Non-invasive Presurgical Investigation in Intractable epilepsy: optimizing selection processes and avoiding redundant studies and tests

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Epilepsy surgery is more expensive and more effective than medical treatment in refractory patients

- Epilepsy surgery is cost-effective in two years
- In a long-term perspective, the surgery became cost-effective between 7 and 8 years after the surgery even without indirect costs

Identifying suitable candidate for epilepsy surgery

1. Good history is the key!
   - Febrile convulsions (lateralized, prolonged), family history, ictal/postictal language abilities, stereotyped auras, presence of sGTCS...
   - Knowledgeable physicians referring appropriate patients to the epileptologist is very important.

Identifying suitable candidate for epilepsy surgery

2. Cognitive and psychiatric evaluation
   - Verbal memory impairment with left TLE, prevalence of psychiatric disorders might be 80% (De Toffol, 2004, Rev Neurol)

3. Interictal EEG
   - Unilateral anterior temporal spikes, localized repetitive fast spikes...

4. High-resolution MRI

Optimizing selection process: Conditio sine qua non

Focal epilepsy
Pharmacoresistant epilepsy
Outpatient clinic - Prior to referral to Epilepsy Center

Epileptogenic zone is NOT in the eloquent brain area to be elucidated in the course of presurgical evaluation in Epilepsy Center

Differential diagnosis of a paroxysmal neurological event: Do neurologists know how to clinically recognize it?

Antoncic J. *Ristic**", "Krkić Mijević", "Zoran Krševan
"Knilo Vojvodić"", "Šarko Jastrešak"**, "Marko Balohavečki"", "Ivan Šaklić", "Aleksandar Soljak"

- 145 physicians
- 12 videos: 6 epileptic seizures, 4 PNES, 2 syncopes
- Better accuracy in epileptic seizures than PNES
- Correct answers in epileptic seizure type was below 50%

Superiority of epilepsy dedicated MRI protocols

*Watch De Toffol et al 2003 - 4 Panel Onseizures/Paroxysms
**Primary aim - identify epileptogenic zone**

**EZ**: minimum amount of brain tissue that should be resected to render the patient seizure-free

- Epileptic cortex: functional abnormality
- Epileptic cortex: structural abnormality
- EEG
- MRI

Concordance of all data dramatically increases chances for seizure freedom following surgery

**Presurgical evaluation**

- **Mandatory** investigation
  - Long-term video EEG monitoring
  - Brain MRI (optimal sequencing)
  - Battery of neuropsychological tests

- **Optional tests**
  - Interictal PET
  - Total and interictal SPECT
  - Magnetoencephalography (MEG)
  - EEG-MRI
  - fNMR Spectroscopy
  - MRI post-processing
  - Source analysis
  - Awake craniotomy and brain stimulation
  - Acute electrocorticography
  - Invasive EEG studies
  - Subdural or SEEG

**Long-term video EEG monitoring**

- In majority of patients plays an *essential role*
- Interictal EEG (increase the amount of data)
- Bitemporal spikes (synchronous or independent) do not preclude successful temporal surgery, provided that they predominate on the side to be resected
- Total EEG
  - It might be misleading in patients with a deeply located focus (e.g., mesial frontal, parietal, occipital, or insular): failing to detect a distinct epileptic discharge, or by showing the seizure spread to distant cortical areas
- Seizure Semiology
  - Initiation from the generator: aura
  - Spread through the epileptic network: sequential semiological signs
  - Inhibition in the epileptic network: postictal semiological signs

**Epileptogenic lesion is in spatial relationship with the epileptogenic zone**

**Most important predictor for favorable post-surgical outcome is the complete resection of the abnormality detected by preoperative MRI**

**Prevalence of epileptogenic lesions among 2740 pts. in Bonn series (1989-2009)**

<table>
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<th>Entity</th>
<th>N</th>
<th>% of all</th>
<th>% of lesions</th>
<th>% of scars</th>
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<td>Focal cortical dysplasia</td>
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<td>Ganglioglioma, DNET</td>
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<tr>
<td>Epileptogenic lesions</td>
<td>1125</td>
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<td></td>
</tr>
</tbody>
</table>

**MRI lesion can’t be identified each time**
Sutton law in epilepsy

Reporter's inquiry: “Why you robbed banks?”

Willie Sutton: “Because that’s where the money is”

Willie Sutton
1901-1980

Sutton’s law in epilepsy: because epilepsy is where the lesion is.

Mortati et al, 2012, Epilepsy Behav

Presurgical evaluation

NONE of the available investigations allow direct delineation of the epileptogenic zone

Eligibility criteria used for entering a presurgical evaluation

1. profile of surgical candidates
2. epilepsy surgery centers experience and training

Decision on surgical treatment

Mandatory investigation

• Long-term video-EEG monitoring
• Brain MRI (optimal sequencing)
• Battery of neuropsychological tests

Optional tests

• Interictal FDG-PET
• Ictal and interictal SPECT
• Magnetoencephalography (MEG)
• EEG-fMRI
• MRI post-processing
• Source analysis
• Awake craniotomy and brain stimulation
• Acute electrocorticography

Surgically remediable epilepsies

MRI-negative PET-positive temporal lobe epilepsy: a distinct surgically remediable syndrome

Bilateral periventricular leucomalacia is a distinct surgically remediable syndrome

The surgically remediable syndrome of epilepsy (prototype): mesial temporal lobe and Sturge-Weber

Mesial temporal lobe epilepsy with no specific histological abnormality: A distinct surgically remediable syndrome

Calcified neurocysticercosis lesions and antiepileptic drug-resistant epilepsy: A surgically remediable syndrome

60% patients with MTLE seizure free in Uganda pilot project of the epilepsy surgery

Work up: video-EEG and brain CT

We did not follow Western protocols blindly. They were not practical or doable in our setting. Had we waited till all the infrastructure was in place – we would still be waiting. We needed to customize the protocols to our Indian conditions. We needed to abbreviate the protocols. Our results bore us out.”

Singh et al, 2011, J Pediat Neurosci

Additional tests

Mainly helpful in MRI-negative pts.

• Positron Emission Tomography (PET)
• Hypometabolic areas on FDG-PET often overlap with ictal onset
• May reveal subtle FCD (in normal brain MRI)
• Ictal SPECT
• Focal area of hyperperfusion, thought to reflect ictal discharge
• Subtraction ictal SPECT co-registered with MRI (SISCOM)
• Magnetoencephalography (MEG)

Belgrade experience

834 pts (2010-2015)

ILAE 1
17/21 (81%)
extra
71/90 (79%)
temp
6 (4+2)
(5.5%)

ILAE 2
17/86 (19%)

ILAE 3
4 (3+1)
(4.8%)

ILAE 4
2 (2)
(2.4%)

89 (60%)

Surgery success

7180 (79%)

Endpoints

10% temp
6%

NLS
9%

Surgery center

44
temp
51%

Post-Op

40
temp
Conclusions

- Epilepsy surgery is expensive but cost-effective.
- Epileptogenic zone is identified by means of clinical observation, neuroimaging, and electrophysiologic studies (and other tests if necessary).
- Surgically remediable syndromes can be easily diagnosed noninvasively in most patients, and early surgical intervention is associated with seizure freedom and prevention of development of irreversible psychological and social disabilities.