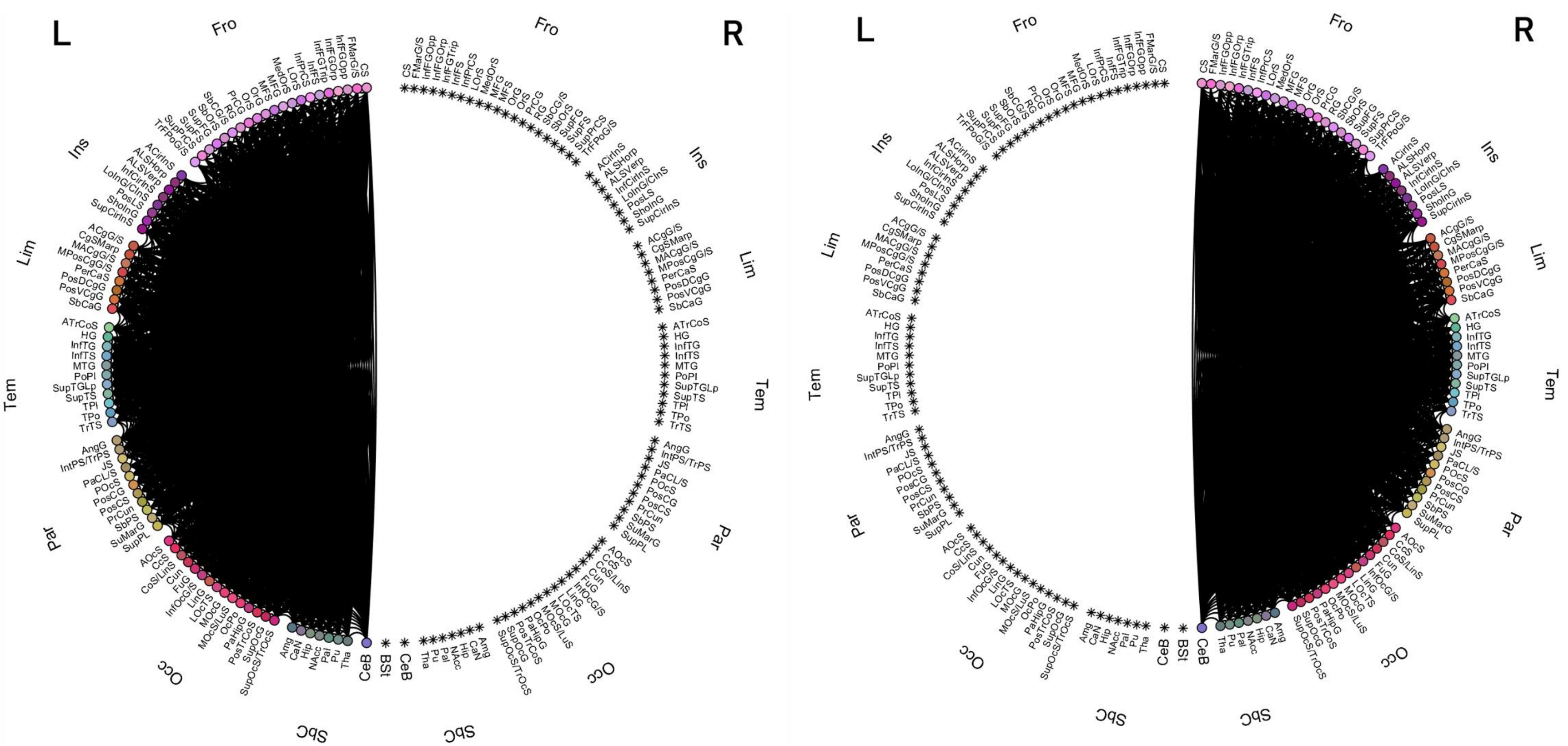


Preprocessing:

- Parcellation and automatic labeling using FreeSurfer – 75 cortical parcels plus 7 subcortical regions for each hemisphere and the brain stem for a total of 165 parcels (Destrieux atlas)
- Connectivity matrices derived by computing the edges as the number of the reconstructed fiber (NF)
- NF normalization by the sum of the volumes of the pair of connected parcels
- Creation of a probabilistic HC template

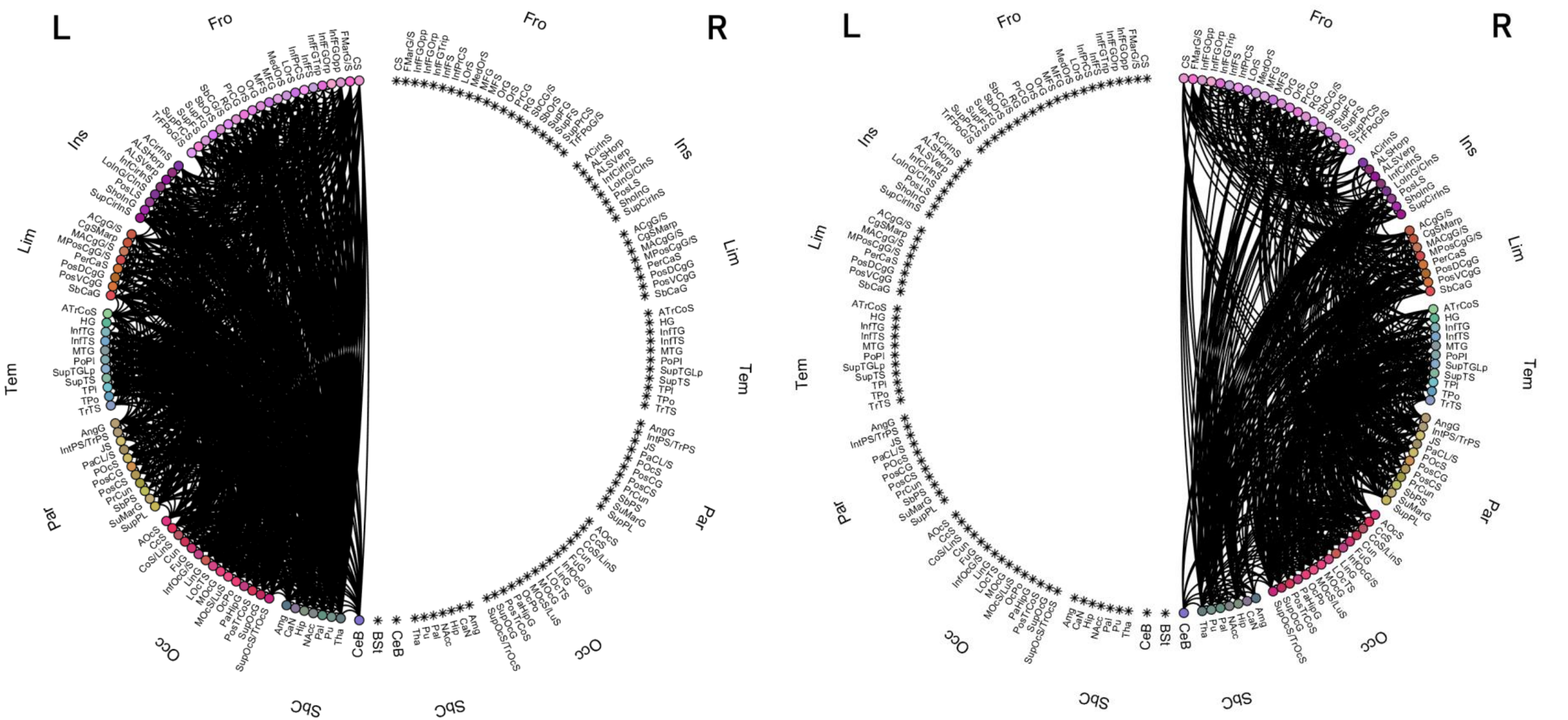
Connectogram visualization

HC Template



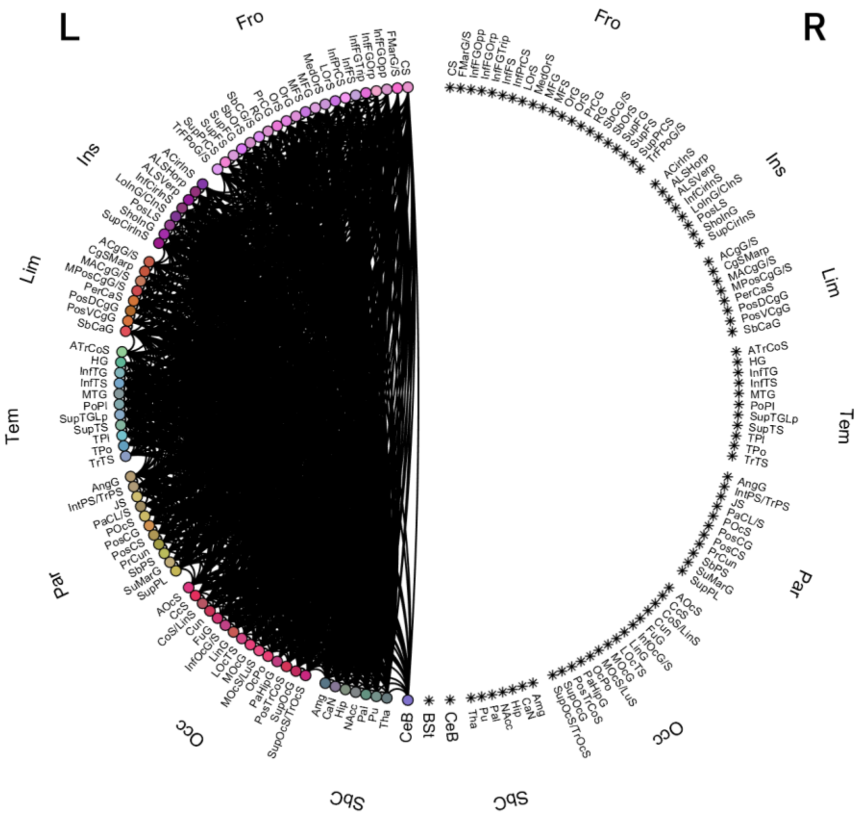
Connectogram visualization

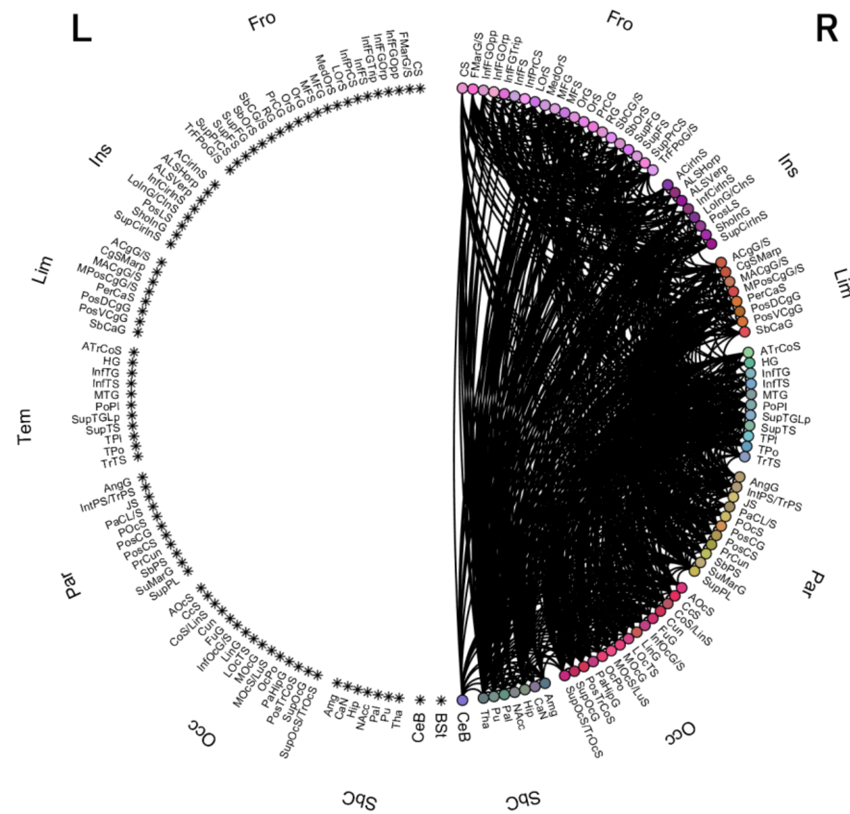
CASE 1



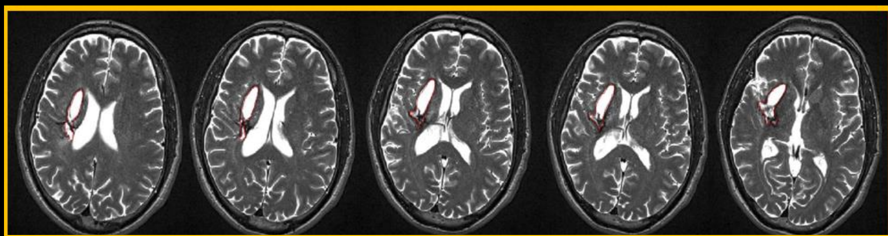
Connectogram visualization

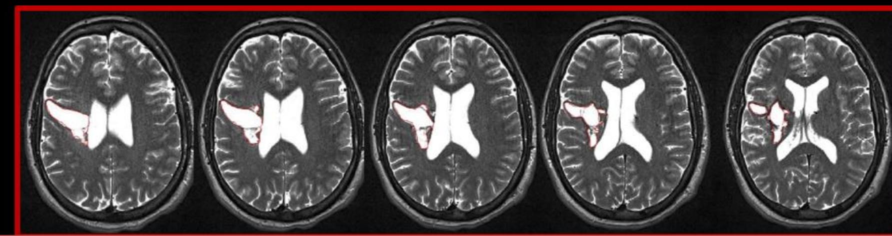
CASE 2



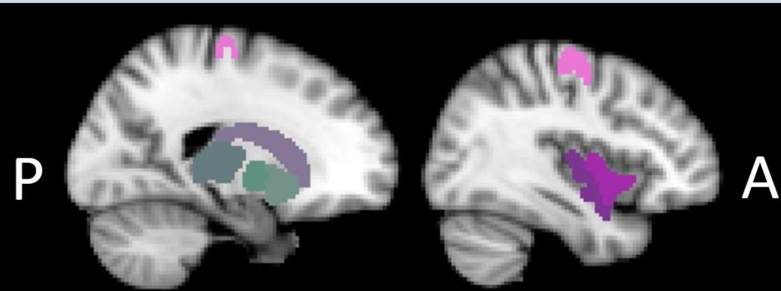


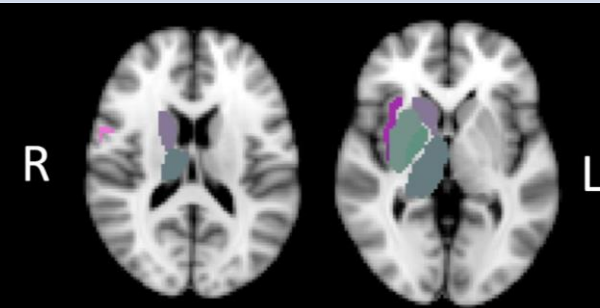
Visualization of connectivity pattern altered by stroke lesion





Case 1	Case 2
Long insular gyrus and central insular sulcus (LoInG/CInS)	Caudate nucleus (CaN)
Short insular gyri (ShoInG)	Precentral gyrus (PrCG)
Pallidum (Pal)	Pallidum (Pal)
Putamen (Pu)	Putamen (Pu)
	Thalamus (Tha)



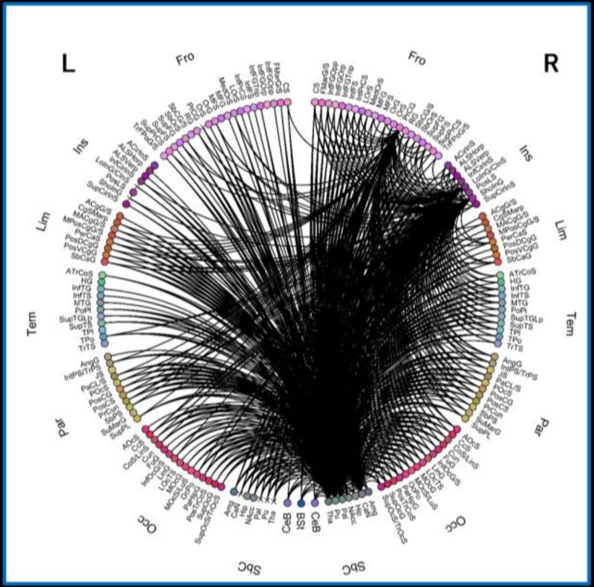


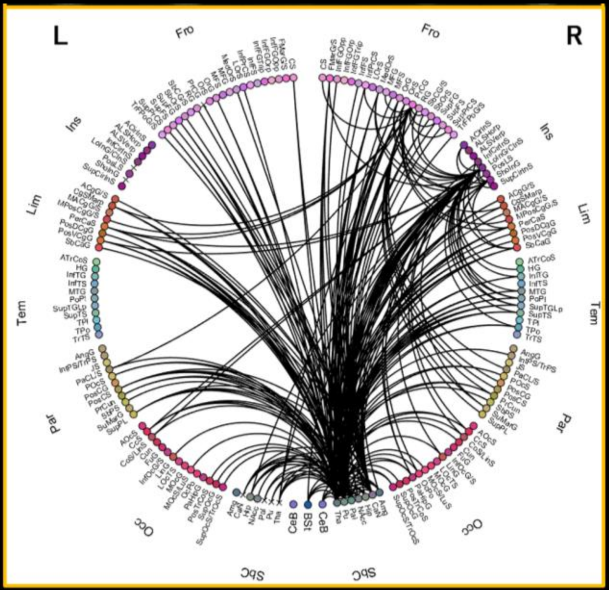
Visualization of connectivity pattern altered by stroke lesion (DTI)

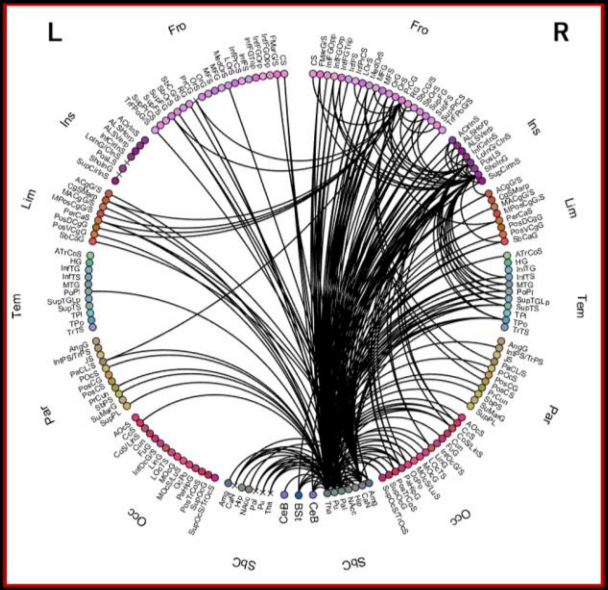
a) HC Template

b) CASE 1

c) CASE 2







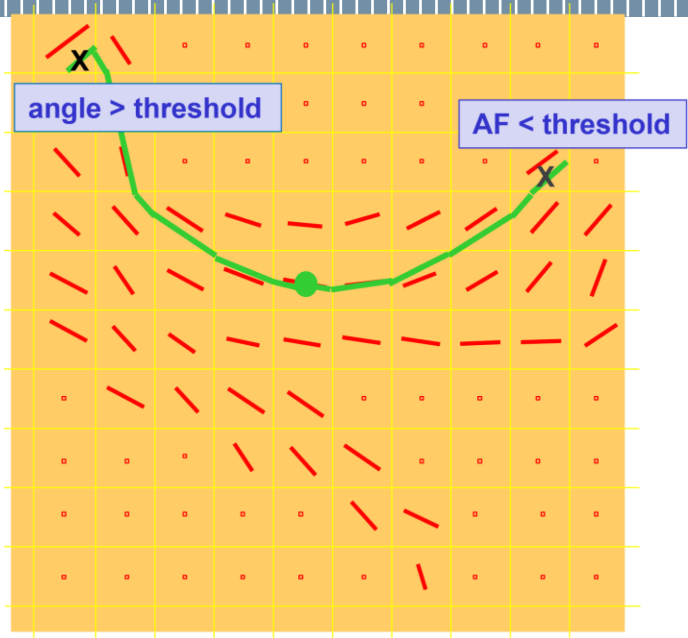
DTI vs CSD structural connectomics

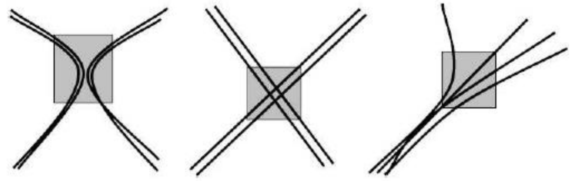
Limitations of DTI:

1. Only simplification of diffusion inside brain, and it can represent only **one major fiber direction** (average direction) **in voxel** (fibers with crossing, kissing, fanning, and curving configurations)

2. Inherently low spatial resolution leads to **partial volume effects**

3. Reconstruction of fiber path is dependent on **data acquisition conditions** (including SNR and number of diffusion encoding directions), as well as axonal geometry

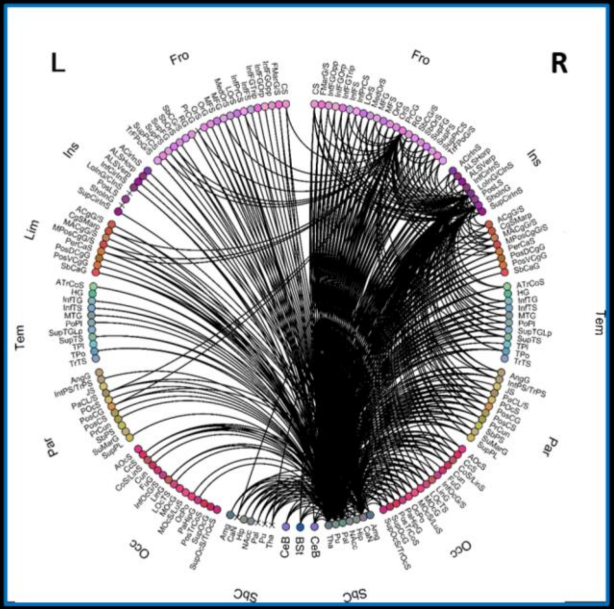




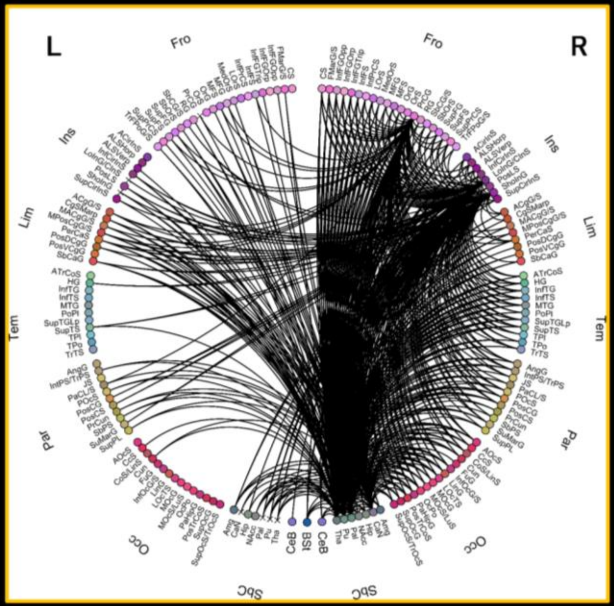
Uncertainty

Visual comparison of processing pipelines (CSD)

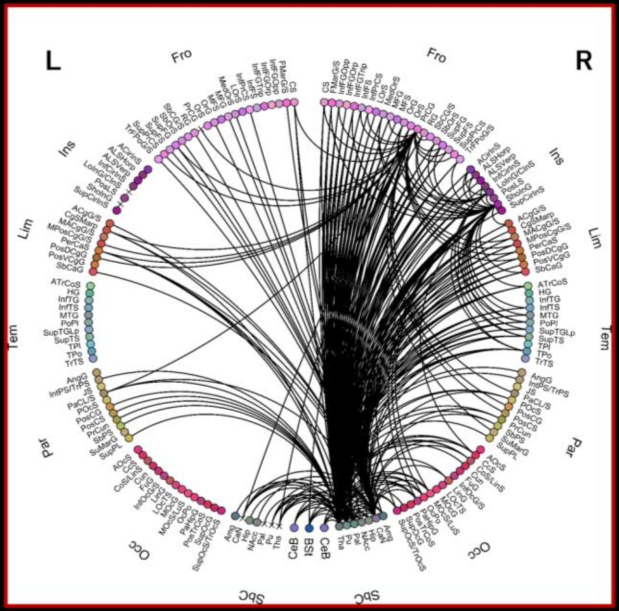
a) HC Template



b) CASE 1



c) CASE 2



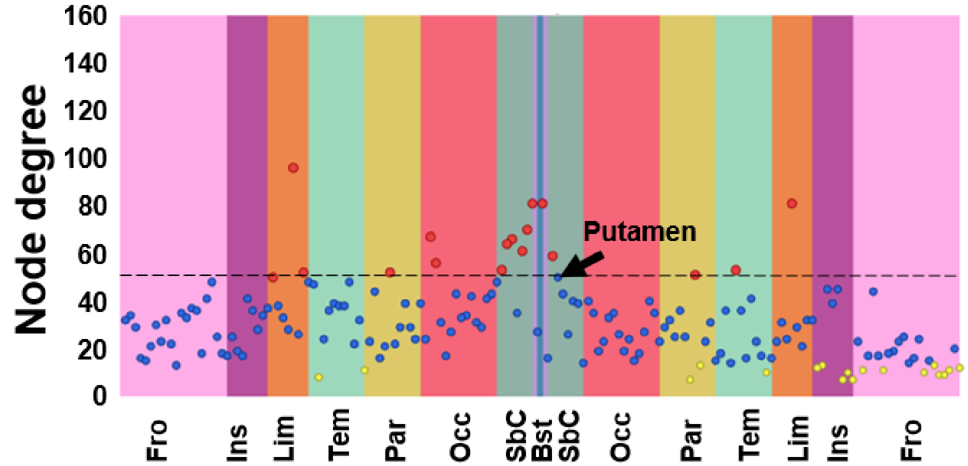
Global topological properties analysis

Graph-based indexes	HC	Case 1	HC-Case1 Delta (%)	Case 2	HC-Case2 Delta (%)
Density	47.509%	18.647%	28.9%*	22.321%	25.2%*
Average Degree	77.915	30.582	60.7%	36.606	53.0%
Average Strength (W)	3.048	1.233	59.5%	1.396	54.2%
Clustering coefficient	0.76	0.614	19.2%	0.604	20.5%
Clustering coefficient (W)	0.019	0.017	10.5%	0.015	21.1%
Characteristic path length	1.542	2.092	-35.7%	1.927	-25.0%
Characteristic path length (W)	18.302	35.211	-92.4%	28.544	-56.0%
Global efficiency	0.735	0.549	25.3%	0.587	20.1%
Global efficiency (W)	0.068	0.039	42.6%	0.045	33.8%
Small-worldness	1.591	2.881	-81.1%	2.531	-59.1%
Modularity	0.193	0.38	-96.9%	0.351	-81.9%
Coreness statistic	0.321	0.402	-25.2%	0.367	-14.3%

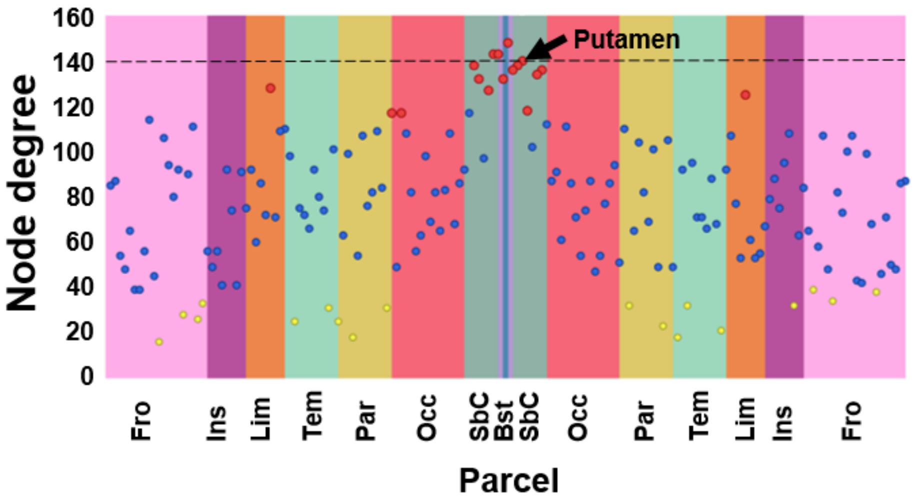
* unnormalized by HC value

Local topological properties analysis

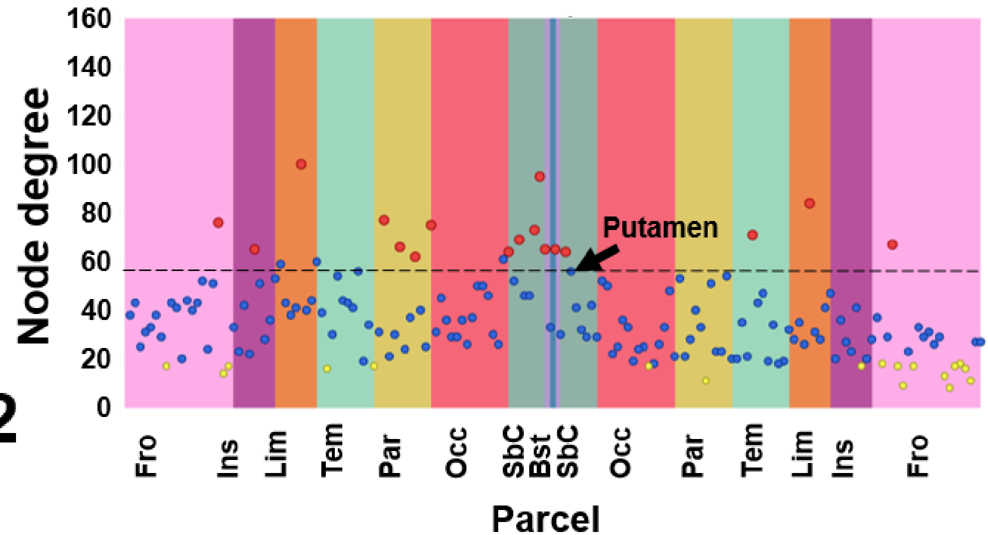
Case 1



HCs



Case 2



Discussion

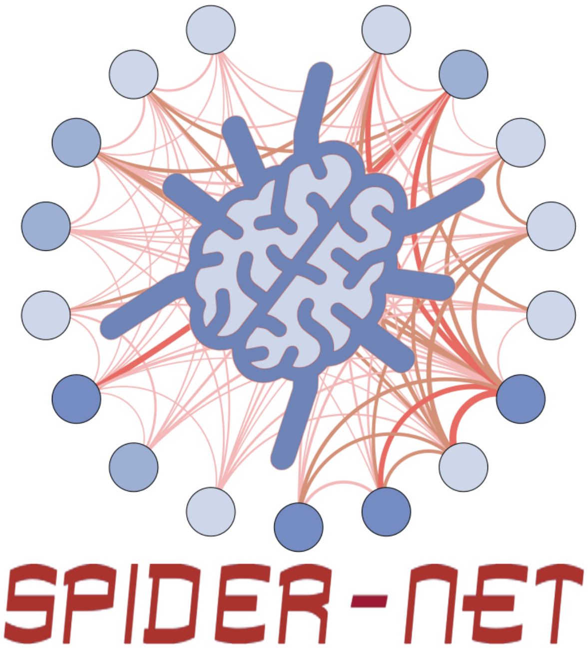
1. In the case 1 pattern of connectomics is significantly different from the case 2, mirroring the greater clinical severity of the former

2. The pattern of disconnection involved both the right hemisphere, where the stroke lesions were present, and the contralateral one

3. The impairment of the cortical areas of interest determined a decrease in both short-range and long-range connections within the hemisphere ipsilateral to the stroke lesion

4. Interhemispheric connectivity was particularly compromised, probably because subcortical nuclei, which are integration hubs of extrapyramidal systems, were affected by the lesions

Neurophysiological and neurological perspectives



- Better insight into cerebral circuits: integration of specific functional and structural information
- Lesional studies
- Studies on neurodegeneration
- AI methods are powerful in black-box analyses. Conversely, SPIDER-NET can help focused explorations

Conclusions and perspectives

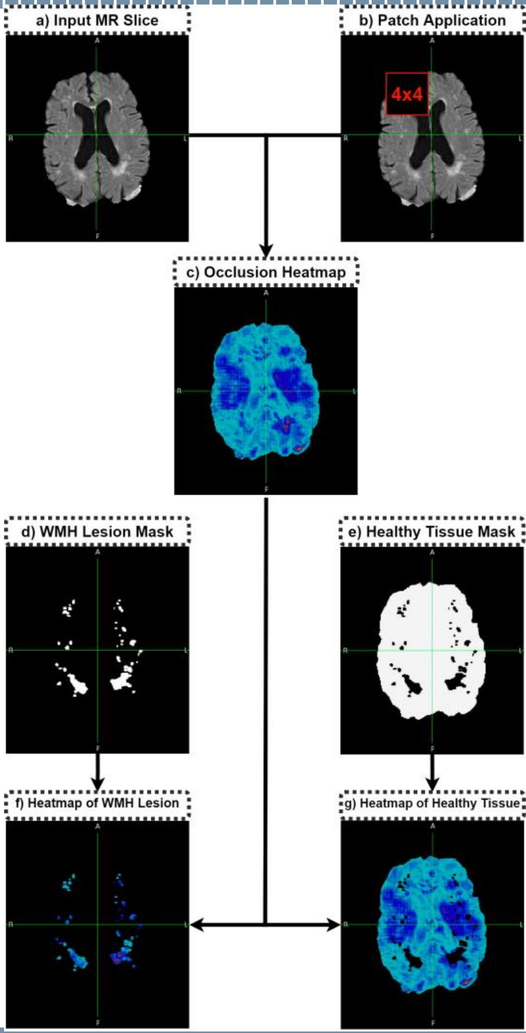
SPIDER-NET

1. will be soon employed on an entire group study to assess differences in the organization of brain connectivity between Alzheimer's Disease (AD) patients and HC subjects

   - In a recent preliminary study, we employed explainable Artificial Intelligence (XAI) to classify AD MRI slices and investigate the contribution of White Matter Hyperintensities (WMHs)

   - We are currently using XAI on connectivity data extracted from the same dataset

   - ❑ Analysis of explainability and connectivity of regions in relation to AD to identify the sub-networks which mostly explain the classification and differ from HC group



Conclusions and perspectives

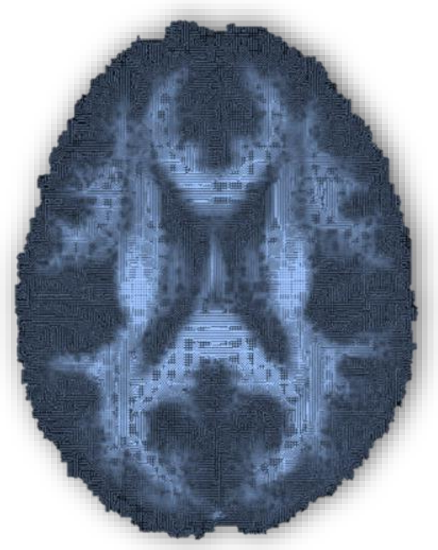
SPIDER-NET

2. may be employed for a posteriori analysis of connectivity measures to test the robustness of the adopted procedures

    - Limitation: gold-standard methodologies are not established yet and even the most widespread connectivity measures and edge weighting are constantly object of research (e.g. DTI)

3. may be generalized to be used with other brain connectivity data (e.g EEG, MEG) or even in other research fields

4. may help in the definition of patient-tailored rehabilitative treatments



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