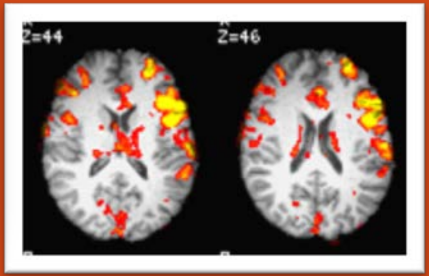
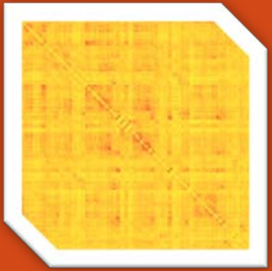





Graph-theoretical analysis of language networks in temporal lobe epilepsy

SiNAPSA Neuroscience Conference '15

Content

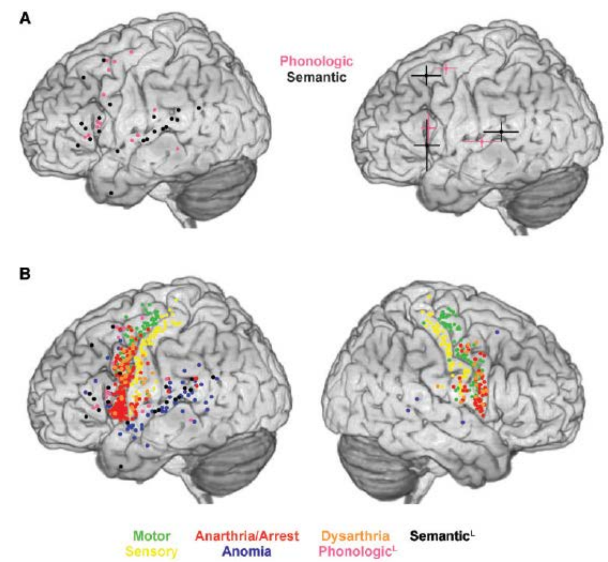
- Introduction
  - Atypical language organization in epilepsy
  - fMRI connectivity and atypical organization language in epilepsy
  - Graph-theory as a tool to understand cognition in epilepsy
- Methods
  - Participants, fMRI pipeline and graph analysis
- Results
  - Activation and connectivity in atypical language organization
  - Efficiency of networks - indicator of atypical language organization
  - Role of age-at epilepsy
- Conclusion
  - contribution of graph-theory to the study of cognition in epilepsy

Introduction

atypical language organization in epilepsy

Language organization and reorganization in epilepsy

- language is the product of a distributed brain network
  - early language processing and final speech bilaterally distributed
  - circuits responsible for naming predominately in the *left hemisphere*



(Tate et al., 2014)

- individuals in whom brain regions for naming reside exclusively or mainly in the right hemisphere

On the Site of the
Faculty of Articulated Speech
(Broca, 1865)

Language organization and reorganization in epilepsy

- language assessment as vital part of pre-operative work-up in drug-resistant epilepsy
  - **Wada test** for lateralizing language function (Wada & Rasmussen, 1958)
    - barbiturate injected into one hemisphere via the carotid artery
    - injected hemisphere looses function for a period of 5-10 minutes
    - neuropsychological testing during this period and immediately afterwards
  - **functional MRI** (Arora et al., 2009; Janecek et al., 2013)
    - **advantages**: localization of activation in regard to lesion and other structures easier recognition of mixed dominance
    - **disadvantage:** fMRI is an activation method, Wada a deactivation method
    - good overall good concordance reported 73-91 %)
- atypical language organization in drug-resistant temporal lobe epilepsy (TLE) in19-43% of cases
  (Benke et al., 2006; Janecek et al., 2013)

FULL-LENGTH ORIGINAL RESEARCH

Language lateralization by fMRI and Wada testing in 229 patients with epilepsy: Rates and predictors of discordance

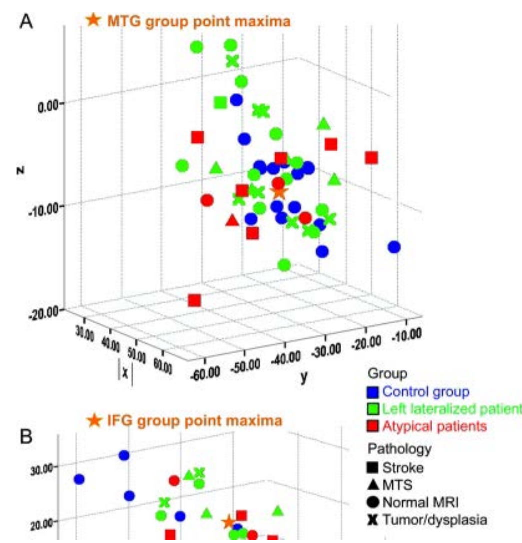
Julie K. Janecek, Sara J. Swanson, David S. Sabsevitz, Thomas A. Hammeke, Manoj Raghavan, Megan E. Rozman, and Jeffrey R. Binder

Department of Neurology and the Comprehensive Epilepsy Center, Medical College of Wisconsin, Milwaukee, Wisconsin, U.S.A.

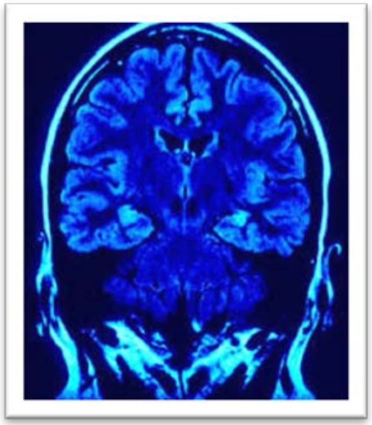
Atypical language organization in TLE

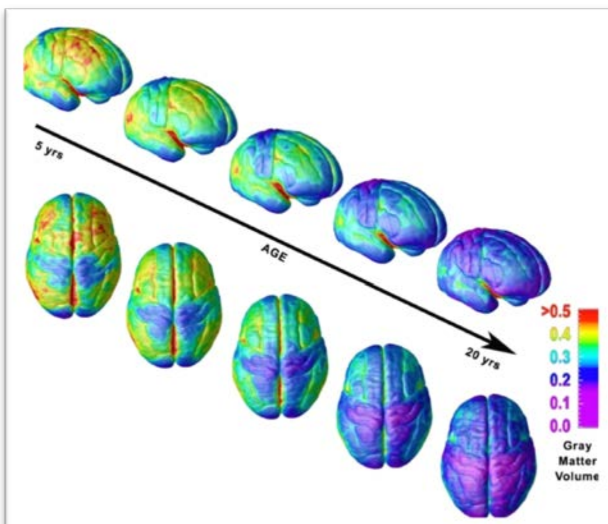
- Inter-hemispheric
  (Benke et al., 2006; Janecek et al., 2013)
  - bilateral language dominance 12-15%
  - right language dominance 6-13%

- Intra-hemispheric
  (Hamberger et al., 2007; Rosenberg et al., 2009; Mbwana et al., 2009)
  - cortical stimulation mapping showed a more posterior distribution of naming sites in TLE patients with hippocampal sclerosis
  - left-dominant TLE patients had more variable area of BOLD activation in the middle temporal gyrus compared to controls
  - additional BOLD activation in left posterior superior temporal sulcus compared to controls

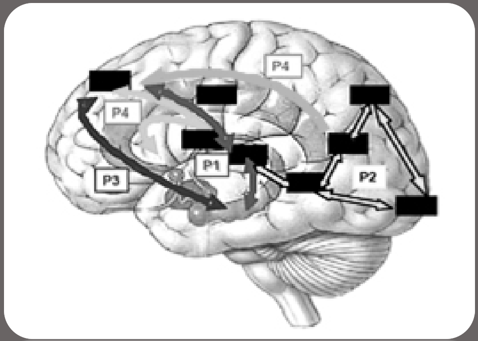


Atypical language organization in TLE





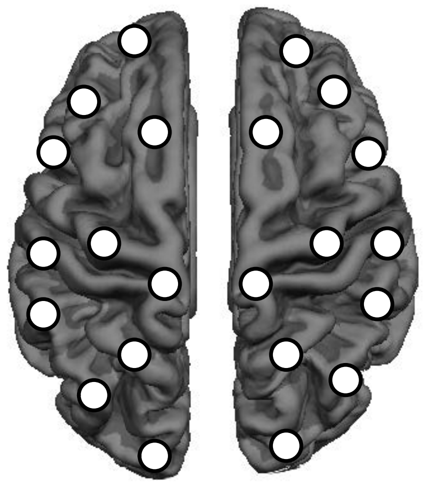
- Predictors of atypical language organization
  - **structural lesion** in the **left** hemisphere , especially left hippocampus (Weber et al., 2006; Hamberger et al., 2007)
  - **left-seizure focus** (Isaacs et al., 2006; Stewart et al., 2014)
  - **early age of "injury"** (Rasmussen and Milner 1977; Rausch et al. 1991) or early or intermediate age of epilepsy onset (12-20 yr of age) (Stewart et al., 2014)
  - handedness only in case of early onset and left-seizure focus (Stewart et al., 2014)

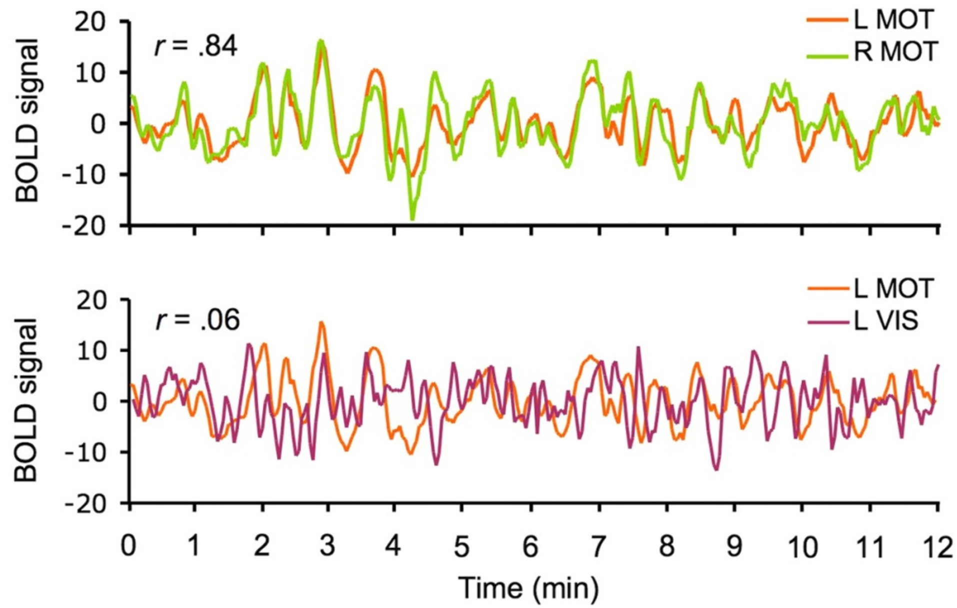


Introduction

fMRI connectivity and atypical organization of language in epilepsy

fMRI connectivity and atypical organization of language in epilepsy





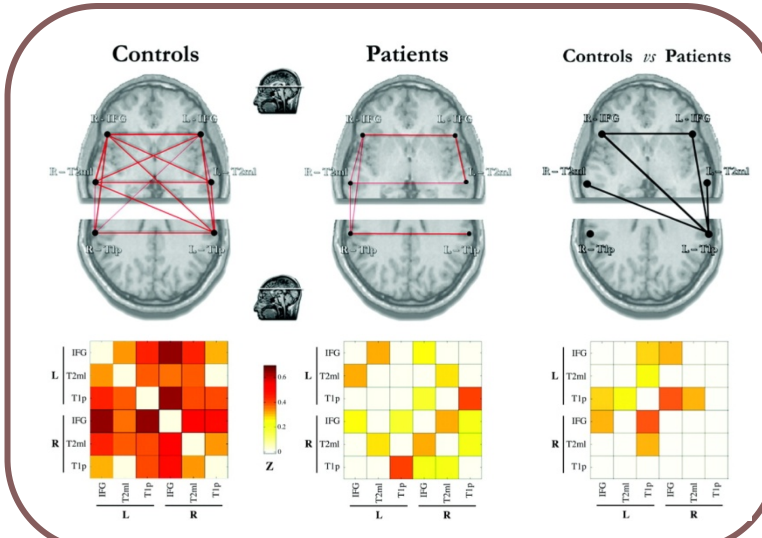
- Functional connectivity **(FC)**
  - **definition**: "…the statistical association or dependency among two or more anatomically distinct time-series" (Friston, 1994)
  - **measures**: Pearson *r*, Spearman *rho*, partial *r*, mutual information…

fMRI connectivity and atypical organization language in epilepsy

- **Pravata et al. 2011**
  - 11 patients with left-sided, 11 right-sided focus (73% TLE), 12 controls
  - reduced FC within left hemisphere and between hemisphere in both groups of patients
  - during verb-generation task reduced FC of language network in patients with left-sided focus
  - in this group lower left intra-hemispheric FC predicted lower verbal IQ (r =.70)

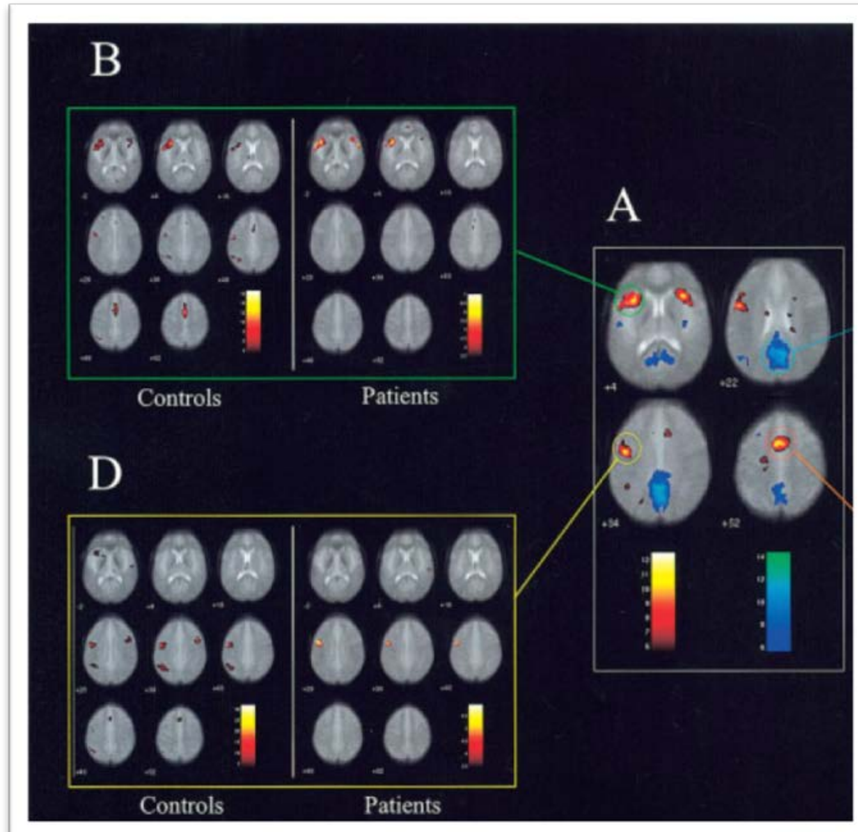
regions of interest (6-mm radius) were:

- the pars triangularis of the IFG
- posterior part of the superior temporal gyrus
- middle-lateral part of the middle temporal gyrus



fMRI connectivity and atypical organization language in epilepsy

- **Waites et al. 2006**
  - 17 patients with left-sided, 8 healthy control participants
  - seed regions defined by separate fMRI study on a control group of 30 healthy control participants
  - no differences in activation
  - during resting-state fMRI reduced FC of language network in patients:
    - left interior frontal gyrus less connectivity with angular gyrus and ACC, more with posterior cingulate cortex
    - left middle frontal gyrus less connectivity with angular gyrus

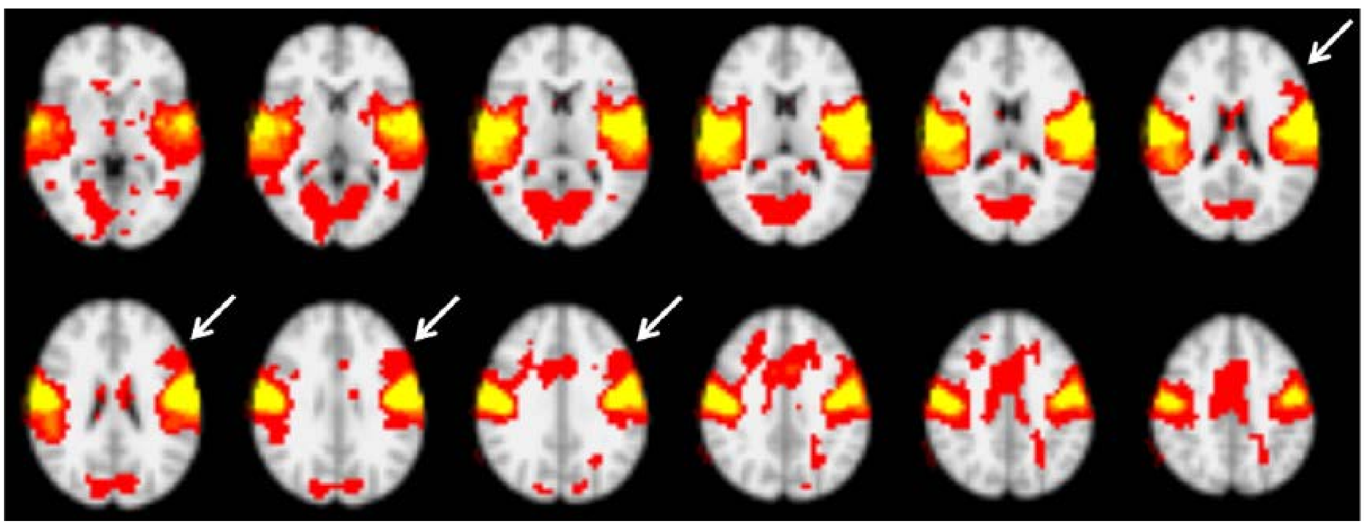


fMRI connectivity and atypical organization language in epilepsy

- **Vlooswijk et al. 2010**
  - 34 patients with cyrptogenic localization-related epilepsy, 27 healthy controls
  - word-generation and text-reading fMRI paradigm
  - no differences in activation, however in patients lower FC:
    - during the word-generation paradigm in prefrontal network
    - during the text-reading task paradigm in frontotemporal network
  - lower FC in prefrontal and frontotemporal networks associated with
    - poorer performance on test of verbal fluency
    - poorer performance on test of reading ability

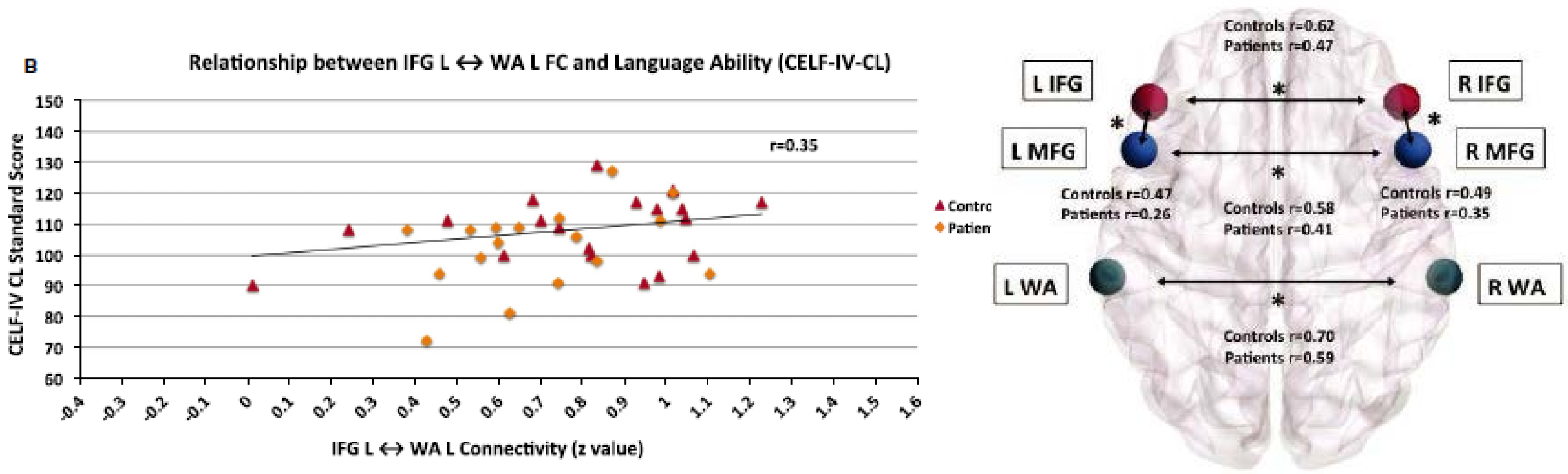
fMRI connectivity and atypical organization language in epilepsy

- **Besseling et al., 2013**
  - 22 children with rolandic epilepsy and 22 controls (8-12 yr)
  - resting-state fMRI, word-generation and reading task
  - no differences in activation (used for ROI selection)
  - reduced functional connectivity of the left inferior frontal gyrus with pre- and post-central gyri and superior temporal gyrus (“Rolandic Network”)
  - no association with neuropsychological assessment of language



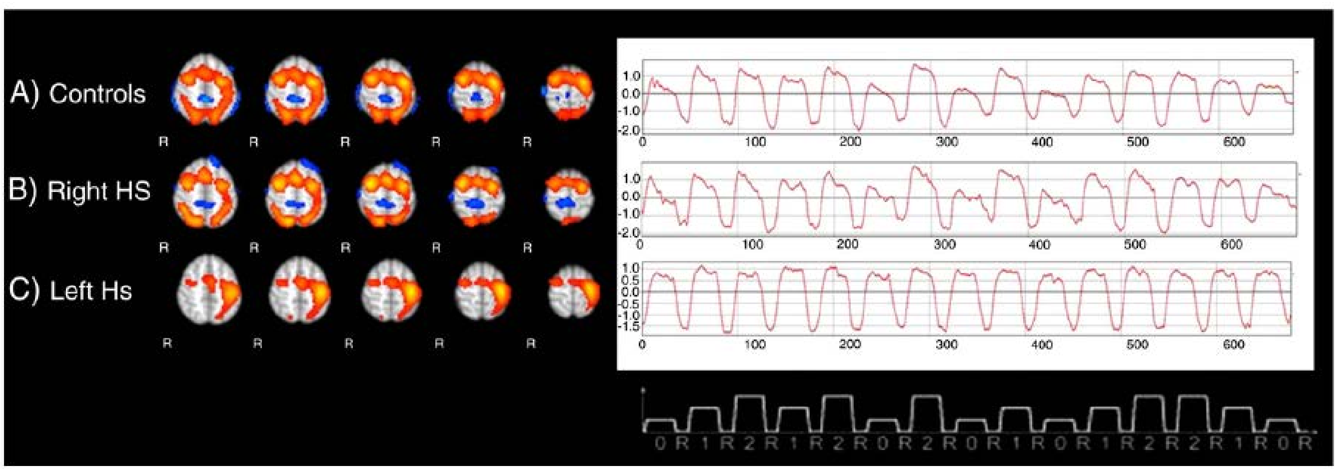
fMRI connectivity and atypical organization language in epilepsy

- **Sepeta et al., 2015**
  - 19 children with left-hemispheric focal epilepsy (~50% temporal), 19 controls
  - regions of interest: inferior frontal gyrus, middle frontal gyrus, Wenicke's area
  - reduced inter-hemispheric and intra-hemispheric connectivity in patients
  - greater FC beween left language regions (IFG, WA) predictive of better verbal ability
  - FC not associated wit age at epilepsy onset or duration of epilepsy



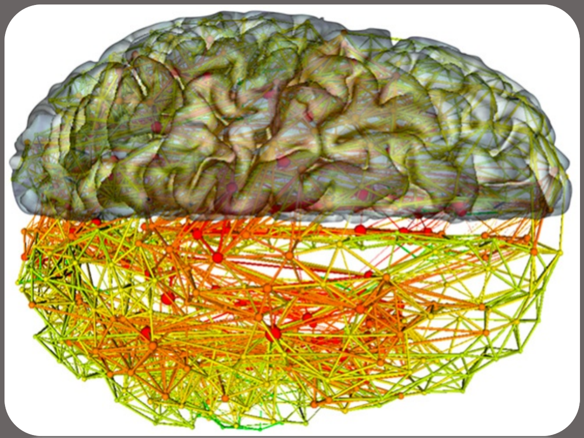
fMRI connectivity and atypical organization language in epilepsy

- **Stretton et al., 2013**
  - 52 TLE patients with hippocampal sclerosis and 30 controls
  - fMRI working-memory task + DTI
    - task-positive networks: 4 regions involving fronto-parietal activation
    - task-negative networks: 2 regions involving deactivation of the default-mode network
  - "…the segregation of the task-positive and task-negative FC networks supporting working memory in TLE is disrupted, and is associated with abnormal structural connectivity of the sclerosed hippocampus."
  - FC of regions which show task-associated increases with those showing task-associated decreases were predictive of poorer performance



Summary of FC research in language and epilepsy

- Summary
  - in children and adults with epilepsy there are differences in FC compared to controls, even in the absence of differences in activation
  - in TLE and left localization-related epilepsy there is evidence of reduced FC between classical language regions
  - in adults with TLE (Pravata et al. 2011) and children (Sepeta et al., 2015) with left-hemispheric focal epilepsy there is some evidence that reduced FC between language regions is associated with lower verbal abilities
  - in patients with TLE an inability to decouple task-unassociated regions may be associated with impaired performance (Stretton et al., 2013)



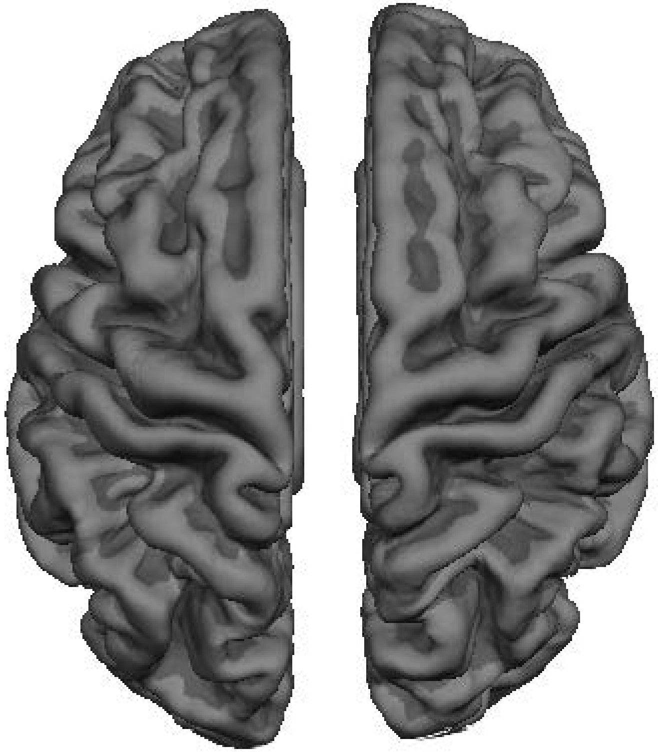
Introduction

Graph-theory as a tool to understand cognition in epilepsy

Graph-theory as a tool to understand cognition in epilepsy

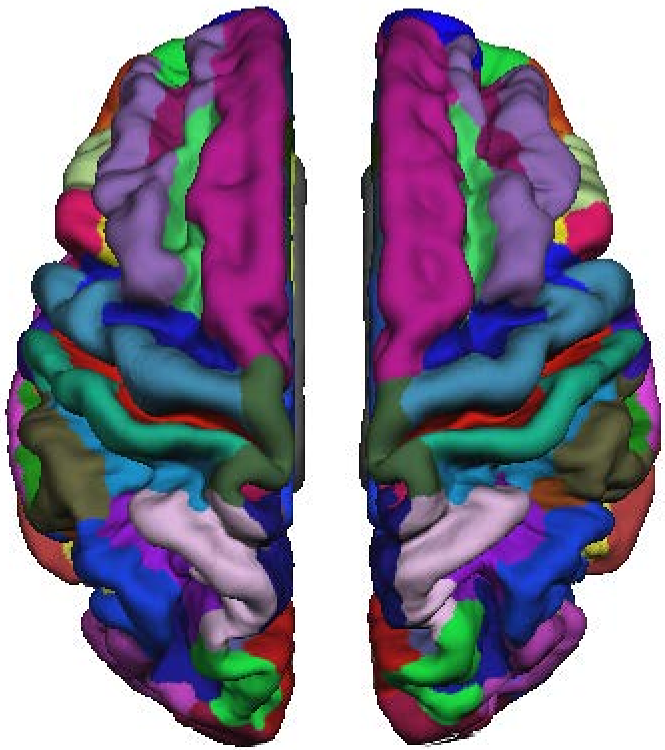
- beyond FC of individual regions towards investigating the connectome in patients with epilepsy - a comprehensive map of neural connections in the brain

- Connectomics and Epilepsy
  - offers an advantage in the delineation of the aberrant functional and structural connections of the whole brain (Engel et al., 2015)
  - graph theory as a tool for the analysis and quantification of network structure and function.
  - follows from the realization that the complexity in the macroscopic behaviour of a system of interacting elements (society cell, or brain), is shaped by interactions among their constituent elements.



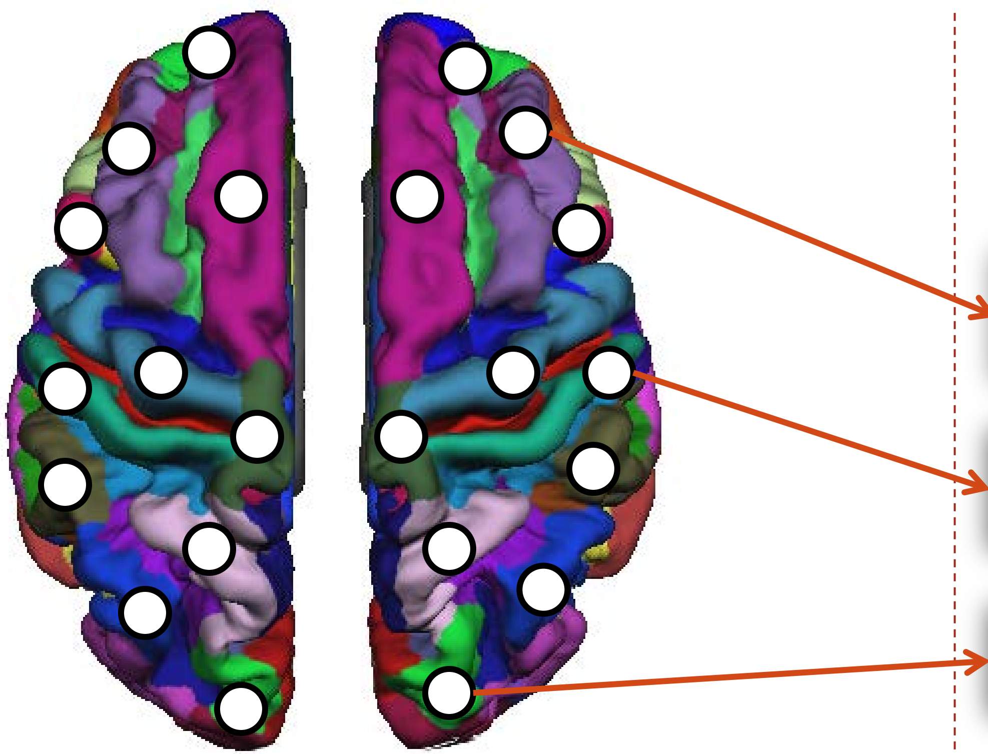
Graph-theory and connectomics

- How to define the elements of a system?
  - anatomical regions (Destrieux et al., 2010)
  - homogeneus functional regions (Craddock et al., 2012)
  - regions based on previous research (Yarkoni et al., 2011)
  - …

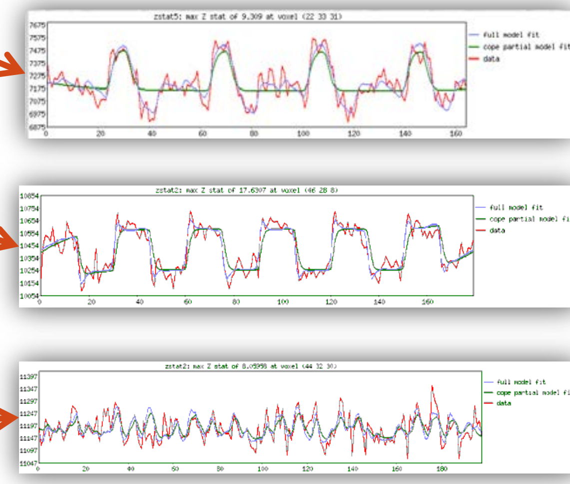


Graph-theory and connectomics

- Example:
  - anatomical parcellation with the FreeSurfer Destrieux anatomical atlas (Destrieux et al., 2010)

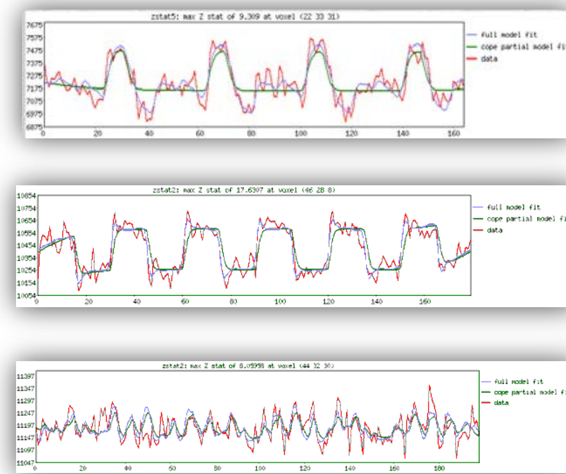


Graph-theory and connectomics



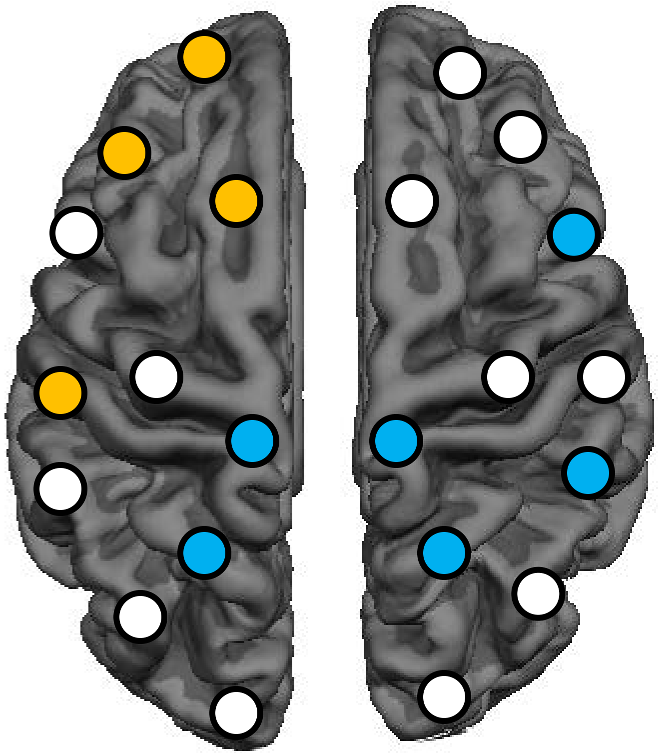
- appropriate fMRI pre-processing pipeline and choice of brain parcellation → time courses

Graph-theory and connectomics

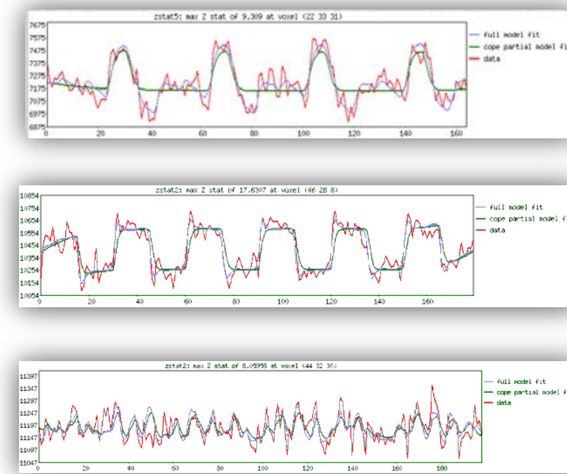


- can be used to identify regions of task-associated increases

↑ BOLD activation



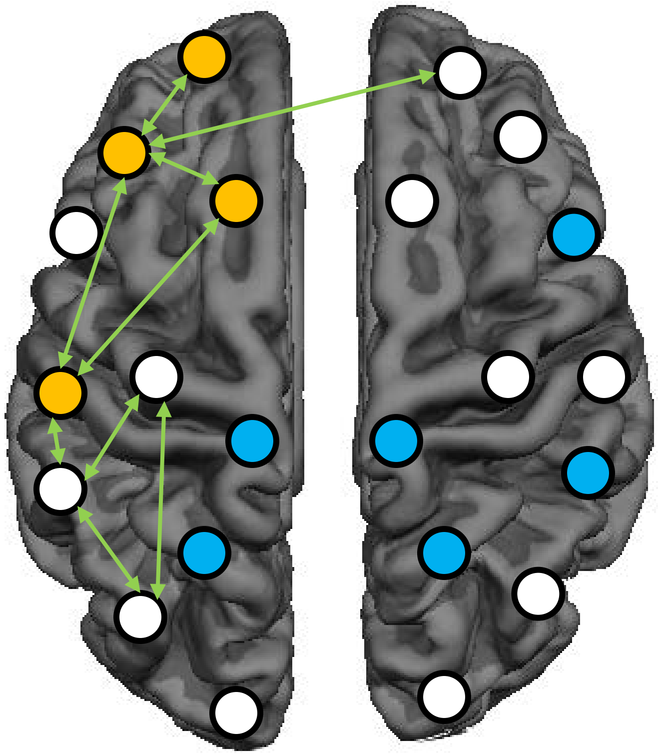
Graph-theory and connectomics



- can be used to identify regions of task-associated increases and decreases in activation

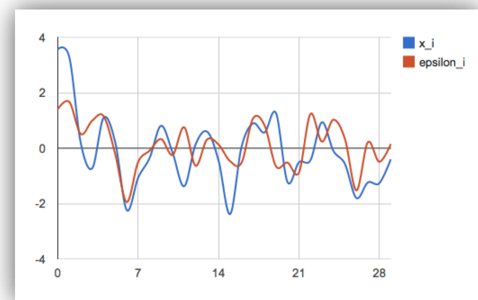
↑BOLD activation

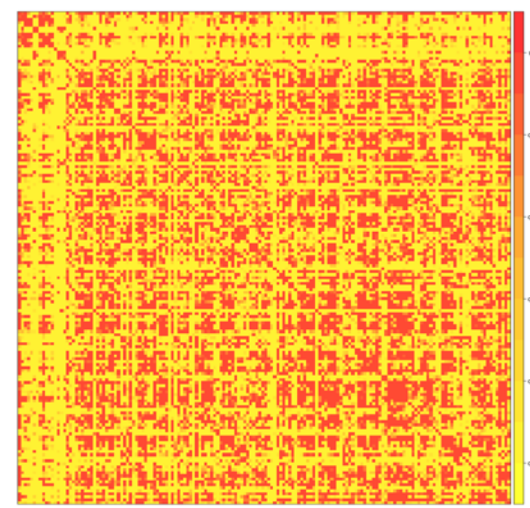
↓BOLD deactivation



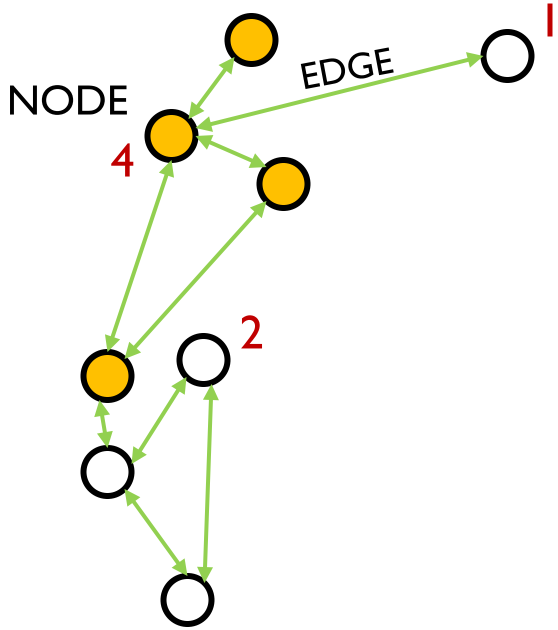
Graph-theory and connectomics

+ DIFFRENTIAL NEWTORKS





- by looking at the impact of a task on the FC among all regions we can find those which show and **increase** in connectivity among regions
  - **+ DIFFRENTIAL NEWTORKS**

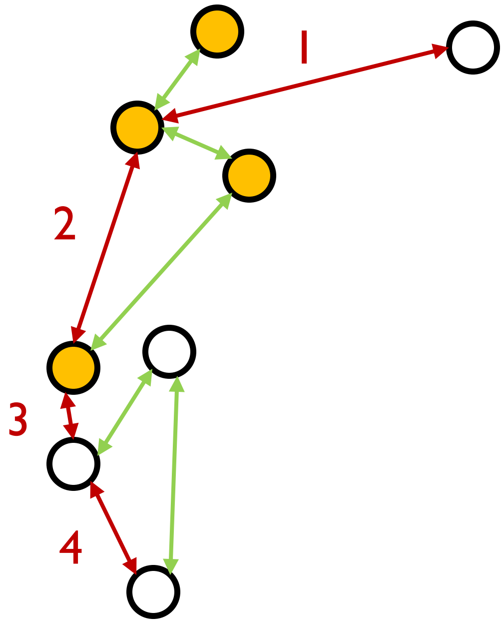


- **NODE** – element of network (obtained by brain parcellation)
- **EDGE** – connection between two elements (obtained by choosing a threshold)

Graph-theory and connectomics

+ DIFFRENTIAL NEWTORKS

NODAL DEGREE
number of connections with other nodes



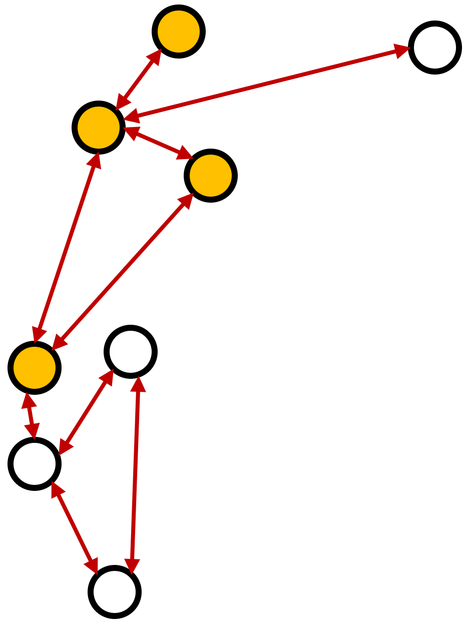
Graph-theory and connectomics

+ DIFFRENTIAL NEWTORKS

PATH LENGTH
number of edges neeeded to get from one node to another

MEAN PATH LENGTH
mean path length average over all nodes

COST
overall level of connectivity



$$E(G) := \frac{1}{N_V(N_V-1)} \sum_{i \in V} \sum_{j \neq i \in V} d_{ij}^{-1}$$

- G…graph
- N_v…number of vertices
- d_{ij}…length of the shortest path from nodes i to j

Graph-theory and connectomics

+ DIFFRENTIAL NEWTORKS

NETWORK EFFICIENCY

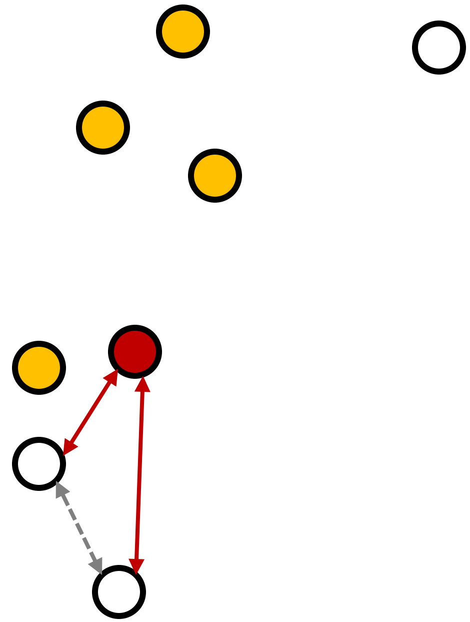
GLOBAL EFFICIENCY

LOCAL EFFICIENCY

REGIONAL EFFICIENCY

Latora and Marchiori, 2001

Ginestet and Simmons, 2011



$$E^{Loc}(G) := \frac{1}{N_V}\sum_{i\in V} E(G_i)$$

- G_i…subnetwork of G which contains all neighbors of i
- while global efficiency is the efficiency of the entire graph G, local efficiency is the averaged efficiency of all first-order neighborhoods
- measures how fault tolerant the system is locally

Graph-theory and connectomics

+ DIFFRENTIAL NEWTORKS

NETWORK EFFICIENCY

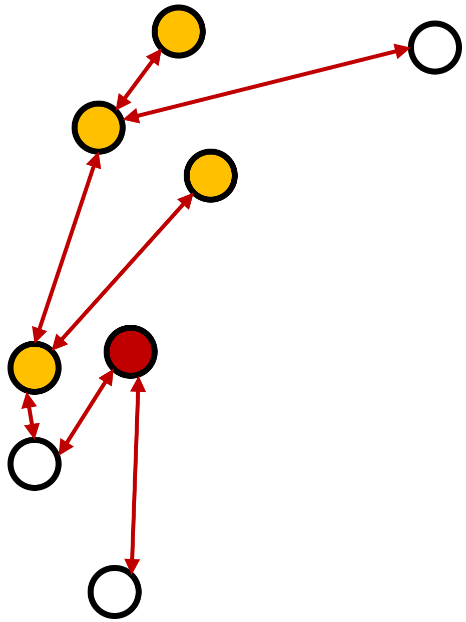
GLOBAL EFFICIENCY

LOCAL EFFICIENCY

REGIONAL EFFICIENCY

Latora and Marchiori, 2001

Ginestet and Simmons, 2011



$$E^{Glo}(G,v) := \frac{1}{N_V - 1} \sum_{j \neq v \in V} d_{vj}^{-1},$$

- is the region-specific global efficiency and sometimes simply referred to as regional efficiency
- quantifies the connectivity of each node to all the other nodes in the network.

Graph-theory and connectomics

+ DIFFRENTIAL NEWTORKS

NETWORK EFFICIENCY

GLOBAL EFFICIENCY

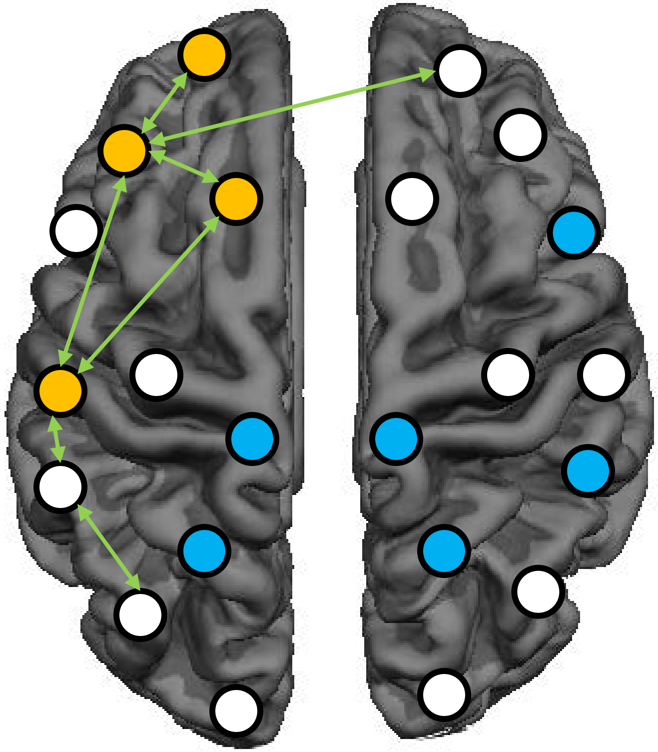
LOCAL EFFICIENCY

REGIONAL EFFICIENCY

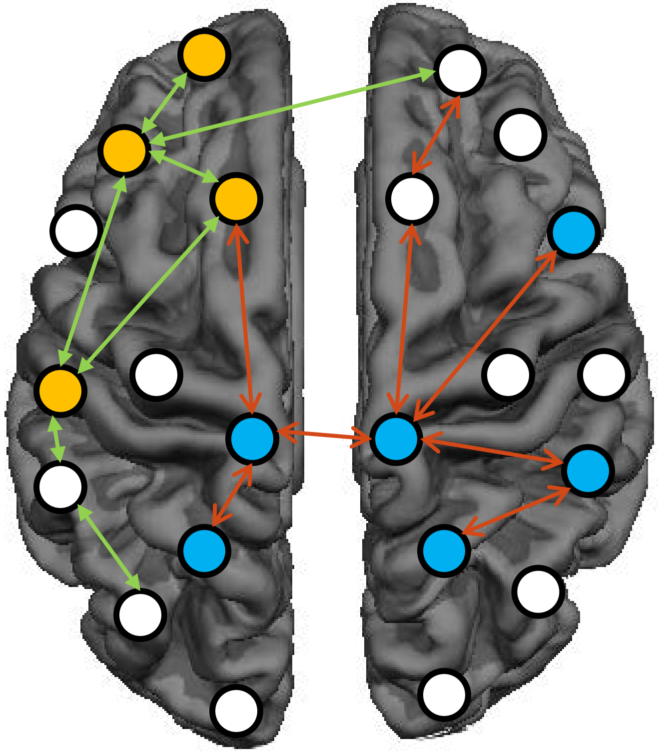
Latora and Marchiori, 2001

Achard and Bullmore, 2007

Ginestet and Simmons, 2011

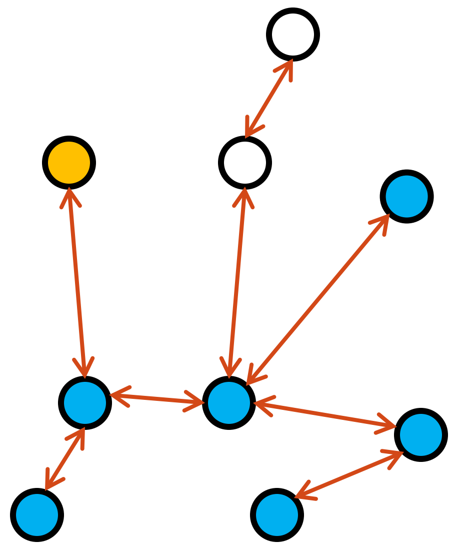


Graph-theory and connectomics

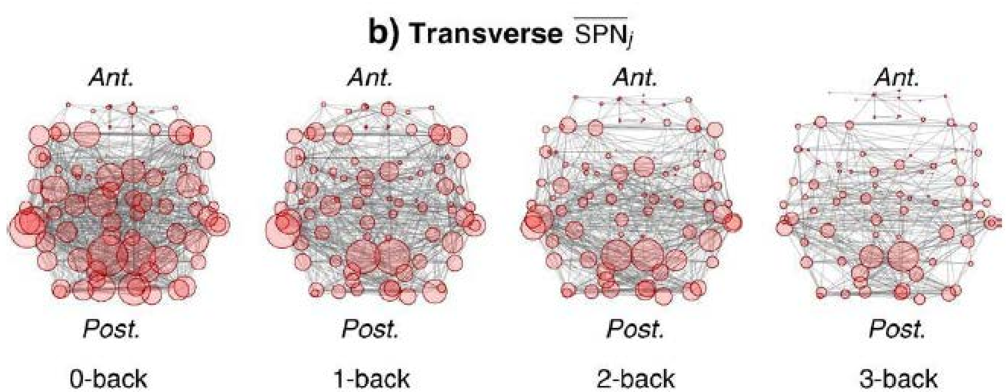


Graph-theory and connectomics

- by looking at the impact of a task on the FC among all regions we can find those which show a **decrease** in connectivity among regions
  - **- DIFFRENTIAL NEWTORKS**



- also possible to calculate the global, local and regional efficiency in networks that show decoupling during a task (i.e. N-back task - Ginestet and Simmons, 2011)



Graph-theory and connectomics

NETWORK EFFICIENCY

GLOBAL EFFICIENCY

LOCAL EFFICIENCY

REGIONAL EFFICIENCY

Graph-theory as a tool to understand cognition in epilepsy

- How does this relate to epilepsy and language?
  - Vlooswijk et al. (2011)
    - fMRI silent-word generation paradigm,
    - 41 patients with frontal and temporal lobe epilepsy had globally as well as locally less efficient networks compared to 23 controls
    - greater disruptions in local efficiency in these patients were associated with lower full scale IQ

- How does this relate to epilepsy and cognition
  - Wang et al. (2014)
    - resting state fMRI study of 26 TLE patients
    - reduced global efficiency and increased local interconnectivity
    - increased local efficiency in patients with left temporal epilepsy being associated with longer duration of epilepsy
    - focal changes in the network parameters of several nodes, including the bilateral angular gyri, left middle temporal gyrus and the left pars triangularis (significance for language)

Study

- **Aim**: to investigate atypical language organization using two fMRI language paradigms and graph-theoretical measures

- **Hypotheses**:
  1. in patients with atypical language organization greater task-modulated activation in right frontal and temporal lobes
  2. in patients with atypical language organization greater task-modulated FC in right frontal and temporal lobes
  3. lower global network efficiency in TLE patients
  4. reduced ability of patients with epilepsy to deactivate task non-relevant regions
  5. age of epilepsy onset to be associated with greater language-associated activation and connectivity of the right hemisphere

Methods

Participants, fMRI pipeline and graph analysis

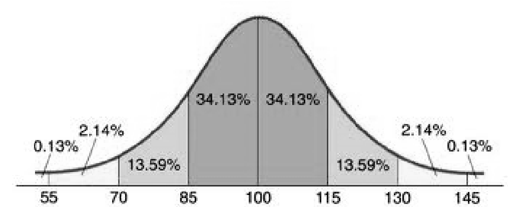
Participants

	Control group	Left language-dominant TLE	Right language-dominant TLE
N	9	6	6
N female	4	3	3
N right-handed	9	5	3
Age	30.7 (7.9)	48.8 (7.1)	35.2 (9.2)
Age at epilepsy onset		34.8 (16.4)	16.5 (12.7)
Duration of epilepsy		14.0 (17.6)	18.7 (10.8)
Hippocampal sclerosis		4	4
Febrile seizures		0	4
Early insult		2	4
Number of AEDs		2.2 (0.8)	2.5 (0.8)
Verbal IQ		96.6 (17.9)	94.5 (6.2)
BNT score		61.6 (35.5)	90.5 (36.6)

- all 12 patients had a left-seizure focus in the temporal lobe

Neuropsychological assessment

- As part of presurgical work-up:
  - Wada test (Pauli et al., 2006)
  - Neuropsychological assessment
    - Test of verbal IQ (Lehrl, 2005)
    - Boston Naming Test (BNT)
  - fMRI language assessment
    - Verbal fluency paradigm
      - 30s task blocks of generating words to a letter interspaced with a control task of reading nonsense words
    - Verb generation paradigm
      - 30s task blocks of generating verbs based on nouns interspaced with a control task of reading nonsense words



Neuroimaging

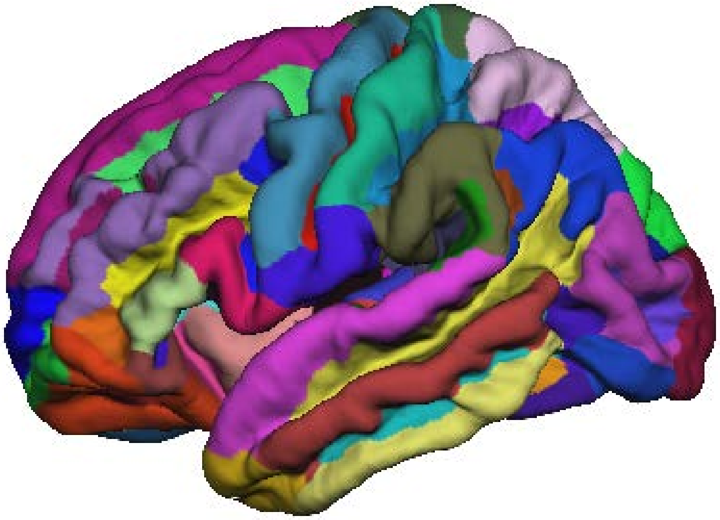
- **MRI sequences** (3T Siemens Trio, 12-chanel standard head coil)
  - T1 weighted 3D-MPRAGE sequence (voxel size = 1x1x1mm^3)
  - T2 weighted 3D-FLAIR sequence (voxel size = 0.5x0.5x0.5mm^3)
  - fMRI tasks - two gradient-echo planar T2*-weighted sequences (TR = 3000 ms, TE = 30 ms, voxel size = 1.5 x 1.5 x 3.75 mm^3, 36 interleaved slices, 130 and 170 volumes)

- **Preprocessing**
  - preprocessing using FSL FEAT (high-pass filter, slice timing correction, motion correction, spatial smoothing, FSL variance normalization (Beckmann and Smith, 2004))
  - Conversion into time-series via to parcellation schemes

Parcellation schemes

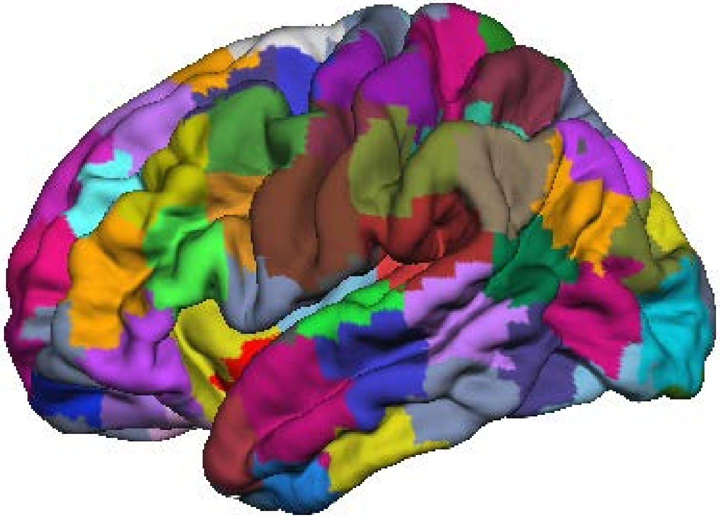
FreeSurfer

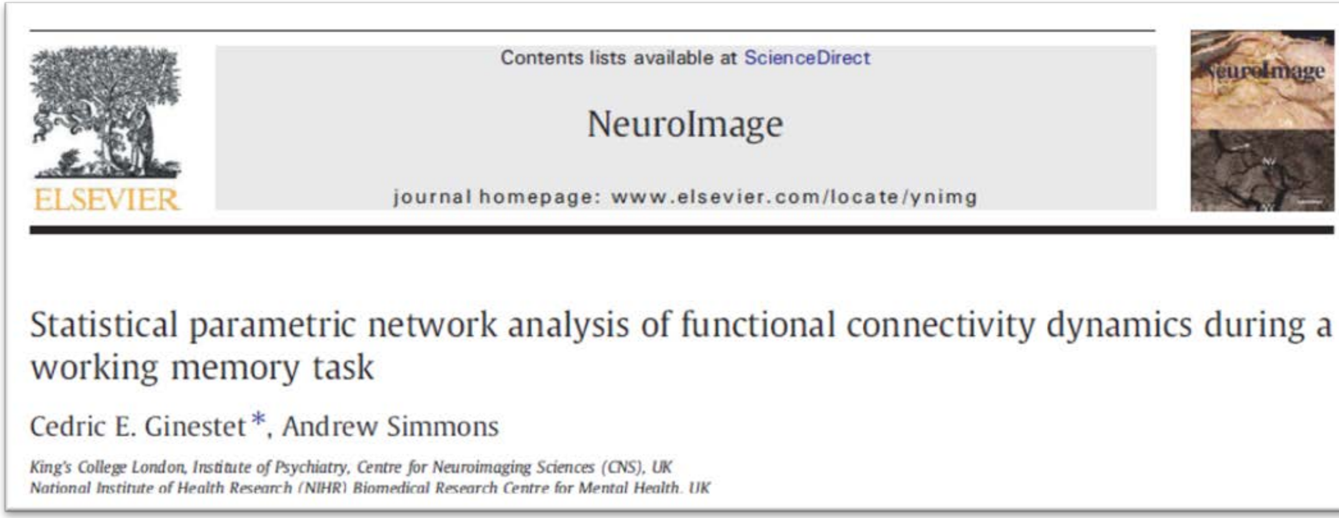
(Destiroux, 2009)



fMRI-based atlas (200 regions)

(Cradock et al., 2011)




Contents lists available at ScienceDirect
NeuroImage
journal homepage: www.elsevier.com/locate/ynimg

Statistical parametric network analysis of functional connectivity dynamics during a working memory task

Cedric E. Ginestet *, Andrew Simmons
King's College London, Institute of Psychiatry, Centre for Neuroimaging Sciences (CNS), UK
National Institute of Health Research (NIHR) Biomedical Research Centre for Mental Health, UK

- Transformation of correlation coefficients
- Networks
  - significance of correlations coefficients (FDR correction)
  - identification of high degree nodes (random networks)
  - task-positive (task-modulated increase in correlation) and task-negative (task-negative increase in correlation) networks
- Age at epilepsy onset
  - activation and nodal degree

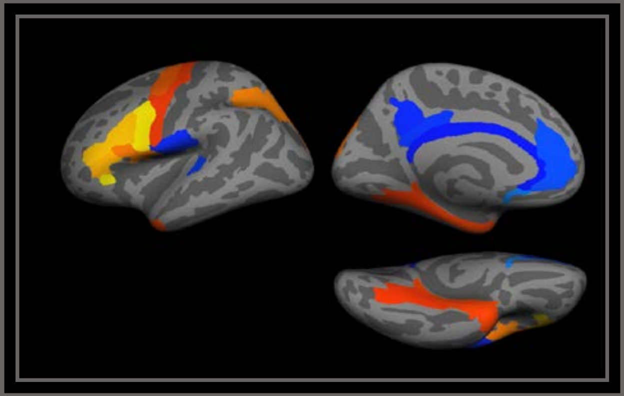
Cerebral Cortex
doi:10.1093/cercor/bht119

Functional Connectivity and Brain Activation: A Synergistic Approach

Dardo Tomasi[1], Ruiliang Wang[2], Gene-Jack Wang[2,3] and Nora D. Volkow[1,4]

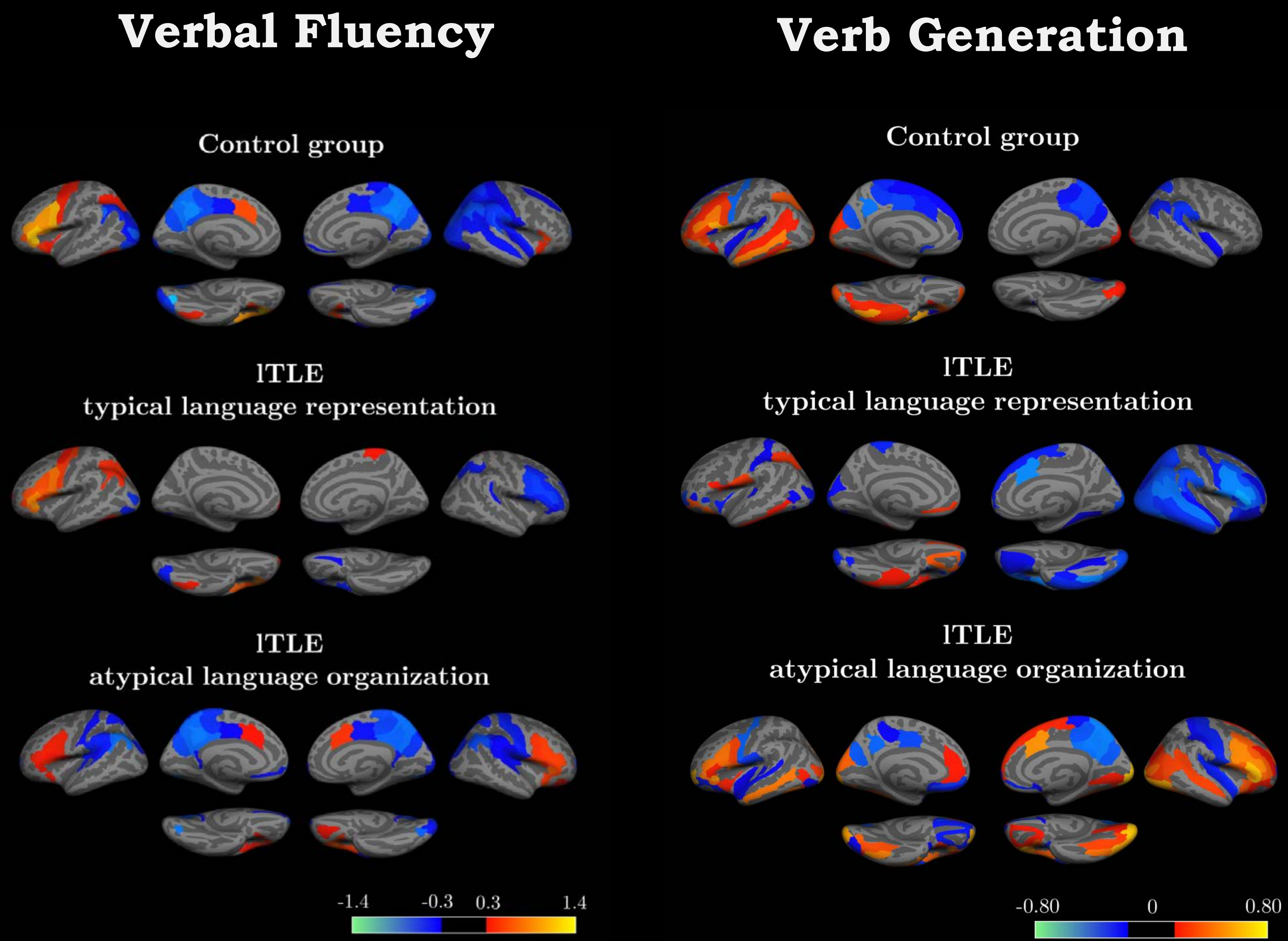
[1]National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD, USA, [2]Department of Biosciences, Laboratory of Neuroimaging (LNI/NIAAA), Brookhaven National Laboratory, Upton, NY, USA, [3]Department of Radiology, Stony Brook University, Stony Brook, NY, USA and [4]National Institute on Drug Abuse, Bethesda, MD, USA

- Additional network efficiency assessment across individual participants with cost-integrated measures
  - for brain regions showing task-modulated increases in the BOLD signal
  - for brain regions showing task-modulated decreases in the BOLD signal
- Correlation analyses
  - BOLD activation/deactiovation and connectivity
  - Network efficiency and clinical variables

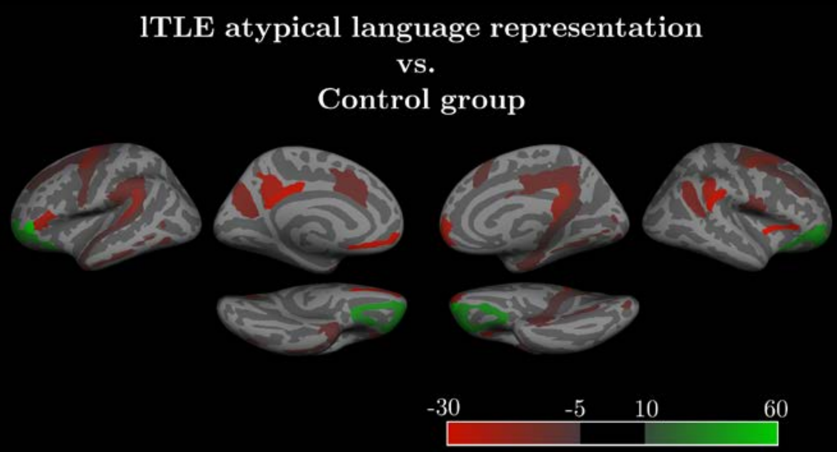


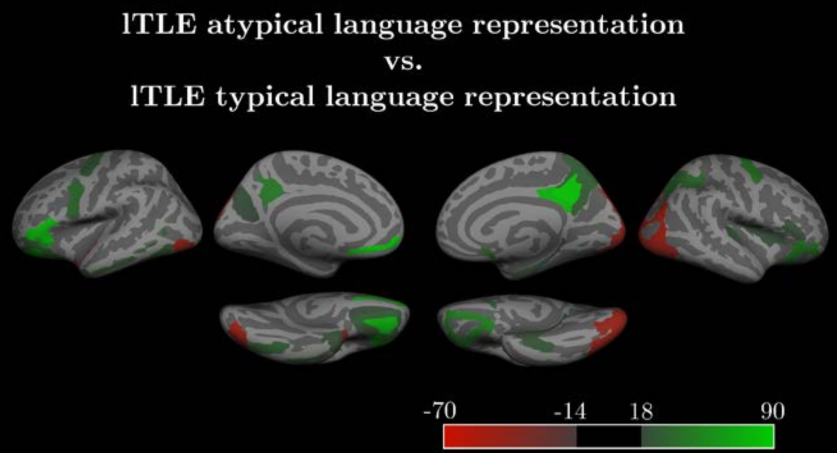
Results

Activation and connectivity in atypical language organization


Verbal Fluency
Verb Generation
Control group
Control group
lTLE
typical language representation
lTLE
typical language representation
lTLE
atypical language organization
lTLE
atypical language organization
-1.4
-0.3
0.3
1.4
-0.80
0
0.80

Task-positive networks

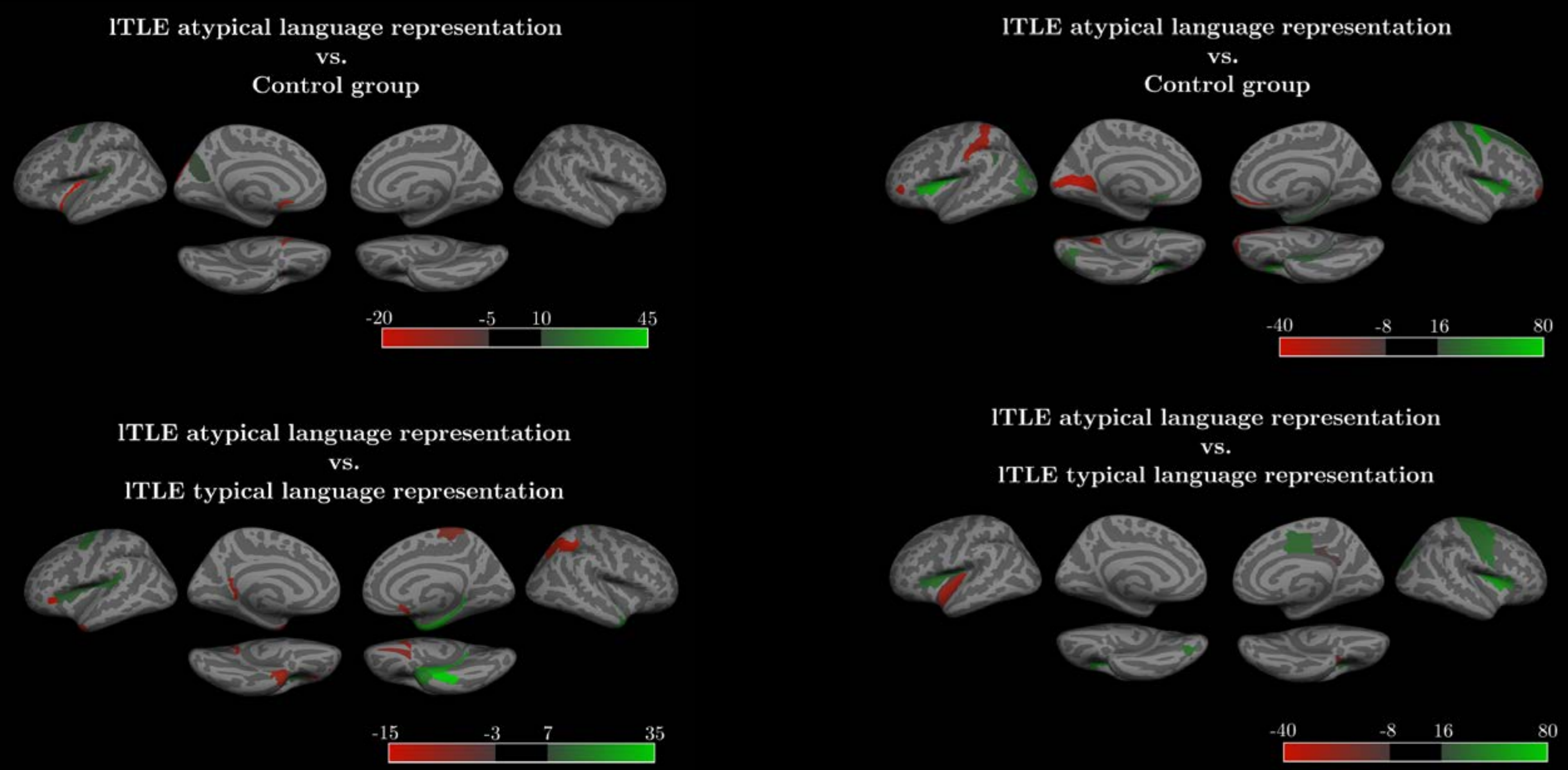




- **Atypical TLE vs. controls**
  - greater nodal degree on both fMRI task:
    - **left:** frontomarginal gyrus, orbital gryus and lateral sulcus,
    - **right**: cuneus, central insula, occipital middle and superior gyrus

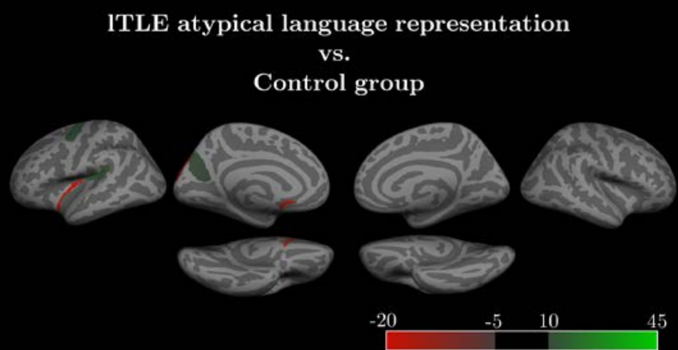
- **Atypical vs. typical TLE**
  - greater nodal degree on both fMRI task:
    - **left:** posterior cingulate cortex, inferior frontal gyrus (orbital, pars triang.) and sulcus, orbital gyrus and sulcus, vertical ramus of the lateral fissure, temporal pole,
    - **right**: posterior cingulate, inferior frontal gyrus (orbital, pars triang.), orbital gyrus superior temporal gyrus, , horizontal ramus of the lateral fissure

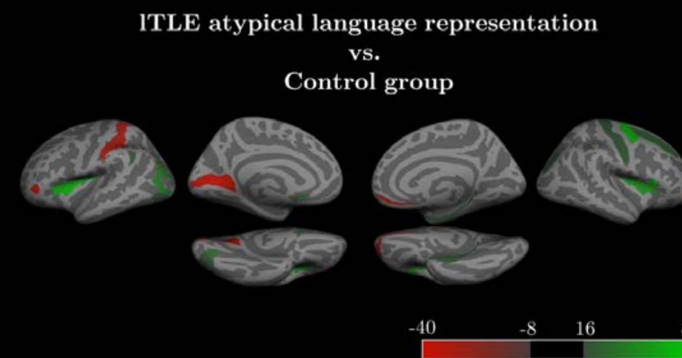
Task-negative networks

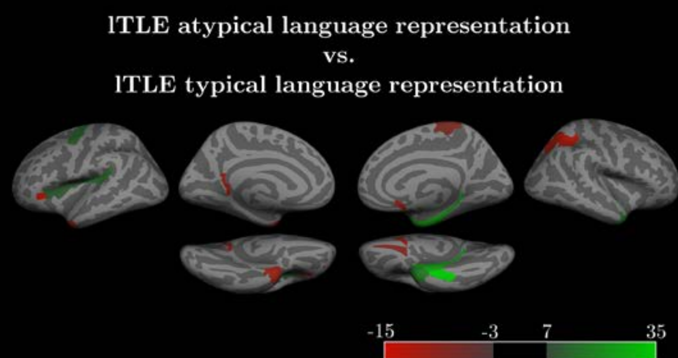


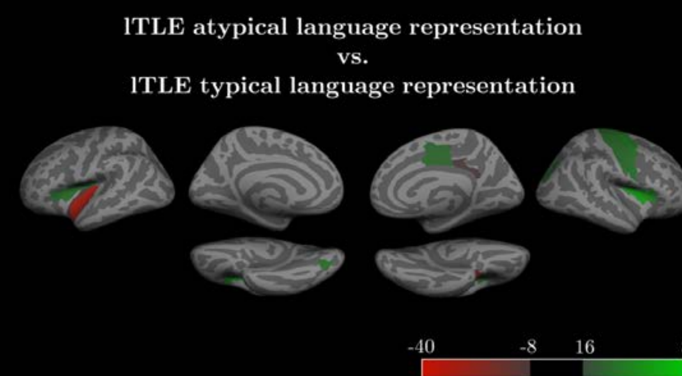
- **Less consistent** (Verbal fluency):
  - **left:** left planum temporale anad posterior part of the lateral fissure , frontomarginal gyrus, orbital gryus and lateral sulcus, parieto-occipital sulcus, superior part of the precentral sulcus, sup. occipital (TLE)
  - **right:** post-central gyrus, temporal pole, sup. occipital (TLE), parahippocampa gyrus (TLE)

Task-negative networks

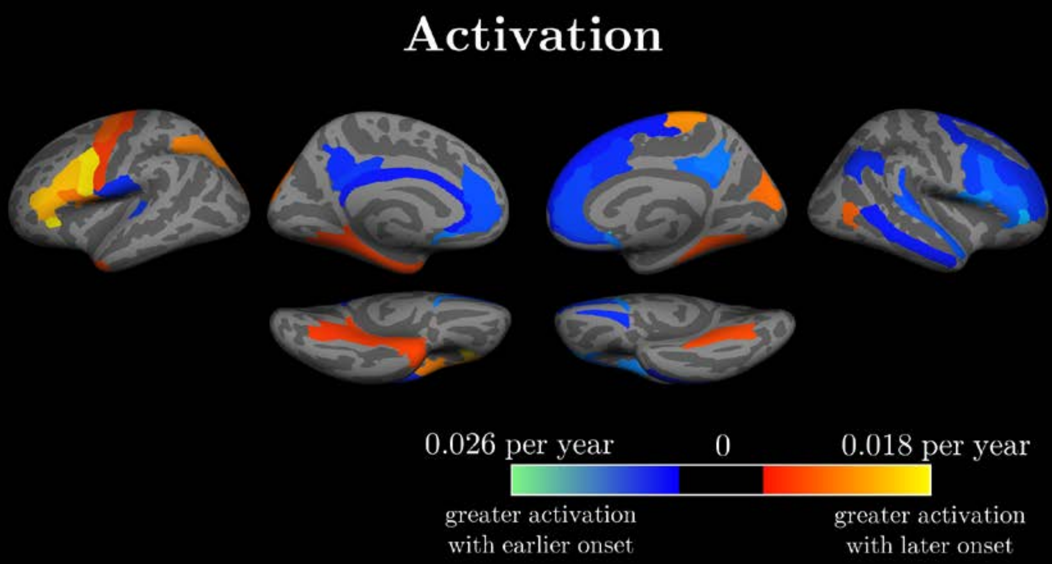


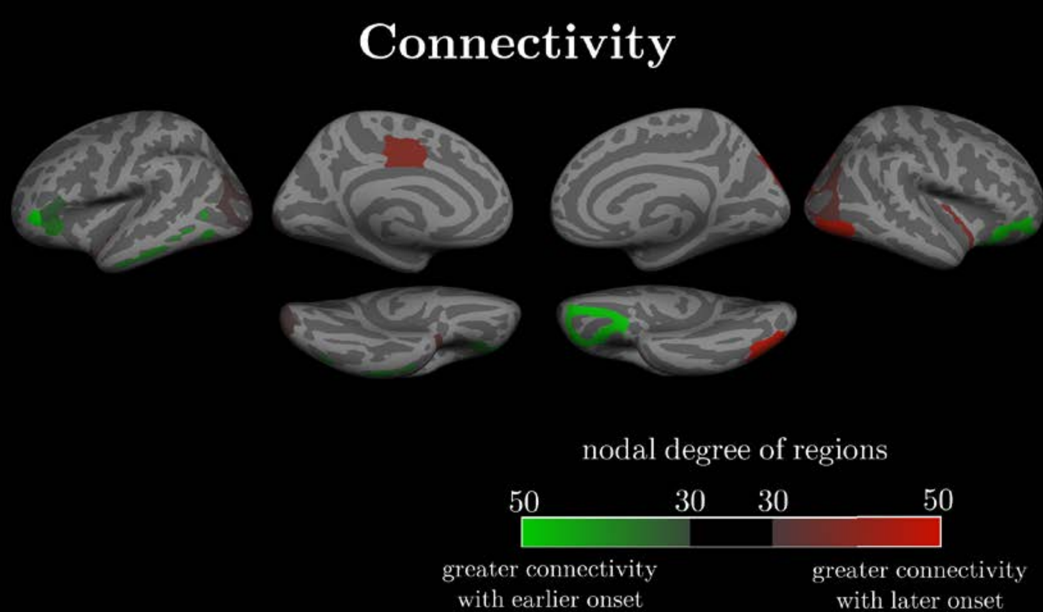






- **Less consistent** (Verb Generation):
  - **Left:** calcarine sulucs, lateral obrital sulcus, post-central sulcus, insular cortex (TLE)
  - **Right:** frontomarginal gyrus, suborbital sulcus, posterior cingulate (TLE), precentral gyrus (TLE), vertical ramus of the lateral fissure (TLE), insular cortex (TLE), superior occipital sulcus (TLE)

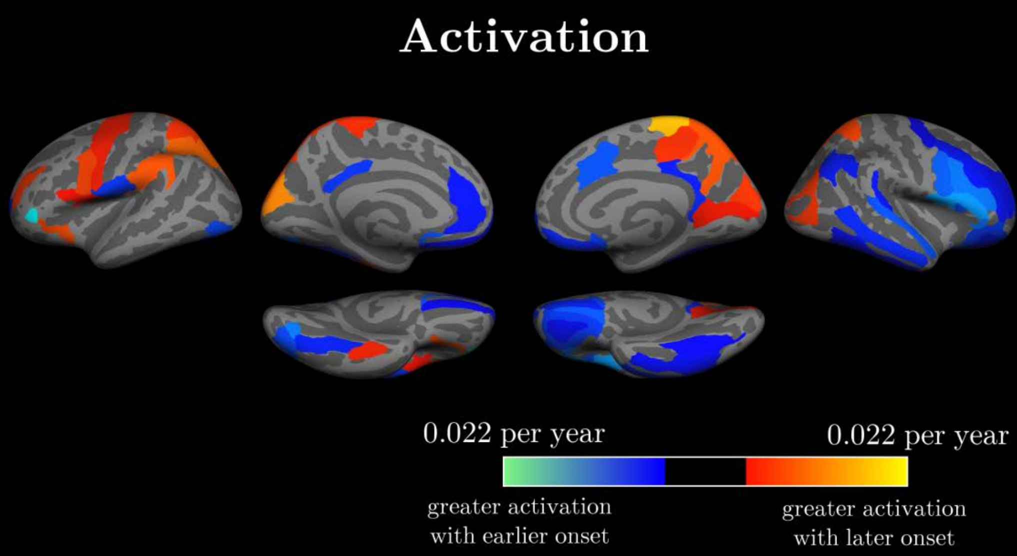


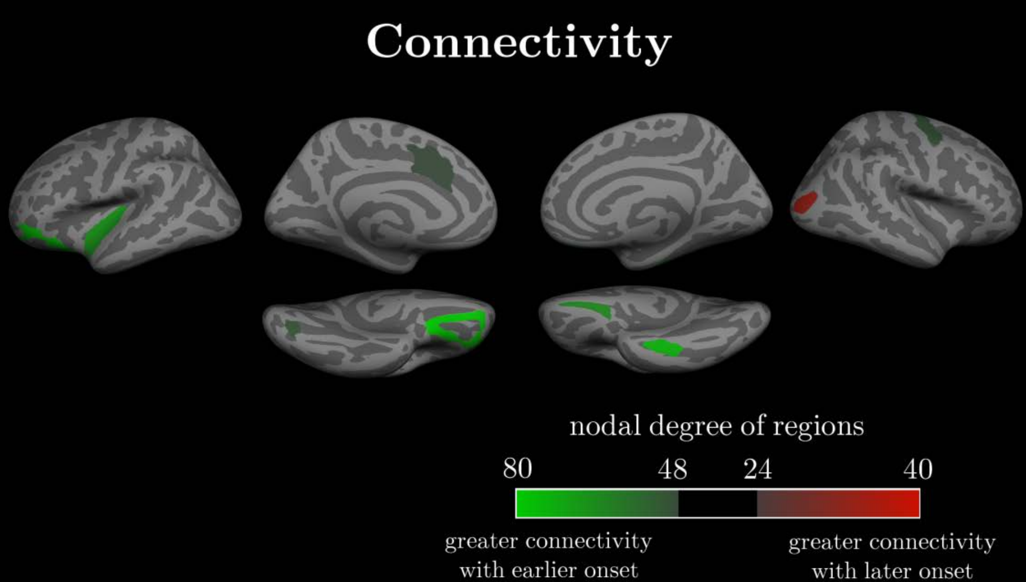


Age at epilepsy onset
(Verbal Fluency)

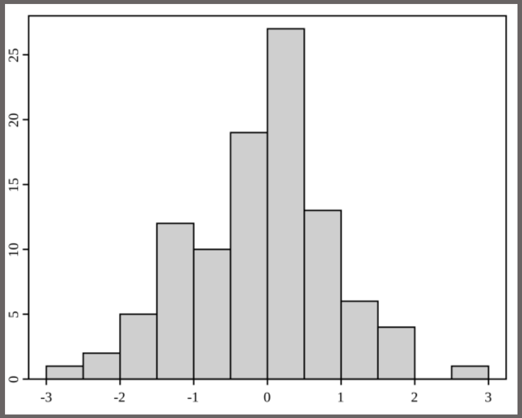
- Right-sided activation associated with earlier onset
- **Greater nodal degree with earlier onset:** bilateral connectivity of the insula and of the left orbital gyrus and lateral orbiral sulcus, inferior temporal sulcus, as well as right orbital gyrus

Age at epilepsy onset
(Verb Generation)



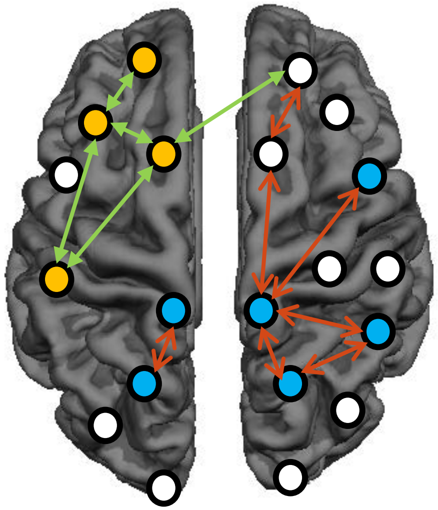


- Right-sided activation in inferior frontal gyrus associated with earlier onset
- **Greater nodal degree with earlier onset:** bilateral connectivity of the insula and of the left orbital gyrus and the right tranverse sulcus



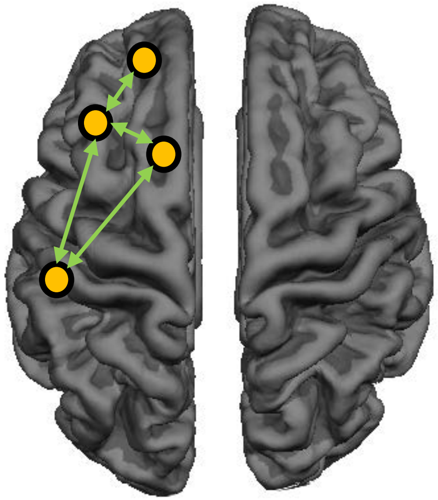
Results

Association between activity and connectivity



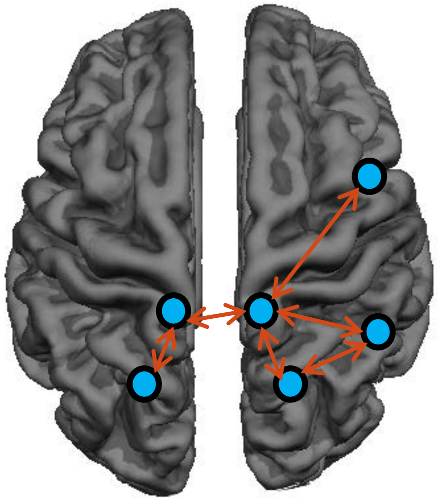
	Verbal fluency			Verb generation		
	r	*df*	*p*	*r*	*df*	*p*
Destrieux atlas						
Control group						
deactivation	-.24	86	.026	-.30	53	.027
activation	-.18	38	.278	-.03	45	.853
Left language-dominant lTLE						
deactivation	-.18	116	.046	.09	76	.439
activation	.38	7	.314	-.30	42	.047
Right language-dominant lTLE						
deactivation	-.13	75	.276	-.45	49	.001
activation	.11	22	.607	-.02	66	.859
fMRI connectivity-based atlas						
Control group						
deactivation	-.57	74	.001	-.51	57	.001
activation	.24	55	.074	.14	59	.281
Left language-dominant lTLE						
deactivation	-.42	124	.001	-.24	79	.031
activation	.30	9	.374	-.03	50	.821
Right language-dominant lTLE						
deactivation	-.24	68	.044	-.48	32	.004
activation	.48	28	.007	.36	89	.001

- Is connectivity associated with the up or down-regulation of activation?



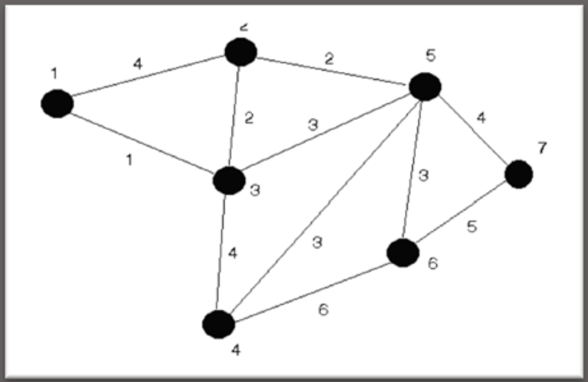
	Verbal fluency			Verb generation		
	r	*df*	*p*	*r*	*df*	*p*
Destrieux atlas						
Control group						
deactivation	-.24	86	.026	-.30	53	.027
activation	-.18	38	.278	-.03	45	.853
Left language-dominant lTLE						
deactivation	-.18	116	.046	.09	76	.439
activation	.38	7	.314	-.30	42	.047
Right language-dominant lTLE						
deactivation	-.13	75	.276	-.45	49	.001
activation	.11	22	.607	-.02	66	.859
fMRI connectivity-based atlas						
Control group						
deactivation	-.57	74	.001	-.51	57	.001
activation	.24	55	.074	.14	59	.281
Left language-dominant lTLE						
deactivation	-.42	124	.001	-.24	79	.031
activation	.30	9	.374	-.03	50	.821
Right language-dominant lTLE						
deactivation	-.24	68	.044	-.48	32	.004
activation	**.48**	**28**	**.007**	**.36**	**89**	**.001**

- Is connectivity associated with the up or down-regulation of activation? Only in TLE patients with atypical language



	Verbal fluency			Verb generation		
	r	*df*	*p*	*r*	*df*	*p*
Destrieux atlas						
Control group						
deactivation	-.24	86	.026	-.30	53	.027
activation	-.18	38	.278	-.03	45	.853
Left language-dominant lTLE						
deactivation	-.18	116	.046	.09	76	.439
activation	.38	7	.314	-.30	42	.047
Right language-dominant lTLE						
deactivation	-.13	75	.276	-.45	49	.001
activation	.11	22	.607	-.02	66	.859
fMRI connectivity-based atlas						
Control group						
deactivation	**-.57**	**74**	**.001**	**-.51**	**57**	**.001**
activation	.24	55	.074	.14	59	.281
Left language-dominant lTLE						
deactivation	**-.42**	**124**	**.001**	**-.24**	**79**	**.031**
activation	.30	9	.374	-.03	50	.821
Right language-dominant lTLE						
deactivation	**-.24**	**68**	**.044**	**-.48**	**32**	**.004**
activation	.48	28	.007	.36	89	.001

- Is connectivity associated with the up or down-regulation of activation? It would seem so.



Results

Efficiency of networks - indicator of atypical language organization

Network efficiency

- **Global efficiency**
  - significant interaction between task x group for both the verbal fluency ($F = 17.3$, $df_1 = 2$, $df_2 = 54$, $p < .001$) and verb generation tasks ($F = 6.0$, $df_1 = 2$, $d_2 = 54$, $p < .004$)
  - Verbal Fluency
    - Control participants higher global efficiency in network consisting of regions with task-related activation:
      - compared to typical TLE (95% CI for diff. = .026 - .068)
      - compared to atypical TLE (95% CI for diff. = .005 - .039)
    - No differences in global efficiency in network consisting of regions with task-related deactivation
  - similar results for Verb Generation
  - the control group had the highest global efficiency for task activation networks, followed by atypical lTLE patients and typical lTLE patients

Network efficiency

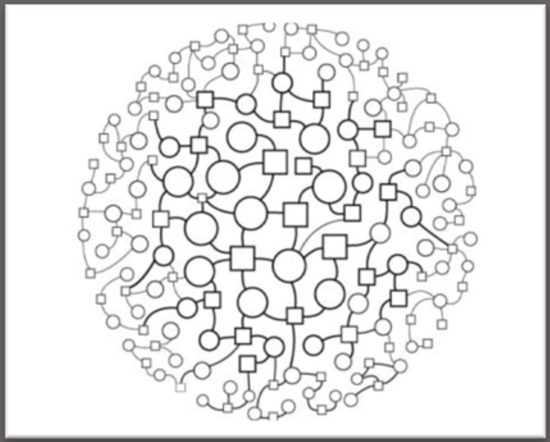
- **Local efficiency**
  - significant interaction between task x group for both the verbal fluency (F = 117.3, df_1 = 2, df_2 = 54, p < .001) and verb generation tasks (F = 20.8, df_1 = 2, df_2 = 54, p < .001)
  - Verbal Fluency
    - Control participants higher local efficiency in network consisting of regions with task-related activation:
      - compared to typical TLE (95% CI for diff. = .089 - .123)
      - compared to atypical TLE (95% CI for diff. = .024 - .050)
    - No differences in local efficiency in network consisting of regions with task-related deactivation
  - different results for Verb Generation
    - for regions with task-related activation atypical TLE patients had higher local efficiency than controls (95% CI = .002-.034) and typical TLE patients (95% CI = .002-.034)
    - for regions with task-related activation typical TLE patients had the highest local efficiency

Network efficiency and clinical outcome

Networks / Clinical var.	Verbal fluency (N=12) Epilepsy onset	Verbal fluency (N=12) Epilepsy duration	Verbal fluency (N=12) Verbal IQ	Verbal fluency (N=12) BNT	Verb generation (N=12) Epilepsy onset	Verb generation (N=12) Epilepsy duration	Verb generation (N=12) Verbal IQ	Verb generation (N=12) BNT
Regions of task deactivation								
LE (task)	**-.63**	.38	-.44	-.34	-.18	-.25	-.30	.46
LE (rest)	-.06	-.01	-.57	.37	.37	-.46	-.33	-.19
GE (act)	-.21	.19	**-.84**	-.06	-.24	-.06	**-.62**	-.17
GE (rest)	.34	-.16	.03	.15	**-.62**	.30	**-.65**	.24
Regions of task activation								
LE (task)	-.24	-.05	-.40	-.28	.14	-.32	-.38	.04
LE (rest)	.23	-.02	-.20	.20	.11	-.21	-.29	-.26
GE (act)	-.13	.24	**-.88**	-.18	-.16	-.08	-.38	-.01
GE (rest)	.46	-.26	.20	.34	**-.67**	.38	-.56	.05

FDR-corrected significant correlatons are given in red (p < .05)

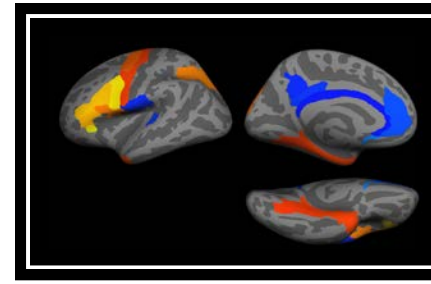
- global efficiency of networks composed of regions showing task-modulated down-regulation of activity during the tasks is associated with verbal IQ
- on the verbal fluency task global efficiency of networks showing task-modulated up-regulation during the task is associated with verbal IQ
- limited statistical power



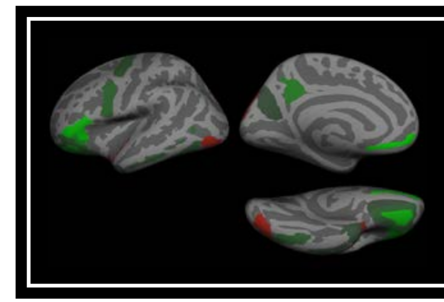
Conclusions

Main findings

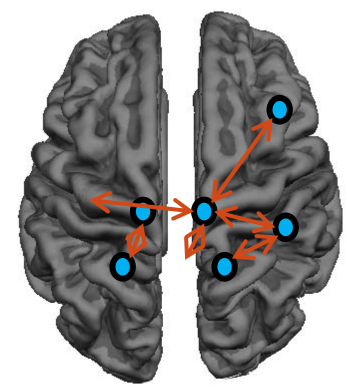
1. TLE patients with atypical language organization showed increased BOLD activation in the classical language regions, the left insula and the left orbital cortex as well as right-sided homologue regions



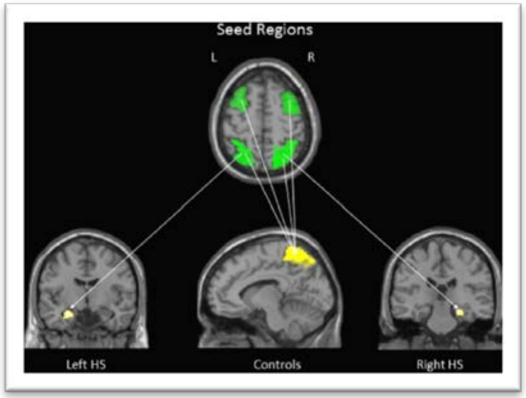
2. Compared to TLE patients with typical language organization and participants in the control group, they also displayed higher FC in some of these right-sided brain regions.



3. Task-activation networks of ITLE patients were less globally efficient
   - may be significant for the ability of the brain to dynamically reduce the activation of task-irrelevant regions.



Main findings



Disrupted segregation of working memory networks in temporal lobe epilepsy

J. Stretton *, G.P. Winston, M. Sidhu, S. Bonelli, M. Centeno, C. Vollmar, R.A. Cleary, E. Williams, M.R. Symms, M.J. Koepp, P.J. Thompson, J.S. Duncan
Epilepsy Society MRI Unit, Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, Queen Square, London WC1N 3BG, UK

The effect of topiramate on cognitive fMRI

Clarissa Lin Yasuda [b,1], Maria Centeno [a], Christian Vollmar [a], Jason Stretton [a,1], Mark Symms [a], Fernando Cendes [b], Mitul A. Mehta [c], Pamela Thompson [a], John S. Duncan [a], Matthias J. Koepp [a,*]

Increased neural activity during overt and continuous semantic verbal fluency in major depression: mainly a failure to deactivate

Heidelore Backes · Bruno Dietsche · Arne Nagels · Mirjam Stratmann · Carsten Konrad · Tilo Kircher · Axel Krug

- the importance of deactivation of parts of the DMN
  - *WM in TLE patients* (Stretton et al., 2013)
  - *Topiramate and verbal fluency in FLE* (Yasuda et al., 2013)
    - a reduction in the task-related deactivation of the default mode network (DMN) in patients taking TPM
  - *depression* (Backes et al., 2014)
    - failure to suppress potentially interfering activity from inferior temporal regions involved in default-mode network functions and visual imagery → poor performance on verbal fluency

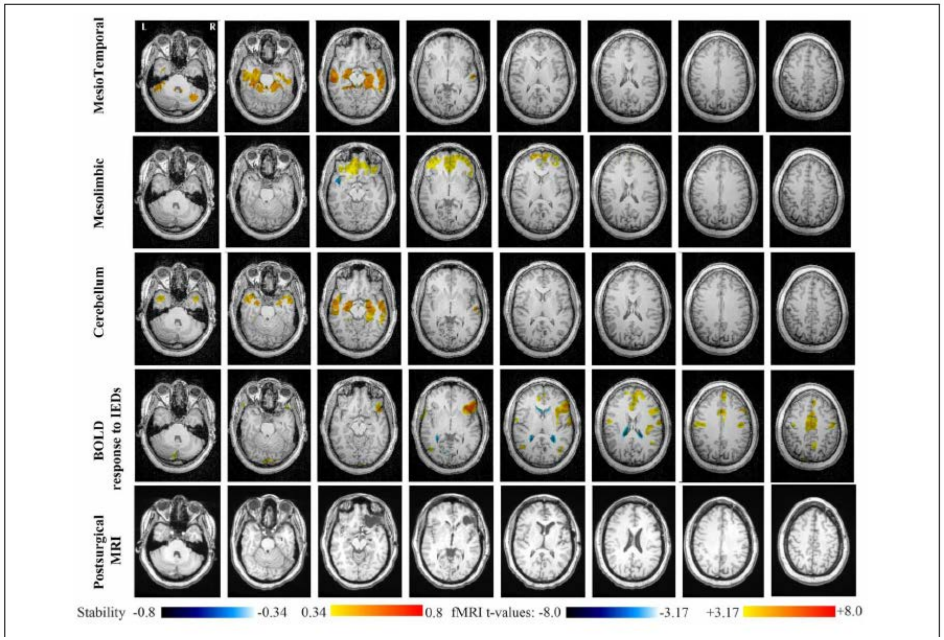
Main findings

4. our results on network efficiency indicate that an inability to dynamically inhibit task-irrelevant regions may be associated with poorer verbal abilities in TLE patients, as measured by a measure of verbal IQ

5. our analyses of task-modulated activation and connectivity indicate that the age which a person develops seizures has significant impact on the ability of their brain to reorganize the brain regions involved in language (Rasmussen and Milner, 1977; Moddel et al., 2009; Stewart et al., 2014)
   - connectivity, of the right inferior frontal gyrus and right orbital gyrus
   - connectivity in left-sided regions of the cortex, especially the orbital cortex, which has a prominent role in semantics (Mandonnet et al., 2007), the ability to distinguish between the content and function words (Diaz and McCarthy, 2009)
   - pruning of connections in the frontal cortex, including the orbital cortex, is thought to be the most protracted, reaching well into adolescence (Zecevic and Rakic, 2001) → early insult or onset of epilepsy may favor the retention of compensatory bilateral connectivity

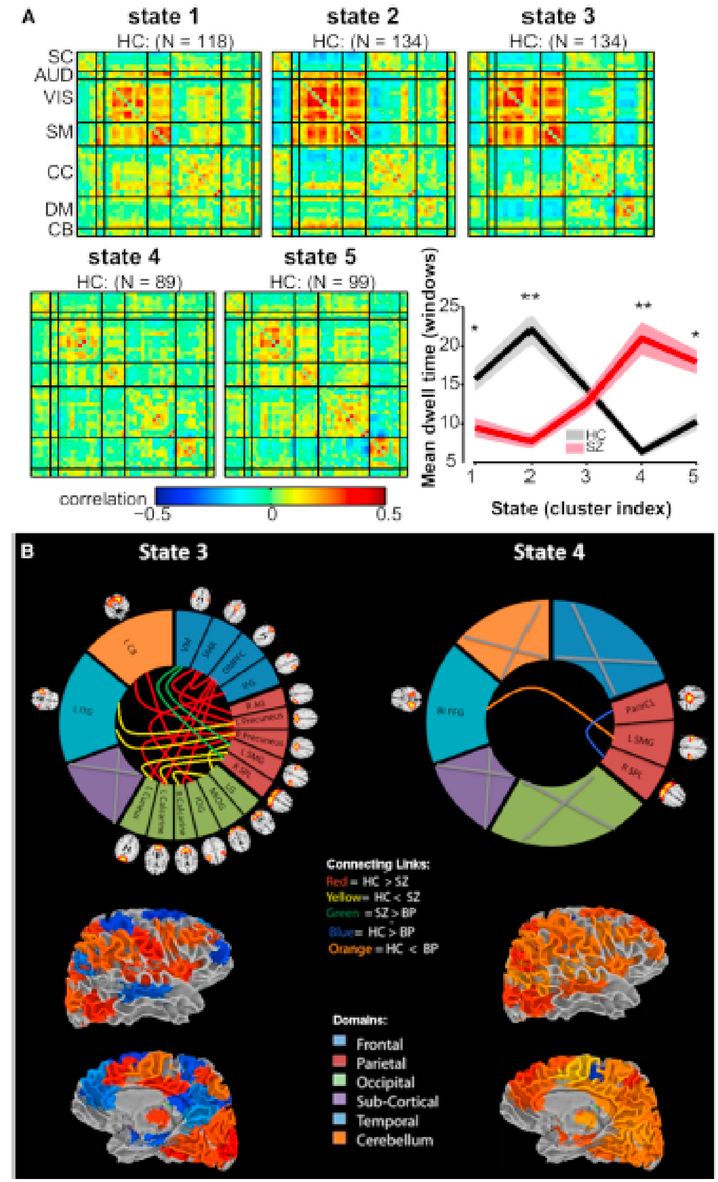
Detection of abnormal resting-state networks in individual patients suffering from focal epilepsy: an initial step toward individual connectivity assessment

*Christian L. Dansereau [1,2,3], Pierre Bellec [3,4], Kangjoo Lee [1,2], Francesca Pittau [2], Jean Gotman [2] and Christophe Grova [1,2,5]**



The Chronnectome: Time-Varying Connectivity Networks as the Next Frontier in fMRI Data Discovery

Vince D. Calhoun,[1,2,*] Robyn Miller,[1] Godfrey Pearlson,[4] and Tulay Adalı[3]
[1]The Mind Research Network & LBERI, Albuquerque, NM 87106, USA
[2]Department of ECE, University of New Mexico, Albuquerque, NM 87131, USA
[3]Department of CSEE, University of Maryland, Baltimore County, Baltimore, MD 21250, USA
[4]Olin Neuropsychiatry Research Center, Hartford, CT 06114, USA
*Correspondence: vcalhoun@unm.edu
http://dx.doi.org/10.1016/j.neuron.2014.10.015



Thank you for your attention

Collaborators:

Kopfklinik Erlangen
Elisabeth Pauli
Angelika Mennecke
Julie Rösch
Kirsten Herfurth
Hajo Hamer
Arnd Dörfler

UKC Ljubljana
Anja Čuš
Blaž Koritnik
Bogdan Lorber

Department of Child, Adolescent & Developmental Neurology, UKC Ljubljana, Slovenia

Slovenian ILAE Chapter