Defining epileptic network using structural and functional imaging

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Introduction

- Brain functioning is complex interplay of dynamic neural systems rely on the integrity of structural and functional networks
- Recent studies stated that functional and structural networks in epilepsy revealed specific disruptions in connectivity and network topology
  - Led to a shift from "focus" to "networks" concept [1]
- Disruptions in these networks may be associated with cognitive and behavioral impairments often seen in patients with chronic epilepsy

1. Eric van Diessen Epilepsia 2013

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Introduction

- EEG is widely used method to quantify epileptic activity across the brain
  - High temporal resolution is advantageous to define seizure focus and associated network
  - However, it have relatively low spatial resolution and can be corrupted by attenuation of the signal by bone or other tissue
- Invasive EEG monitoring can measure electrical activity directly from cortex, but spatial resolution is still relatively low
  - The recording can only be obtained from preselected regions of cortex
  - Also involves more significant risk
- Imaging methodologies make it possible to investigate networks across the whole brain

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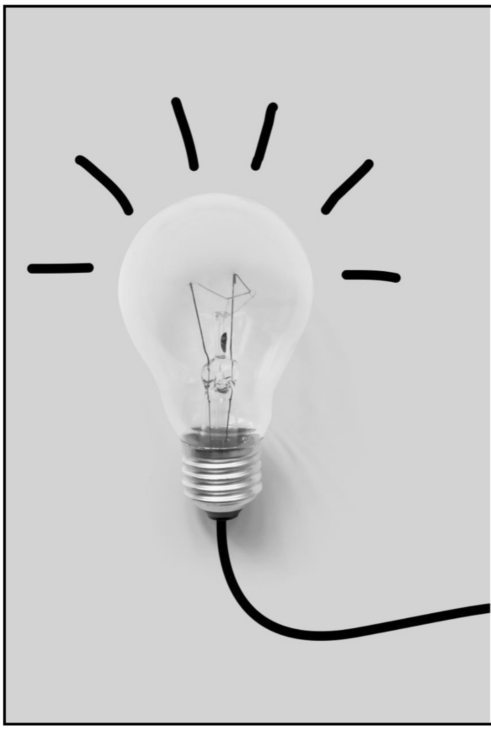

Concepts in Functional and Structural Networks: Functional connectivity

- Different brain areas are functionally connected depends on the level of synchronous temporal activity, irrespective of signal amplitude, called "synchronization [1]
- Different neurophysiologic techniques, such as (intracranial) electroencephalography (EEG) and magnetoencephalography (MEG), widely used to localize epileptiform activity and to provide information on how brain areas are functionally connected

1: Varela et al., 2001

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Concepts in Functional and Structural Networks: Functional connectivity

- Initially, connectivity studies focused on linear correlations between two signals as a function of the frequency during seizure propagation[1]
- Later, complex, nonlinear correlations introduced to investigate functional coupling between different brain areas i.e.
  - Synchronization [1]
  - Phase lag index [2]
  - Coherence [3]
  - etc.

1; Stam & Van Dijk, 2002, 2: Stam et al., 2007, 3; Baccala & Sameshima, 2001

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Complex, nonlinear correlations to investigate functional coupling between different

> Epilepsia. 2015 Mar;56(3):393-402. doi: 10.1111/epi.12918. Epub 2015 Jan 29.

Mapping the coherence of ictal high frequency oscillations in human extratemporal lobe epilepsy

Marija Cotic [1], Osbert C Zalay, Yotin Chinvarun, Martin del Campo, Peter L Carlen, Berj L Bardakjian

Affiliations + expand

PMID: 25630492 DOI: 10.1111/epi.12918

Free article

Abstract

Objective: High frequency oscillations (HFOs) have recently been recorded in epilepsy patients and proposed as possible novel biomarkers of epileptogenicity. Investigation of additional HFO characteristics that correlate with the clinical manifestation of seizures may yield additional insights for delineating epileptogenic regions. To that end, this study examined the spatiotemporal coherence patterns of HFOs (80-400 Hz) so as to characterize the strength of HFO interactions in the epileptic brain. We hypothesized that regions of strong HFO coherence identified epileptogenic networks believed to possess a pathologic locking nature in relation to regular brain activity.

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Functional connectivity

- Functional connectivity in neurophysiologic studies is usually analyzed in separate frequency bands:
  - Delta band (0–4 Hz)
  - Theta band (4–8 Hz)
  - Alpha band (8–13 Hz)
  - Beta band (13–30 Hz)
  - Gamma band (>30 Hz)
  - HFO
  - Very Low frequency band

  as each frequency band is associated with distinct networks and functions [1]

1; Basar et al., 2001

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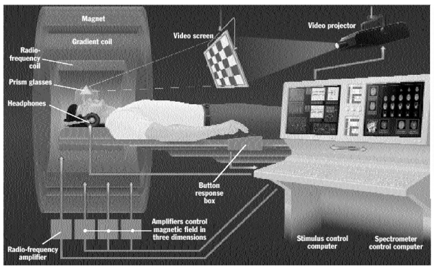
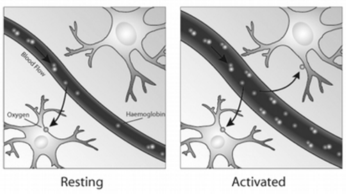
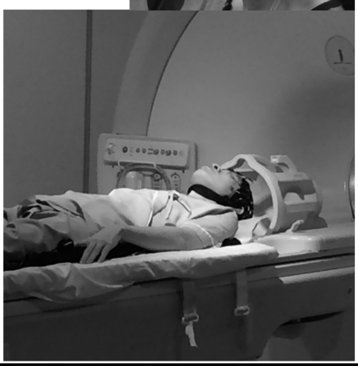
Functional connectivity: fMRI, EEG-fMRI





EEG-fMRI



Intense brain activity ~ increase in oxygen demand
Oxygen provided in blood flow
Measure Blood MR signal
Repeat every 1-4 sec.
Detect tiny metabolical changes
Blood Oxygenation Level Dependent (BOLD)

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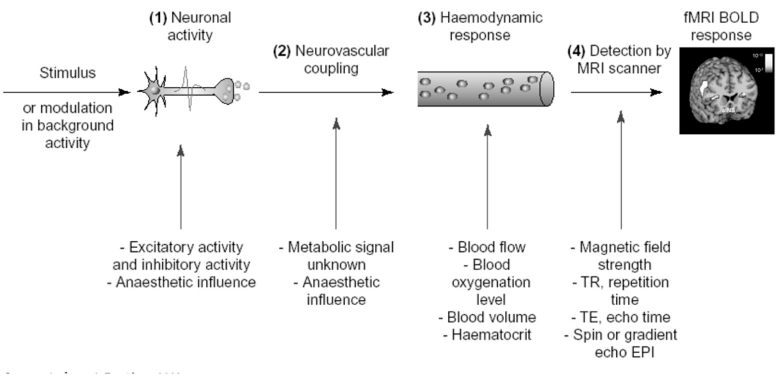
Functional connectivity: fMRI, EEG-fMRI



- Using spontaneous low frequency fluctuations in the blood oxygenation level–dependent (BOLD) signal, functional MRI (fMRI) enables functional connectivity investigations with a higher spatial, but lower temporal resolution compared to neurophysiologic recordings
- Integrated with EEG (EEG-fMRI) will improv the temporal resolution
- Because BOLD signal changes relate to underlying neural activity
- fMRI provides only an indirect measure of functional connectivity

1; Basar et al., 2001

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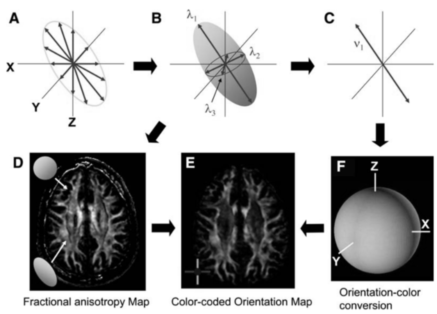
Structural connectivity

- Structural connectivity is inferred from diffusion tensor imaging (DTI)
- This imaging technique is based on the directionality of diffusion of water molecules in the brain.
  - The diffusivity of water molecules is facilitated along axons in white matter, and is restricted in the direction perpendicular to axonal tracts [1]
- Alternatively, structural connectivity i.e. cortical thickness, or (sub) cortical gray matter volumes are quantified on three-dimensional T1-weighted MR images



An anisotropy map (D) created from the shape, in which dark regions are isotropic (spherical) and bright regions are anisotropic (elongated).

1; Basser & Jones, 2002

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Strengths and weaknesses of different modalities used in network analytic studies

Modality	Strengths	Weaknesses
Functional networks		
EEG	Widely used in clinical practice High temporal resolution Suitable to study ictal networks	Low spatial resolution (less for high-definition EEG) Sensitive to volume conduction artifacts
Intracranial recordings	Direct electrical recordings of neuronal activity High temporal and spatial resolution No myogenic artifacts	Only available in a surgical setting No whole brain network analysis possible
MEG	High temporal and spatial resolution Source space analysis allows identification of anatomic network specification	Sensitive to movement artifacts Not widely available
fMRI	High spatial resolution Allows the study of subcortical networks separately Widely available	Low temporal resolution Assumption of BOLD changes in respect to electrophysiologic changes in the epileptic brain
Structural networks		
Cortical thickness	Inferred from standard MRI sequences High spatial resolution	Analysis of individual networks complicated Analysis of subcortical structures not possible
DTI	Physical network connections can be studied Both cortical and subcortical structures and their interconnectedness can be studied	Several technical pitfalls when analyzing DTI data Many arbitrary choices in the process of data extraction

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Functional MRI and functional connectivity mapping

- Functional MRI is a widely used non-invasive neuroimaging technique detect and localize areas of the brain engaged in performing a specific task
  - Typically uses echo-planar image acquisition parameters that are sensitive to the changes in blood oxygenation occurring with neuronal activation (Blood Oxygenation Level Dependent or BOLD acquisitions)[1]
- Signal intensity in the BOLD images is increased when oxyhemoglobin concentrations increase due to neuronal activation
- In conventional block-design fMRI studies, a series of images is collected during at least two different activation states (e.g. rest and stimulation) and their signal intensities are compared statistically on a voxel by voxel basis

1; Logothetis, et al. 2001, Ogawa, et al. 1990

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Functional MRI and functional connectivity mapping

- The primary challenge in using fMRI in epilepsy is that interictal and ictal seizure activity is spontaneous and its timing cannot be controlled
- Two general approaches to overcome this problem.
  - The first approach is to combine fMRI acquisitions with scalp EEG measurements [1] The EEG will provide the timing of the epileptic activity for conventional fMRI analysis.
  - The second is to use a data-driven approach to identifies interictal BOLD response in the fMRI data without EEG

1; Gotman, et al. 2004

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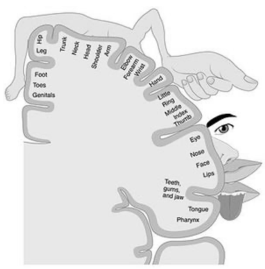
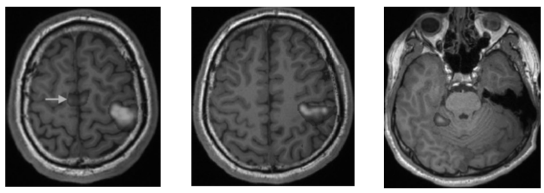
Functional MRI and functional connectivity mapping

- Simple fMRI activation maps can determine the level of involvement of distinct regions of a network to perform a task at the time of acquisition
- However, fMRI potentially can also reveal additional information about the functional coupling within this network using functional connectivity mapping
- Functional connectivity uses linear correlations of low frequency (<0.1 Hz) fMRI BOLD signal oscillations usually at rest or during steady-state performance of a task [1]



Motor cortex mapping is the among the easiest and most highly reliable of BOLD/fMRI methods.



BOLD-fMRI maps obtained during performance of right-sided finger tapping. The contralateral (left-side) primary sensorimotor cortex is most strongly activated. Also note bilateral activation of the supplementary motor area (green arrow) and ipsilateral (right-side) superior cerebellum

1; Rogers, et al. 2007

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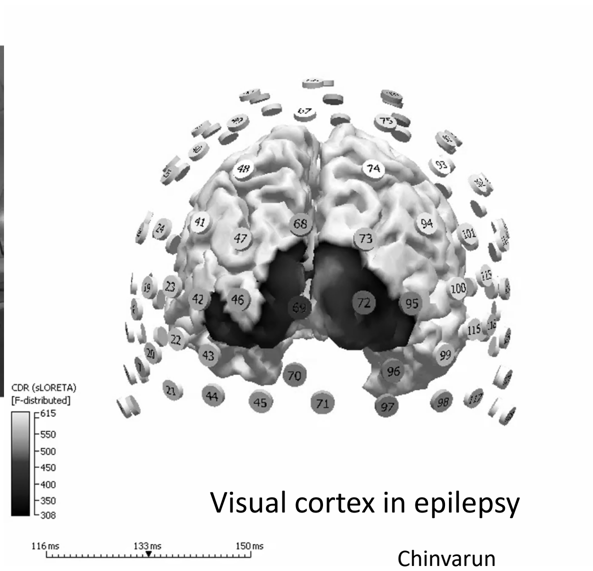
EEG-fMRI to to localize eloquent cortex



Visual cortex in epilepsy

Chinvarun

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Functional MRI and functional connectivity mapping

- Two most commonly used methods of determining functional connectivity are seed based methods and independent component analysis (ICA)
- Both are based on temporal series of BOLD signals
- The seed based approaches require the identification of a seed voxel (certain **voxel** or cluster of **voxels)** or region, and the linear correlation across time of other voxels or regions to that seed is considered the measure of connectivity

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Functional MRI and functional connectivity mapping

- The ICA method attempts to transform original data time series into individual components assuming that all of signal sources and noise are statistically independent and mixed linearly to create the observed signal.

- This technique used successfully with fMRI data [1]

- The advantage of these techniques in epilepsy is that all of components of signal (presumably from independent sources) identified result in a large number of components

1; Calhoun, et al. 2003, Moritz, et al. 2005)

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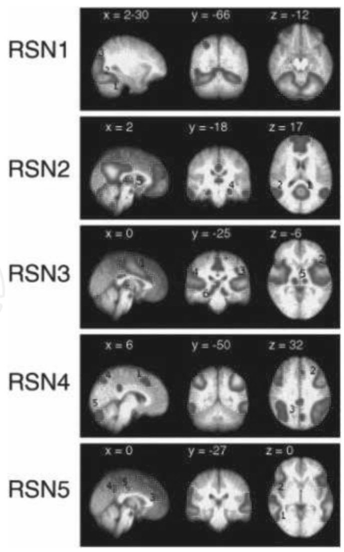
Networks defined in healthy controls

- Varying numbers of resting–state networks have been described, they generally can be divided into approximately five overlapping spatial maps [1]
  - Visual cortex network– lateral and medial occipital cortex
  - Default-mode network – anterior cingulate, posterior cingulate, lateral inferior parietal cortex, hippocampus and prefrontal cortex
  - Sensorimotor and auditory network – pre and post-central gyrus, superior temporal gyrus, insula, thalamus and hippocampus
  - Dorsal pathway – lateral frontal regions and dorsal parietal cortex
  - Ventral pathway – lateral temporal, and inferior prefrontal cortex



1; De Luca, et al. 2006

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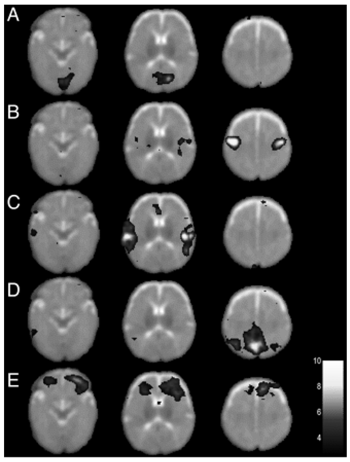
Networks defined in healthy controls

- The networks similar to visual, auditory and motor processing in adults have been detected in infants [1]
  - This suggests the order of maturation of various networks in the brain
  - May explain development of specific cognitive functions as a child ages



Resting-state networks in a single infant

1; Fransson, et al. 2007

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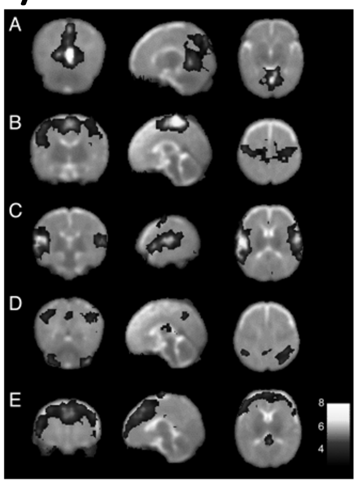
Networks defined in healthy controls

- Resting-state patterns were found in
  - Primary visual areas
  - Somatosensory and motor cortices bilaterally
  - Bilateral temporal/inferior parietal cortex encompassing the primary auditory cortex
  - Posterior lateral and midline parts of the parietal cortex as well as the lateral aspects of the cerebellum
  - Medial and lateral sections of the anterior prefrontal cortex



Group resting-state networks in infants

1; Fransson, et al. 2007

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Networks defined in healthy controls

- In order to understand how epilepsy and its treatment can affect normal cognitive function and behavior,
  - it is useful to investigate the changes within the known resting-state networks of these patients.

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Language and memory networks

- Chronic drug-resistant temporal lobe epilepsy (TLE) is associated with progressive memory impairment [1]
  - Related to damage of hippocampus and other mesial temporal lobe structures [2]
- Also, surgical treatment of TLE can also have a negative impact on language and memory functions
  - Further declines in verbal memory and word finding after respective surgery to treat seizures occurring in as many as 40% of TLE patients [3]

1; Fisher, et al. 2000, Helmstaedter, et al. 2003), 2; Kilpatrick, et al. 1997 3; Langfitt & Wiebe 2008).

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Language and memory networks

- In patients with good seizure outcome, quality of life improved even if some memory loss occurred [1]
- However, in patients without post-surgical seizure control, quality of life decreased when memory loss occurred [2]
- These findings illustrate the importance of quantifying and understanding these cognitive functions, and using this information to accurately predict risk of cognitive decline after resective surgery

1; Langfitt et al. , 2; Langfitt, et al. 2007

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Language and memory networks

- Functional MRI provides a way to probe the functional integrity of these networks, and allows quantification of the relationships between cognition and connectivity in order to address these issues
- Functional MRI has been very successful for lateralizing language dominance as well as identifying and localizing language networks. There is a wide variety of stimulation tasks used for this purpose.
  - Some of the more widely used tasks include word generation[2] for activating the inferior frontal language regions (Broca's Area)
  - Tasks such as reading[3] and listening to speech[4] for identifying temporoparietal language regions (Wernicke's Area)

1; Deblaere, et al. 2002, Ramsey, et al. 2001).,, 2; Gaillard, et al. 2002, Rutten, et al. 2002b., 3; Binder, et al. 2008b, Bookheimer 2007)

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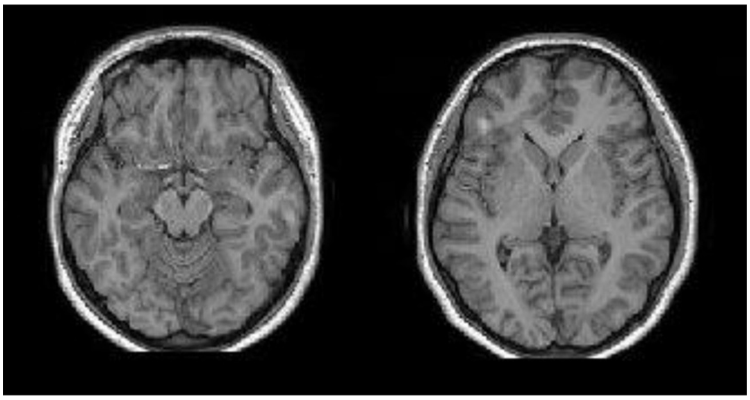
Language and memory networks

fMRI task: auditory description/ comprehension task



Bilateral Broca's and left Wernicke's area

1; Byron Bernal a, Alfredo Ardila 2014

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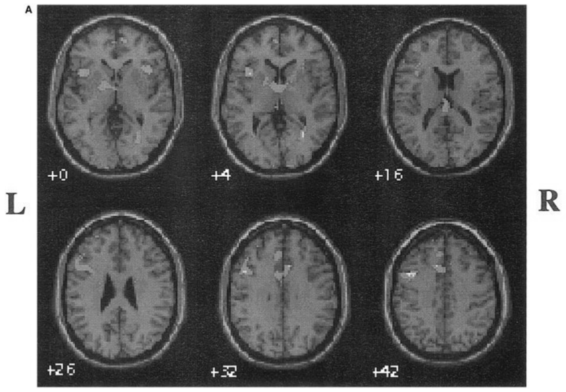
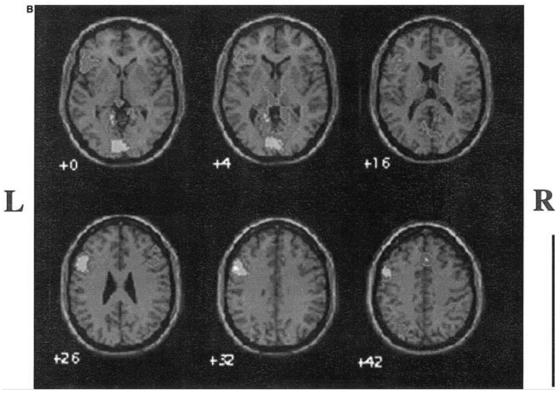
Language and memory networks

Word generation for activating the inferior frontal language regions (Broca's Area)



children



adults

SPM maps for semantic verbal fluency in children and adults

1; ; Gaillard, et al. 2002

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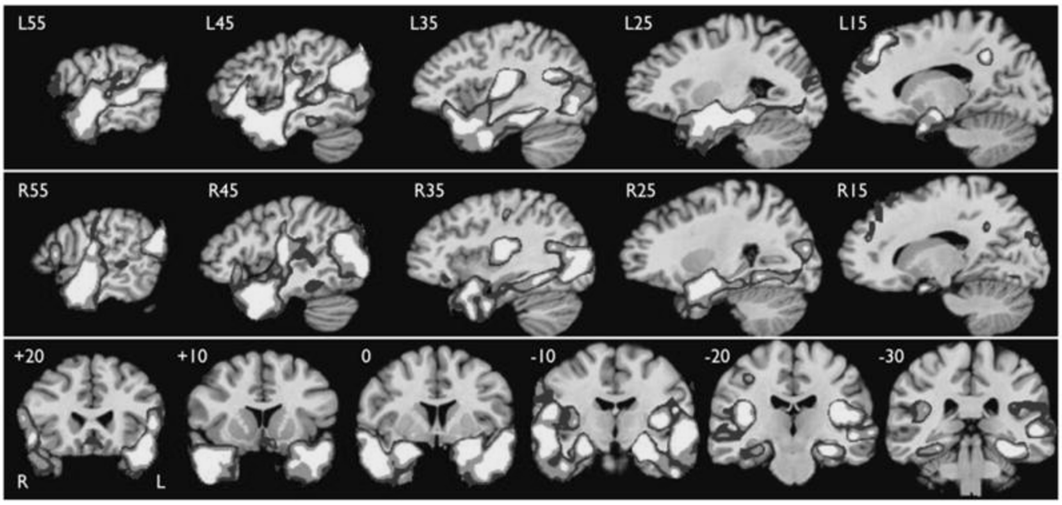
Language and memory networks

fMRI using Story-Math protocol task provides a reliable method for activation of surgical regions of interest in ATL



The bilateral activation conceptual processing involves both temporal lobes

1; ; Binder, et al. 2008b

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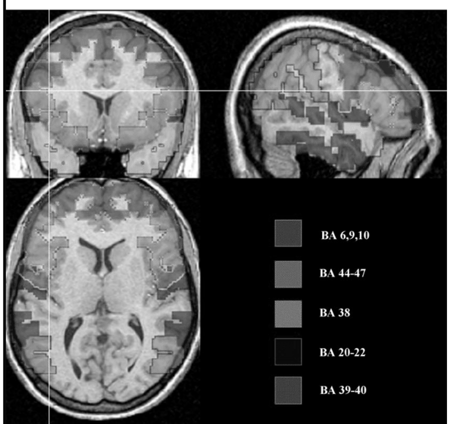
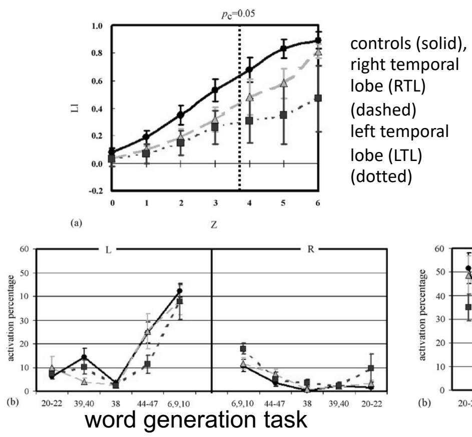
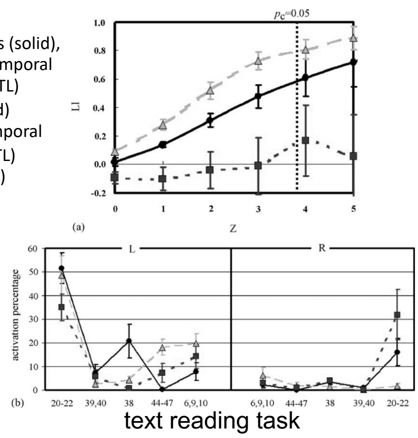
Language and memory networks

Differences of cerebral activation related to language functions in post-operative temporal lobe epilepsy (TLE) patients. Right (RTL) and left temporal lobe (LTL) resected patients, and healthy controls







The cerebral language representation in post-operative LTL epilepsy patients is more bi-hemispherically lateralized than in controls and RTL patients.

1; Deblaere, et al. 2002, Ramsey, et al. 2001)

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Language and memory networks

- The combination of multiple fMRI tasks has been found to be more accurate than a single task[1] and these methods can also be modified for use in children[2]
- For these reasons, fMRI, when available, is quickly becoming the preferred technique for determining language lateralization and localization.

1; Arora, et al. 2009, Deblaere, et al. 2002, Ramsey, et al. 2001, Rutten, et al. 2002a 2; Arora, et al. 2009, Gaillard, et al. 2002

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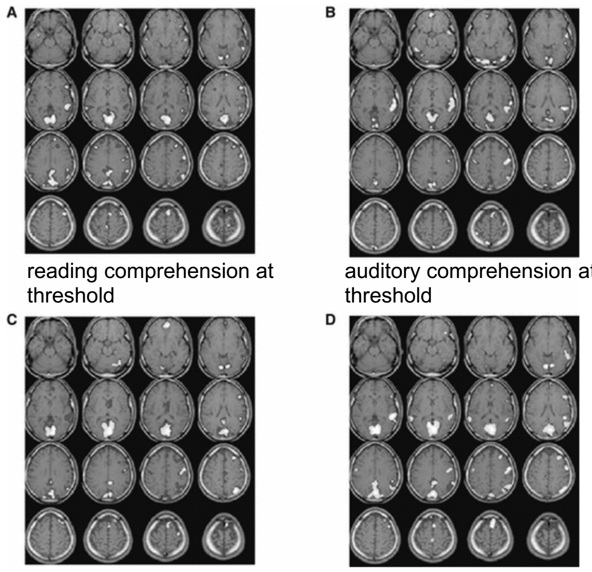
Combination of multiple fMRI tasks Language lateralization in epilepsy patients: fMRI validated with the Wada procedure



reading comprehension at threshold

auditory comprehension at threshold

verbal fluency at threshold

conjunction analysis at threshold

Overall fMRI was in agreement with the Wada test

Epilepsia, Volume: 50, Issue: 10, Pages: 2225-2241, First published: 22 September 2009, DOI: (10.1111/j.1528-1167.2009.02136.x)

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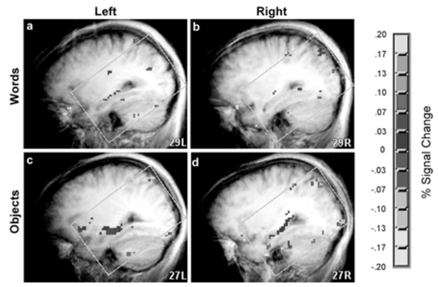
Language and memory networks

- Assessment of memory functions slower to develop, because of fMRI memory paradigms more complicated and require more trials to provide detectible signal changes than language paradigms
- Some fMRI memory paradigms designed to activate mesial temporal structures used with varying levels of success to predict post-surgical memory declines
  - Increased fMRI activation in the mesial temporal lobe ipsilateral to the surgical resection was correlated with increased post-surgical declines
  - Thus supporting the “functional adequacy model” of hippocampal function



Activity in the left and right hippocampal regions.

1; Frings, et al. 2008b, Rabin, et al. 2004, Richardson, et al. 2006, Wagner, et al. 2007

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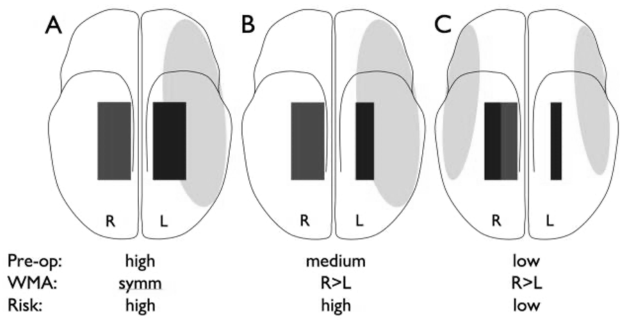
Language and memory networks

- This model predicts that severity of decline depends on the function of the region resected and not on the ability of the contralateral region to support function after surgery “functional reserve model” [1]
- Positive predictive values of 56 to 100% [2]



healthy subjects | Chronic left TLE without shift | Chronic left TLE with shift

Yellow ovals ; language systems

Red rectangles; verbal episodic memory encoding systems in MTL

Blue rectangles; non-verbal episodic memory encoding systems in MTL.

1; Chelune 1995., 2; Richardson, et al. 2004)

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Language and memory networks

- In cohort study, the positive predictive value of memory fMRI activation asymmetry in the anterior temporal lobe was 20-35%
- However, when fMRI language lateralization, calculated using multiple regions across frontal and temporal lobes, and pre-operative neuropsychological scores included
  - The positive predictive value rose to 70-100%

1; Bonelli, et al. 2010)

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Language and memory networks

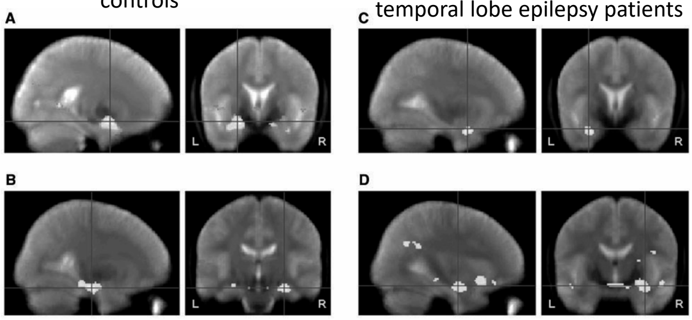
controls

comparison between controls, left and right temporal lobe epilepsy patients

Main effects in controls are shown in A and B.

(A) Word encoding: Lt. hippocampal activation

(B) face encoding: Rt. hippocampal activation



(C) Less left hippocampal activation for encoding words in left temporal lobe epilepsy compared with controls.

(D) Less right hippocampal activation for encoding faces in right temporal lobe epilepsy compared to controls.

1; Frings, et al. 2008b, Rabin, et al. 2004, Richardson, et al. 2006, Wagner, et al. 2007

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Language and memory networks

- In right temporal lobe epilepsy, greater right than left anterior hippocampal functional magnetic resonance imaging activation on face encoding predicted greater visual memory decline after right anterior temporal lobe resection

- In left temporal lobe epilepsy, greater left than right anterior hippocampal activation on word encoding correlated with greater verbal memory decline after left anterior temporal lobe resection

1; Silvia B. Bonelli Brain 2010

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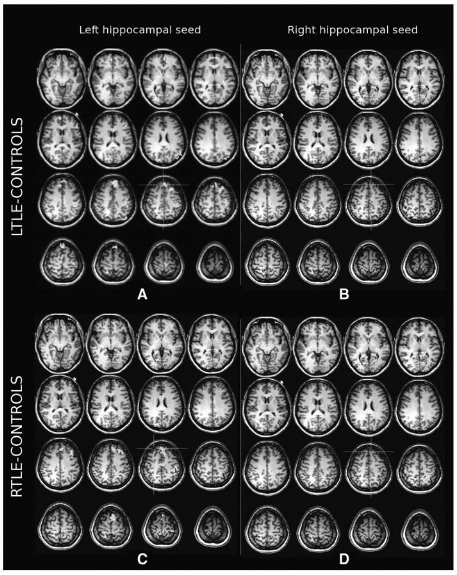
Language and memory networks : functional connectivity

- One promising repeated finding is that the functional connectivity between the anterior cingulate and left inferior frontal gyrus was found to be decreased in TLE compared to healthy controls during rest [1] and during block-design performance of a word-generation task [2]

1; Waites, et al. 2006.,, 2; Vlooswijk, et al. 2010).



Yellow areas indicate significantly higher FC with the seeded hippocampal area compared to controls;

Blue areas indicate significantly lower FC with the hippocampal seed compared to controls

Reductions in FC may be greatest in the left hemisphere and in patients with left TLE

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Language and memory networks : functional connectivity

- Similarly, the functional connectivity of the left hippocampus and other regions involved with memory was also decreased relative to controls [1]

- The functional adequacy model, higher fMRI connectivity of the ipsilateral hippocampus to the superior temporal gyrus was associated with greater decline of verbal memory performance after surgery [2]

1; Addis, et al. 2007 .,2; Wagner, et al. 2007.

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Language and memory networks : Error and variability in fMRI methods

- Many possible sources of error and variability in fMRI methods.
  - First, variability in task performance.
  - Many patients have cognitive deficits which reduce their ability to cooperate, understand and remember the directions of the task. Including children that variation even more
  - For many cognitive tasks, it is difficult to impossible to monitor externally how well the tasks are being performed
  - fMRI analysis methods are not standard, differences in statistical thresholds and regions of interest can also lead to uncertainty [1]

1; Abbott, et al. 2010, Branco, et al. 2006, Sidtis 2007, Suarez, et al. 2008).

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The default-mode network

- There are regions of the brain regularly observed to reduce fMRI activity (deactivate) during performance of demanding cognitive tasks or goal directed behavior [1]
- When studied in a wakeful resting state using positron emission tomography (PET)
  - Increases in cerebral metabolic rate for oxygen (CMRO2) and cerebral blood flow (CBF) detected in these regions
- The data suggest the existence of baseline activation level in these areas at rest above the mean level of the brain, reflect internal modes of cognition e.g. mind wandering or daydreaming in this state
  - These regions referred to as “default-mode network” (DMN, network)

1.; Fox, et al. 2005., 2; Raichle, et al. 2001, 2; Buckner, et al. 2008

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The default-mode network

- The default-mode network” such as ventral medial prefrontal cortex, posterior cingulate/retrosplenial cortex, bilateral inferior parietal lobule, lateral temporal cortex, dorsal medial prefrontal cortex, and hippocampus

The main resting state networks of the human brain

Motor and sensory networks
Visual network
Auditory network
Sensorimotor network
Networks mediating higher brain functions
Default mode network
Attention networks
Dorsal attention network
Ventral attention network
Alertness network
Salience network
Executive control network
Reward emotion network
Language networks

1.; Fox, et al. 2005., 2; Raichle, et al. 2001, 2; Buckner, et al. 2008

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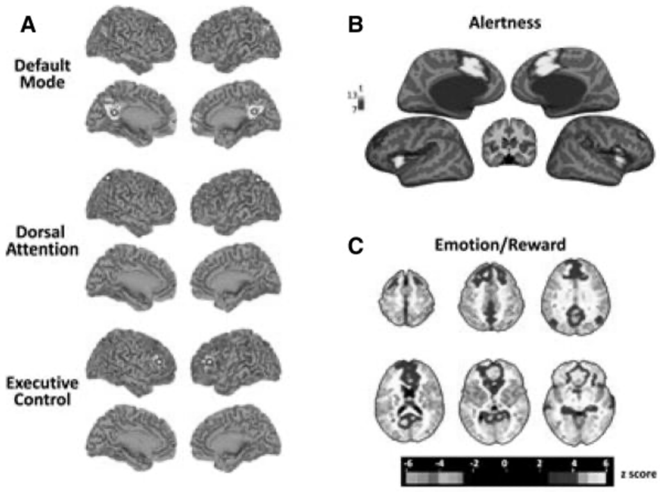
The default-mode network

(A) Connectivity maps of the default, dorsal attention, executive control
(B) Alertness
(C) Reward emotion networks in normal subjects.



1.; Buckner, et al. 2008

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Abnormalities in the Default-Mode Network

- Alterations in the physiologic activities controlled by DMN such as abstract thinking, cognitive tasks, or memory retrieval are observed in TLE as well as in other conditions such as Alzheimer’s disease, autism, and attention deficit/hyperactivity disorder [1]
- It was posited that loss in DMN connectivity along with its recurrent deactivation by interictal discharges may have a role in decreasing the cognitive performance in patients with TLE [2]

1.; Broyd et al., 2009., 2; Laufs et al., 2007

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Abnormalities in the Default-Mode Network

- The relationship between DMN and epilepsy first reported in activation studies of generalized spike-and-wave (GSW) bursts in patients with idiopathic generalized epilepsy (IGE) [1]
  - In these studies, simultaneous measures of EEG and fMRI [2] acquired in individual or groups of IGE patients with frequent GSW bursts on EEG.
  - The EEG used to determine timing of any GSW bursts occurring during fMRI scanning

1.; Archer, et al. 2003, Gotman, et al. 2005, Hamandi, et al. 2006, Laufs, et al. 2006, Salek- Haddadi, et al. 2003)..,
2; Gotman, et al. 2004

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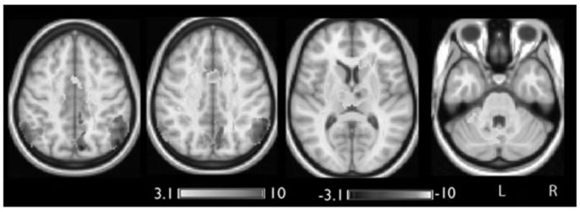
Abnormalities in the Default-Mode Network

- These findings suggest that activation in thalamus indicated this region's involvement in generation or spread of generalized epileptic discharges.
- Also, the combination of the activation of thalamus with the deactivation of the DMN may lead to the lapse in responsiveness associated with absence seizures in IGE [1]



- GSWDs characterized by highly synchronized activity in the thalamocortical network
- GSWD-related activations detected in the thalamus, mesial frontal cortex, and cerebellum; decreases in BOLD signal in parietal areas and precuneus

1.; Gotman, et al. 2005, Hamandi, et al. 2006

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Abnormalities in the Default-Mode Network

- More recent studies attempted to resolve timing differences between fMRI changes in the DMN and other regions in response to GSW bursts
- Both studies showed fMRI deactivations in DMN generally occurring prior to increased thalamic response [1]
  - In several instances fMRI signal change in DMN started prior to the event onset on EEG
  - Another study [2] found parietal activation occurring prior to thalamic activation

1.; Carney, et al. 2010, Moeller, et al. 2010a).

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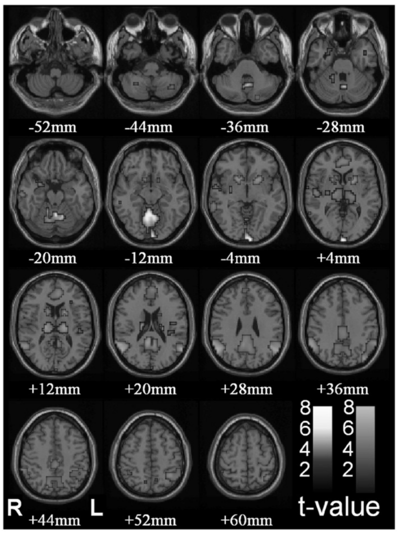
Abnormalities in the Default-Mode Network

- The earliest change in BOLD signal occurs in the DMN, prior to onset of epileptiform events.
- This region also shows altered FC in patients with Absence seizure (AS)
- Convincing evidence for potential link between function of DMN and absence seizures and GSW bursts, but the direct mechanism of this relationship remains unknown



- **Thalamic increases and "default mode" cortical decreases are the most prominent changes in AS**
- fMRI decreases seen in bilateral lateral parietal, medial parietal, and cingulate cortex and basal ganglia

1.; Bai X 2008

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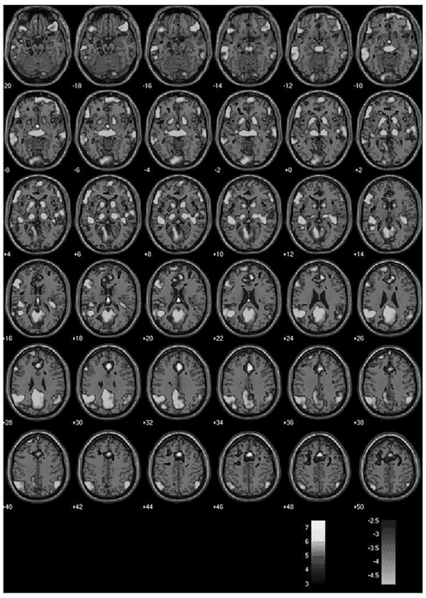
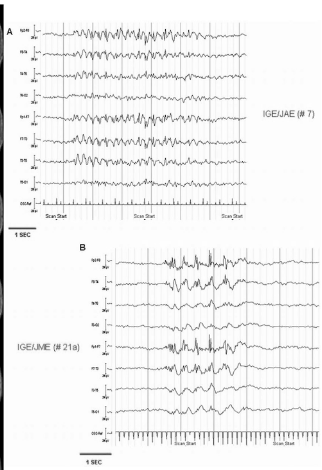
Abnormalities in the Default-Mode Network

EEG-fMRI in JME

- BOLD signal increase in bilateral cingulated gyrus
- BOLD signal decrease in bilateral thalamic, bilateral caudate, right medial frontal gyrus,, left superior temporal gyrus, right precuneus, bilateral inferior parietal lobuli





The precuneus gates GSW discharges in the thalamo-(fronto) cortical network

1.; Anna E. Vaudano 2009

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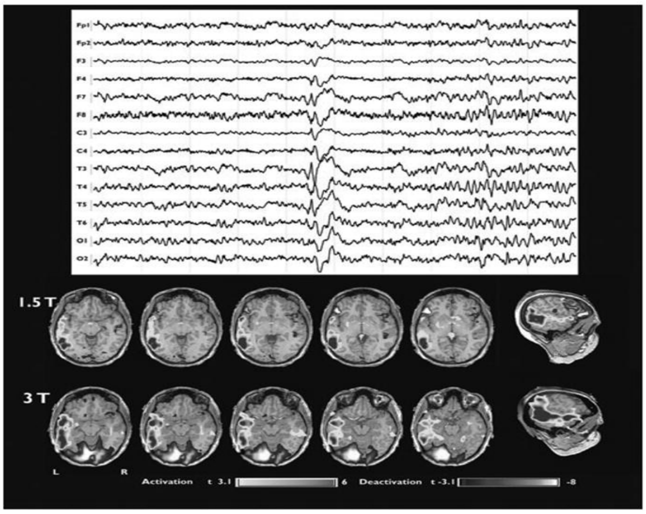
Abnormalities in the Default-Mode Network

- There is a smaller, but growing, about DMN with focal epilepsy
- Using simultaneous EEG and fMRI protocol, deactivation has been detected in DMN regions in response to interictal EEG spiking [1]



Left temporal spike and wave in EEG and BOLD response [2]

1.; Kobayashi, et al. 2006, Laufs, et al. 2007.,, 2; Jean Gotman and Francesca Pittau 2011

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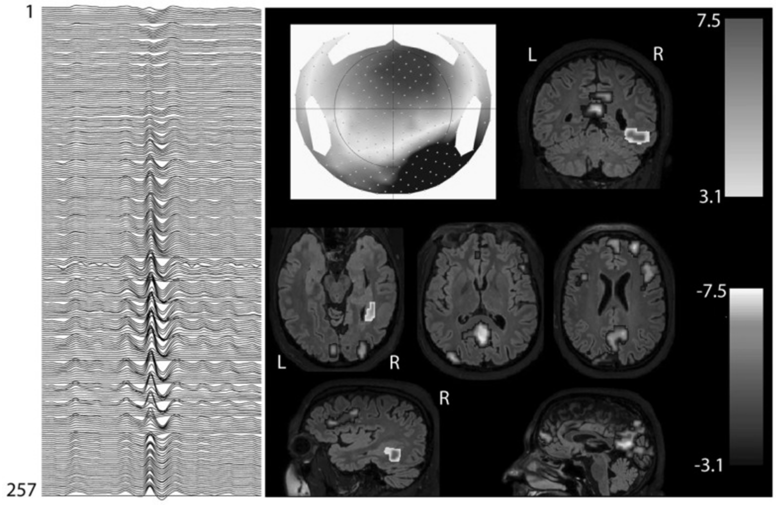
Abnormalities in the Default-Mode Network

- Patients with right hemispheric extended periventricular nodular heterotopia: right posterior temporal spikes with phase reversal at P8
- BOLD increase is concordant with the spike topography
- Whereas BOLD decrease is present in default-mode network (DMN).



1.; Francesca Pittau et al., 2014

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Abnormalities in the Default-Mode Network

- The DMN in interictal state, without temporally associating changes directly with interictal spiking
- In unilateral TLE patients, revealed decreased connectivity between hippocampus (predominantly ipsilateral to the epilepsy) and the rest of the DMN compared to healthy controls [1]
  - Using a seed-based functional connectivity analysis in unilateral TLE patients performing a verbal memory task [2]

1.; Zhang, et al. 2010a., 2; Frings, et al. 2009

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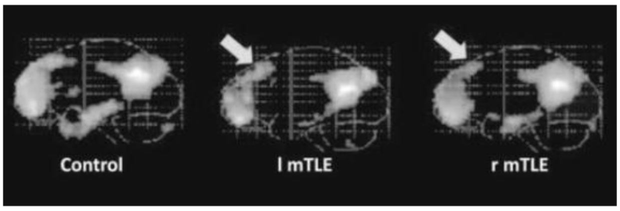
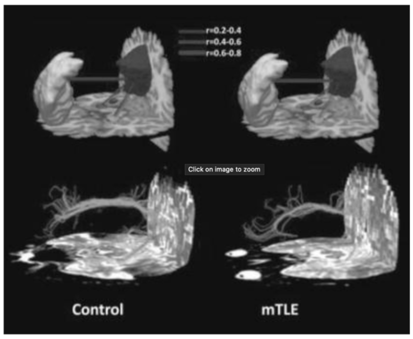
Abnormalities in the Default-Mode Network



- Comparison of the DMN in control subjects, and right and left TLE patients. (analysis of BOLD coherent fluctuations, in 29 control subjects, 27 right and 25 left TLE patients
- The significantly smaller areas of the dorsal medial prefrontal cortex, and of the mesial and inferior temporal lobe in TLE patients in comparison with controls.



- The connectivity among different regions of the default mode network is lower in TLE than in normal subjects
- Connectivity between precuneus/posterior cingulate cortex and both right and left temporal lobes is weaker in TLE

1.; Zhang et al. (2010b), 2; Laufs et al., 2007

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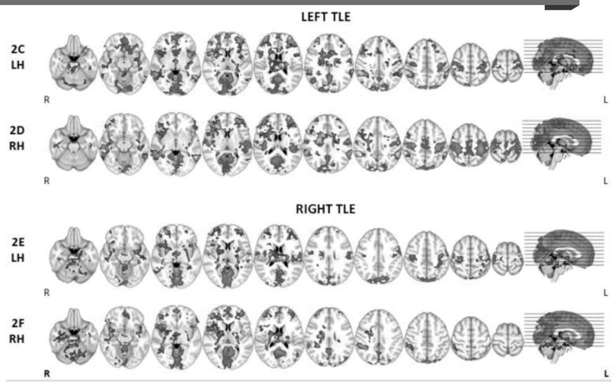
Perception and attention networks

- Auditory system in the bilateral superior temporal lobes including Heschl's gyrus, planum temporale and the temporal poles
- Auditory function is integral in language (i.e. auditory sentence comprehension) and memory (i.e. verbal memory), known impaired in TLE [1]
- The results showed increases in connectivity in TLE in primary visual cortex, coupled with decreases in higher order visual processing regions such as MT+ when compared to controls that decreased with duration of disease [2]



TLE associated with reduced connectivity involving areas of sensorimotor cortex (visual, somatosensory, auditory, primary motor)

Left TLE had more marked connectivity changes than right TLE.

1; Fisher, et al. 2000, Helmstaedter, et al. 2003.,, 2; Zhang, et al. 2009a

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Conclusions and future directions

- Epilepsy can affect the functional networks of brain and various fMRI methods used to determine this
  - These changes may be related to behavioral, cognitive or disease characteristics

- The comparison between functional and structural connectivity in epilepsy may provide the answers

- Large scale neuroimaging studies that incorporate both structural and functional imaging with genetic, physiological and neuropsychological testing may provide the greatest potential in uncovering mechanisms and effects of network alterations in the brain in epilepsy

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