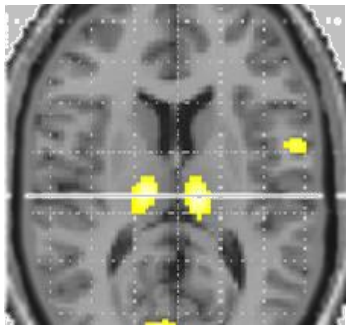
Changes in network architecture in temporal lobe epilepsies

66th Annual Meeting of the American Epilepsy Society
Tuesday, 4th of November 2012



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NeFF
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Forschungsschwerpunkt Frankfurt

Bundesministerium
für Bildung
und Forschung

epilepsy society

BIC
Brain Imaging Center
Frankfurt am Main

Special thanks to:

Enzo Tagliazucchi (BIC, Frankfurt)
Roman Rodionov (UCL, London)

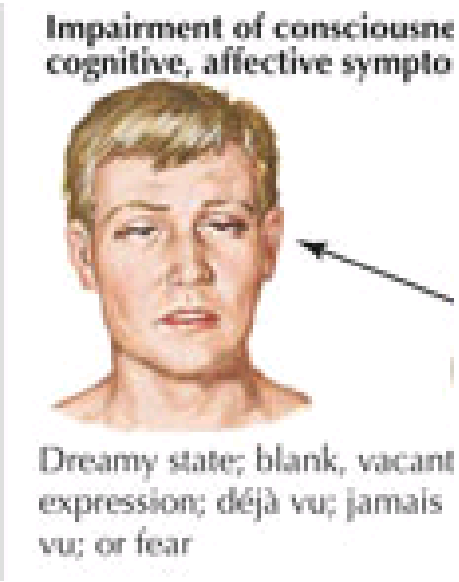
Outline:

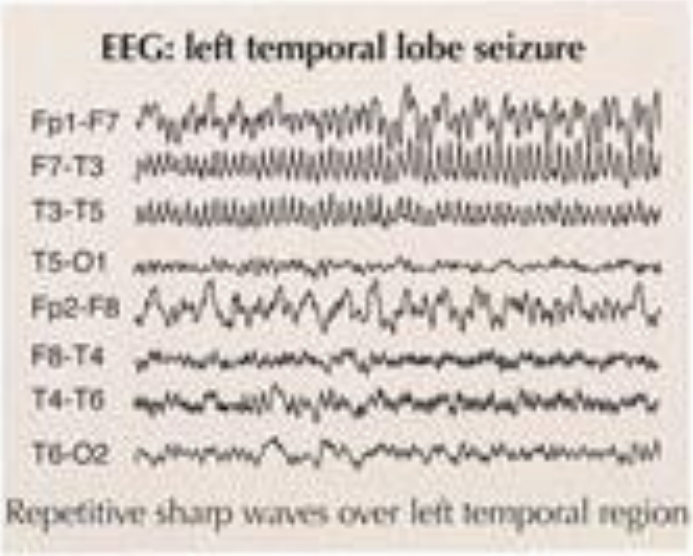
1. background: example (connectivity) studies TLE
2. brief methodological excursion: graph analysis
3. Results
4. Implications

Two main clinical features of temporal lobe epilepsies:

interictally: **cognitive impairment (memory)**

ictally: **dyscognitive seizures with reduced consciousness**





interictal epileptic discharge-correlated BOLD-fMRI

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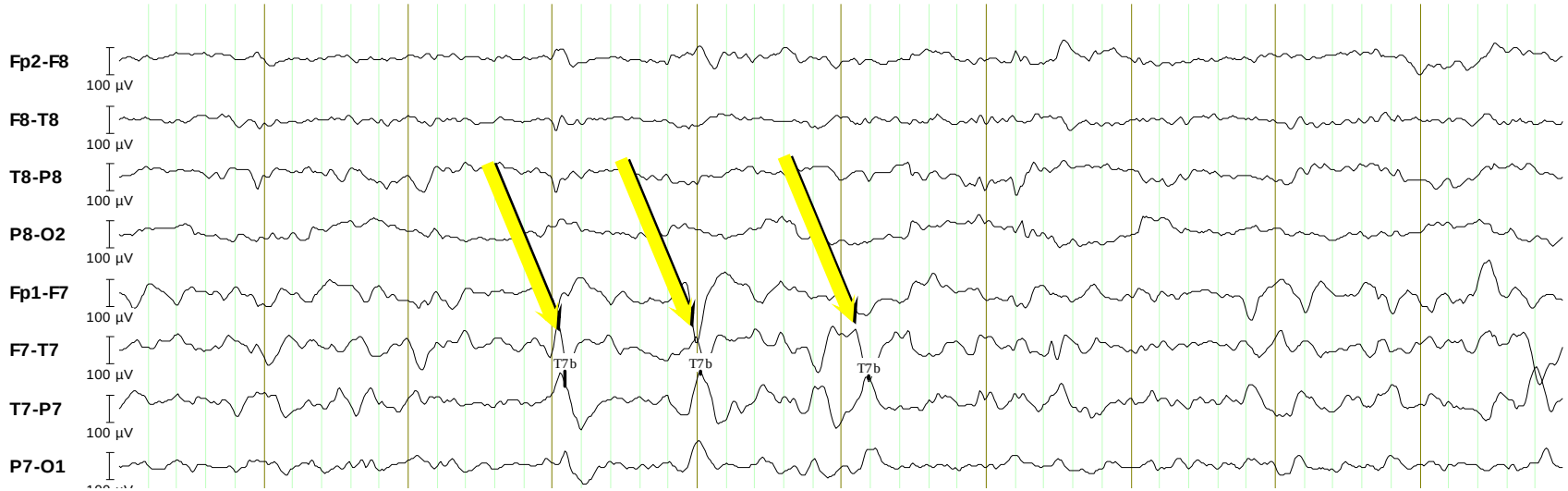
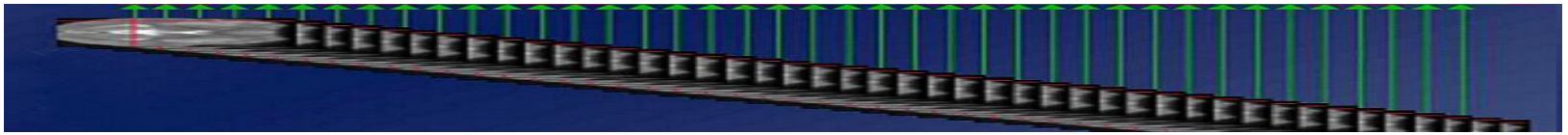
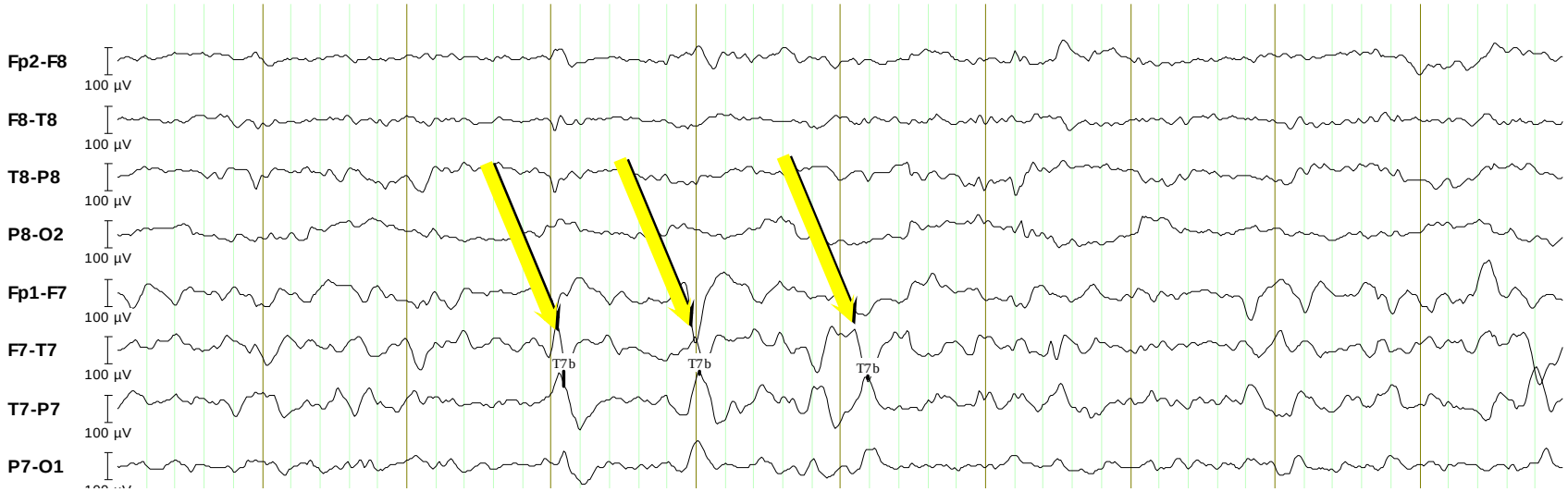


spikes:



interictal epileptic discharge-correlated BOLD-fMRI



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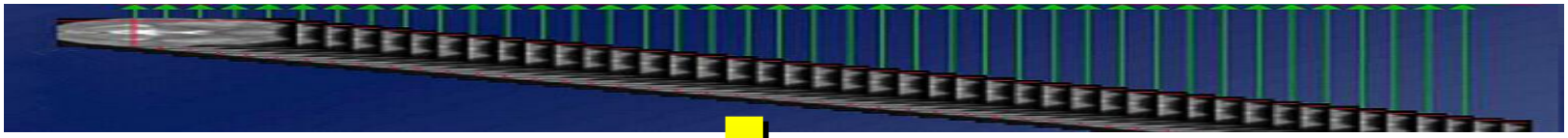
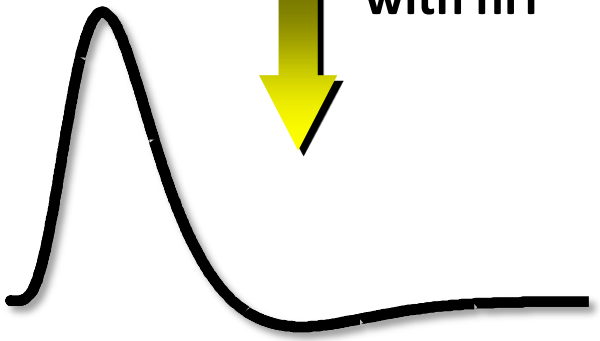


convolution with hrf



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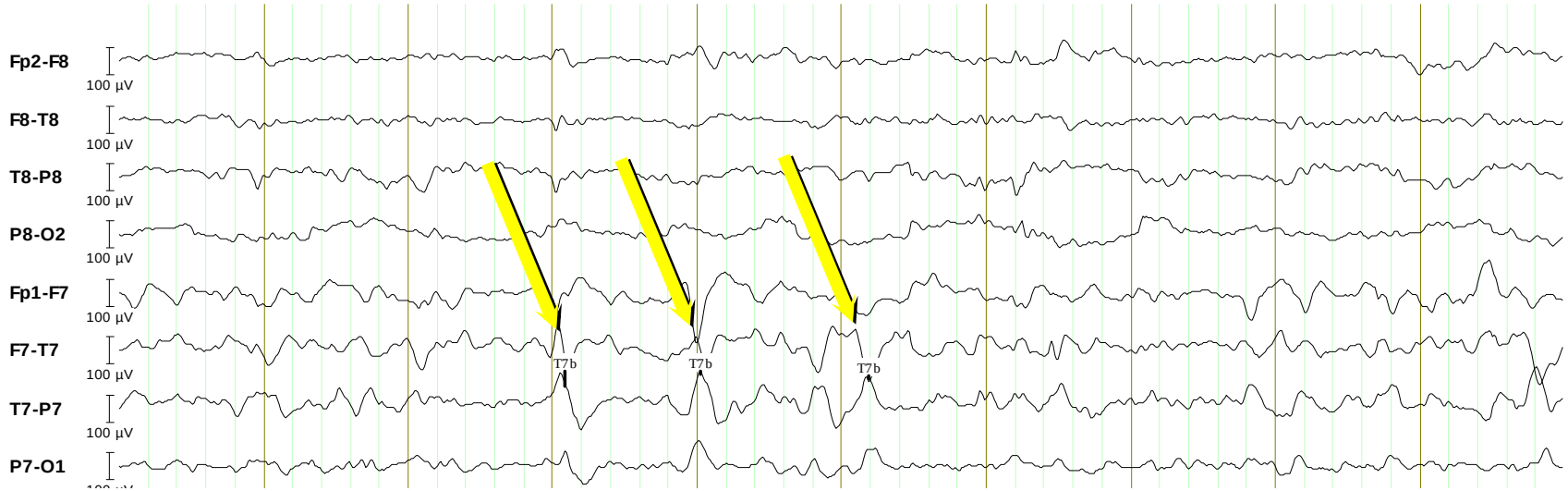

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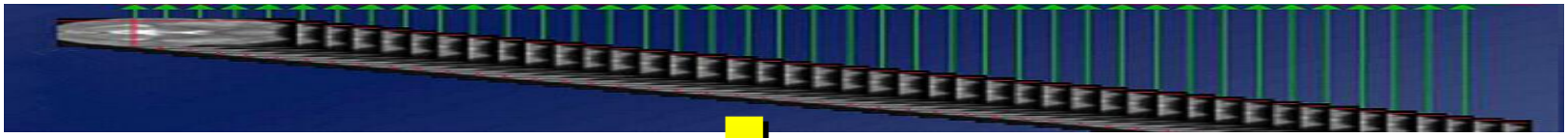

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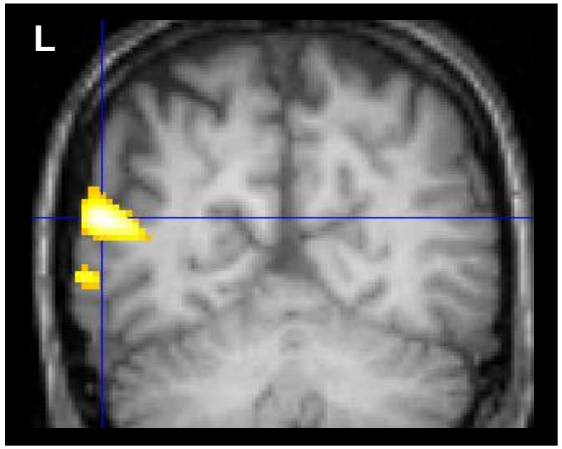
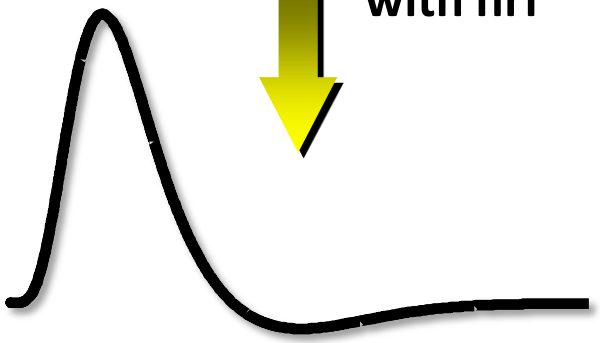
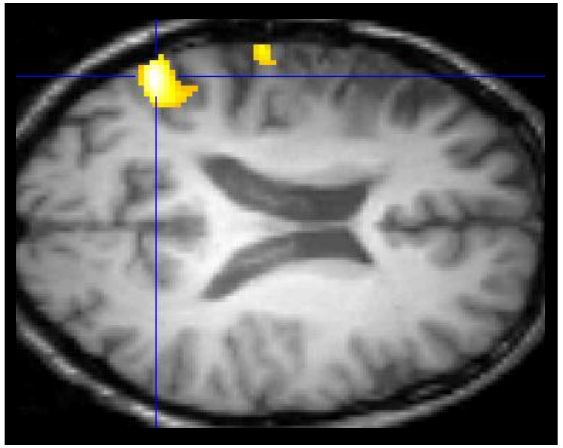
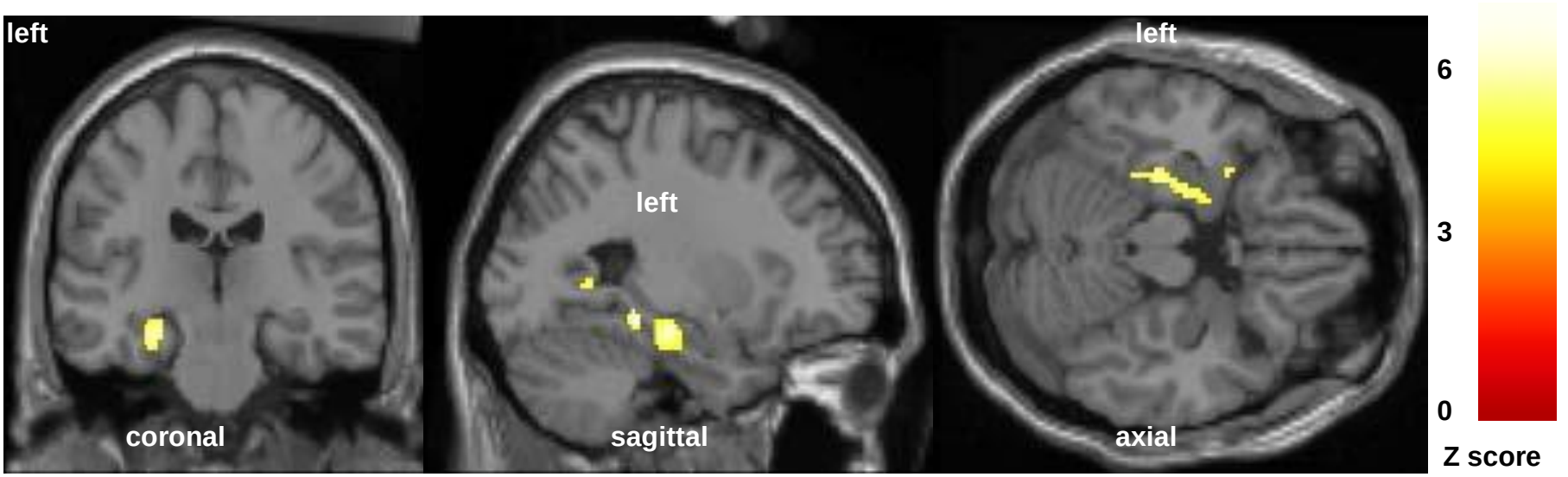






group analysis of patients with (left) TLE



BOLD signal increases to interictal epileptic discharges (slice planes [x,y,z]=[-26,-35,1]).

Laufs et al. 2007

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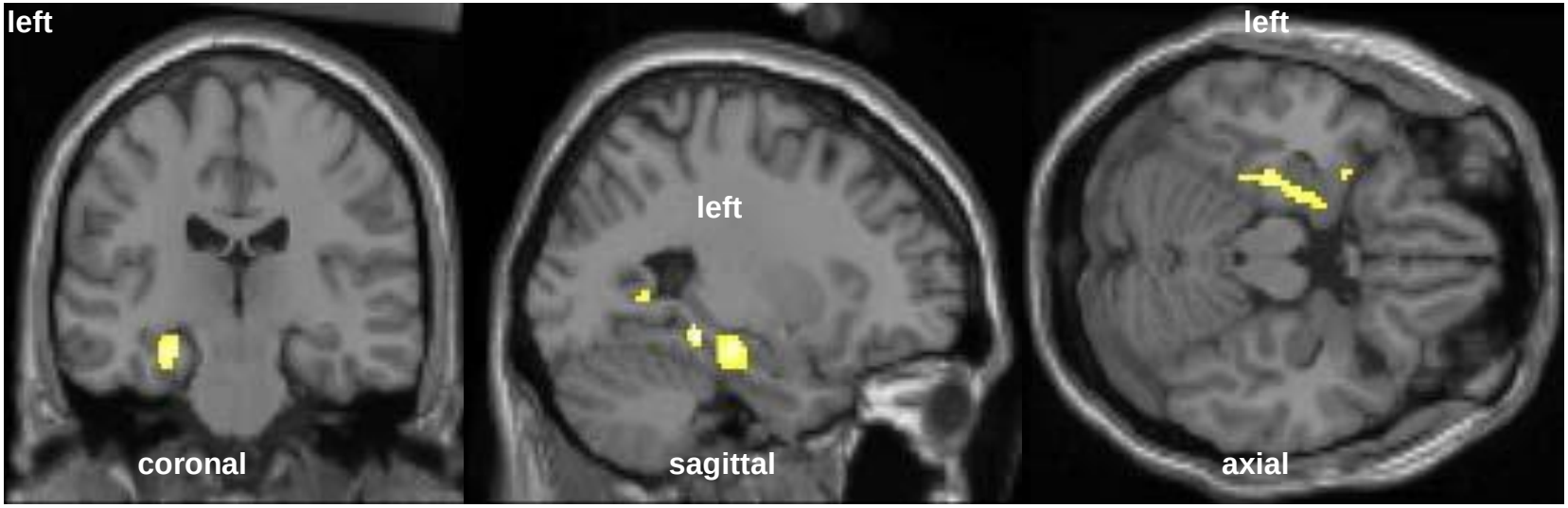

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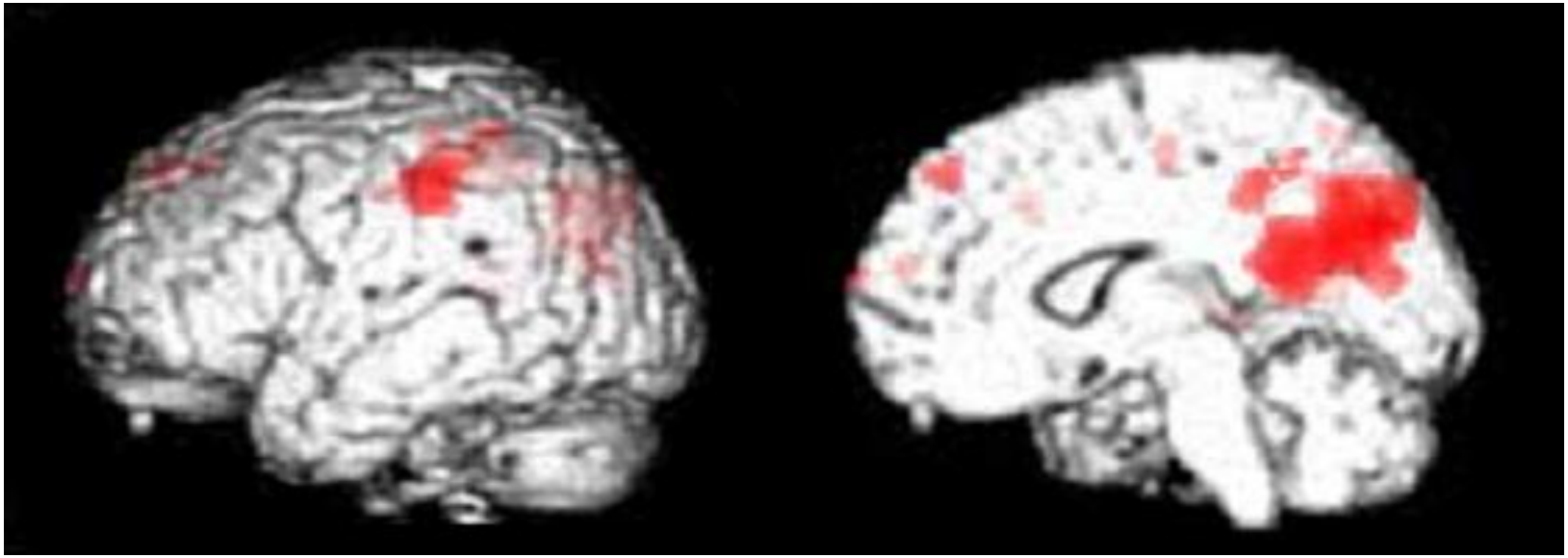
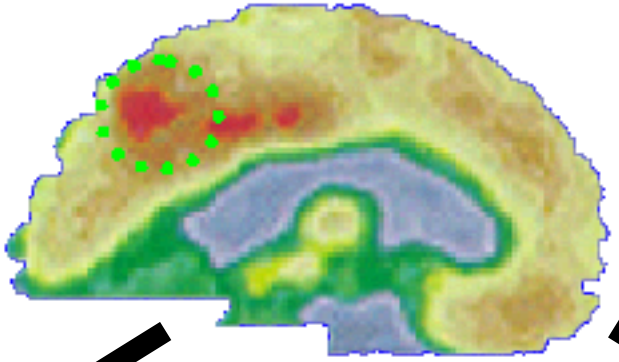
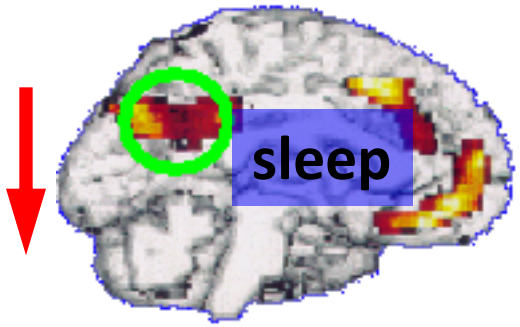


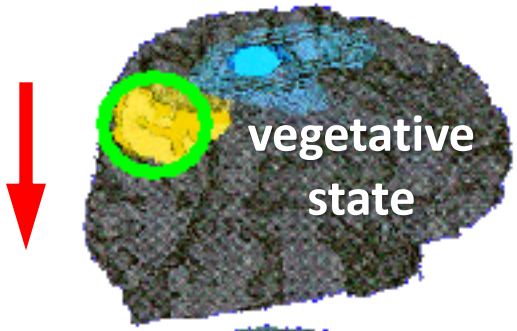
BOLD signal decreases in response to interictal epileptic discharges.

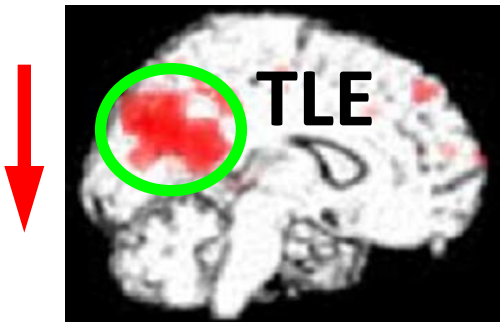
Laufs et al. 2007

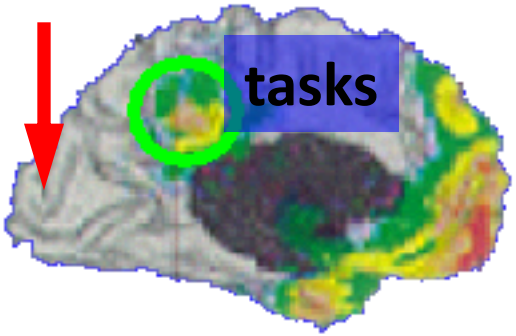
states of reduced consciousness ⟷ **rest** (default mode) ⟷ perception and action

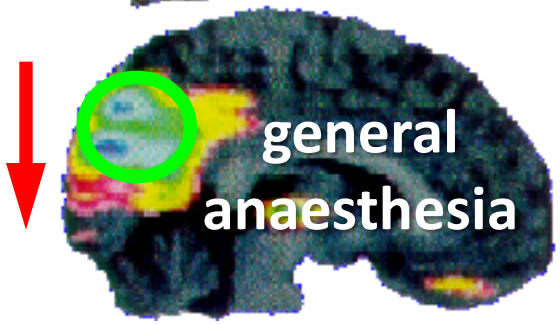








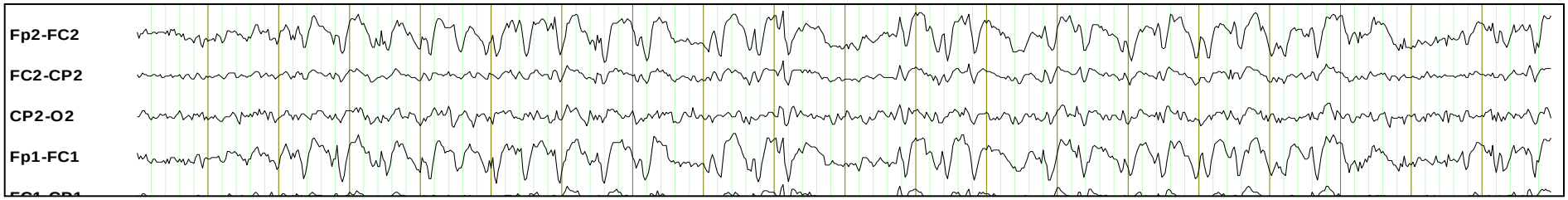




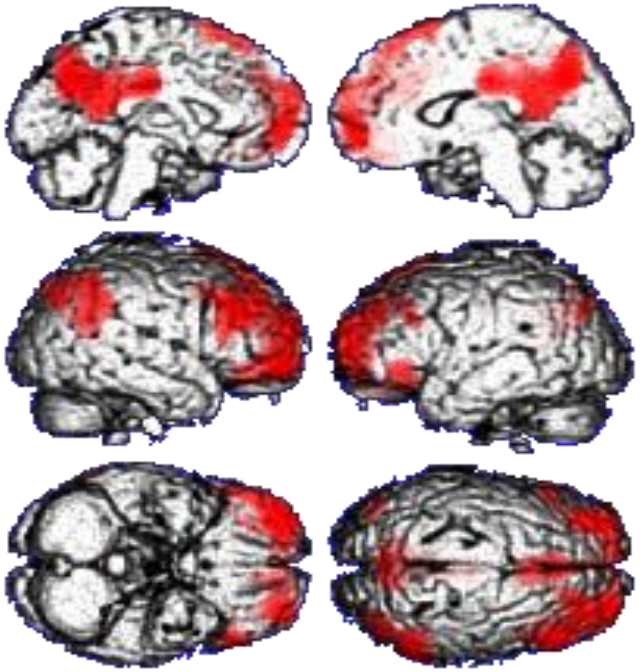
Laureys et al. 2004 Laufs et al. 2007 Gusnard and Raichle 2001

fMRI correlates of generalised spike-wave activity

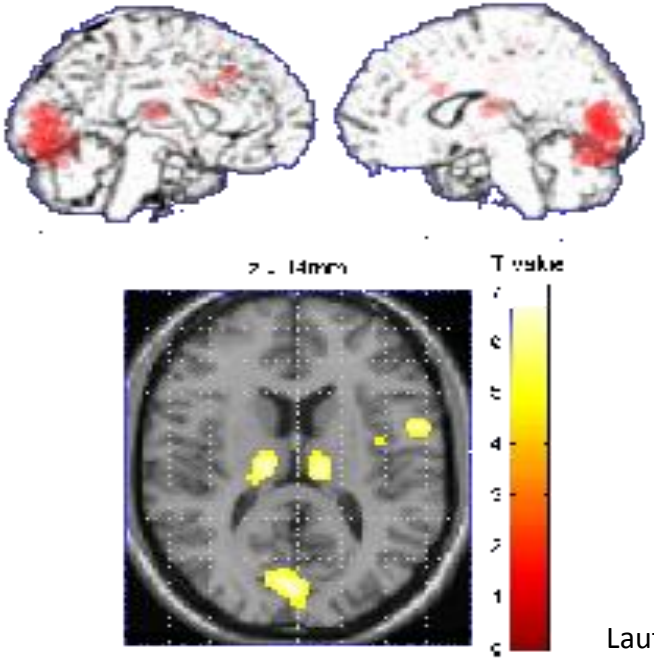
absence seizures: another example of impaired consciousness



reduced activity in DMN

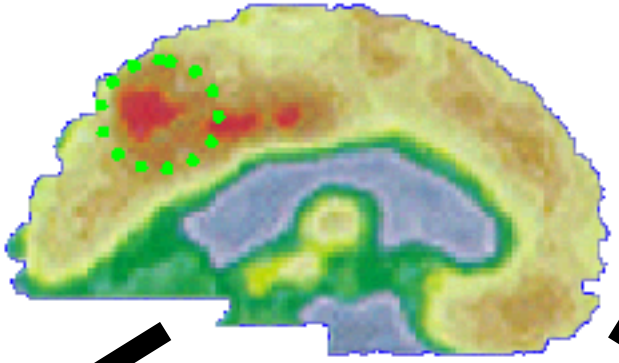


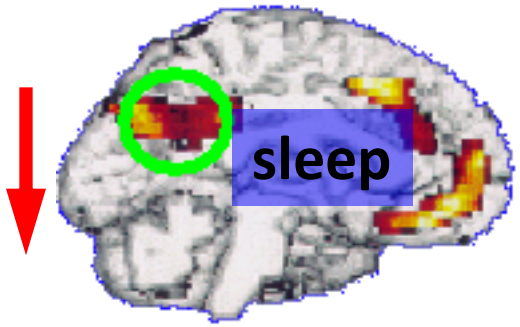
increased activity in thalamus

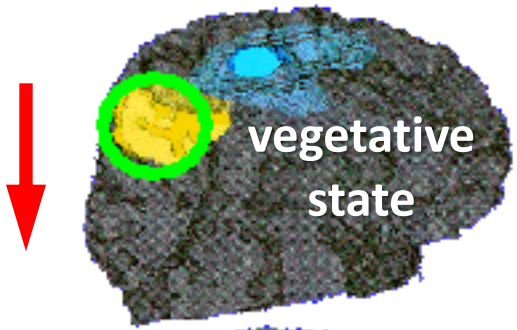


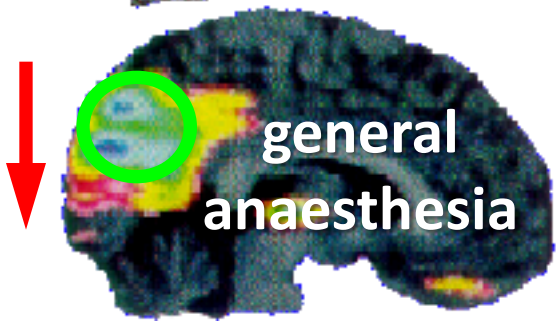
Laufs, Lengler et al. 2006
Hamandi et al. 2006
Gotman et al. 2005
...

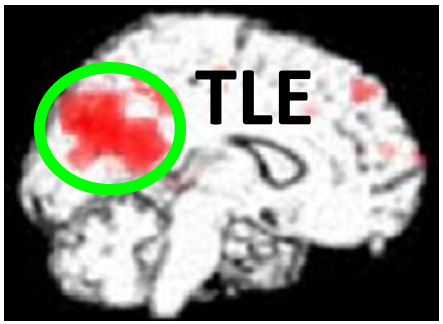
states of reduced consciousness ⟷ **rest** (default mode) ⟷ perception and action

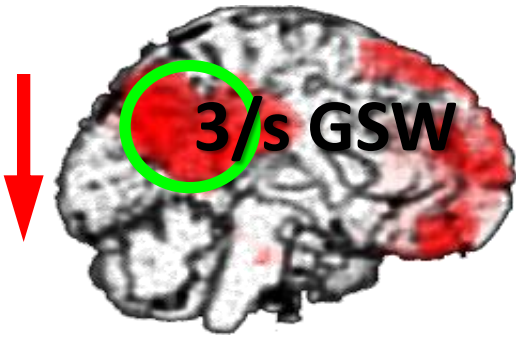


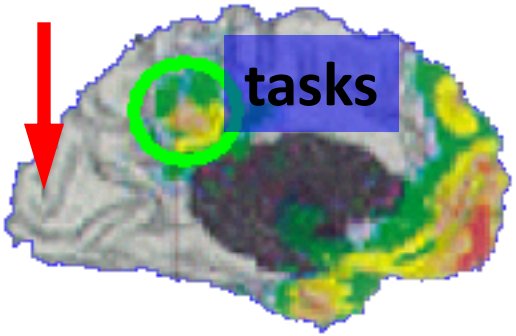












Laureys et al. 2004

Laufs et al. 2006, 2007

Gusnard and Raichle 2001

- **networks are affected beyond the epileptogenic zone**
- **fMRI suitable to detect such networks**
- **we know pathology persists interictally**

- networks are affected beyond the epileptogenic zone
- fMRI suitable to detect such networks
- we know pathology persists interictally

=> study networks with fMRI at rest (e.g. seed correlation)

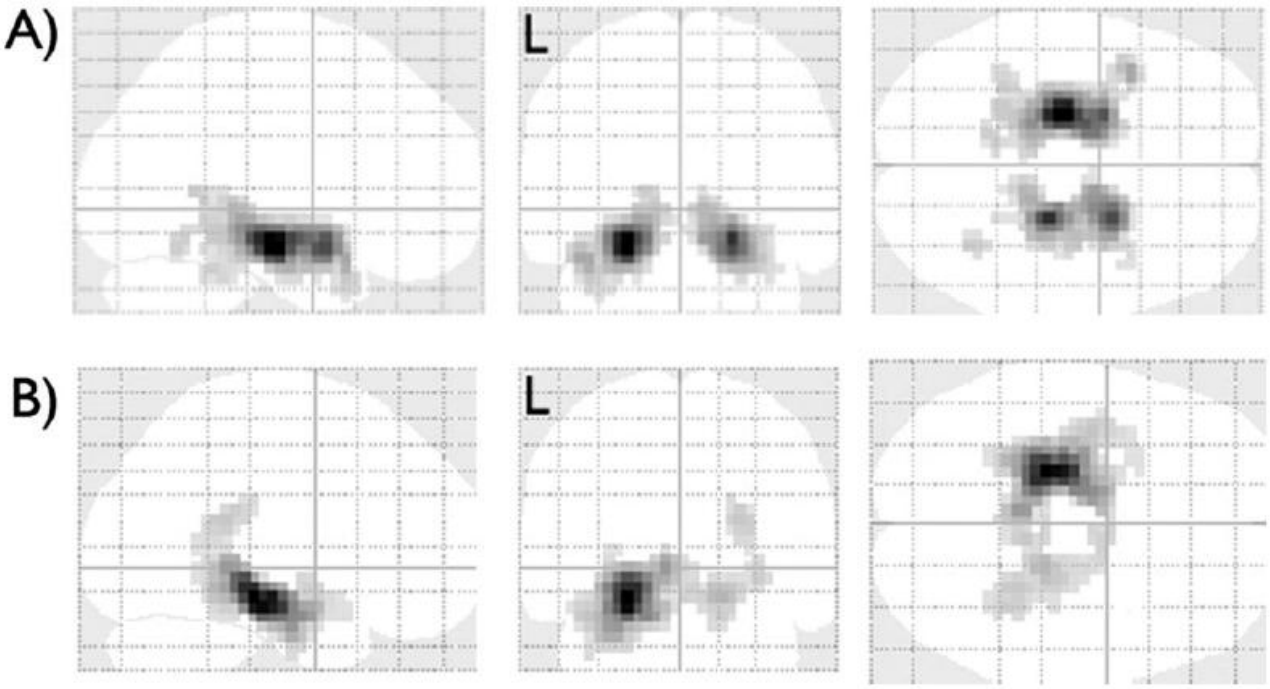


Figure 1.

Resting state functional connectivity maps to the left hippocampus. (**A**) Control subject used in the study. (**B**) LTLE patient in the study.

- networks are affected beyond the epileptogenic zone
- fMRI suitable to detect activity changes in networks
- we know pathology persists interictally

=> link functional connectivity to (memory) function

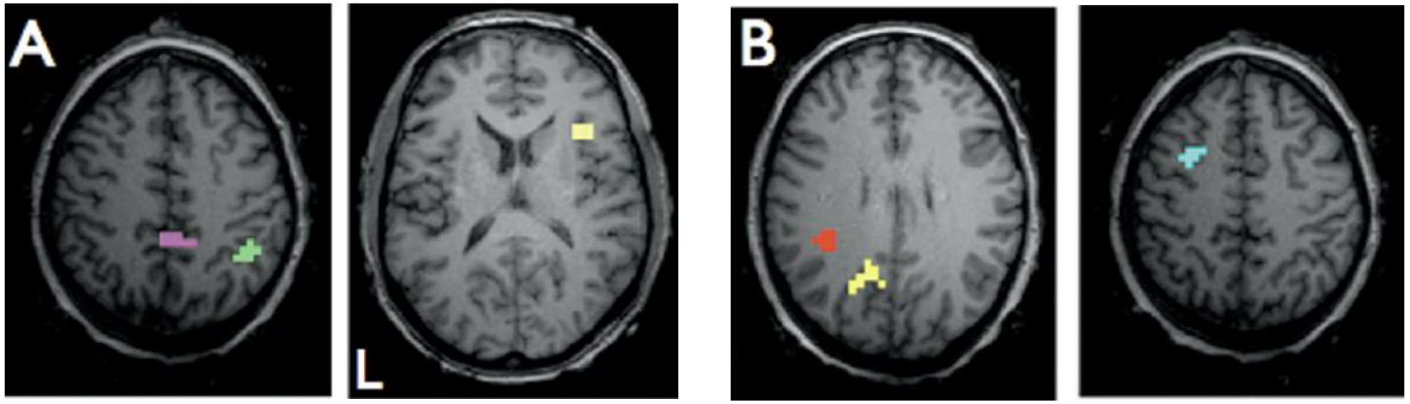
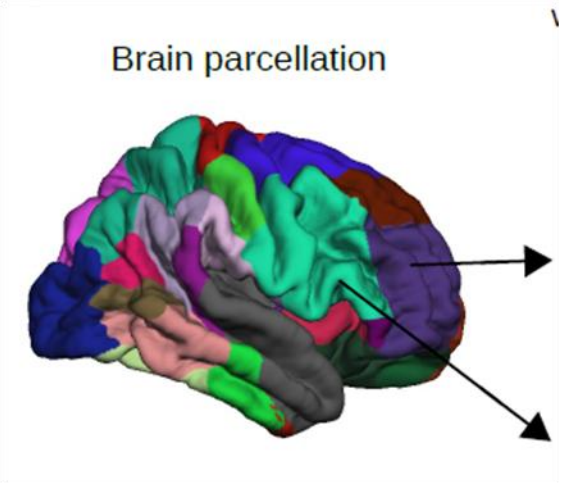


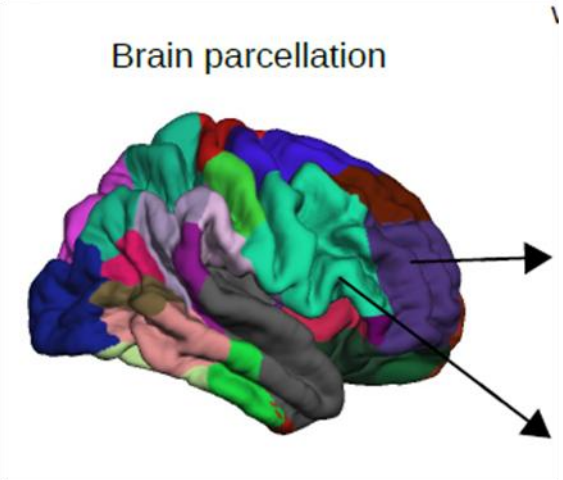
Figure 2.

Regions showing significant correlation between resting state connectivity to the LH and CVLT-II* percentage retention score across group of 11 LTLE patients. (**A**) Cluster in the mid-right precuneus (magenta), right inferior parietal lobule (green), and right insula (yellow) showing positive correlation (decreased connectivity with decreased score). (**B**) Cluster in the left precuneus (yellow), left inferior parietal lobule (red), and left middle frontal gyrus (cyan) demonstrating a negative correlation (increased connectivity with decreased score. * Calif. Verbal Learning Test

from seed correlation to full brain connectomics



Functional brain network analysis



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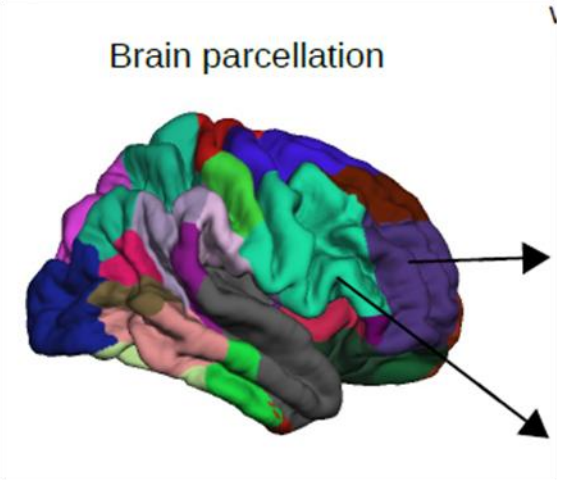
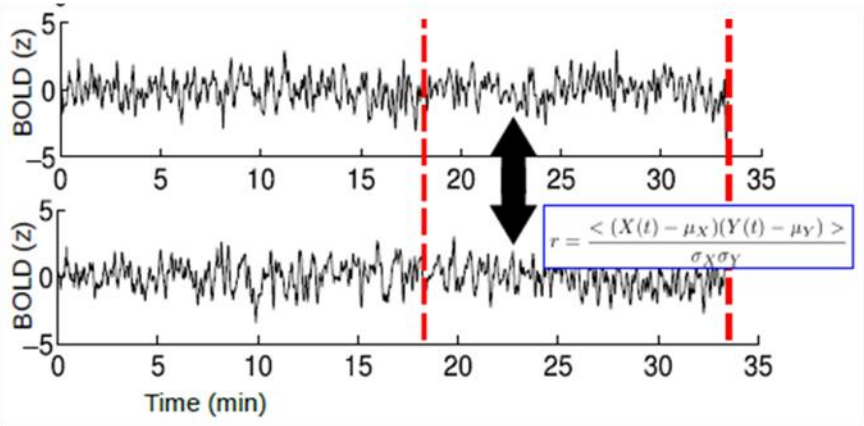
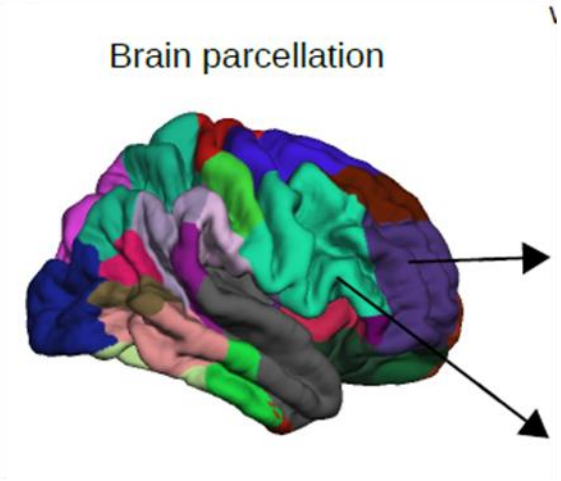
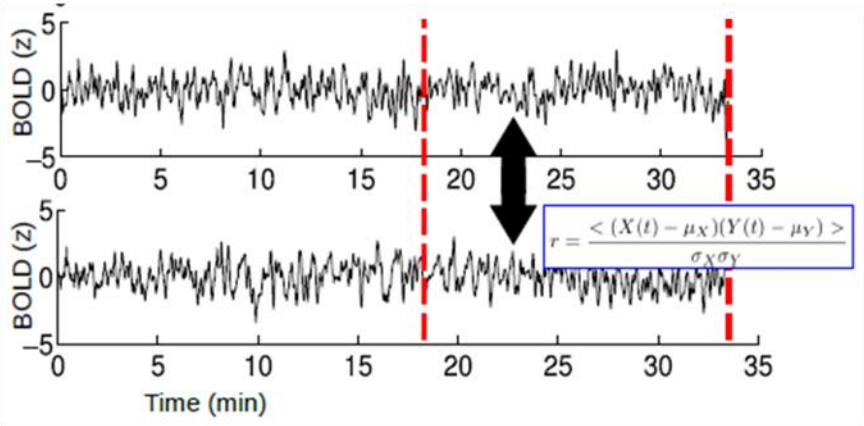




pair-wise correlations

Functional brain network analysis





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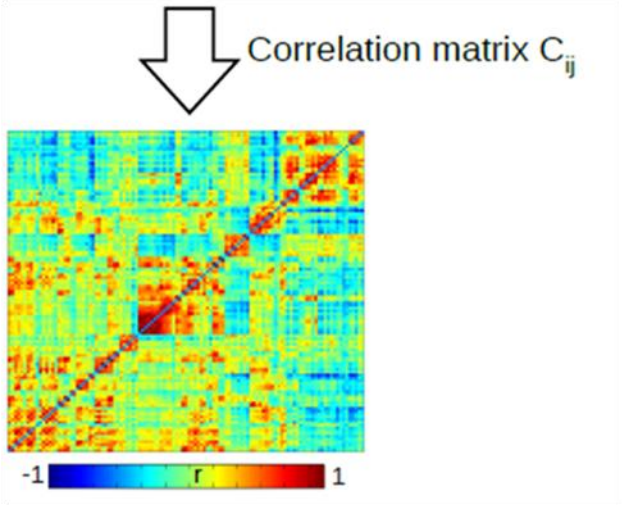

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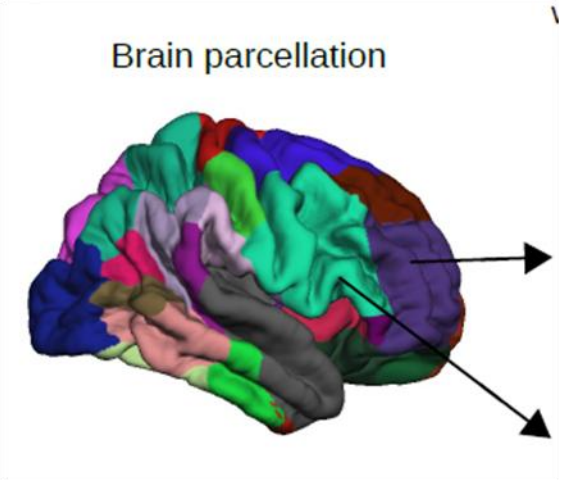

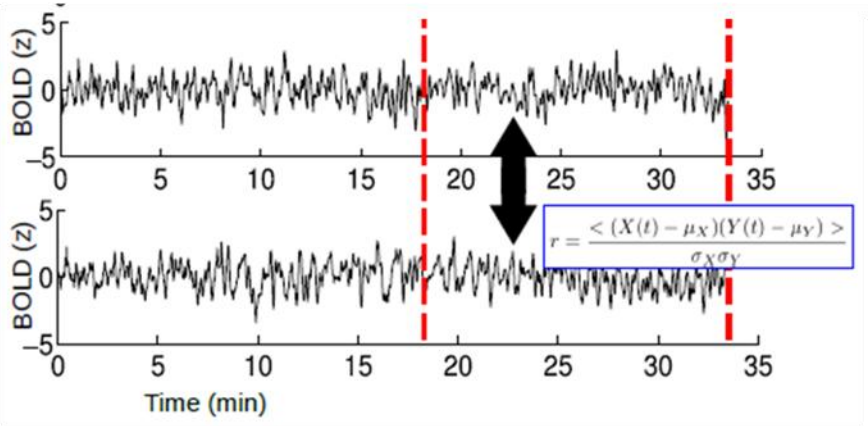

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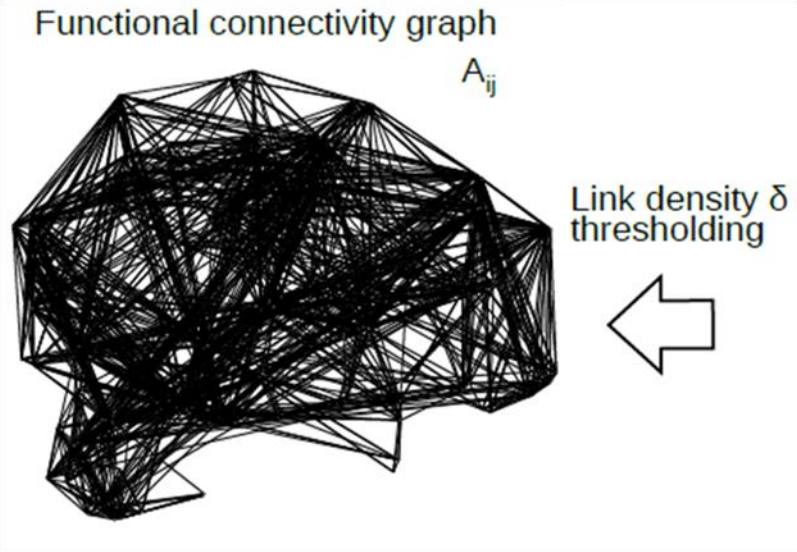
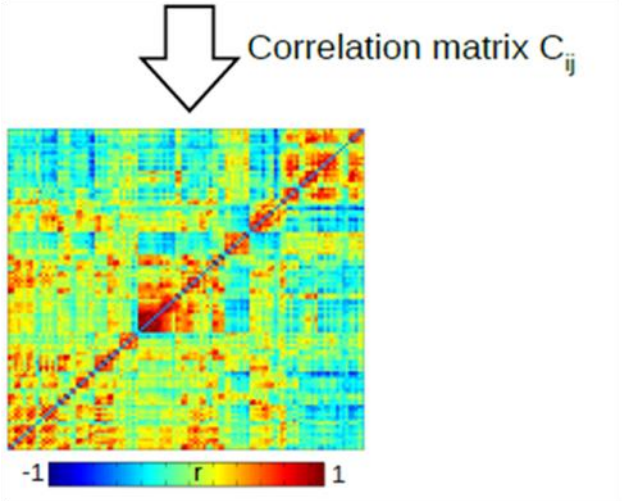


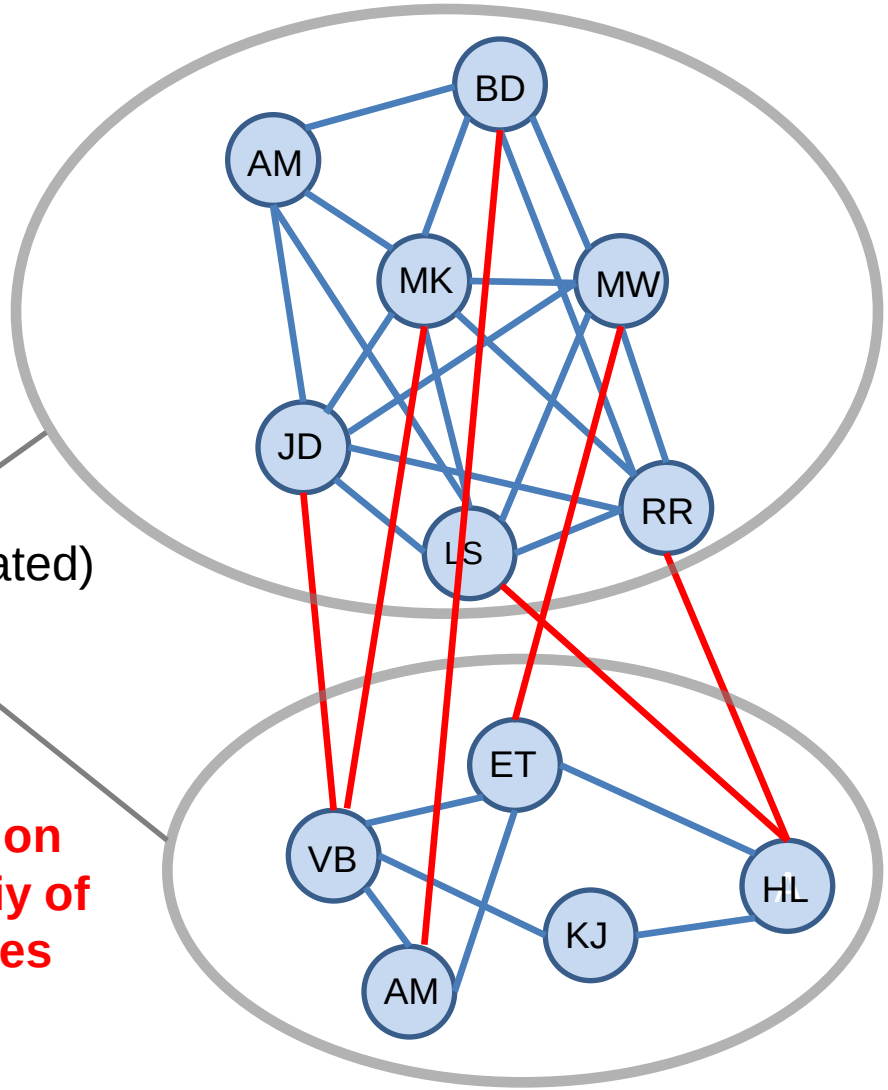


Bringing functional connectivity to life

A graph is a group of **nodes** *(people, colleagues, actors, brain regions etc.)* and a group of **edges** representing relationships *(love, hate, co-authorships, movie co-starrings, functional connectivity etc.)*

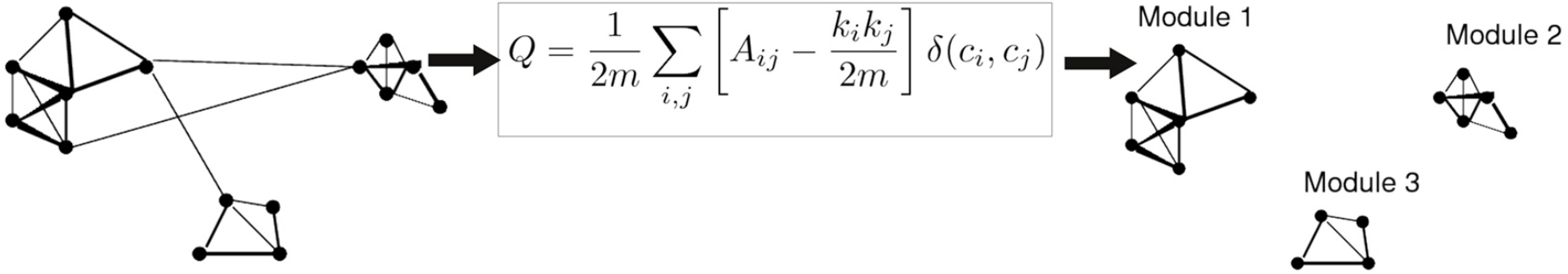
Integrated (but segregated) social groups

Increased integration destroys the identitiy of segregated modules



Bringing functional connectivity to life

Extracting functional modules by modularity (Q) optimization



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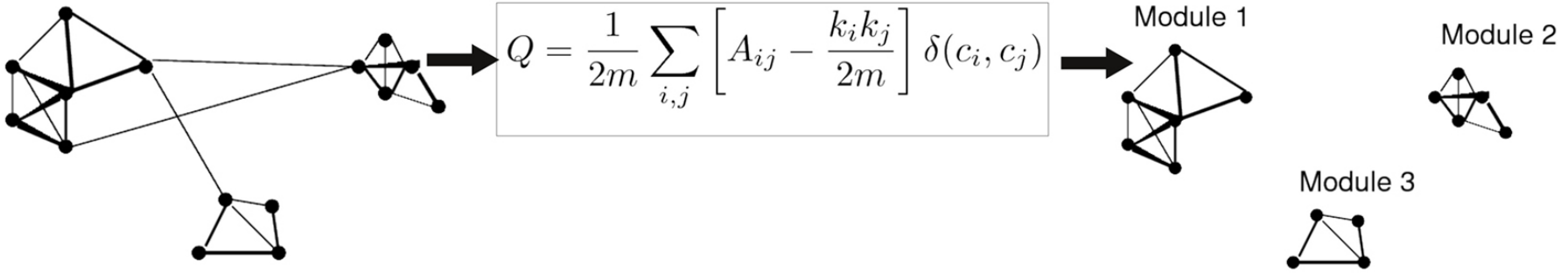
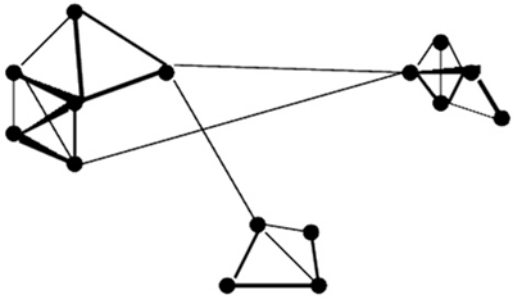
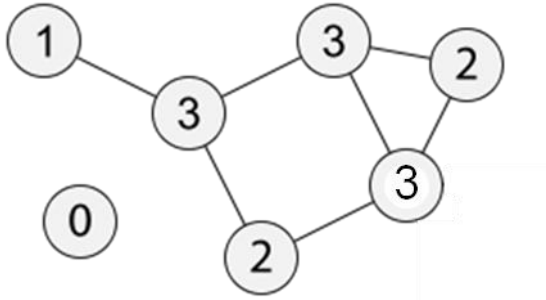


modularity ~ extent of segregation <-> integration

Bringing functional connectivity to life

centrality measure: node degree





node degree = number of ties a node has

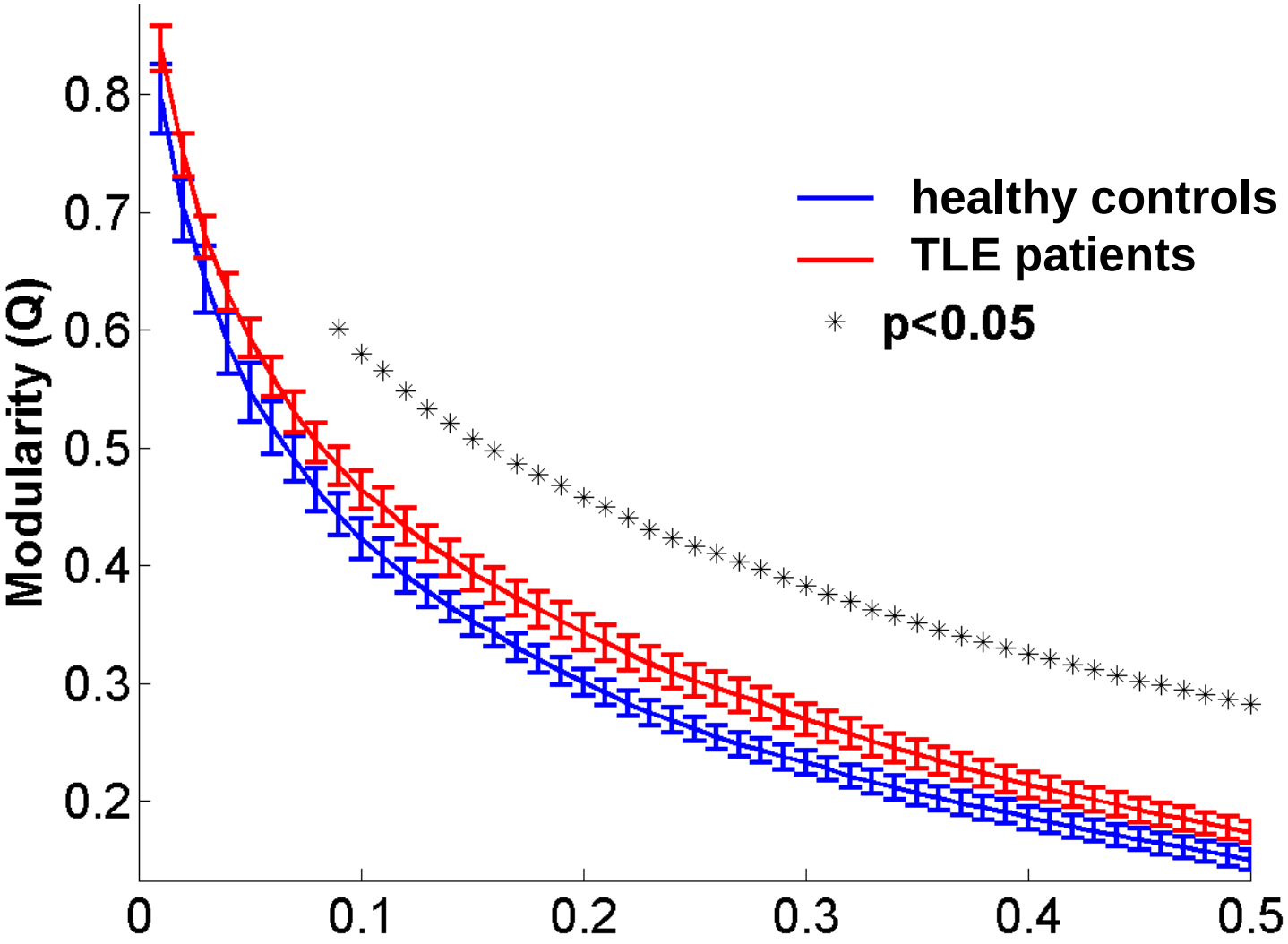
"risk of a node for catching whatever is flowing through the network"

data:

controls = 20
left TLE = 7
right TLE = 14

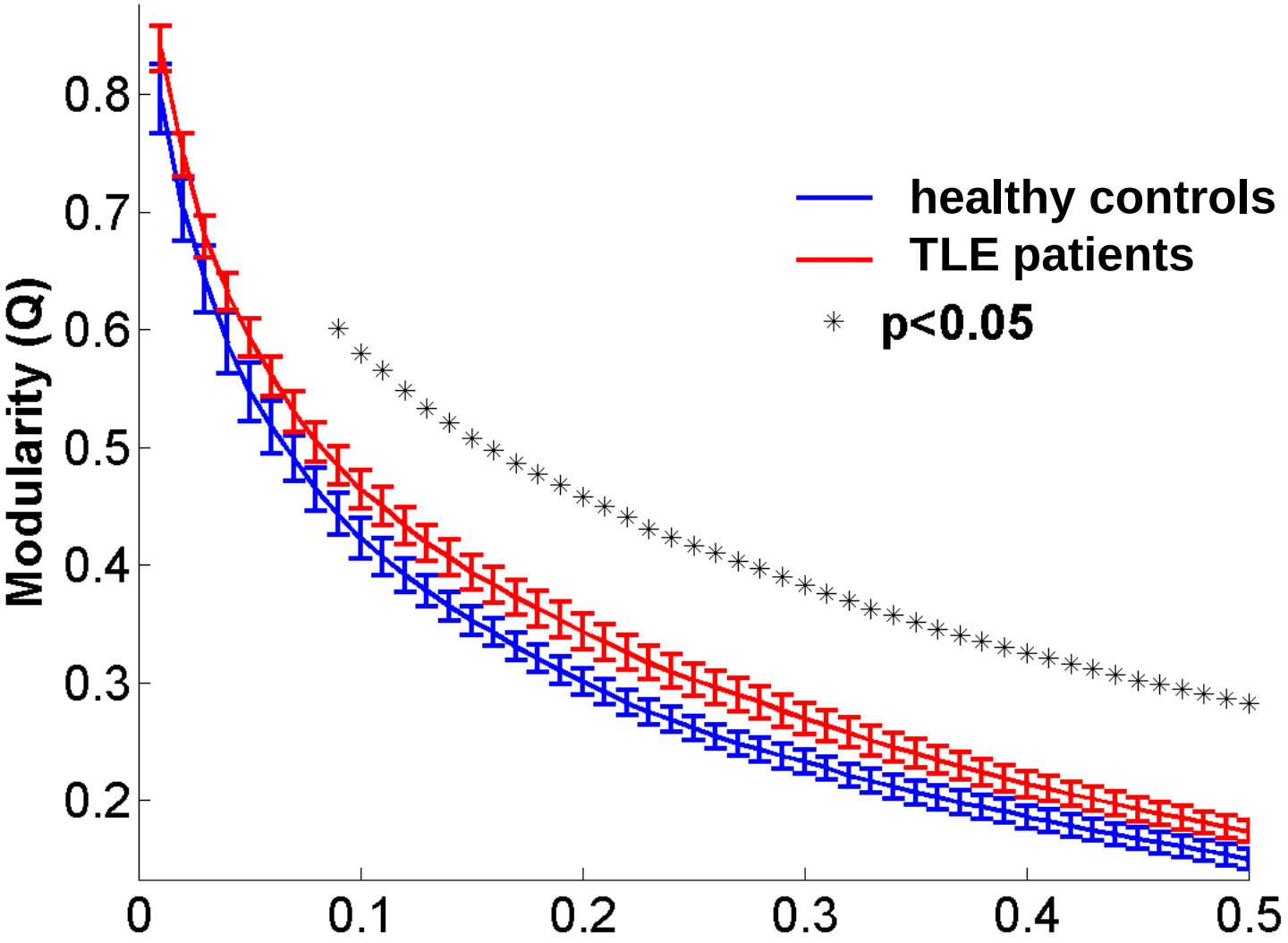
20 minutes resting state
eyes closed
TR = 3 s
400 volumes

modularity: TLE vs. controls



(the more links, the less reliable, i.e. small correlation value as threshold)

overall higher segregation in TLE



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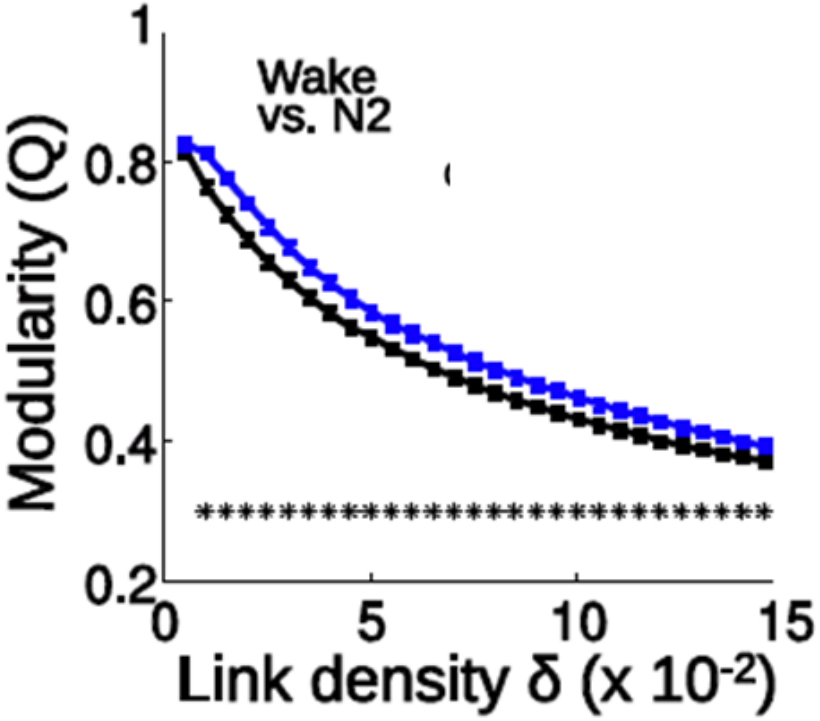
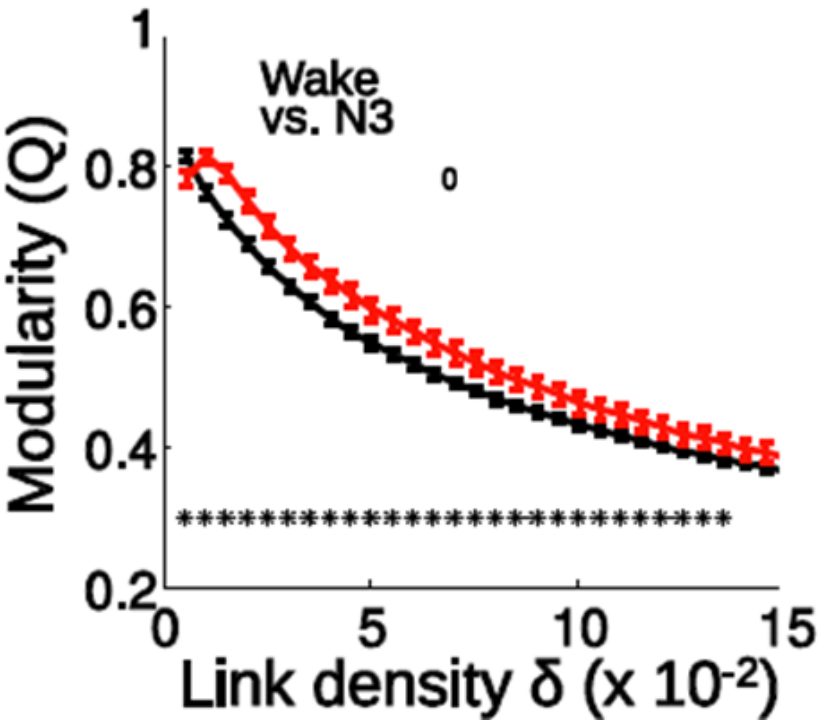
higher segregation (modularity) also in sleep vs. wakefulness





Tagliazucchi et al. 2012

node degree = number of ties a node has

"risk of a node for catching whatever is flowing through the network"

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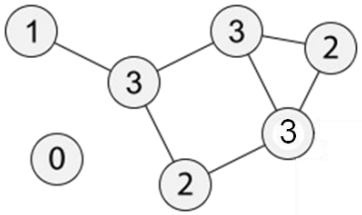
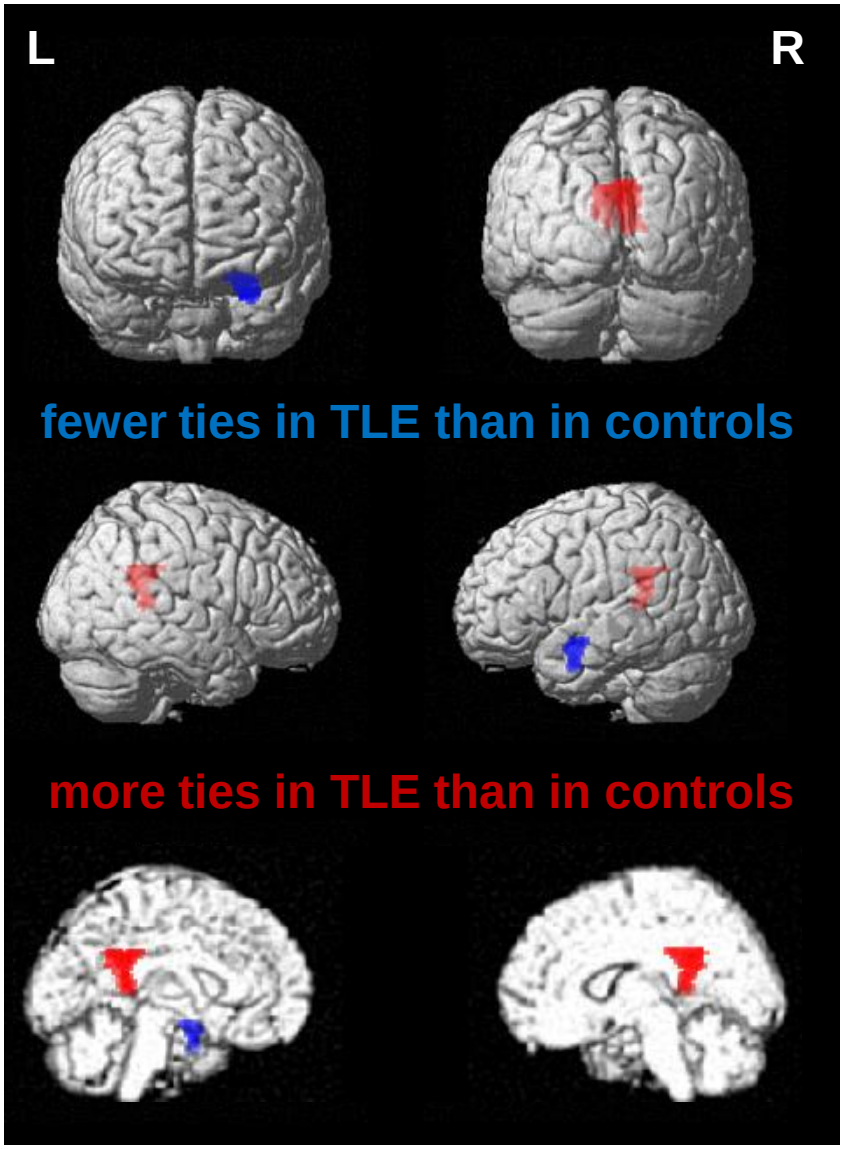
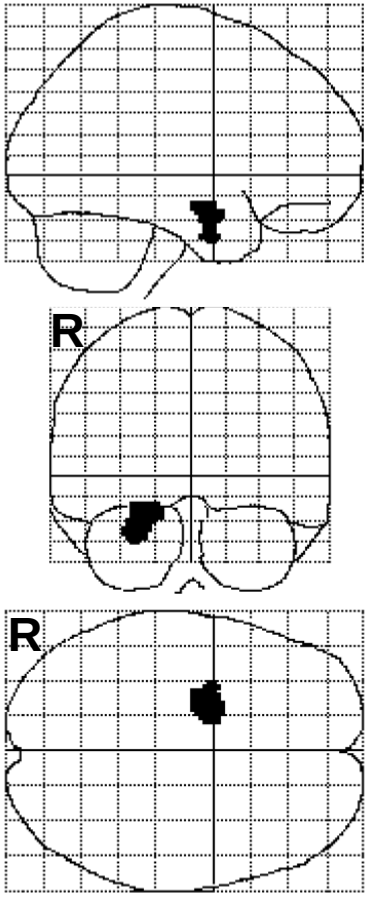
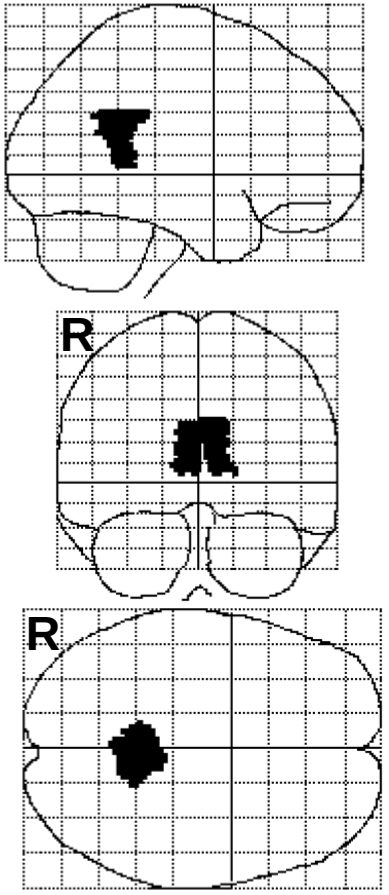




TLE < controls



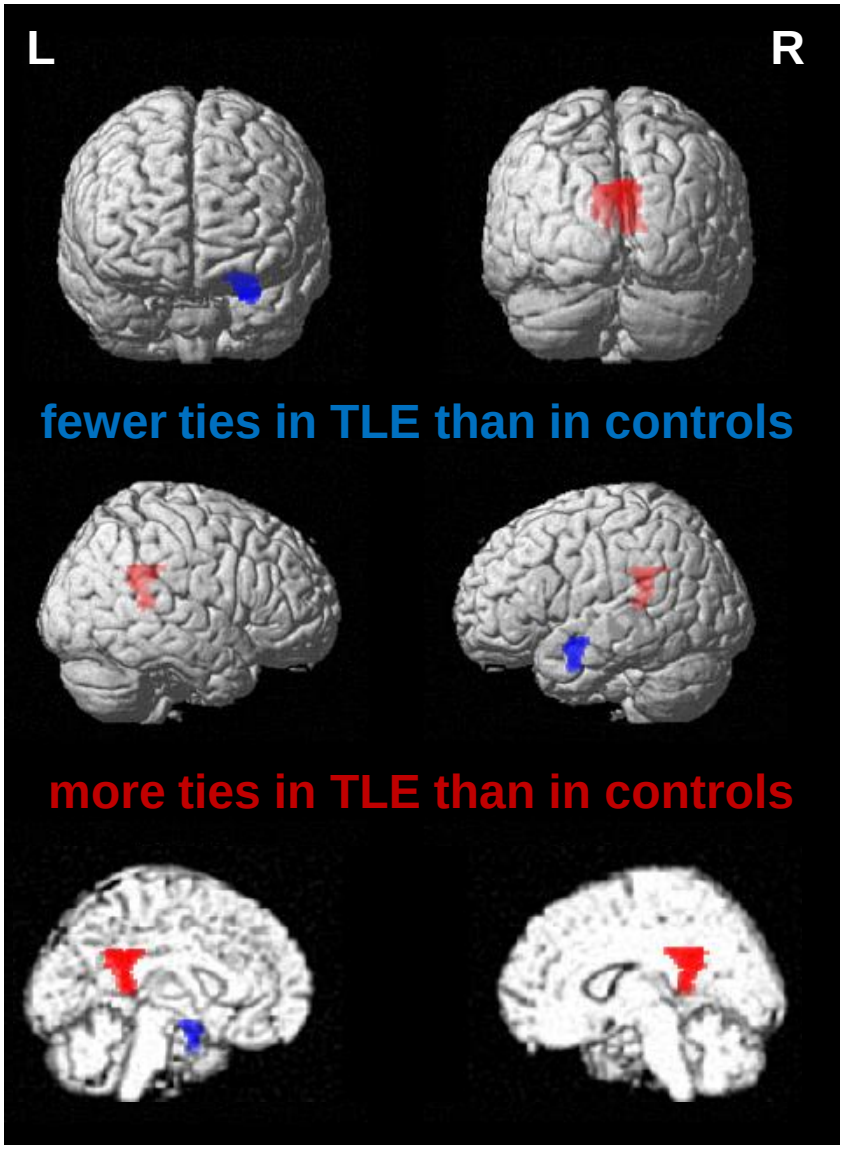
TLE > controls



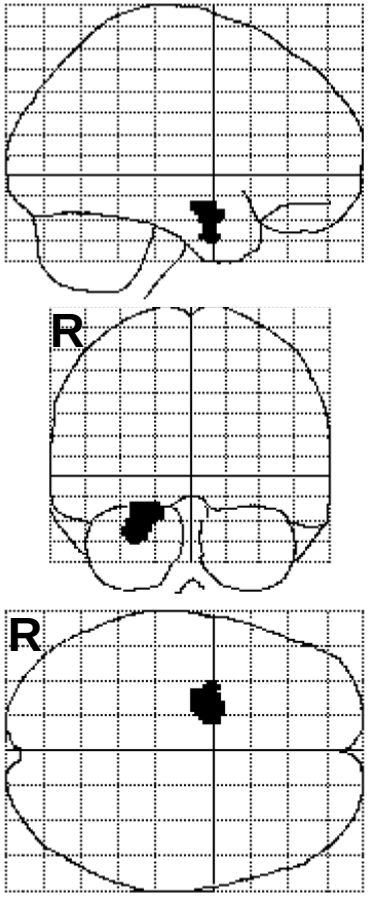
node degree = number of ties a node has

"risk of a node for catching whatever is flowing through the network"

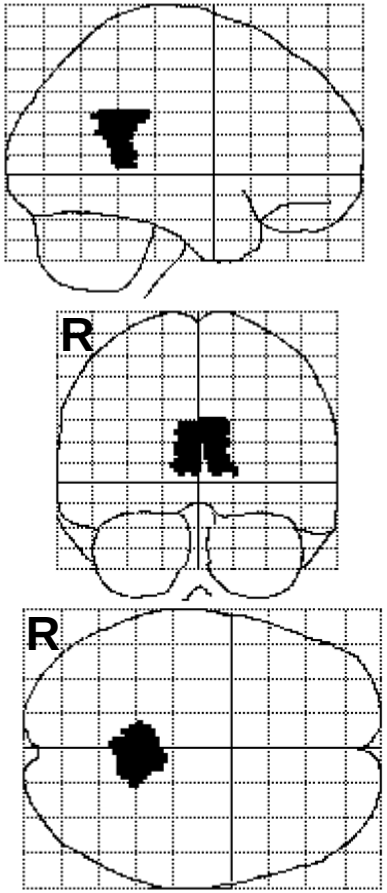
or: "potential of a node to influence what is going on in the network"



TLE < controls
amygdala



TLE > controls
posterior cingulate



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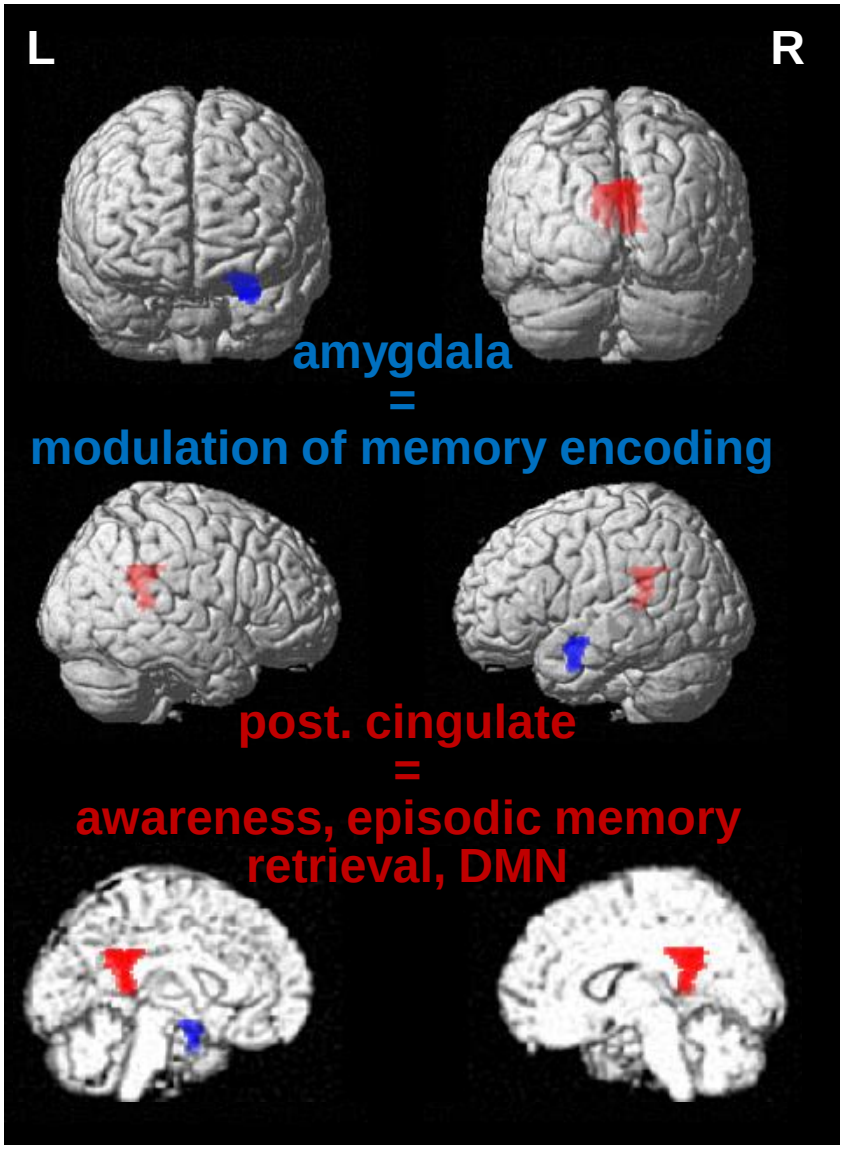
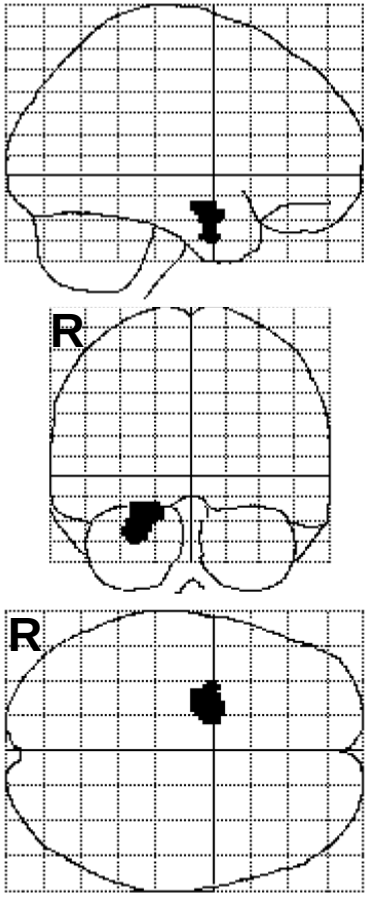


TLE < controls
amygdala



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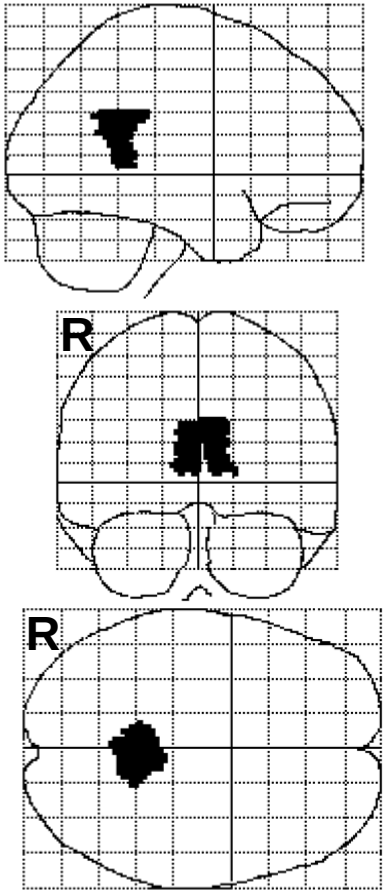


Where might extra links to posterior cingulate come from?

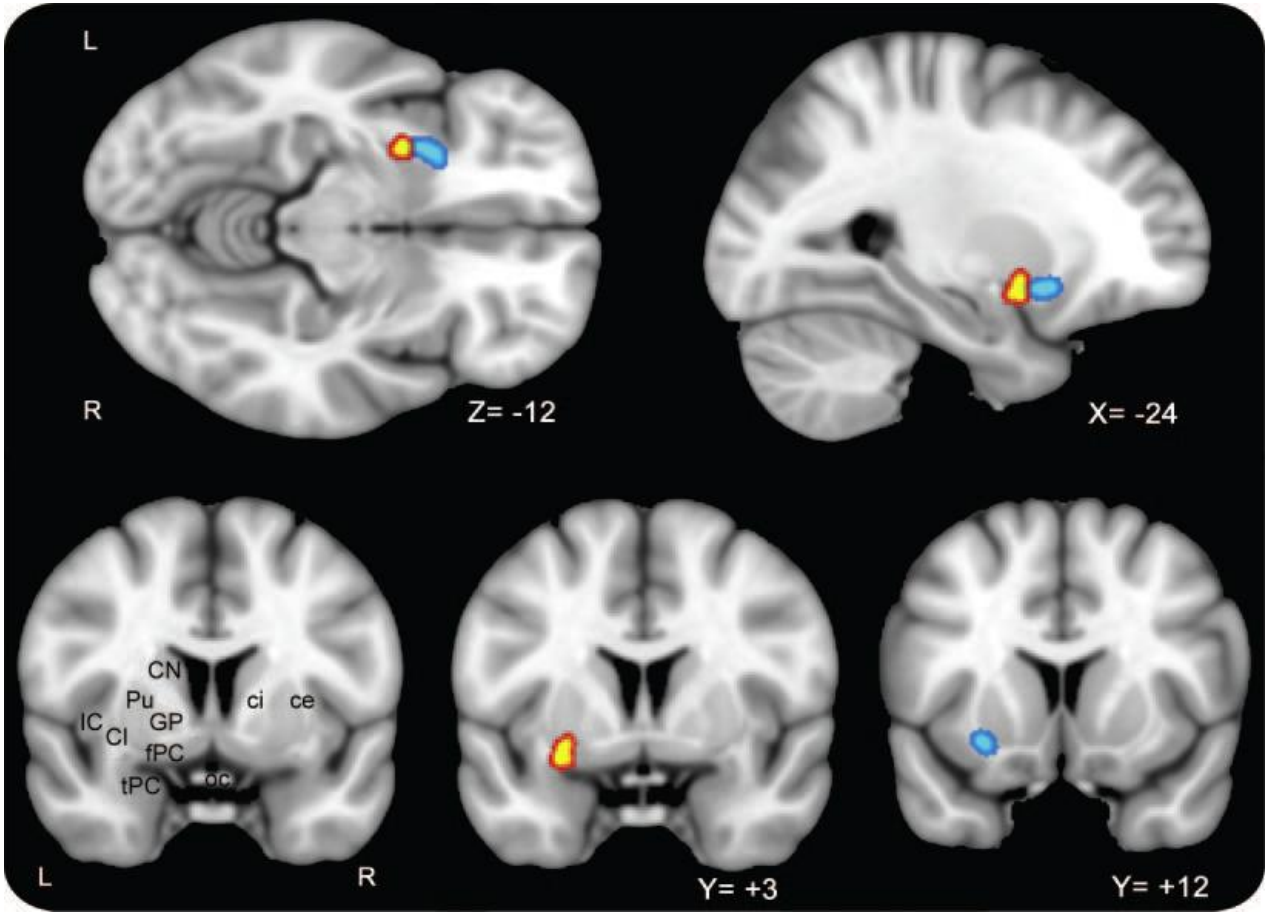
Functional connectivity with seed in “area tempestas”...

Functional connectivity with seed in “area tempestas”...

...in right TLE patients reveals higher functional connectivity to DMN regions than in controls.

What is “area tempestas”?

Group analysis of patients with focal epilepsies (non-TLE + TLE)

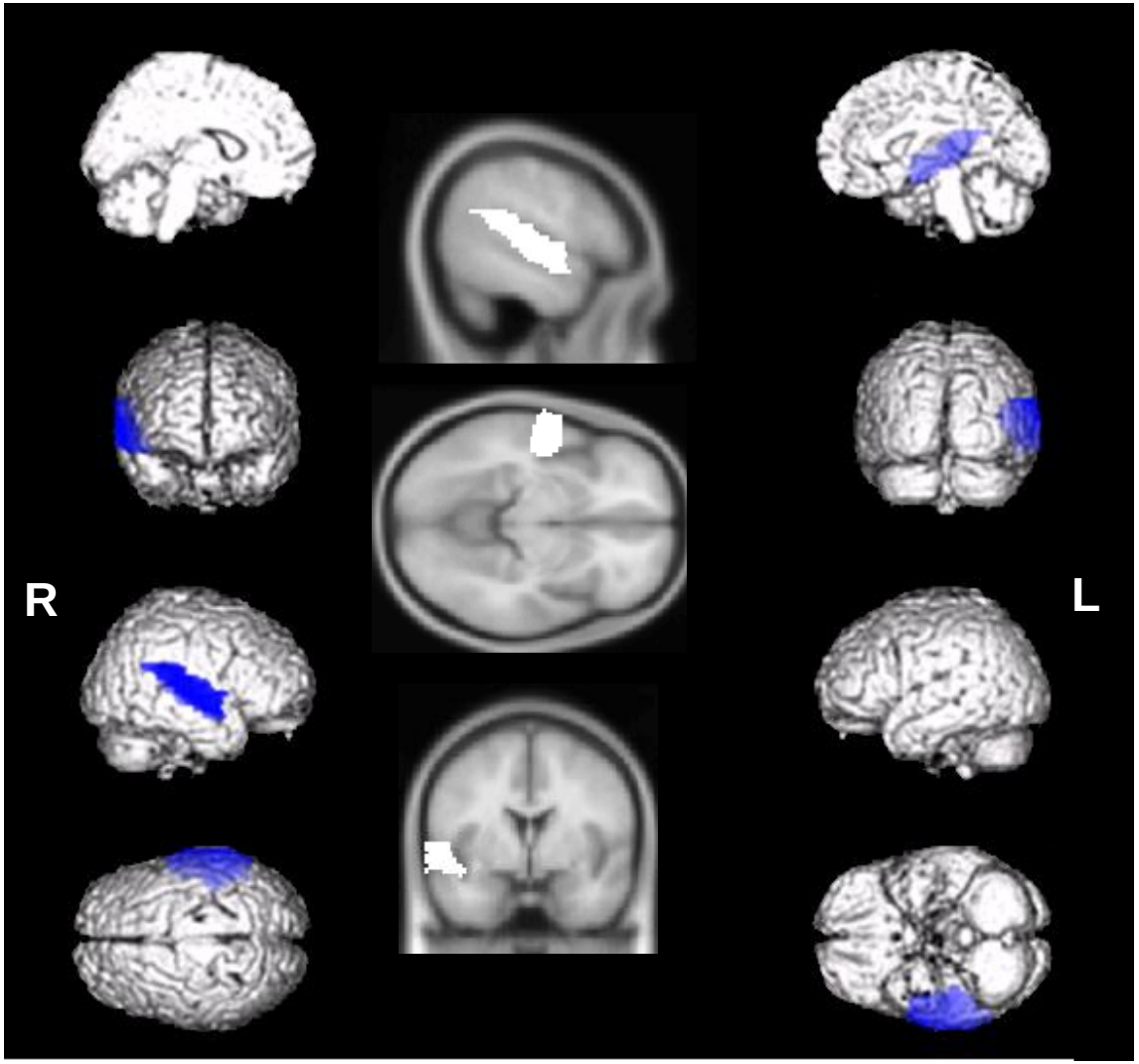


Clusters around the peak voxels for **spike-correlated EEG-fMRI** group analysis (yellow) and **correlation between flumazenil binding and seizure frequency** (blue) are superimposed on a T1 template. ce capsula externa; ci capsula interna; Cl claustrum; CN caudate nucleus; fPC frontal piriform cortex; GP globus pallidus; IC insular cortex; oc optic chiasm; Pu putamen; tPC temporal piriform cortex.

Laufs, Richardson et al. 2011

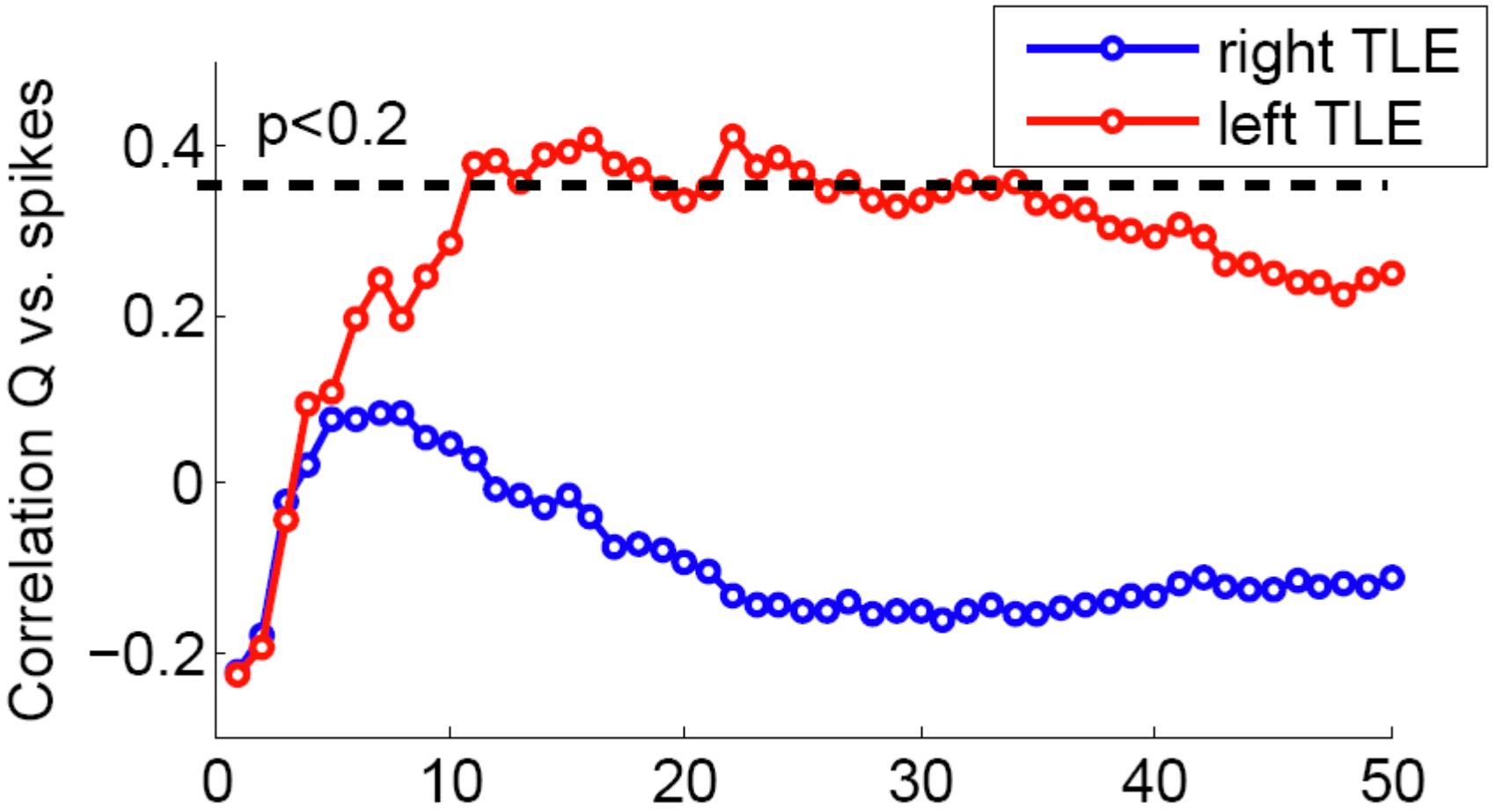
Can we link back to the EEG?
(interictal epileptic discharges)

correlation of node degree with # of IED (left TLE only)



right superior temporal gyrus (uncorrected)

correlation of modularity with # of IED



Link density = number of [possible] links between nodes

(the more links, the less reliable, i.e. small correlation value as threshold)

...are IED responsible after all?

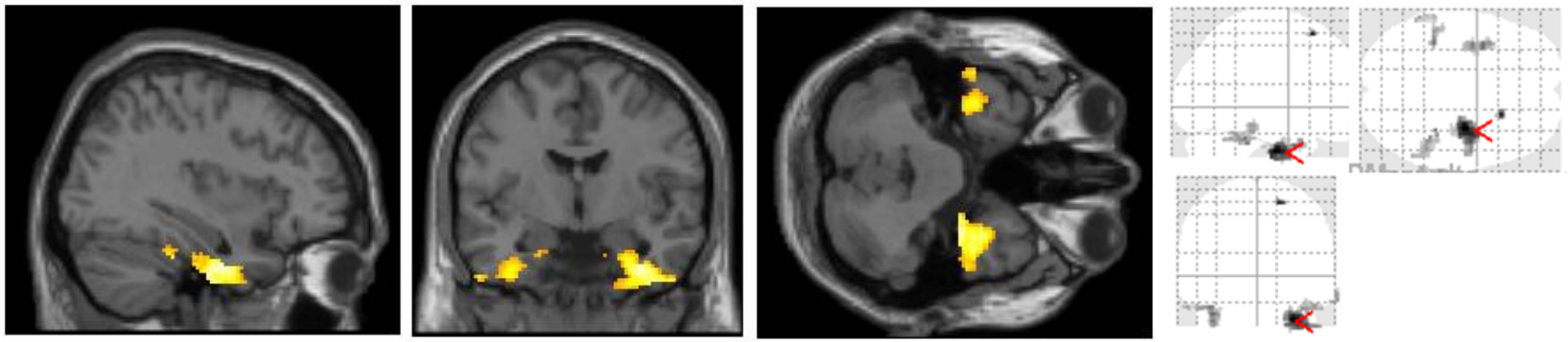
-> BOLD surrogate of “aberrant neuronal activity”

-> assuming IED cause high BOLD amplitude changes

-> look at BOLD signal variance

BOLD signal variance

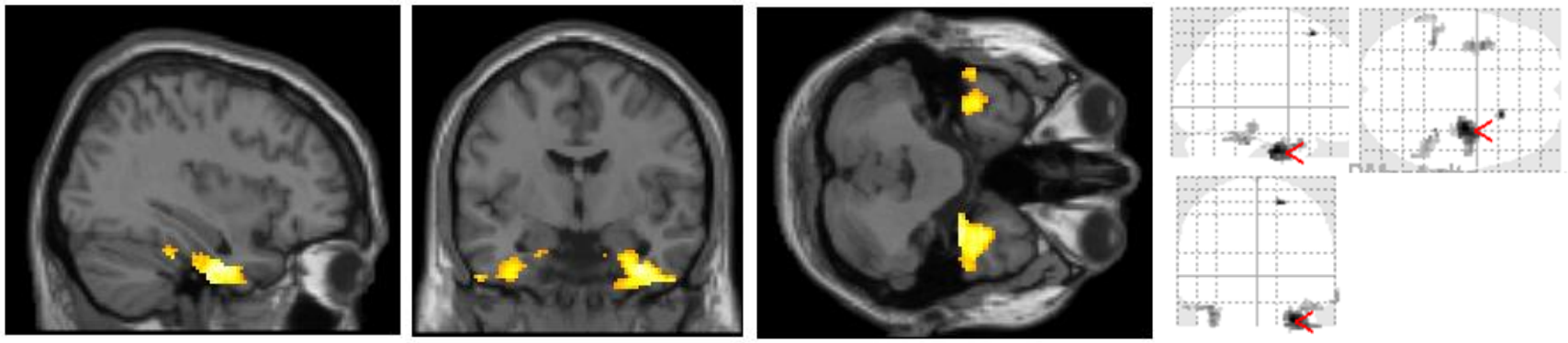
surrogate of aberrant neuronal activity



BOLD signal variance in TLE > controls (p<0.001 uncorrected)

BOLD signal variance

surrogate of aberrant neuronal activity

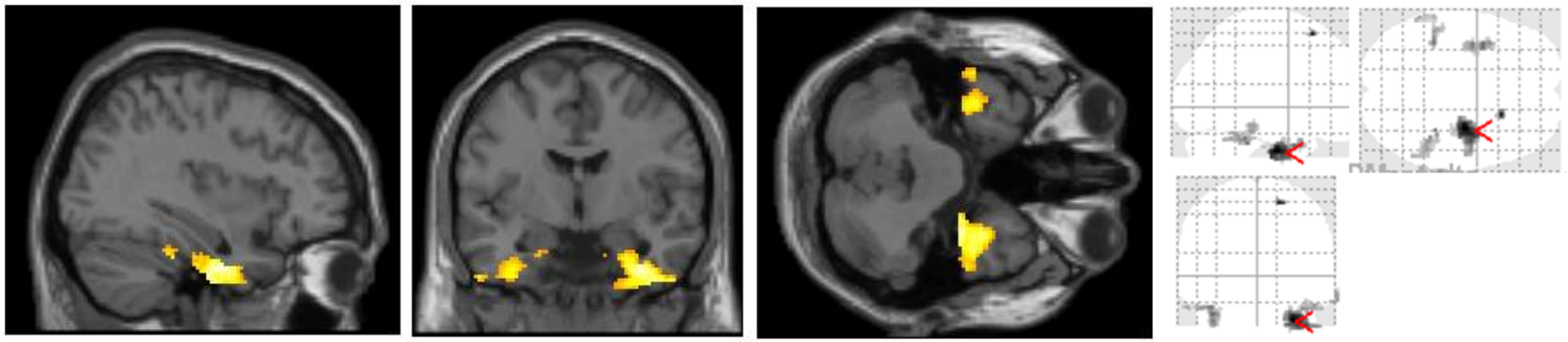


BOLD signal variance in TLE > controls (p<0.001 uncorrected)

Correlation of BOLD variance with # of IED

BOLD signal variance

surrogate of aberrant neuronal activity



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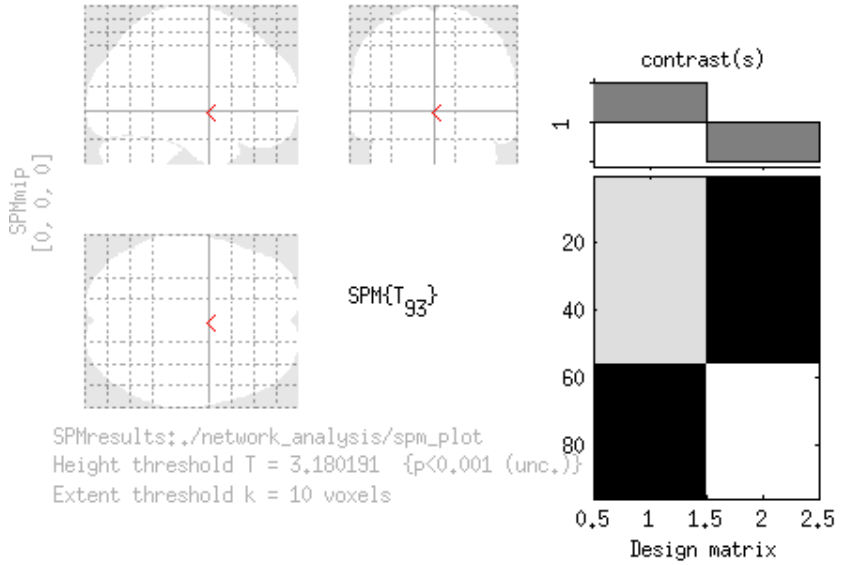

No correlation with scalp IED!

Conclusion

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- **decreased integration (Q) in TLE**

  –> global network dysfunction?

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  -> connections from crucial hubs like “area tempestas”
  -> compensatory “over connection” (memory retrieval)?

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- trend for higher segregation (Q) with more IED
  -> IED “causal”:
- **increased variance in TLE, no scalp IED-correlation**
  -> spiking in TLE cause for segregation?
  -> spiking not visible on scalp EEG but reflected in BOLD signal

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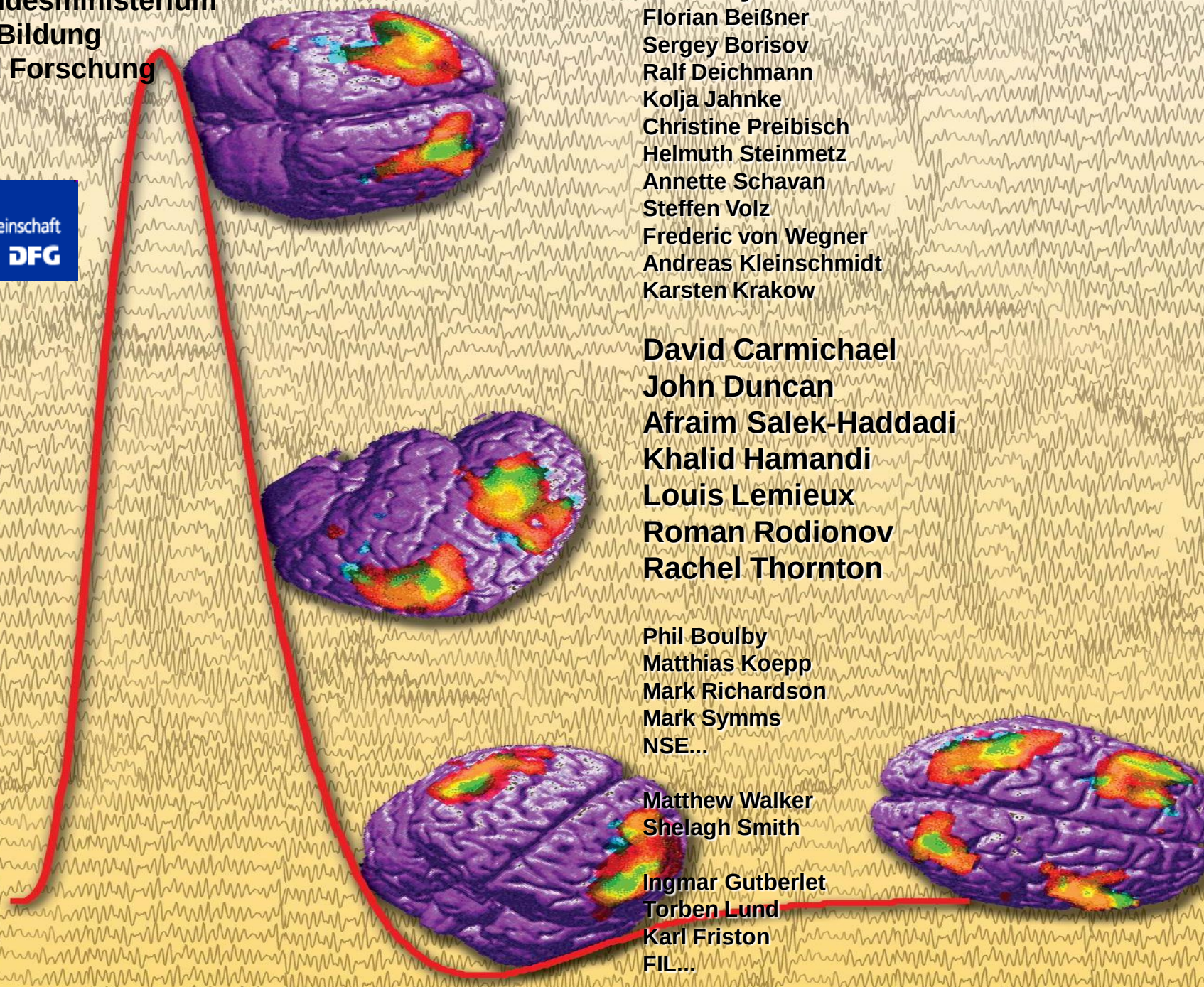

Thank you:

Sandra Anti

Florian Beißner
Sergey Borisov
Ralf Deichmann
Kolja Jahnke
Christine Preibisch
Helmuth Steinmetz
Annette Schavan
Steffen Volz
Frederic von Wegner
Andreas Kleinschmidt
Karsten Krakow

David Carmichael
John Duncan
Afraim Salek-Haddadi
Khalid Hamandi
Louis Lemieux
Roman Rodionov
Rachel Thornton

Phil Boulby
Matthias Koepp
Mark Richardson
Mark Symms
NSE...

Matthew Walker
Shelagh Smith

Ingmar Gutberlet
Torben Lund
Karl Friston
FIL...


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