ACMEGS
AMERICAN CLINICAL MEG SOCIETY

2017 ACMEGS Annual Conference
Thursday, February 9, 2017
Sheraton Grand Phoenix • Phoenix, Arizona

8:00am Arrival / Breakfast Reception

8:30 am ACMEGS Presidential Address 2017
Welcome and Introduction (Richard Burgess, Cleveland)

8:45am Current Issues and Enduring Questions in Clinical MEG (Part 1) Chair: Rick Burgess, Cleveland

- *Beyond the Spike: Alternative Markers for the Epileptic Network* - ***Stefan Rampp, Erlangen***
- *Network Connectivity in Generalized Epilepsy* – ***Adham Elshahabi, Tuebingen***
- *Localizing significance of interictal MEG DC transients* – ***Ernst Rodin, Salt Lake City***

10:15am Added Insight from MEG - Neurodegenerative Diseases Chair: Heidi Kirsch, San Francisco

- *Regional functional connectivity predicts distinct cognitive impairments in Alzheimer's disease* - ***Kamalini Ranasinghe, San Francisco***
- *Fronto-temporal connectivity in nondemented Parkinson's disease* – ***Tony Wilson, Omaha***
- *Somatosensory cortical activity is related to the mobility and strength impairments seen in children with cerebral palsy* - ***Max Kurz, Omaha***

11:45am Annual ACMEGS Photo Shoot Chair: Anto Bagic, Pittsburgh

12:00 pm Lunch

12:45pm Update on Movement Related Evoked Fields Chair: Tony Wilson, Omaha

- *What is cortico-kinetic coherence mapping* – ***Xavier de Tiege, Brussels***
- *Comprehensive sensorimotor mapping* – ***Xavier de Tiege, Brussels***

1:45pm Current Issues and Enduring Questions in Clinical MEG (Part 2) Chair: Anto Bagic, Pittsburgh

- *High-resolution MEG source imaging approach to accurately localize Broca's area* – ***Roland Lee, San Diego***
- *MEG inter-ictal high frequency oscillations: A potential biomarker of epilepsy surgical outcome* – ***Jayabal Velmurugan, San Francisco***
- *Benefits of Combined MEG/EEG in Presurgical Evaluation of Epilepsy: A Study of 250 Patients* – ***Michael Wagner, Hamburg***

3:15pm Coffee Break

3:30pm Update on Educational Initiatives Chair: Richard Burgess, Cleveland

- *The State of MEG Fellowships*
- *Update and Announcements on MEG/EEG-Technologist Activities*

4:00pm What's on the Horizon: Vendor Innovations and Plans Chair: Richard Burgess, Cleveland

- *Compumedics – Curtis Ponton, PhD, Vice President, Chief Science Officer*
- *Elekta – Mikkaa Putaala, Director, Business Line MEG*
- *York Instruments - Gordon J. Haid, Vice President, Global Sales and Marketing*
- *Ricoh - Takahito Uga, Marketing Senior Manager*

4:30pm Meeting Adjourn

The ACMEGS Business Meeting follows at 4:45pm (see next page). All are welcome to attend, but only ACMEGS members may vote. All registered attendees at the ACMEGS meeting are invited to our annual dinner at 6:30 pm.

4:45pm Business Meeting Chair: Richard Burgess, Cleveland

- *President's Report – Richard Burgess, Cleveland*
- *Financial Report* - Susan Bowyer, Detroit
- *Membership Report* - Susan Bowyer, Detroit
- *Public Relations Committee* - Susan Bowyer, Detroit
- *New Business*
- *Board Elections* - Richard Burgess, Cleveland

6:30pm **Casual ACMEGS Dinner**

The Arrogant Butcher
CityScape
2 E Jefferson St #150
Phoenix, AZ 85004

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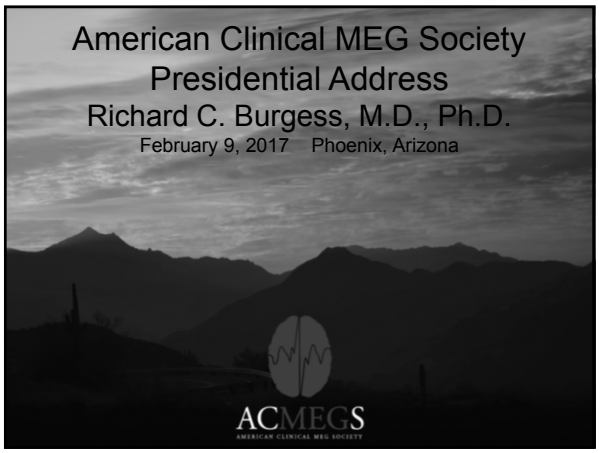
Presidential Address

Richard C. Burgess, Cleveland



State of Magnetoencephalography

- MEG sites
- ACMEGS membership
- Costs and revenues
- Education
- Annual meetings
- Advocacy, standardization, and quality improvement
- Hardware and software vendors
- International outreach
- Challenges

ACMEGS Board of Directors

- Anto Bagic
- Susan Bowyer
- Richard Burgess
- Michael Funke (Meeting director)
- Angel Hernandez (Course co-director)
- Heidi Kirsch
- Tony Wilson (Course co-director)

ACMEGS Membership

- Institutional Members:
  - Representing the clinical MEG laboratories in the United States
- Individual Members:
  - Increased memberships
  - Technologist members

Costs and Revenues

- Costs
  - Helium recycling systems have decreased costs and increased security.
- Revenues
  - Established CPT codes and more widespread coverage have made the administrative and financial logistics easier on patients and providers.
  - Example: Texas Medicaid coverage.

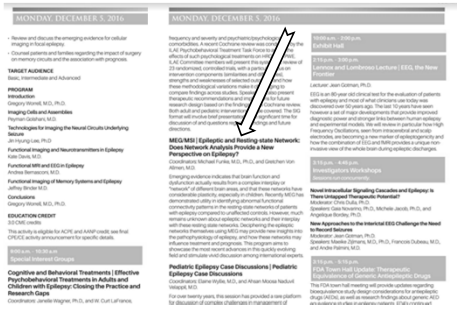
ACMEGS Education

- Physician Education
  - Annual course
  - SIGs and programs at other society meetings
- Clinical Fellowship Training
  - Positions available
  - Guidelines/Survey in progress
- MEG Technologist Education Efforts
  - ACMEGS speaker participation in local & national meetings
- MEG Technologist Certification
  - Teaching modules
  - Examination questions

Neurologists' increased exposure to MEG

- ACGME - approved fellowships in CNP and Epilepsy
- Exposure to MEG during fellowship and questions on board exams
- MEG seen as part of the Standard of Care

MEG SIG at AES in Houston



MONDAY, DECEMBER 5, 2016

- Review and discuss the emerging evidence for cellular imaging in focal epilepsy.
- Counsel patients and families regarding the impact of surgery on memory circuits and the association with prognosis.

TARGET AUDIENCE
Basic, Intermediate and Advanced

PROGRAM
Introduction
Gregory Worrell, M.D., Ph.D.

Imaging Cells and Assemblies
Peyman Golshani, M.D.

Technologies for Imaging the Neural Circuits Underlying Seizure
Jin Hyung Lee, Ph.D

Functional Imaging and Neurotransmitters in Epilepsy
Kate Davis, M.D.

Functional MRI and EEG in Epilepsy
Andrea Bernasconi, M.D.

Functional Imaging of Memory Systems and Epilepsy
Jeffrey Binder M.D.

Conclusions
Gregory Worrell, M.D., Ph.D.

EDUCATION CREDIT
3.0 CME credits

This activity is eligible for ACPE and AANP credit; see final CPE/CE activity announcement for specific details.

9:00 a.m. - 10:30 a.m.
Special Interest Groups

Cognitive and Behavioral Treatments | Effective Psychobehavioral Treatments in Adults and Children with Epilepsy: Closing the Practice and Research Gaps
Coordinators: Janelle Wagner, Ph.D., and Mr. Curt LaFrance.

MONDAY, DECEMBER 5, 2016

frequency and severity and psychiatric/psychological comorbidities. A recent Cochrane review was conducted by the ILAE Psychobehavioral Treatment Task Force and found that ILAE Committee members will present this systematic review of 23 randomized, controlled trials, with a particular focus on intervention components, similarities and differences, strengths and weaknesses of selected studies, and how these methodological variations make it challenging to compare findings across studies. Speakers will also present research design based on the findings of the Cochrane review. Both adult and pediatric interventions will be covered. The SIG format will involve brief presentations and significant time for discussion of and questions regarding challenges and future directions.

MEG/MSI | Epileptic and Resting-state Network: Does Network Analysis Provide a New Perspective on Epilepsy?
Coordinators: Michael Funke, M.D., Ph.D., and Gretchen Von Allmen, M.D.

Emerging evidence indicates that brain function and connectivity can be viewed as "networks" of brain regions or "network" of different brain areas, and that these networks have considerable plasticity, especially in children. Recently MEG has demonstrated utility in identifying abnormal functional connectivity patterns in the resting-state networks of patients with epilepsy compared to unaffected controls. However, much remains unknown about epileptic networks and their interplay with normal brain networks. Studying epileptic and normal networks themselves using MEG may provide new insights into the pathophysiology of epilepsy, and how these networks may influence treatment and prognosis. This program aims to showcase the most recent advances in this quickly evolving field and stimulate vivid discussion among international experts.

Pediatric Epilepsy Case Discussions | Pediatric Epilepsy Case Discussions
Coordinators: Elaine Wyllie, M.D., and Ahsan Moosa Naduvil Hospital, M.D.

For over twenty years, this session has provided a rare platform for discussion of complex challenges in management of

10:00 a.m. - 3:00 p.m.
Exhibit Hall

3:15 p.m. - 3:55 p.m.
Lennox and Lombroso Lecture | EEG, the New Frontier
Lecturer: Jean Gotman, Ph.D.

EEG is an 80-year old clinical test for the evaluation of patients with epilepsy and most of what clinicians use today was discovered over 50 years ago. The last 10 years have seen a revival in the field of electroencephalography with increased diagnostic power and stronger links between human epilepsy and experimental models. We will review in particular how High Frequency Oscillations, seen from intracerebral and scalp electrodes, are becoming a new marker of epileptogenicity and how the combination of EEG and fMRI provides a unique non-invasive view of the whole brain during epileptic discharges.

3:55 p.m. - 4:45 p.m.
Investigators Workshops
Scientific Program

Novel Intracellular Signaling Cascades and Epilepsy: Is There Untapped Therapeutic Potential?
Moderator: Chris Dulla, Ph.D.
Speakers: Gea Novarino, Ph.D., Michele Jacob, Ph.D., and Angelique Bordey, Ph.D.

New Approaches to the Interictal EEG Challenge the Need to Record Seizures
Moderator: Jean Gotman, Ph.D.
Speakers: Meeike Zijlmans, M.D., Ph.D., Frances Dubeau, M.D., and Andre Palmini, M.D.

4:55 p.m. - 5:15 p.m.
FDA Town Hall Update: Therapeutic Equivalence of Generic Antiepileptic Drugs

The FDA town hall meeting will provide updates regarding bioequivalence study design considerations for antiepileptic drugs (AEDs), as well as research findings about generic AED equivalence in clinical practice patients. (FAILS CONTINUED

ACMEGS Sessions at ACNS

Annual Meeting Program

Saturday, February 11, 2017

1163: The Frontal Lobe Club
Session Director: Daniela Minecan, MD, FACNS

3:45pm — The Functional Anatomy of the Frontal Lobe — *Daniela Minecan, MD, FACNS*
4:00pm — Frontal Lobe Seizure Subtypes with a Focus on Semiology — *Rafeed Alkawadri, MD*
4:20pm — Frontal Lobe Seizures – Invasive Monitoring Approaches — *Juan Bulacio, MD*
4:40pm — Frontal Lobe Seizures – What about the Children? — *TBD*
5:00pm — Wrap Up & Recommendations for Frontal Lobe Epilepsy — *Stephan U. Schuele, MD, MPH, FACNS*

1164: Proponents vs. Opponents: You Really Mean I Need to Order a MEG in 2017?
Session Director: Anto Bagic, MD, PhD, FACNS

3:45pm — Informed Skeptic – We Wish, We Profess, but thus Spoke the NAEG Centers' Directors — *Anto Bagic, MD, PhD, FACNS*
4:10pm — Enlightened Proponent – If you just could See How it Works in Our Hands… — *Richard C. Burgess, MD, PhD, FACNS*
4:35pm — Enlightened Opponent – Know What you Have & When to Use It! — *Ronald Lesser, MD, FACNS*
5:00pm — Discussion

Saturday, February 11, 2017

1113: Competing Techniques for Refining the Location of the Epileptogenic Zone: Magnetoencephalography & High Density EEG
Session Director: Richard C. Burgess, MD, PhD, FACNS

8:00am — Comparison of Intracranial EEG Potentials with Source Localization from Scalp EEG & MEG: Location Accuracy & Implantation Guide — *Eliane Kobayashi, MD, PhD*
8:30am — Simultaneous High Density Scalp EEG & MEG — *Robert C. Knowlton, MD*
9:00am — Theoretical & Practical Considerations for Localization of the Epileptogenic Zone from High Density EEG & MEG — *Richard C. Burgess, MD, PhD, FACNS*

1114: Cortical Stimulation: Theory & Practice
Session Director: Giridhar Kalamangalam, MD, DPhil, FACNS

8:00am — Physiology of Non-Invasive Cortical Stimulation — *Mark Hallett, MD, FACNS*
8:20am — Measuring & Modifying Cortical Excitability with AEDs — *Uli Zimmann, MD*
8:40am — Modelling the Effects of Cortical Stimulation: Afterdischarge — *Giridhar Kalamangalam, MD, DPhil, FACNS*
9:00am — From Science to Bedside: Eloquent Function Mapping — *Anthony L. Ritaccio, MD*
9:20am — Panel Discussion

ACMEGS at ICCN 2018

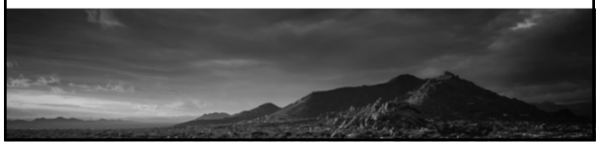
SAVE THE DATE
31st International Congress of Clinical Neurophysiology
of the International Federation of Clinical Neurophysiology (IFCN)
ICCN★2018
Washington, DC
May 1-6, 2018
Hosted by:
American Clinical Neurophysiology Society (ACNS)
Canadian Society of Clinical Neurophysiologists (CSCN)

- Watch for multiple ACMEGS sponsored courses and sessions.
- With special attention to and participation by international experts.

ACMEGS Annual Meeting

Travel Awards

Available to personnel from ACMEGS institutional member sites



ACMEGS Clinical Practice Guidelines

- Position statement #2

clinicalneurophys.com Journal of Clinical Neurophysiology 2017

SPECIAL ARTICLE MEG/MSI in Noninvasive Presurgical Mapping

American Clinical MEG Society (ACMEGS) Position Statement #2: The Value of Magnetoencephalography (MEG)/Magnetic Source Imaging (MSI) in Noninvasive Presurgical Mapping of Eloquent Cortices of Patients Preparing for Surgical Interventions

Anto I. Bagić,* Susan M. Bowyer,† Heidi E. Kirsch,‡ Michael E. Funke,§ Richard C. Burgess,‖ For the ACMEGS Position Statement Committee

*University of Pittsburgh Comprehensive Epilepsy Center (UPCEC), University of Pittsburgh Medical School, Pittsburgh, Pennsylvania, U.S.A.; †Neuromagnetism Laboratory, Department of Neurology, Henry Ford Hospital, Detroit, Michigan, U.S.A.; ‡Biomagnetic Imaging Laboratory, UCSF Epilepsy Center, San Francisco, California, U.S.A.; §MEG Center, Department of Pediatrics, McGovern Medical School, The University of Texas Health Sciences Center at Houston, Houston, Texas, U.S.A.; and ‖Magnetoencephalography Laboratory, Cleveland Clinic Epilepsy Center, Cleveland, Ohio, U.S.A.

New MEG Vendors

- Compumedics/KRISS,
- Ricoh/Yokogawa
- York Instruments/Oxford Inst

Teaming with Vendors

- Our labs depend on the vendors.
- Vendors need our help to team up with them.
- Most knowledgeable advisors to the vendors are in ACMEGS.
- Vendors provide support to the Society
- Manufacturers keep the members apprised of "What's on the Horizon"

Corporate Support for ACMEGS

- Platinum $50k and above
- Gold $25k to $49,999
- Silver $10k to $24,999
- Bronze $5k to $9,999

Recognition and thanks to our corporate supporters.
ELEKTA NEUROMAG: Platinum Supporter

ACMEGS Outreach

- ACMEGS Website and on-line resources
- Engagement with other MEG societies
- Participation in ISACM (Sendai May, 2017)
- Multiple committee and board roles in ICCN planning (Washington DC, April 2018)

ACMEGS Outreach

And sometimes it's a struggle…

(European Consortium on Diagnostic Methods in Epilepsy, ["E-Epilepsy"])

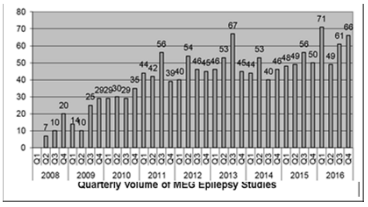

Epilepsia

GRAY MATTERS

LETTERS

Challenges: First the Good News

- Patient self referrals: Selecting a center on the basis of the presence of a MEG
- Physician referrals to MEG centers are up



Challenges: Still to Work On

- REFERRERS: There remains a lack of understanding of and appreciation for the benefits of MEG by neurologists, and even epileptologists.
- PRACTIONERS: Despite the ACMEGS Clinical Practice Guidelines, there are still widespread disaparities in MEG procedures and reporting.

Challenges: Care-delivery vs Margin-generation

- MEG labs are an expensive cost-center
  - Fee for service vs risk-based environments
  - Advocacy vs gate-keeping is a false choice
- Maximize the value of MEG
  - Do what is right for each individual patient
  - Become fully integrated into the patient's evaluation
- Increase the magnetoencephalographer's profile
  - Advise on when a MEG may help and what it may add
  - Present the results in Case Management conference with clear explanations of the meaning and confidence

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Beyond the Spike: Alternative Markers for the Epileptic Network

Fronto-temporal connectivity in nondemented Parkinson's disease

Stefan Rampp, Erlangen

In recent years, novel markers for the epileptic network beyond interictal spikes and ictal seizure correlates have been described. Fast activity, from high gamma oscillations to ripples and fast ripples may be correlated to the pathomechanisms of epilepsy. Detection is possible using mainly invasive recordings, however recent advances may offer methods for non-invasive evaluation. Slow wave at the other end of the frequency spectrum are detected using both invasive and non-invasive means. While this type of activity also occurs associated e.g. with large lesions and after intracranial surgery, certain subtypes may be utilized to localize the epileptic network. Complimentary to such frequency-based markers, alterations of the connectivity structure provide further insights in location and dynamics of epilepsy related areas. The presentation will give an overview of such alternative markers for the epileptic network. Current methods and clinical applications are presented and illustrated with case examples.

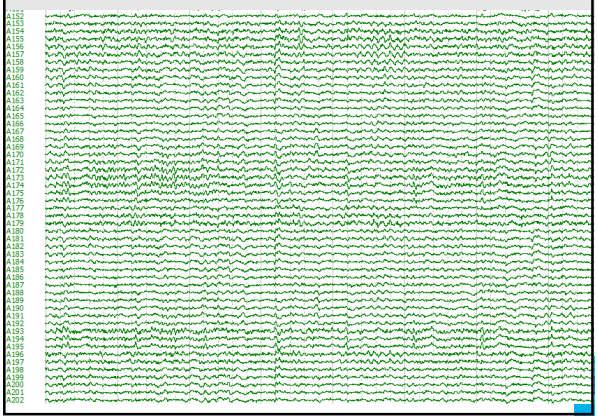
Beyond the Spike: Alternative Markers for the Epileptic Network

Stefan Rampp

Universitätsklinikum Erlangen

Disclosures

- Advisory for Elekta Oy, Helsinki, Finland
- Executive board member of the International Society for the Advancement of Clinical MEG
- Executive board member of the European MEG Society



Patient example

- 25y female patient
- Seizures since age 4:
  - Somatosenbile auras tongue (prickling feeling)
  - Tonic -> Clonic (facial right)
  - Rare generalized tonic clonic seizures
- Ictal EEG: Right fronto-central onset (but not very clear patterns)

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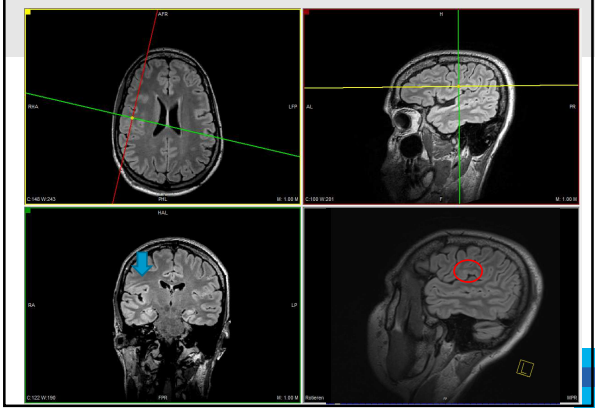
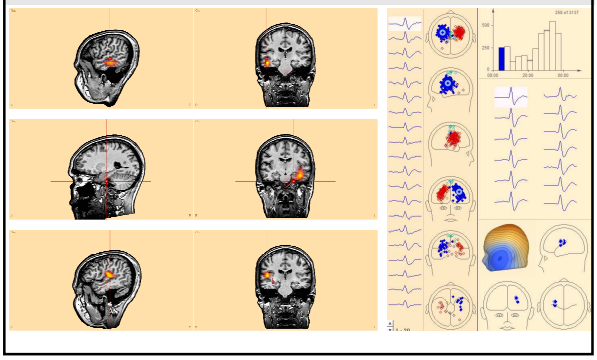


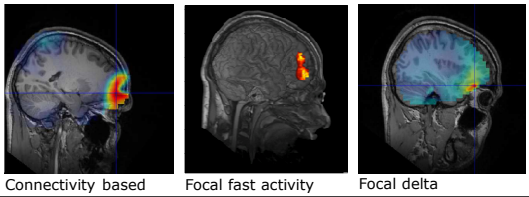
MEG and Video-EEG localizations



Alternative markers?

- Higher sensitivity (cases with no spikes)
- Higher specificity (cases with too many spikes)
- Automated?

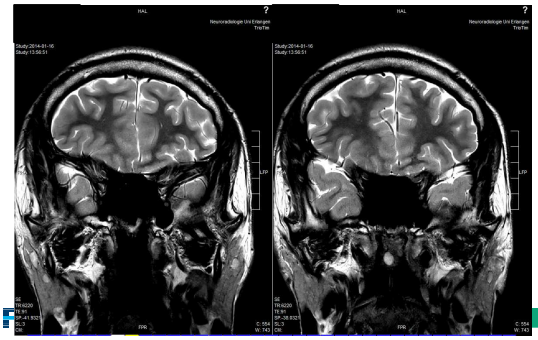
FLE due to fronto-polar FCD 2b



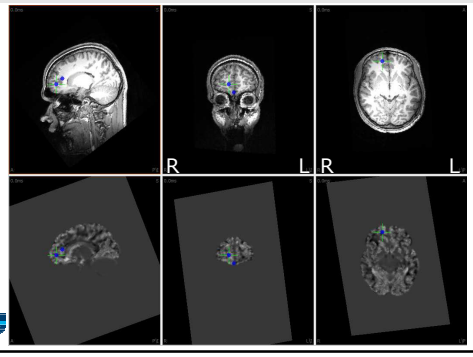
Connectivity based | Focal fast activity | Focal delta

Localization using connectivity: The idea

Example case

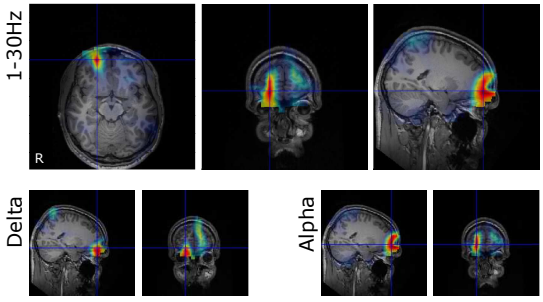


MEG Spike Localization
Voxel based morphometry (VBM)



FAU

Imaginary part of coherence:
All-to-all, node degree



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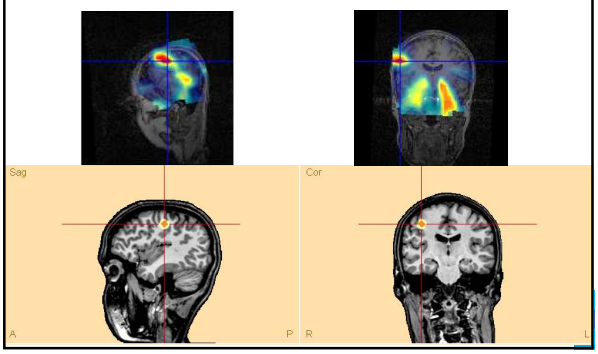
Example: Central FCD



Pilot study of 13 patients

- Patients
  - 9 FCD II (1 patient with 2 FCDs), 1 TLE, 2 FLE, 1 OLE
  - Incl. 3 with previous surgery (FCD, FLE, OLE)
- 8-10 minutes of resting state data
- 2 MEG systems (CTF, 4D Neuroimaging)
- Comparison vs. spike localization and lesion
  - Concordant: 8 (62%) patients
  - Partial: 3 (23%)
  - Misses: 2 (15%)

More on connectivity in MEG…

8:45am Current Issues and Enduring Questions in Clinical MEG (part 1)
Chair: Rick Burgess, Cleveland

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- *Localizing significance of interictal MEG DC transients* – ***Ernst Rodin, Salt Lake City***

FAU

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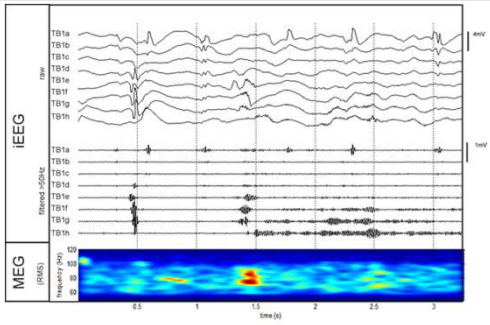
MEG correlates of epileptic high gamma oscillations in invasive EEG

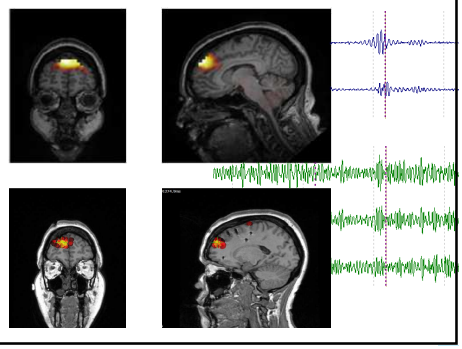
*Stefan Rampp, *Martin Kaltenhäuser, †Daniel Weigel, †Michael Buchfelder, ‡Ingmar Blümcke, §Arndt Dörfler, and *Hermann Stefan



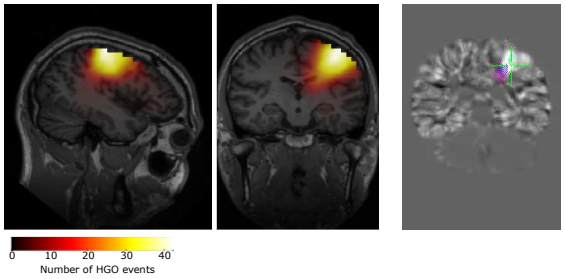
HFO 100-150Hz

MEG (automated)

MEG/iEEG (manual)



High gamma: 50-100Hz



More on fast activity in MEG…

1:45pm Current Issues and Enduring Questions in Clinical MEG (part 2)
Chair: Anto Bagic, Pittsburgh

- *High-resolution MEG source imaging approach to accurately localize Broca's area* – ***Roland Lee, San Diego***
- *MEG inter-ictal high frequency oscillations: A potential biomarker of epilepsy surgical outcome* – ***Jayabal Velmurugan, San Francisco***
- *Benefits of Combined MEG/EEG in Presurgical Evaluation of Epilepsy: A Study of 250 Patients* – ***Michael Wagner, Hamburg***

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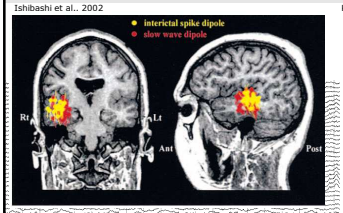
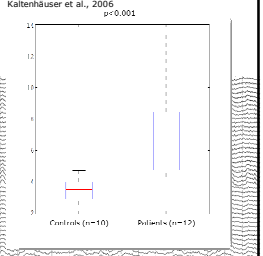
Epileptic slow waves (delta/theta)

Ishibashi et al., 2002

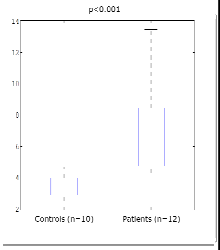


Kaltenhäuser et al., 2006



Localization approach

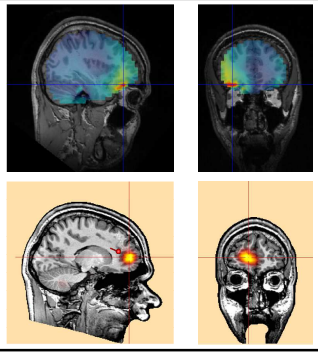
- 15 healthy controls
- 10 minutes resting state MEG
- Rejection of bad channels and time segments with artifacts
- DICS 1-4Hz
- Normalization
- z-score transformation

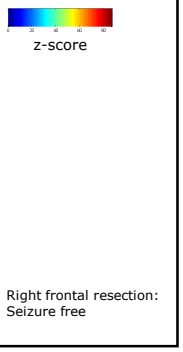


Example 1: Right frontal FCD

Delta

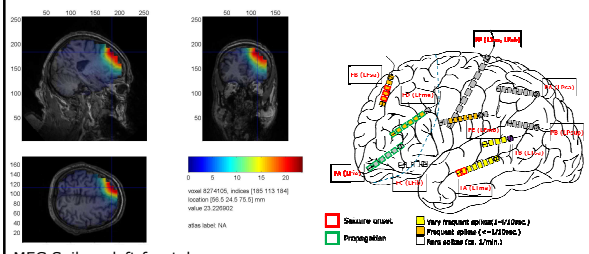
Spikes





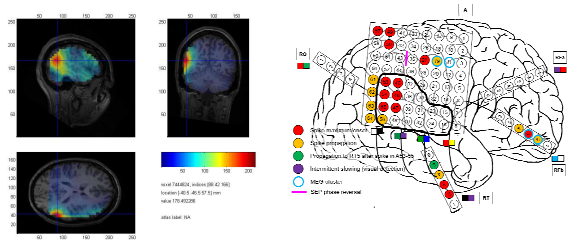
Right frontal resection:
Seizure free

Example 2: Left frontal atrophy (post-inflamation?)



MEG Spikes: left frontal
Left frontal resection: Improvement, but not seizure free

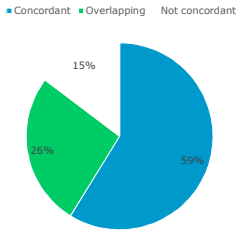
Example 3: Right temporo-parietal FCD 2a (preoperative MRI negative)



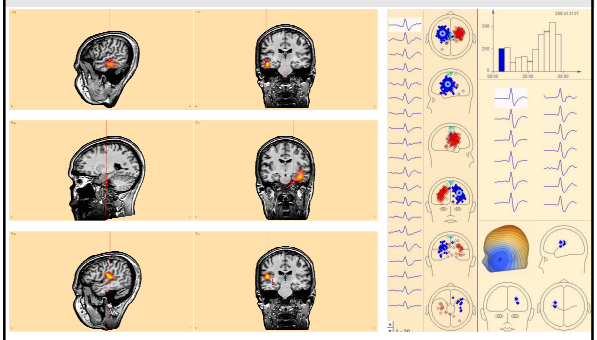
MEG Spikes: right frontal (also iEEG spikes)
Right parietal resection: Improvement, but not seizure free
Histology: Parts of FCD 2a

Focal delta localization

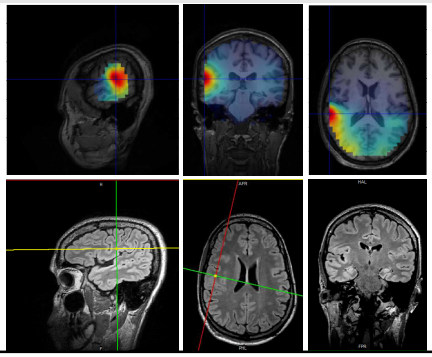
- 50 patients
- Different etiologies (FCD, HS, tumors, MR negative, …)
- Comparison with presurgical focus localization (MR, VEEG, iEEG, PET, SPECT, MEG)
- 34 patients (68%) with significant delta increase
- 29 patients (85%) concordant or overlapping
- 5 patients with no or 1-3 spikes



MEG and Video-EEG localizations

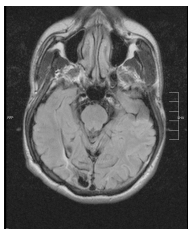


Delta-localization

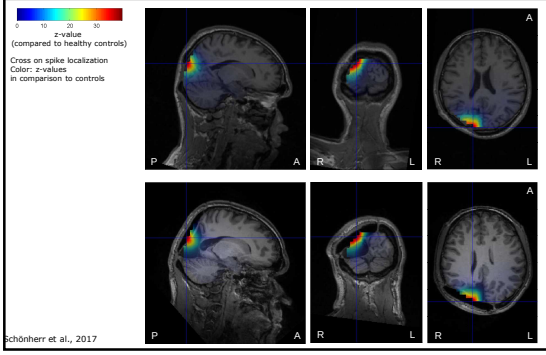


Patient

- Male patient
- Focal epilepsy since 20 years
- Semiology: optic, vision loss, but also epigastric, staring, stereotyped movements of both arms
- Cystic lesion occipital right
- First surgery 19 years ago
- EEG:
  - Interictal: 90% temporal right, 10% occipital right
  - Ictal: unclear, temporal and occipital
- MEG: 90% occipital right near lesion, 10% temporal right
- Invasive EEG: Occipital seizure onset



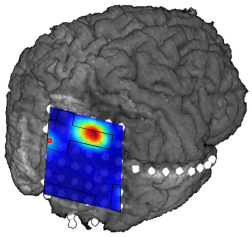
Spikes and focal delta



Schönherr et al., 2017

Focal delta in invasive EEG

- Invasive evaluation (subdural EEG)
- 1h of awake data
- Artifacts manually excluded
- Spectral analysis
- Visualization of relative power in delta band

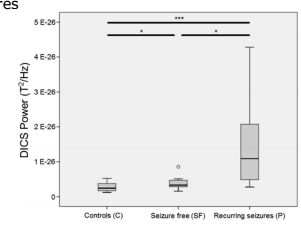


Schönherr et al., 2017

The delta between postoperative seizure freedom and persistence: Automatically detected focal slow waves after epilepsy surgery

Margit Schönherr[a], Hermann Stefan[a], Hajo M. Hamer[a], Karl Rössler[b], Michael Buchfelder[b], Stefan Rampp[b,*]

- 15 patients with recurrent seizures
- 12/15 monofocal distribution
- Median distance between delta peak and spike localization: 2.1cm
- 15 seizure free patients after surgery
- 15 controls
- AUC for recurring seizures: 0.84



Alternative markers

- Promising results for presurgical evaluation
- More than just „spike stand-ins“?
- Potential for automated procedures!

But:

- Spectrum of methodologies, no standards
- Mixed (contradicting?) observations for connectivity
- More work on reliability and validity

ACMEGS
AMERICAN CLINICAL MEG SOCIETY

Network Connectivity in Generalized Epilepsy

Adham Elshahabi, Tuebingen

Localizing significance of interictal MEG DC transients

Ernst Rodin, Salt Lake City

Regional functional connectivity predicts distinct cognitive impairments in Alzheimer's disease

Kamalini Ranasinghe, San Francisco

Alzheimer's disease (AD) is characterized by progressive loss of memory and other cognitive functions. A wealth of physiological studies in animal models suggests that abnormal oscillations within localized neuronal ensembles and network hyperexcitability are key mechanisms underlying network dysfunction in the early stages of AD. In this translational investigation, we aimed to characterize spatiotemporal dynamics of brain oscillations and their relationships to cognitive deficits in patients with AD. We studied three clinical variants of AD spectrum including amnestic/dysexecutive (Amn/dys), logopenic variant primary progressive aphasia (lvPPA), and posterior cortical atrophy (PCA), and age-matched normal controls. We used magnetoencephalographic imaging (MEGI) to characterize the neural oscillatory patterns during rest and task engaged states, and also to study the incidence of subclinical epileptiform activity, in AD patients. Specifically, we examined (1) the band-specific resting state functional connectivity patterns in different variants of AD; (2) correlations between region specific functional dysconnectivity and cognitive deficits; (3) high-gamma-band (65-4-150 Hz) activity during an auditory feedback compensation task—producing a vowel while listening to real-time unexpected shift in pitch feedback; and (4) the incidence and potential cognitive impact of subclinical epileptiform activity in AD patients using 24-hour overnight EEG and 1-hour MEG exams.

We found that each AD variant shows distinct anatomic patterns of reduced functional connectivity within alpha and beta band oscillations. In contrast, within delta-theta band, all three variants showed spatially nonspecific patterns of hypersynchorny. Within alpha-band, region-specific resting-state functional connectivity deficits predicted specific cognitive deficits in AD spectrum. High-gamma-band activity during pitch-perturbation revealed a significantly enhanced evoked activity in AD patients compared to age-matched controls, indicating lack of sensorimotor integration of speech motor control in AD. We found that 42 % of AD patients have subclinical epileptiform activity, detected by extended EEG and/or MEG, and such activity associated with faster declines in global cognition determined by the Mini–Mental State Examination.

The current results demonstrate the first evidence of direct neuronal activity patterns recorded using MEG in a comprehensive evaluation including all clinical variants of AD during rest as well as task-engaged states. Distinctive spatiotemporal patterns of decreased alpha and beta synchronizations of resting state activity in AD spectrum suggest diverse mechanisms for network failure in each AD syndrome. Additionally, shared patterns of increased delta-theta synchronizations indicate some potentially unifying mechanisms. The current results further emphasize that AD patients with silent network hyperexcitability are at a higher risk for accelerated cognitive decline. Collectively our data suggest that comprehensive neurophysiological assessments will enable identification of some of the earliest manifestations of network dysfunction in AD.

Reference: Spatiotemporal patterns of network dysfunction in Alzheimer's disease

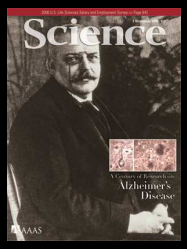
Kamalini G Ranasinghe, Leighton B Hinkley, Alexander J Beagle, Hardik Kothare, Alice La, Danielle Mizuiri, Susanne M Honma, Maria-Louisa Gorno Tempini, Bruce L Miller, Paul A Garcia, Heidi E Kirsch, John F Houde, Srikantan S Nagarajan, Keith A Vossel

Spatiotemporal Patterns of Network Dysfunction in Alzheimer's Disease

Kamalini Ranasinghe, MD PhD

UCSF Memory and Aging Center

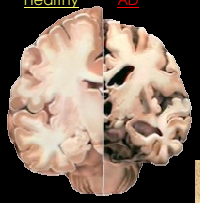
Alzheimer's Disease



Clinical / Behavioral

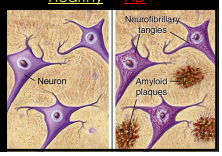
Gross anatomy

Healthy AD



Cellular/ molecular

Healthy AD



Missing link …

What happens to neuronal firing ?

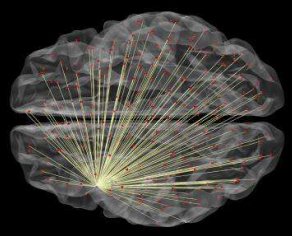
Functional Deficits of Neural Activity Patterns in AD

60 seconds of resting

in 3 clinical variants of AD:

1. Memory Predominant AD (AD-Amn/Dys)
2. Logopenic primary progressive aphasia (AD-LPA)
3. Posterior cortical atrophy (AD-PCA)

Global Connectivity (Synchrony)

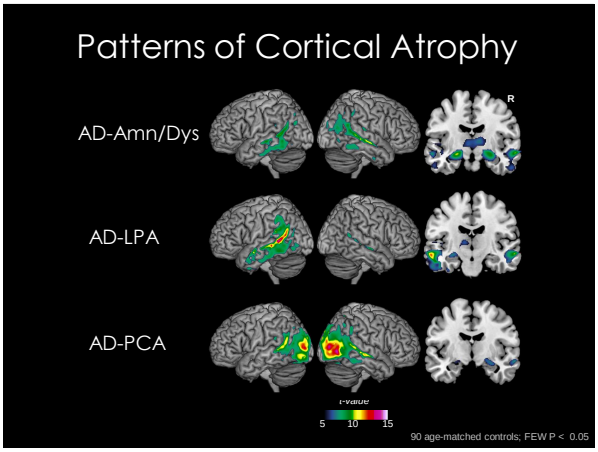


δ-θ (2-8 Hz) α (8-12 Hz) β (12-30 Hz)

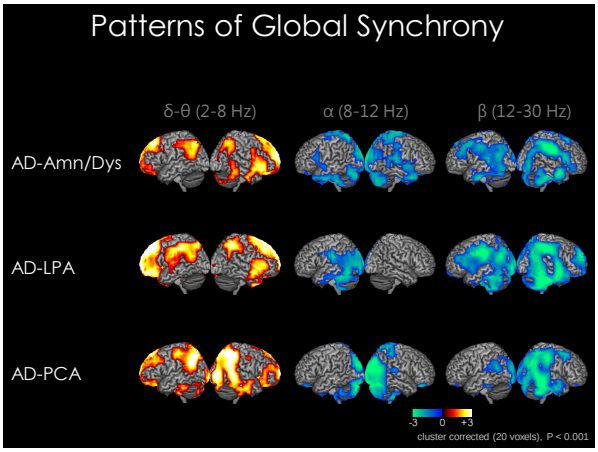
Participant Demographics

	Amn/Dys	LPA	PCA	Controls
	n=30	n=15	n=13	n=20
Age	60 ± 8	62 ± 9	62 ± 7	64 ± 5
Female	63%	67%	69%	60%
Handedness (R)	87%	67%	92%	80%
Education	16 ± 2	17 ± 4	15 ± 2	17 ± 2
MMSE	21 ± 1	21 ± 1	18 ± 1	-
CDR	1 ± 0.1	1 ± 0.1	1 ± 0.1	-

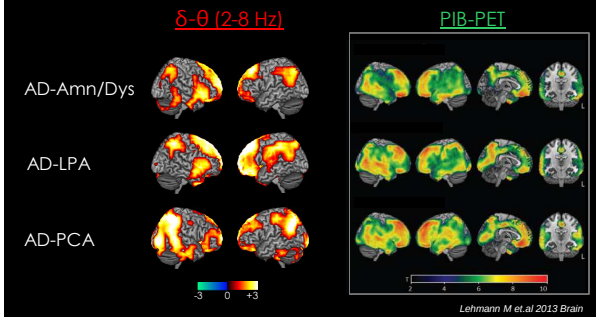
Patterns of Cortical Atrophy



Patterns of Global Synchrony

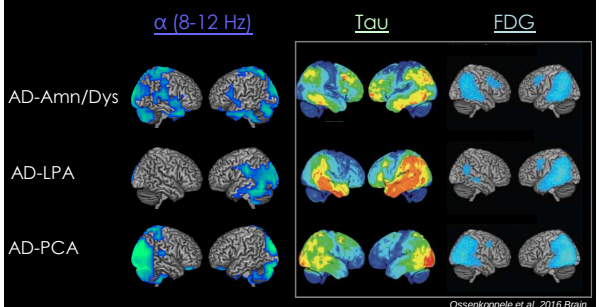


δ-θ Hypersynchrony and PIB-amyloid Uptake of AD variants



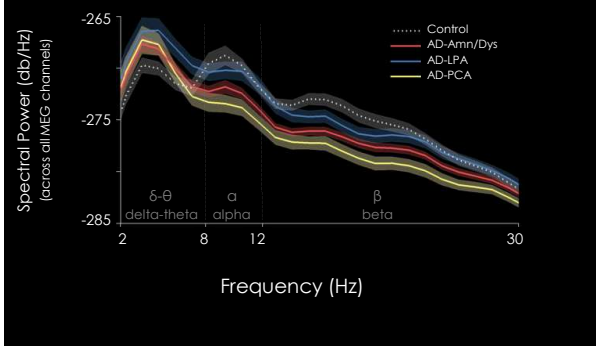
Lehmann M et.al 2013 Brain

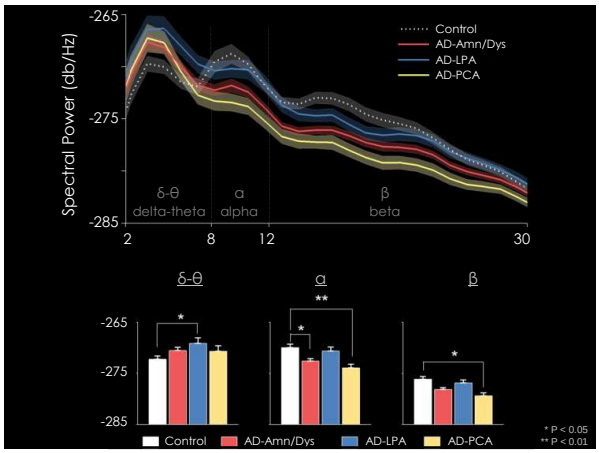
α (8-12 Hz) Hyposynchrony, FDG and Tau imaging



Ossenkoppele et.al 2016 Brain
Lehmann et.al 2013 Brain

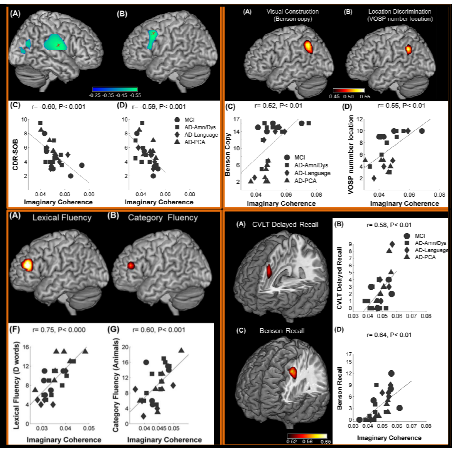
Spectral Power





- What's new:
  i. Direct neural activity patterns in 3 AD variants
  ii. Unbiased whole brain approach
- What we found:
  i. Unique neural activity patterns in each AD variant
  ii. Striking resemblance of frequency specific global deficits to Amyloid and Tau

Regional FC defects predict cognitive deficits

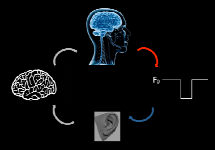


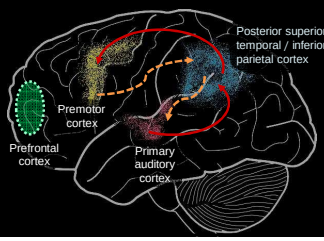
- Summary:
  i. reductions in region-specific alpha-band resting-state functional connectivity predict, and might contribute to, specific cognitive deficits in AD spectrum.

  ii. MEGI functional connectivity could be an important biomarker to map and follow defective networks in the early stages of AD.

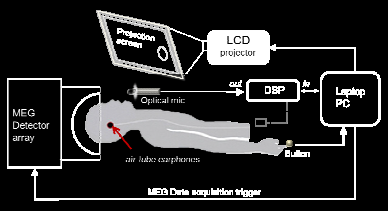
Sensorimotor Integration in AD

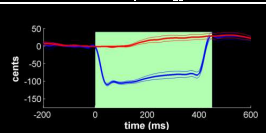
(Pitch Reflex)



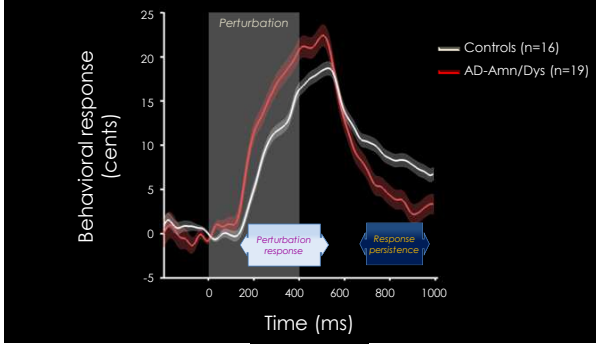


Vocal response to Pitch-perturbation (experimental setup)

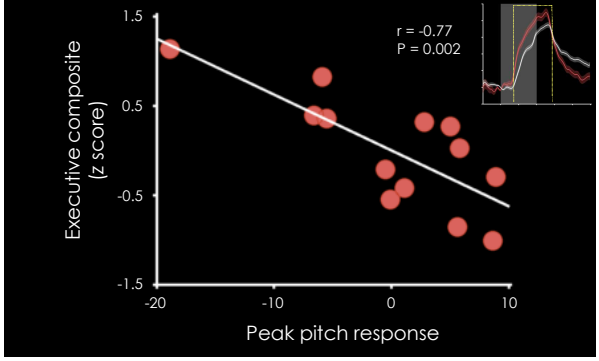


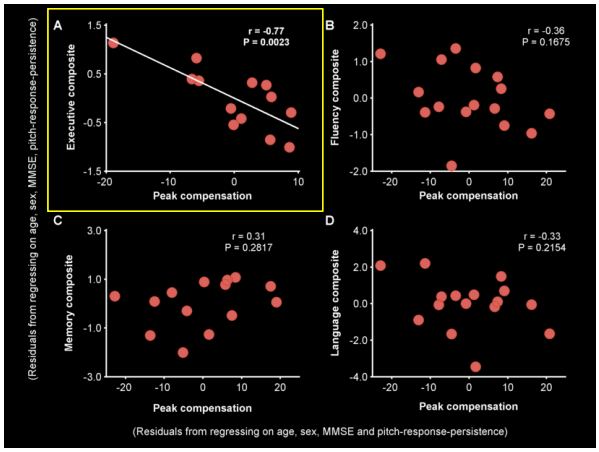


Behavioral response to pitch perturbation

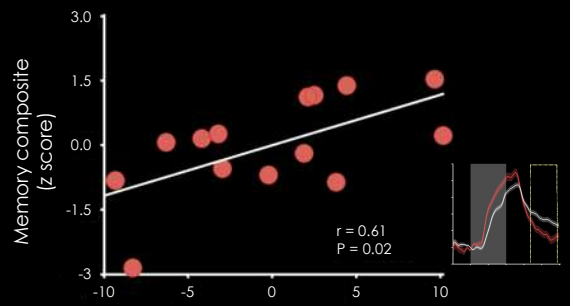


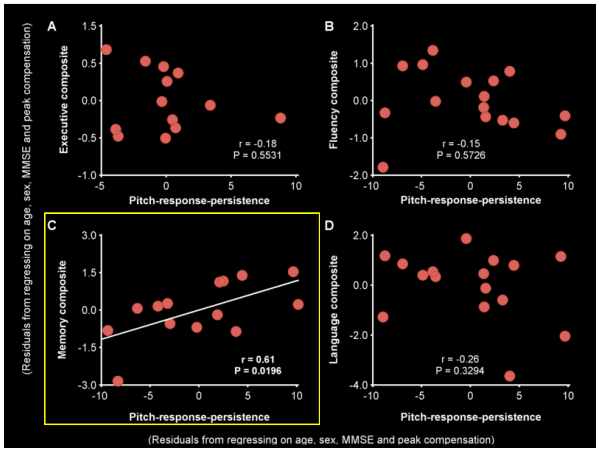
Increased peak compensation predicted executive dysfunction



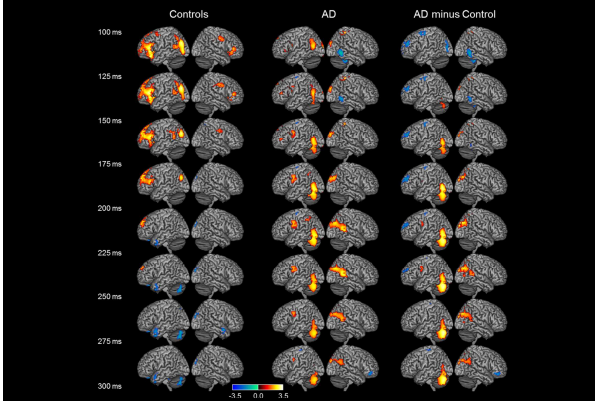


Reduced response persistence predicted memory dysfunction



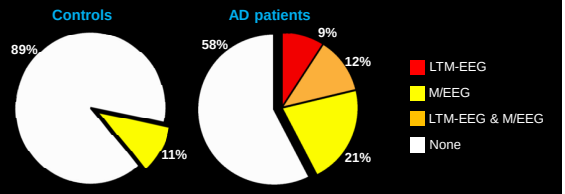


Neural response to Pitch-perturbation



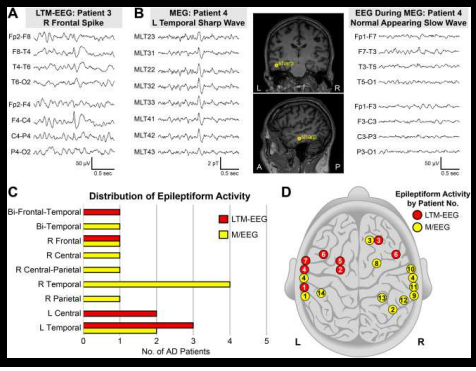
- Summary:
  i. AD patients demonstrate an abnormal pitch reflex
  ii. The elevated compensation and loss of response persistence are sensitive as well as specific indicators of executive dysfunction and memory dysfunction, respectively, in AD.
  iii. MEGI derived high-gamma-band activity trakcs the neural signatures of the abnormal pitch reflex in AD.

Incidence of subclinical epileptiform activity in AD

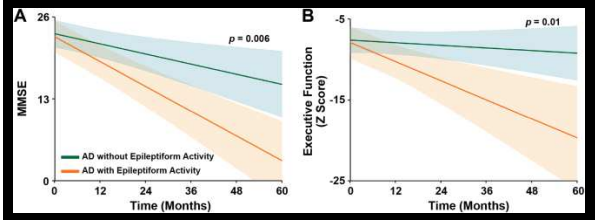


	Controls Epileptiform Activity	AD Epileptiform Activity	P Value
LTM-EEG – no./total no. (%)	0/19 (0)	7/33 (21.2)	**0.039**
M/EEG – no./total no. (%)	2/19 (10.5)	11/33 (33.3)	0.099
Combined LTM-EEG and M/EEG – no./total no. (%)	2/19 (10.5)	14/33 (42.4)	**0.027**

Subclinical epileptiform activity in AD (examples)



Subclinical epileptiform activity and longitudinal change in cognition in AD



- Summary:
  i. Extended monitoring detects subclinical epileptiform activity in a substantial proportion of patients with AD.
  ii. Patients with this indicator of network hyperexcitability are at risk for accelerated cognitive decline and might benefit from antiepileptic therapies.

Thank You

Mentors:

UCSF Memory and Aging Center
Keith Vossel, MD MSc
Bruce Miller, MD

UCSF Biomagnetic Imaging Laboratory
Sri Nagarajan, PhD

UCSF Speech Neuroscience Laboratory
John Houde, PhD

Katherine Rankin, PhD
Heidi Kirsch, MD MSc
Paul Garcia MD
Alex Beagle, BA
Alice La, BA
Leighton Hinkley, PhD
Hardik Kothare, MSc
Naomi Kort, PhD
Danielle Mizuiri, MA
Susanne Honma, RT

Patients and their families

Fronto-temporal connectivity in nondemented Parkinson's disease

Tony Wilson, Omaha

Parkinson's disease (PD) is the second most common neurodegenerative disorder in the United States, but its neurobiology is not fully understood. This talk will focus on recent translational studies conducted at the Omaha MEG Center that have investigated motor and cognitive function in patients with mild to moderate PD. These pharmaco-MEG studies have utilized advanced oscillatory analyses and dynamic functional connectivity to characterize the pathophysiology of PD, and to identify the impact of dopaminergic medications on aberrant neural circuitry.

University of Nebraska Medical Center

Frontotemporal Connectivity in Parkinson's Disease

Tony W. Wilson, Ph.D.
Associate Professor of Neurological Sciences
Scientific Director, Center for MEG

Disclosures

My laboratory is supported by:

National Science Foundation
WHERE DISCOVERIES BEGIN

NIH National Institute of Mental Health

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development
Health research throughout the lifespan

NIH National Institute on Drug Abuse
Advancing Addiction Science

American Heart Association.
life is why™

Outline

- MEG studies of motor function in PD
- Spontaneous activity in the motor cortices
- Dynamic functional connectivity during working memory processing in patients with PD

Elekta 306-sensor MEG System installed at the University of Nebraska Medical Center

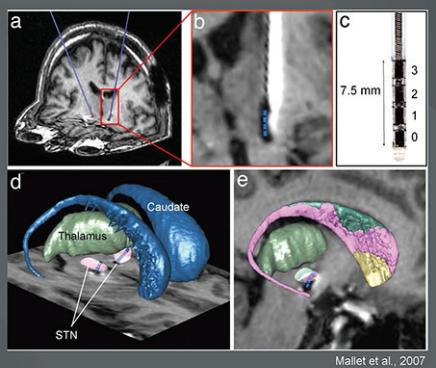
Parkinson's Disease

Second most common neurodegenerative disorder

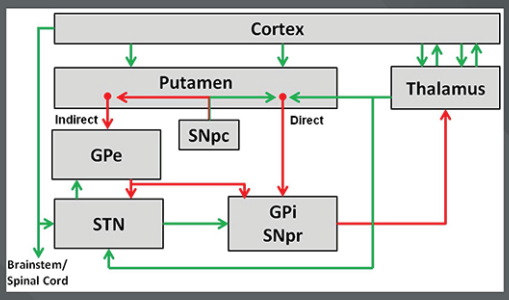
Progressive and symptoms include muscle rigidity, resting tremor, and brady- or hypo-kinesia

Symptomatology primarily due to loss of dopaminergic neurons in the substantia nigra pars compacta

Current treatments include dopamine replacement therapy (e.g., Levo-dopa) and deep-brain stimulation.



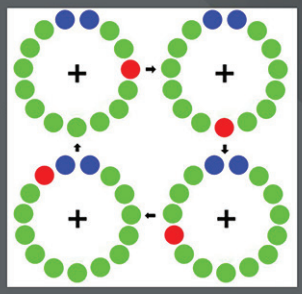
Mallet et al., 2007



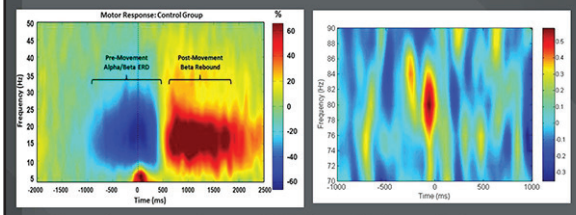
Clock-Paced Motor Tasks

Participants watch a "clock" to pace index finger movements

- One movement every six seconds
- When red dot reaches the blue dots near the "12:00 o'clock" position.



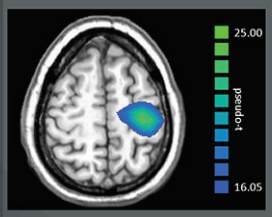
Movement-Related Oscillations



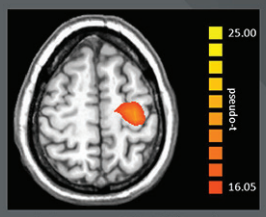
Beamformer analyses of MEG oscillatory activity

- Peri-movement beta ERD
- Movement-onset gamma response
- Post-movement beta rebound (ERS)

Neural Generators

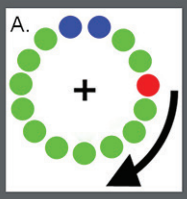


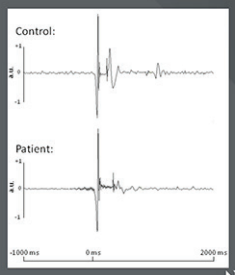
Pre-movement Beta ERD



Post-movement Beta Rebound

MEG Studies of Motor Function in PD

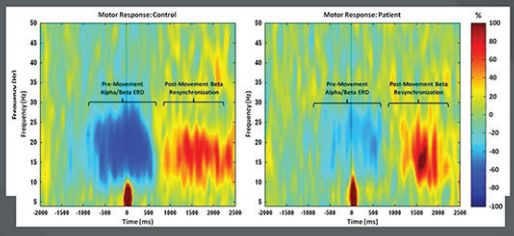




19 patients with PD were recorded in the practically-defined drug OFF state and after medication administration.

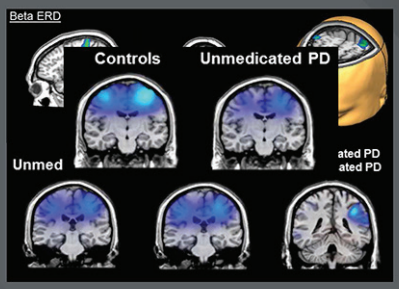
16 demographically-matched controls were also recorded

Time-Frequency Data



Heinrichs-Graham et al., 2014
Cerebral Cortex

Beamforming Results



Heinrichs-Graham et al., 2014
Cerebral Cortex

Conclusions

Patients with PD exhibit pathological beta oscillatory activity in the motor network.

Un-medicated patients are unable to "break through" this pathological beta synchronization during movement planning.

Beta abnormalities were limited to the primary motor cortices and supplementary motor area (PMBR) and eliminated by medication.

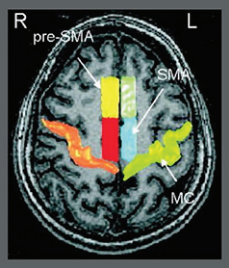
Spontaneous Beta Activity in PD

The intra-operative (DBS) studies interpreted beta synchrony as abnormal because it was decreased by DBS and symptoms improved.

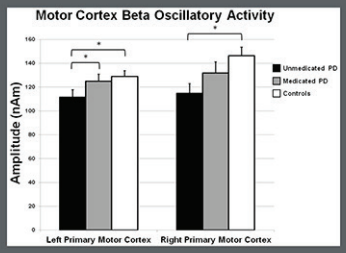
Primary Questions:

- Do unmedicated patients with PD exhibit aberrant cortical beta during rest compared to controls?
- Abnormal beta synchrony **and** amplitude?
- Effects of dopamine replacement therapy?

Brain Regions of Interest

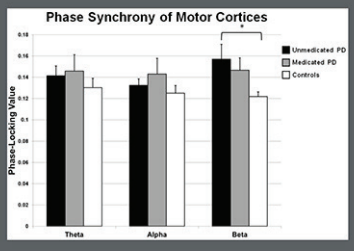


Beta-Specific Amplitude Deficits



Heinrichs-Graham et al., 2014
Journal of Neurophysiology

Beta-Specific Hyper-Synchrony



Heinrichs-Graham et al., 2014
Journal of Neurophysiology

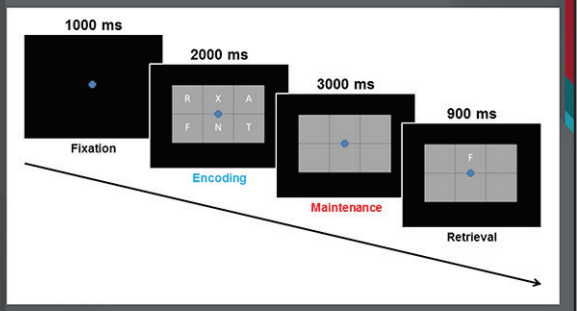
Conclusions

Un-medicated patients have reduced resting beta activity in the primary motor cortices, which is normalized by medication.

Un-medicated patients have hyper-synchrony between the primary motor cortices, which decreases after medication.

Both of these observations would be predicted based on the connectivity pattern of the basal ganglia-thalamo-cortical motor network.

Working Memory



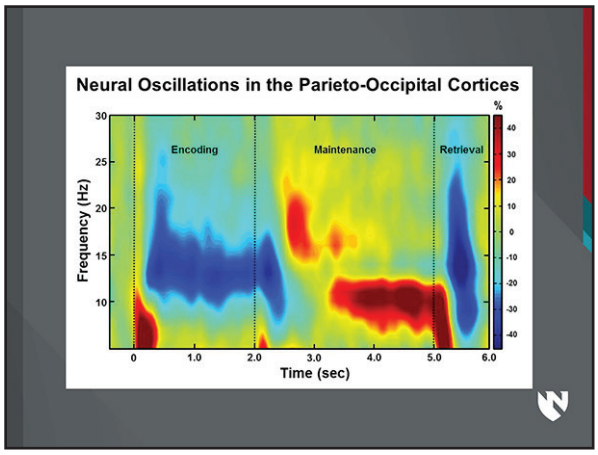
Participants & Performance

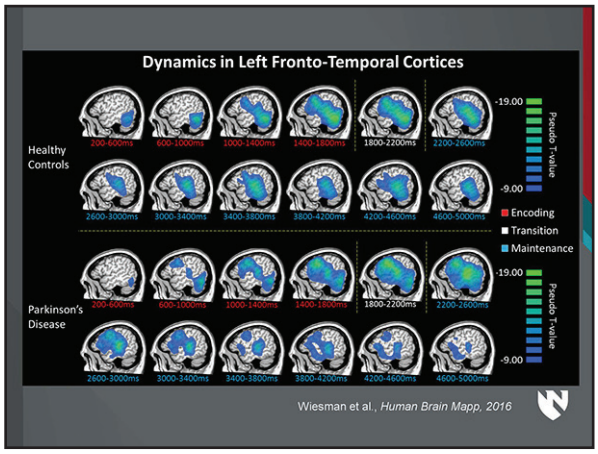
16 patients with PD (age: 63 yrs) recorded in the practically-defined drug off state

17 demographically-matched healthy adults

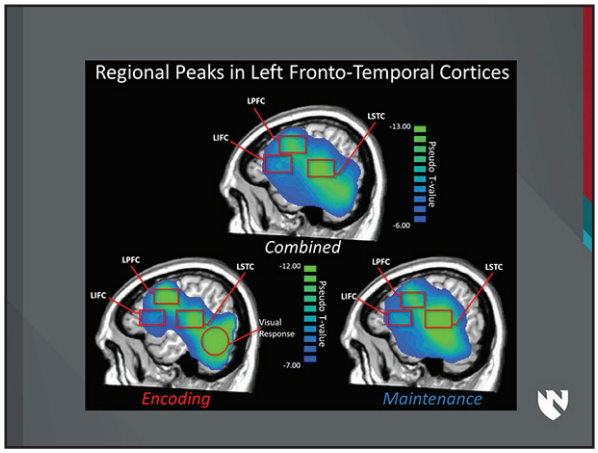
Patients with PD performed significantly worse on the working memory task (68% vs. 81%; p = 0.006)

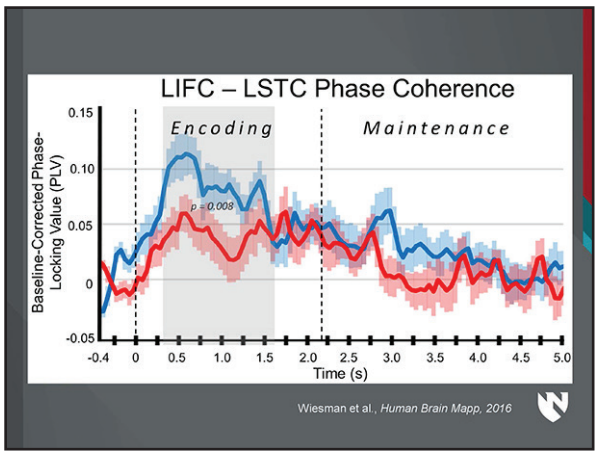
Only correct trials used in the analysis and we used the same number of mean trials per group





Wiesman et al., *Human Brain Mapp, 2016*




LIFC – LSTC Phase Coherence
Encoding
Maintenance
Baseline-Corrected Phase-Locking Value (PLV)
0.15
0.10
0.05
0
-0.05
p = 0.008
-0.4
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
Time (s)
Wiesman et al., Human Brain Mapp, 2016


DICoN Laboratory


University of Nebraska Medical Center
BREAKTHROUGHS FOR LIFE.
Nebraska Medical Center

Somatosensory cortical activity is related to the mobility and strength impairments seen in children with cerebral palsy

Max Kurz, Omaha

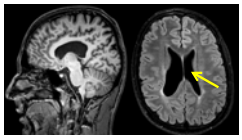
Cerebral palsy (CP) is a pediatric neurologic condition that results from a perinatal brain insult. Although the incurred brain damage does not progress, many of these children often display motor impairments that advance throughout development. This has fueled the clinical impression that these impairments primarily reside in the musculoskeletal system. However, this perspective has recently been redirected towards the possibility that the structural damage may actually ignite a cascade of neuroplastic changes that impact the cortical oscillations that underlie the processing of sensory feedback and production of motor actions. This presentation will provide an overview of a series of magnetoencephalography studies that we have conducted at the University of Nebraska Medical Center that are on the leading-edge of this new perspective. These experiments have shown that the cortices of children with CP display uncharacteristic neural oscillations in the beta-frequency (14-30 Hz) during the motor planning and execution stages of a target force matching motor task. Our experimental work has also revealed that the somatosensory cortical oscillations are uncharacteristic following peripheral stimulation of the foot, and that the somatosensensory cortices of children with CP may hyper-gate redundant peripheral stimulations. These uncharacteristic somatosensory cortical oscillations appear to be tightly coupled with the mobility and strength impairments seen in these children. Overall, these pioneering experimental results provide a new understanding of the nexus of the impaired motor actions seen in children with CP.

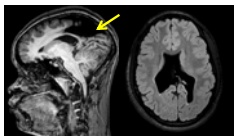
The Impact of Cerebral Palsy on the Neuromagnetic Cortical Oscillations

Max J. Kurz, PhD
UNMC Center for Magnetoencephalography
Department of Physical Therapy
Munroe-Meyer Institute for Genetics and Rehabilitation
University of Nebraska Medical Center

UNMC

Cerebral Palsy (CP)





- ~4/1000 children born in the United States have CP.
- Non-progressive brain defect or lesion that occurs in utero, during birth or shortly after.
- Total lifetime economic burden to our society is estimated to be nearly one million dollars per child.
- No direct correlation between degree of insult on the MRI and motor impairments.

Musculoskeletal Impairments

GMFCS I

GMFCS III

- Assume that the impaired motor actions reside in the musculoskeletal machinery.
- Musculoskeletal impairments can progress throughout development.
- Contractures, skeletal abnormalities, muscular weakness and poor coordination.

Treatment Trends

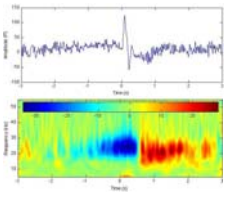
- **Orthopedic surgeries** directed at improving joint range of motion, realign bony structures, and alter muscle insertions.
- **Therapeutic strategies** focus on strength training and flexibility.
- Outcomes are often mixed and unreliable.

Research Goals

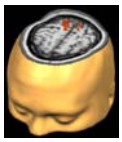
•Structural damage may promote neuroplastic changes that affect the brain activity that underlies the production of a motor action.

•To identify how CP affects the cortical oscillations that underlie the processing of sensory feedback and the execution of motor actions.

UNMC Center for MEG



- Elekta Neuromag System
- Time Frequency Representations
- Beamforming algorithm to identify the source of the cortical activity.

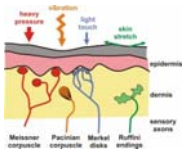


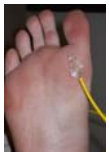
Sensory Deficits

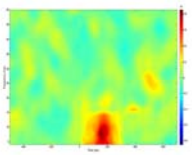
- Proprioception, stereognosis and tactile discrimination deficits.
- Neurophysiology of these sensory processing deficits are unknown.
- Link between the uncharacteristic sensory processing and motor impairments are unknown.

Sanger & Kukke (2007). J Child Neurol 22(3):289-93.
Wingert et al. (2008). Arch Phys Med Rehab 90:447-453.

MEG Methods







- Mechanoreceptors provide feedback about the pressures applied to the bottom of the foot.
- Sensory information from the foot is used for gait adaptations.
- Children with CP with GMFCS I-III (n=11) and aged-matched controls (n=11).
- Beamforming analyses was used to quantify the oscillations of the somatosensory cortices between 4-14 Hz.

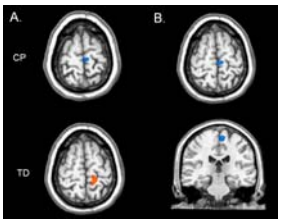
Kurz et al. (2014). J Neurophys, 111(3):573-9.
Kurz et al. (2015). J Neurophys, 113(9):3143-50.

Gait & Strength Methods

- Preferred and fast-as-possible walking speeds.
- Velocity, stride length and cadence.
- Ankle strength measured with an isokinetic dynamometer.

Kurz et al. (2014). J Neurophys, 111(3):573-9.
Kurz et al. (2015). J Neurophys, 113(9):3143-50.

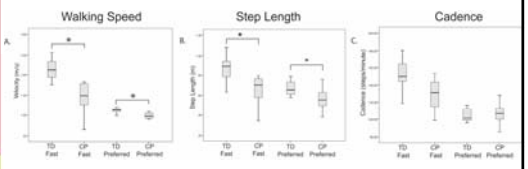
MEG Results



Somatosensory cortices of the children with CP were desynchronized with the tactile stimulation.

Kurz et al. (2014). J Neurophys, 111(3):573-9.
Kurz et al. (2015). J Neurophys, 113(9):3143-50.

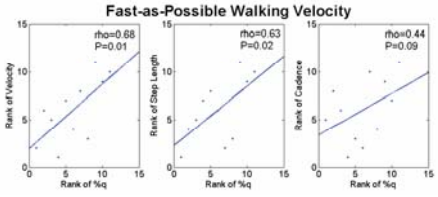
Mobility Results



Children with CP walked slower and used a shorter step length

Kurz et al. (2014). J Neurophys, 111(3):573-9.
Kurz et al. (2015). J Neurophys, 113(9):3143-50.

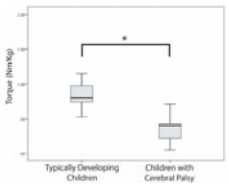
Correlations

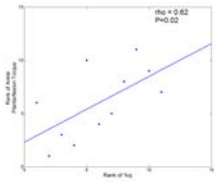


- Faster walking velocity was associated with greater synchronization within the somatosensory cortices
- Longer step length was associated with greater synchronization within the somatosensory cortices

Kurz et al. (2014). J Neurophys, 111(3):573-9.
Kurz et al. (2015). J Neurophys, 113(9):3143-50.

Strength Results





- Children with CP had weaker plantarflexors.
- Greater strength was associated with greater synchronization within the somatosensory cortices.

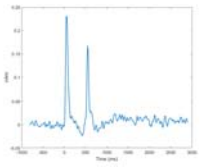
Kurz et al. (2014). J Neurophys, 111(3):573-9.
Kurz et al. (2015). J Neurophys, 113(9):3143-50.

Scientific Insights

- Activity within the somatosensory cortices is aberrant in children with CP.
- Uncharacteristic somatosensory activity is strongly linked with the mobility and strength impairments.

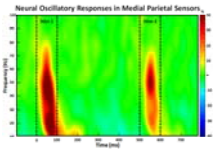
Sensory Gating

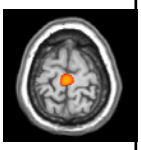
- Reduced cortical response to repetitive and redundant sensory information.
- Filtering of sensory information that does not provide new information.
- Uncharacteristic in individuals with schizophrenia, autism and Alzheimer's disease.
- Somatosensory gating mechanisms of children with CP is unknown.



Bramon et al. (2004). Schizoprenia Res 70(2-3):315-329.
Matsuzaki et al. (2014). PLoS One 9(7):e102599.
Jessen et al. (2001) Am J Psychiatry 158:1319-1321.

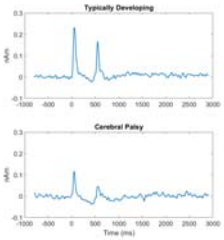
Sensory Gating Methods

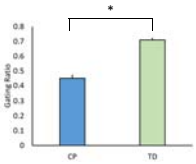





- Children with CP (n=15; Age = 15± 3 yrs.; GMFCS II-III) and TD children (n=20; Age = 14 ± 3 yrs.).
- Paired pulse electrical stimulation of the tibial nerve.
- Applied to the most affected leg of the children with CP and the non-dominant leg of the typically developing children.
- Beamformed 10-75Hz oscillatory activity.
- Extracted the time course from the peak voxel within the respective images.

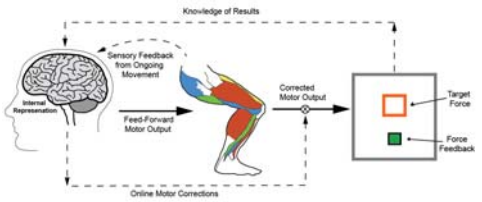
Results





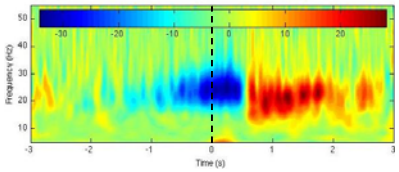
- Children with CP have weaker somatosensory activity.
- Children with CP have a hyper-gating response.
- May filter-out salient sensory information.

Scientific Insights



- Processing of sensory feedback is devoid in children with CP.
- Affects the development of the internal model that is used to predict motor actions that will successfully attain a goal.

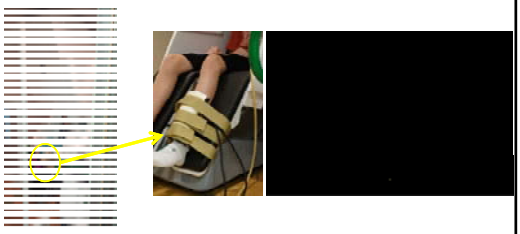
Beta Oscillations



- Zero is movement on set.
- Beta event related synchronization (ERD; 15-30 Hz) occurs prior to the onset of movement.
- Beta oscillations remain but become weaker during the movement.

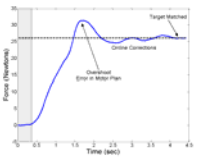
Heinrichs-Graham et al. (2014). Cereb Cortex 24(10):2669-2678
Tzagarakis et al. (2010). J Neurosci 30(4):11270-11277.
Wilson et al. (2010). Brain & Cognition 73(2):75-84.

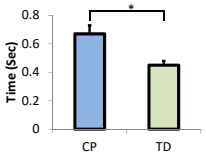
Methods

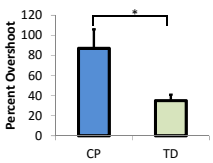


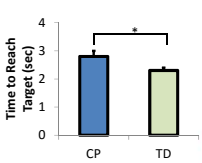
- 18 children with CP (GMFCS I-III) and 20 age-matched controls.
- Custom built magnetically silent force transducer.
- Beta ERD sensorimotor cortical activity imaged from -500 to 0 ms and 0 to 500 ms.
- Integrated biomechanical analysis of force production.

Behavioral Results

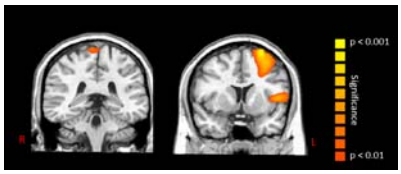






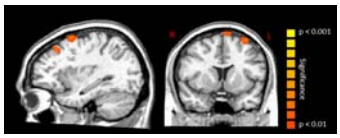


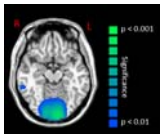
Motor Planning Results



- Children with CP had a stronger beta ERD than the TD children within the primary motor cortices, left premotor cortices and left inferior frontal gyrus.

Motor Action Results





- Children with CP had a stronger beta ERD in the left premotor, supplementary motor area (SMA).
- Children with CP had weaker beta ERD within the occipital cortices and visual/MT area.

Concluding Remarks

1. Activity of the somatosensory cortices is aberrant in children with CP.
2. Uncharacteristic somatosensory cortical activity related to motor impairments.
3. Atypical cortical activity during the planning and motor execution stages.
4. Uncharacteristic activity in the occipital cortices and MT/visual areas while performing visuomotor transformation.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What is cortico-kinetic coherence mapping

Xavier de Tiege, Brussels

ACMEGS
AMERICAN CLINICAL MEG SOCIETY

Comprehensive sensorimotor mapping

Xavier de Tiege, Brussels

ACMEGS
AMERICAN CLINICAL MEG SOCIETY

High-resolution MEG source imaging approach to accurately localize Broca's area

Roland Lee, San Diego

MEG inter-ictal high frequency oscillations: A potential biomarker of epilepsy surgical outcome

Jayabal Velmurugan, San Francisco

Compared to conventional interictal spikes mapping, the specificity of epileptogenic zone localization with HFO's is very high, and surgical removal of these tissues generating HFOs had resulted in a better outcome (Haegelen C et al. 2013, T Akiyama et al. 2011, Jacobs et al., 2010). The significance of non-invasively (MEG) interictal pathological high frequency oscillations (HFOs in 30-200Hz) in patients with focal epilepsies is relatively least known. The present study investigated thirty patients (M: F=21:9; age=23.1±9.5years) with drug resistant temporal (n=16), frontal(n=11), parietal(n=2) and occipital(n=1) lobe epilepsies underwent MEG recording as a part of pre-surgical evaluation. Surgical resection of the presumed epileptogenic zone was performed, and outcomes were assessed after a follow-up of 16.8±6.6 months. IED (33±8.4/patient) were extracted and time-frequency decomposition was computed with at 30-80Hz (gamma band or γ) & 80-200Hz (ripple band or Ŕ). It was subjected to source localization over a cortical grid using an adaptive spatial filter. Congruency of HFO source localization with resection areas was estimated and compared. Kappa(k) statistics were computed to measure inter-HFO band (γ/Ŕ) localization with resection areas. Occurrence of HFOs prevailed during IED (n=25;83.3%) than pre-IED (n=14;46%) and post-IED (n=6;20%) period. The HFO spectral power (fT2/Hz) ratio of IED to pre-IED was significantly greater ($p<0.05$) than IED to post-IED, among all patients. Better concordance of HFO source localization with presumed epileptogenic zones was observed in 26/30(γ) and 22/30(Ŕ) patients. Multi-lobar/widely distributed HFO localization were noted in 4/30(γ) and 8/30patients (Ŕ). Among 26 patients with Engel, I outcome, 24(92.3%; γ) & 21(95.4%; Ŕ) had concordant HFO localization. Among four patients with poor outcome (Engel-III&IV), 1(25%; γ) & 3(75%; Ŕ) had multilobar distributed HFO localization. Inter-agreement between HFO localization and surgical resection areas were substantial [k=0.78(γ)&0.81(Ŕ); S. E=0.08]. Patients with multilobar Ŕ epileptogenic activity ($p=0.04$) had a poorer outcome than with γ activity ($p=0.36$). The congruency of HFO activity corresponded with the surgical resection sites in >92% of the patients. Focal HFOs could predict patients with better outcome (92.3 to 95.4%). Multilobar HFOs in Ŕ better-predicted patients with poorer outcome. These observations suggest that interictal MEG HFOs could reliably be used as a biomarker for localizing the epileptogenic zone and predicting the surgical outcome.

Inter ictal high frequency oscillations (30-80Hz) & (80-200Hz) on magnetoencephalography (MEG) in patients with drug resistant epilepsy: Comparison with clinical outcomes

Velmurugan Jayabal

Visiting fellow (Fulbright fellowship) Department of Radiology & Bio-medical imaging, University of California, San Francisco

UCSF University of California San Francisco

Department of Clinical Neurosciences & Department of Neurology, NIMHANS (National Institute of Mental Health &Neurosciences), India

1

Conflict of interests:

None

2

Rationale:

- High frequency oscillations (HFOs) (80 to 200 Hz) are being recognized as EEG markers for epileptic tissues (*Jacobs et al., 2012*).
- HFOs in focal epilepsy were studied with intracranial depth & subdural electrodes *(Bragin et al., 1999; Staba et al., 2002;Jacobs et al., 2008; Ochi et al., 2007)* and less frequently on scalp EEG *(Andrade-Valenca et al., 2011; Zelmann et al., 2014)*.
- Compared to conventional inter-ictal spikes mapping, the specificity of epileptogenic zone localization with HFO's is very high and surgical removal of these tissues generating HFOs had resulted in better outcome (*Haegelen C et al 2013, T Akiyama et al 2011, Jacobs et al., 2010).*
- Though few studies had investigated MEG HFOs in patients with epilepsy (*Van Klink et al 2016, Von Ellenrieder et al 2016*), nevertheless, the epileptogenicity of these HFO sources detected in MEG had never been validated or compared with their clinical outcome
- Therefore, the significance of non-invasively detected inter-ictal pathological high frequency oscillations (HFOs in 30-200Hz) during MEG in these patients with focal epilepsies is relatively less known compared to studies with other modalities.

3

Aim of the study:

To investigate the role of inter-ictal HFO sources with MEG in patients with pharmacologically intractable epilepsies undergoing surgery.

Objectives of the study:

i. To assess sensor-level spatiotemporal topographies of inter-ictal HFOs

ii. To localize inter-ictal HFOs observed in MEG

iii. Establish the role of HFO localization in surgical outcome.

4

Methods:

Number of patients	N=30 (Male = 21)
Age of the patients	**23.1±9.5** years
TLE (Temporal)	**16**
ETLE (Extra-temporal)	**14** Frontal =11 Parietal= 2 Occipital= 1

- Subjects underwent all pre-surgical investigations (presumed EZ →surgery)
- MEG data duration : 90 min/subject
- Sampling rate : 2000Hz
- Analysis : Field trip & Brainstorm
- Statistics : SPSS 21
- For co-registration : T1 MPRAGE MRI sequence
- Post-surgical outcome: **16.8±6.6 months** (at least after 1 year)

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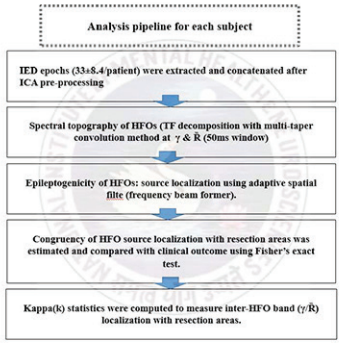


6

Clinical parameters of the subjects

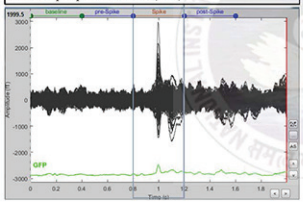
S.NO	Age	Gende	MRI	Presumed EZ	HPE	port surgical f/u	Outcome
1	25	m	left arachnoid cyst	Left temporal lobe	HS-I, porencephalic cyst	18 months	Engel I
2	32	f	Right MTS	right temporal lobe	MTS-IA	12	Engel I
3	10	m	Right temporal DNET	Right temporal lobe	MTS-IA	15	Engel I
4	22	m	Left med. temp. gliosis	Left temporal lobe	MTS-IA, calcified cyst on h	13	Engel I
5	20	m	Left MTS	Left temporal lobe	MTS-IA	21	Engel I
6	25	m	Left MTS+DNET	Left temporal lobe	Ganglioglioma	34	Engel I
7	39	m	Left MTS	Left temporal lobe	HS-ILAE Type1	30	Engel I
8	26	f	Right MTS	Right temporal lobe	MTS-IA	14	Engel I
9	43	f	Left mts	Left temporal lobe	MTS-IA	17	Engel I
10	18	m	Left temporal GW diff. loss	Left temporal lobe	MTS-II	14	Engel I
11	29	m	Left MTS	Left temporal lobe	MTS Ib	24	Engel I
12	39	m	Rt. MTS + Left temporal cyst	Right temporal lobe	MTS Ii	22	Engel I
13	34	m	Left MTS	Left temporal lobe	HS-I	12	Engel I
14	40	m	Left MTS	Left temporal lobe	MTS-IA	12	Engel I
15	19	f	Right MTS	right temporal lobe	MTS Ib	13	Engel I
16	12	f	Left MTS	Left temporal lobe	MTS-IA	27	Engel I
17	18	m	Right frontal FCD	Right frontal lobe	FCD IIb	14	Engel I
18	18	m	Left frontal DNET(ant. To motor)	Left frontal lobe	DNET (low grade glioneur	12	Engel I
19	23	m	Right frontal cavernoma	Right frontal lobe	Cavernoma	16	Engel I
20	11	f	Right medial & basifrontal FCD	Right basifrontal lobe	Ganglioglioma	14	Engel I
21	18	m	Left MFG FCD type II	Left frontal lobe	FCD IIb	12	Engel III
22	17	m	Right frontal FCD	Right frontal lobe	FCD IIb	8	Engel I
23	43	f	Left sup. Frontal DNET	Left frontal lobe	Anaplastic oligoastrocyto	12	Engel III
24	10	m	Left frontal ganglioglioma	Left frontal lobe	FCD IIb	12	Engel I
25	23	m	Left frontal cortical thickening	Left frontal lobe	FCD IIb	15	Engel I
26	16	m	Left MFG cavernoma	Left frontal lobe	Cavernous angioma	13	Engel I
27	14	m	Left frontal FCD (IFG)	Left frontal lobe	FCD Ic	12	Engel I
28	11	f	Right parietal gliosis	Right parietal lobe	FCD IIb (parito-temporal)	14	Engel II
29	16.5	m	Left post temporal/ parietal DNET	Left parietal lobe	Ganglioglioma (left pariet	17	Engel I
30	14	m	Left occipital gliosis	Left occipital lobe	FCD IIa with polymicrogyr	14	Engel III

7

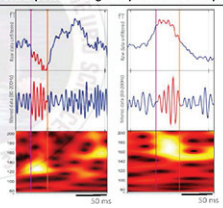
Results:

(I) TLE: 25 year old gentle man (#P6)who was diagnosed with right temporal lobe DNET concordant with all pre-surgical investigations underwent MEG before surgery

Peri-IIED epochs (n=3) were extracted and concatenated, from the pre-processed data (ICA)

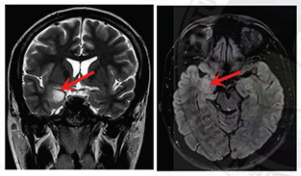


HFOs in the raw unfiltered and filtered traces with spectral power changes in pre-IED and IED period

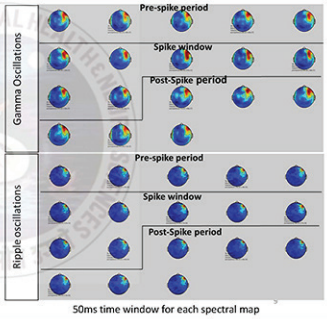


Results:

(I) TLE: 25yr/m diagnosed with right temporal DNET



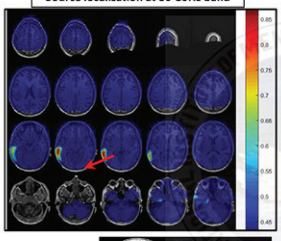
Spatio-temporal assessment



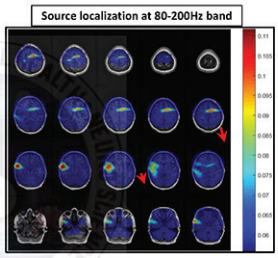
50ms time window for each spectral map

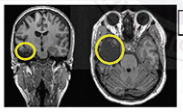
Results:

Source localization at 30-80Hz band



Source localization at 80-200Hz band



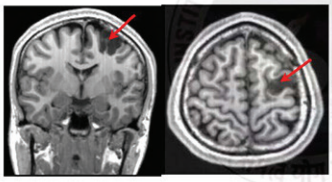


Rt. temporal post-op cavity

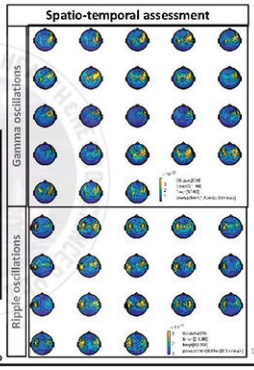
Histopathology : Ganglioglioma
Post-op follow up : 34 months
Clinical outcome : Engel-I

Results:

(II) ETLE: 18yr/m diagnosed with left frontal DNET anterior to motor cortex



Spatio-temporal assessment

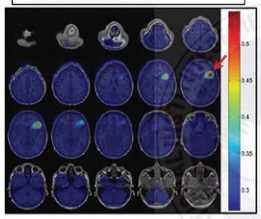


50ms time window for each spectral map

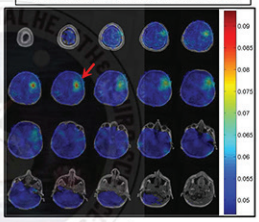
11

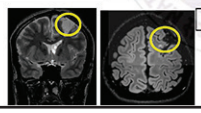
Results:

Source localization at 30-80Hz band



Source localization at 80-200Hz band

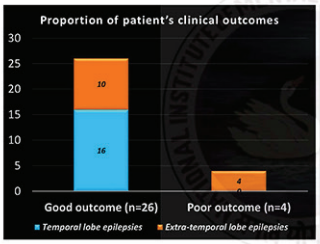


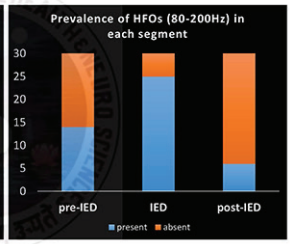


Lt. frontal resection cavity

Histopathology : low grade glioneural tx (DNET)
Post-op follow up : 13months
Clinical outcome : Engel-I

12





13

Results:

Table 1: ***Concordance rate of focal HFO localization with EZ/ surgical resection area (R)***

Gamma band localization	26/30
ripple band localization	22/30
Presumed EZ is defined from clinical semiology, MRI, video EEG, and PET scan (if any)	

Table 2: ***Inter-agreement between HFO localization & surgical resection areas***

	Gamma frequency band	Ripple frequency band
Kappa statistics	0.78 (S.E=0.08)	0.81 (S.E=0.08)

substantial (good) agreement

Table 3	Sensitivity	Specificity
Gamma band source localization	88.9%	33%
Ripple band source localization	80.77%	75%

Summary of the study:

- The prevalence of HFOs (80-200Hz) and their spectral density was higher during IED segment.
- HFOs source localization (gamma &ripple band) during IED had a good **spatial concordance rate of ~92%** with the surgical resection site.
- Patients who showed **very focal MEG HFO localization had a very good clinical outcome** and patients who had **multi-lobar HFO localization in ripple band had poorer clinical outcome** (p=0.04) at the post-surgical follow up assessment. These results are comparable to the results of inter-ictal HFOs studies using invasive EEG (*Haegelen C et al 2013, T Akiyama et al 2011, Jacobs et al 2010*).
- Limitation: The **morphological characteristics** *(Burnos et al 2016)*, **quantification** (*Van Klink et al 2016*), and **classification** *(Dumplemann et al 2015)* **of these inter-ictal HFOs** are required to be performed in this cohort of temporal & extra-temporal lobe epilepsies.
- The present study attempted to study the **electrophysiological and clinical role of HFOs** with the surgical outcome in patients with DRE. The findings suggests that these **inter-ictal MEG HFOs** could reliably be used as a **biomarker in localizing the epileptogenic zone** and might aid in predicting the **surgical outcome**

15

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Dr. Heidi Kirsch
Staffs and students of
Speech Neuroscience lab

Benefits of Combined MEG/EEG in Presurgical Evaluation of Epilepsy: A Study of 250 Patients

Michael Wagner, Hamburg

Rationale

Combined Electroencephalography (EEG) and Magnetoencephalography (MEG) recordings of epileptic spikes can be used to assess, how well either modality alone or the combination of both allow for the characterization of epileptiform brain activity. Such insight may aid in deciding whether simultaneous EEG should be part of a planned MEG acquisition, or whether MEG should be performed in addition to EEG.

Methods

At Overlook Medical Center (Summit, NJ, USA), over the course of the last three years (2014 to 16), 297 patients were recorded using simultaneous MEG and EEG. 306 channels of MEG (Elekta Triux, Helsinki, Finland) and 25 channels of EEG (standard 10-20 plus 3 subtemporal channels bilaterally) were used. Spikes of similar voltage and/or magnetic field topography were averaged. Realistic boundary element head models were created based on patients' individual MRIs. ECDs were calculated for both EEG and MEG data. The resulting 297 reports were charted retrospectively. Spikes showing synchronous EEG and MEG activity but displaced ECDs were additionally analyzed using cortical Current Density Reconstruction (CDR) with cortical orientation and connectivity constraints. All data analysis was performed using the Curry software (Compumedics, Charlotte, NC, USA).

Results

A total of 656 spike types were identified. In 49% of patients, simultaneous EEG helped identify and characterize additional spike types compared to MEG alone, while MEG was able to augment EEG in 17% of patients. 42% of spike types were synchronous in EEG and MEG. For every sixth of those, however, EEG and MEG ECDs did not co-localize. Mostly, these were EEG ECDs in the temporal lobe tip that had counterpart MEG ECDs posteriorly displaced by two or more centimeters. This source location ambiguity was resolved in all cases by cortical CDR that co-localized both EEG and MEG generator cortex to the tip of the temporal lobe.

Conclusion

Combined EEG and MEG recordings are beneficial over either modality alone. Situations where dipole results are ambiguous regarding source cortex or where EEG and MEG dipoles do not co-localize can be resolved by using cortical CDR methods.

Benefits of Combined MEG/EEG in pre-Surgical Evaluation of Epilepsy: a Study of 297 Patients

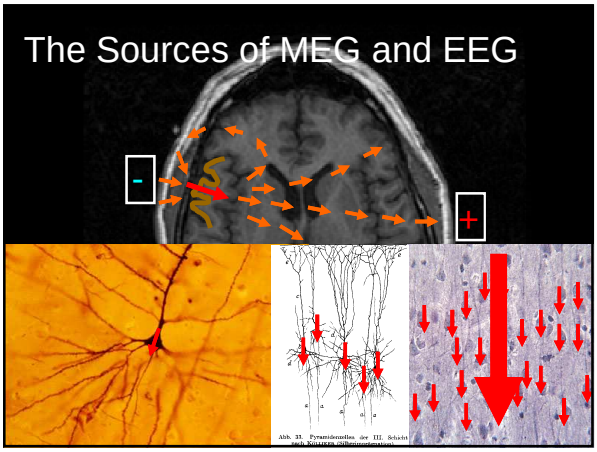
Michael Wagner[1], John S. Ebersole[2]

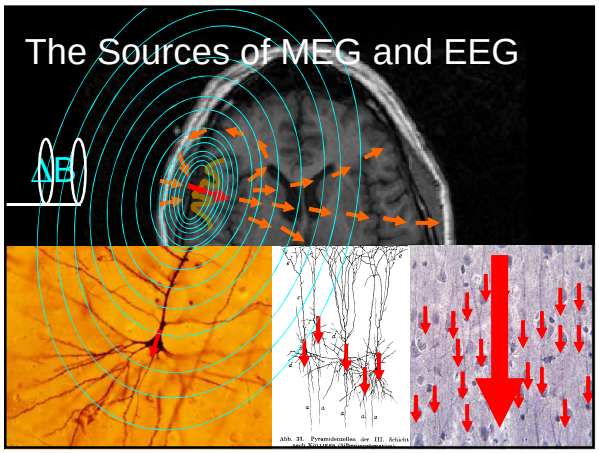
[1]Compumedics Neuroscan, Hamburg, Germany
[2]Overlook Medical Center, Summit, NJ

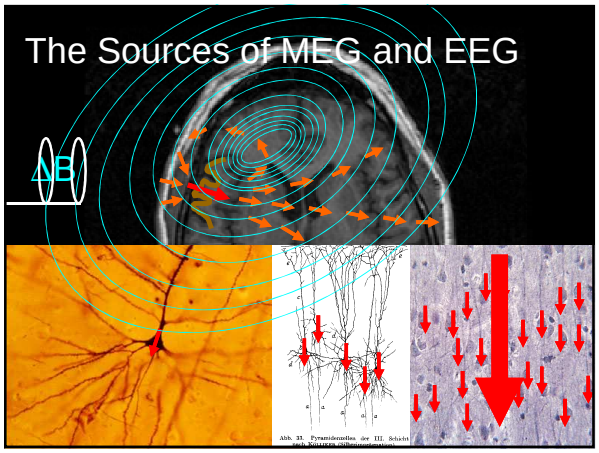
Disclosures

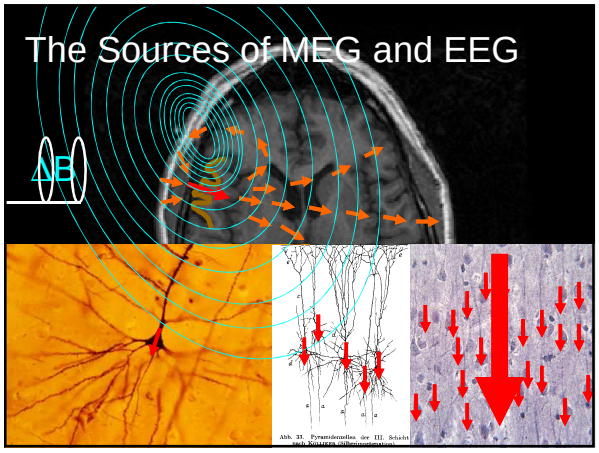
- Michael Wagner
  - Compumedics: employee
- John Ebersole
  - Compumedics: Medical Advisory Board member

The Sources of MEG and EEG




The Sources of MEG and EEG
ΔB


The Sources of MEG and EEG
ΔB

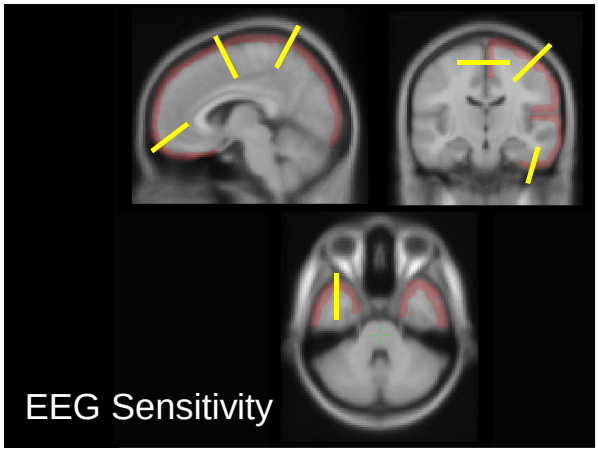

The Sources of MEG and EEG
ΔB

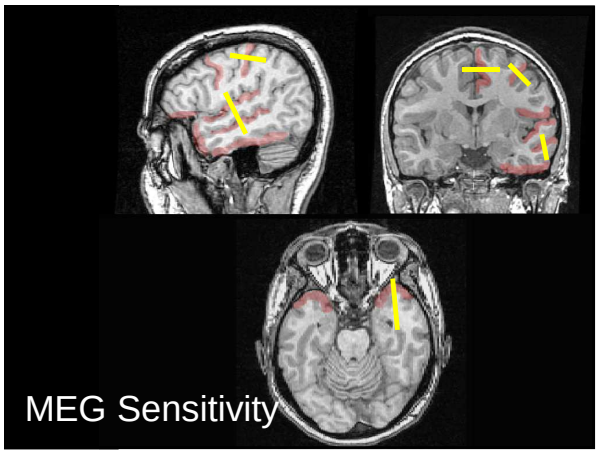
EEG/MEG Characteristics

EEG	MEG
Smaller No. of channels	Larger No. of channels
Sees tangential sources	Even better
Sees radial sources	No
Sees deep sources	Not so much
Head modeling important	Not so much
Lower SNR	Higher SNR
> 10 cm²	> 4-6 cm²

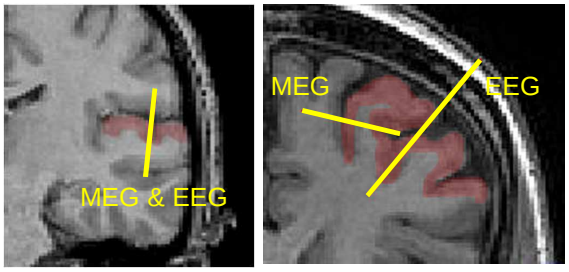
EEG/MEG are Complementary

EEG	MEG
Smaller No. of channels	Larger No. of channels
Sees tangential sources	Even better
Sees radial sources	No
Sees deep sources	Not so much
Head modeling important	Not so much
Lower SNR	Higher SNR
> 10 cm²	> 4-6 cm²





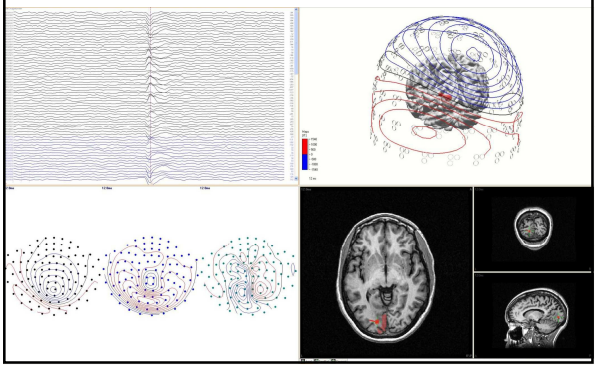
What EEG and MEG See



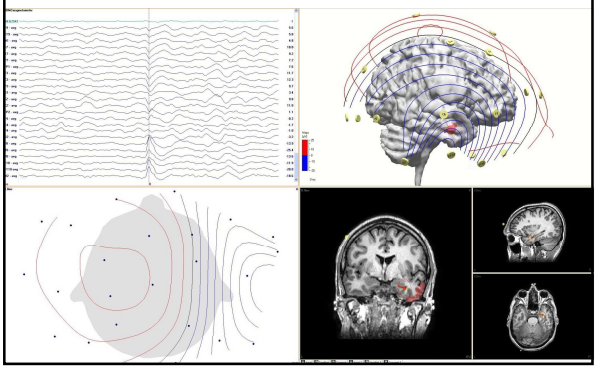
Same Different

Dipoles

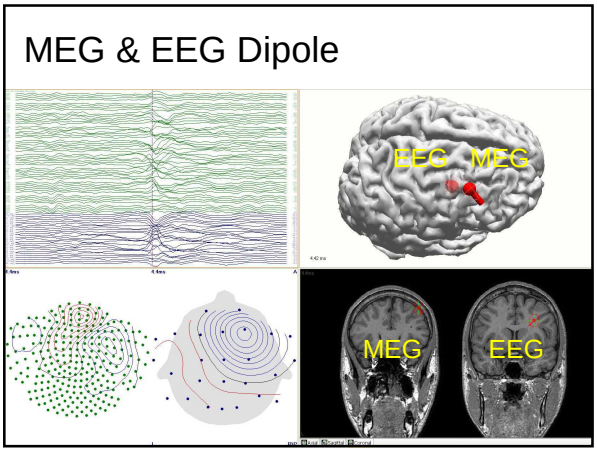
MEG Dipole



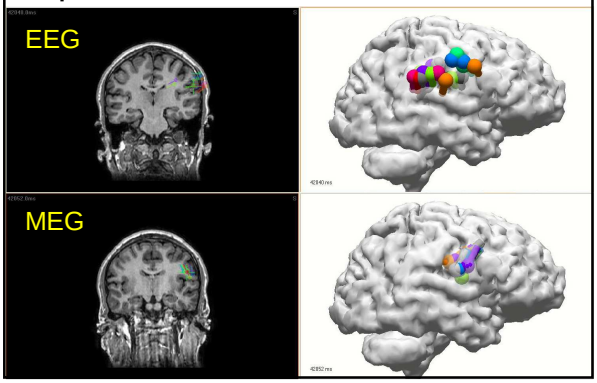
EEG Dipole



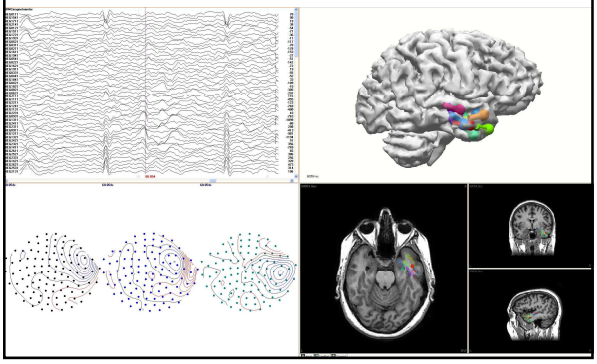
MEG & EEG Dipole



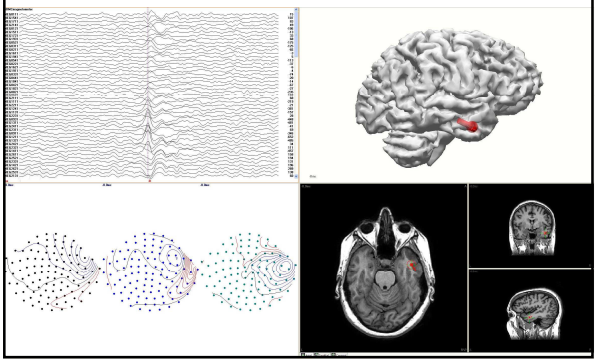
Dipole Clusters



Clustering vs. Spike Averaging



Clustering vs. Spike Averaging



MEG/EEG Scenarios

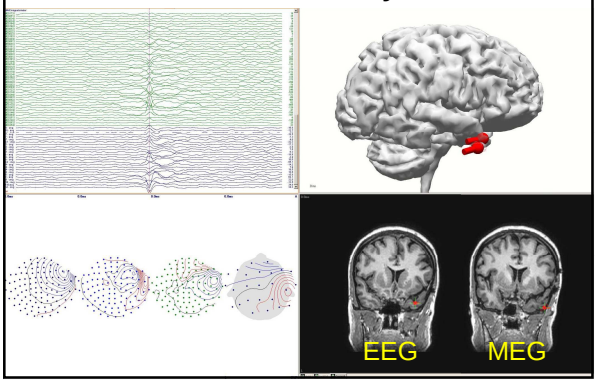
Scenarios

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

MEG Tan, EEG Tan, Sync

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

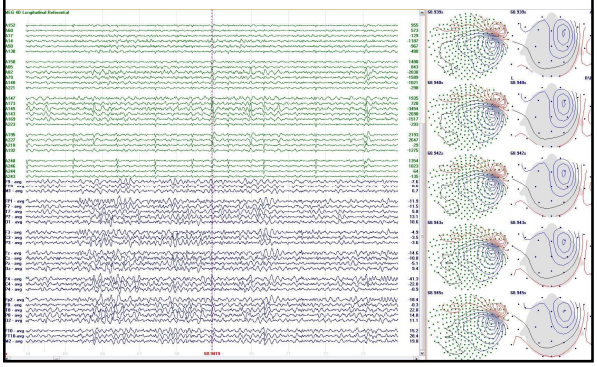
MEG Tan, EEG Tan, Sync



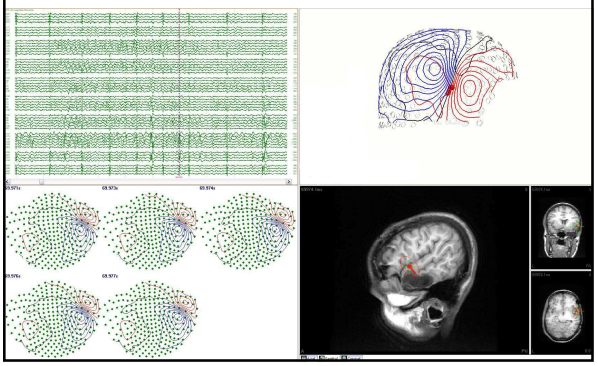
MEG Tan, no EEG

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

MEG Tan, no EEG



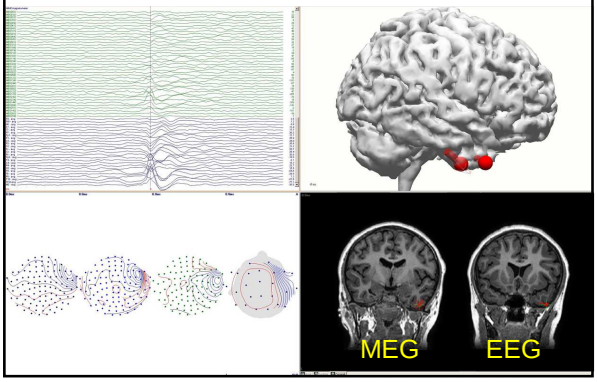
MEG Tan, no EEG



MEG Tan, no EEG

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

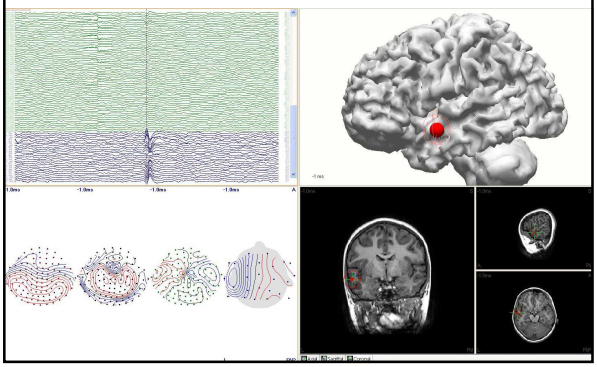
MEG Tan, EEG Rad, Syncc



No MEG, EEG Rad

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

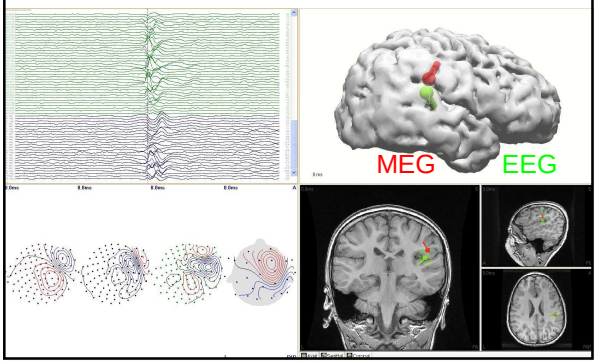
No MEG, EEG Rad



MEG Tan, EEG Any, MEG Leads

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

MEG Tan, EEG Any, MEG Leads



MEG Tan, EEG Any, EEG Leads

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
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Tan	Any	MEG leads	(radial comp. of prop.)
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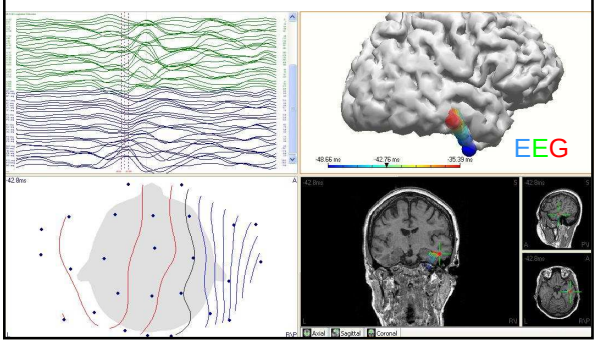
MEG Tan, EEG Any, EEG Leads



EEG alone Sees all Aspects

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

MEG alone Sees all Aspects

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

MEG+EEG see all Aspects

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

EEG adds Crucial Information

MEG	EEG	Synchrony	EEG Adds
Tan	Tan	Sync	-
Tan	-	-	-
Tan	Rad	Sync	Radial component
-	Rad	-	Location, orientation
Tan	Any	MEG leads	(radial comp. of prop.)
Tan	Any	EEG leads	Location, orientation

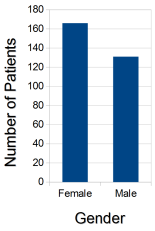
A Study of 297 Patients

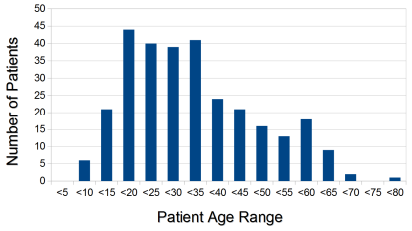
Study Characteristics

- Overlook Hospital, Summit, NJ
- January, 2014 to December, 2016
- 297 reports evaluated
- Elekta MEG+EEG (306+25 channels)
- Curry software
  - Spike marking
  - Spike detection using template morphology
  - Realistic BEM head models
  - Dipole analysis
  - Overlay with MRI-derived anatomy

Study Characteristics

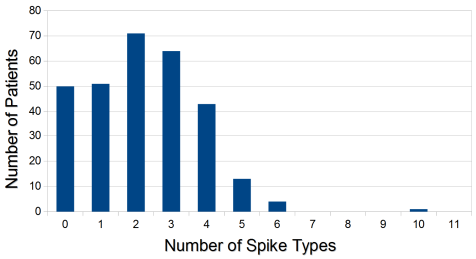
- Overlook Hospital, Summit, NJ
- January, 2014 to December, 2016
- 297 reports evaluated





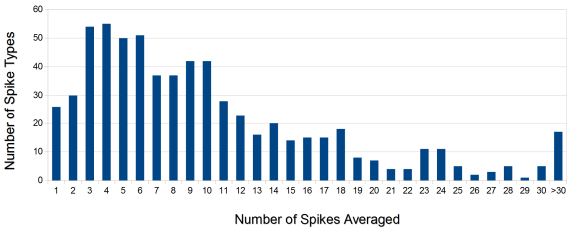
Study Characteristics

- 297 reports evaluated
- 656 spike types (model-worthy)

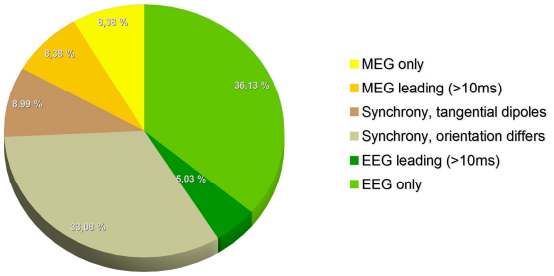


Study Characteristics

- 297 reports evaluated
- 656 spike types (model-worthy)
- spike averaging (manual or template-based)

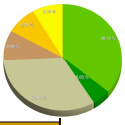


Scenarios



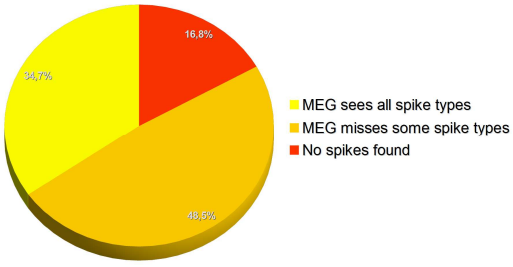
Percentage of Spikes

Scenarios



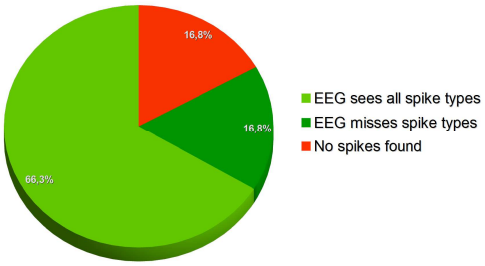
MEG	EEG	Synchrony	
Tan	Tan	Sync	9.0%
Tan	-	-	8.4%
Tan	Rad	Sync	33.1%
-	Rad	-	36.1%
Tan	Any	MEG leads	8.4%
Tan	Rad	EEG leads	5.0%

MEG misses Spike Types



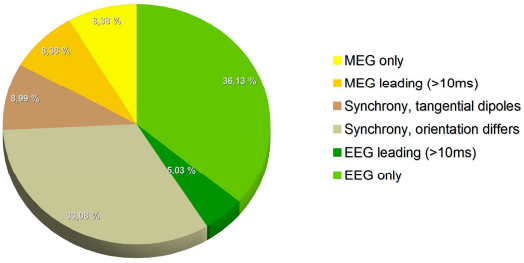
Percentage of Patients

EEG misses Spike Types



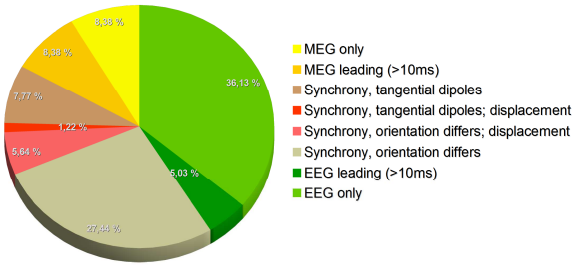
Percentage of Patients

Synchrony



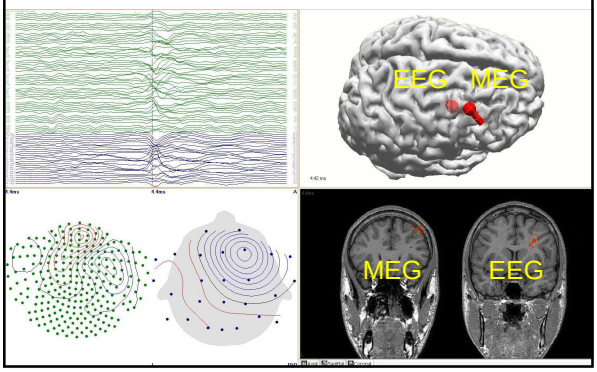
Percentage of Spikes

Synchrony and Displacement

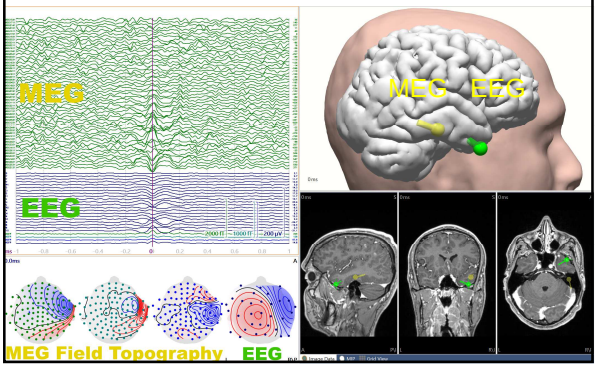


Percentage of Spikes

Displacement Scenarios

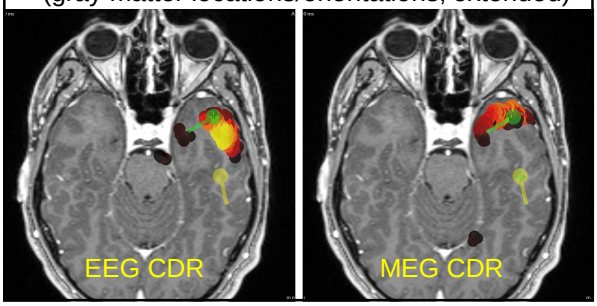


Displacement Scenarios



Displacement Scenarios

- Resolved by Currend Density Analysis (gray matter locations/orientations, extended)



Conclusions

- Simultaneous EEG-MEG
  - augmented MEG alone in 49% of patients
  - augmented EEG alone in 17% of patients
- Synchronous EEG / MEG spikes
  - account for 42% of spikes
  - 7% of spikes are synchronous with ECD displacement
- ECD displacement
  - mainly for temporal lobe spikes
  - resolved by cortical CDR

Coworkers

Overlook Hospital
- John Ebersole
- Jeffrey Politsky
- Joseph Camerone

Compumedics Neuroscan
- Curtis Ponton
- Manfred Fuchs
- Jörn Kastner
- Reyko Tech
- Fernando Gasca

The State of MEG Fellowships
Update and Announcements on MEG/EEG-Technologist Activities

Richard C. Burgess, Cleveland

ACMEGS
AMERICAN CLINICAL MEG SOCIETY

What's on the Horizon: Vendor Innovations and Plans

Compumedics – Curtis Ponton, PhD, Vice President, Chief Science Officer
Elekta – Mikkaa Putaala, Director, Business Line MEG
York Instruments - Gordon J. Haid, Vice President, Global Sales and Marketing
Ricoh - Takahito Uga, Marketing Senior Manager

AMERICAN CLINICAL MAGNETOENCEPHALOGRAPHY SOCIETY
2017 Annual Conference ♦ February 9, 2017

Evaluation Form

Please identify yourself: ☐ Neurologist ☐ Neurosurgeon ☐ Radiologist

☐ MEG/EEG Technologist ☐ Other _____

Please rate each speaker's effectiveness in conveying the material of his/her presentation using 5 as most effective and 1 as least effective:

	Most Effective				**Least Effective**	
Faculty						**Comments**
Stefan Rampp	5	4	3	2	1	
Adham Elshahabi	5	4	3	2	1	
Ernst Rodin	5	4	3	2	1	
Kamalini Ranasinghe	5	4	3	2	1	
Tony Wilson	5	4	3	2	1	
Max Kurz	5	4	3	2	1	
Xavier de Tiege	5	4	3	2	1	
Roland Lee	5	4	3	2	1	
Jayabal Velmurugan	5	4	3	2	1	
Michael Wagner	5	4	3	2	1	

Please rate using 5 as most effective and 1 as least effective:

Rate your overall satisfaction with the opportunity to network with colleagues.	5	4	3	2	1
Rate your overall satisfaction with the quality of this conference/workshop.	5	4	3	2	1
Please rate your satisfaction with the organization of the conference/workshop.	5	4	3	2	1
How would you rate the cost of registration versus what you personally got out of the conference?	5	4	3	2	1

What topics should be addressed at future meetings?

What features should be added to future meetings?

What features should be deleted from future meetings?

.

Did you perceive commercial bias in any of the presentations? ☐ Yes ☐ No
Explain: