Intra-lesional stereo-EEG activity in Taylor’s focal cortical dysplasia

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ABSTRACT — Focal cortical dysplasia are a frequent histological finding in epilepsy surgery series. Among the different types of focal cortical dysplasia, distinctive anatomical, electrical and clinical details have been identified for Taylor’s focal cortical dysplasia, and in a recent article we reported a better post-surgical outcome in Taylor’s focal cortical dysplasia than in other histological subtypes of cortical dysplasias. In the present study, we analysed the intra-lesional electrical activity directly recorded inside Taylor’s focal cortical dysplasia during a stereo-EEG diagnostic procedure in 21 patients selected from among the 27 cases in which post-operative neuropathological examination demonstrated this kind of lesion.

Our data show the existence of a peculiar interictal pattern characterised by the presence of repetitive and rhythmic spike and poly-spike and wave, frequently associated with short bursts of fusiform micro poly-spikes. Moreover, an almost pathognomonic ictal pattern (mid-amplitude 14-18 Hz rhythmic activity followed by a low voltage recruiting fast activity) is present in 12 of these 21 patients. These electrical peculiarities suggest a high level of epileptogenicity of Taylor’s focal cortical dysplasia and could possibly explain the high percentage of post-surgical success among patients with this kind of lesion.

KEY WORDS: focal cortical dysplasia, intracerebral recordings, epilepsy surgery

In patients with localisation-related refractory epilepsy, magnetic resonance (MR) has dramatically increased the possibility of identifying, in life, a probable cortical dysplasia (CD) [1-5], and the incidence of this pathology is particularly high in surgical series [6-11].

Among focal CD, particular features have been identified for Taylor’s type cortical dysplasia [12-15].

In two recent papers, we reported the clinical, electrical, neuroradiological and neuropathological features of patients with focal CD, proposing a new classification based on easily recognised histopathological characteristics [16, 17]. In particular, we confirmed the existence of distinctive anatomoelectro-clinical details for Taylor’s focal cortical dysplasia (TFCD), including a better prognosis for post-surgical outcome.

Only one report [18] in the literature deals with electrical activity recorded directly inside the dysplastic pathological tissue during a stereo-EEG procedure. Since this study suggests the presence of peculiar interictal patterns, it might be useful to study in
depth ictal and interictal (MR controlled) stereo-EEG activity in a group of patients with Taylor’s FCD.

Patient characteristics and general clinical results

From May 1996 to December 2001, 321 patients underwent surgery for localisation-related refractory epilepsy at the ‘Claudio Munari’ Epilepsy Surgery Centre. Anatomopathological examination [14] demonstrated FCD in 81 (25%) of these patients. The general clinical characteristics of this group of patients are listed in Table 1.

According to the histological classification that we have recently proposed [16], FCD were subdivided into: architectural FCD (42 patients, 52%), cytoarchitectural FCD (12 patients, 15%) and Taylor’s FCD (27 patients, 33%).

General features of Taylor’s type patients (Table 1) show no significant difference as regards these parameters with respect to the total population, since the lower age at intervention in Taylor’s patients does not depend upon an earlier onset of the illness, but mainly on a prompter indication for surgical treatment (i.e. shorter duration of the illness).

Since seizure frequency seemed to be higher in Taylor’s FCD, we analysed the distribution of patients presenting monthly, weekly, daily and plurality seizure frequency in the three groups.

The results of this analysis (Table 2) confirm that the percentage of patients presenting daily/pluri-daily seizures is significantly higher in Taylor’s FCD (78%) than in other CD patients (22%).

The MR technique [17] (Table 3) revealed a higher sensitivity in Taylor’s patients, since a lesion was identified pre-operatively in 74% of these cases and the suggested diagnosis was correct in 16 patients (59% of total population and 80% of positive MR patients). The most frequent finding was focal thickening of the cortex with blurring of the grey-white matter junction in association with increased signal intensity in the subcortical white matter on T2-w images and decreased signal in white matter on T1-w images (figure 1A, B).

It is important to note the lower incidence of mesial temporal sclerosis (MTS) and the absence of double pathology in the Taylor’s group, but these data could be explained by the reduced presence of temporal lobe epilepsy (TLE) in Taylor’s FCD. The site of surgery in this group was, in fact, temporal in six cases (22%), frontal in 11 (41%) and parietal in 2 (7.4%), while at least bilobar resection was performed in eight cases (29.6%) and included temporal structures in only three.

Presurgical diagnostic procedures (Table 4), which always started with a careful anamnestic definition of the semiology of the episodes, usually included ictal video-EEG monitoring of the patients in both the total population and Taylor’s FCD, while stereo-EEG exploration was more frequently performed in Taylor’s type than in the total population. This difference could also be due to the reduced incidence of TLE in Taylor’s type patients.

Despite the presence of some negative prognostic parameters (i.e. high seizure frequency, high incidence of extratemporal and/or multilobar epileptogenic regions), post-surgical outcome in Taylor’s patients (Table 5) was consistently more favourable than in architectural and cytoarchitectural ones. These features strongly suggest the

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**Table 1. General Characteristics of the analysed population.**

<table>
<thead>
<tr>
<th>General Charact.</th>
<th>Total population</th>
<th>Archi + cytoarchi</th>
<th>Taylor’s FCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>F 40 – M 41</td>
<td>F 27 – M 27</td>
<td>F 13 – M 14</td>
</tr>
<tr>
<td>Age at surgery</td>
<td>26 yrs (2-53; ± 11)</td>
<td>28 yrs (2-53; ± 11)</td>
<td>22 yrs (3-42; ± 11)</td>
</tr>
<tr>
<td>Age at onset</td>
<td>7 yrs (0-26; ± 7)</td>
<td>8 yrs (0-26; ± 7)</td>
<td>7 yrs (0-24; ± 7)</td>
</tr>
<tr>
<td>Duration</td>
<td>18 yrs (1-42; ± 9)</td>
<td>20 yrs (1-42; ± 9)</td>
<td>14 yrs (2-35; ± 8)</td>
</tr>
<tr>
<td>Seizure freq/m</td>
<td>69</td>
<td>61</td>
<td>85</td>
</tr>
<tr>
<td>Abnor. Neurol. Ex.</td>
<td>18 pts (22%)</td>
<td>8 pts (15%)</td>
<td>10 pts (37%)</td>
</tr>
</tbody>
</table>

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**Table 2. Seizure frequency.**

<table>
<thead>
<tr>
<th>Seizure Freq.</th>
<th>Total population</th>
<th>Archi + cytoarchi</th>
<th>Taylor’s FCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monthly</td>
<td>17 (21%)</td>
<td>13 (24%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Weekly</td>
<td>31 (38%)</td>
<td>29 (54%)</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Daily</td>
<td>9 (11%)</td>
<td>2 (4%)</td>
<td>7 (26%)</td>
</tr>
<tr>
<td>Pluri-daily</td>
<td>24 (30%)</td>
<td>10 (18%)</td>
<td>14 (52%)</td>
</tr>
</tbody>
</table>

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**Table 3. MRI findings.**

<table>
<thead>
<tr>
<th>MR</th>
<th>Total population</th>
<th>Archi + cytoarchi</th>
<th>Taylor’s FCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>37 pts (46%)</td>
<td>17 (31%)</td>
<td>20 pts (74%)</td>
</tr>
<tr>
<td>MTS</td>
<td>10 pts (12%)</td>
<td>9 (17%)</td>
<td>1 pts (3%)</td>
</tr>
<tr>
<td>Dual Pathology</td>
<td>17 pts (21%)</td>
<td>17 (31%)</td>
<td>– pt (–%)</td>
</tr>
<tr>
<td>Negative</td>
<td>17 pts (21%)</td>
<td>11 (21%)</td>
<td>6 pts (23%)</td>
</tr>
</tbody>
</table>
This 27-year-old, right-handed woman started having seizures at age 6 years. She initially benefited from medical treatment, but, at the age of 13 years, seizures reappeared and became drug-resistant. At surgery (July 2001) she was 26 years old and presented a mean of 15 seizures per month. Episodes could be preceded by a not well specified visual illusion in a low percentage of cases, but the patient was always unable to call, showing a slight right deviation of eyes and head and a dystonic posturing of the left hand. Loss of contact lasted 10-20 seconds and could be accompanied by falling; in general verbal functions returned promptly after the seizure.

The MR images shown in this figure (Coronal T1-w/IR TSE [A] and T2-w/FLAIR [B]) evidenced a lesion in the right inferior parietal lobule and in the underlying white matter, whose features evoked a FCD, probably of Tailor’s type. Particularly in FLAIR sequences, the lesion seemed to involve the white matter under the post-central gyrus.
Scalp EEG interictal abnormalities mainly involved the right parieto-central region, frequently the posterior temporal; numerous sequences of rhythmic theta waves seemed to have a phase-reversal under the electrode C4, but these sharp waves were well-represented also under Cz. The topography of ictal discharges (rhythmic activity followed by a low voltage fast discharge) strongly overlapped that of interictal abnormalities, thus evoking the ictal involvement of extra-lesional structures. Both electro-clinical findings and the poor definition of the borders of the lesional area at MR led to the stereo-EEG exploration shown in this figure (lateral [C] and frontal [D] views of the stereotactic scheme). Sixteen intra-cerebral electrodes were implanted in the right parietal (8 electrodes), temporal (six electrodes) and occipital (two electrodes) regions. The lesional area (reconstructed in the stereotactic space in figure 1 [C]) was mainly explored by electrode L.
Stereo-EEG methods and results

In most of the Taylor's type patients, non-invasive anatomo-electro-clinical data, always verified by video-EEG study, did not clearly locate the epileptogenic zone. For this reason, stereo-EEG was performed in 86% of the cases (i.e. 23 patients), allowing a more precise definition of the epileptogenic zone and resection plan tailored to individual anatomical and electro-clinical characteristics. In these 23 patients, 10 to 16 intracerebral electrodes were implanted under general anaesthesia (see figure 1C, D for an example of a stereotactic scheme). The intra-parenchymal trajectory of these MR-compatible multilead electrodes was planned on stereo-arteriographic and 3D MR images. The procedure used was that described by Talairach and Bancaud [19] (1966) and later refined by Munari and Bancaud [20] (1985) and Munari et al. [21] (1994). In our centre, the procedure has been integrated with advanced computer-aided imaging and surgical techniques [16].

The position of the intracerebral contacts (five to 18 leads per electrode) was verified by 3D MR, performed a few days after implantation (figure 2 b). With this technique, it was possible to identify the number of patients in which the lesion was actually explored by one or more electrodes; in the five patients with negative MR, the cortical specimens were analysed in relation to the anatomical location of the intracranial electrodes. The combination of these methods demonstrated that in only two cases (one with negative MR), we lacked reliable information about intra-lesional electrode activity. Consequently, we analysed interictal and ictal electrical features of the remaining 21 cases.

Interictal lesional activity

Background activity was totally absent in 16 patients (76.2%), and was partially preserved in five (23.8%). Depression of the intra-lesional amplitude was an uncommon finding (one case), and although slow waves were present in eight cases (38.1%), they represented the predominant activity in only one.

Spikes and poly-spikes, more or less followed by a slow wave, were present in all cases. In three patients we identified only slow spikes, while in 18 patients (85.7%) spike- and poly-spike- and waves were the predominant pattern. They tended to present with a rhythmic modality in 19 of 21 cases (90.5%), thus representing the most peculiar interictal activity of this kind of lesion (figure 2a and 2b), especially when repetitive fast spikes (or poly-spikes) were followed by high amplitude slow waves and interspersed by relatively flat periods. Another striking peculiarity of Taylor's electrical pattern consisted of brief discharges of low voltage, fast rhythmic activity with regular morphology. These short bursts of fusiform micro poly-spikes were relatively rare during waking (sporadic in five cases, frequent in two and predominant in only one), but increased in frequency during slow sleep. They were frequent in nine cases and became the predominant pattern in five (i.e. 14 patients, 66.7%). In the remaining cases, drowsiness and slow sleep induced a worsening of the trace with faster spikes, increased frequency and more frequent spreading into non-lesional areas.

Ictal lesional activity

The most frequent initial ictal pattern in the intra-lesional leads was the abrupt appearance of a mid-amplitude rhythmic activity, with sharp morphology and frequency between 14 and 18 Hz. This rhythmic discharge lasted, in general, for 2-4 s and was replaced by low voltage, fast activity with a recruiting tonic evolution (figure 4). This initial modality, always identical in each single case, was observed in 12 patients (57.1%), but a low voltage, fast discharge, more or less tonic, was present in another seven (33.3%). In the remaining two explorations, the beginning of the seizures was characterised by increased interictal spike and waves frequency and a very particular kind of sinusoidal rhythmic activity.

As in the example of ictal discharge shown in figure 4, extra-lesional structures were generally involved, with a short delay in ictal activity.

In the great majority of cases, the post-ictal period consisted of a brief electrical silence (4-20 s), followed by the re-appearance of the spike- and poly-spike- and waves activity.

### Table 4. Pre-surgical diagnostic procedures.

<table>
<thead>
<tr>
<th>Pre-surgical dgn</th>
<th>Total population</th>
<th>Taylor's FCD</th>
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<tbody>
<tr>
<td>VEEG – SEEG –</td>
<td>2 pts (2.5%)</td>
<td>– pt (–%)</td>
</tr>
<tr>
<td>VEEG + SEEG –</td>
<td>26 pts (32%)</td>
<td>4 pts (14%)</td>
</tr>
<tr>
<td>VEEG + SEEG +</td>
<td>53 pts (67%)</td>
<td>23 pts (86%)</td>
</tr>
</tbody>
</table>

### Table 5. Post-surgical outcome (according to Engel's 1993 classification) [22]

<table>
<thead>
<tr>
<th>Outcome (follow-up &gt; 1 yr)</th>
<th>Archi + cytoarchi</th>
<th>Taylor's FCD</th>
</tr>
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<tbody>
<tr>
<td>Ia</td>
<td>28 pts (51.9%)</td>
<td>21 pts (80.8%)</td>
</tr>
<tr>
<td>Ib, c, d</td>
<td>7 pts (12.9%)</td>
<td>– pts</td>
</tr>
<tr>
<td>II</td>
<td>3 pts (5.6%)</td>
<td>– pts</td>
</tr>
<tr>
<td>III</td>
<td>5 pts (9.3%)</td>
<td>2 pts (7.7%)</td>
</tr>
<tr>
<td>IV</td>
<td>9 pts (16.7%)</td>
<td>3 pts (11.5%)</td>
</tr>
</tbody>
</table>

* 1 patient died one week after surgery.
Relationships between lesion and epileptogenic zone

At the end of each exploration, the analysis of interictal and ictal data, together with the clinical effects of intracerebral electrical stimulation led to the identification of the epileptogenic zone, considered as the cortical areas that were the primary origin of the ictal discharges [18, 19, 21]. The zone thus identified was related to lesion location showing that: in none of the patients was the epileptogenic zone reliably less extended than the lesion; in only three cases (14.3%) did these two cerebral volumes overlap; in ten cases (47.6%) the epileptogenic zone exceeded the limits of the lesion but involved only contiguous cerebral structures; in eight patients (38.1%), the epileptogenic zone included the lesion but extended widely beyond its MR limits.

Surgery and surgical outcome

In these 21 patients, surgery was planned on the basis of stereo-EEG findings, taking into account the limits imposed by functional anatomy. Consequently, surgery limited to lesional tissue was performed in only three cases; these patients presented a lesion that was at least bi-lobar, also involving the central area and for this reason all these ‘pure’ lesionectomies were incomplete.
In the remaining 18 patients, a corticectomy was associated with the lesionectomy (figure 5), the latter being complete in 16 cases and incomplete in two.

For 20 patients (excluding one who died one week after surgery), a post-operative follow-up period of at least 12 months was available (mean 30 months ± 21, ranging from 12 to 69). Following surgery, 17 patients are completely seizure-free (class IA of Engel [22]), while three patients still presented seizures, without worthwhile improvement in two cases (class IV of Engel). Among the IA patients (85% of these 20), we found three cases in which the lesionectomy performed was incomplete; the other two patients with incomplete lesionectomy are in Engel’s classes III and IV; the third patient still presenting seizures is in class IV despite a complete lesionectomy associated with incomplete resection of the stereo-EEG-defined epileptogenic zone.

Conclusions
We have presented a selected population of patients with localisation-related refractory epilepsy associated with Taylor’s FCD, in which electrical activity was directly recorded from the dysplastic tissue.

Our data show the existence of some electrical, interictal and ictal peculiarities that suggest a high level of epileptogenicity of this kind of lesion. This notion, in partial but consistent agreement with data published by Palminti et al. 1995 [8], Chassoux et al., 2000 [18] and Chassoux in this...
issue, should be considered as a possible explanation of the high percentage of post-surgical success in patients with Taylor’s FCD, especially when compared with other types of dysplastic lesions. In fact, although in the present study we did not analyse the electrical features of architectural and cytoarchitectural CD, we have already described how these CD do not show such strikingly peculiar stereo-EEG activity and how they present a significantly lower rate of post-operative freedom from seizures [16].

Despite the proven epileptogenicity of the lesional tissue, in the great majority of our patients we preferred to perform a cortical excision extending beyond the anatomical limits of the Taylor’s FCD. In fact, our stereo-EEG data, especially data concerning the topography of the ictal discharges, strongly supported the necessity of an extended resection. The identification and subsequent exeresis of the extra-lesional epileptogenic structures probably contributed to the high percentage of totally seizure-free patients after at least one year follow-up in the Taylor’s FCD group (80.8%) and particularly in the 20 intra-lesionally-explored subjects (85%). It must also be noted that three out of five cases in which an incomplete resection of the lesion (figure 5) was performed, but with complete exeresis of the epileptogenic zone, are in class IA.

Unfortunately, our results cannot answer some mandatory questions regarding the possible efficacy of a pure lesion-
ectomy in these same patients. A prospective ‘randomized’ study is necessary to better clarify this aspect. Moreover, interesting results could emerge from further analysis concerning the scalp EEG ictal and inter-ictal features and the correlation of some neuropathological sub-classifications (i.e. the presence or absence of balloon cells in the surgical specimen) with neuroradiological and stereo-EEG data.

**Acknowledgements**

We would like to thank all the members of the Claudio Munari Epilepsy Surgery Centre, our colleagues at our hospital and at Istituto Neurologico C. Besta in Milano, who collaborated substantially in the collection and analysis of these data.

Figure 5. Patient P.D.: post-operative (6 months) MR in coronal T1-w/IR sequence, showing the lesionectomy associated with a parietal corticectomy.

Neuropathological examination demonstrated the presence of Taylor’s FCD with balloon cells not only in correspondence with the intermediate and dorsal leads of electrode L, but also with the interior mesial parietal cortex explored by the mesial contact of the same electrode and electrode X. No lesion was found in the interior parietal peri-lesional dorsal cortex and in the superior parietal lobules.

Patient was seizure-free after 15 months of follow-up (October 2002), with no sensorimotor deficit and an inferior left quadrantanopia. Functional caution induced us to not extend the resection to the parietal white matter, also considering that the post-central gyrus (electrode N) was not significantly involved by ictal discharge.

A big thank-you is reserved for our magister ludi, Claudio Munari, to whom this workshop and this volume are dedicated. We hope that in some part of the « world of the ideas » he can appreciate our work, recognising his hand in it and the grateful feeling in our hearts.

**References**