Influence of somatosensory input on paroxysmal activity in benign rolandic epilepsy with ‘extreme somatosensory evoked potentials’

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Summary
We studied six patients suffering from benign rolandic epilepsy of childhood with central temporal spikes who presented so-called ‘extreme somatosensory evoked potentials (SEPs)’ following peripheral somatosensory stimulation. Stimuli were delivered to the fingers of one hand using both a triggered tendon hammer and low-intensity electrical stimulation. The electrical stimulation was delivered in sequences in different conditions (i.e. random order, 1, 3 and 10 Hz). Both tapping and electrical stimulation produced scalp evoked potentials in all subjects, characterized by a spike followed by a slow wave, similar in morphology and scalp distribution to the spontaneously occurring spikes. This paroxysmal activity was sensitive to stimulus rate; the number of evoked spikes was inversely related to the frequency of stimulation, being maximal at 1 Hz and disappearing at high frequencies (10 Hz). Spontaneous spikes disappeared during high-frequency stimulation but were present during low-frequency stimulation. Averaged SEPs at 3-Hz stimulation showed a late high-amplitude component, identical in morphology and distribution to the single evoked spike. We therefore conclude that, in these subjects, the so-called ‘extreme SEPs’ are evoked spikes and that evoked and spontaneous spikes share common cortical sensorimotor generators. The evidence that these generators can be influenced by afferent input provides important information regarding the functional mechanisms involved in modulating cortical excitability in benign rolandic epilepsy. Moreover, we suggest that peripheral electrical stimulation can be used as an additional activation test in this kind of epilepsy.

Keywords: epilepsy; EEG; somatosensory evoked potentials; EEG spike; hyperexcitability of sensorimotor cortex

Abbreviation: SEP = somatosensory evoked potential

Introduction
It is well known that afferent peripheral stimulation (visual, somatosensory and auditory) can be a provocative stimulus of focal or generalized paroxysmal activity and partial seizures in epilepsy. In particular, somatosensory stimulation can produce clinical symptoms or EEG paroxysmal activity in myoclonic epilepsy or in epilepsy of the sensorimotor areas.

In reflex myoclonic epilepsy both muscle stretch (Rosen et al., 1977; Hallett et al., 1979) and light tactile stimulation (Sutton and Mayer, 1974; Sutton, 1975) can induce myoclonic jerks. In this form of epilepsy it has been suggested that there may be hyperexcitability of the cerebral sensorimotor cortex because of the presence of high-amplitude somatosensory evoked potentials (SEPs) (Rothwell et al., 1984; Obeso et al., 1985, 1986; Shibasaki et al., 1986; Mima et al., 1997) and the fact that a time-locked focal EEG event in the sensorimotor strip contralateral to the muscle involved precedes the myoclonic jerks (Shibasaki and Kuroiwa, 1975).

Among the different kinds of epilepsy of the somatosensory areas there is a form of benign epilepsy of childhood with centrotemporal spikes (Wolf, 1985; Commission on Classification and Terminology of the International League against Epilepsy, 1989; Holmes, 1993) where tapping the foot or hand elicits high-voltage evoked potentials (occasionally up to 400 µV in amplitude) in the parasagittal and contralateral...
parietal regions, respectively, in children with motor seizures and spontaneous rolandic spikes (De Marco and Tassinari, 1981; Dalla Bernardina et al., 1990, 1992) and in children with behavioural problems (De Marco and Negrin, 1973). Tassinari and De Marco (1985) called this rare form of rolandic epilepsy ‘benign epilepsy with extreme SEPs’. The term ‘extreme SEPs’ is used to denote both the single high-amplitude evoked activity recorded by continuous EEG after tapping and the high-amplitude late components observed in averaged SEPs following 3-Hz median nerve stimulation. The authors advocate the use of this term with reference to an abnormal activation of the sensory pathways as distinct from the spontaneous rolandic spikes, though others (Holmes, 1993) consider this activity as evoked too.

In previous studies, the effect of different parameters such as stimulus intensity and frequency of peripheral stimulation in eliciting ‘extreme SEPs’ was not quantified in the continuous EEG activity setting. Moreover, the scalp distribution of this evoked activity and its temporal relationship to peripheral stimulation have not been investigated in detail. Finally, a relationship between spontaneous rolandic spikes and this evoked phenomenon in the same epileptic patients has been suggested but never analysed in terms of scalp topography and reactivity to afferent stimulation.

In an attempt to answer these unsolved questions, we studied six patients classified as having benign rolandic epilepsy with ‘extreme SEPs’, using both triggered tapping and electrical finger stimulation. We observed that both tapping and electrical stimulation produced a well-defined scalp event characterized by a single spike followed by a slow wave. This evoked spike was consistent in latency, morphology and scalp distribution across different recordings and across subjects.

In individual patients the spontaneous spikes presented the same morphology and scalp distribution as the evoked spikes. The effect of frequency of electrical stimulation was dramatic. While low-frequency stimulation produced the maximum number of evoked spikes, high-frequency stimulation led to the disappearance of both evoked and spontaneous spikes. We also studied the relationship between averaged SEPs and evoked spikes.

Methods and subjects

Patients

Six patients (five females, one male), ranging in age from 9 to 11 years, participated in the study. All subjects were right-handed. The protocol was approved by the Ethical Committee of Verona University, and subjects and their parents gave their written informed consent for the study. All patients were referred to the Child Neurology Section of the University Hospital of Verona and were diagnosed as having benign epilepsy with centrotemporal spikes and ‘extreme SEPs’ in response to tapping stimulation of the finger (Table 1). None of the subjects showed any brain lesions on radiological investigation and all were normal at the neurological examination. All subjects presented with at least one seizure in their clinical history.

Daytime seizures were confined to one side of the body and included clonic movements of the face and arm. Arrest of speech usually occurred during the seizure. Consciousness was rarely impaired. Nocturnal seizures were characterized by clonic movements of the mouth and gurgling sounds in the throat. Patients with nocturnal seizures presented a secondary generalized seizure. Only Patient 1 was being treated with carbamazepine (200 mg/day) at the time of recording.

EEG recording

The EEG signal was amplified using a DC Syn Amp amplifier (Neuroscan, Herdon, VI) with a bandpass from DC to 60 Hz. The data were digitized with 16-bit resolution at a sampling rate of 500 Hz for off-line analysis. Twenty-eight EEG channels were used with scalp electrodes mounted on an elastic cap (Electro-Cap International, Eaton, Ohio, USA) and a linked ears reference, according to the 10–20 international system of electrode placement, with additional electrodes placed along the longitudinal axis and over the centroparietal (CP1 and CP2), parietal (P5 and P6), temporo-central (TC1 and TC2) and temporo-occipital (TO1 and TO2) regions. Impedance was kept below 3.0 kΩ. Bipolar surface electrodes were placed over the right abductor pollicis brevis using a belly–tendon montage to check muscle relaxation. During the experiment, the EEG was continuously monitored on-line. Data were stored on computer and analysed off-line.

Stimulation procedure

Each subject was seated in an armchair with the elbow semiflexed and the forearm supine; they were fully relaxed and supported by the arms of the chair. At rest and under stimulation conditions, the position of arms and hands was monitored visually to avoid movements and inappropriate contact with the fingers capable of producing paroxysmal scalp activity. The recordings were performed while the subjects were awake, with their eyes open, and looking at a fixation point.

Several stimulus modalities were employed to elicit paroxysmal scalp activity. (i) Taps were delivered to the fingers of both hands by a triggered tendon hammer on each finger. The exact point of percussion was marked on the palm of the distal segment of the finger. Taps were delivered to each finger in a random sequence with one stimulus every 1–10 s for a period of 3 min. The number of stimuli ranged from 30 to 60 for each finger. The tap produced a time marker triggered by the tendon hammer. (ii) Electrical stimulation was delivered to the finger where tapping elicited scalp activity most frequently. This was done with a pair of ring electrodes placed around the digit. The electrical stimulus, consisting of a brief pulse (0.2-ms duration), was delivered...
### Table 1 Clinical findings

<table>
<thead>
<tr>
<th>Patient (sex)</th>
<th>Age (years)</th>
<th>Age at onset (years)</th>
<th>Seizure</th>
<th>EEG</th>
<th>Family</th>
<th>NMR</th>
<th>Follow-up</th>
<th>Treatment</th>
<th>Tapping</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (F)</td>
<td>9</td>
<td>5</td>
<td>Complex partial</td>
<td>R+L central-temporal spikes</td>
<td>–</td>
<td>Normal</td>
<td>No seizures from the age of 6 years</td>
<td>CBZ*</td>
<td>R – L</td>
</tr>
<tr>
<td>2 (F)</td>
<td>8</td>
<td>4</td>
<td>Complex partial</td>
<td>R+L central spikes</td>
<td>–</td>
<td>Normal</td>
<td>No seizures from the age of 7 years</td>
<td>R+L</td>
<td>I – II, III</td>
</tr>
<tr>
<td>3 (F)</td>
<td>9</td>
<td>7</td>
<td>Complex partial</td>
<td>R+L central-temporal spikes</td>
<td>+</td>
<td>Normal</td>
<td>One seizure</td>
<td>–</td>
<td>R – L</td>
</tr>
<tr>
<td>4 (F)</td>
<td>10</td>
<td>7</td>
<td>Complex partial</td>
<td>R+L central-temporal spikes</td>
<td>–</td>
<td>Normal</td>
<td>Two seizures from the age of 7 years</td>
<td>–</td>
<td>L – I, II, III</td>
</tr>
<tr>
<td>5 (M)</td>
<td>10</td>
<td>8</td>
<td>Complex partial</td>
<td>R+L central-temporal spikes</td>
<td>+</td>
<td>Normal</td>
<td>No seizure from the age of 8 years</td>
<td>–</td>
<td>R – I, II</td>
</tr>
<tr>
<td>6 (F)</td>
<td>9</td>
<td>9</td>
<td>Complex partial</td>
<td>R central spikes</td>
<td>–</td>
<td>Normal</td>
<td>One seizure</td>
<td>–</td>
<td>R – I, II, III</td>
</tr>
</tbody>
</table>

R = right; L = left; CBZ = carbamazepine. *Only Patient 1 was being treated with carbamazepine (200 mg/day) at the time of recording.

with an intensity 1.2 (in four subjects) and 2.5 times (in all subjects) the sensory threshold. Sensory threshold was defined as the intensity of stimulation at which 50% of the single shock stimuli randomly administered to the individual fingers were detected. None of the subjects perceived the stimuli as painful.

Digital nerve stimulation was carried out according to different modalities; either 40 electrical stimuli were applied in a random order for a period of 3 min with interstimulus intervals ranging from 1 s to 10 s, or electrical stimuli were delivered at 1 Hz, 3 Hz or 10 Hz for a period of 3 min for each stimulus frequency.

### Off-line data analysis: spike detection and averaging

Spontaneous spikes were detected visually on both bipolar and referential montages and read into a topographical analysis system in epochs of 500 ms. The voltage differences between neighbouring electrodes were linearly interpolated from the four nearest values and transformed into a color (grey/white) scale, providing continuous representation of scalp voltages.

For the spontaneous spikes, the epochs were aligned with reference to a digital marker positioned on the main negative peak recorded from the most active channel (Merlet et al., 1996). The epoch ranged from −130 to +370 ms relative to the negative peak, as before.

Baseline correction was performed for the first 100 ms of all epochs. Spike averaging was used to enhance the signal-to-noise ratio (Gregory and Wong, 1984; Ebersole, 1994; Merlet et al., 1996). Before averaging, the individual spike distributions were compared in terms of scalp locations, maximal amplitude of negative and positive peaks and orientation of the zero potential line. In each condition, only scalp activity showing the scalp distribution and morphology typical of rolandic spikes (characterized by a spike followed by a slow wave) was selected to obtain an average of 10 spikes. To determine whether the sample size was adequate, the variance was assessed as a function of increasing sample size. For spontaneous and evoked spikes the variance reached a completely stable level at 10 spikes.

The scalp topography analysis was performed on the spike average. In order to test the influence of a possible ear activation we reformatted the spike average using the common average reference. However, the scalp topography was determined using the linked ear reference. The means and standard deviations of the latency, duration and peak-to-peak amplitude were computed on the single spikes selected for the spike averaging.

In order to quantify the effect of peripheral stimulation on the evoked paroxysmal EEG activity, we used the parameter of persistence defined as percentage of evoked spikes per number of stimuli applied in 3 min of recording.
**Statistical analysis**
Components of spontaneous and evoked spikes were identified on the basis of latency, duration, peak morphology and scalp distribution. Amplitudes were measured peak-to-peak at the locations where they were maximal. Paired *t* tests were performed on the number of evoked spikes described as persistence across various conditions of stimulation (tapping, random, 1- and 3-Hz electrical stimulation). Paired *t* tests were also performed on the latency of each spike component and duration of the main N1 component, to compare each of the four conditions (tapping, random, 1- and 3-Hz electrical stimulation). Since amplitudes were not distributed normally, pair-wise non-parametric comparisons (Wilcoxon’s test) were performed for the various stimulation conditions. *P* < 0.05 was taken as the significance threshold.

**Somatosensory evoked potentials (SEPs)**
Cortical SEPs were obtained by stimulating the finger where tapping evoked the maximal and most frequent scalp activity. The stimuli were square waves of 0.1-ms duration and 3-Hz frequency and had an intensity 2.5 times greater than the perception threshold. In four subjects, the SEPs were also recorded by stimulating the fifth finger. The amplifier band employed for the 28 EEG channels was from 5 to 2000 Hz. A linked-ears reference was used. The averaged potentials were obtained from 500 artefact-free responses and the first 100 ms of each response was analysed. All tests were repeated at least once to ensure reliability of the evoked potentials. Ten age-matched volunteers served as controls for the SEPs elicited by stimulation of the first and fifth fingers.

**Results**

**Spontaneous scalp activity**
All patients showed spontaneous spikes predominantly confined to one hemisphere. Occasionally the spikes occurred bilaterally, and in these cases they were independent. The unilateral spontaneous activity was distributed over the central and temporal electrodes and was characterized by a spike followed by a slow wave (Fig. 1, Subject 4). Averaging of this scalp activity revealed a spike and wave complex which was consistent in its morphology across all the subjects and characterized by a small initial positive peak (P1), a first major negative peak (N1), a second positive peak (P2) and a late slow negative wave (N2). The mean P1–P2 interval was 86.91 ms (*SD* = 12.2 ms). Using a monopolar reference the voltage mapping of the spontaneous spikes showed maximum N1 negativity over the central, parietal and temporo-central electrodes with a time-locked positivity in the frontal regions (Figs 1 and 2). This dipole configuration was present in all patients and did not change with the common average reference. The mean P1–N1 peak-to-peak amplitude was 150 µV (*SD* = 70 µV). The electrode site where the N1 spike showed the maximal amplitude was the same for each paroxysm in each subject: left central and parietal electrodes (C3 and P5) in three patients; left central, parietal and temporo-central electrode (C3, P5 and TC1) in two patients; and right central, temporo-central and parietal (C4, TC2 and P6) electrodes in one subject.

**Scalp activity evoked by tapping**
Tapping stimulation of either hand evoked scalp activity contralateral to the site of stimulation in all subjects. In each subject, one hand was more sensitive than the other to tapping stimulation in terms of number of evoked spikes (right hand in five subjects and left hand in one). Also, the fingers of the same hand showed a different stimulation sensitivity in eliciting scalp activity (Fig. 3). The stimulation of the first finger produced the greatest amount of evoked scalp activity throughout the 3-min recordings. The tapping of the second and third finger produced progressively lower amounts of evoked scalp activity. No scalp activity was observed on tapping the fourth and fifth fingers. Persistence, as evaluated by stimulating the first finger, was different in the various conditions. In particular, the persistence of evoked activity when using tapping stimulation was ~50%, indicating the presence of an evoked spike for every two stimuli applied (Fig. 4).

In all subjects the average scalp activity produced by tapping showed a waveform characterized by P1, N1, P2 and N2 components, similar to those observed for the spontaneous activity (Fig. 2). The initial P1 peak (mean latency 43 ms) was more pronounced for each individual after the spike average and was followed by an N1 component peaking at 78.3 ms (Fig. 2, Table 2). The P2 peak and N2 component were present in all subjects.

The mean duration of the main N1 negative component was 80 ms and the mean peak-to-peak N1 amplitude 159.83 µV. All the evoked activity was contralateral to the stimulation site.

The major N1 component showed a dipole configuration similar to that of the N1 of the spontaneous spike in all subjects (Fig. 2).

**Scalp activity evoked electrical stimulation of the digits**
In all subjects, the electrically evoked activity showed a similar morphology and similar topographic distribution to that evoked by tapping (Fig. 2). The mean peak latencies of the spike components (P1, N1, P2 and N2) and spike duration (P1–P2) for electrically evoked activity were slightly shorter than those obtained by tapping, but the difference was not significant (Fig. 2, Table 2).

Electrical stimulation of the digits with an intensity 2.5 times higher than the sensory threshold was delivered in sequences under different conditions (random, 1 Hz and 3 Hz) and produced an evoked spike with the same morphology in the same subject (Fig. 5, Table 2).
Somatosensory input in rolandic epilepsy

Fig. 1 Scalp representation of raw dataset of spontaneous averaged spikes ($n = 10$) in Subject 4. Calibration tic on vertical bar is 26 $\mu$V (negativity upwards), linked ears reference. The main complex of the spike and slow wave is distributed over the central, temporal and parietal electrodes. The main components of the spontaneous paroxysmal activity (P1, N1, P2 and N2) are represented in the record from the selected electrode P6 (on the right). The frontal positive counterpart of the N1 component is represented in the record from the selected electrode Fz (on the left). The voltage topography of this dipole is represented in Fig. 2.

Fig. 2 Topographic representation of the scalp voltage field at the time of the N1 peak in the averaged spikes ($n = 10$) in Subject 4. The selected electrode is P6 for all the different conditions: spontaneous spike, evoked spike by tapping stimulation and digital electrical stimulation at intensities of 1.2 and 2.5 times the sensory threshold. The vertical cursor denotes the time of the voltage maps. For the evoked spikes, ‘S’ indicates the time of the stimulus. Calibration tic on vertical bar is 26 $\mu$V (negativity upwards). The isopotential contours are shown in steps of 15 $\mu$V. Grey is negative and white positive; the negative component (N1) in the scalp topography is shaded in to emphasize the frontal positive counterpart of the dipole configuration of the spontaneous and evoked spikes.

No significant changes were observed in latency and duration under different conditions of electrical stimulation (Table 2). No significant changes in amplitude were observed between random and 1-Hz electrical stimulation. A significant decrease ($P < 0.02$) in amplitude was found for the evoked activity following 3-Hz electrical stimulation compared with the other stimulus conditions.

In the four subjects in whom electrical digital stimulation was delivered with an intensity 1.2 times the sensory threshold, the evoked paroxysmal activity showed the same persistence, morphology and scalp distribution as the paroxysmal activity produced by an intensity 2.5 times the threshold (Fig. 2). The mean P1 peak latency was 41.2 ms (SD = 6.8 ms) while the N1 component peaked at 75 ms (SD = 5.5 ms). The P2 peak and N2 components showed latencies of 115 ms (SD = 12.5 ms) and 200 ms (SD =
The mean duration of the negative N1 component was 77 ms (SD = 5.5 ms). The mean N1 peak-to-peak amplitude was 170.72 µV (SD = 50 µV).

In all subjects, the electrical digital stimulation delivered in the random condition produced a significantly greater number ($P < 0.05$) of evoked spikes (persistence = 68%, SD = 21%) compared with tapping stimulation (persistence = 48%, SD = 20%) (Figs 4 and 5). The 1-Hz frequency stimulation produced an increase in persistence ($P < 0.05$) of evoked spikes (persistence = 85%, SD = 10%) compared with the persistence of spikes evoked by electrical stimulation delivered in random conditions (Figs 4 and 5). A significant decrease in persistence ($P < 0.01$) was noted for the 3-Hz stimulation (persistence = 47%, SD = 20%) (Figs 4 and 5).

### Table 2

<table>
<thead>
<tr>
<th></th>
<th>P1 (ms)</th>
<th>N1 (ms)</th>
<th>P2 (ms)</th>
<th>N2 (ms)</th>
<th>P1–P2 (ms)</th>
<th>P1–N1 (µV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tapping, random</td>
<td>43.00 ± 6.44</td>
<td>78.3 ± 4.8</td>
<td>121.6 ± 9.6</td>
<td>210 ± 18</td>
<td>80.00 ± 7.6</td>
<td>159.83 ± 57</td>
</tr>
<tr>
<td>Electrical, random</td>
<td>41.33 ± 5.92</td>
<td>73.83 ± 4.62</td>
<td>117.3 ± 11.2</td>
<td>210 ± 10</td>
<td>76.6 ± 4.8</td>
<td>176.33 ± 49</td>
</tr>
<tr>
<td>Electrical, 1 Hz</td>
<td>42.16 ± 6.17</td>
<td>75.33 ± 5.88</td>
<td>124.5 ± 6.02</td>
<td>214 ± 16.2</td>
<td>81.00 ± 4.19</td>
<td>156.00 ± 58</td>
</tr>
<tr>
<td>Electrical, 3 Hz</td>
<td>45.66 ± 5.78</td>
<td>81.00 ± 4.42</td>
<td>125.6 ± 7.68</td>
<td>210 ± 14.1</td>
<td>79.83 ± 3.86</td>
<td>118.66 ± 47</td>
</tr>
</tbody>
</table>

Data are presented as means and standard deviations.
No clinical seizures were observed during low- and high-frequency stimulation.

Electrical stimulation at 10 Hz did not produce any evoked paroxysmal activity during the 3-min recordings. However, two subjects (Subjects 3 and 4) presented brief trains of evoked spikes lasting only a few seconds at the beginning of the high-frequency stimulation (Fig. 5). Spontaneous spikes were still present among the evoked spikes during the low-frequency stimulation (1 Hz), ranging from 10 to 15 over a period of 3 min, but rarely occurred during 3-Hz stimulation. No spontaneous spikes were observed during high-frequency stimulation (10 Hz).

**Somatosensory evoked potentials (Fig. 6, Tables 3 and 4)**

All patients presented a high-amplitude late component (mean latency 80 ms; amplitude 30 µV) with maximum negativity over the centroparietal and temporal regions contralateral to the peripheral stimulation. In each patient, the late SEP component showed a scalp topography similar to the paroxysmal activity evoked by electrical and tapping stimulation. It was centred over the centroparietal and centrottemporal regions and was mirrored by a frontal positivity, with the isoelectric line over the central regions. By contrast, in our normal subjects the late component N60 obtained by stimulation of first and fifth fingers showed a diffuse distribution over the central regions contralateral to the side stimulated with a radial orientation. The latency of the late high-amplitude SEP component and that of the N1 peak of the spike evoked at 3-Hz stimulation showed no significant difference. The mean amplitude of the late SEP component (N60 = 36.6 µV) was lower than the amplitude of the N1 component of the spike evoked by 3-Hz electrical stimulation (N1 = 118 µV), but it was significantly higher than the mean amplitude of the N60 recorded in the normal subjects (N60 = 3.1 µV, SD = 1.9 µV, from the first finger and N60 = 2.9 µV, SD = 2 µV, from the fifth finger) (Tables 3 and 4).

The early N20 component of SEP showed a normal peak latency and amplitude in all patients, while the later components were masked by the 'extreme SEPs'. In four subjects, the SEPs obtained by stimulation of the fifth finger were normal in latency, amplitude and morphology.

**Discussion**

Epilepsy with extreme SEPs is a form of benign rolandic epilepsy of childhood. The occurrence of abnormal scalp
responses following stimulation of the fingers, or the sole of the foot, with a tendon hammer has been described in various studies (De Marco and Negrin, 1973; De Marco and Tassinari, 1981; Tassinari and De Marco, 1985; Dalla Bernardina et al., 1990).

In this study we have demonstrated that low-intensity electrical digital stimulation was capable of eliciting spikes. The evoked spikes had a similar latency, morphology and topography to those elicited by tapping stimulation. The effect of frequency was important: compared with electrical digital stimulation, 1-Hz stimulation produced a greater number of evoked spikes, while 3-Hz stimulation caused a decrease in the number of evoked spikes. During 10-Hz stimulation evoked spikes almost disappeared. In patients with this form of epilepsy the evoked spikes. During 10-Hz stimulation evoked spikes while 3-Hz stimulation caused a decrease in the number of evoked spikes, stimulation performed in the random condition, 1-Hz effect of frequency was important: compared with electrical digital stimulation was capable of eliciting spikes.

One of the main findings of the present study is the possibility of eliciting high-amplitude scalp activity after electrical stimulation of digital nerves. Both a very low stimulus intensity (just above the sensory threshold) and a relatively high stimulus intensity below pain threshold (2.5 times the sensory threshold) evoked EEG spikes.

Direct comparison of the focal spikes evoked by tapping with those evoked by electrical stimulation was possible using a triggered tendon hammer which enabled us to evaluate the temporal relationship between the tapping stimulus and the evoked activity. We found that tapping and electrical stimulation produced paroxysmal scalp activity with the same morphology and topography and with almost the same latency. This finding strongly suggests that, with both these types of peripheral stimulation, common sensory pathways and similar cortical sources are involved in generating the abnormal EEG activity.

That the generators of the evoked paroxysmal activity are cortical is suggested by the fact that, when using electrical stimulation, the minimum afferent conduction time from digit to sensory cortex is ~20 ms (Burke et al., 1975; Chiappa, 1990).

SEP studies with upper limb stimulation have shown that a parietal negative potential (N20) is the first cortical activity of the somatosensory cortex, mainly generated from area 3b (Allison et al., 1989, 1991, 1992). It is followed by frontal and parietal responses which are assumed to be of different origin (Mauguiere et al., 1983; Desmedt and Bourget, 1985; Deiber et al., 1986; Rossini et al., 1989). Most of these investigators claim that early SEP components, ranging from 20 to 45 ms and distributed over the centroparietal scalp region, originate predominantly from the somatosensory cortex.

Likewise, the somatosensory cortical areas may be the hypothetical site where an early hypersynchronous neuron discharge takes place in response to afferent stimulation, in view of the fact that, in our subjects, the first positive component (P1) of the evoked spikes peaked with a mean latency of 43 ms. This hypothesis is supported by the fact that low-intensity electrical digital stimulation produces prominent activation of cutaneous fibres which converge mainly on the somatosensory area (Buchthal and Rosenfalck, 1965).

Scalp activity evoked by peripheral stimulation

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### Table 3 Peak latencies and amplitudes of SEP components following finger stimulation in normal subjects

<table>
<thead>
<tr>
<th></th>
<th>N20</th>
<th>P22</th>
<th>P25</th>
<th>N30</th>
<th>N60</th>
<th>P100</th>
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<tbody>
<tr>
<td>Finger I</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>21 ± 1.4</td>
<td>22.6 ± 1.3</td>
<td>25.6 ± 1.6</td>
<td>32 ± 1.8</td>
<td>59 ± 6.6</td>
<td>120 ± 4.2</td>
</tr>
<tr>
<td>Amplitude (µV)</td>
<td>2.5 ± 2.2</td>
<td>3.1 ± 2.1</td>
<td>4.2 ± 2.4</td>
<td>3.4 ± 2.3</td>
<td>3.1 ± 1.9</td>
<td>3.6 ± 2</td>
</tr>
<tr>
<td>Finger V</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>21.8 ± 1.2</td>
<td>23 ± 1.4</td>
<td>25.7 ± 1.7</td>
<td>33 ± 1.9</td>
<td>61 ± 4.2</td>
<td>122 ± 5.8</td>
</tr>
<tr>
<td>Amplitude (µV)</td>
<td>2.4 ± 2.3</td>
<td>3.5 ± 2.1</td>
<td>3.6 ± 1.8</td>
<td>3.7 ± 1.9</td>
<td>2.9 ± 2</td>
<td>2.6 ± 1.7</td>
</tr>
</tbody>
</table>

Data are presented as means and standard deviations (n = 10 subjects).

### Table 4 Peak latencies and amplitudes of SEP components following finger stimulation in four patients (Subjects 1, 4, 5 and 6)

<table>
<thead>
<tr>
<th></th>
<th>N20</th>
<th>P1</th>
<th>N1</th>
<th>P2</th>
<th>P1-N1</th>
<th>P22</th>
<th>P25</th>
<th>N30</th>
<th>N40</th>
<th>N60</th>
<th>P100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finger I</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>Latency (ms)</td>
<td>21.25 ± 1.5</td>
<td>37.5 ± 3.1</td>
<td>71.2 ± 7.4</td>
<td>120 ± 10</td>
<td></td>
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<tr>
<td>Amplitude (µV)</td>
<td>3.7 ± 1.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>36.6 ± 10</td>
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<td></td>
</tr>
<tr>
<td>Finger V</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>22.5 ± 1.1</td>
<td></td>
<td></td>
<td></td>
<td>23.1 ± 1.1</td>
<td>26 ± 2.1</td>
<td>32 ± 1.9</td>
<td>42 ± 3.2</td>
<td>63 ± 2.2</td>
<td>115 ± 2.1</td>
<td></td>
</tr>
<tr>
<td>Amplitude (µV)</td>
<td>3.5 ± 2.1</td>
<td></td>
<td></td>
<td></td>
<td>2.1 ± 1.1</td>
<td>3.6 ± 1.8</td>
<td>3.7 ± 1.9</td>
<td>3.1 ± 2</td>
<td>3.3 ± 2</td>
<td>3.1 ± 4</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as means and standard deviations.
Effect of stimulus rate on the evoked spikes

A refractory period of the group of neuronal cells involved in producing the ‘extreme SEP’ activity may be a possible explanation for the decrease in persistence accompanying the increase in stimulus rate. Since the evoked spikes last >100 ms in all subjects, during the 10-Hz stimulation (interstimulus interval = 100 ms) the cortical generators of the spikes may still be in the refractory period on arrival of the new afferent input.

However, this hypothesis cannot account for the decrease in persistence and amplitude of the evoked spikes at 3-Hz stimulation because the interval between stimuli (333 ms) is much longer than the spike duration.

The effect of stimulus frequency on SEPs has been extensively researched (Pratt et al., 1980; Abbruzzese et al., 1990; Delberghe et al., 1990; Onishi et al., 1991; Garcia-Larrea et al., 1992). In particular, in a recent PET study (Ibanez et al., 1995) the progressive decrease in SEP amplitude from low to high frequency of stimulation was associated with a linear increase in regional cerebral blood flow. Complex inhibitory mechanisms mediated by GABAergic connections with parietal regions (Whitsel et al., 1989) have been adduced in order to explain the reduction in excitatory post-synaptic potentials in those cells which generate the SEP components. Similar inhibitory mechanisms can be postulated for the decrease in the persistence and amplitude of spikes evoked by stimulation at the 3-Hz frequency.

Repetitive peripheral stimulation has not only inhibitory but excitatory effects on cortical generators of the evoked spikes. The increase in number of evoked spikes during 1-Hz stimulation in comparison with the random condition suggests that 1-Hz stimulation is a special stimulus rate to which the cortical excitability becomes more sensitive. Furthermore, the increase in number of evoked spikes during 1-Hz stimulation may be related to the hypothetical hypersynchronization of afferent input at the cortical level (Dichter and Ayala, 1987) as documented in biological models (Masukawa et al., 1996).

The clinical importance of these observations includes the possibility of using a peripheral stimulus to bring about excitatory or inhibitory modulations of the paroxysmal activity, and as such clearly warrants further investigation.

The relationship between evoked and spontaneous spikes

Bilateral independent spontaneous spikes occurred over the centrotemporal regions in all subjects. The spontaneous spikes presented the typical morphology and scalp distribution of rolandic spikes, characterized by a spike followed by a slow wave. The spike presented a posterior negativity and an anterior positivity with the isoelectric line over the central regions, as described in previous studies (Gregory and Wong, 1984; Luders et al., 1987; Wong and Weinberg, 1988; Niedermeyer, 1992; Van der Meij et al., 1992; Baumgartner et al., 1996). In order to establish the relationship between evoked and spontaneous spikes, we compared the spontaneous spikes recorded on the same hemisphere as the evoked spikes, using spike average and scalp topography. We found that the morphology and scalp distribution of the evoked spikes was similar to that of the spontaneous spikes in the same subject. Moreover, high-frequency stimulation suppressed both the spontaneous and evoked spikes.

It is therefore likely that spontaneous rolandic spikes with a similar behaviour to the evoked spikes share common generators. An initial source in the sensory cortex and a subsequent involvement of the motor and secondary sensory areas is also consistent with clinical seizure, in which some patients have reported paraesthesias of the mouth and hand preceding the clonic jerk in the face and arm (Lombroso, 1967; Luders et al., 1987; Holmes, 1993).

We suggest that, in this form of benign epilepsy, the afferent sensory input may be capable of modulating the generators of the spontaneous and evoked spikes with potentially significant clinical implications.

Significance of high-amplitude late SEP components

The standard SEPs elicited by 3-Hz stimulation of the first finger produced a high-amplitude late component in our patients, as described in previous studies (Tassinari and De Marco, 1985; Dalla Bernardina et al., 1990, 1992). The early N20 component of the SEP showed a normal peak latency, amplitude and morphology, while the later components were masked by a high-amplitude complex similar in latency, morphology and scalp distribution to the single spike elicited at 3-Hz stimulation, but smaller in amplitude. However, in four subjects, in whom tapping stimuli failed to evoke cortical spikes, stimulation of the fifth finger produced normal late SEPs. We are therefore of the opinion that the high-amplitude
complex in the averaged SEPs is simply the average of the evoked spikes elicited by electrical stimulation. The decrease in the amplitude of this complex compared with the single spike is probably due to the averaging of traces without evoked spikes because the persistence is ~50% at 3-Hz stimulation, as documented during the continuous EEG recording.

Moreover, the high-amplitude late SEPs observed in our patients can be differentiated from the late negative component (N60) of normal SEPs on the basis of a number of characteristics. The dipole configuration was similar for both the evoked spikes and the late high-amplitude component of SEPs, while the N60 obtained by stimulation of the fifth finger showed a diffuse radial low-amplitude distribution, as observed in our normal subjects and in previous studies (Desmedt and Tomberg, 1989; Garcia Larrea et al., 1991).

In addition, evoked spikes of maximum amplitude can be elicited by electrical stimulation adjusted to just 1.2 times the stimulation threshold. This behaviour is at variance with that of SEPs components following mechanical stimulation, which increase in amplitude with enhancement of the stimulus intensity (Buchthal and Rosenfalck, 1966; Lesser et al., 1979).

Therefore, for all the above-mentioned reasons the high-amplitude late component of SEPs in benign rolandic epilepsy should be regarded as the result of the averaging of the spikes evoked by electrical stimulation. The term ‘extreme SEPs’ in our opinion is ambiguous and redefinition of the phenomenon may be necessary in the rolandic epilepsy group.

Conclusions
The possibility of evoking a spike by electrical digital stimulation constitutes an important and useful tool for testing and monitoring cortical excitability in rolandic epilepsy.

The use of a well-quantified stimulus enabled us to investigate the effects of different somatosensory afferent input parameters in this form of benign idiopathic epilepsy.

Our data suggest that spontaneous and evoked spikes share common generators, probably located in the sensorimotor cortex.

The sensitivity to the stimulus rate affords new insights into the excitatory and inhibitory mechanisms involved in modulating the paroxysmal activity of the rolandic area and therefore offers prospects of possible therapeutic strategies. We would suggest the use of peripheral electrical stimulation as an additional activation test in the clinical setting, particularly for epilepsy of the sensorimotor areas.

References


