Centre of Excellence for Epilepsy: A paradigm shift in Neuroscience research

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Understanding development of diseased state in the human brain is complicated!
Center of Excellence for Epilepsy Research

(A Department of Biotechnology funded collaborative project of National Brain Research Centre, Manesar & All India Institute of Medical Sciences, New Delhi)

**MEG and Brain Mapping Facility**

Manjari Tripathi, Professor, Neurology AIIMS  
P Sarat Chandra, Professor, Neurosurgery, AIIMS  
Subrata Sinha, Director, NBRC  
Parvat Mandal, Professor, NBRC  
Ajay Garg, Addl Professor, Neuroradiology, AIIMS  
CS Bal, Professor, Nuclear Medicine, AIIMS  
Arpan Banerjee, Associate Professor, NBRC

**Clinical Electrophysiology Lab**

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Sheffali Gulati, Addl Professor, Pediatric Neurology, AIIMS  
VK Paul, Professor & Head, Pediatrics, AIIMS

**Epilepsy Surgery Facility**

P Sarat Chandra, Professor, Neurosurgery, AIIMS  
BS Sharma, Professor and Head, Neurosurgery, AIIMS

**Prof. P. N. Tandon Epilepsy Neurobiology Lab**

Jyotirmoy Banerjee, Asst Professor, NBRC  
Aparna Dixit, Asst Professor, NBRC  
Chitra Sarkar, Professor Neuropathology, AIIMS
Of 50 million people with epilepsy worldwide, ~80% reside in resource-poor countries.

- 10 million in India
- 30% of all neurological disorders

30% of the total epilepsy patients suffer from Drug-Resistant Epilepsy

- 10 million in India
- 30% of all neurological disorders

Urban: 2 - 3 Million
Rural: 6 - 7 Million
Life time prevalence: 2%
DRUG RESISTANT EPILEPSY (RE)

• may be identified early in the course of disease
• Is also “de novo”

• Failure to first drug: only 30% chance of responding to second drug
• Failure to the second drug: <1% chance to respond to the third drug
• Newer AEDs do not significantly change the above-mentioned equations, and in countries like India, only increase the cost burden.

Patient has to undergo resective surgery!
While success in 75% offers the only hope for these patients (otherwise <1% chances of cure) - failure of 1/3 rd is also NOT trivial.

Complexity of epileptogenicity

Seizure control

<table>
<thead>
<tr>
<th>Complexity</th>
<th>Seizure Control</th>
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<tbody>
<tr>
<td>Low</td>
<td>Complete</td>
</tr>
<tr>
<td>Moderate</td>
<td>Improved</td>
</tr>
<tr>
<td>High</td>
<td>Absent</td>
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35% Not seizure-free
65% Seizure-free

15% Seizures not improved
20% Seizures improved
40% Seizure-free on AEDs
25% Seizure-free and off AEDs (cured)

Long-term results of resective surgery
Accurate localization of epileptogenic zone

We need a better picture!!

The most common cause of failed epilepsy surgery is thought to be inaccurate localization!

“Folks, the main reason you’re not getting a good picture is because you bought yourselves a microwave oven.”
In Epilepsy surgery, lesion ≠ area of electrical generation

In many cases with intractable epilepsy, no structural abnormality, only functional derangement of abnormal neural networks

These abnormal ‘epileptogenic zone’ is still not well-defined.
Understanding Epileptogenic Network Associated with DRE: A Multidisciplinary Approach

- Imaging Techniques eg. PET, SPECT, MRI
- Electrophysiology eg. EEG, ECoG
- Advanced Techniques eg. MEG
- Fluctuation/Noise analysis of Electrical Data
- Non-regression analysis of Electrical Data
- Immuno-histochemistry for synaptic markers
- Gene Expression studies
- Cellular Electrophysiology eg. patch-clamp

Advanced MEG facility for better localization of epileptogenic zone

A 10,000 sq feet facility built at NBRC, with 3 floors including a reception, a 8 bedded male and female bedded ward, and seminar room. The MEG is lodged in a separate magnetically shielded room. The facility is ready and the training of personnel has also been accomplished. 458 patients with drug resistant epilepsy have been studied so far.

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<td>HIMACHAL</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td><strong>458</strong></td>
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Advantages of MEG

- Detects abnormal Functional state in absence of anatomical abnormalities
- Non-invasive, real time, small duration (1-3 hrs), easy for children.
- High level of spatial resolution: unlike functional MRI (fMRI) and positron emission tomography (PET).
- No distortion while passing through skull

Also very useful:
- Mapping eloquent cortex
- Mapping language dominance
- Dementia and aging
- Psychiatric disorders
- Traumatic Brain Injuries

Superconducting QUantum Interference Devices: “SQUID”s
MEG is the ‘key element’ of the centre

MEG involves the measurement of neuromagnetic signals emanating from the brain. Magnetic activity measured outside the head is produced primarily by intracellular electrical currents.
MEG: Higher Resolution

- **MEG**: Higher Resolution
- **EEG**: 1 msec
- **fMRI**: 1 sec
- **CT**: 10 min
- **MRI**: 1 min
- **PET**: 1 hour
- **SPECT**: 10 min

Time Resolution (sec)

Spatial resolution (mm)
Synchronization of MEG data over NKN

NBRC LAN

VPN LINK

NKN

VPN LINK

AIIMS LAN

MEG DATA SERVER-1

VPN LINK

MEG DATA SERVER-2

VPN LINK

DAQ LAN

MEG LAN-1

MEG LAN-2
Why NKN is important?

• NKN is providing unified high-speed network connectivity between NBRC, Manesar and AIIMS, New Delhi.

• The MEG data acquisition for each patient and its subsequent analysis are of several gigabytes in size, so NKN is the ideal mode of data sharing between the institutes.

• MEG data is synchronized in real-time over the NKN between NBRC and AIIMS making the data available simultaneously at both the ends.
- 3/F
- Sz duration: 1.5 yrs
- Frequency: 5-6/day
- vEEG: generalized polyspike with amplitude more on left. 4 drugs
- MRI: Left frontal cortical dysplasia
- PET: Left frontal hypometabolism

MEG dipole

MEG dipole here helped in surgical resection of a very subtle cortical dysplasia. Patient was seizure free following surgery.
Localization of epileptogenic zone

With conventional investigations
Increased accuracy by 50%

Epileptogenic zone
With conventional investigations

"What we get now are specific, targeted and labelled brain specimens for intra-cytological studies"

Ideal model system to understand epileptogenic networks
Cellular Electrophysiological Studies of Targeted Brain Samples obtained from patients undergoing Epilepsy Surgery

Least Abnormal Area
- MRI -ve
- PET -ve
- ECoG score 0-1
- MEG -ve

Most Abnormal Area
- MRI +ve
- PET +ve
- ECoG score 2-5
- MEG +ve

Blinded Sample

Whole-cell patch clamp to record Postsynaptic Currents (PSCs)
Intracellular Recordings from Single Neurons in Brain Slice Preparations

Excessive excitatory currents in tissues resected from MEG +ve epileptogenic zone

Banerjee et al, 2015, Epilepsy Research, 117, 11-16
Summary

• Centre of Excellence for Epilepsy Research is bridging the gap between basic scientists and clinicians, a necessity to excel in neuroscience research.

• NKN is playing a crucial role in sharing of MEG data between NBRC, Manesar and AIIMS, New Delhi.

• High resolution MEG data when used along with the MRI, PET and ECoG data, increases the accuracy of localization of epileptogenic zone.

• Systems biology approach helps understand the epileptogenic network, thereby aiding in finding a treatment for drug-resistant epilepsy.
Acknowledgements

Scientific Faculty from NBRC, Manesar and AIIMS, New Delhi

PhD students and Research Fellows

Institutional Support:

All India Institute of Medical Sciences (AIIMS), New Delhi

National Brain Research Centre (NBRC), Manesar, India

Department of Biotechnology, Ministry of Science & Technology, Government of India for the generous funding.

National Knowledge Network (NKN) for providing high-speed connectivity
THANKS