Electrophysiology of focal clonic seizures in humans: a study using subdural and depth electrodes

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Summary

Focal clonic seizures are a frequent epileptic phenomenon. However, there are few data about their pathogenesis. Eleven patients with focal epilepsy who experienced focal clonic seizures during prolonged video-EEG monitoring were included in this study. Nine patients had subdural electrodes on the precentral gyrus and one patient had additional bilateral subthalamic nucleus (STN) depth electrodes. In five patients, the EEG was co-registered with the EMG of muscles which were involved in the clonic seizures. The frequency, pattern and evolution of the ictal EEG were analysed and their relationship to STN and EMG activity was studied. Focal clonic seizures were always associated with a polyspike–wave pattern in the EEG of the primary motor area (frequency range 1.6–3.4 Hz), while neighbouring electrodes not overlying the precentral gyrus showed different EEG patterns. At seizure onset, the ictal EEG derived from the precentral gyrus consisted of repetitive spiking for 8–28 s (median 19.5 s), accompanied by a continuous increase in muscle tone. This evolved to a pattern of polyspike–wave complexes which were associated with clinical clonus and lasted for 14–202 s (median 30.5 s). The clonic muscle contractions consisted of bursts of compound muscle action potentials (CMAPs) which occurred synchronously in agonistic and antagonistic muscles and were separated by periods of complete muscle relaxation. Each series of CMAPs followed the polyspikes in the EEG with a latency of 17–50 ms. The periods of muscle relaxation occurred during the EEG slow waves. Only some of the cortical spikes were followed by ipsilateral STN spikes. CMAPs followed the cortical polyspikes independently of whether or not STN spikes were seen. The study suggests that focal clonic seizures are focal tonic–clonic seizures. The epileptic clonus consisted of simultaneous contractions of agonistic and antagonistic muscles at regular intervals and was generated by localized polyspike–wave activity in cortical primary motor areas. Activation of the STN did not appear to be an essential component of clonic seizures.

Keywords: clonic; tonic; seizure; subthalamic nucleus; human

Abbreviations: CMAP = compound muscle action potential; STN = subthalamic nucleus

Introduction

When epileptic activity includes the primary motor area, clonic convulsions of a certain part of the body can evolve (Ikeda et al., 1999). Clonic seizures occur frequently in patients with focal epilepsy (Mauguiere and Courjon, 1978). In a series of 252 patients with focal epilepsy, clonic seizures were observed in 57% of the patients with frontal lobe epilepsy and in 29% of the patients with temporal lobe epilepsy (Manford et al., 1996).

The pathomechanism of clonic contractions as a manifestation of seizures is unclear. Tetanic 50 Hz electrical stimulation of the primary motor area in awake humans elicited 3–8 Hz clonic muscle responses which resembled focal epileptic clonus and supported the hypothesis that focal clonus is triggered by supraspinal, most probably cortical, mechanisms (Hamer et al., 2002).

In an attempt to elucidate the pathophysiology of this seizure type further, we analysed focal clonic seizures in humans by registration of EEG derived from subdural electrodes placed on the motor strip and depth electrodes placed in the subthalamic nucleus (STN) in combination with surface EMG recordings of muscles involved in the epileptic clonus.
### Table 1 Patients’ characteristics

<table>
<thead>
<tr>
<th>No. and initials</th>
<th>Age/sex</th>
<th>Epilepsy syndrome</th>
<th>Aetiology</th>
<th>Semiology*</th>
<th>Recordings</th>
<th>Location/no. of electrodes of subdural grids/strips</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 D.S. 49/M</td>
<td>M</td>
<td>Right temporal lobe epilepsy</td>
<td>Focal neuronal heterotopia</td>
<td>Auditory aura→left arm/face clonic seizure</td>
<td>Subdural electrodes</td>
<td>8 × 8 f-c-t; two 2 × 6 t;</td>
</tr>
<tr>
<td>2 E.B. 13/F</td>
<td>F</td>
<td>Right fronto-central epilepsy</td>
<td>Dysplasia</td>
<td>Autonomic aura→left arm/face clonic seizure→gen. tonic-clonic seizure</td>
<td>Subdural electrodes</td>
<td>Left cheek – – 4 × 11 f-c-p; 4 × 4 f; 4 × 4 p; two 2 × 6 t;</td>
</tr>
<tr>
<td>3 K.B. 16/F</td>
<td>F</td>
<td>Right frontal lobe epilepsy</td>
<td>Low grade astrocytoma</td>
<td>Left face tonic seizure→left face clonic seizure→gen. tonic-clonic seizure</td>
<td>Subdural electrodes</td>
<td>– – 5 × 8 f-c;</td>
</tr>
<tr>
<td>4 F.D. 39/M</td>
<td>M</td>
<td>Left temporal lobe epilepsy</td>
<td>Traumatic defect</td>
<td>Complex motor seizure→right face clonic seizure</td>
<td>Subdural electrodes</td>
<td>5 × 8 f-c-t; two 2 × 6 t-o; three 1 × 6 t;</td>
</tr>
<tr>
<td>5 R.H. 15/F</td>
<td>F</td>
<td>Right frontal lobe epilepsy</td>
<td>Dysplasia</td>
<td>Hypermotor seizure→left arm/face clonic seizure</td>
<td>Subdural electrodes</td>
<td>Left triceps m. – 8 × 8 f-c-t; 2 × 6 f-t; 4 × 4 f; four 1 × 6 mes-f;</td>
</tr>
<tr>
<td>6 R.G. 26/M</td>
<td>M</td>
<td>Multifocal epilepsy</td>
<td>Perinatal hypoxic brain injury</td>
<td>Bilateral asymmetric tonic seizure→left arm/face clonic seizure</td>
<td>Subdural electrodes</td>
<td>Left biceps m., left triceps m. – 5 × 8 f-c; 4 × 11 t; 4 × 11 p-o;</td>
</tr>
<tr>
<td>7 R.C. 20/M</td>
<td>M</td>
<td>Right frontal lobe epilepsy</td>
<td>Dysplasia</td>
<td>Left arm/face clonic seizure→gen. tonic-clonic seizure</td>
<td>Subdural electrodes</td>
<td>– – 8 × 8 f-c-t; two 1 × 11 mes-f; 2 × 6 f;</td>
</tr>
<tr>
<td>8 B.B. 29/M</td>
<td>M</td>
<td>Right parietal lobe epilepsy</td>
<td>Low grade astrocytoma</td>
<td>Left arm/face clonic seizure→gen. tonic-clonic seizure</td>
<td>Subdural electrodes</td>
<td>– – 8 × 8 f-c-p;</td>
</tr>
<tr>
<td>9 M.G. 26/M</td>
<td>M</td>
<td>Right parieto-temporal epilepsy</td>
<td>Ganglioglioma</td>
<td>Stimulation induced: left arm/face clonic seizure→gen. tonic-clonic seizure</td>
<td>Subdural electrodes</td>
<td>– – 8 × 4 f-c-t; 2 × 6 p; 1 × 6 t; 1 × 4 c;</td>
</tr>
<tr>
<td>10 L.W. 39/M</td>
<td>M</td>
<td>Right parietal lobe epilepsy</td>
<td>Infarction</td>
<td>Left face/arm tonic seizure→left clonic seizure →gen. tonic-clonic seizure</td>
<td>Scalp electrodes</td>
<td>Left biceps m. – –</td>
</tr>
<tr>
<td>11 A.D. 38/M</td>
<td>M</td>
<td>Left fronto-central epilepsy</td>
<td>Dysplasia</td>
<td>Right arm tonic seizure→right arm clonic seizure</td>
<td>Scalp electrodes</td>
<td>Right biceps m. Bilateral electrodes –</td>
</tr>
</tbody>
</table>

Age in years; M = male; F = female; gen. = generalized; m. = muscle; STN = subthalamic nucleus; f = frontal; c = central; t = temporal; p = parietal; o = occipital; mes = mesial.
*Semiology is as classified by clinical staff during routine monitoring after analysis of the video; for the semiological seizure classification, see Lüders et al. (1998).
Patients and methods
In this study, we retrospectively identified all patients who suffered from focal clonic seizures during video-EEG monitoring with subdural electrodes on the motor strip at the Cleveland Clinic Foundation or the University of Marburg between 1991 and 2000. Routine electrical stimulation had to uncover electrodes whose stimulation elicited contractions of muscles that participated in the epileptic clonus. Thus, 11 patients were identified. Two of these patients were excluded from the study because their recordings were unavailable. Two additional patients were included in this study because they contributed complementary information although they did not have recordings with subdural electrodes (see below).

All nine patients with subdural electrodes were referred for invasive monitoring because they were considered possible candidates for epilepsy surgery and non-invasive results did not reveal enough localizing information to justify a resective procedure (Table 1). The number and location of the subdural plates to be inserted were determined by a consensus meeting based on the non-invasively obtained information. In eight of the nine patients (all except patient R.G.), the subdural electrodes covered the ictal onset zone and the lesion if and to the extent to which it was identified by MRI. All patients except patient B.B. who was monitored in 1992 received an additional MRI scan of the brain after insertion of the electrodes in order to confirm the exact location of the subdural grids and strips. After video-EEG monitoring, electrical stimulation of each subdural electrode was performed to map eloquent cortex. A detailed description of the electrical stimulation procedure is given elsewhere (Hamer et al., 2002). It was assumed that the electrodes whose stimulation elicited muscle responses of the body part which was also involved in the clonic seizures overlaid or were in close proximity to the motor cortex which generated the epileptic clonus. There were no conflicting results with regard to location of the precentral gyrus between MRI and stimulation findings, and no motor responses were elicited by electrodes distant from the motor strip. In one of these nine patients, electrical stimulation (50 Hz stimulation for 5 s with 0.3 ms bipolar square waves of 7 mA current intensity) of an electrode overlying the hand area of the postcentral gyrus elicited a focal clonic seizure of the left hand with a Jacksonian march to the arm and face that was followed by a secondarily generalized tonic–clonic seizure (Table 1).

One of the two additional patients contributing complementary information had recordings from the STN (Table 1). This was a 38-year-old man with left fronto-central epilepsy due to cortical dysplasia in this region. The seizures consisted of right arm tonic–clonic seizures evolving to right head version followed by secondarily generalized tonic–clonic seizures. The seizures were refractory to multiple anticonvulsant drugs. He underwent multiple subpial cortical transections in the primary motor area of the face and arm with a restricted resection of a small area of cortex anterior to the eloquent cortex. After surgery, his focal motor seizures persisted in clusters once every hour. A vagal nerve stimulator was implanted which also did not result in any improvement. Two weeks later, bilateral depth electrodes (Medtronic, Inc., Minneapolis, MN, USA) were implanted into the left and right STN guided by stereotaxic MRI and neurophysiological monitoring (Guridi et al., 2000; Dinner et al., 2002). Each electrode had four contacts each 1.27 mm in diameter, 1.5 mm in length and separated from each other by 1.5 mm. Because STN stimulation also did not result in any significant improvement of his epilepsy, the patient had another video-EEG monitoring with simultaneous recording

Table 2 Characteristics of focal clonic seizures

<table>
<thead>
<tr>
<th>No. and initials</th>
<th>No. of seizures</th>
<th>Duration of clonic seizure (s)</th>
<th>EEG Pattern</th>
<th>Clonus frequency (Hz)</th>
<th>Polyspike frequency* (Hz)</th>
<th>Duration of wave* (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 D.S.</td>
<td>1</td>
<td>26</td>
<td>Polyspike–wave</td>
<td>2.6</td>
<td>18–33</td>
<td>114–226</td>
</tr>
<tr>
<td>2 E.B.</td>
<td>2</td>
<td>14</td>
<td>Polyspike–wave</td>
<td>2.6</td>
<td>19–33</td>
<td>150–251</td>
</tr>
<tr>
<td>3 K.B.</td>
<td>2</td>
<td>46</td>
<td>Polyspike–wave</td>
<td>2.8</td>
<td>20–30</td>
<td>184–284</td>
</tr>
<tr>
<td>4 F.D.</td>
<td>1</td>
<td>29</td>
<td>Polyspike–wave</td>
<td>1.8</td>
<td>14–21</td>
<td>200–264</td>
</tr>
<tr>
<td>5 R.H.</td>
<td>1</td>
<td>18</td>
<td>Polyspike–wave</td>
<td>2.3</td>
<td>15–26</td>
<td>200–304</td>
</tr>
<tr>
<td>6 R.G.</td>
<td>1</td>
<td>34</td>
<td>Polyspike–wave</td>
<td>2.0</td>
<td>14–26</td>
<td>183–305</td>
</tr>
<tr>
<td>7 R.C.</td>
<td>1</td>
<td>22</td>
<td>Polyspike–wave</td>
<td>3.1</td>
<td>20–29</td>
<td>119–205</td>
</tr>
<tr>
<td>8 B.B.</td>
<td>2</td>
<td>24</td>
<td>Polyspike–wave</td>
<td>2.1</td>
<td>22–41</td>
<td>165–234</td>
</tr>
<tr>
<td>9 M.G.</td>
<td>1</td>
<td>60</td>
<td>Polyspike–wave</td>
<td>2.2</td>
<td>15–23</td>
<td>186–325</td>
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<tr>
<td>10 L.W.</td>
<td>1</td>
<td>202</td>
<td>Polyspike–wave</td>
<td>2.2</td>
<td>19–45</td>
<td>188–256</td>
</tr>
<tr>
<td>11 A.D.</td>
<td>3</td>
<td>33</td>
<td>Polyspike–wave</td>
<td>2.6</td>
<td>18–42</td>
<td>123–203</td>
</tr>
<tr>
<td></td>
<td></td>
<td>37</td>
<td>Polyspike–wave</td>
<td>2.4</td>
<td>18–29</td>
<td>171–238</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>Polyspike–wave</td>
<td>3.4</td>
<td>22–45</td>
<td>138–217</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Polyspike–wave</td>
<td>1.9</td>
<td>13–28</td>
<td>221–420</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Polyspike–wave</td>
<td>1.6</td>
<td>12–31</td>
<td>253–361</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Polyspike–wave</td>
<td>1.8</td>
<td>12–31</td>
<td>246–447</td>
</tr>
</tbody>
</table>

*Values given as range.

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of EEG by scalp and STN electrodes as well as EMG of the right biceps muscle.

Another patient with right parietal lobe epilepsy underwent non-invasive video-EEG monitoring with scalp electrodes. In this patient, the ictal EEG was recorded from F4 and C4 (International 10/20 System), and EMG was derived simultaneously from the left triceps, biceps and brachioradialis muscle.

A Patient KB

Seizure onset

Clonic seizure phase (27 s after onset)

B Patient EB

Initial (tonic) phase 20 s later Clonic seizure

A35

A36

A37

A38

A39

A40

A41

EMG

500 µV

100 µV

1 s
In five patients, bipolar surface EMG leads were placed on muscles which were involved in the clonic seizures (Table 1). The EMG leads were attached in a belly-tendon montage. Video-tapes of the focal clonic seizures which were included in this study were analysed to verify that the recorded muscles took part in the epileptic clonus. Four patients had EMG leads on arm muscles and, in one patient, with clonic seizures of the left face, one electrode was placed on the cheek of the involved side with a reference electrode on the ipsilateral mastoid (Table 1).

The patients experienced a total of 16 focal clonic seizures during prolonged video-EEG monitoring. Focal clonic seizures were defined as series of myoclonic contractions occurring at regular intervals, typically in the range of 0.5–5 Hz (Lüders et al., 1998; Hamer et al., 1999). The focal clonic seizures involved the arm and face of one side in seven patients, only one side of the face in two patients, the arm only in one patient and one entire side of the body in another patient. Focal clonic contractions as classified by the clinical staff during routine monitoring were the first behavioural symptoms in five patients (Table 1). At the beginning of these seizures, a certain degree of responsiveness usually was preserved. However, alteration or loss of consciousness occurred during the course of the clonic seizures, especially before the secondary generalization.

Gold cup electrodes were used for all surface EEG and EMG recordings. The subdural grids consisted of 3 mm diameter platinum disc electrodes of 0.127 mm thickness embedded in flexible Silastic with an interelectrode distance of 1 cm. The EEG and EMG activity were recorded digitally with a high pass filter of 0.5 Hz, a low pass filter of 70 Hz and a sampling frequency of 200 Hz. These filter settings were the maximal values of the EEG equipment in the monitoring unit. Because the duration of compound muscle action potentials (CMAPs) is ~15–20 ms, a low pass filter of 70 Hz allows recording of these potentials. However, we cannot exclude that the amplitude and waveform of the CMAPs were different in this set-up as compared with recordings with wider filter settings and higher sampling rates.

The pattern, frequency and evolution of the cortical EEG of focal clonic seizures were analysed and their relationship to STN and EMG activity was studied. The EEG recorded from electrodes on the motor strip was compared with EEG recorded from neighbouring electrodes.

**Results**

The focal clonic seizures had a median duration of 30.5 s (range 14–202 s, Table 2). During the clonic phase of the seizures, the EEG derived from subdural electrodes overlying the motor strip always showed a polyspike–wave pattern (Fig. 1). The waveform of each polyspike–wave complex consisted of 2–6 polyspikes recurring with a frequency of 12–45 Hz followed by a negative slow wave (Table 2). The duration and amplitude of the polyspikes and EEG slow waves varied within and between subjects (Fig. 1). The frequency of the polyspike–wave complexes was in the range of 1.6–3.4 Hz (median 2.25 Hz; Table 2) and slowed down towards the end of the focal clonic seizures. However, when the focal clonic seizure evolved to a generalized tonic–clonic seizure, the frequency tended to increase before the occurrence of the secondarily generalized seizure. The polyspike–wave complexes could also be recorded by scalp electrodes (Fig. 2). The beginning of seizure activity in precentral subdural electrodes consisted of repetitive spiking in 10 of the 11 patients, preceded by low-voltage fast activity in three patients (Fig. 1; Table 1: patients D.S., B.B. and K.B.). Polyspike–wave complexes appeared later in the seizures, coinciding with the appearance of clonic muscle activity. The initial repetitive spiking was accompanied by a tonic muscle contraction recorded in all patients with EMG leads (Fig. 1; Table 1). This increase in muscle tone did not result in a significant movement or posturing in two of these patients (patients E.B. and R.H.) so that it was not noticed as a separate tonic seizure phase during routine video analysis. Retrospective video analysis in the remaining five patients without EMG leads revealed focal tonic seizure phases coinciding with the repetitive spiking in three patients (K.B., F.D. and B.B.). The tonic muscle contraction was not as impressive clinically as the clonic phase, with jerking of one limb or one side of the face. In the patients D.S. and R.C., the body parts involved in the seizures initially were under the blanket or turned away from the camera so that the semiology could not be analysed at seizure onset.

The tonic seizure phases were of shorter duration (median 19.5 s; range 8–28 s) compared with the clonic seizure phases (median 30.5 s). There was a gradual transition from the tonic to the clonic seizures over several seconds. During the tonic muscle contraction, the EMG showed a complete interference pattern in which single CMAPs were not recognizable (Fig. 1B).
The only patient who did not show repetitive spiking as the initial part of the precentral seizure activity was patient M.G., who suffered from a focal clonic seizure elicited by electrical stimulation of an electrode on the postcentral gyrus. From the beginning of the seizure, the ictal EEG consisted of polyspike±wave complexes similar to the EEG pattern observed during spontaneous clonic seizures. Clinically, the seizure started with a focal clonic seizure of the left hand without a tonic phase preceding it (Table 1).

During the clonic seizure phase, the polyspike±wave pattern was confined to electrodes on the pre- and postcentral gyrus in eight out of nine patients (88%) with subdural electrodes, while neighbouring electrodes of the same grid showed different seizure patterns, such as spike±wave complexes or rhythmic slowing (Fig. 1). However, ictal polyspike–wave patterns were not recorded exclusively in the central area. In three patients, this pattern appeared first in the parietal or temporal lobe and stopped when the clonic seizure evolved in the motor strip. In two other patients, the EEG seizures started in electrodes anterior to the precentral gyrus and in mesio-frontal electrodes, with low voltage fast activity followed by repetitive spiking which stopped or was followed by rhythmic slowing/spike–wave complexes when the seizure pattern evolved in the central electrodes.

The rhythmic clonic muscle response consisted of bursts of CMAPs which occurred synchronously in agonistic and antagonistic muscles (see insert) and were separated by periods of complete relaxation of both muscles. Note that the clonic muscle response exactly matched the cortical polyspike–wave complexes. The series of CMAPs followed the polyspikes (see vertical line) and the muscle relaxation occurred during the EEG wave.

**Fig. 2** EEG and EMG recordings of a focal clonic seizure of the left arm in patient L.W. EEG: referential montage of scalp electrodes with the contralateral scalp electrode as reference electrode (F4 and C4 placed according to the International 10/20 System). EMG: bipolar recording of the left triceps and biceps muscle. The rhythmic clonic muscle response consisted of bursts of compound muscle action potentials (CMAPs) which occurred synchronously in agonistic and antagonistic muscles (see insert) and were separated by periods of complete relaxation of both muscles. Note that the clonic muscle response exactly matched the cortical polyspike–wave complexes. The series of CMAPs followed the polyspikes (see vertical line) and the muscle relaxation occurred during the EEG wave.
contractions of agonistic and antagonistic muscles were never observed. The series of CMAPs occurred 17±50 ms after the beginning of the polyspikes in the EEG, whereas the muscle relaxation started with a latency of 9±55 ms after the initiation of the EEG slow waves. Therefore, the frequency of the clonic muscle response exactly matched the frequency of the polyspike–wave complexes in the cortical EEG. However, there was no clear 1 : 1 relationship between single CMAPs and individual cortical spikes as part of the polyspike–wave complexes. There were no systematic changes of the latencies between polyspikes and CMAPs throughout the seizure course.

In the patient with bilateral STN electrodes, the polyspike–wave pattern seen in the cortical EEG was associated with a similar but reduced pattern in the ipsilateral STN (Fig. 3): only some of the cortical spikes were followed by ipsilateral STN spikes. Because the cortical activity was recorded by scalp electrodes in patient A.D., an exact correlation between
cortical and STN spikes could not be performed. The STN spikes were of approximately the same waveform, duration and amplitude in all ipsilateral STN electrodes. In contralateral STN electrodes, usually no spikes were detected. The EEG slow waves following the polyspikes were recorded in cortical electrodes and bilaterally in STN electrodes. The waves derived from STN electrodes were of shorter duration and reached their maximum ~40–70 ms earlier than the waves generated by the cortical motor strip. The slow waves were smaller in contralateral as compared with ipsilateral STN electrodes (Fig. 3). The series of CMAPs always followed the cortical polyspikes independently of whether or not STN spikes occurred (Fig. 3).

Discussion
In this study, co-registration of subdural EEG of the motor strip, recordings from STN electrodes and surface EMG were performed in an attempt to clarify the pathophysiology of focal clonic seizures in humans. The findings suggest that focal clonic seizures are indeed focal tonic–clonic seizures and originate from the motor strip. The epileptic clonus consisted of simultaneous contractions of agonistic and antagonistic muscles at regular intervals and was generated by localized polyspike–wave activity in the cortical primary motor area. Activation of the STN apparently was not essential in the generation of clonic seizures.

Focal tonic–clonic seizures
Although epileptic syndromes and their causes are diverse, the cellular mechanisms of seizure generation appear to fall into two broad categories of tonic, high frequency repetitive discharges or rhythmic and synchronized spike/polyspike–wave complexes (McCormick and Contreras, 2001). In the present study, all EEG seizures showed a transition from repetitive spike discharges at seizure onset to polyspike–wave complexes later in the seizure. This electrographic seizure evolution has also been reported in cellular recordings of hippocampal pyramidal neurons (McCormick and Contreras, 2001). This EEG pattern was accompanied clinically by progression of a focal tonic to a focal clonic seizure. The tonic phase, however, was so subtle in two cases that it was documented in EMG recordings but was not noticed during video analysis. The results suggest that the majority of focal clonic seizures are actually focal tonic–clonic seizures with a tonic phase of variable expression. A retrospective video analysis of focal clonic seizures also reported that a large percentage of focal clonic seizures are preceded by focal tonic seizures (Noachtar and Arnold, 2000).

Increasing intensity of cortical electrical stimulation in humans at the same high frequency converted an intermittent clonic muscle response to a continuous tonic response (Hamer et al., 2002). This supports the view that the initial tonic seizure phase represented an intense, high frequency epileptic stimulation of the motor cortex and that the transition from the tonic phase to the clonic phase reflected a progressive decrease of epileptic excitation in the motor cortex or a progressive increase of inhibitory influences. It was beyond the scope of the current study to examine possible differences between focal and generalized tonic–clonic seizures or between focal and generalized polyspike–wave patterns in EEG.

Relationship between cortical and STN activity
In the one patient with recordings from the STN, all STN spikes were preceded by spikes recorded from the primary motor cortex. This may indicate spread of the ictal activity from the cortex to the STN, and is consistent with the analysis of interictal EEG (Dinner et al., 2002) and data from animal experiments demonstrating a direct glutamatergic cortico-STN pathway (Parent and Hazrati, 1995; Dinner et al., 2002). The activity at the STN appeared mainly ipsilateral to the cortical activity. Not all cortical spikes elicited STN spikes, and the cortical EEG waves following the polyspikes outlasted the waves recorded in STN electrodes. The series of CMAPs always followed the cortical polyspikes independently of the existence of STN spikes. This leads to the assumption that the clonic muscle response is driven by the cortical ictal pattern and that the STN, which has an important influence on basal ganglia outflow activity (Deransart et al., 1998; Tronnier et al., 1999; Dybdal and Gale, 2000), has no or only limited influence on the specific clonic seizure pattern. This is supported by another study in humans, which could not record epileptic ictal discharges in the basal ganglia during secondarily generalized seizures (Rektor et al., 2002). The observation of the present study that unilateral activation of the STN was recorded during focal seizures does not contradict reports that bilateral STN inhibition by high frequency stimulation can reduce cortical seizure activity (Benazzouz et al., 1995; Tronnier et al., 1999; Benazzouz and Hallett, 2000; Dybdal and Gale, 2000; Dinner et al., 2002). The spread of cortical spikes to the STN may contribute to the continuation of the seizure activity of the cortex in general, which is supported by the finding that unilateral disinhibition of the STN is likely to be proconvulsant in rats (Dybdal and Gale, 2000).

Comparison of epileptic and stimulation-induced clonus
Tetanic electrical stimulation of the motor strip in awake humans elicited clonic muscle responses which closely resembled focal epileptic clonus in frequency, appearance of muscular activation and latencies between stimuli and CMAP (Hamer et al., 2002). The results of this study also indicated that clonus is generated cortically. It was suggested that the clonic muscle activation in spite of continuous stimulation is induced by a temporary hyperpolarization of pyramidal tract neurons by GABAergic interneurons which
were activated by recurrent axon-collaterals of the pyramidal tract neurons (Stefanis and Jasper, 1964; Ghosh and Porter, 1988; Hamer et al., 2002). In the present study, the recording of localized polyspike–wave activity in primary motor areas may have been an expression of this pathomechanism. It is hypothesized that the slow waves following the polyspikes reflect the transient hyperpolarization of pyramidal tract neurons that is terminated by a rebound excitation. Further studies should address the question of whether or not the primary motor area contains neuronal networks which facilitate this ictal pattern.

References


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