The human brain resting state networks based on high time resolution EEG

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Part 1: Introduction

Part 2: Tutorial on using software

Part 1: Introduction

What is neuroimaging?

<u>99% of the time</u>

(example)

-Measure BOLD signals in two groups of subjects

-At each voxel in the brain, compare the BOLD signals by computing a *t*-test (millions of *t*-tests, one for each voxel)

-Set an appropriate threshold (correct for multiple tests), and report significant voxels (hot-spots or cold-spots)

Example: comparing Schizophrenic patients with normal control subjects

◆ Human Brain Mapping 25:60–69(2005)

Beyond Hypofrontality: A Quantitative Meta-Analysis of Functional Neuroimaging Studies of Working Memory in Schizophrenia

David C. Glahn,[1,2*] J. Daniel Ragland,[3] Adir Abramoff,[4] Jennifer Barrett,[1]
Angela R. Laird,[2] Carrie E. Bearden,[5] and Dawn I. Velligan[1]

Schizophrenic patients
control subjects

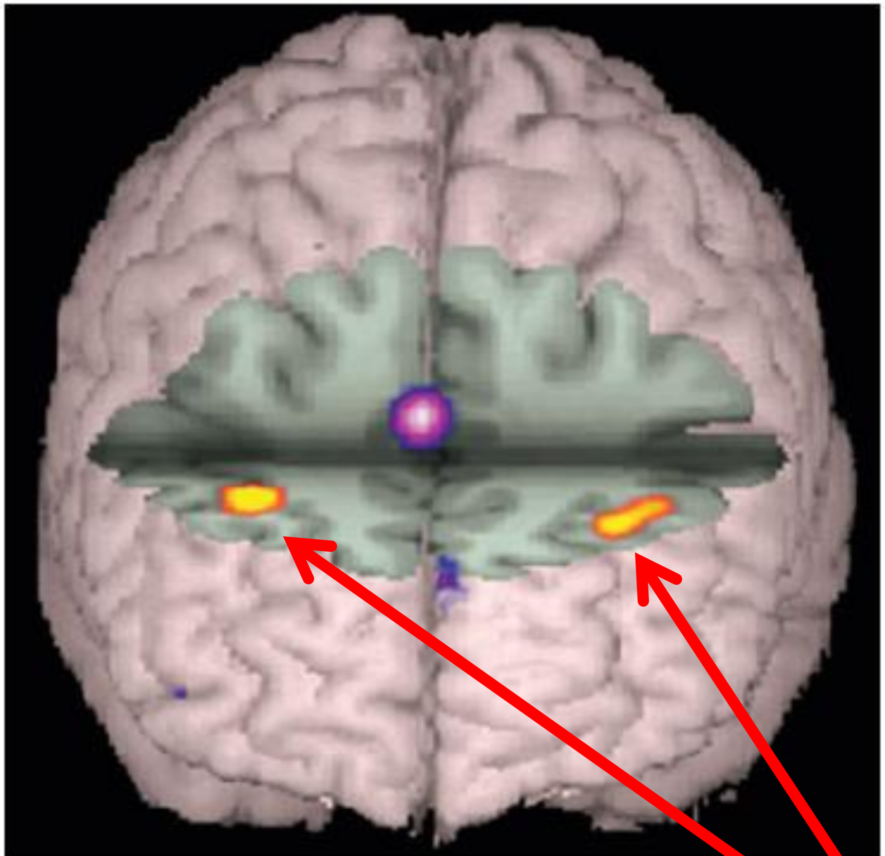


Figure 2.

Volume rendering of between-group contrasts where relative increased activity for healthy subjects is presented in red-yellow (DLPFC; BA9) and relative increased activity for patients with schizophrenia is shown in purple-pink (anterior cingulate; BA32). Although patients with schizophrenia engaged the DLPFC less than comparison subjects, they overactivated a portion of the anterior cingulate. Evidence of reduced DLPFC activation and increased activity in the anterior cingulate may be consistent with the notion that schizophrenia disrupts or reverses the normal functional connectivity of prefrontal and limbic structures.

◆ Human Brain Mapping 25:60–69(2005)

ity: A Quantitative
tional Neuroimaging
mory in Schizophrenia

Hypometabolism in schizophrenia: is it localized only here???

There is nothing wrong with classical neuroimaging

However, it gives <u>very</u> limited information

Can behavioral disorders, therapy effects, or cognition be assigned to some few hot-spots in the brain?

NO

Alternative approach: from hot-spots to distributions (networks)

Different parts of the brain work in a certain <u>relationship</u> to each other

Break the <u>relations</u>, and you have an emergent behavioral disorder

What is the "resting state"?

- Wakeful rest
- Mind-wandering
- Spontaneous thoughts
- Daydreaming
- Retrieving memories
- Stimulus independent thoughts
- Absence of goal-directed neuronal action and external input

- REST = Random Episodic Spontaneous Thoughts

- EEG: resting, eyes closed, awake

What is the “resting state”?

Resting brain ≠ Inactive brain

NEUROSCIENCE

The Brain’s Dark Energy

Marcus E. Raichle

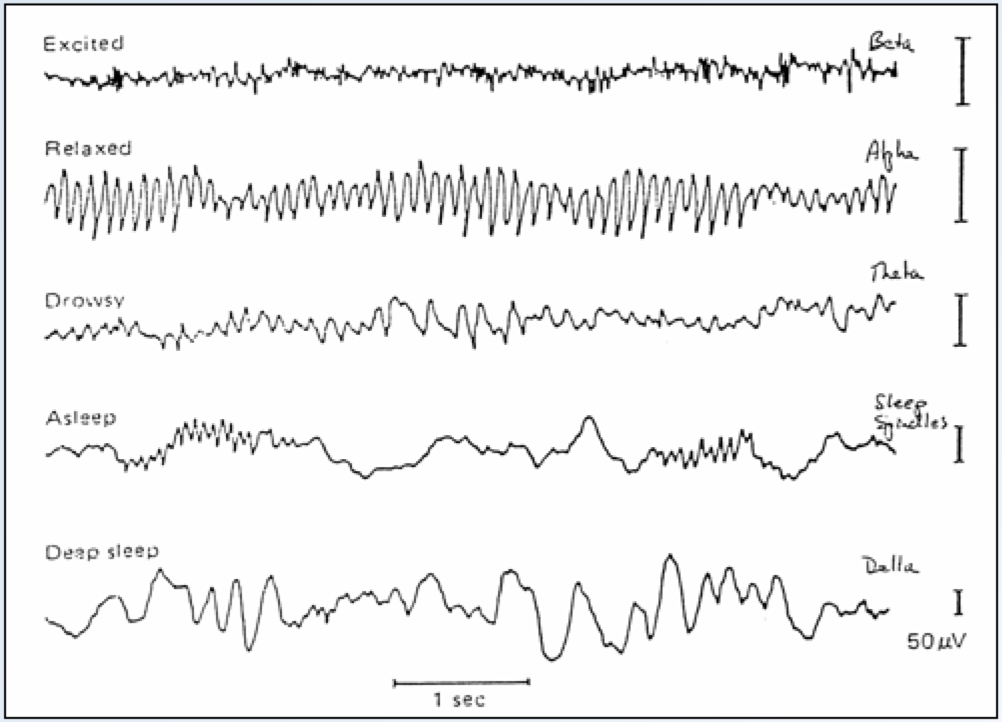
SCIENCE VOL 314 24 NOVEMBER 2006

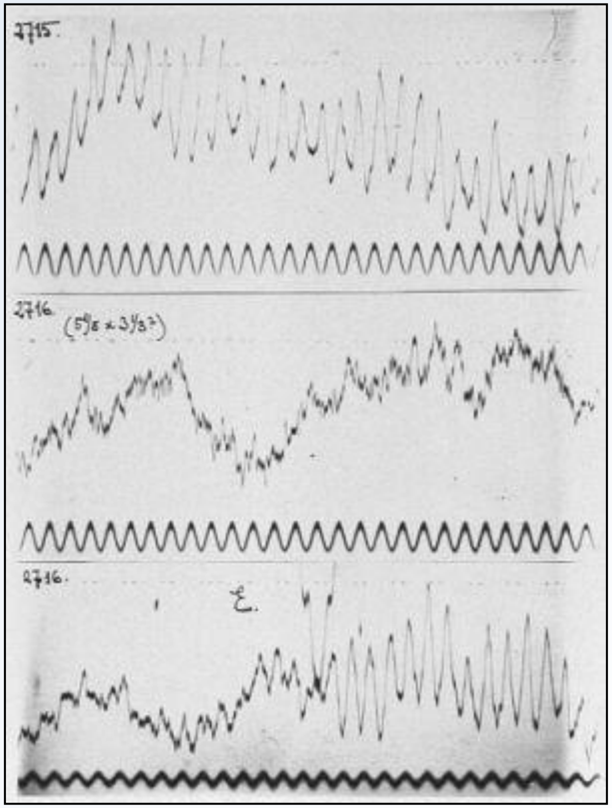
it is estimated that 60 to 80% of the energy budget of the brain supports communication among neurons and their supporting cells (*2*). The additional energy burden associated with momentary demands of the environment may be as little as 0.5 to 1.0% of the total energy budget (*2*).

The resting state is important

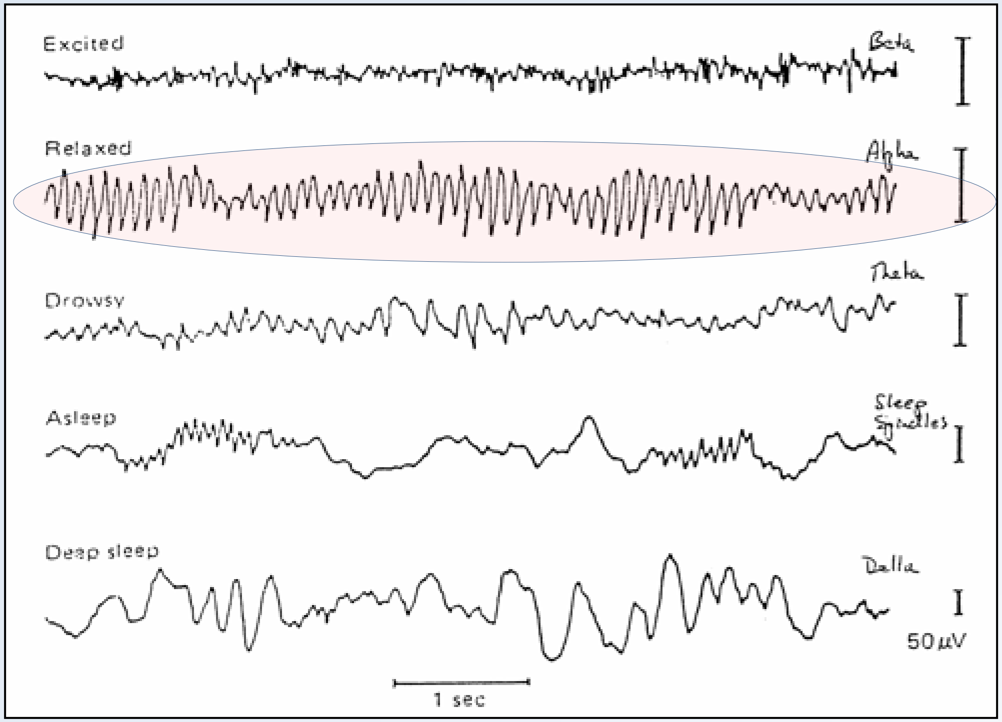
It is the dynamic substrate of the "present", momentary state of the brain, and determines the fate of incoming information

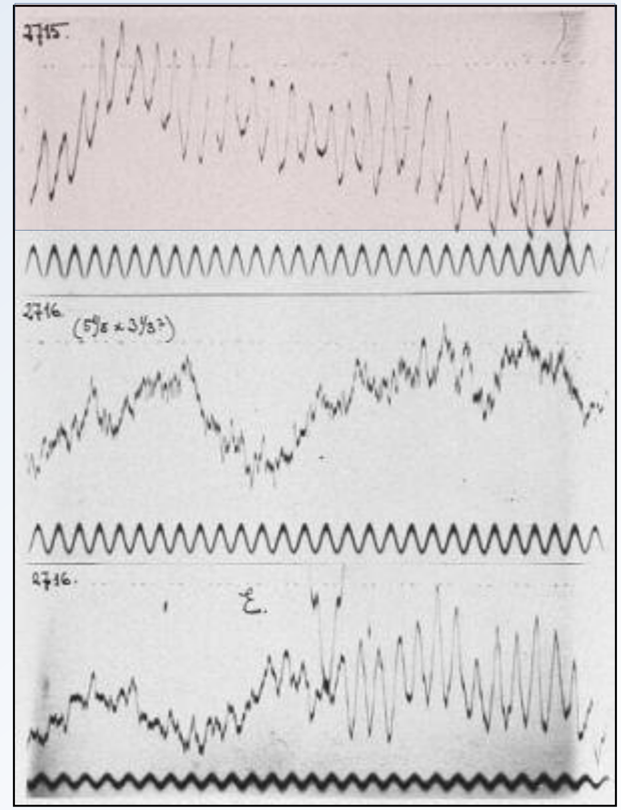
Resting state, first observations: EEG, Hans Berger, 1929





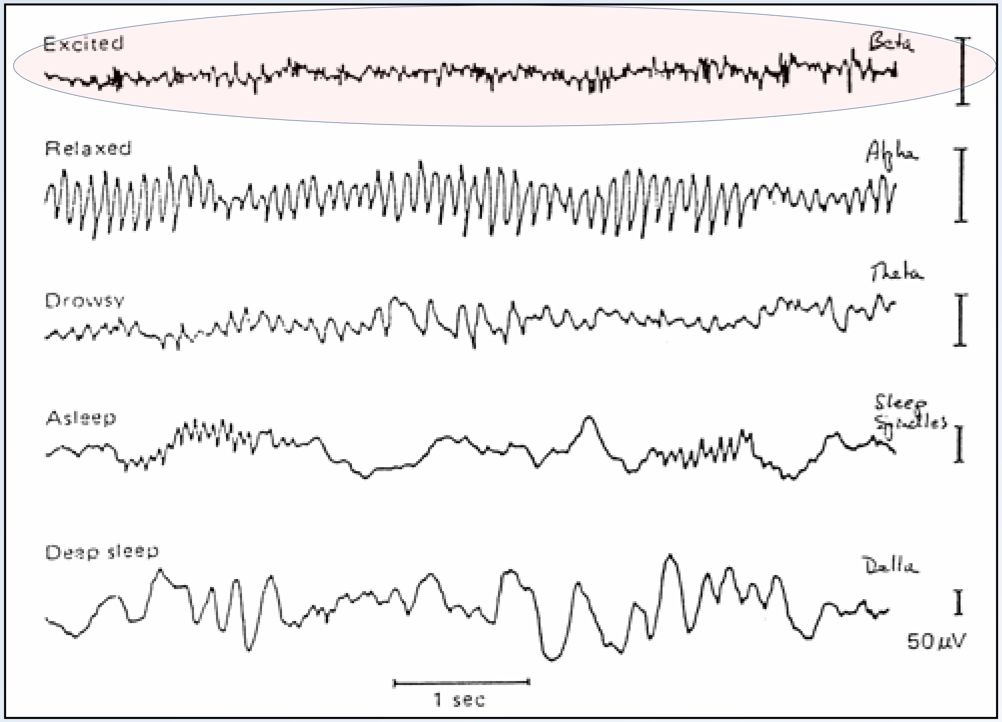
Resting state, first observations: EEG, Hans Berger, 1929

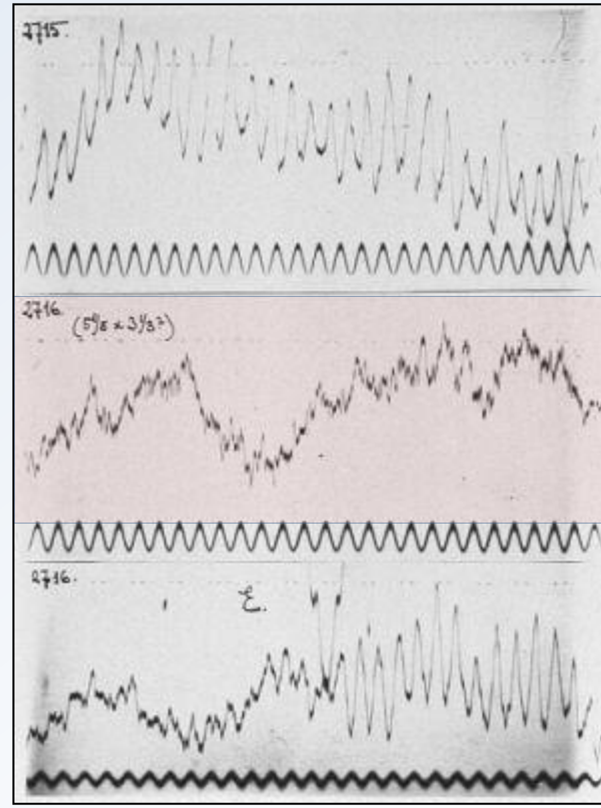




Rest (eyes closed)

Resting state, first observations: EEG, Hans Berger, 1929





Eyes-open

<u>What are “resting state networks (RSN)”?</u>

New definition (less than 10 years old), old ideas

First famous network: “default mode”, but it is just one of the many “resting state networks”

Default mode network (DMN): a set of brain regions that are jointly active during rest, and that jointly deactivate in any task.

Default mode network example

BRAIN CONNECTIVITY
Volume 1, Number 1, 2011

DOI: 10.1089/brain.2011.0019

REVIEW ARTICLES

The Restless Brain

Marcus E. Raichle

De

BRAI
Volur
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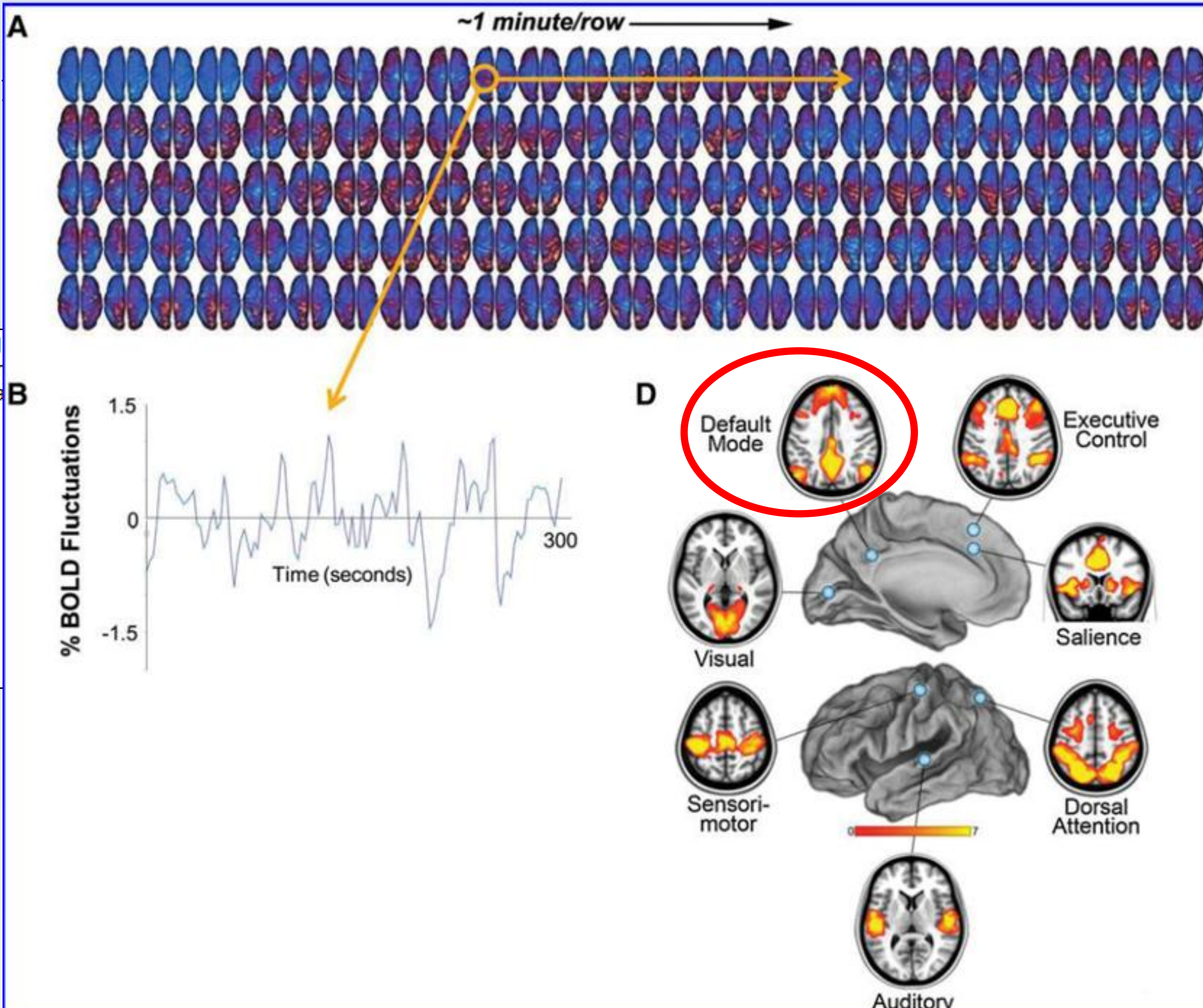
DOI:

.ES



What are "resting state networks"?

A network is composed of a group of brain regions, with "correlated" time varying activities.

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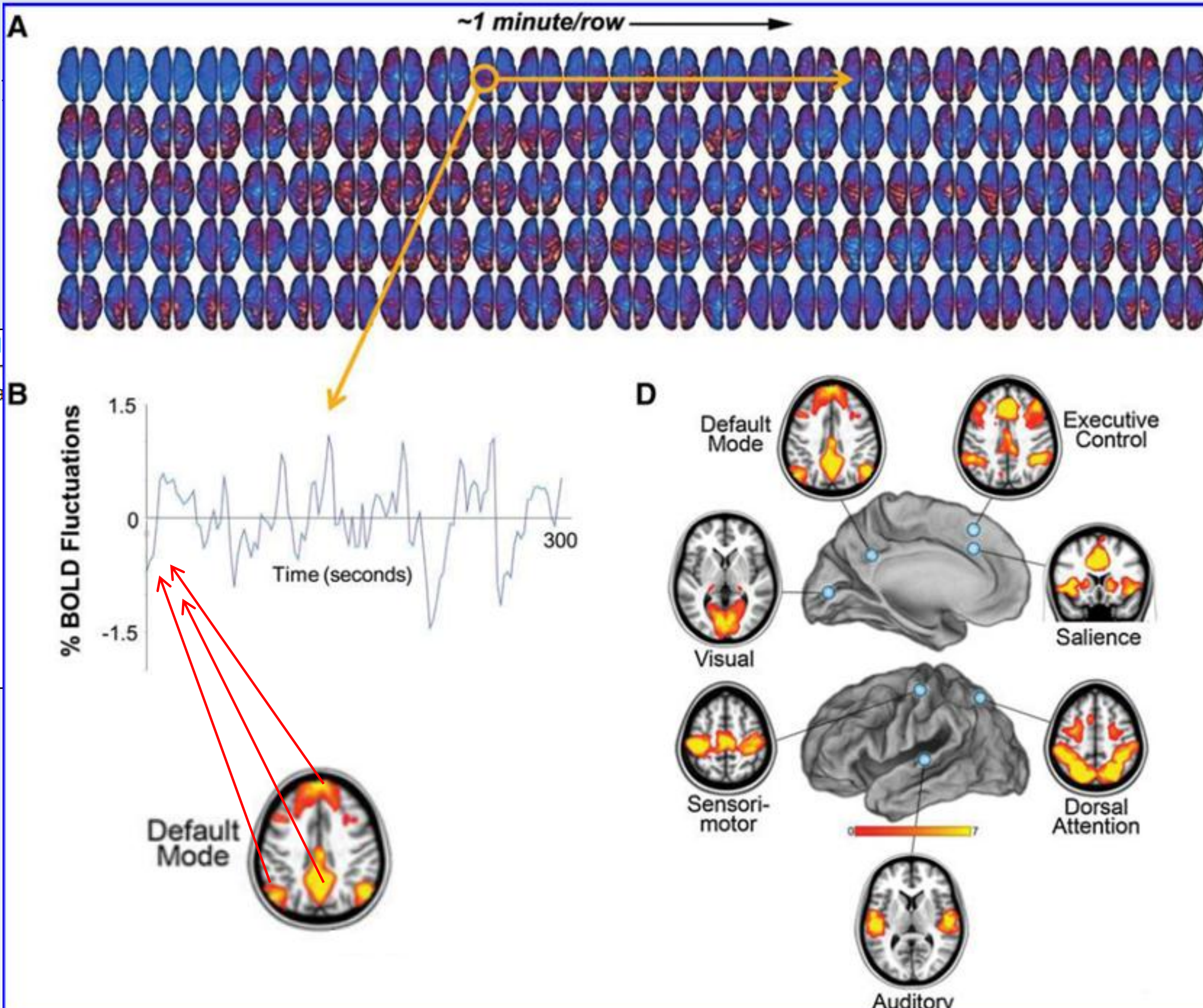

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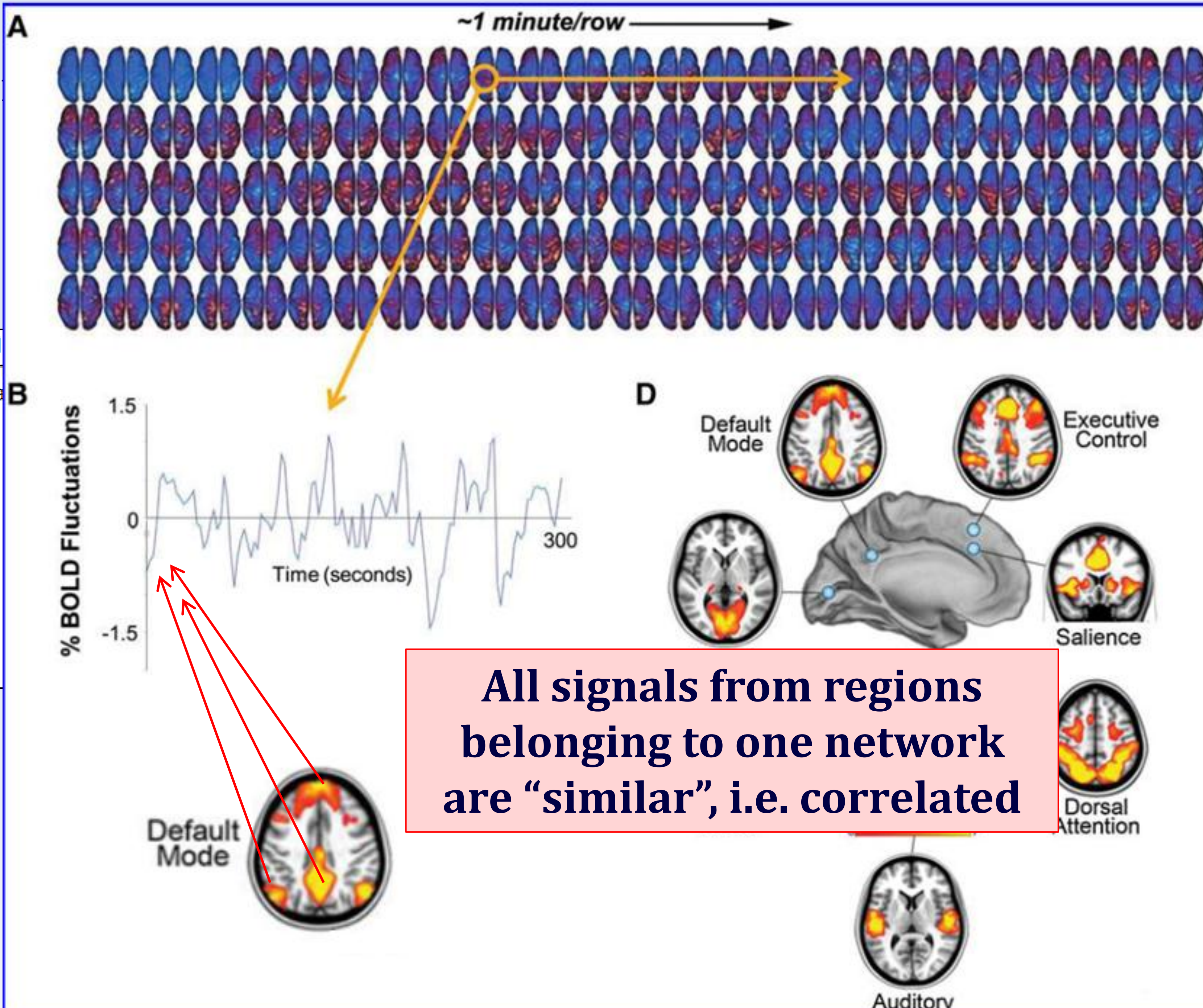

What are “resting state networks”?

A network is composed of a group of brain regions, with “correlated” time varying activities.

Different networks work independently of each other.

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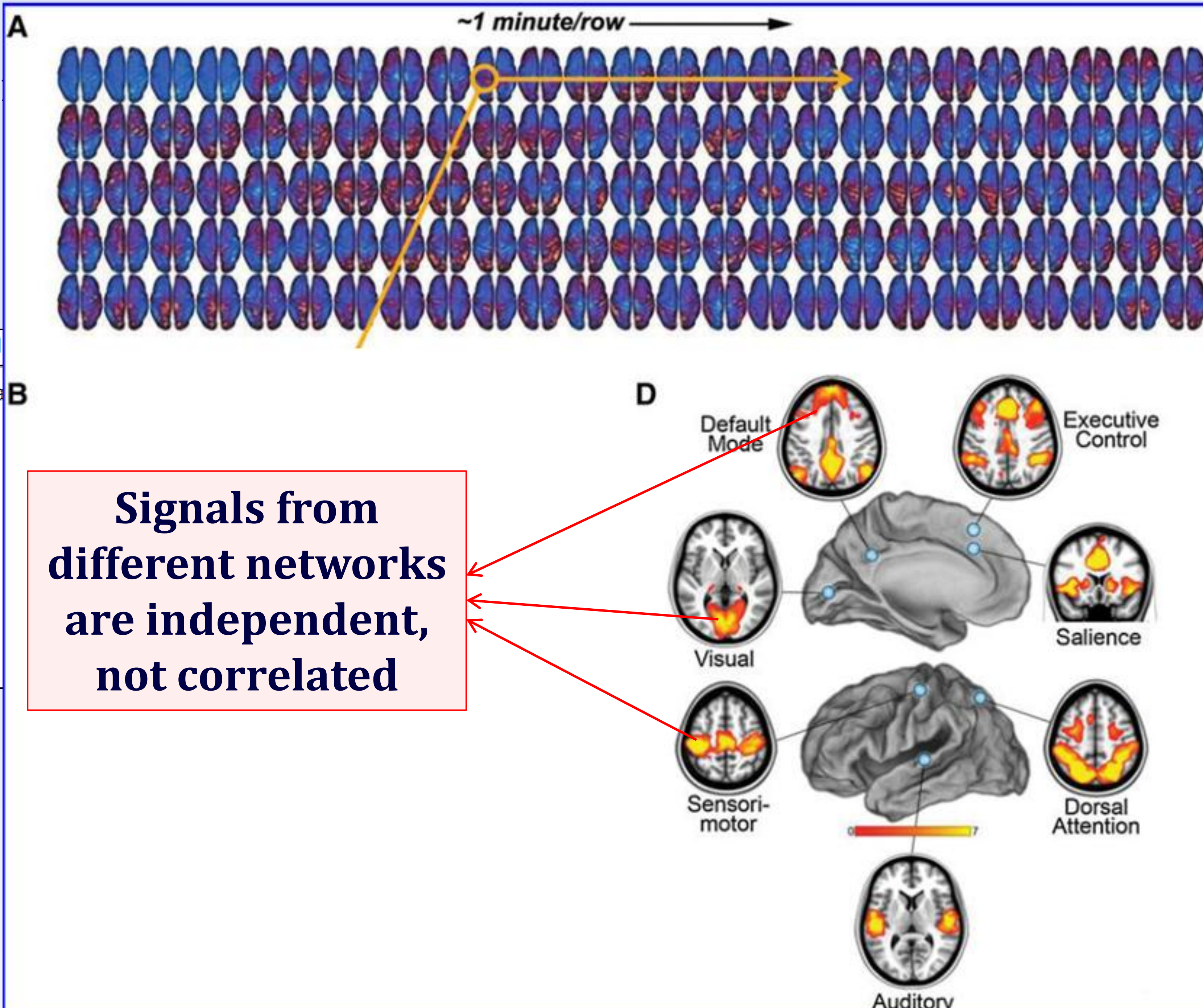
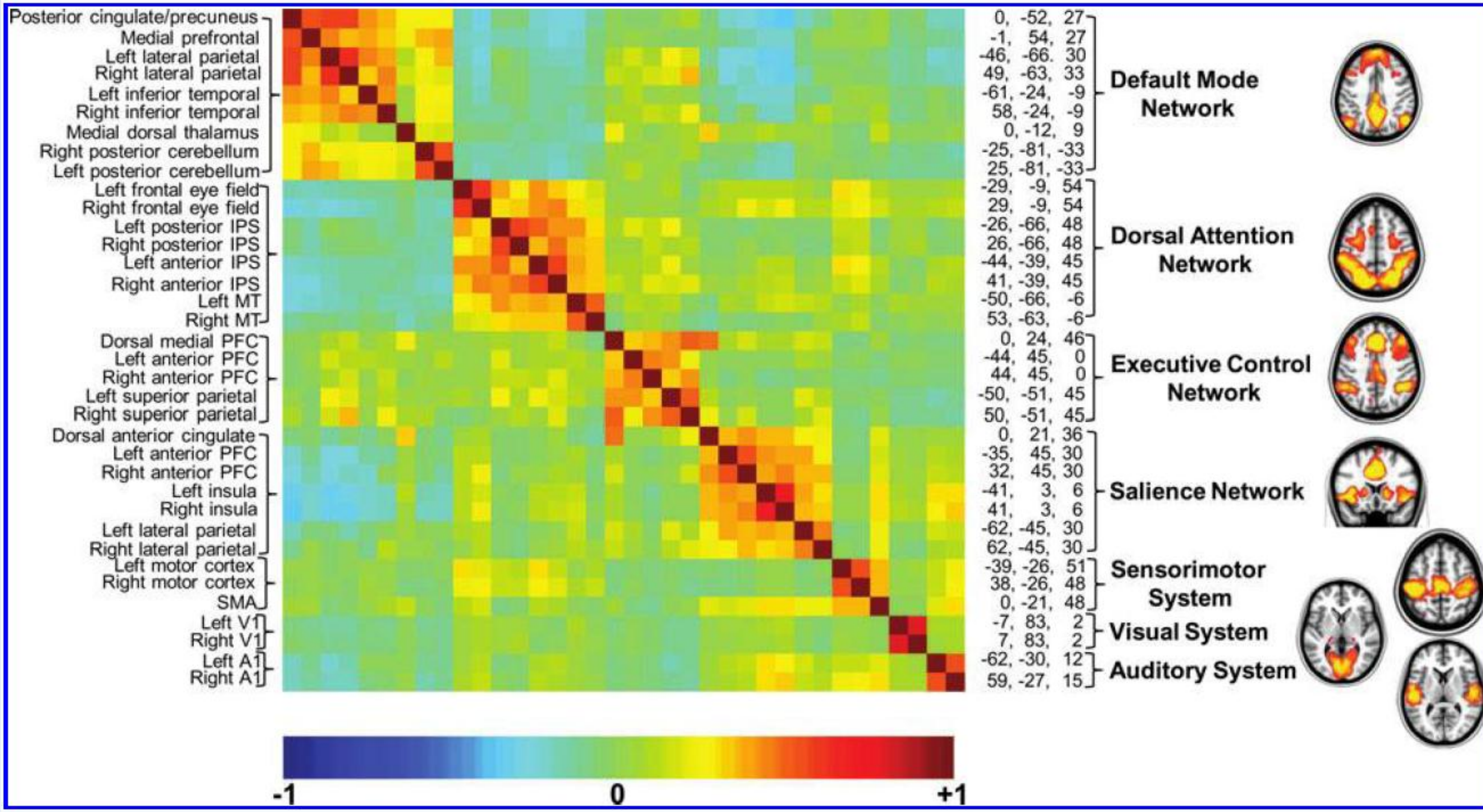


Signals from different networks are independent, not correlated

Default mode network example



Resting state networks

Most of the recent literature, based on fMRI experiments, use many different methods of analysis such as ICA (independent components analysis), correlation analysis, clustering techniques, all with converging results

frontiers in
SYSTEMS NEUROSCIENCE

ORIGINAL RESEARCH ARTICLE
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A baseline for the multivariate comparison of resting-state networks

Elena A. Allen[1]*, Erik B. Erhardt[1], Eswar Damaraju[1], William Gruner[1,2], Judith M. Segall[1,3], Rogers F. Silva[1,2], Martin Havlicek[1,2], Srinivas Rachakonda[1], Jill Fries[1], Ravi Kalyanam[1,2], Andrew M. Michael[1], Arvind Caprihan[1], Jessica A. Turner[1,4], Tom Eichele[5], Steven Adelsheim[4], Angela D. Bryan[1,6,7], Juan Bustillo[4,8], Vincent P. Clark[1,6,8], Sarah W. Feldstein Ewing[1], Francesca Filbey[1,9], Corey C. Ford[10], Kent Hutchison[1,6,8], Rex E. Jung[1,11], Kent A. Kiehl[1,6,8], Piyadasa Kodituwakku[12], Yuko M. Komesu[13], Andrew R. Mayer[1,10], Godfrey D. Pearlson[14,15,16], John P. Phillips[1,10], Joseph R. Sadek[4,17], Michael Stevens[14,15], Ursina Teuscher[1,6], Robert J. Thoma[1,4,6] and Vince D. Calhoun[1,2,4,8,15]

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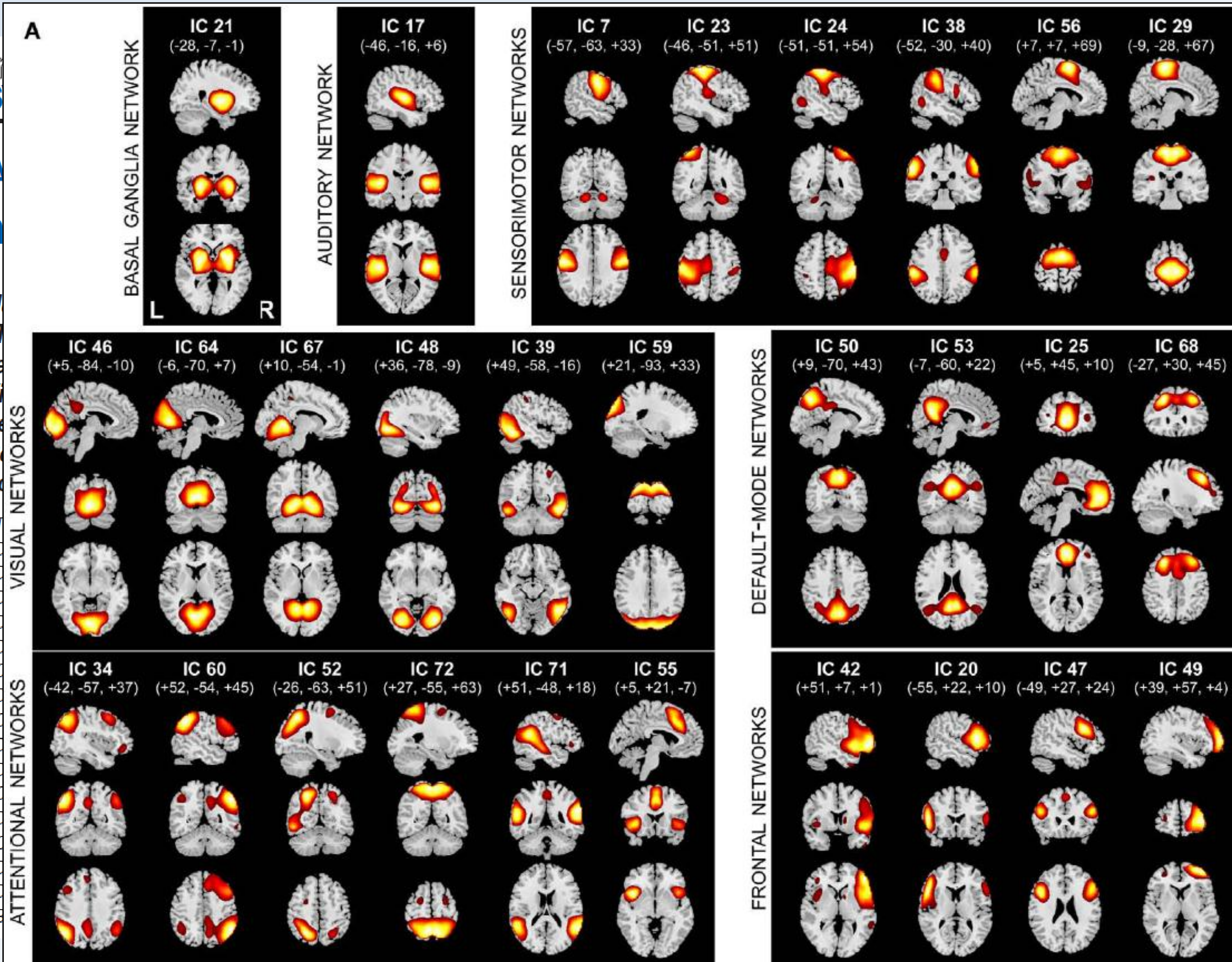
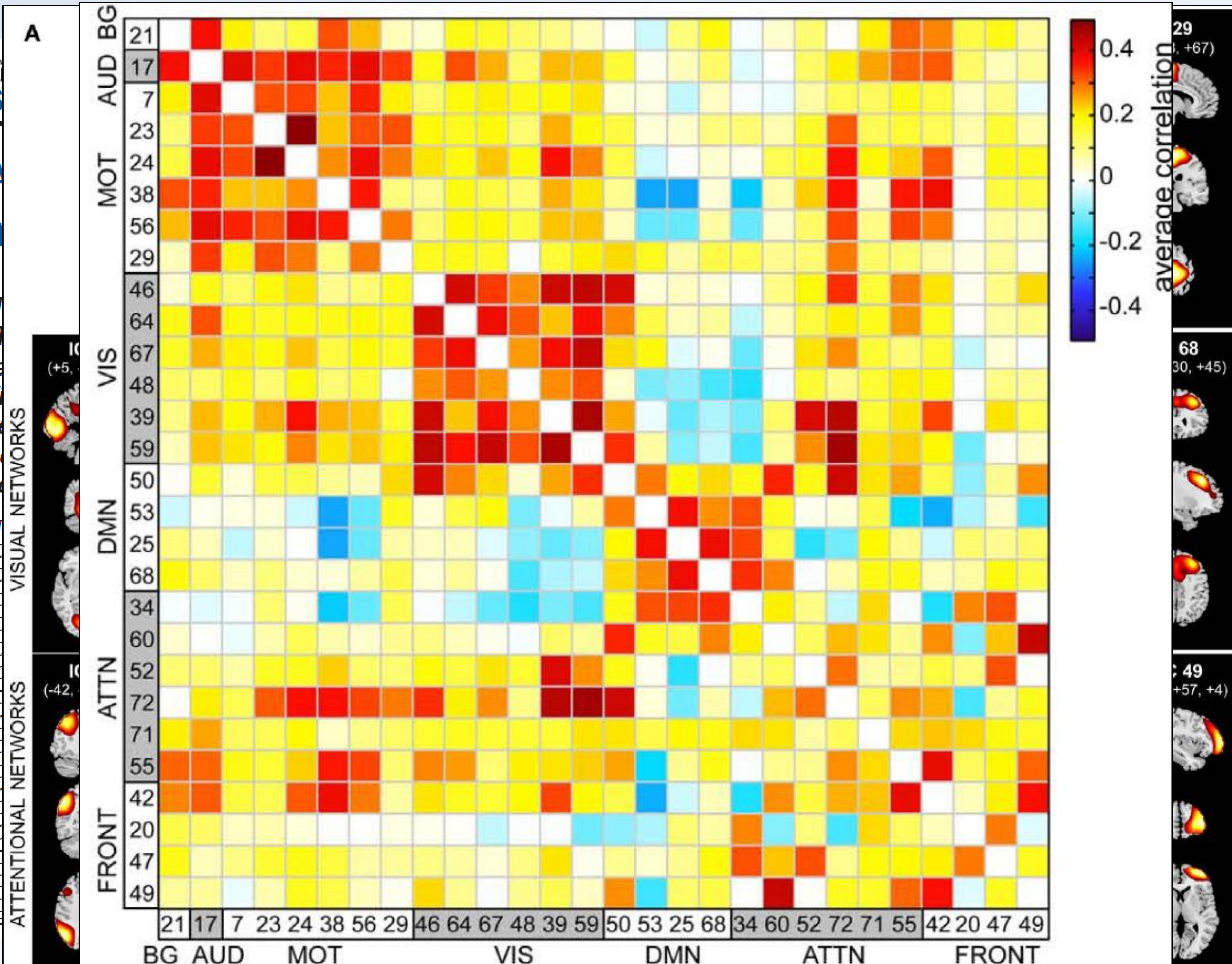


A
BASAL GANGLIA NETWORK
IC 21
(-28, -7, -1)
L
R
AUDITORY NETWORK
IC 17
(-46, -16, +6)
SENSORIMOTOR NETWORKS
IC 7
(-57, -63, +33)
IC 23
(-46, -51, +51)
IC 24
(-51, -51, +54)
IC 38
(-52, -30, +40)
IC 56
(+7, +7, +69)
IC 29
(-9, -28, +67)
VISUAL NETWORKS
IC 46
(+5, -84, -10)
IC 64
(-6, -70, +7)
IC 67
(+10, -54, -1)
IC 48
(+36, -78, -9)
IC 39
(+49, -58, -16)
IC 59
(+21, -93, +33)
DEFAULT-MODE NETWORKS
IC 50
(+9, -70, +43)
IC 53
(-7, -60, +22)
IC 25
(+5, +45, +10)
IC 68
(-27, +30, +45)
ATTENTIONAL NETWORKS
IC 34
(-42, -57, +37)
IC 60
(+52, -54, +45)
IC 52
(-26, -63, +51)
IC 72
(+27, -55, +63)
IC 71
(+51, -48, +18)
IC 55
(+5, +21, -7)
FRONTAL NETWORKS
IC 42
(+51, +7, +1)
IC 20
(-55, +22, +10)
IC 47
(-49, +27, +24)
IC 49
(+39, +57, +4)

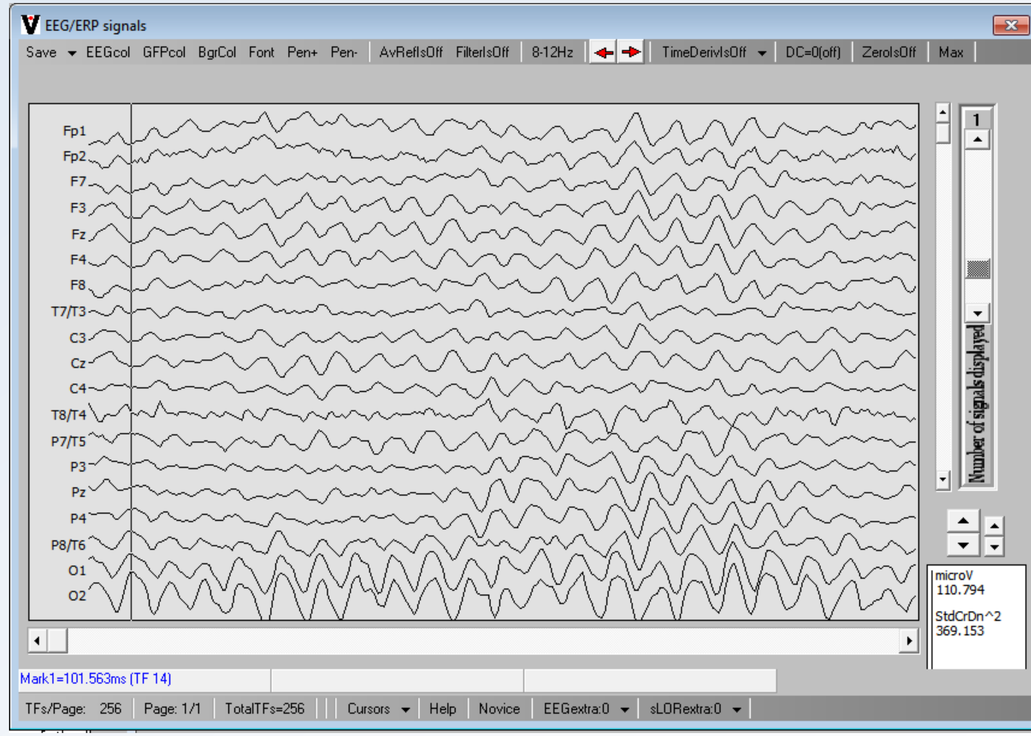

A
BG
AUD
MOT
VIS
DMN
ATTN
FRONT
21 17 7 23 24 38 56 29 46 64 67 48 39 59 50 53 25 68 34 60 52 72 71 55 42 20 47 49
0.4
0.2
0
-0.2
-0.4
average correlation
VISUAL NETWORKS
ATTENTIONAL NETWORKS

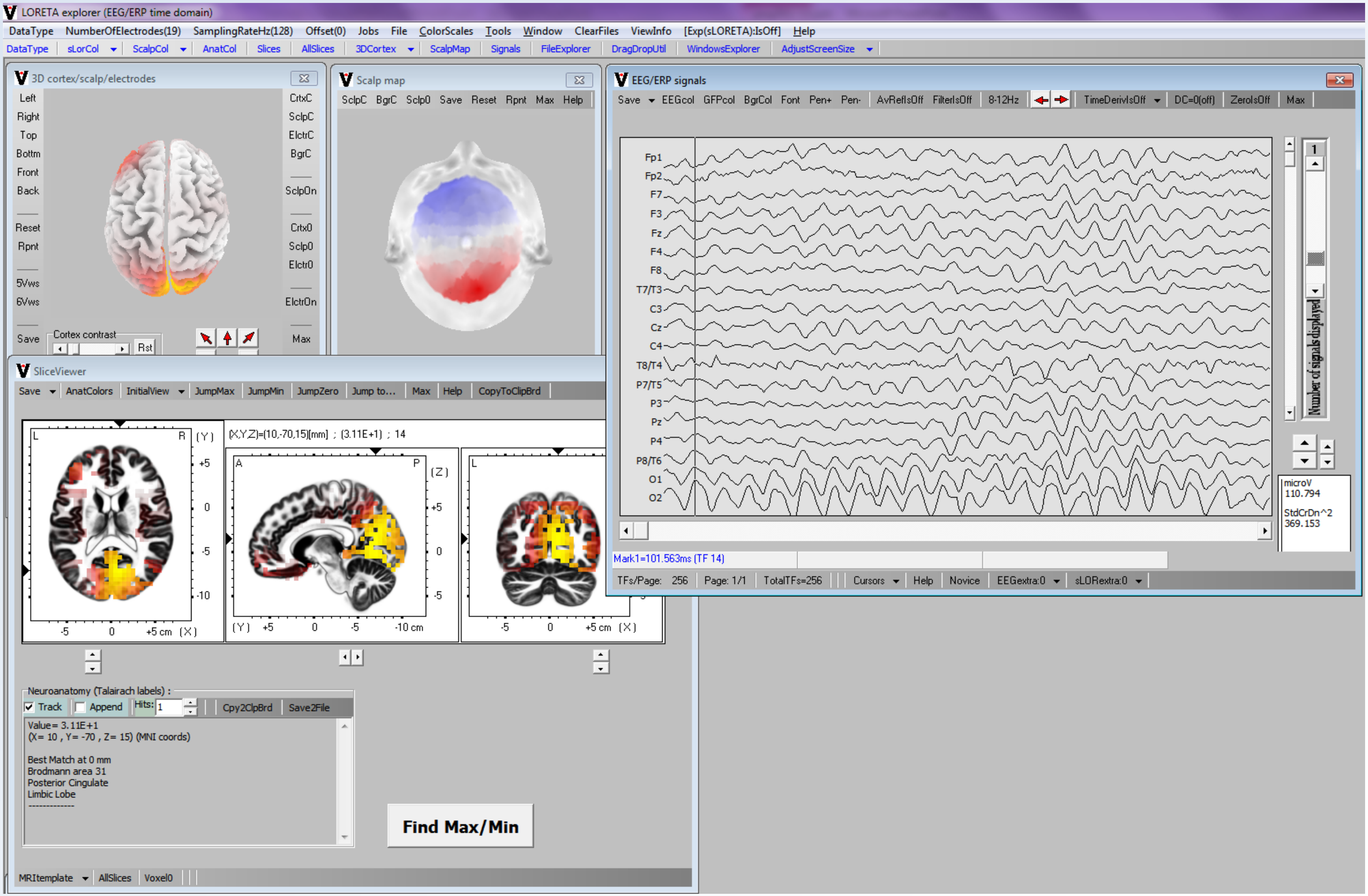
The resting state is important

It is the dynamic substrate of the "present", momentary state of the brain, and determines the fate of incoming information

During rest, the brain goes through all working modes: sensory, attention, executive control, language, ... and rest

E.g.: Attention deficit = abnormal attention network, decreased time, weak interconnections, ...


EEG/ERP signals
Save EEGcol GFPcol BgrCol Font Pen+ Pen- AvRefIsOff FilterIsOff 8-12Hz TimeDerivIsOff DC=0(off) ZeroIsOff Max
Fp1
Fp2
F7
F3
Fz
F4
F8
T7/T3
C3
Cz
C4
T8/T4
P7/T5
P3
Pz
P4
P8/T6
O1
O2
1
Number of signals displayed
microV
110.794
StdCrDn^2
369.153
Mark1=101.563ms (TF 14)
TFs/Page: 256 Page: 1/1 TotalTFs=256 Cursors Help Novice EEGextra:0 sLORextra:0


LORETA explorer (EEG/ERP time domain)
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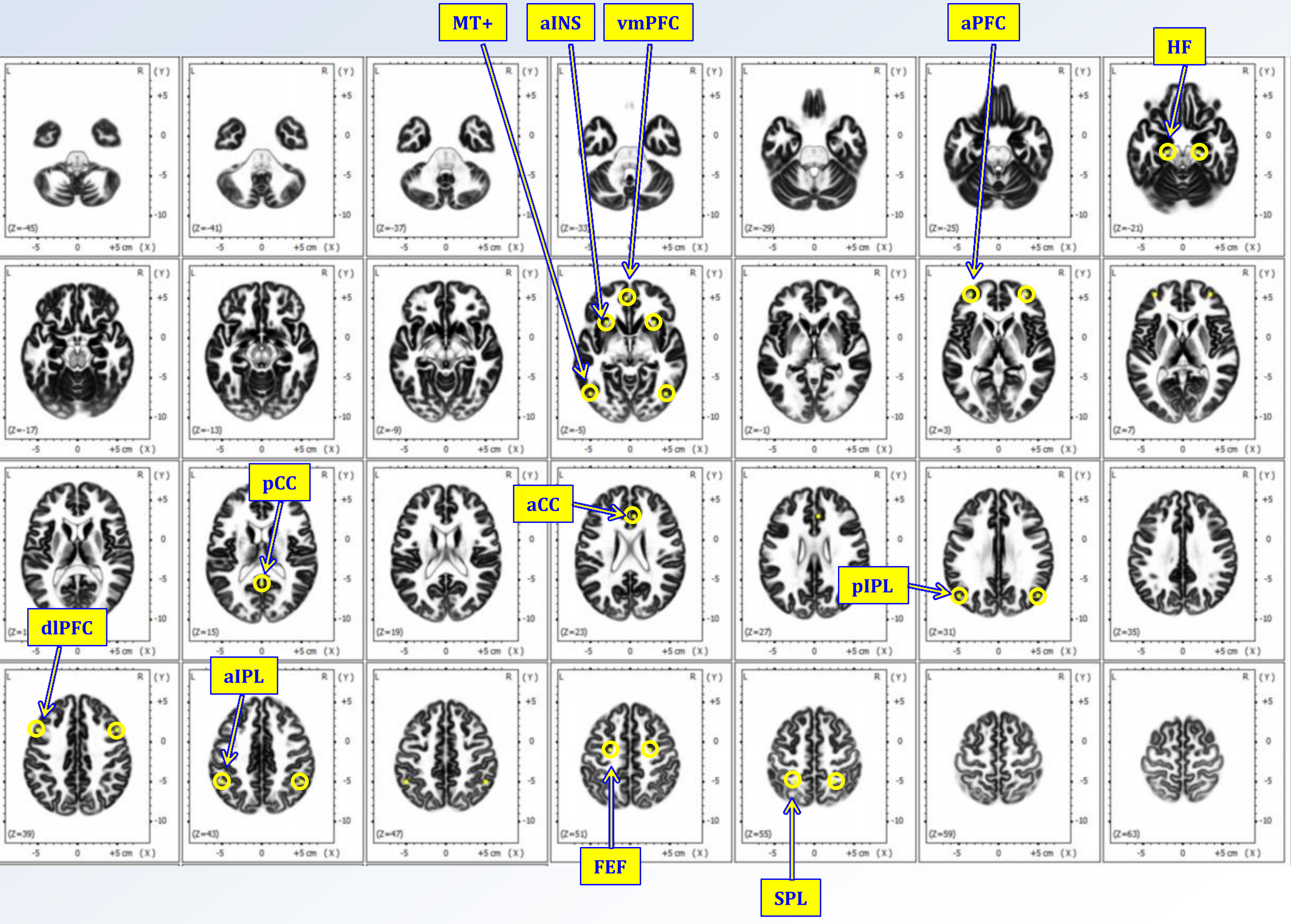
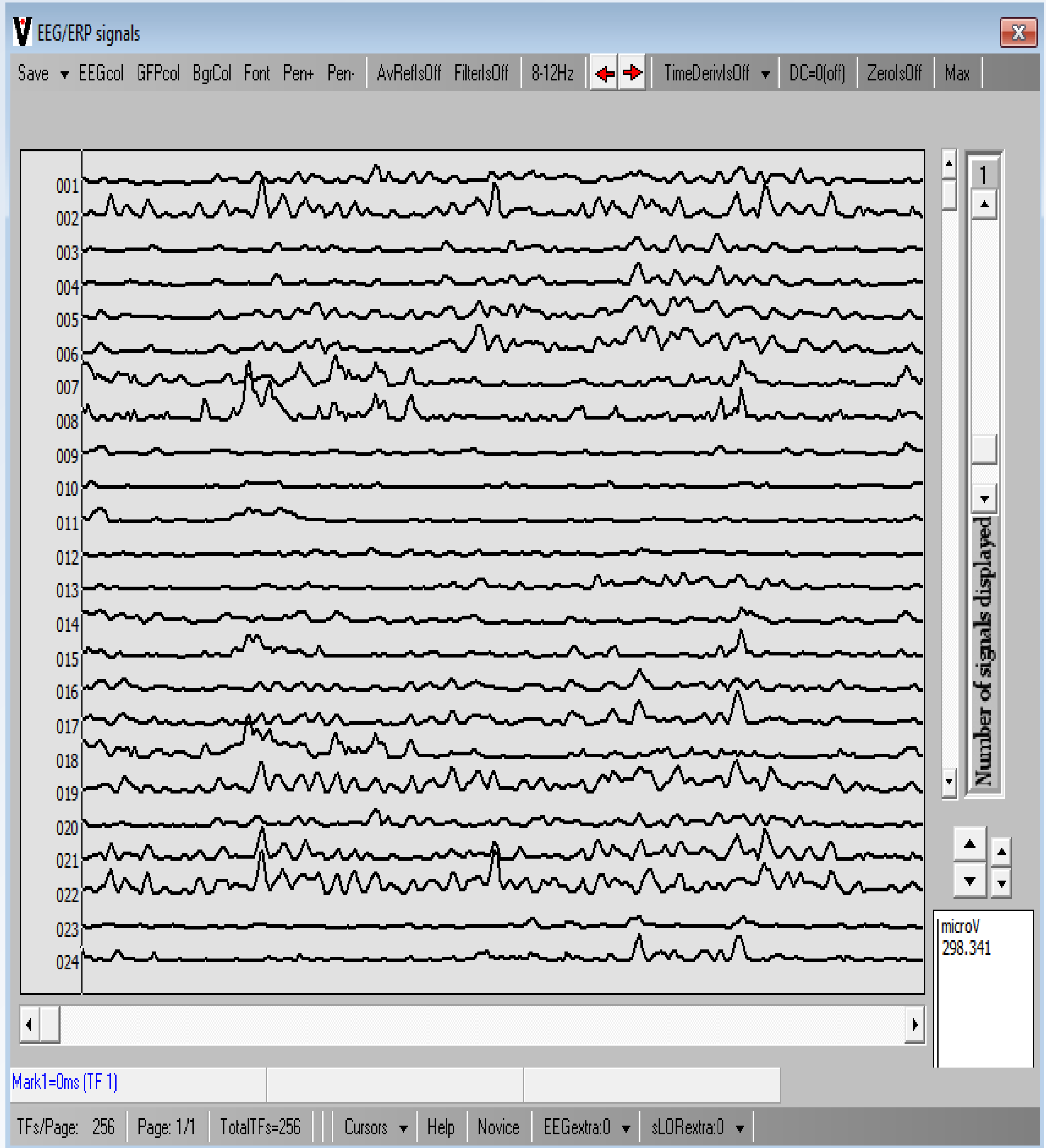
DataType sLorCol ScalpCol AnatCol Slices AllSlices 3DCortex ScalpMap Signals FileExplorer DragDropUtil WindowsExplorer AdjustScreenSize
3D cortex/scalp/electrodes
Left Right Top Bottm Front Back Reset Rpnt 5Vws 6Vws Save
CrtxC SclpC ElctrC BgrC SclpOn Crtx0 Sclp0 Elctr0 ElctrOn Max
Cortex contrast Rst
Scalp map
SclpC BgrC Sclp0 Save Reset Rpnt Max Help
EEG/ERP signals
Save EEGcol GFPcol BgrCol Font Pen+ Pen- AvRefIsOff FilterIsOff 8-12Hz TimeDerivIsOff DC=0(off) ZeroIsOff Max
Fp1 Fp2 F7 F3 Fz F4 F8 T7/T3 C3 Cz C4 T8/T4 P7/T5 P3 Pz P4 P8/T6 O1 O2
Number of signals displayed
microV 110.794
StdCrDn^2 369.153
Mark1=101.563ms (TF 14)
TFs/Page: 256 Page: 1/1 TotalTFs=256 Cursors Help Novice EEGextra:0 sLORextra:0
SliceViewer
Save AnatColors InitialView JumpMax JumpMin JumpZero Jump to... Max Help CopyToClipBrd
(X,Y,Z)=(10,-70,15)[mm] ; (3.11E+1) ; 14
Neuroanatomy (Talairach labels) :
Track Append Hits: 1 Cpy2ClpBrd Save2File
Value= 3.11E+1
(X= 10 , Y= -70 , Z= 15) (MNI coords)
Best Match at 0 mm
Brodmann area 31
Posterior Cingulate
Limbic Lobe
Find Max/Min
MRItemplate AllSlices Voxel0


MT+
aINS
vmPFC
aPFC
HF
pCC
aCC
pIPL
dlPFC
aIPL
FEF
SPL

Intracranial electric neuronal activity

-47.5	-69	-2.5	lMT+
47.5	-69	-2.5	rMT+
-26	-8	50	lFEF
26	-8	50	rFEF
-25.5	-54	56	lSPL
25.5	-54	56	rSPL
-35	54.5	9.5	laPFC
35	54.5	9.5	raPFC
-48	17	38.5	ldlPFC
48	17	38.5	rdlPFC
3	31	27	aCC
-52	-47.5	47	laIPL
52	-47.5	46	raIPL
-31	21	-1	laINS
31	22	-2	raINS
-22.5	-22	-17.5	lHF
22.5	-22	-17.5	rHF
0	51	-7	vmPFC
1	-55	17	pCC
-48.5	-67.5	28	lpIPL
48.5	-67.5	28	rpIPL
2	-92	-6	Vis
-55	-25	10	lAud
55	-25	10	rAud



Intracranial electric neuronal activity

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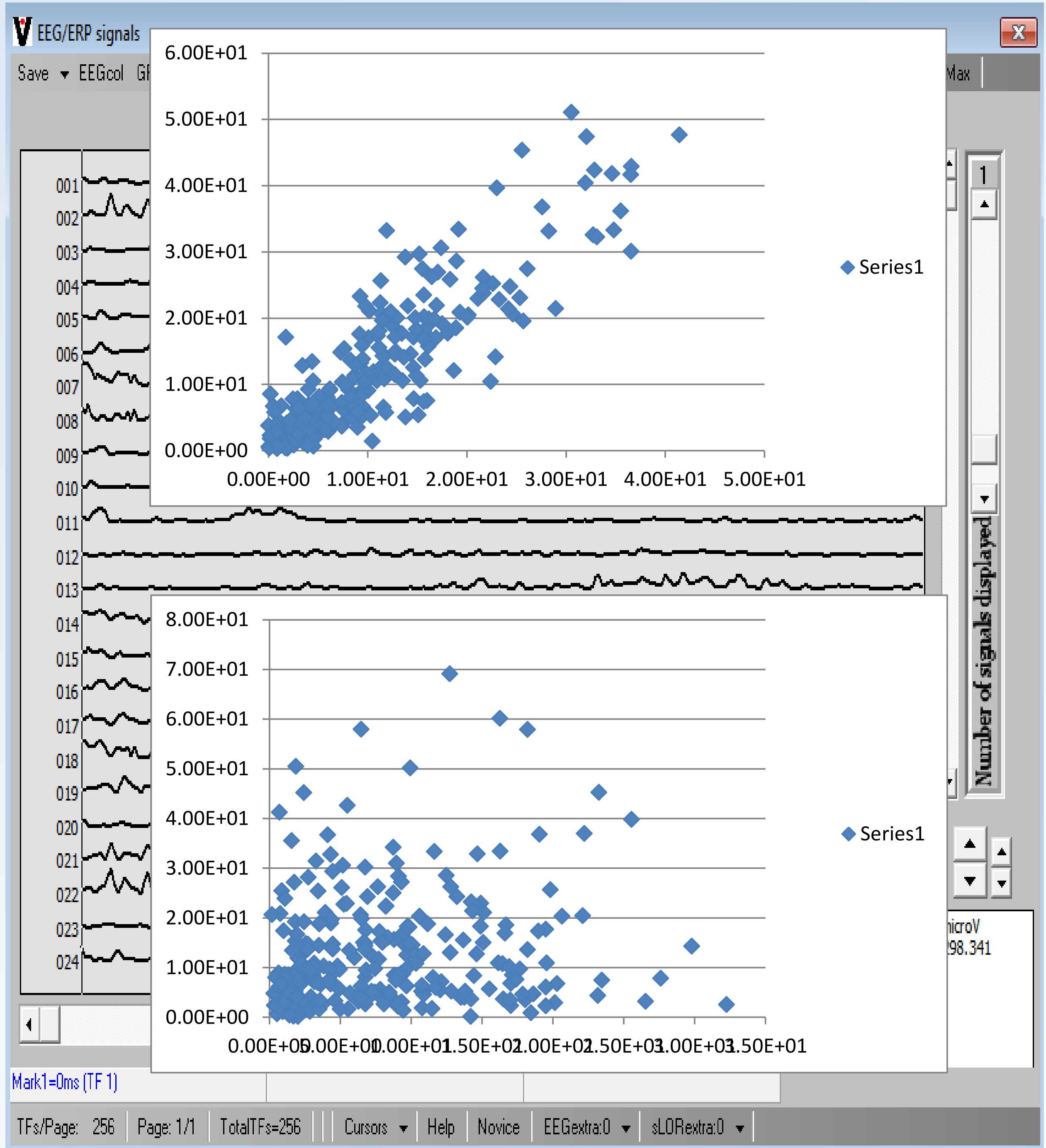
52	-47.5	46	raIPL
-31	21	-1	laINS
31	22	-2	raINS
-22.5	-22	-17.5	lHF
22.5	-22	-17.5	rHF
0	51	-7	vmPFC
1	-55	17	pCC
-48.5	-67.5	28	lpIPL
48.5	-67.5	28	rpIPL
2	-92	-6	Vis
-55	-25	10	lAud
55	-25	10	rAud



Intracranial electric neuronal activity

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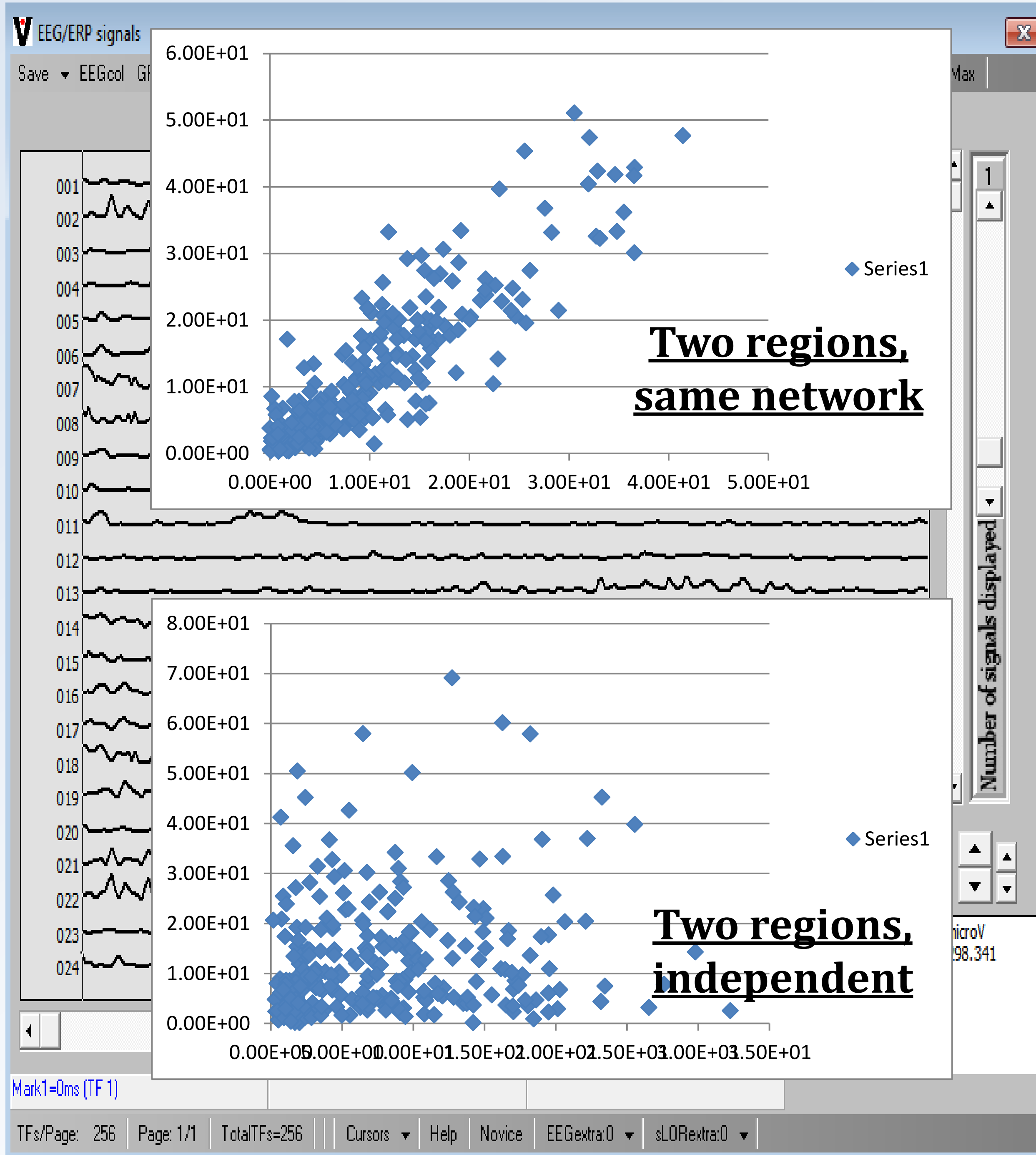
-31	21	-1	laINS
31	22	-2	raINS
-22.5	-22	-17.5	lHF
22.5	-22	-17.5	rHF
0	51	-7	vmPFC
1	-55	17	pCC
-48.5	-67.5	28	lpIPL
48.5	-67.5	28	rpIPL
2	-92	-6	Vis
-55	-25	10	lAud
55	-25	10	rAud



In words, the procedure for the discovery of brain networks (intuitive, exploratory method):

1. Stick needles into the brain, cover the whole cortex (non-invasively, virtual electrodes, LORETA).
2. Take each distinct pair of intracranial electrodes, and compute the "similarity" between the signals.
3. If two signals are very similar, i.e. highly correlated – coherent – synchronized, then assign them into the same network.
4. If two signals are very dissimilar, make sure they belong to different network.
5. Scan all distinct pairs of intracranial signals.

Exploratory analysis using this intuitive method is not feasible

6239 cortical grey matter voxels
6239*6238/2 = 19’459’441 plots

For each EEG frequency band of interest, e.g.:
Delta: 1.5-6 Hz
Theta: 6.5-8.0 Hz
Alpha1: 8.5-10 Hz
Alpha2: 10.5-12.0 Hz
Beta1: 12.5-18.0 Hz
Beta2: 18.5-21.0 Hz
Beta3: 21.5-30.0 Hz

At least 40 seconds of EEG

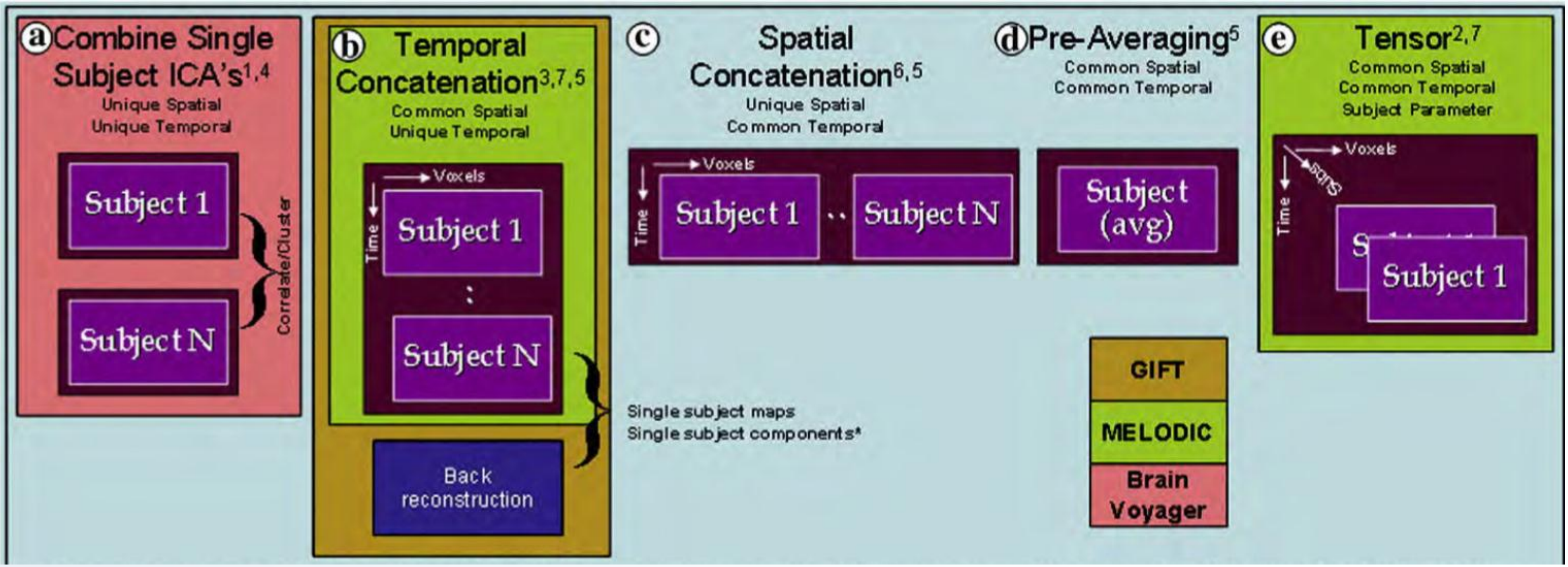
ICA (independent components analysis)

Published in final edited form as:
Neuroimage. 2009 March ; 45(1 Suppl): S163–S172. doi:10.1016/j.neuroimage.2008.10.057.

A review of group ICA for fMRI data and ICA for joint inference of imaging, genetic, and ERP data

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

Vince D. Calhoun[a,b,*], **Jingyu Liu**[a,b], and **Tülay Adalı**[c]

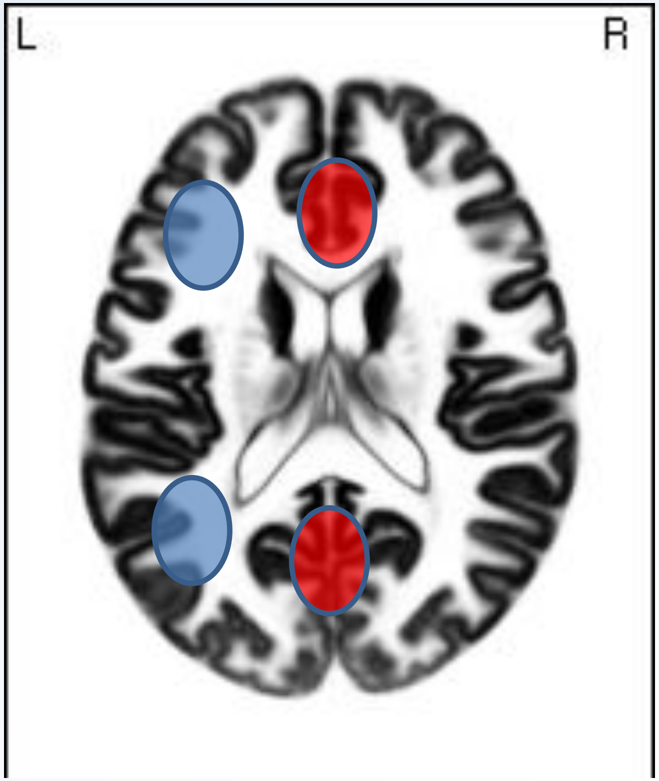


ICA (independent components analysis)

If brain activity is organized and structured in such a way that there are several different groupings (networks) of regions, where within a group (network) all activity is correlated, but between groups (networks) there is independence, then ICA should produce spatial "components" that correspond to the networks.

ICA (independent components analysis)

If brain activity is organized and structured in such a way that there are several different groupings (networks) of regions, where within a group (network) all activity is correlated, but between groups (networks) there is independence, then ICA should produce spatial "components" that correspond to the networks.



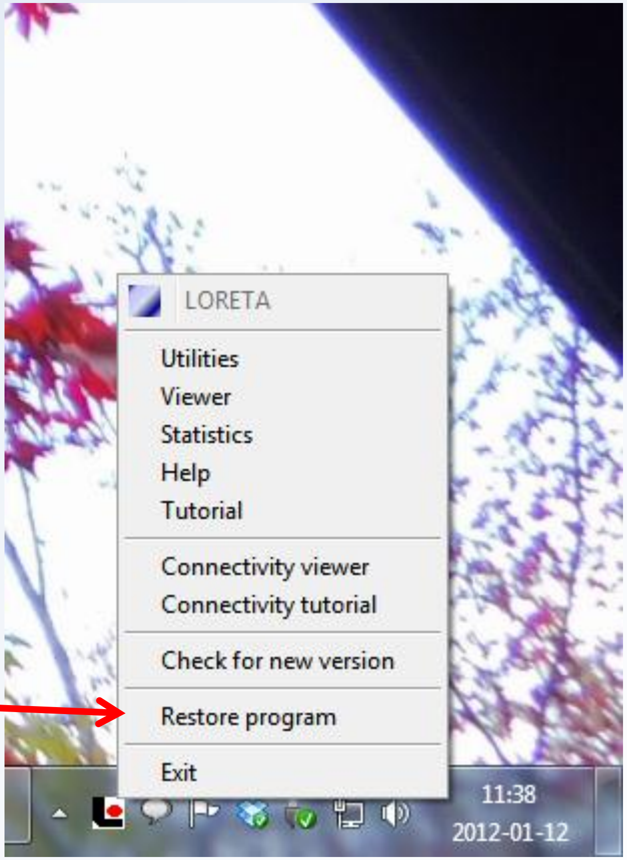
blue↔blue

red ↔red

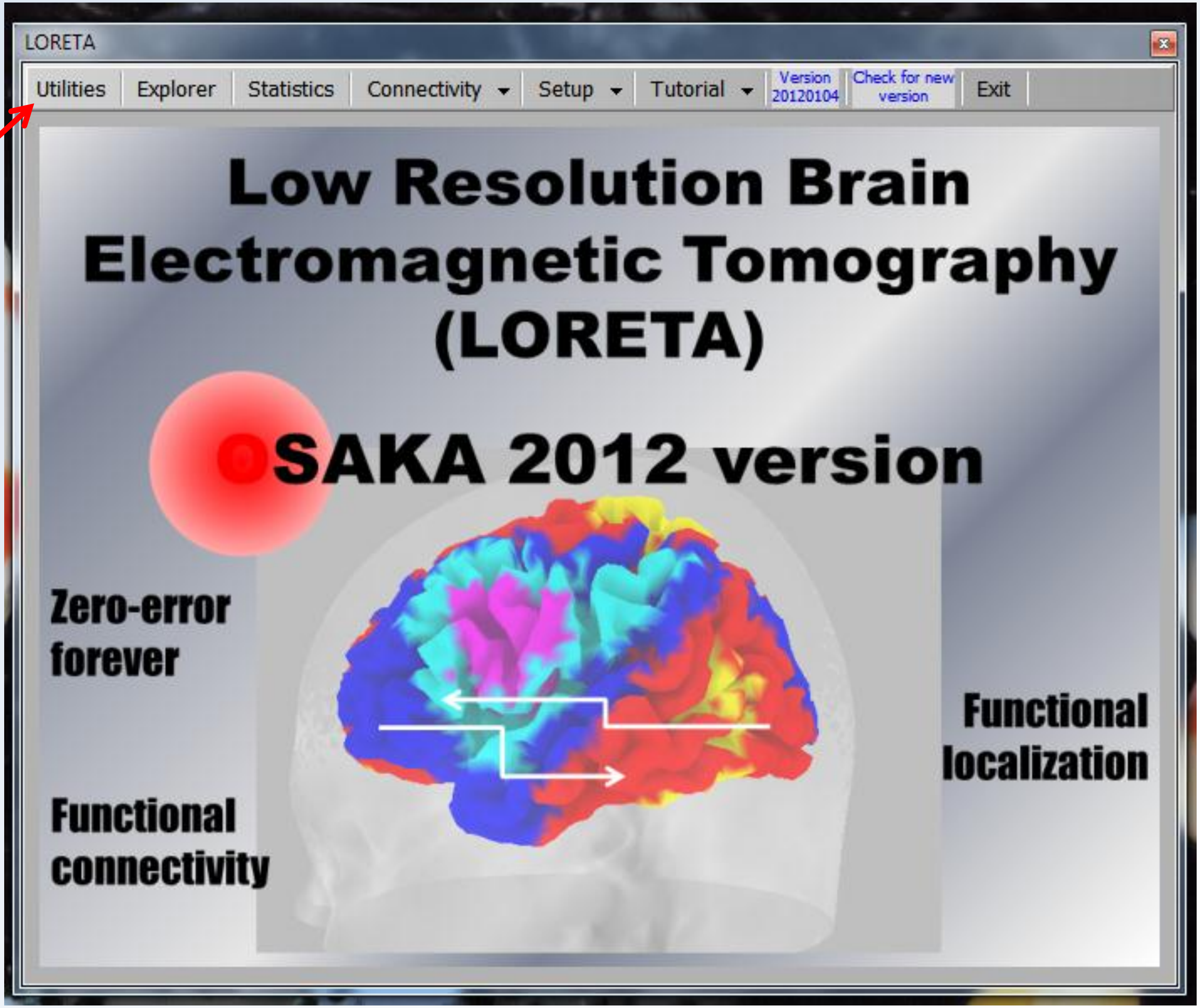
Part 2: Tutorial on using software

Run / open the main LORETA program
Open the Utilities module
Make electrode coordinates (skip if already made)
Compute transformation matrix (skip if already made)
Create frequency bands file
Compute cross-spectra (skip if already made)
Compute sLORETAs (skip if already made)
Compute Brain Networks
Statistical Analysis of Resting State Networks

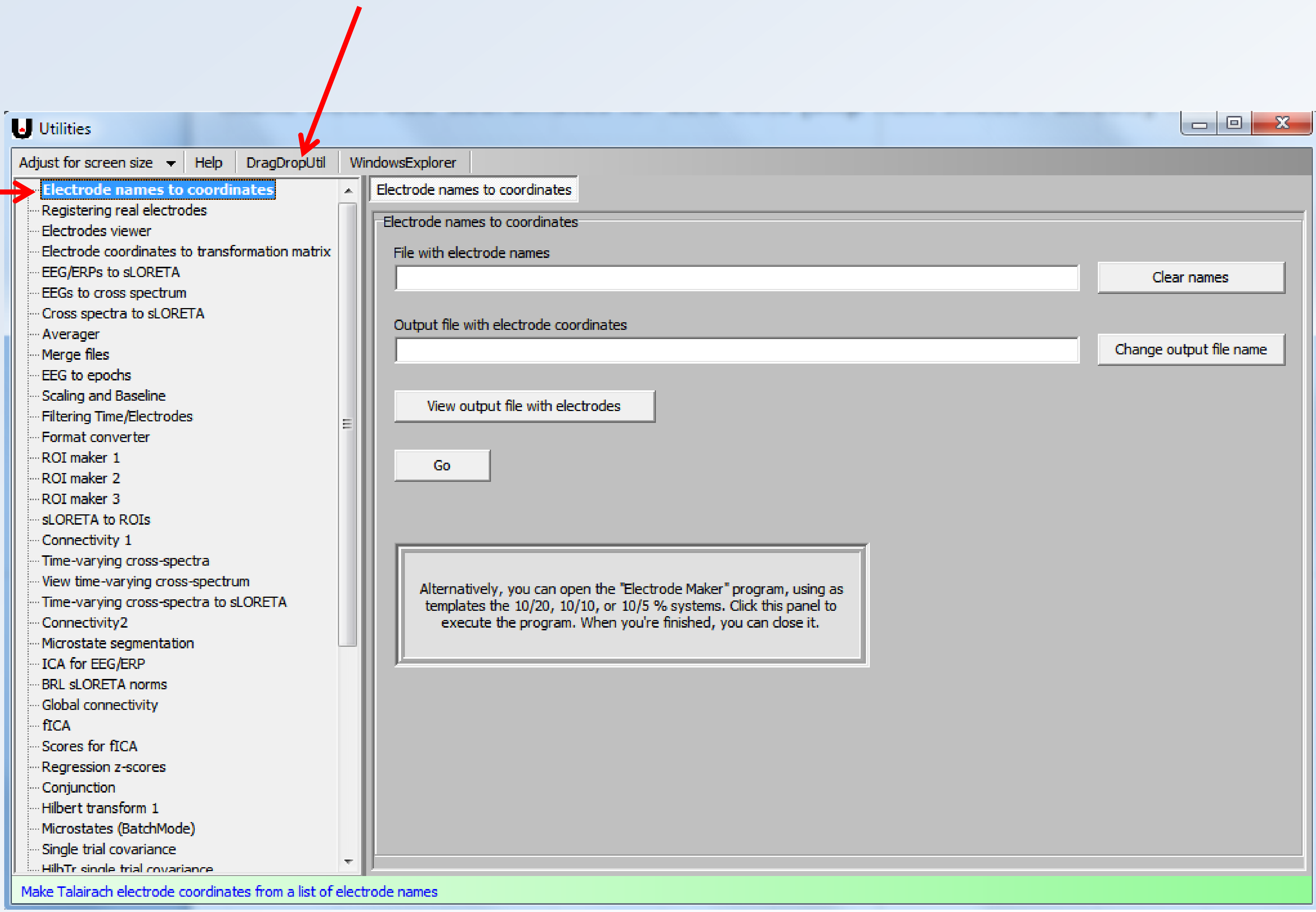
Run / open the LORETA software



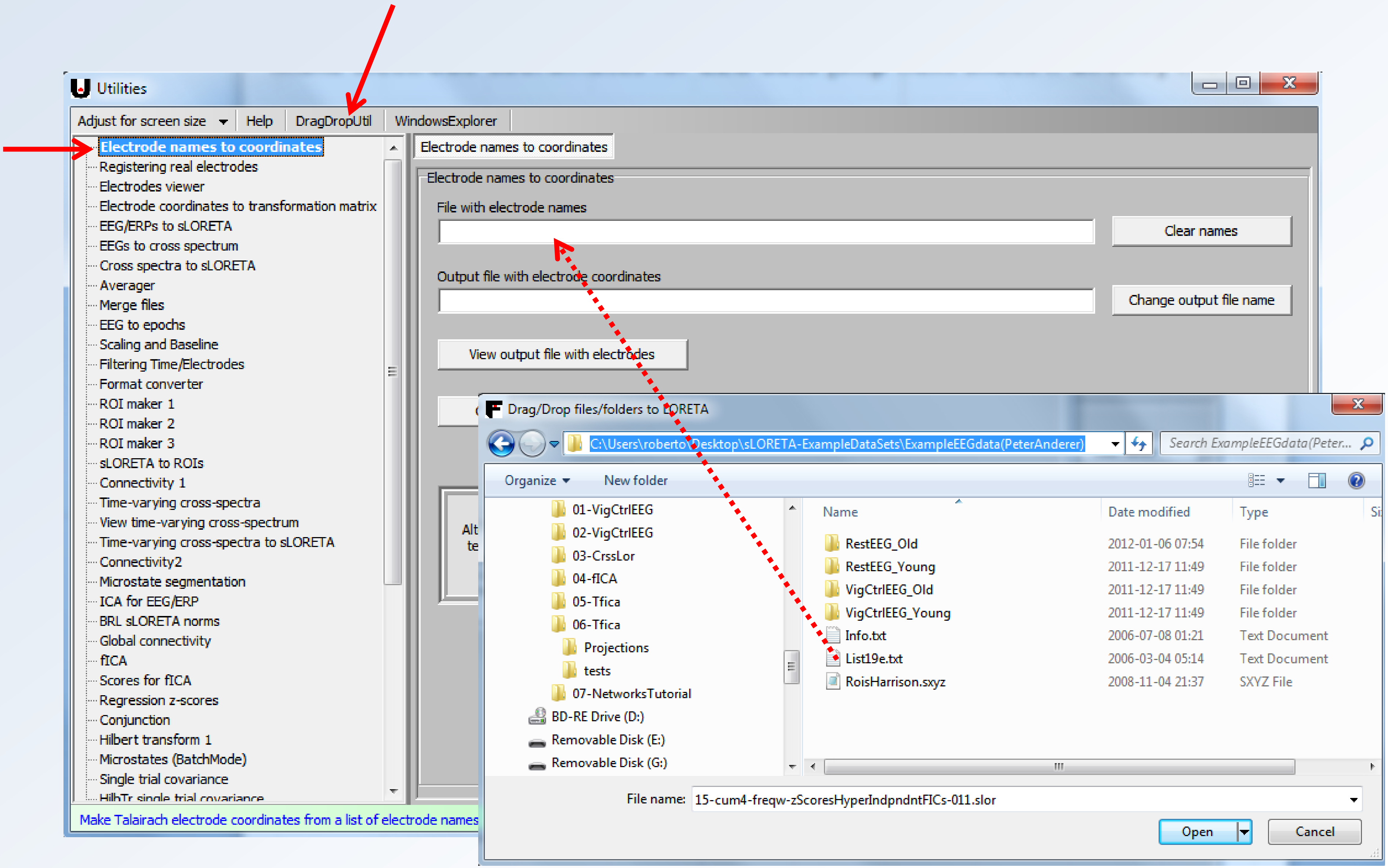
Open the Utilities



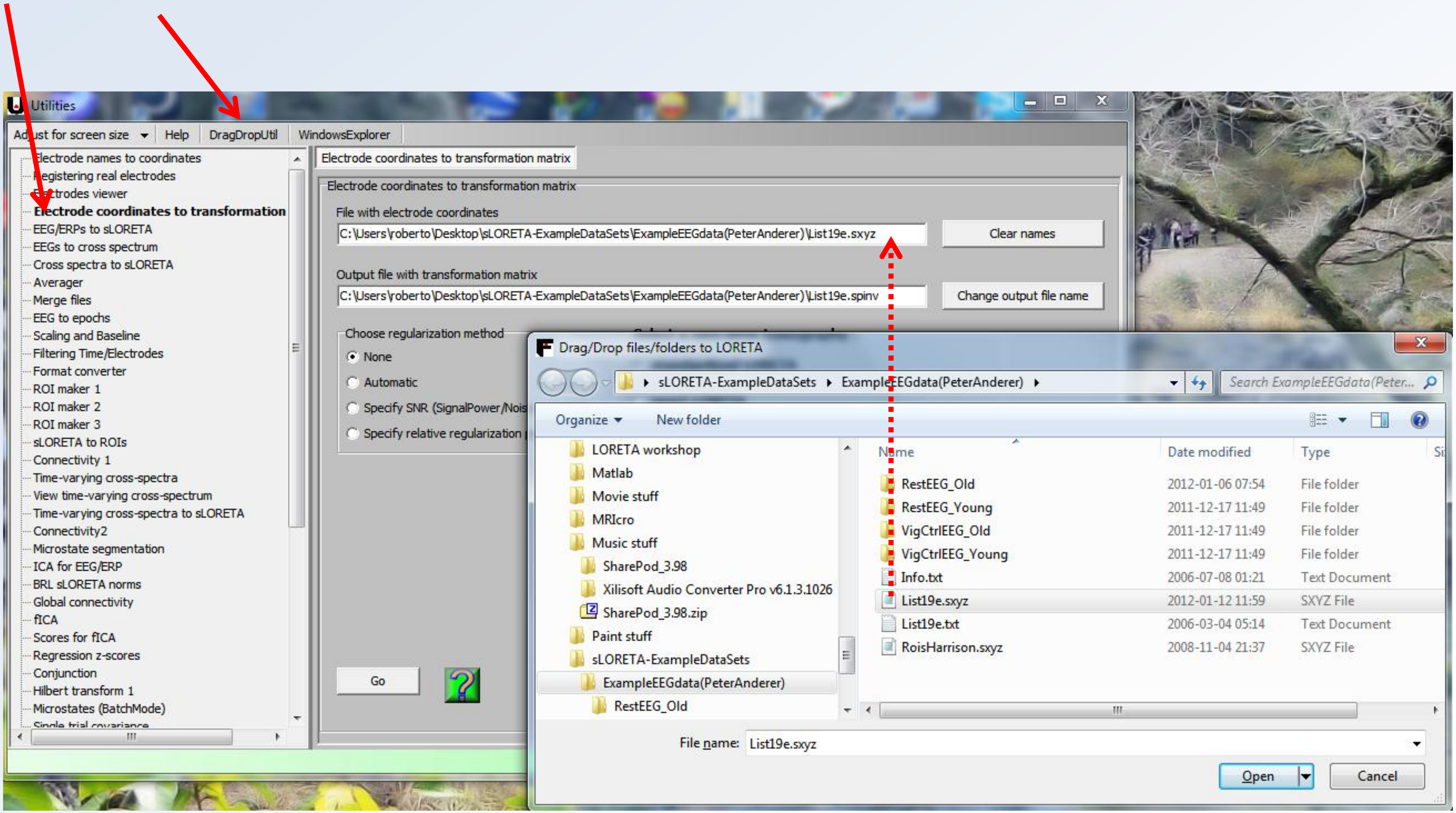
Make electrode coordinates for EEG data (skip next slides if already made!)



Make electrode coordinates for EEG data (skip next slides if already made!)
Drag and drop the text file with electrode names (List19e.txt), from the desktop folder with the example EEG data. Click “Go”. The file (List19e.sxyz) is created.

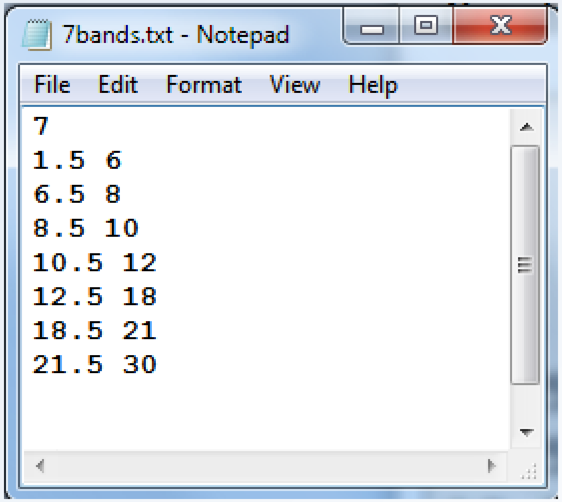


Make the transformation matrix (skip next slides if already made!)
Drag and drop the file (List19e.sxyz) with electrode coordinates, from the desktop folder with the example EEG data. Click “Go”. The file (List19e.spinv) is created.



Create a text file in the notepad with the following text:

```
7
1.5 6
6.5 8
8.5 10
10.5 12
12.5 18
18.5 21
21.5 30
```

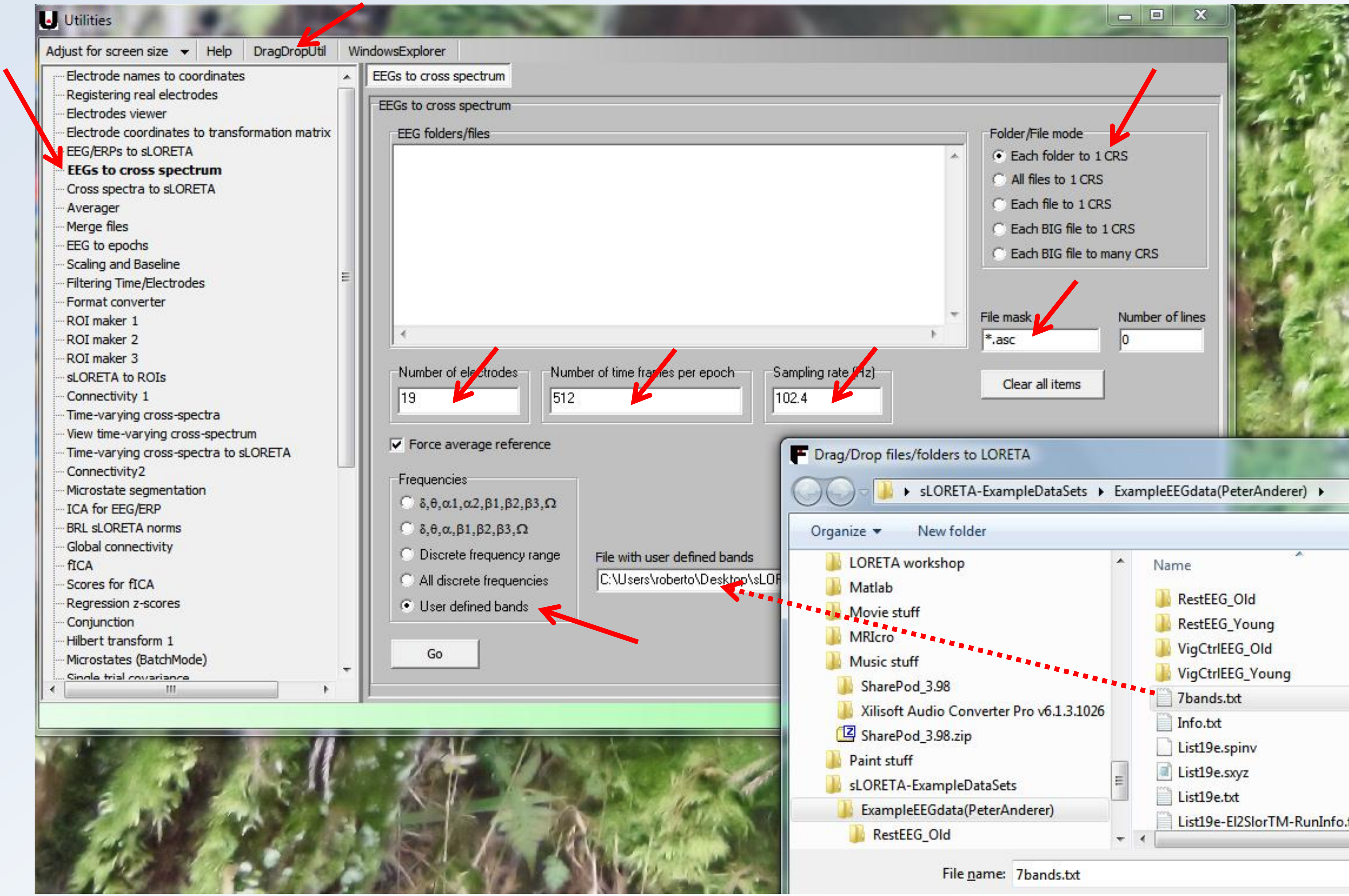


This is a "User defined frequency band file". You can make analysis with any bands of your interest. In this case, seven (7) bands are defined. The next seven lines have the "start" and "end" frequency, separated by space. These are the 7 classical bands, without the additional full band (1.5 30). Save this text file with name:

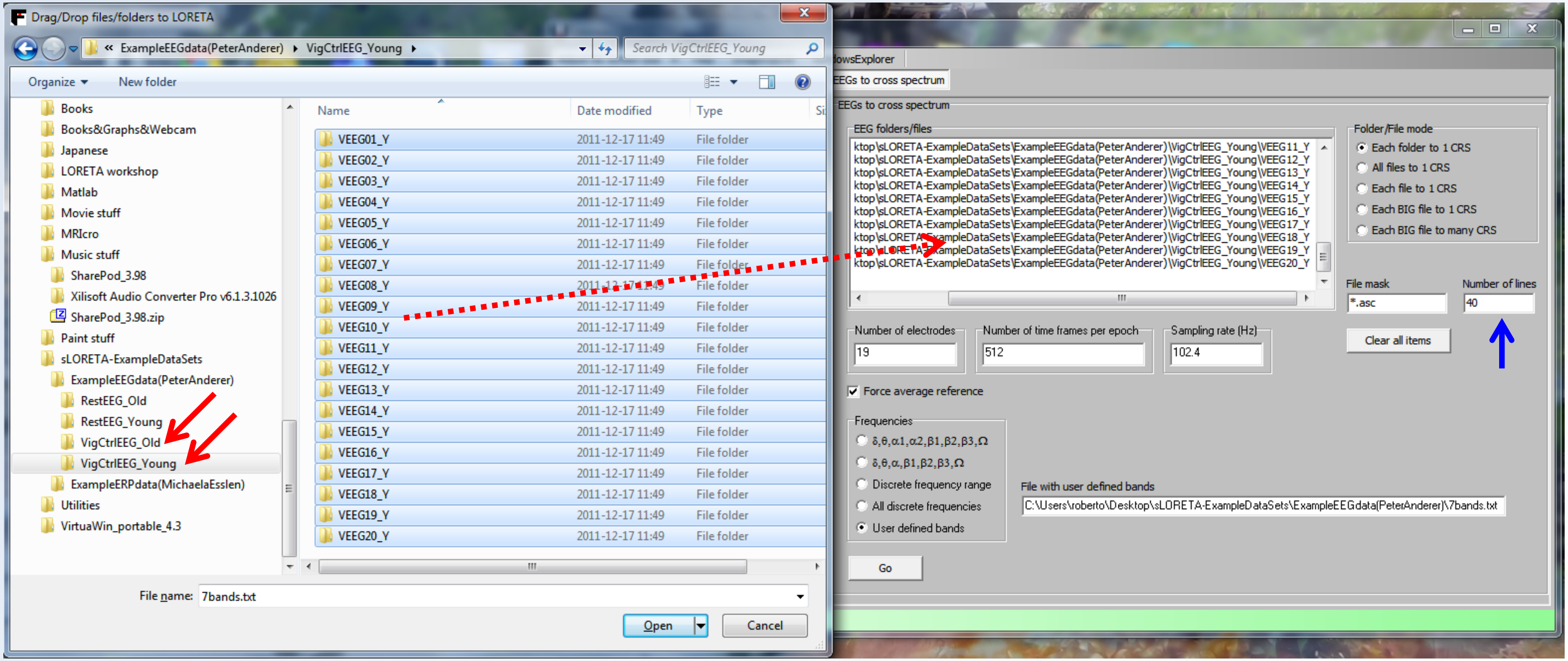
7bands.txt

Save to the EEG folder!

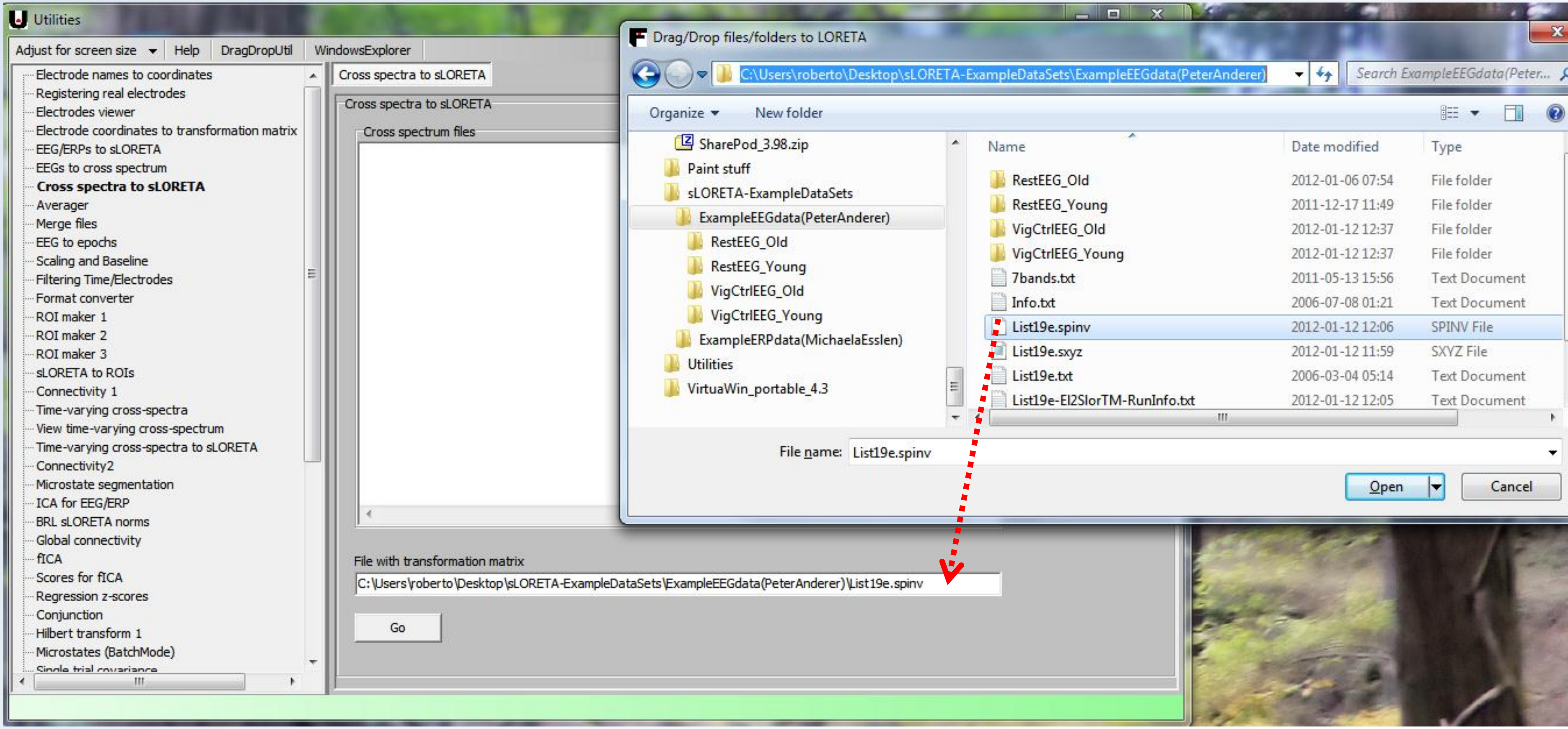
Compute the cross-spectra for vigilance controlled EEG, for old and young subjects. (skip next slides if already made!) Note every detail marked with arrows. Drag/drop “7bands.txt” to the box “File with user defined bands”



Compute the cross-spectra for vigilance controlled EEG, for old and young subjects. (skip next slides if already made!) Note every detail marked with arrows. Finally, drag/drop the 20 folders for old and 20 folders for young, vigilance controlled EEG. Note that there must be a total of 40 lines (blue arrow), indicating 40 folders. And click “Go”.

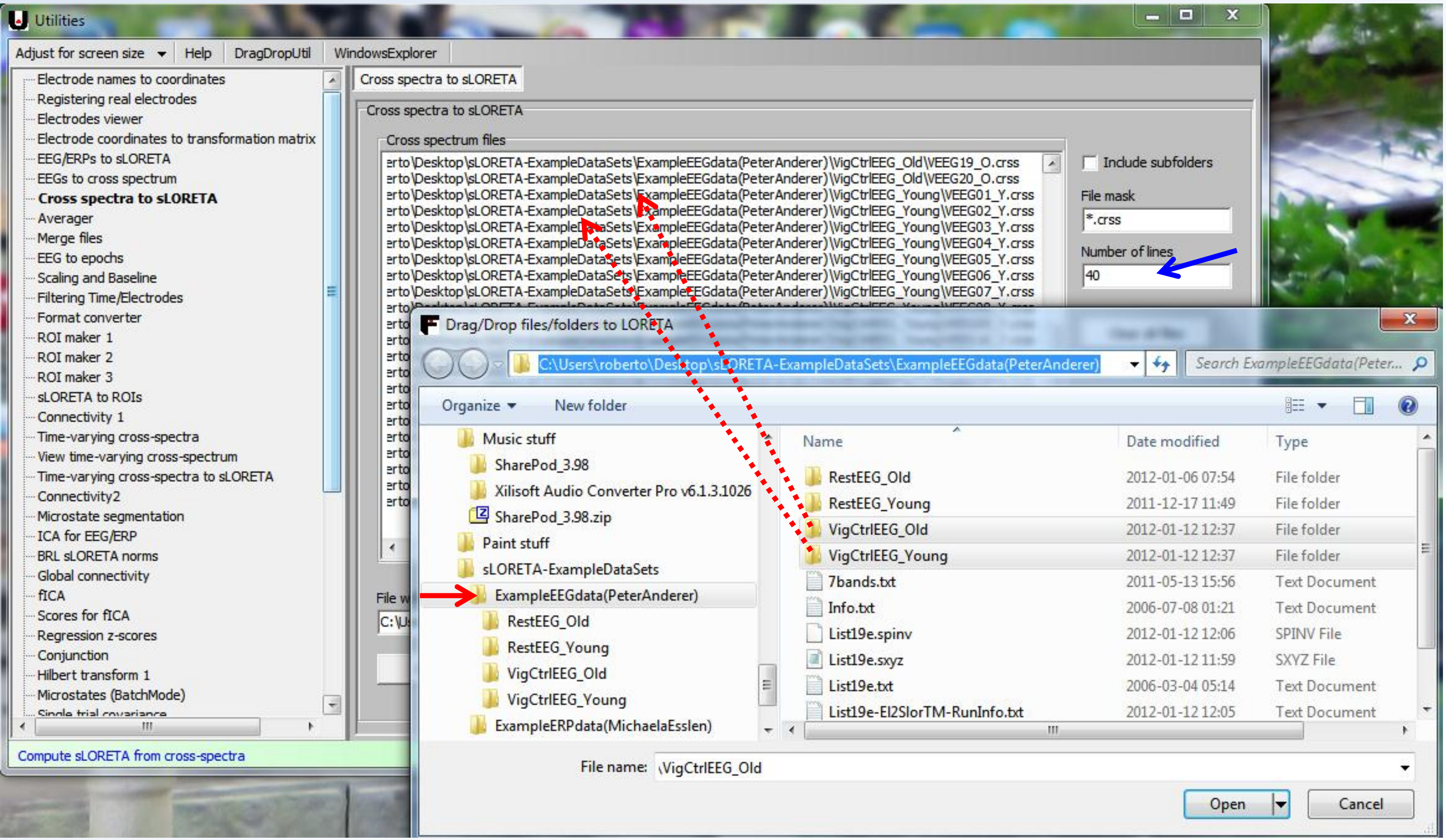


Compute sLORETA from cross-spectra (skip next slides if already made!)
First drag and drop the transformation matrix (List19e.spinv) as indicated



Compute sLORETA from cross-spectra (skip next slides if already made!)

Finally, drag and drop the folders VigCtrlEEG_Old and VigCtrilEEG_Young as indicated. These folders contain the cross-spectra. Note the “Number of lines = 40” cross-spectra. Click “Go”.



Computing brain networks

Computing brain networks

Resting state networks in EEG are computed in a very similar way to fMRI, using independent components analysis (ICA). An excellent review paper on fMRI-ICA is: Calhoun VD, Liu J, Adali T. Neuroimage. A review of group ICA for fMRI data and ICA for joint inference of imaging, genetic, and ERP data. 2009 Mar;45(1 Suppl):S163-72.

The papers describing LORETA-ICA are:

Pascual-Marqui RD and Biscay-Lirio RJ. Interaction patterns of brain activity across space, time and frequency. Part I: methods. arXiv:1103.2852v2 [stat.ME], 2011-March-15, http://arxiv.org/abs/1103.2852

RD. Pascual-Marqui, K Kochi, D Lehmann, M Koukkou, T Kinoshita. Functional independent components: revealing cortico-cortical, cross-frequency interactions. Japanese Journal of Pharmaco-EEG 2011, Vol 12 : 53-58

Computing brain networks

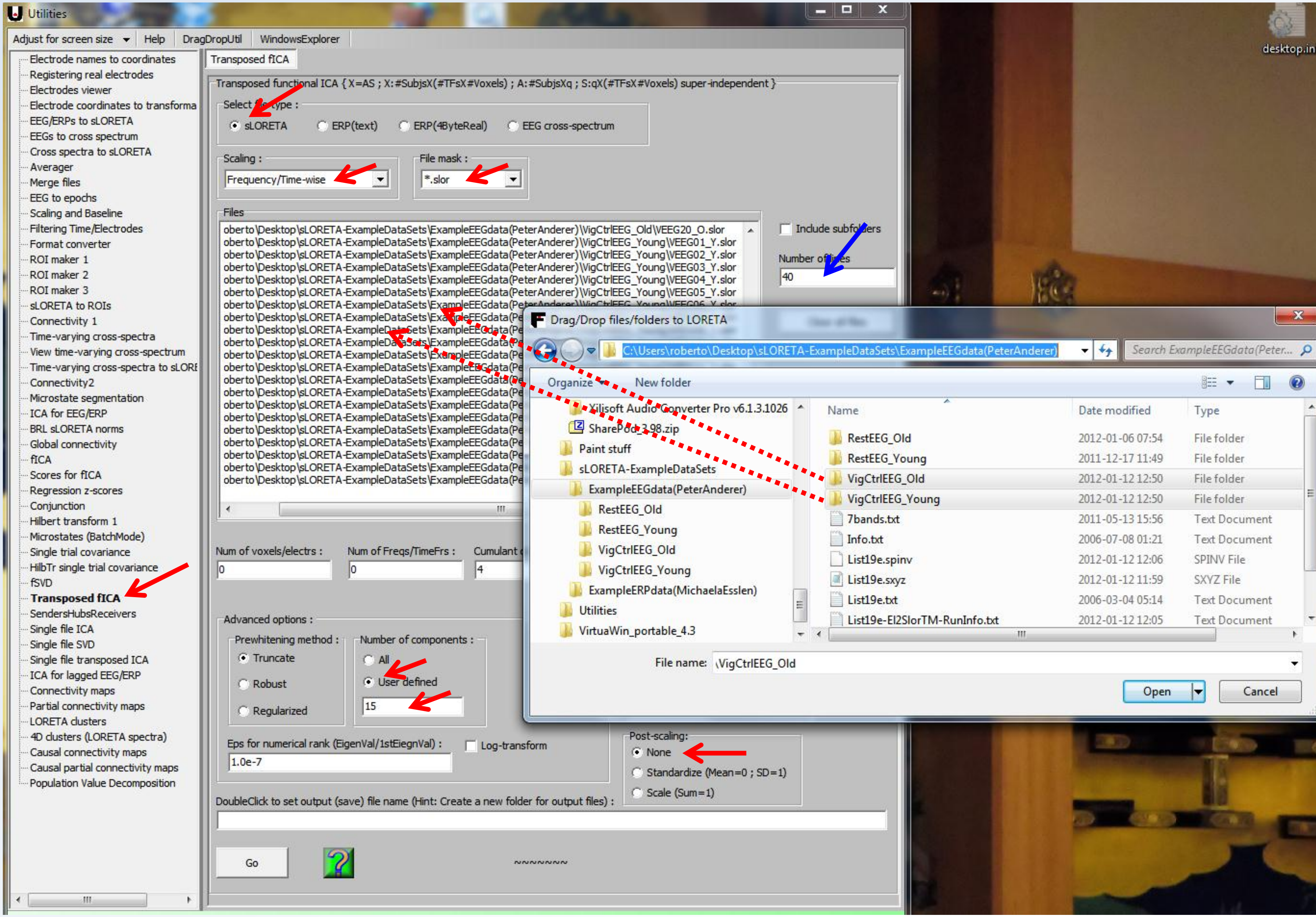
In fMRI, the basic material are images of metabolic brain activity that change with time.

In EEG, the basic material are images of electric cortical activity for each frequency band (sLORETA files, with 7 images, one for each band: delta, theta, alpha1, alpha2, beta1, beta2, beta3).

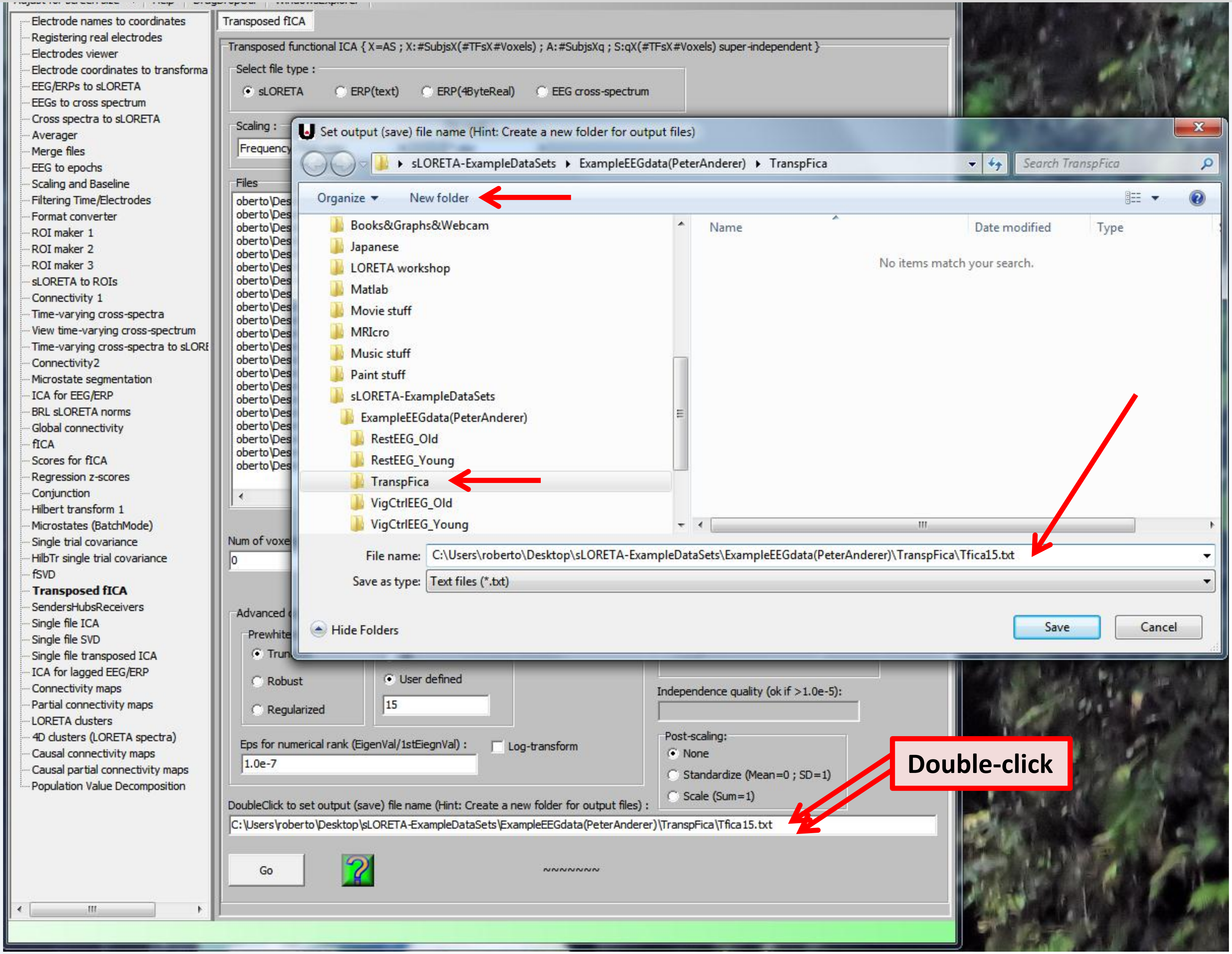
An fMRI resting state network is a single static image of metabolic brain activity. The brain areas in a network activate together, but different networks do not activate together.

An sLORETA resting state network consists of many images of electric cortical activity, one for each frequency (e.g. 7 images). The "brain areas *AND* frequencies" in a network always activate together, but different networks do not activate together.

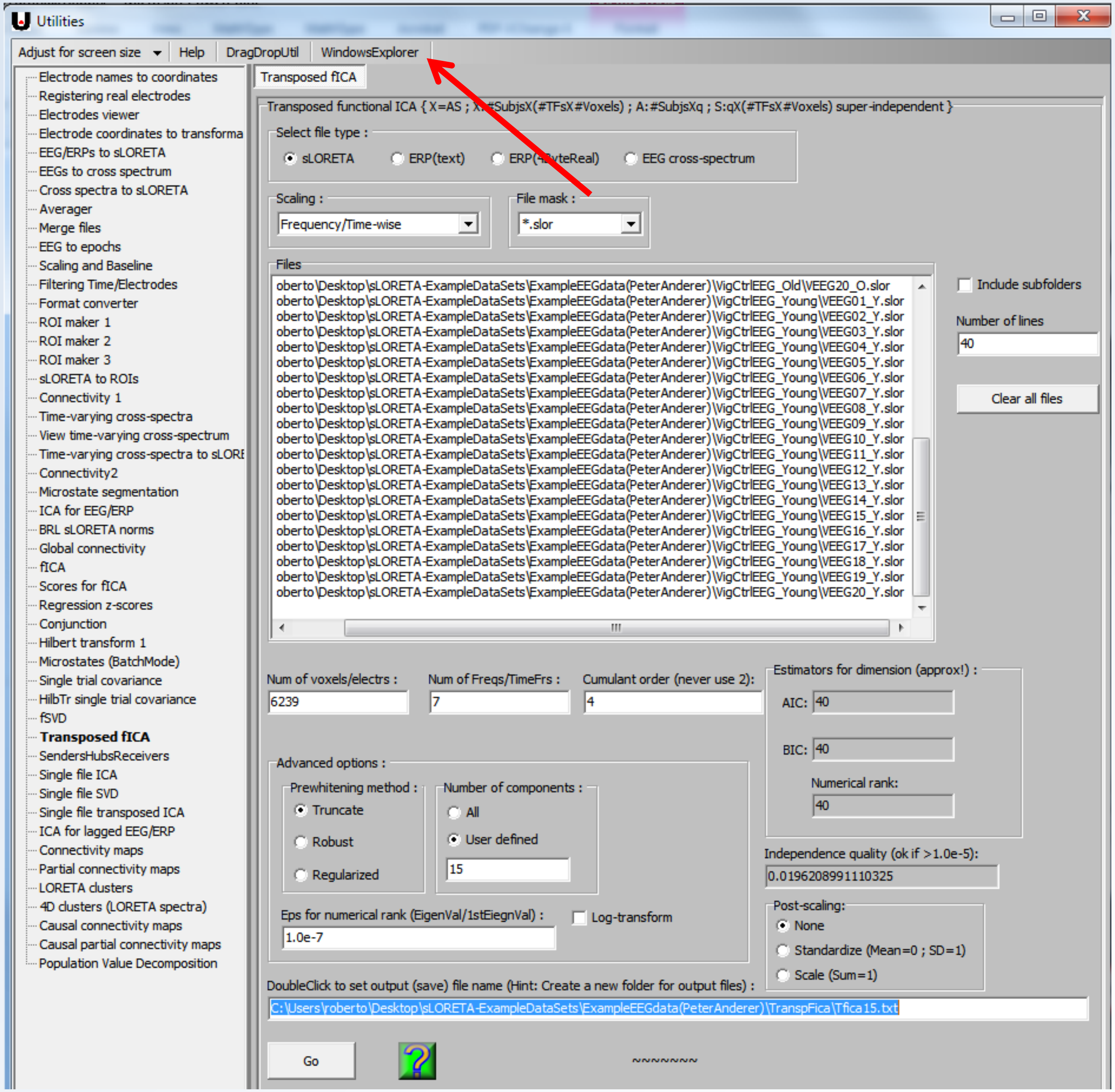
Select “Transposed fICA” in the “Utilities” module. Drag/drop indicated folders with sLORETA files. Select all parameters as indicated.



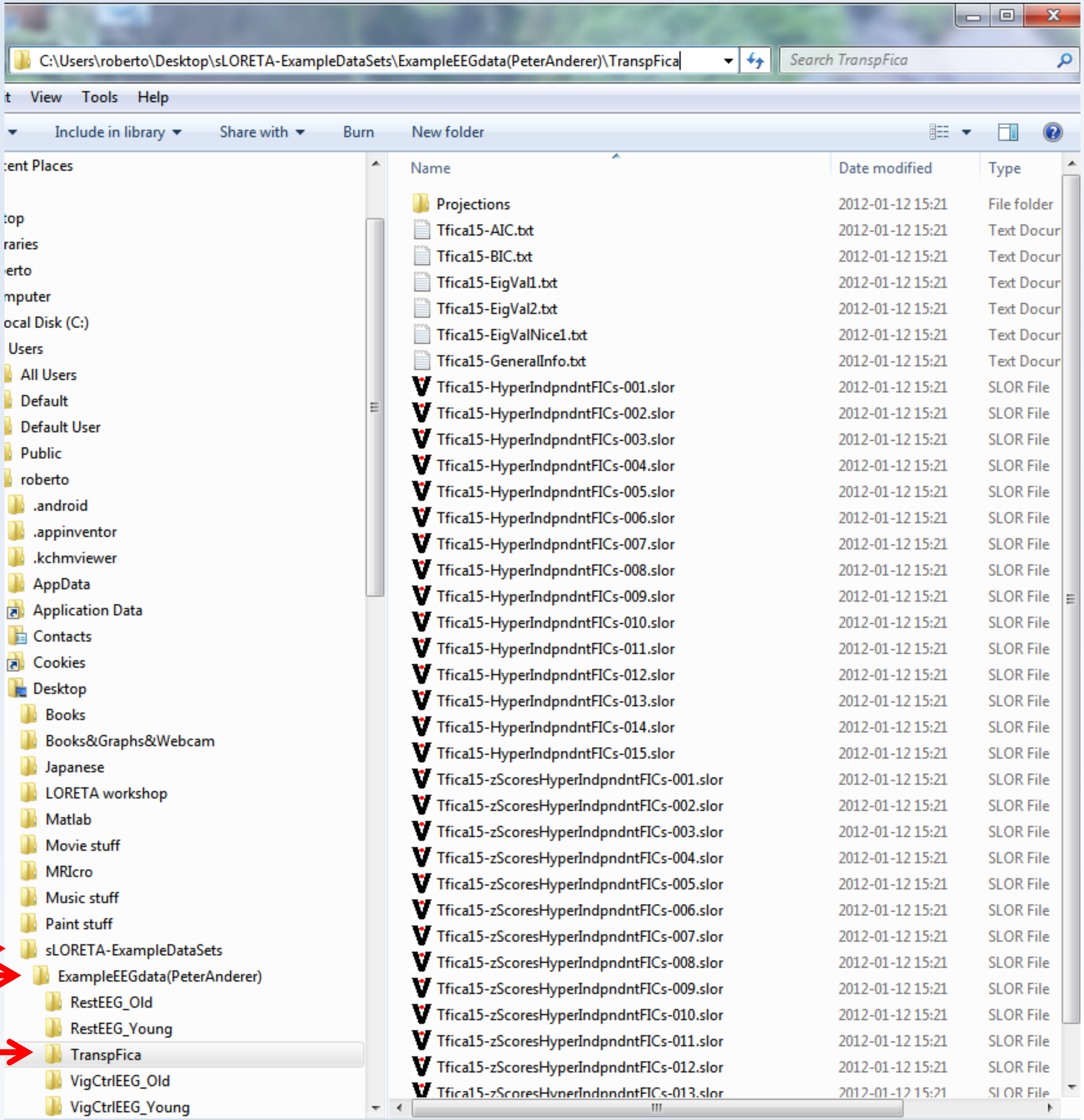
Double-click as indicated, and create a "New Folder" within the EEG folder (any name, e.g. "TranspFica"), and within the new folder, define a file name for the results of the ICA analysis (e.g. Tfica15). Click "Save", then click "Go".



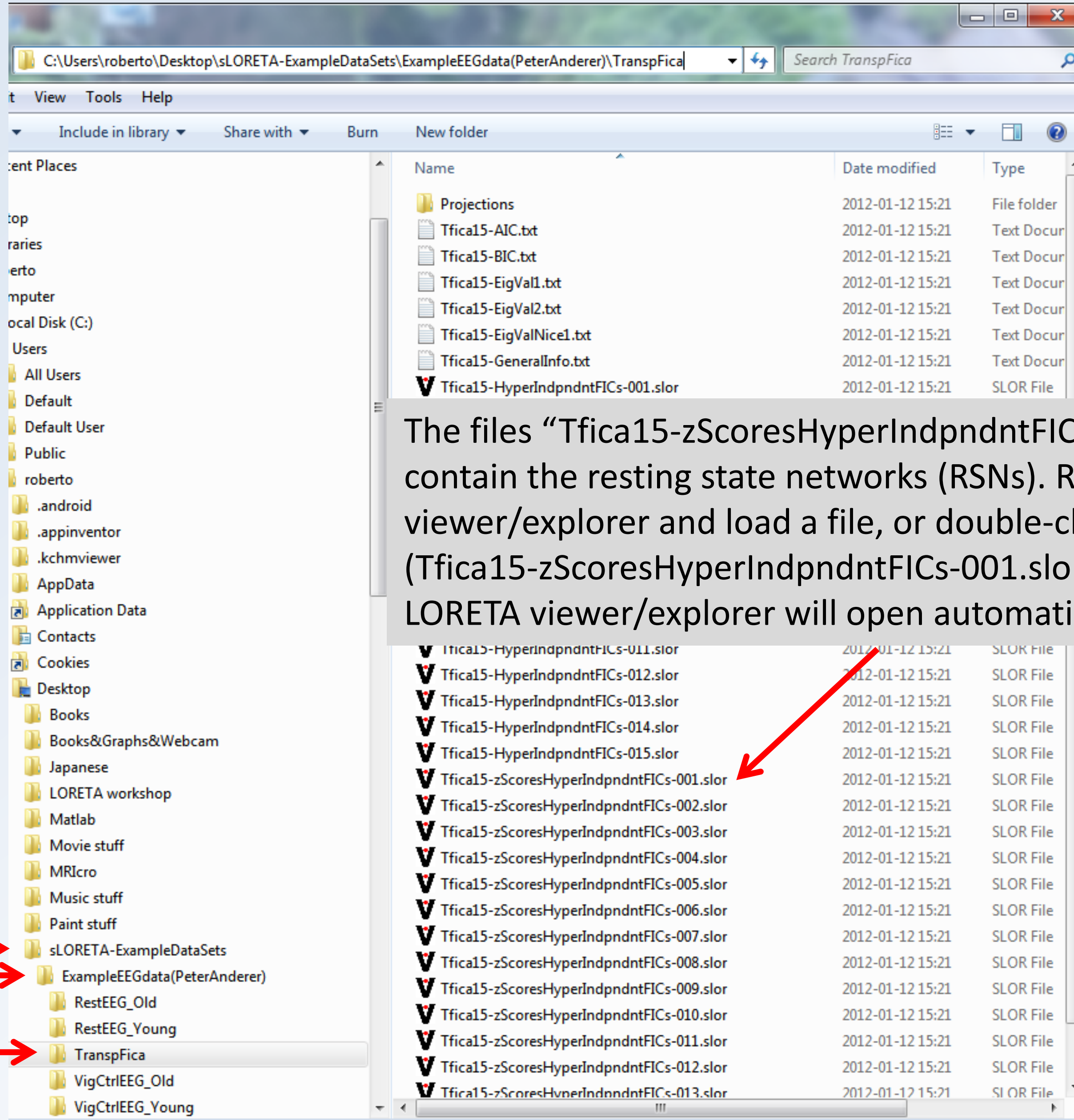
Open the windows explorer, e.g. click as indicated. Navigate to the folder with the ICA results.



The results for the Transposed fICA analysis:

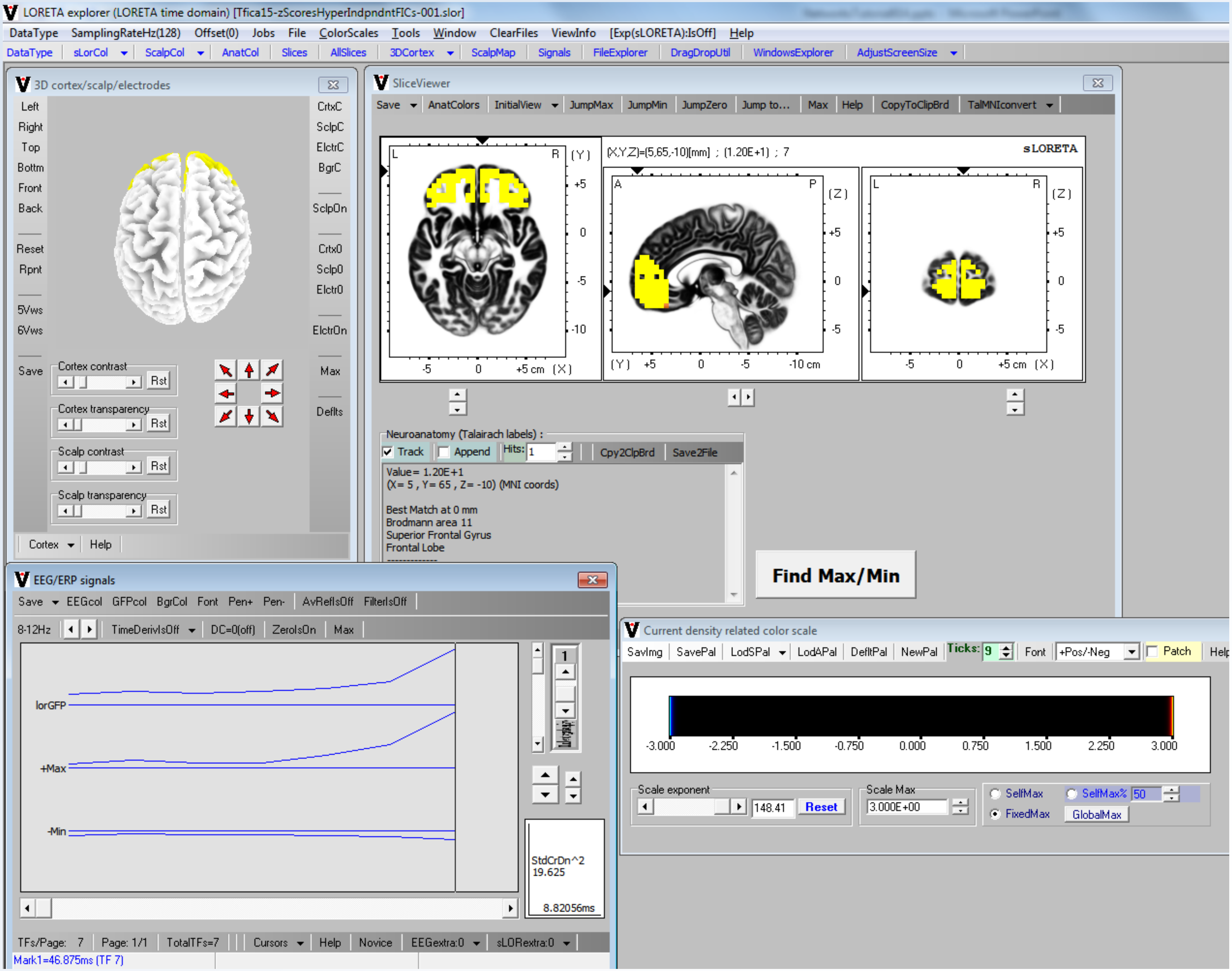


The results for the Transposed fICA analysis:



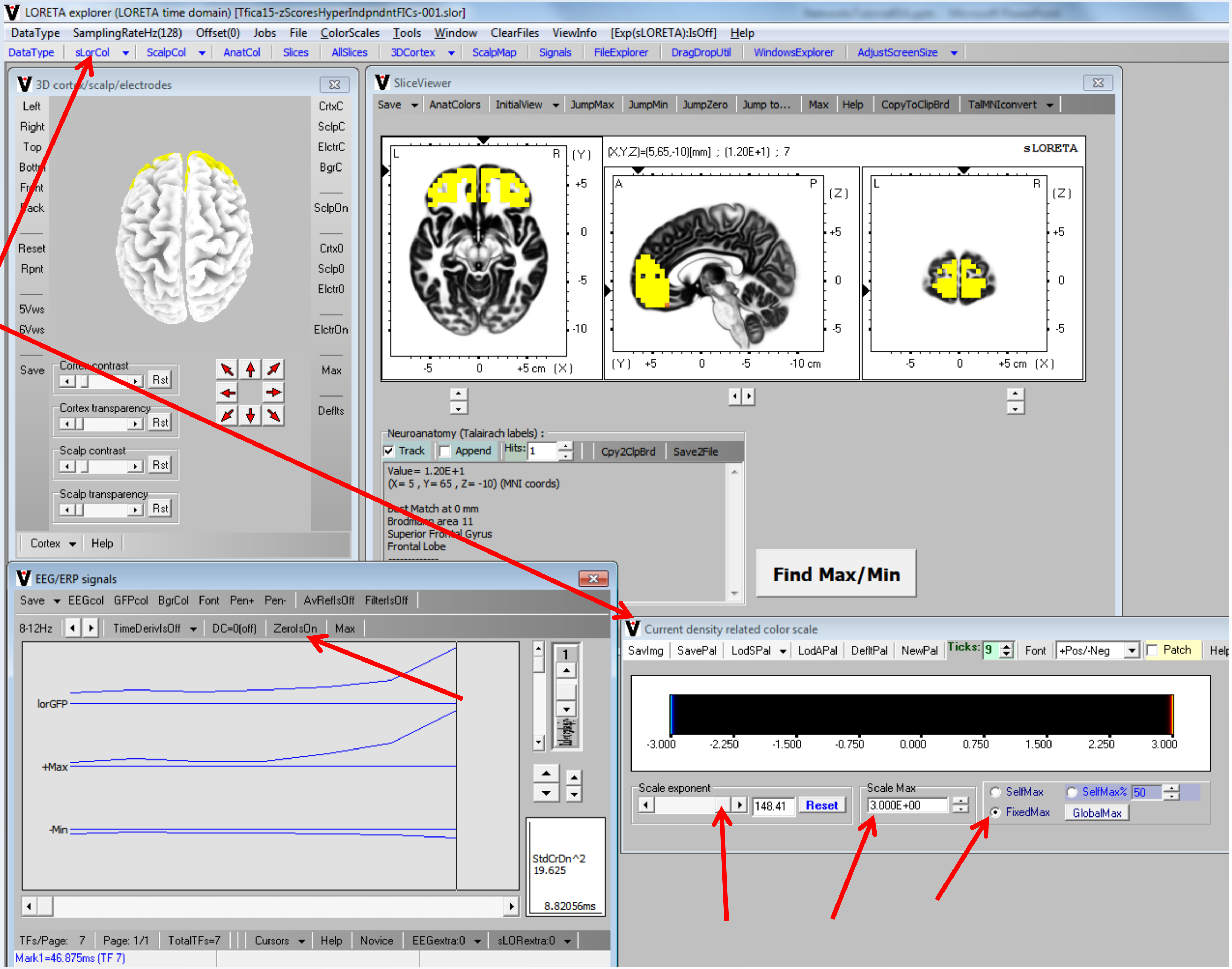
The files “Tfica15-zScoresHyperIndpndntFICs-0XX.slor” contain the resting state networks (RSNs). Run the LORETA viewer/explorer and load a file, or double-click the first file (Tfica15-zScoresHyperIndpndntFICs-001.slor), and the LORETA viewer/explorer will open automatically.

The next slide shows the preferred display layout.



LORETA explorer (LORETA time domain) [Tfica15-zScoresHyperIndpndntFICs-001.slor]
DataType SamplingRateHz(128) Offset(0) Jobs File ColorScales Tools Window ClearFiles ViewInfo [Exp(sLORETA):IsOff] Help
DataType sLorCol ScalpCol AnatCol Slices AllSlices 3DCortex ScalpMap Signals FileExplorer DragDropUtil WindowsExplorer AdjustScreenSize
3D cortex/scalp/electrodes
Left Right Top Bottm Front Back Reset Rpnt 5Vws 6Vws Save
CrtxC SclpC ElctrC BgrC SclpOn Crtx0 Sclp0 Elctr0 ElctrOn Max Deflts
Cortex contrast
Cortex transparency
Scalp contrast
Scalp transparency
Rst
Cortex Help
SliceViewer
Save AnatColors InitialView JumpMax JumpMin JumpZero Jump to... Max Help CopyToClipBrd TalMNIconvert
(X,Y,Z)=(5,65,-10)[mm] ; (1.20E+1) ; 7
sLORETA
Neuroanatomy (Talairach labels) :
Track Append Hits: 1 Cpy2ClipBrd Save2File
Value= 1.20E+1
(X= 5 , Y= 65 , Z= -10) (MNI coords)
Best Match at 0 mm
Brodmann area 11
Superior Frontal Gyrus
Frontal Lobe
Find Max/Min
EEG/ERP signals
Save EEGcol GFPcol BgrCol Font Pen+ Pen- AvRefIsOff FilterIsOff
8-12Hz TimeDerivIsOff DC=0(off) ZeroIsOn Max
lorGFP
+Max
-Min
StdCrDn^2
19.625
8.82056ms
TFs/Page: 7 Page: 1/1 TotalTFs=7 Cursors Help Novice EEGextra:0 sLORextra:0
Mark1=46.875ms (TF 7)
Current density related color scale
SavImg SavePal LodSPal LodAPal DefltPal NewPal Ticks: 9 Font +Pos/-Neg Patch
-3.000 -2.250 -1.500 -0.750 0.000 0.750 1.500 2.250 3.000
Scale exponent 148.41 Reset
Scale Max 3.000E+00
SelfMax SelfMax% 50
FixedMax GlobalMax

Select all windows and parameters as indicated by the arrows. In the next slide.

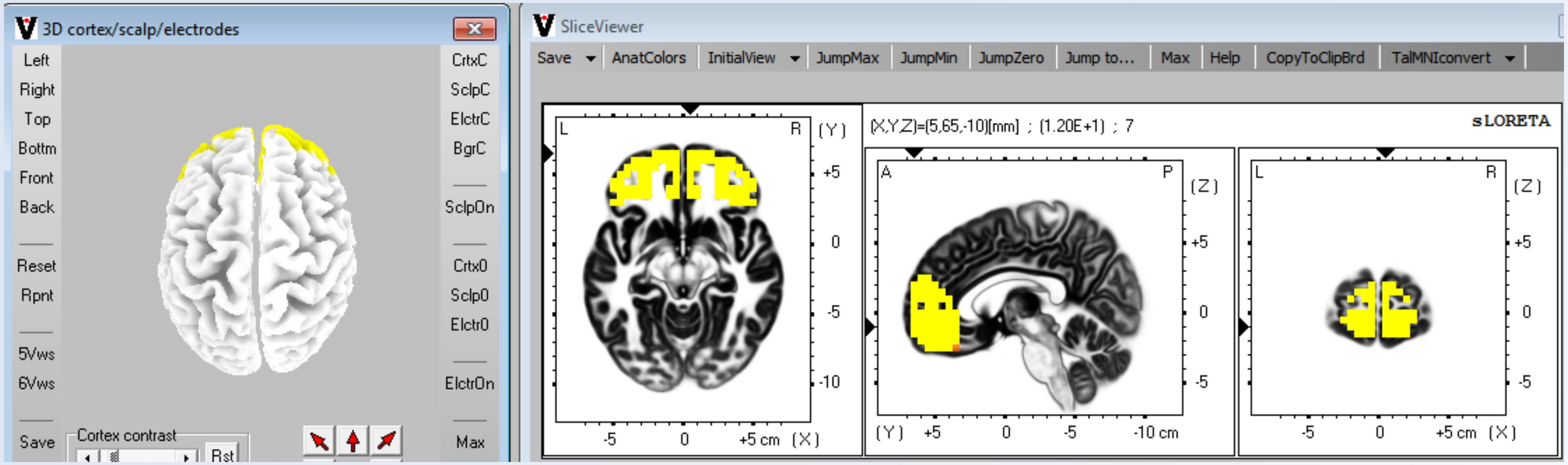

LORETA explorer (LORETA time domain) [Tfica15-zScoresHyperIndpndntFICs-001.slor]
DataType SamplingRateHz(128) Offset(0) Jobs File ColorScales Tools Window ClearFiles ViewInfo [Exp(sLORETA):IsOff] Help
DataType sLorCol ScalpCol AnatCol Slices AllSlices 3DCortex ScalpMap Signals FileExplorer DragDropUtil WindowsExplorer AdjustScreenSize
3D cortex/scalp/electrodes
Left Right Top Bottom Front Back Reset Rpnt 5Vws 6Vws Save
CrtxC SclpC ElctrC BgrC SclpOn Crtx0 Sclp0 Elctr0 ElctrOn Max Deflts
Cortex contrast Rst
Cortex transparency Rst
Scalp contrast Rst
Scalp transparency Rst
Cortex Help
SliceViewer
Save AnatColors InitialView JumpMax JumpMin JumpZero Jump to... Max Help CopyToClipBrd TalMNIconvert
(X,Y,Z)=(5,65,-10)[mm] ; (1.20E+1) ; 7
sLORETA
Neuroanatomy (Talairach labels) :
Track Append Hits: 1 Cpy2ClpBrd Save2File
Value= 1.20E+1
(X= 5 , Y= 65 , Z= -10) (MNI coords)
Best Match at 0 mm
Brodmann area 11
Superior Frontal Gyrus
Frontal Lobe
Find Max/Min
EEG/ERP signals
Save EEGcol GFPcol BgrCol Font Pen+ Pen- AvRefIsOff FilterIsOff
8-12Hz TimeDerivIsOff DC=0(off) ZeroIsOn Max
lorGFP
+Max
-Min
StdCrDn^2
19.625
8.82056ms
TFs/Page: 7 Page: 1/1 TotalTFs=7 Cursors Help Novice EEGextra:0 sLORextra:0
Mark1=46.875ms (TF 7)
Current density related color scale
SavImg SavePal LodSPal LodAPal DefltPal NewPal Ticks: 9 Font +Pos/-Neg Patch Help
-3.000 -2.250 -1.500 -0.750 0.000 0.750 1.500 2.250 3.000
Scale exponent 148.41 Reset
Scale Max 3.000E+00
SelfMax SelfMax% 50
FixedMax GlobalMax

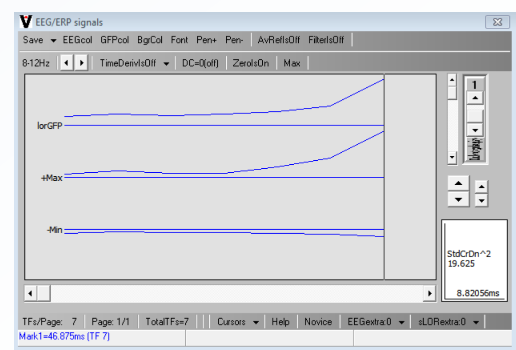
How to interpret what you see:

1. The color scale is set to display activation only if it has a z-score higher that 3, which is significant.
2. In the “EEG/ERP signals” window, the two lower curves correspond to positive maximum, and minimum negative activation, for each frequency band (there are 7 bands along the x-axis).
3. In the previous slide, the results show maximum activation in frontal cortex for high frequency Beta3 band.
4. This is a simple case, with only one dominant frequency (Beta3). For other brain networks, if there is more than one dominant frequency, it is necessary to check each of those frequencies individually.

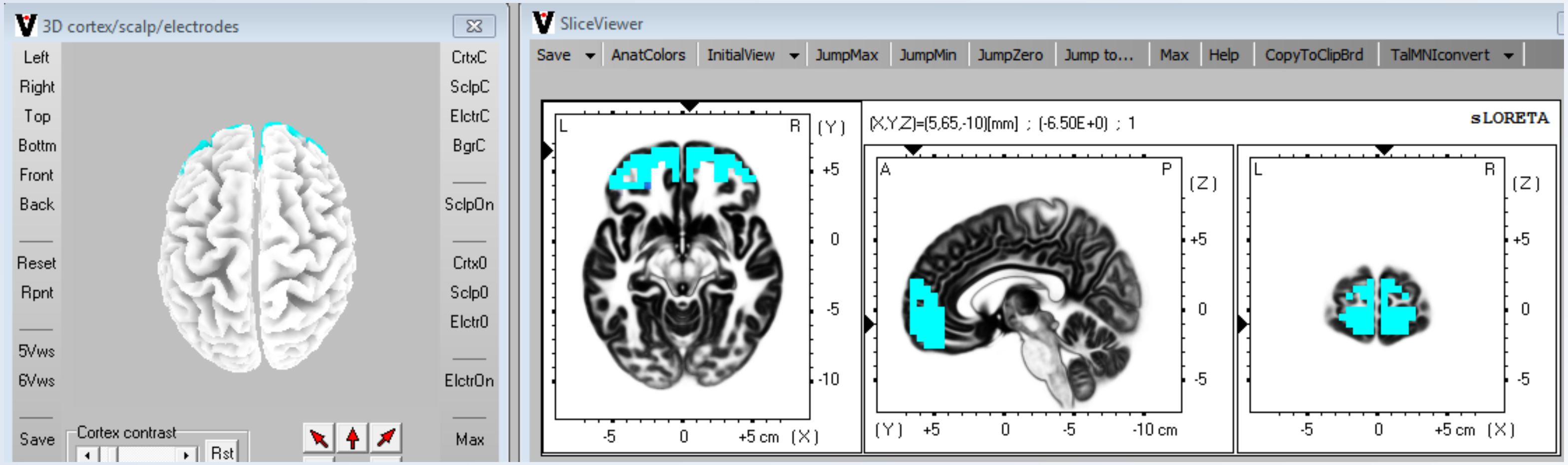
The next slides summarize some of the main networks

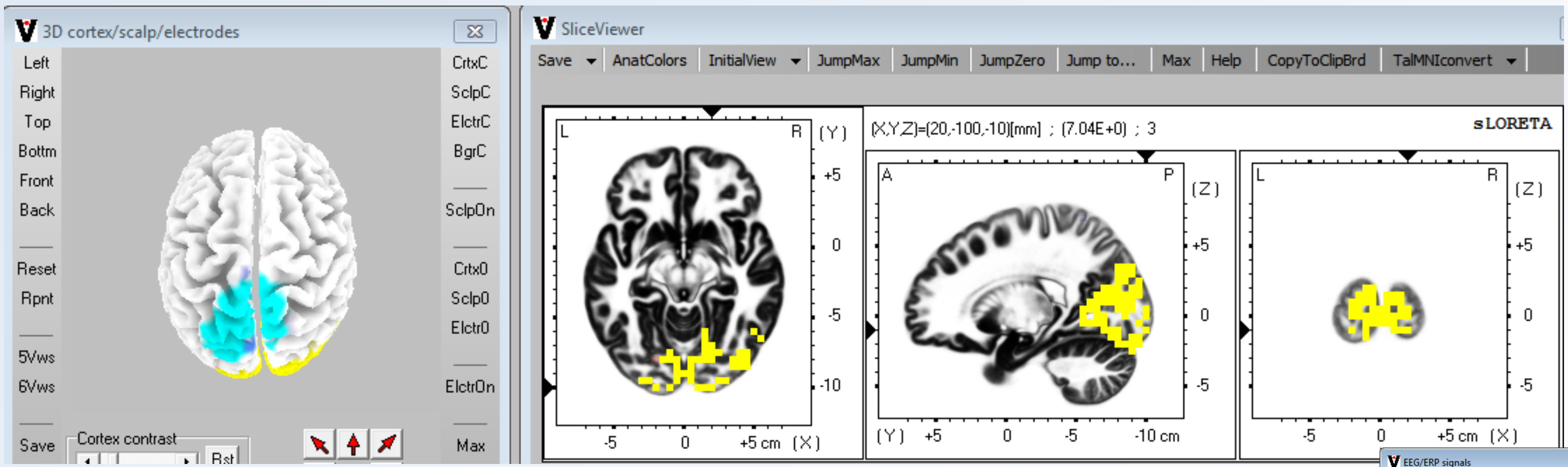
LORETA resting state network 1: Frontal Beta3

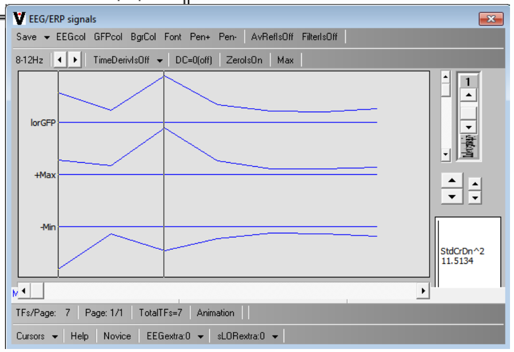




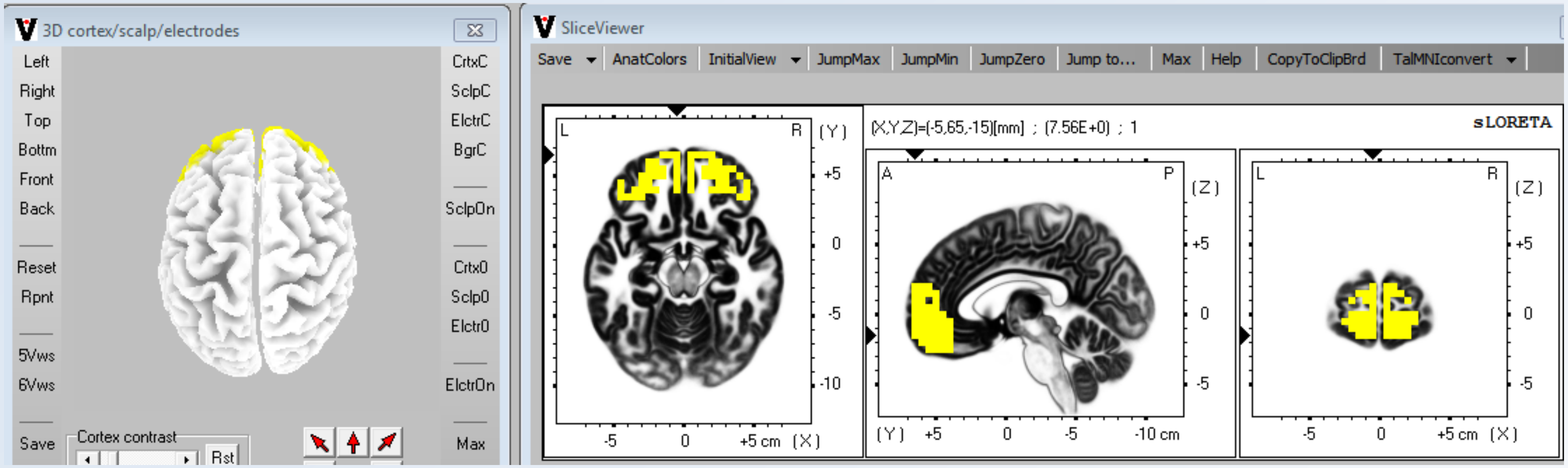
LORETA resting state network 2: (Frontal Delta AND Parietal Alpha1) anti-correlated with Occipital Alpha1

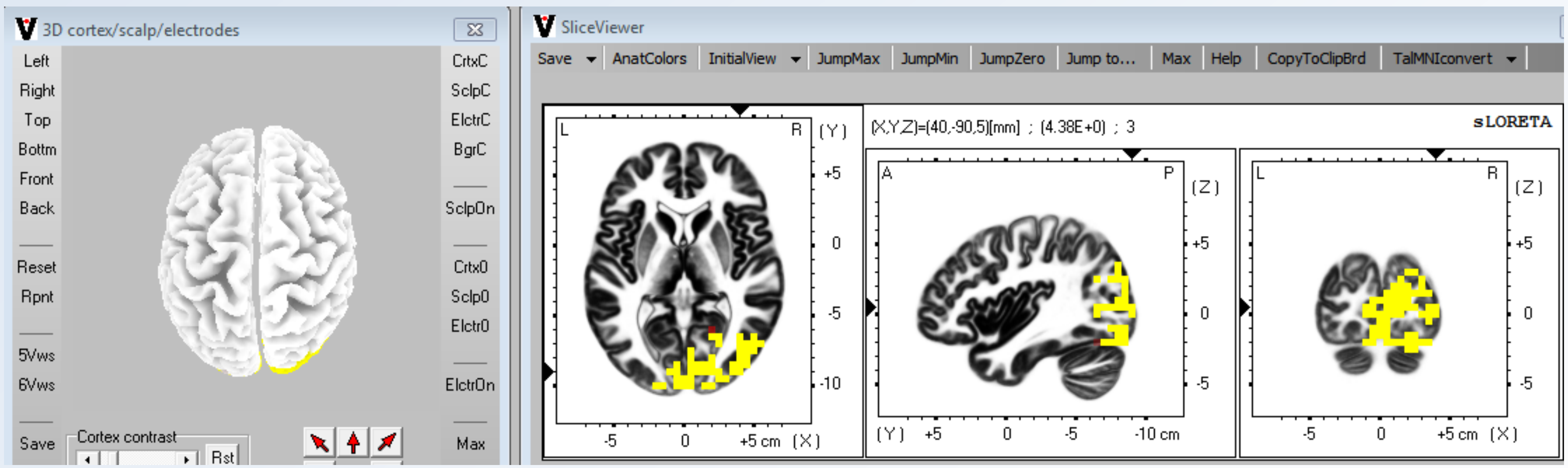


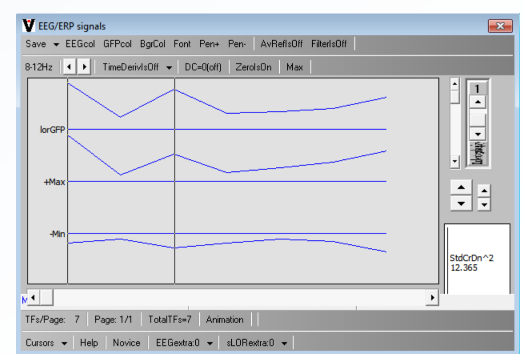




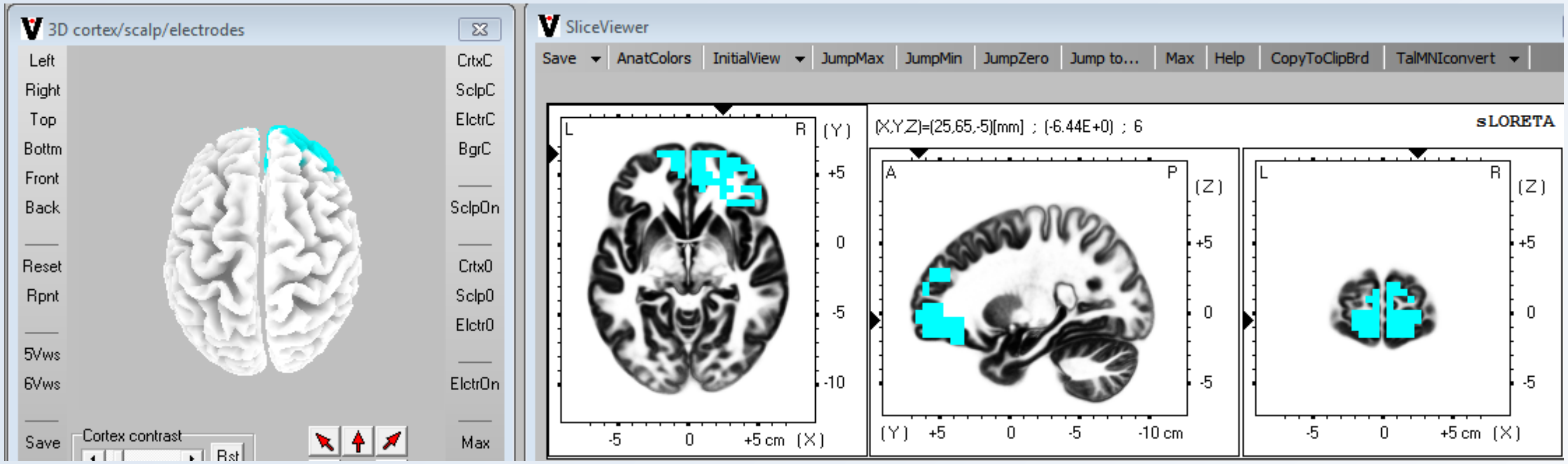
LORETA resting state network 3: Frontal Delta with Occipital Alpha1

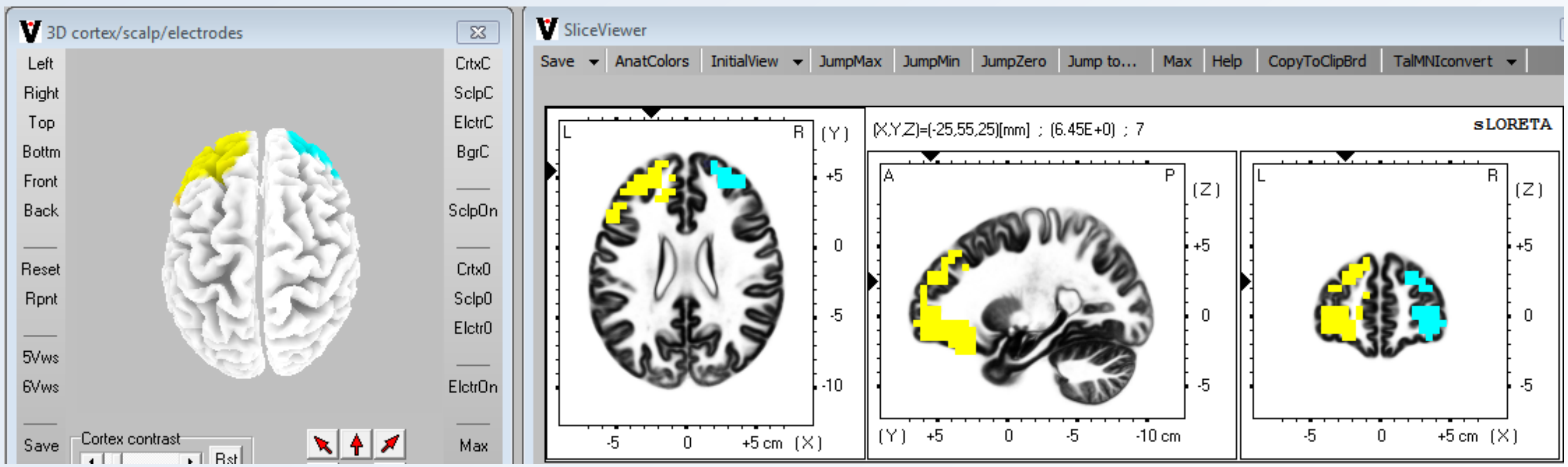


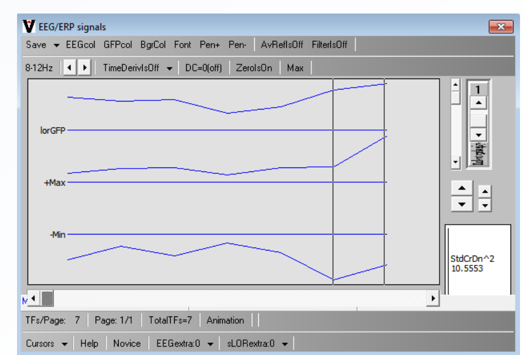




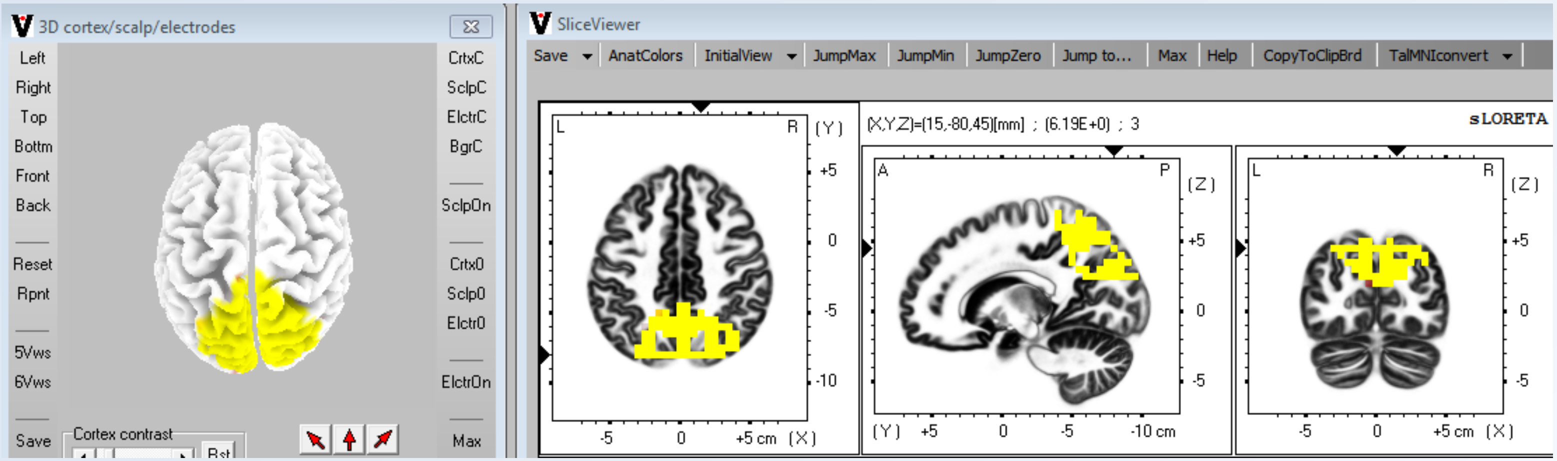
LORETA resting state network 4: Right Frontal Beta2 anti-correlated with Left Frontal Beta3

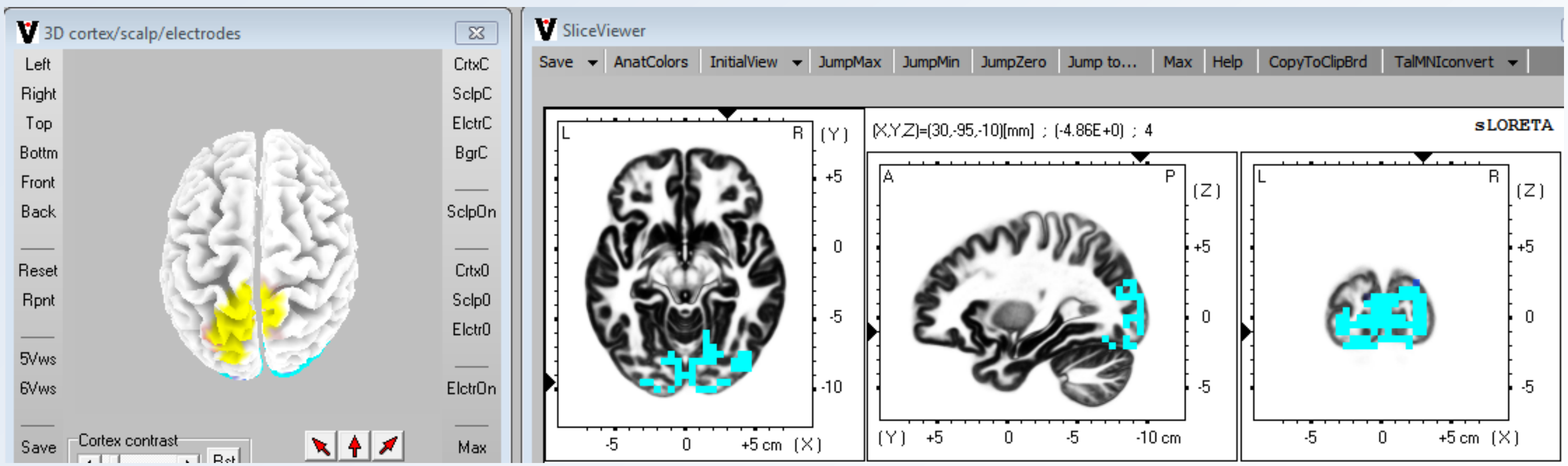


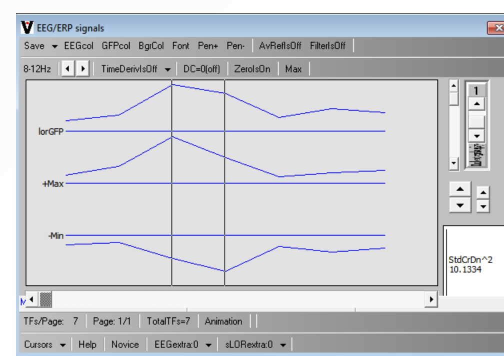




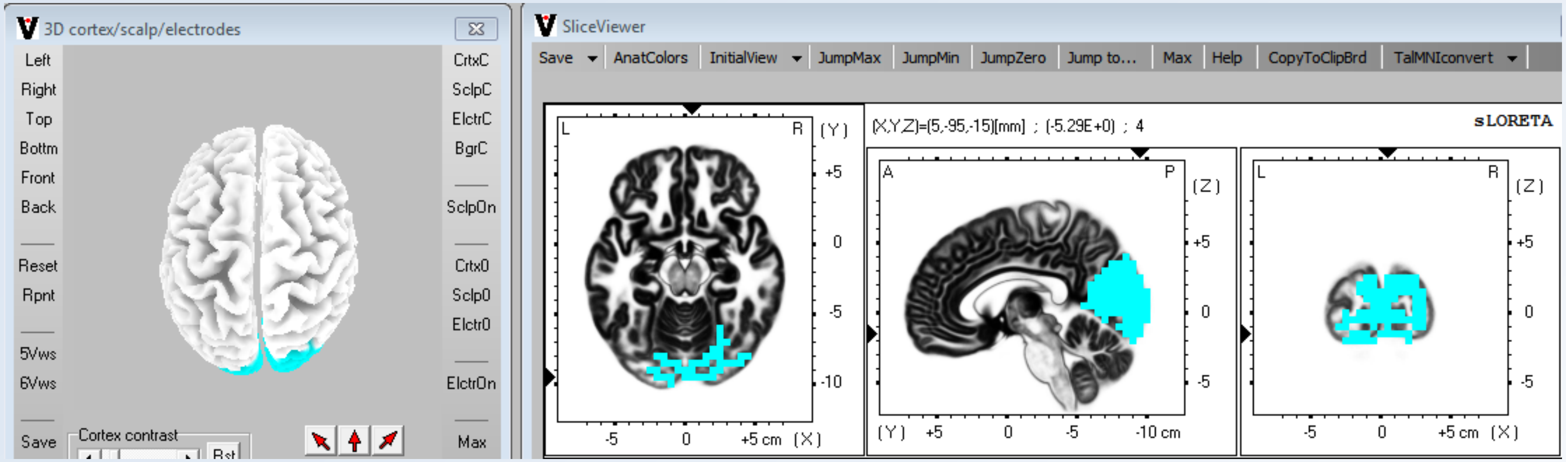
LORETA resting state network 5: Parietal Alpha1 anti-correlated with Occipital Alpha2

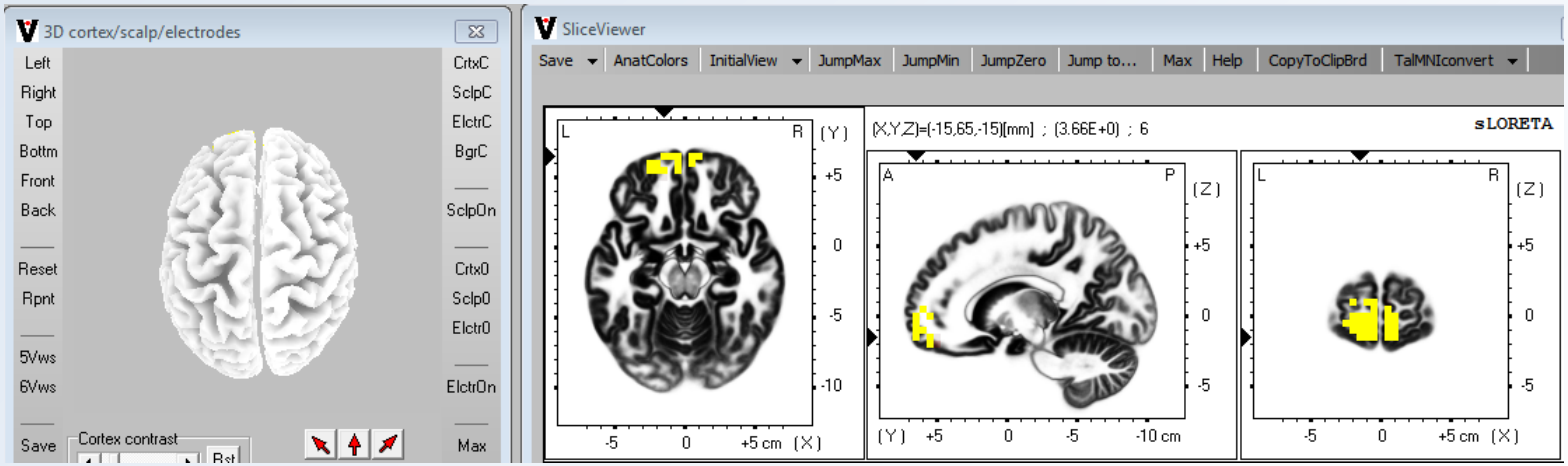


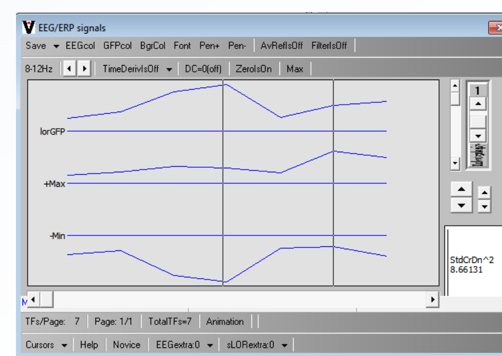




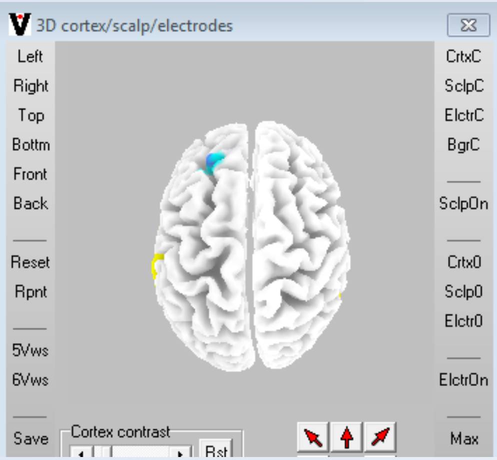
LORETA resting state network 6: Occipital Alpha anti-correlated with Frontal Beta2

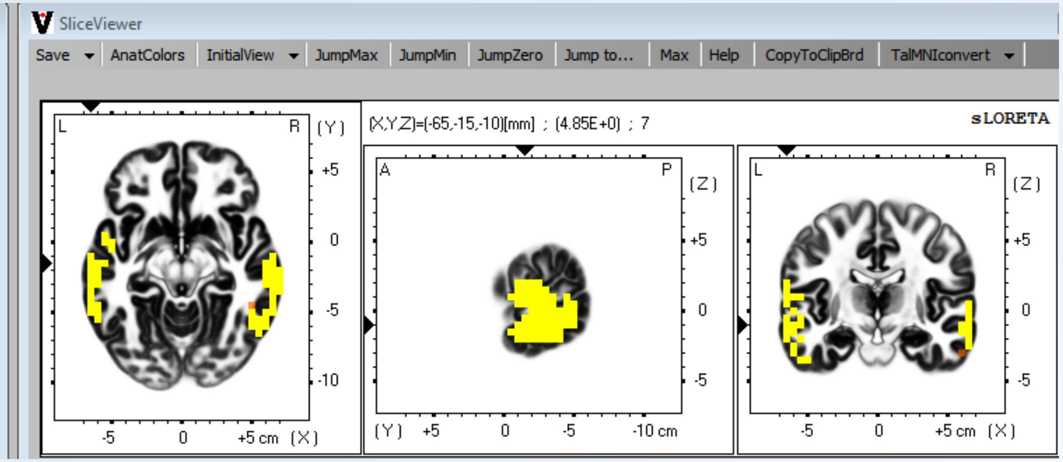


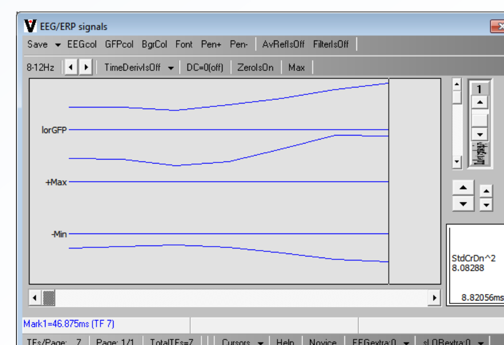




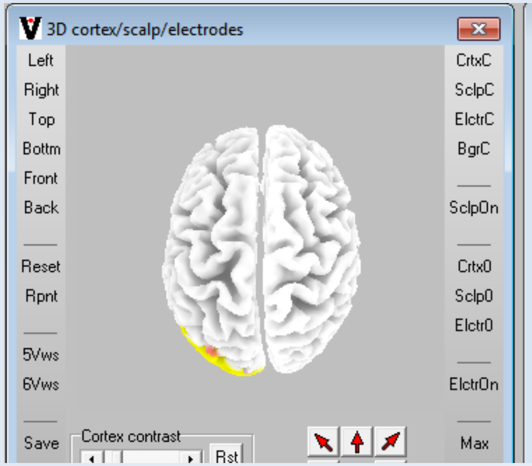
LORETA resting state network 9: Temporal (auditory) cortices Beta2 and Beta3

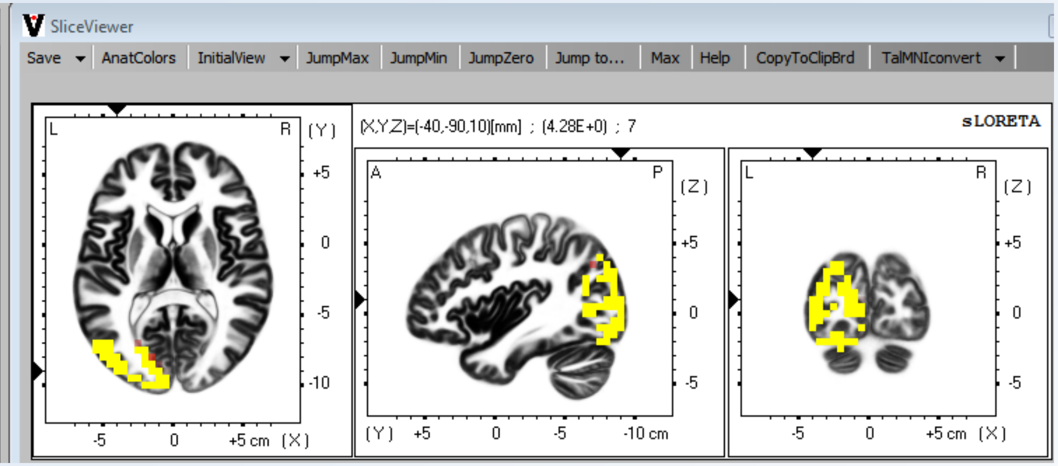


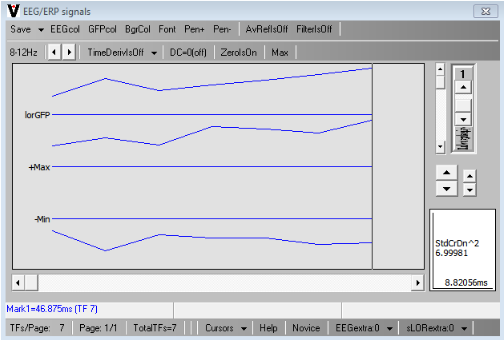




LORETA resting state network 11: Left Occipito-Parietal cortex Alpha2 to Beta3





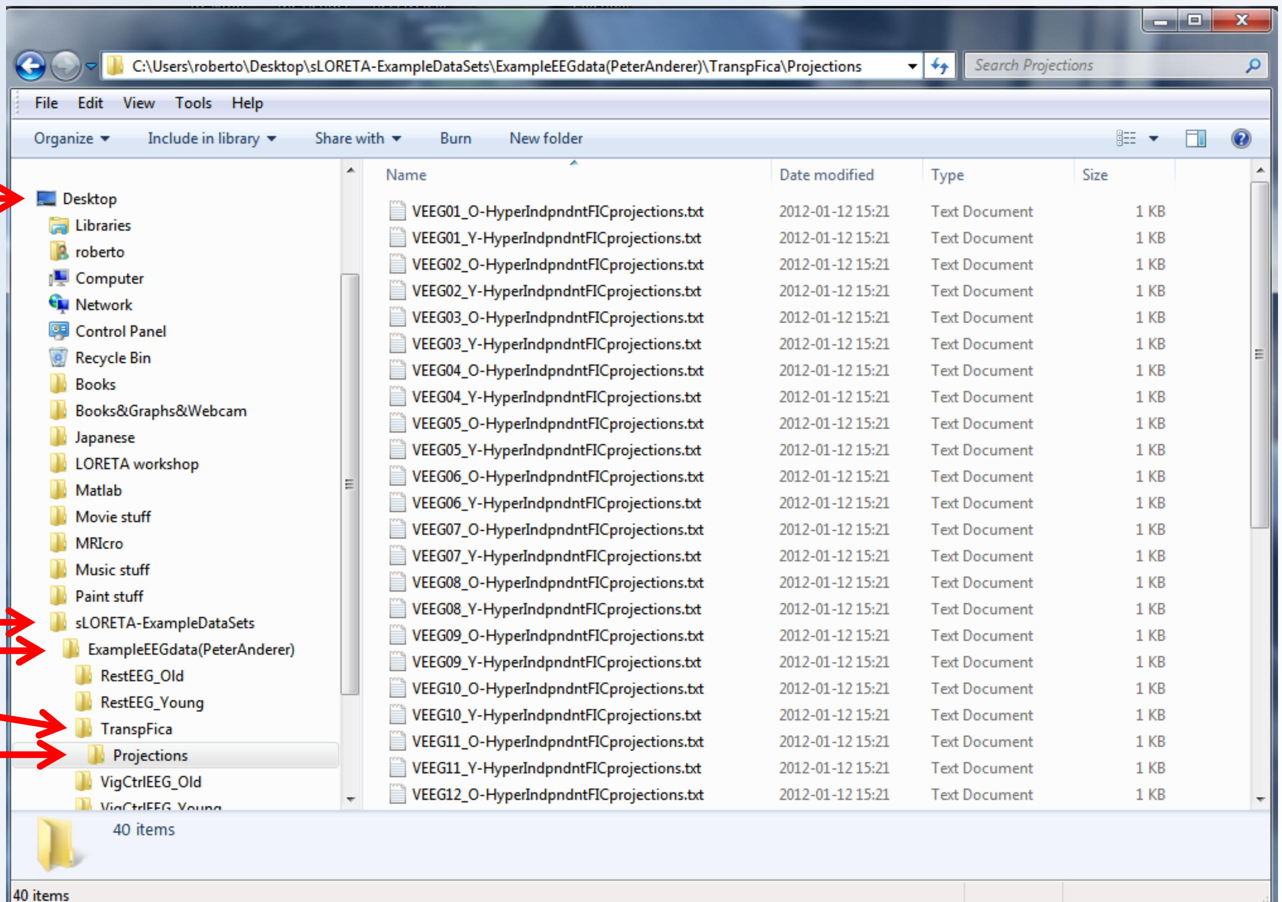


Statistical Analysis of Resting State Networks

The previous 15 resting state networks are common to both groups of subjects (young and old normal controls).
Both types of brain use the same resources (common networks).

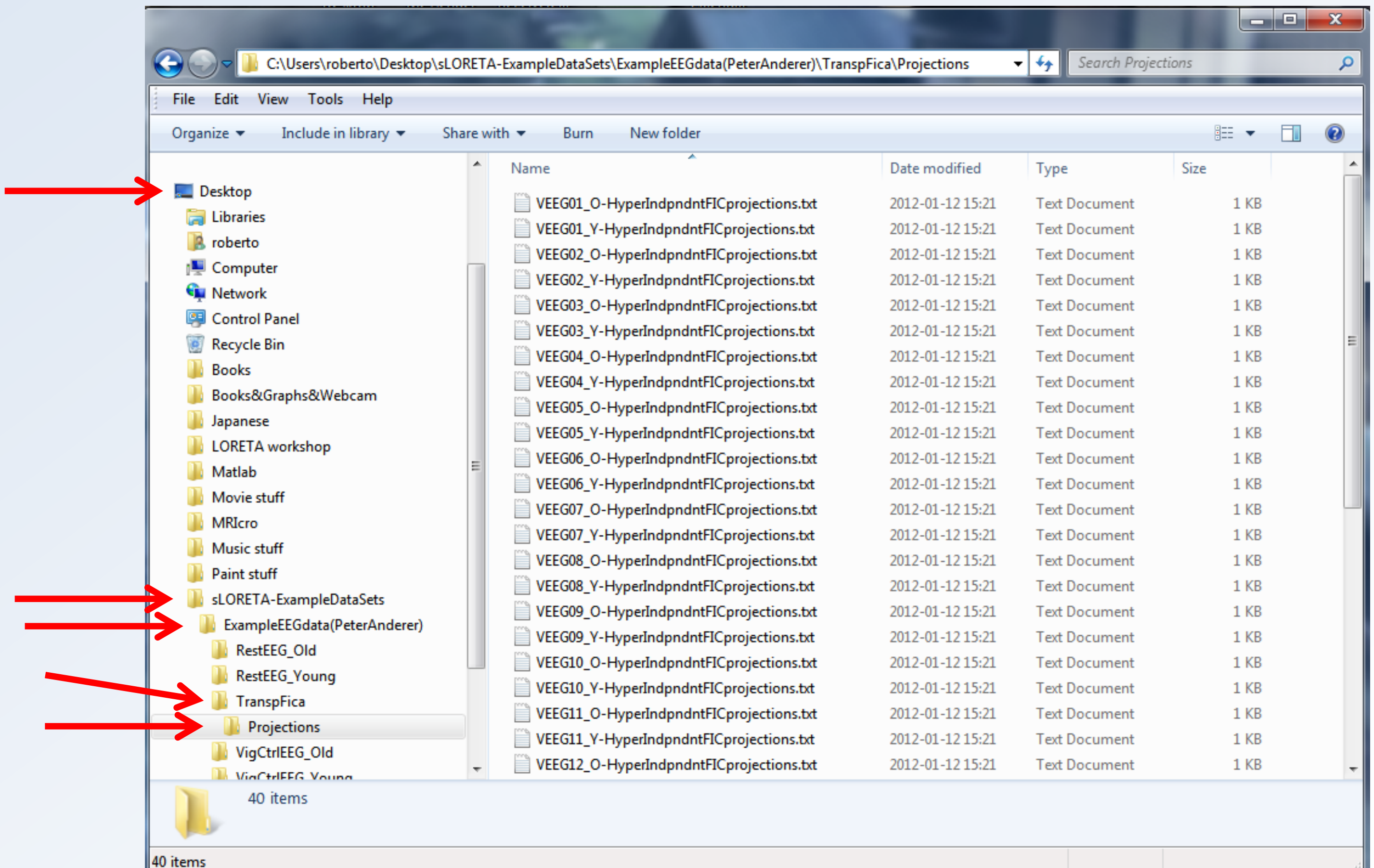
However, it may happen that the older subjects use some networks in a different way as compared to the younger subjects.

The usage of the networks for each subject consist of the files located in the “Projections” folder:

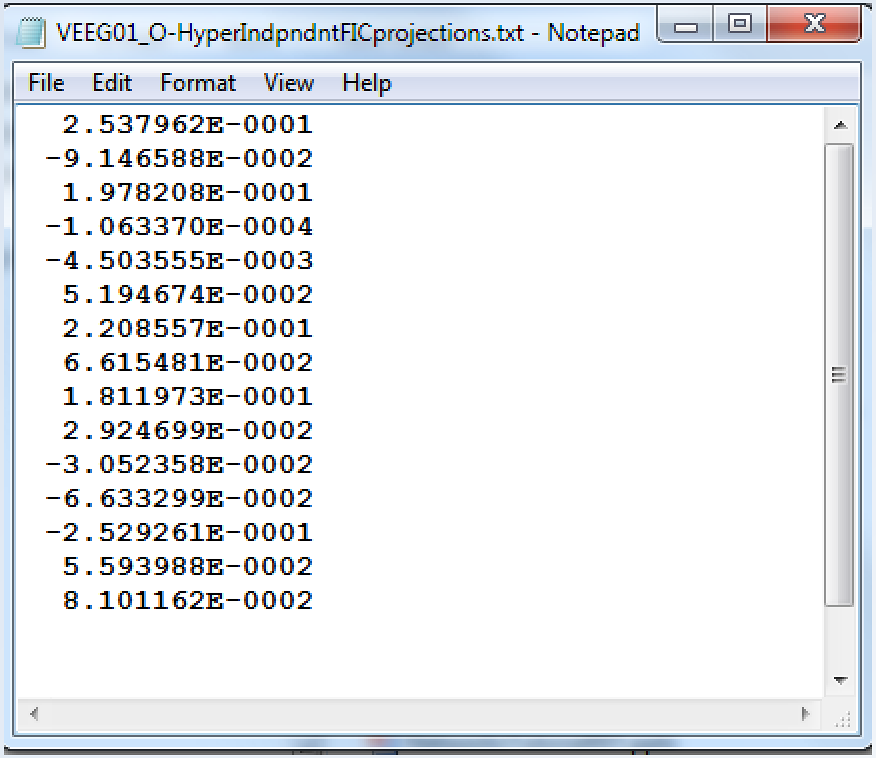


For instance:
VEEG01_O-HyperIndpndntFICprojections.txt corresponds to old subject number 1;
VEEG01_Y-HyperIndpndntFICprojections.txt corresponds to young subject number 1;

These text files contain 15 coefficients, expressing how each network is used.



For instance, the coefficients for VEEG01_O-HyperIndpndntFICprojections.txt are


VEEG01_O-HyperIndpndntFICprojections.txt - Notepad

File Edit Format View Help

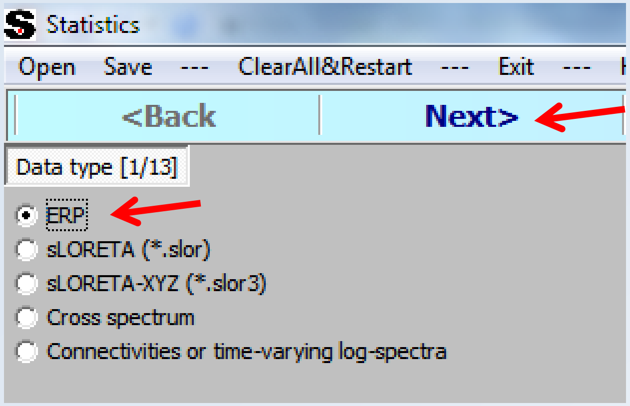
```
 2.537962E-0001
-9.146588E-0002
 1.978208E-0001
-1.063370E-0004
-4.503555E-0003
 5.194674E-0002
 2.208557E-0001
 6.615481E-0002
 1.811973E-0001
 2.924699E-0002
-3.052358E-0002
-6.633299E-0002
-2.529261E-0001
 5.593988E-0002
 8.101162E-0002
```

One coefficient for each network, expressing how that subject uses that network.

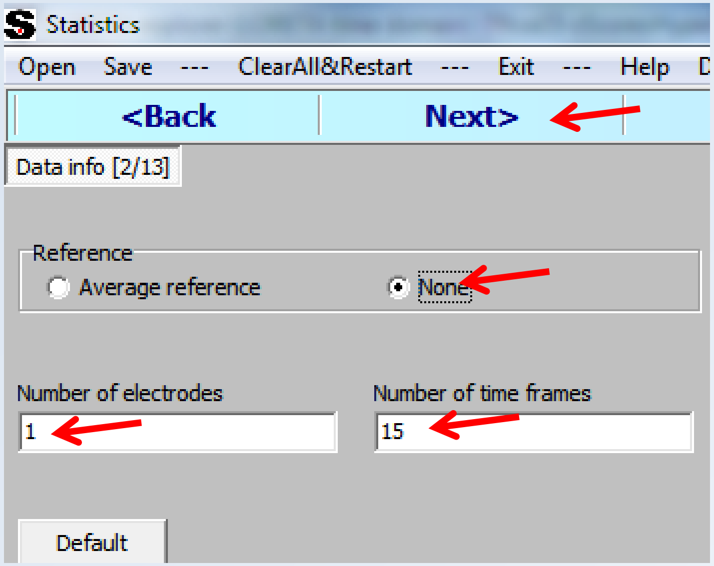
Statistical analysis can be performed on these 15 numbers, comparing Old and Young groups, in search of how the old brain uses the Resting State networks differently from the young brain.

For statistical analysis, these files will be treated as ERP files, with 1 fictitious electrode and 15 fictitious time frames.

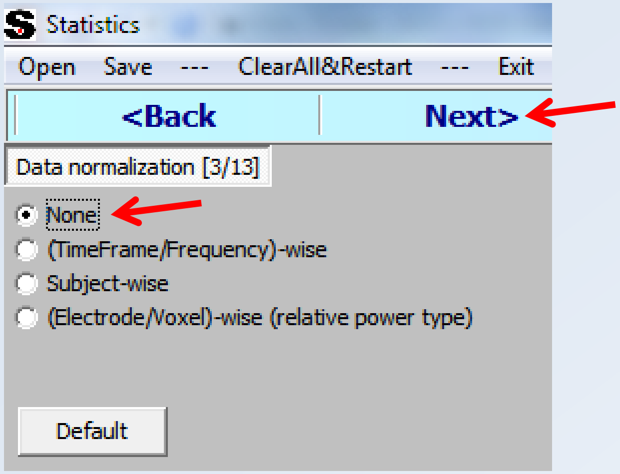
Run the Statistics module and note the arrows:



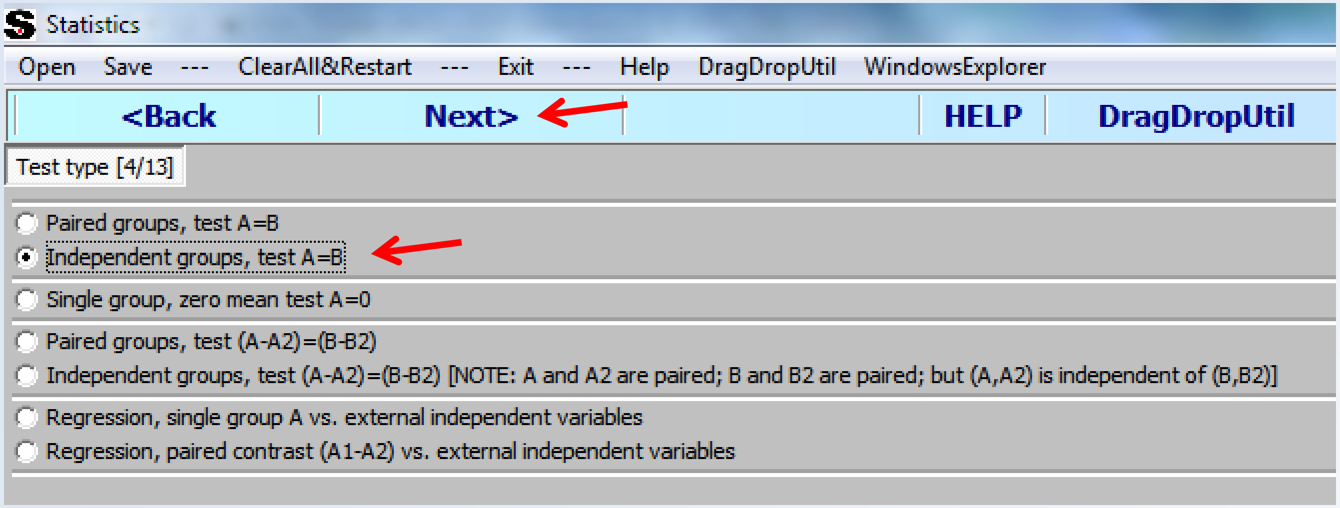
Continuing Statistics, note the arrows:



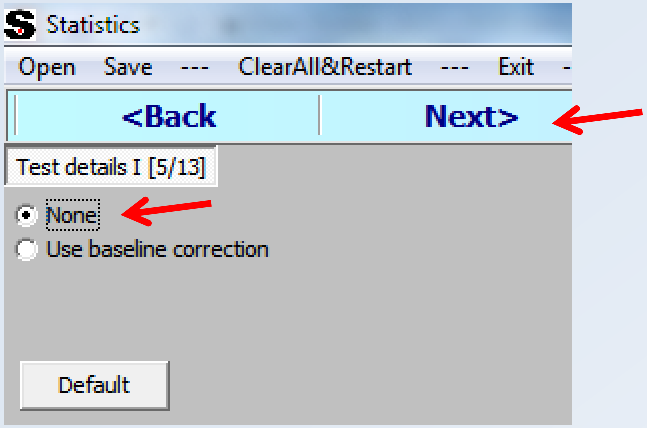
Continuing Statistics, note the arrows:



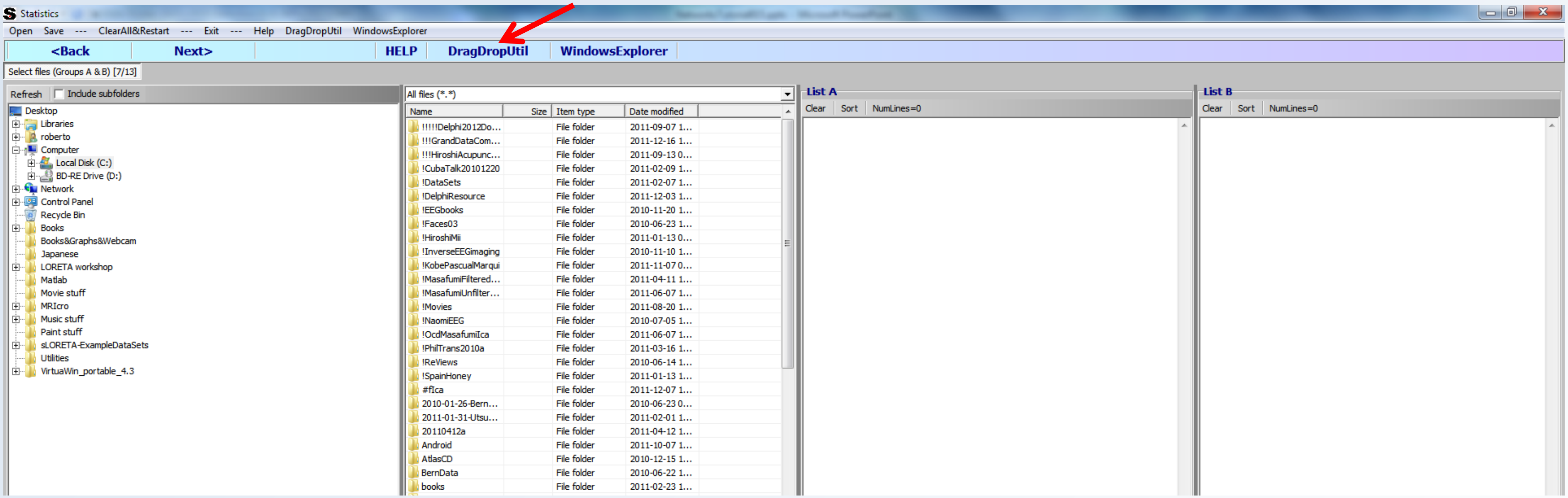
Continuing Statistics, note the arrows:



Continuing Statistics, note the arrows:

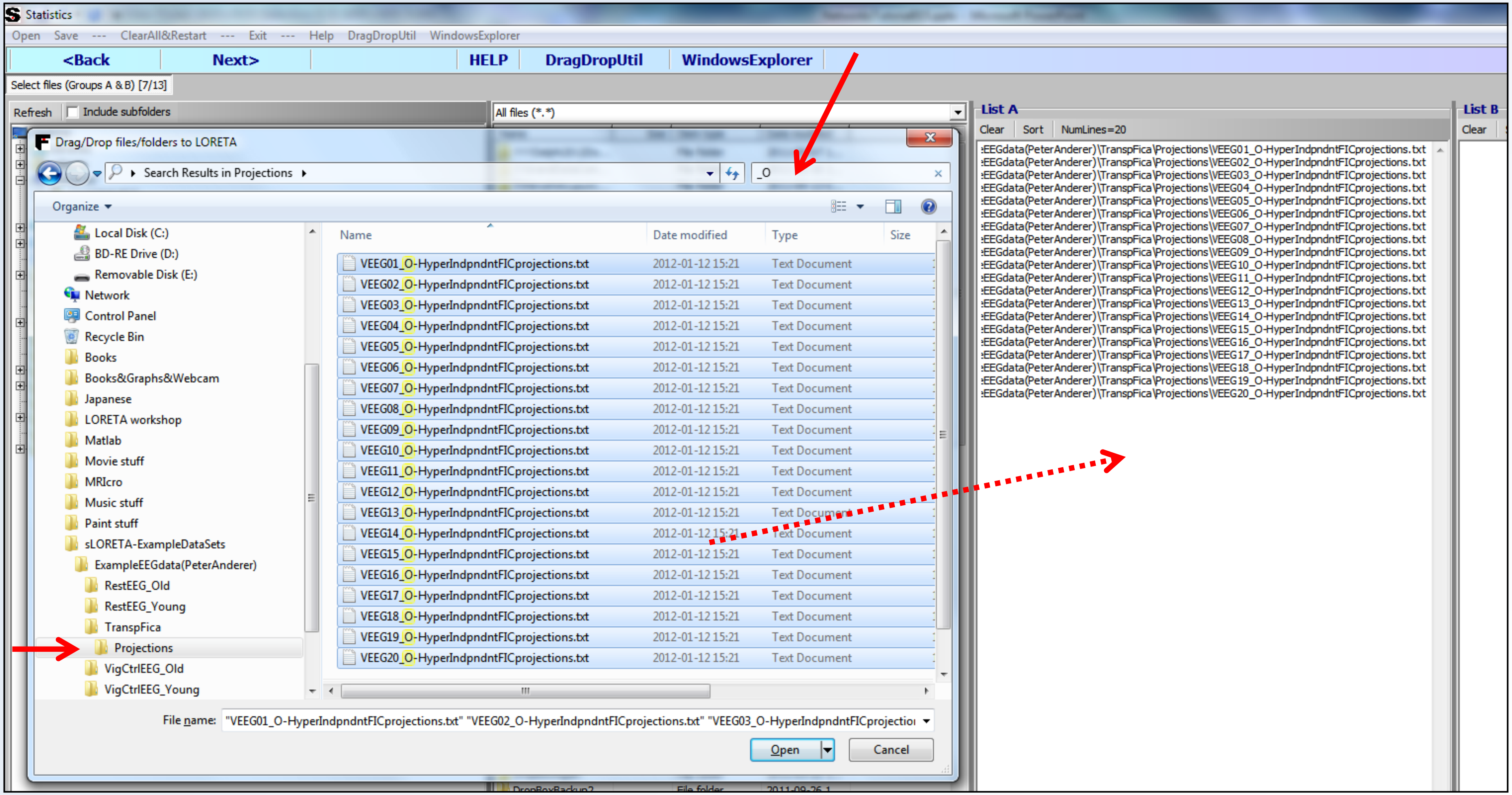


Continuing Statistics, note the arrows:



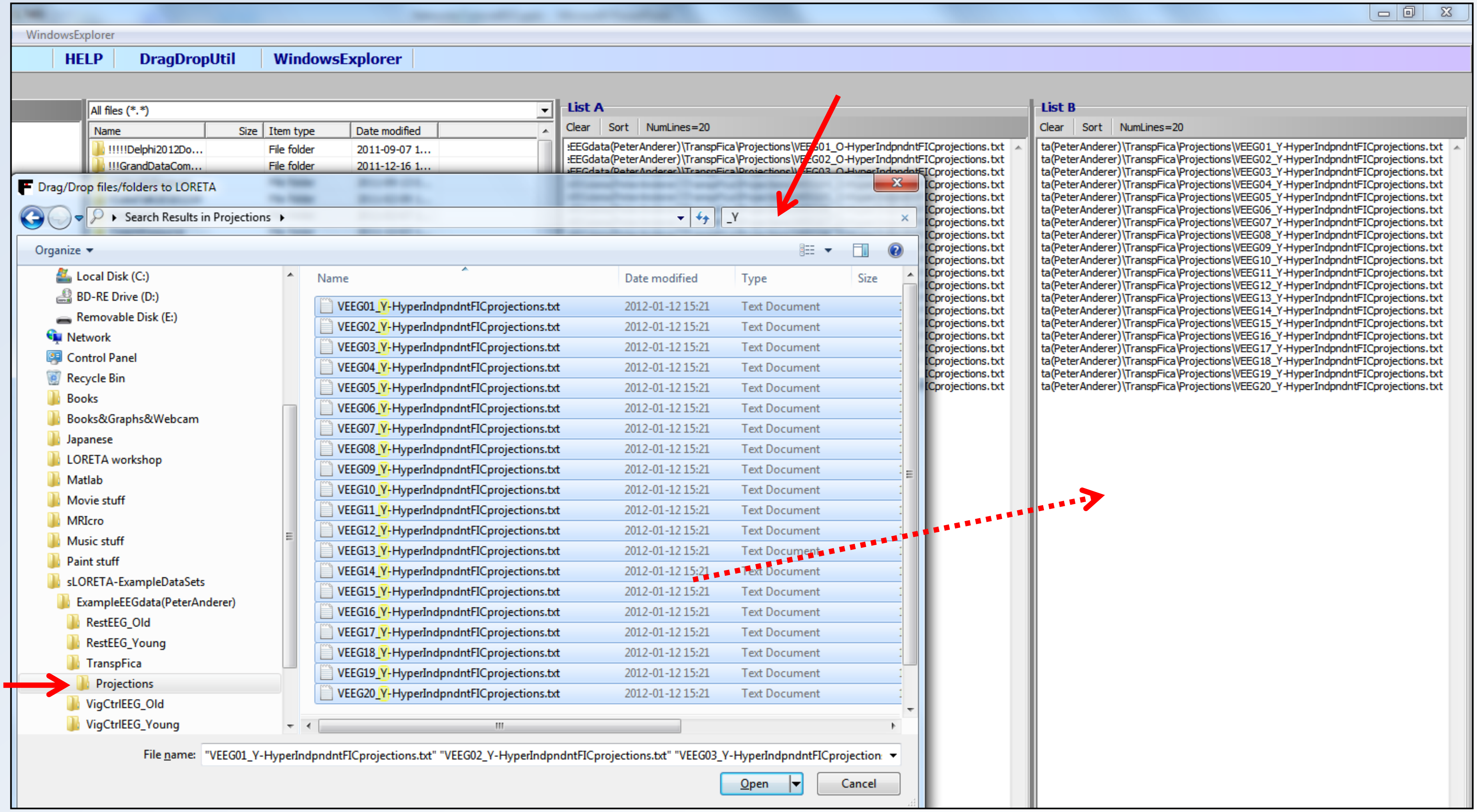
At this point the files with the coefficients (projections) must be selected carefully, placing (drag/drop) the old subjects in list A, and the young subjects in list B. This can be achieved manually, using the left side panels. But more conveniently using the DragDropUtil (red arrow).

Continuing Statistics, note the arrows:



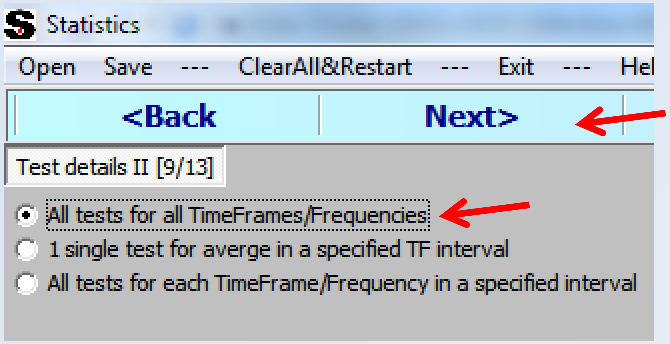
The filenames for old subjects include the unique characters "_O". The search function finds these 20 files, and they are selected and drag/dropped in list A.

Continuing Statistics, note the arrows:

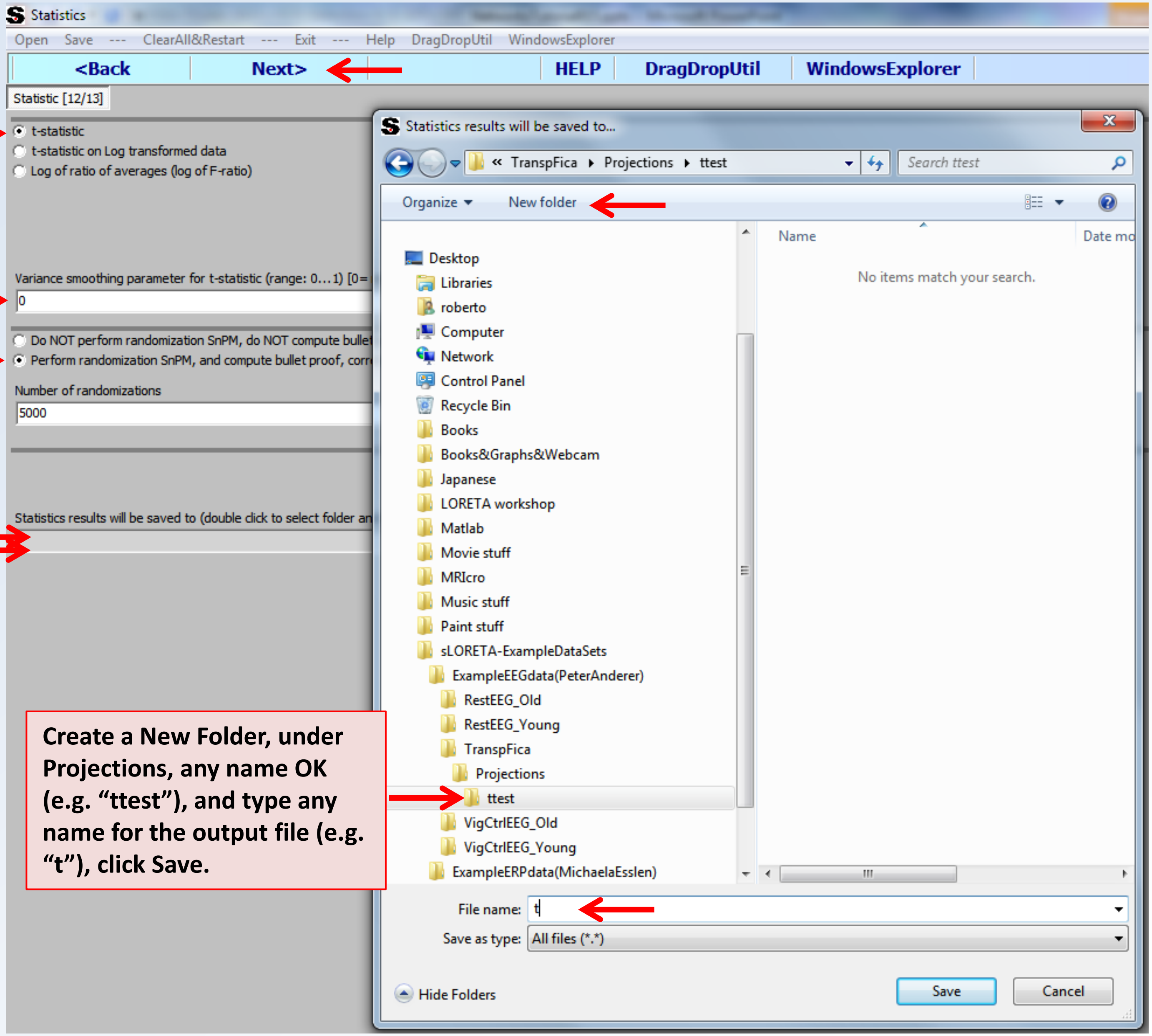


The filenames for young subjects include the unique characters "_Y". The search function finds these 20 files, and they are selected and drag/dropped in list B. Now click next.

Continuing Statistics, note the arrows:



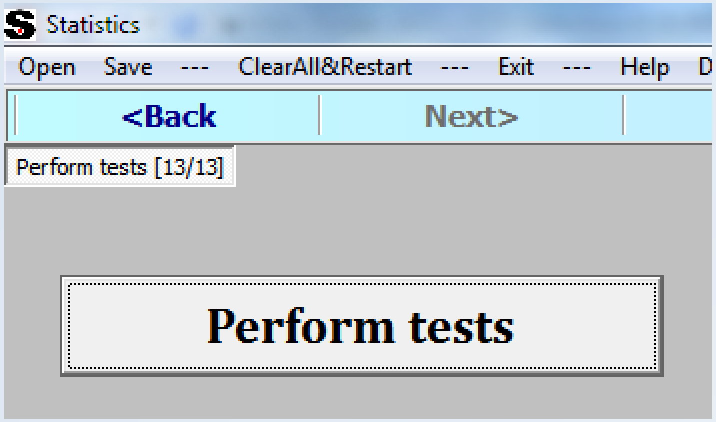
Continuing Statistics, note the arrows:



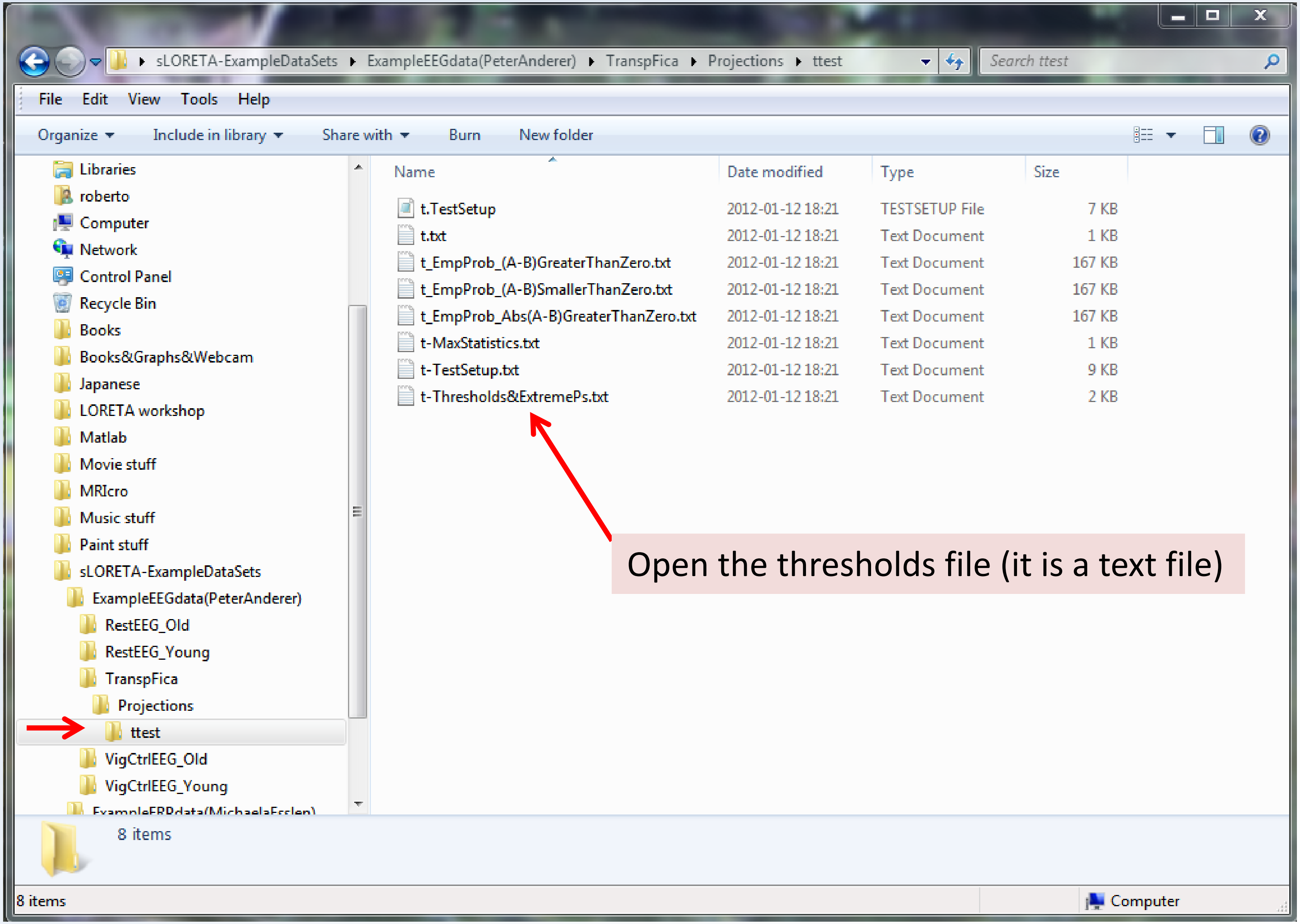
Double-click

Create a New Folder, under Projections, any name OK (e.g. “ttest”), and type any name for the output file (e.g. “t”), click Save.

Finally click perform tests, and wait till finished.



Open the windows explorer, navigate to the "ttest" folder:



t-Thresholds&ExtremePs.txt - Notepad

	t(0.01)	t(0.05)	t(0.10)	ExtremeP
One-Tailed (A>B):	3.605	2.932	2.629	0.00320
One-Tailed (A<B):	-3.559	-2.979	-2.658	0.00680
Two-Tailed (A<>B):	3.815	3.232	2.920	0.00600

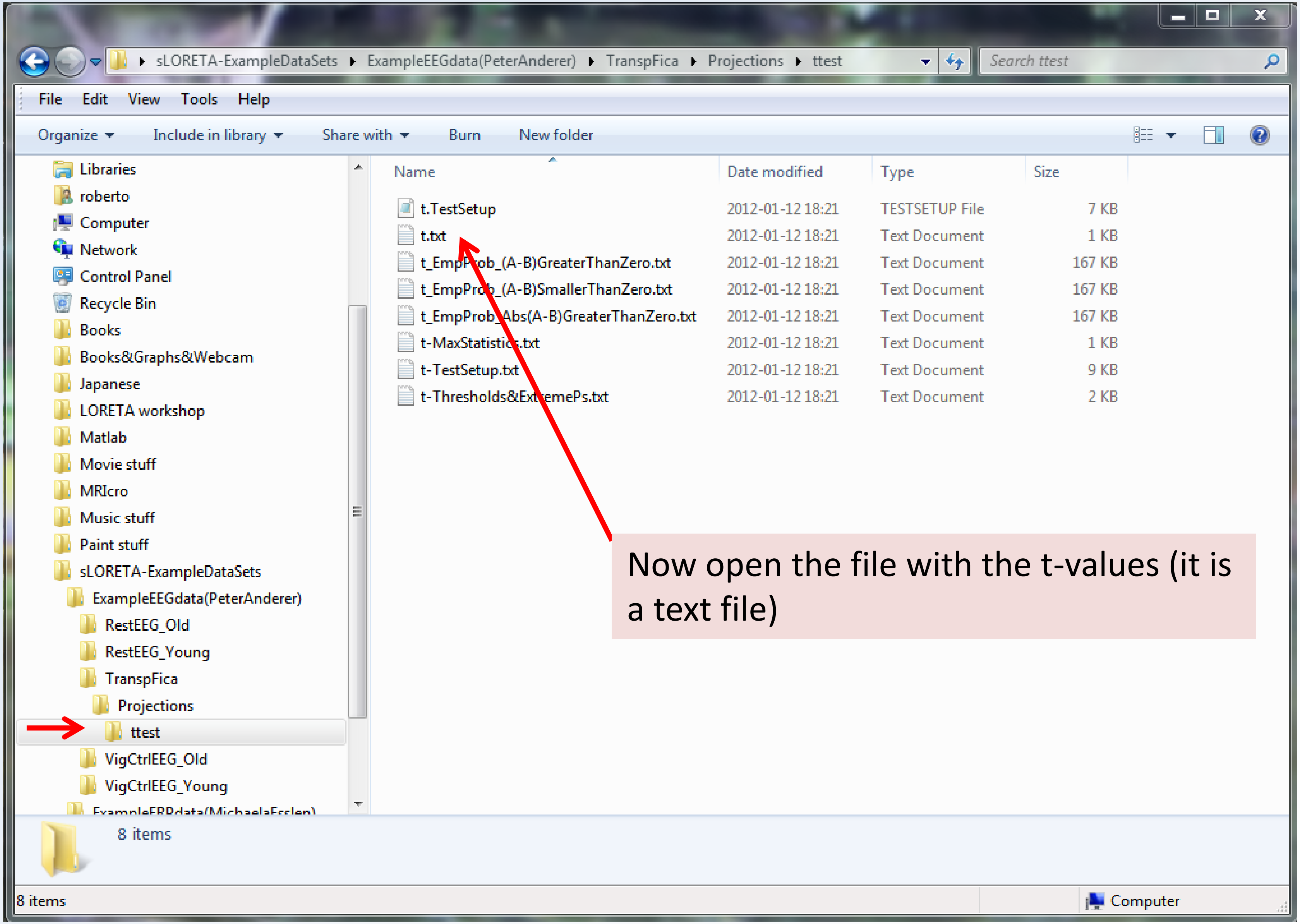
Exceedence proportion tests:

Thrsh(1Tailed>0)	Prob(1Tailed>0)	Thrsh(1Tailed<0)	Prob(1Tailed<0)	Thrsh(2Tailed)	Prob(2Tailed)
0.398516	0.442400	-0.373899	0.675600	0.398516	0.706800
0.797033	0.678000	-0.747797	0.277000	0.797033	0.526800
1.195549	0.298400	-1.121696	0.158400	1.195549	0.185400
1.594066	0.249400	-1.495595	0.113800	1.594066	0.146400
1.992582	0.078800	-1.869494	0.024400	1.992582	0.024400
2.391099	0.018800	-2.243392	0.033400	2.391099	0.014800
2.789615	0.004200	-2.617291	0.007400	2.789615	0.002600
3.188132	0.000600	-2.991190	0.000800	3.188132	0.000000
3.586648	0.000200	-3.365088	0.000600	3.586648	0.000000
3.985164	0.003000	-3.738987	0.006800	3.985164	0.005800

There is significant difference between the way the old and young subjects use the resting state networks!

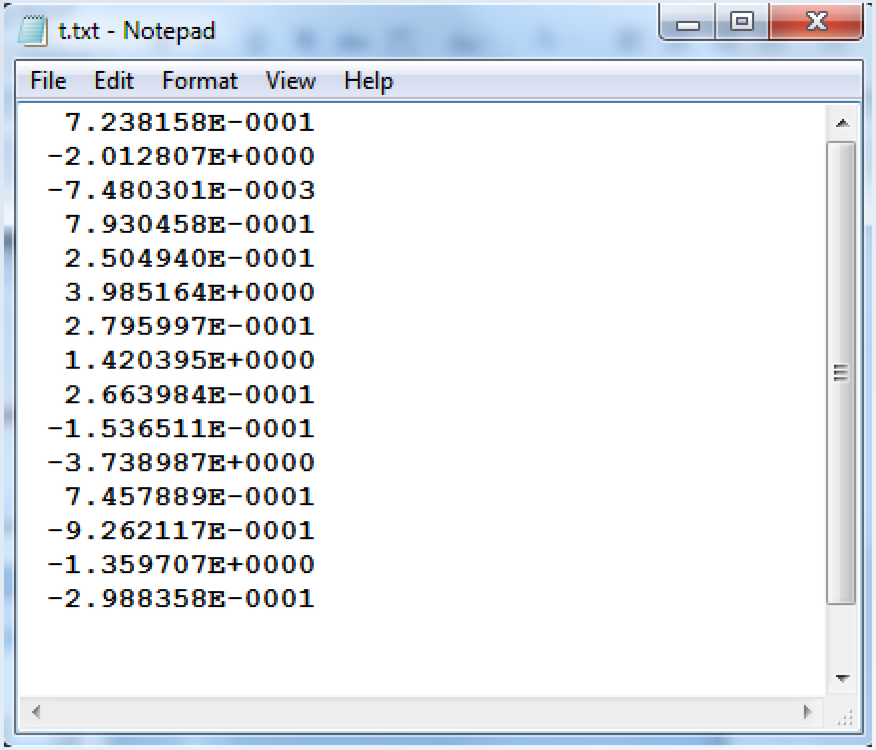
The highlighted threshold value is t=1.99, for p=0.02

Open the windows explorer, navigate to the “ttest” folder:



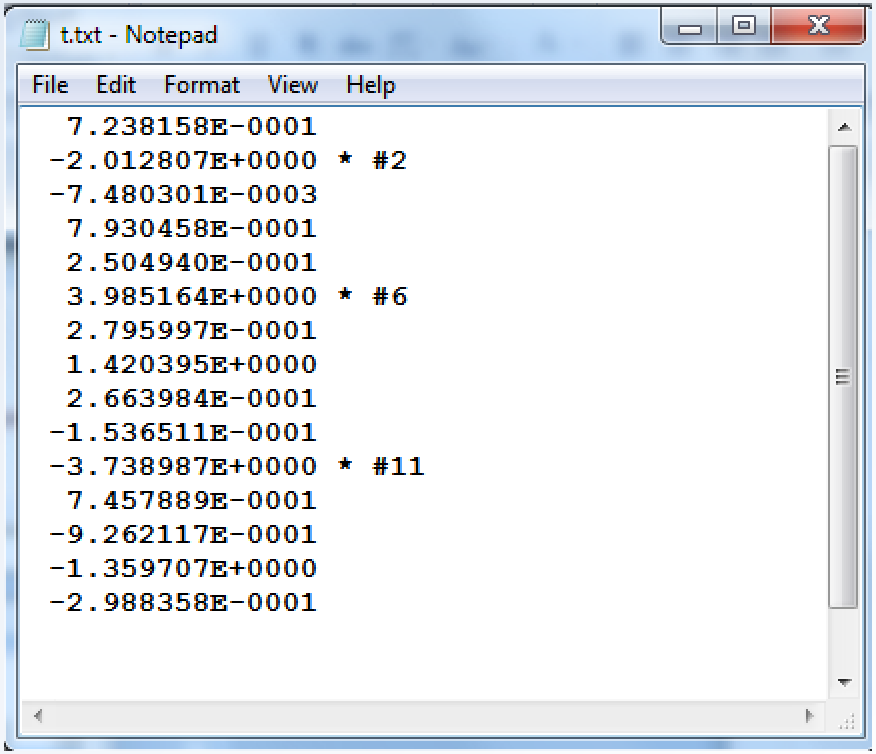
Now open the file with the t-values (it is a text file)

Original t-values:



```
 7.238158E-0001
-2.012807E+0000
-7.480301E-0003
 7.930458E-0001
 2.504940E-0001
 3.985164E+0000
 2.795997E-0001
 1.420395E+0000
 2.663984E-0001
-1.536511E-0001
-3.738987E+0000
 7.457889E-0001
-9.262117E-0001
-1.359707E+0000
-2.988358E-0001
```

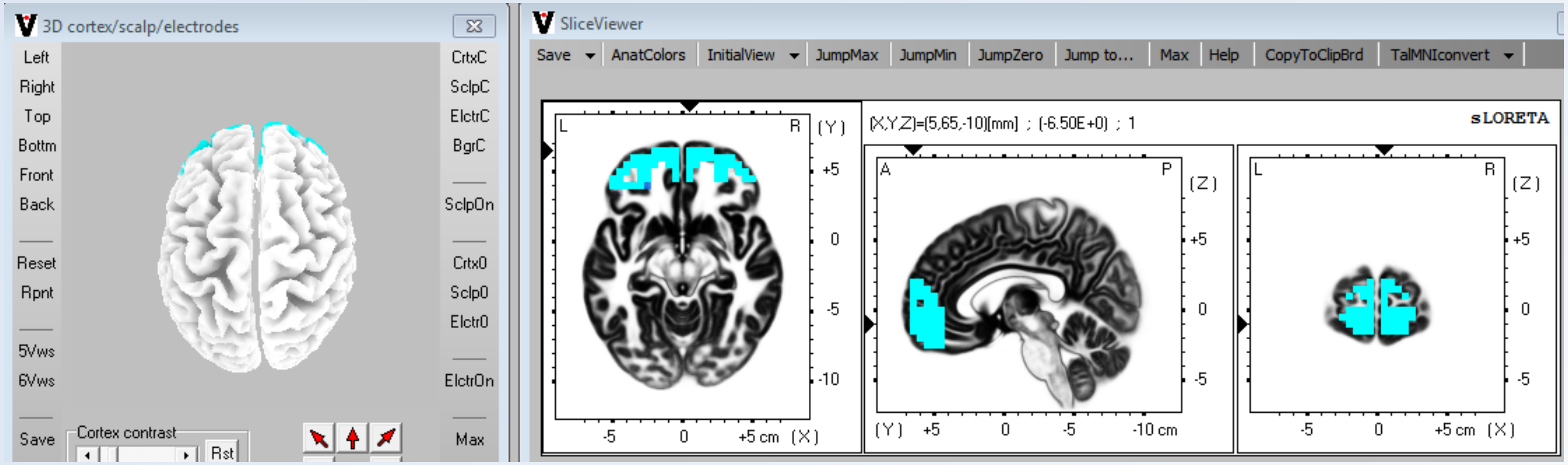
Indicating significant results (t=2, p=0.024)

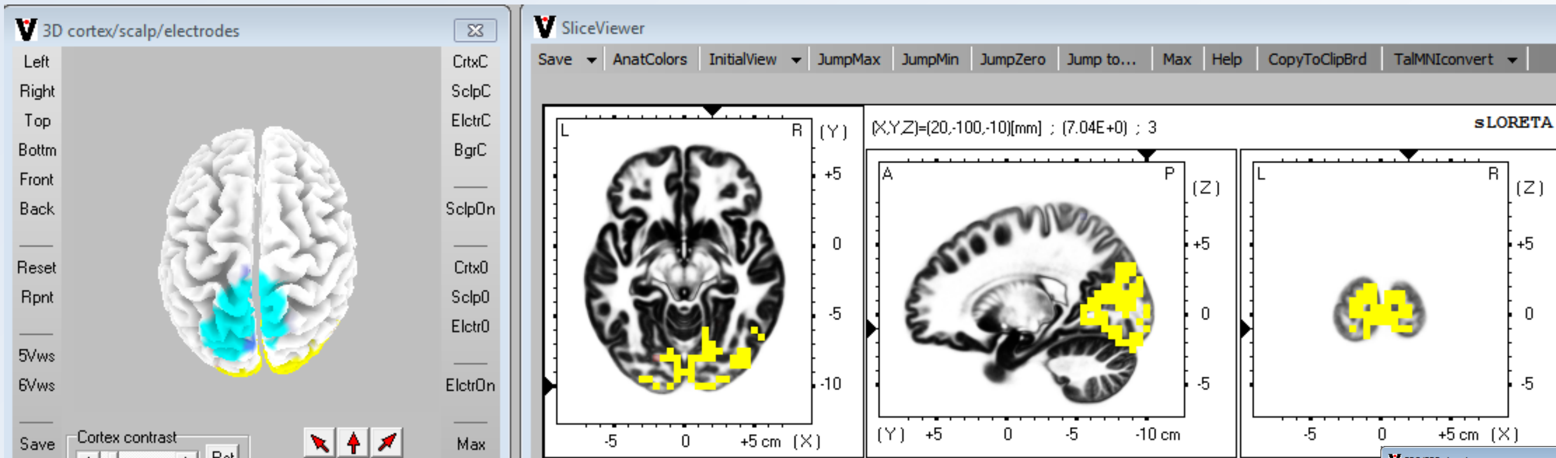


```
 7.238158E-0001
-2.012807E+0000 * #2
-7.480301E-0003
 7.930458E-0001
 2.504940E-0001
 3.985164E+0000 * #6
 2.795997E-0001
 1.420395E+0000
 2.663984E-0001
-1.536511E-0001
-3.738987E+0000 * #11
 7.457889E-0001
-9.262117E-0001
-1.359707E+0000
-2.988358E-0001
```

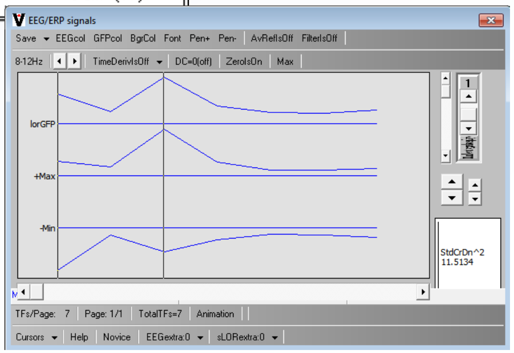
The use of the resting state networks numbered 2, 6, and 11 are significantly different between old and young subjects

LORETA resting state network 2: (Frontal Delta AND Parietal Alpha1) anti-correlated with Occipital Alpha1

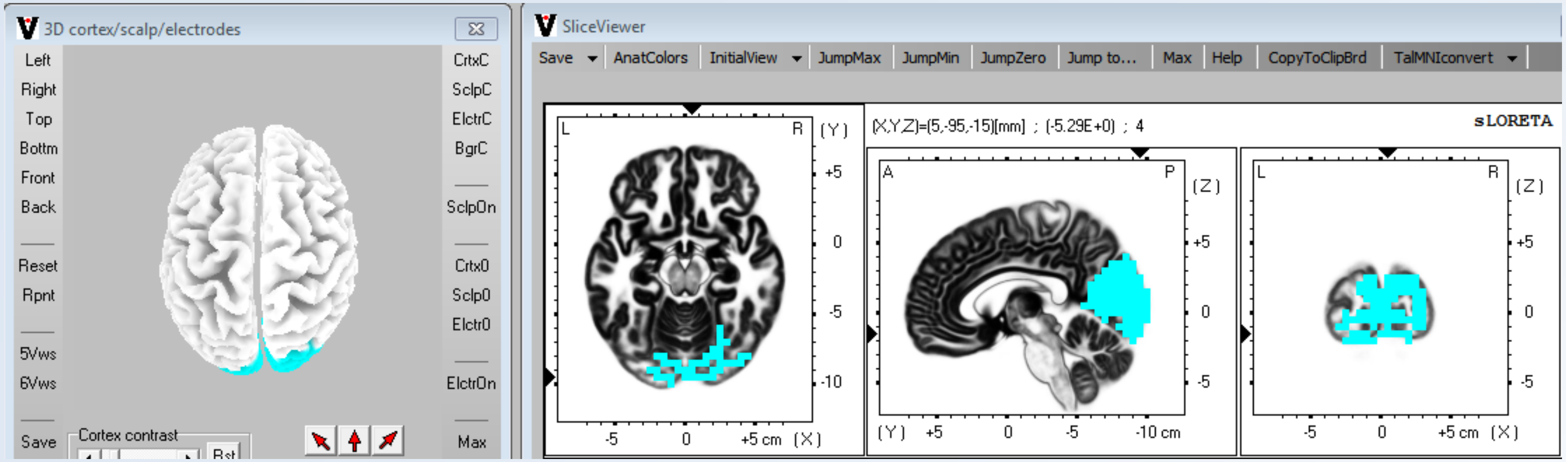


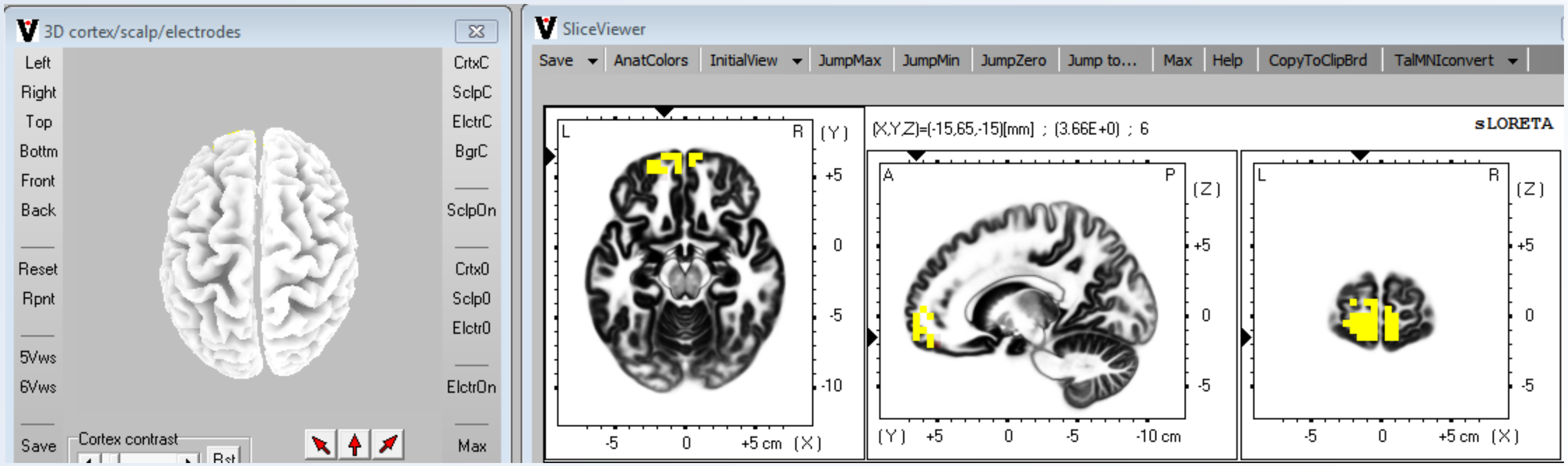


t=-2, invert sign: Old have reduced occipital alpha AND excess frontal delta compared to young (normal aging?)

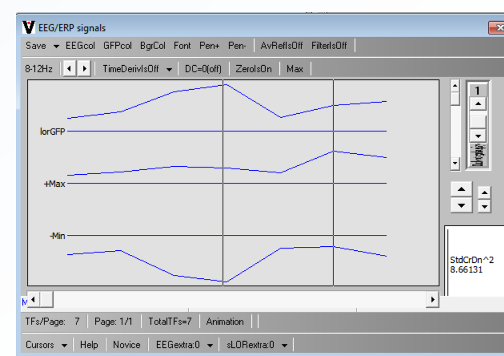


LORETA resting state network 6: Occipital Alpha anti-correlated with Frontal Beta2

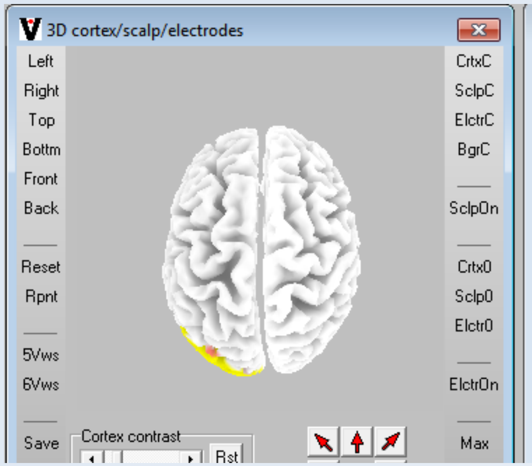


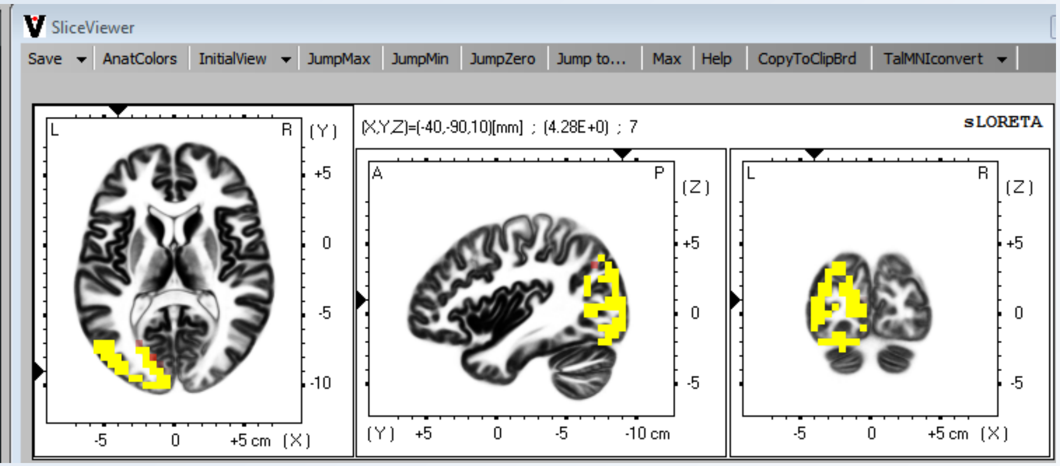


t=+4: Old have reduced occipital alpha AND excess frontal beta compared to young (normal aging, hyper-excitable frontal areas try to compensate age effect?)



LORETA resting state network 11: Left Occipito-Parietal cortex Alpha2 to Beta3





t=-3.7, invert sign: Old have reduced left occipito-parietal high frequencies compared to young (normal aging, insufficiently excitable association cortex and language areas?)