PHENOMENOLOGY DEPENDENT APPROACH OF EPILEPSY TREATMENT (MRI-negative case study)

Automotor Seizures

LORELLA MINOTTI, MD
NEUROLOGY DEPARTMENT, UNIVERSITY HOSPITAL
GIN INSERM U836-UJF-CEA, GRENOBLE
Complex motor seizures

- “… three types of complex motor seizures can be distinguished … ”complex” refers to the complex characteristics of the movement and does not mean that the patient loses awareness during the seizure”.

- Automotor seizures: complex motor seizures in which the main manifestations consist of automatisms involving the distal segments of the hands and feet or the mouth and tongue…
Automotor seizures

- Typical of **temporal** lobe epilepsy but occasionally can also be seen with **frontal** lobe seizures

- **Frontal lobe automotor** seizures tend to be of **shorter duration** than temporal lobe automotor seizures

- **Unilateral automatisms** are more frequently an expression of an **ipsilateral epileptogenic zone** and likely a manifestation of limb dystonia in the contralateral limb

- 95% of the automotor seizures are associated with **altered consciousness** (preservation of consciousness observed almost exclusively in patients with nondominant mesial temporal epilepsy)
Automotor seizures

- Rare in patients < 3 years (Automotor seizures = 0 in patients aged 1 month to 3 years of age)\textsuperscript{1}

- Progressively increase afterwards becoming the major seizure component in adulthood\textsuperscript{1,2}

\textsuperscript{1}Guadalupe Fernandez-Baca Vaca et al, 2018; Fogarasi et al, 2007
35 year-old R-handed male patient

- No relevant personal or familial history
- Seizure onset: 15 years
- Drug-resistant (VPA, TPR, LVT, OXC, CLB)
- 1-2 seizures / month (daytime)
- Precipitant factors: none
- Normal neurological exam
- MRI: normal
- Npsy: verbal memory deficit, dysexecutive signs
Automotor seizures in the temporal lobe: which network?

<table>
<thead>
<tr>
<th>Ictal features</th>
<th>Mesial</th>
<th>Mesio-Lateral</th>
<th>Lateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oroalimentary automatisms</td>
<td>15 (62.5)</td>
<td>11 (61.1)</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>Upper-limb elementary automatisms</td>
<td>16 (66.7)</td>
<td>10 (55.6)</td>
<td>3 (23.1)</td>
</tr>
<tr>
<td>Verbal automatisms</td>
<td>4 (16.7)</td>
<td>7 (38.9)</td>
<td>0</td>
</tr>
</tbody>
</table>

Mesial subtype

(AN-Hc-HcG-EC)

- High frequency of auras (epigastric, experiential, fear)
- Frequent automatisms (oroalimentary, gestural)
- Long duration of seizures

Temporo-polar subtype

- Short EEG-clinical delay
- Short delay first sign-LOC

Mesiolateral subtype

- Initial loss of contact
- Early vocalizations
- Early oral and verbal automatisms

Lateral subtype

- Auditory aura
- Rare automatisms
- Frequent SGTC seizures
- Short duration of seizures

Maillard et al. 2004
35 year-old R-handed male patient

- Seizure semiology:
  - bad taste in the throat, nausea, intent to spit (hand paraesthesiae in the past)
  - then LOC, spitting, OAA, +/- sialorrhea, postictal aphasia
  - R head version, R face contraction -> 2d TCG
Seizure semiology: valuable localizing information

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Lobar location</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bipedal automatisms</td>
<td>Frontal &gt; temporal</td>
<td>FLE: 30% / TLE: 10%</td>
</tr>
<tr>
<td><strong>Ictal spitting / drinking</strong></td>
<td>Temporal (R)</td>
<td>rare</td>
</tr>
<tr>
<td>Ictal emeticus</td>
<td>Temporal (R)</td>
<td>rare</td>
</tr>
<tr>
<td>Ictal urinary urge</td>
<td>Temporal (R)</td>
<td>rare</td>
</tr>
<tr>
<td>Piloerection</td>
<td>Temporal (L)</td>
<td>rare</td>
</tr>
<tr>
<td>Postictal cough</td>
<td>Temporal</td>
<td>TLE: 40%</td>
</tr>
<tr>
<td>Postictal nose wiping</td>
<td>Temporal &gt; frontal (ipsi)</td>
<td>TLE: 50% / FLE: 10%</td>
</tr>
</tbody>
</table>

**Side lateralisation**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Lobar location</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head version (→ SGTCS)</td>
<td>Contralateral</td>
<td>TLE: 35% / ETE: 40%</td>
</tr>
<tr>
<td>Unilateral dystonia</td>
<td>Contralateral</td>
<td>TLE: 35% / ETE: 20%</td>
</tr>
<tr>
<td>Ictal speech</td>
<td>Non dominant</td>
<td>10-20%</td>
</tr>
<tr>
<td>Conscious automatisms</td>
<td>Non dominant</td>
<td>rare</td>
</tr>
<tr>
<td>Unilateral eye blinking</td>
<td>Ipsilateral</td>
<td>rare</td>
</tr>
<tr>
<td>Figure of 4</td>
<td>Controlateral</td>
<td>65% of SGTCS</td>
</tr>
<tr>
<td>Postictal dysphasia</td>
<td>Dominant</td>
<td>20%</td>
</tr>
</tbody>
</table>

Rosenow & Lüders 2001; So, 2006
# Seizure semiology: valuable localizing information

<table>
<thead>
<tr>
<th>Aura</th>
<th>Location</th>
<th>Lateralization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somato-sensory</td>
<td>Parietal (S1)</td>
<td>contralateral</td>
</tr>
<tr>
<td>Visual</td>
<td>Occipital (V1)</td>
<td>contralateral</td>
</tr>
<tr>
<td>Auditory</td>
<td>Temporal (T1)</td>
<td>contralateral</td>
</tr>
<tr>
<td>Gustatory</td>
<td>Insula</td>
<td>-</td>
</tr>
<tr>
<td>Olfactory</td>
<td>Temp (Am) - Front (Orb)</td>
<td>-</td>
</tr>
<tr>
<td>Vestibular</td>
<td>T-P-O junction ??</td>
<td>-</td>
</tr>
<tr>
<td>Experiential (DV)</td>
<td>Temporal (EC)</td>
<td>-</td>
</tr>
<tr>
<td>Emotional (fear)</td>
<td>Temp (Am) - Front (Orb)</td>
<td>non dominant ?</td>
</tr>
<tr>
<td>Abdominal</td>
<td>Temporal &gt; extraT</td>
<td>-</td>
</tr>
</tbody>
</table>

Rosenow & Lüders 2001; So, 2006
Functional differentiation of the insula

1768 studies - functional MRI; voxel-based meta-analysis

- Insula A-V: emotional tasks
- Insula anterior dorsal: cognitive tasks
- Insula central: olfactory and gustatory tasks
- Insula posterior: sensori-motor tasks

Kurt et al, 2010
First tonic or fast discharge in the insula (12 pts)

Onset in cognitive insula associated with no aura (P1,2,3) or cognitive aura (P4,5,6)
Onset in sensory motor insula associated with sensory aura (P7,8,9,10,11)
Onset in chemo-sensitive insula associated with gustatory aura (P12)
35 year-old R-handed male patient: interictal EEG
35 year-old R-handed male patient: interictal EEG

F7-Fb1
Fb1-Tp1
Tp1-T5
FP1-F7
F7-T3
T3-T5
T5-01
FP1-F3
F3-C3
C3-P3
P3-01
Fz-Cz
Cz-Pz
F8-Fb2
Fb2-Tp2
Tp2-T6
Fp2-F8
F8-T4
T4-T6
T6-O2
FP2-F4
F4-C4
C4-P4
P4-O2
EKG
35 year-old R-handed male patient: ictal EEG
35 year-old R-handed male patient: ictal EEG
### Automotor seizures (TL) : scalp EEG features

<table>
<thead>
<tr>
<th>TL (n=58)</th>
<th>TL (%)</th>
<th>T+ (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INTERICTAL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral S/SW</td>
<td>8.5%</td>
<td>43.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Precentral S/SW</td>
<td>1.7%</td>
<td>43.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>ICTAL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal anterior onset</td>
<td>0%</td>
<td>8.7%</td>
<td>0.002</td>
</tr>
<tr>
<td>T-P onset</td>
<td>8.7%</td>
<td>26.1%</td>
<td>0.004</td>
</tr>
<tr>
<td>Precentral onset</td>
<td>0%</td>
<td>21.7%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Barba et al. 2007
35 year-old R-handed male patient: ictal EEG

- Repeted HR MRI = 0
- fMRI: L dominance for language
- 18-FDG-PET:
Metabolic changes and electro-clinical patterns in mesio-temporal lobe epilepsy: a correlative study

50 pts with HcS

Mesial
IA: 7/13 (54%)

Anterior mesio-lateral
IA: 6/16 (37%)

Widespread mesio-lateral
IA: 4/15 (26%)

- Epilepsy Surgery: most effective treatment to achieve seizures control in well-selected patients suffering from refractory focal epilepsy, both children and adults

- Precise definition and complete resection of the epileptogenic zone (EZ): main determinants of post-surgical seizure freedom

- Invasive EEG (iEEG) recordings: still required in more complex cases (MRI-negative cases)

- Primary goal of iEEG procedures: to complete the non-invasive evaluation to provide precise information on the localization of the EZ, its relationships with eloquent cortex (EC), and the feasibility of a tailored surgical resection
Automotor seizures (MRI-negative cases)

- Unilateral TLE
  - eligible for a standard temporal lobectomy without iEEG if clinical, functional, and EEG features are concordant for a clear unilateral TLE\(^1\)
  - but... what about the cognitive outcome\(^2\)

- Pseudo-TLE

- Temporal “plus” epilepsy

Automotor seizures: pseudo-TLE

- Epileptic generator localized outside the TL can be clinically silent until the discharge propagates to TL structures, therefore mimicking TL seizures both clinically and on scalp EEG

- Attention to ictal clinical symptoms, to atypical EEG findings, to discrete extratemporal abnormal MRI data or to unusual interictal PET\(^1\) and ictal SPECT patterns, that might point to extra-temporal areas

- These areas might include the orbito-frontal cortex\(^2\), the posterior cingulate gyrus\(^3\), the temporo-occipital junction\(^4\), and the insula\(^5\)

Automotor seizures: pseudo-TLE

22 year-old, R-handed female

Sz semiology: epigastric constriction, +/- gustatory aura, +/- LOC, staring, OAA, nose rubbing, post-ictal confusion and drowsiness
Four patients showed dialeptic seizures or automotor seizures, with seizure spread to medial temporal or IPL areas.

Metabolic changes in occipital lobe epilepsy with automatisms

Chong H. Wong\textsuperscript{1,2}, Armin Mohamed\textsuperscript{1,3}, Lingfeng Wen\textsuperscript{3,4}, Stefan Eberl\textsuperscript{3,4}, Ernest Somerville\textsuperscript{2,5}, Michael Fulham\textsuperscript{1,3} and Andrew F. Bleasel\textsuperscript{1,2} *

Patients without automatisms during seizures

Patients with automatisms during seizures (visual aura -> automotor)
Multimodal imaging reveals the role of $\gamma$ activity in eating-reflex seizures

Thomas Blauwblomme,1 Philippe Kahane,1,2,3,6 Lorella Minotti,1,2,3 Frédéric Grouiller,1,2,7 Alexandre Krainik,1,2,5 Laurent Vercueil,1,2,3 Stéphan Chabardès,1,2,4 Dominique Hoffmann,4 Olivier David1,2,5

Blauwblomme et al, 2011
Automotor seizures: pseudo-TLE

35 year-old, R-handed female

Sz semiology: No aura, LOC, mild OAA, +/- postictal amnesia
Automotor seizures: pseudo-TLE
Automotor seizures: pseudo-TLE
Automotor seizures: pseudo-TLE
OFC epilepsy is rare and unrecognized and therefore underestimated.

Most of the available literature reports anecdotal cases, with the largest reports including up to 16 patients (6 Canadian epilepsy monitoring units between 1988 and 2014) [1].

Heterogeneous and non-specific clinical presentations have been reported: cephalic and various vegetative auras and non motor and motor manifestations.

No aura, or poor symptomatology at ictal onset.

Ictal discharges confined to the OFC: clinically silent (temporal).

Clinical manifestations: related to the spread of the discharge.

Chibane et al. 2017
Automotor seizures: temporal “plus” cases

- Refer to a form of multilobar epilepsy in which seizures involve a complex epileptogenic network including TL structures and closely connected neighbouring structures (insular cx, orbitofrontal cx, frontal and parietal operculum, TPO junction).

- 27.5% of TLE patients submitted to SEEG recordings.

- 10% of patients undergoing a standard TL surgery.

- Prominent involvement of the TL (electro-clinical features suggestive of TLE, MRI either unremarkable or show signs of HS).

- iEEG demonstrate an ictal discharge originating simultaneously from the TL and the neighboured extra-temporal structures, or two co-existing seizure types with temporal and extra-temporal ictal onset, respectively.

Barba et al. 2007; Barba et al. 2016
Automotor seizures: temporal “plus” cases

39 year-old, R-handed male

Sz semiology: staring, LOC, OAA (swallowing) and severe post-ictal aphasia
35 year-old R-handed male patient: hypothesis on EZ
35 year-old R-handed male patient: SEEG
35 year-old R-handed male patient: ant Hc DES 1 Hz/3mA
35 year-old R-handed male patient: ant Hc DES 1 Hz/3mA
35 year-old R-handed male patient: Amy DES 50Hz/2mA
35 year-old R-handed male patient: Amy DES 50Hz/2mA
All seizures were found to invade the insula, most often after a relay in the ipsilateral hippocampus (19/21 pts).

2 pts: seizures originated in the insular cortex itself...

Seizures propagating to the insular cortex were found to be fully controlled by surgery, whereas those originating in the insular cortex persisted after temporal cortectomy.
Insular SEEG pattern: not relevant (Fisher’s test, p = 0.585)

Absolute values of delay of insular involvement: longer in seizure-free patients than the others (39 vs. 8 sec) (Mann-Whitney test, p = 0.055)

Histology was not predictive of outcome (p = 0.108).

SOZ (mesial vs. ML vs. L): no prognostic factor (chi-square test, p = 0.274)

Insular EV: not statistically different between group Ia and the others (Mann-Whitney test, p = 0.606; Figs. 4 and S1)
35 year-old R-handed male patient: postsurgical MRI

Surgery July 2010: Histo = 0
Initially SF (EEG N)
>2yrs (ttt=0) few seizures recurred; SF ON PER
ICV=96 / IOP=108 / V&nonVM improvement
Automotor seizures (MRI-negative cases)

❖ The most challenging TLE cases, especially in patients with unimpaired memory because of the increased risk for postoperative memory loss after TL resection

❖ Heterogeneous organisation of the EZ within TL structures (involvement of mesial and/or neocortical areas)

❖ The EZ may even incorporate a network that extends beyond the TL (temporal « plus » or pseudo-TL epilepsies)

❖ A meticulous analysis of seizure semiology with a focus on seizure evolution provides valuable localising information

❖ In case of iEEG, the spatial sampling needs to be extensive, in temporal lobe as well as in extratemporal areas