Polygraphic Investigations and Back-Averaging Techniques in the Study of Epileptic Motor Phenomena

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16.1 Introduction

The term *polygraphy* refers to the simultaneous recording of multiple physiologic measures. The main aim of polygraphic monitoring is to correlate behavioral manifestations with changes occurring in a set of physiologic parameters. Therefore, to obtain the maximum yield from a polygraphic study, it is necessary to tailor it to the clinical problem that is going to be investigated by selecting the parameters that are relevant to the nature and the characteristics of this specific clinical manifestation [1, 2].

In epileptology, polygraphic investigations (PI) can be extremely useful to detect subtle and unnoticed clinical manifestations, to define the clinical characteristics of different epileptic conditions, to describe the semiology of epileptic seizures contributing to the syndromic diagnosis, to evaluate the clinical relevance of some paroxysmal activity (ictal? interictal? subclinical?), to clarify the physiopathogenetic mechanisms of epileptic phenomena, and to monitor and evaluate the effects of drugs.

As a general methodological approach, it is advisable that before a PI is set up, the epileptic phenomena that are the subject of the investigation have been previously evaluated.

with the usual video-EEG (or other) recordings. Indeed, the PI complemented with video recording is intended to document what has been collected on anamnestic data or observed by previous investigations. Consequently, various parameters will be associated to EEG recording, to evaluate the muscular activity (electromyogram, usually with surface electrodes), the respiratory and cardiac functions, the degree of performance or responsiveness, and other parameters that might be relevant for the specific clinical condition that has to be investigated [1].

In addition video-polygraphy can be of paramount importance in the differential diagnosis of non-epileptic manifestations or when both non-epileptic and epileptic phenomena are combined in the same patient [3, 4].

The aim of this chapter is to illustrate the usefulness of polygraphic recording in the detection and characterization of epileptic motor phenomena. In addition we will introduce some concepts on the contribution of computerized techniques such as back-averaging of the polygraphic signal to further describe some epileptic motor phenomena and to obtain valuable information on their underlying pathophysiological mechanisms.

16.2 Polygraphic Features of Epileptic Motor Manifestations

Motor manifestations often represent one of the most overt clinical phenomena of an epileptic seizure. PI with recording of surface EMG activity can be helpful to identify and characterize the type of motor events, the pattern of muscular activation, and the temporal correlation with changes of the EEG activity; in addition they can be a very effective tool to identify even subtle and apparently subclinical muscular manifestations such as mild contractions or sporadic muscle twitches that can be missed by the observer.

Therefore PI with surface EMG recording can be crucial to identify and to define different types of motor phenomena that can occur either isolated or in various combinations, to constitute the clinical manifestations of the different types of epileptic seizures.

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16.2.1 Myoclonus

Myoclonus is defined as positive myoclonus when it is characterized by a massive, shock-like muscular contraction that involves one or more body segments [5]. It appears in the EMG as a brief burst of muscular potentials (Fig. 16.1a) synchronous on agonist and antagonist muscles, with or without an EEG correlate. The opposite phenomenon, a "negative" myoclonus, is a brief interruption of a tonic muscular contraction (Fig. 16.1b), sometimes clinically indistinguishable from the positive myoclonus [6]. Negative myoclonus is defined as an interruption of tonic muscular activity lasting <500 ms without evidence of preceding positive myoclonia [5]. When associated with a paroxysmal EEG event, a negative myoclonus is defined as "epileptic negative myoclonus" (Fig. 16.1c) [7–9]. Polygraphic recordings can be crucial to identify negative myoclonus and sometimes to distinguish it from positive myoclonus. In epileptic negative myoclonus, the interruption of the muscular activity occurs synchronously on agonist and antagonist muscles; when epileptic negative myoclonus is focal, involving one or both limbs on the same side of the body, it is usually associated with a contralateral EEG spike located in the centroparietal region [9]. Epileptic negative myoclonus has been recognized as a seizure type by the Task Force of the International League Against Epilepsy on Classification and Terminology [5].

16.2.2 Spasms

A spasm is characterized by a massive and slow contraction reaching a climax and progressively decreasing, more often involving axial and proximal muscular groups. PI with multiple EMG channels have shown that epileptic spasms may occur with complex patterns of muscular activation, recruiting cranial as well as limb and axial muscles (Fig. 16.2) [10, 11]. Spasms can be devoid of any EEG correlate or they can be associated with an EEG flattening, with a diffuse low-voltage fast activity [12] or with a slow wave [11, 13].

16.2.3 Tonic Contractions

The polygraphic feature of a tonic contraction is a slow, sustained contraction maintained over time that involves several muscular groups and that is usually associated with fast-recruiting EEG activity.

16.2.4 Clonic Contractions

Clonic contractions are characterized by a series of muscle jerks, whose amplitude, symmetry, frequency, and topography can vary, and that are often associated with contralateral EEG epileptic paroxysms [12].

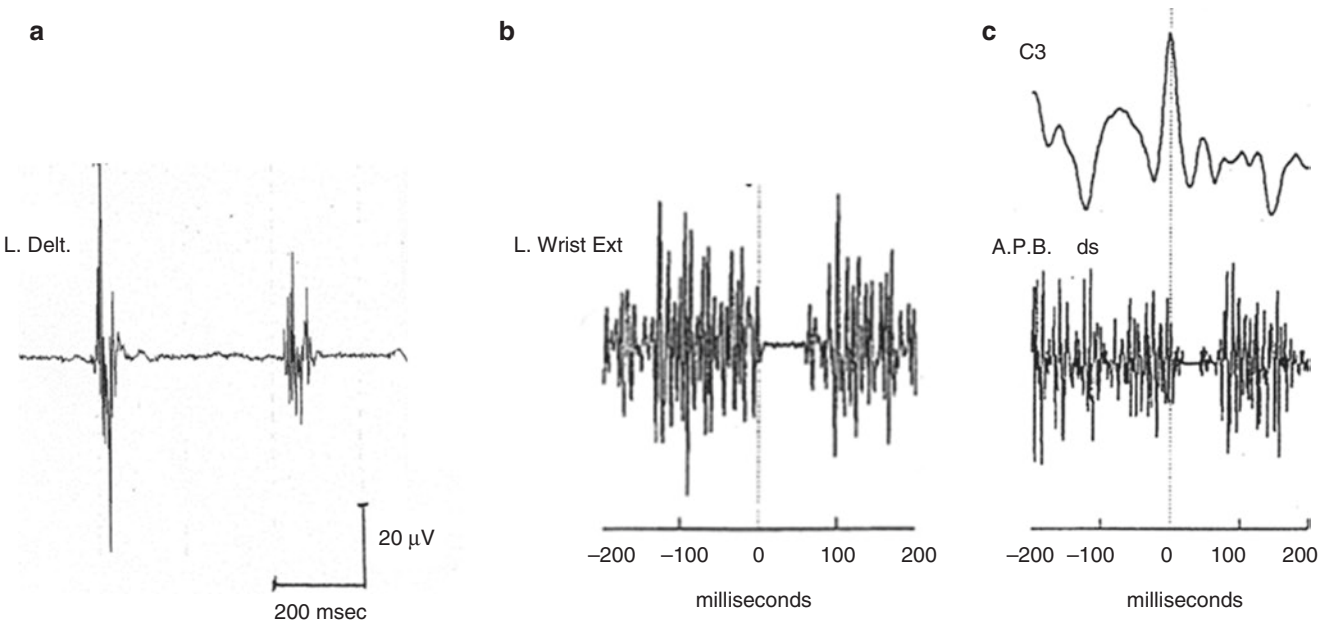


Fig. 16.1 (**a**) Two positive myoclonia in the left deltoid. (**b**) Negative myoclonus in the left wrist extensor in an outstretched left upper limb. Negative myoclonus requires a tonic contraction to be detected (the vertical marker is positioned at the onset of the EMG silent period). (**c**) Epileptic negative myoclonus in the right abductor pollicis brevis. The onset of the EMG silent period is time-locked to the peak of the spike in C3

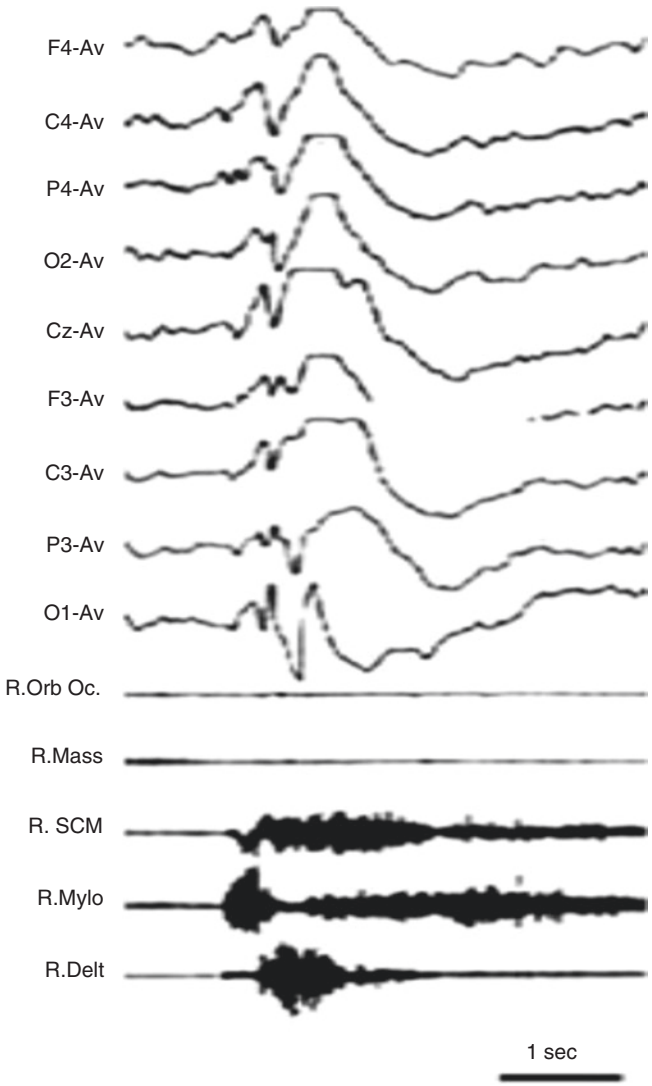


Fig. 16.2 Epileptic spasm. A massive and slow contraction reaching a climax and progressively decreasing involves the proximal limb muscles and the sternocleidomastoideus. The spasm is associated with a slow wave encompassing a spike. *R.* right, *Mass* masseter, *SCM* sternocleidomastoideus, *Mylo* mylohyoideus, *Delt* deltoid

16.2.5 Atonic Phenomena

The main feature of atonic phenomena is a sudden global or focal loss of muscular tone that corresponds in the EMG to an abrupt flattening and that can be related to different types of EEG epileptic abnormalities such as generalized spike- or polyspike-and-wave discharges, diffuse fast rhythmic spikes (Fig. 16.3), bilateral synchronous fast waves intermixed with slow waves, or no EEG changes at all [2, 12]. PI can be helpful to document the combination of myoclonic and atonic phenomena in conditions such as myoclonic-astatic epilepsy [14].

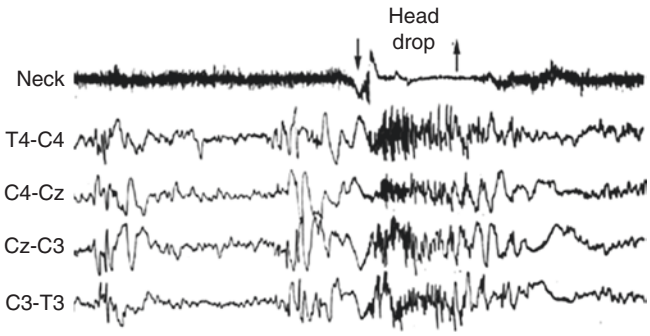


Fig. 16.3 Polygraphic recording of an atonic seizure showing the abrupt loss of muscular tone in the neck muscles, corresponding in the EMG to an abrupt flattening that clinically results in a head drop. The muscular atonia is associated with diffuse fast rhythmic spikes in the EEG

16.3 Polygraphic Patterns in Different Types of Epileptic Seizures or Syndromes

16.3.1 Generalized Tonic-Clonic Seizures

The manifestations of generalized tonic-clonic seizures consist of a more or less stereotyped sequence of motor phenomena [15, 16]. At seizure onset there is an initial tonic phase of sustained muscular contraction lasting 10–20 s and involving all skeletal muscles that corresponds clinically to a flexion involving the whole body, followed by a longer extension phase. Then a diffuse vibratory contraction follows, eventually evolving to massive clonic manifestations that progressively slow down until the seizure ends. The clonic manifestations are usually brief. PI have shown that few seconds after the last clonic jerk, often a new tonic contraction can occur, involving mainly facial and masticatory muscles. In the EEG, the initial phase is usually associated with a desynchronization, sometimes preceded by generalized bursts of polyspike-and-waves and followed by a recruiting rhythm. During the evolution of the seizure, the recruiting rhythm starts to be intermixed with slow waves of decreasing frequency and increasing amplitude that at a certain point correspond to the fragmentation of the tonic massive contraction and to the appearance of the clonic manifestations. The end of the motor manifestations is associated with a flattening of the EEG activity lasting several seconds.

16.3.2 Tonic Seizures

The tonic seizures are characterized clinically by muscular tonic contraction, lasting about 5–20 s, and accompanied by

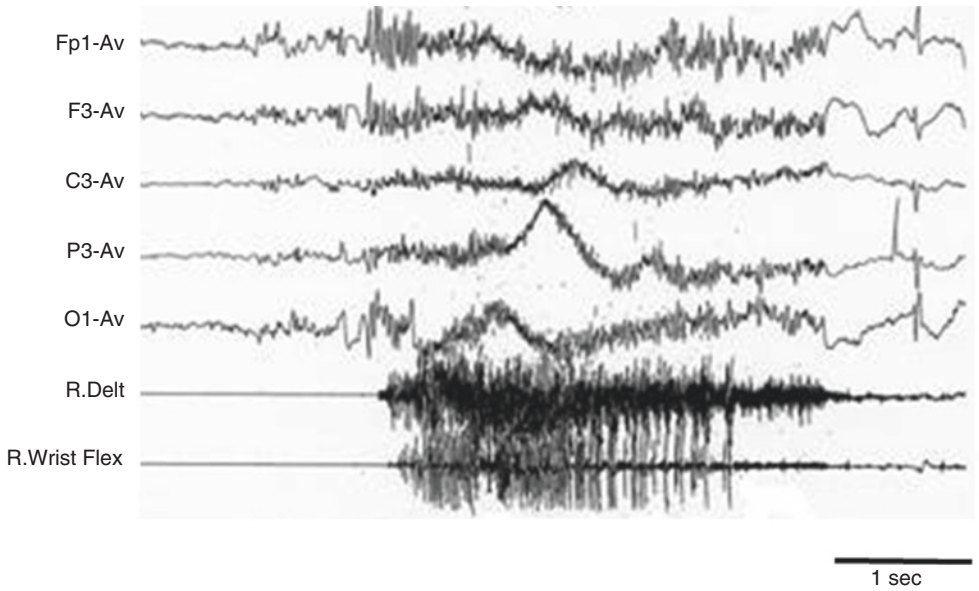


Fig. 16.4 Polygraphic recording of a tonic seizure, characterized by a muscular tonic contraction in the recorded muscles associated with rhythmic fast activity (around 20 Hz) in the EEG. *R.* right, *Delt* deltoid, *Wrist Flex* wrist flexor

impairment of consciousness, involving, with varying degrees of intensity, mainly muscles of the head, trunk, limb girdles, and, to a lesser extent, legs [17–19]. PI can show different EEG patterns such as (a) flattening of the tracing, (b) fast activity (around 20 Hz) of progressively increasing amplitude (Fig. 16.4), and (c) recruiting rhythmic discharge at about 10 Hz, sometimes of high amplitude from the onset. In the EMG channels, the tonic contraction is associated with an interference pattern in all muscles involved by the seizure. In short tonic seizures, the EMG activity is maximal at the onset and then decreases; in longer seizures, the intensity of the EMG activation progressively increases reflecting the increasing intensity of the contraction. In global tonic seizures, an axial preponderance of the muscular activation is evident. An asymmetric tonic contraction or a massive myoclonia at the end of the tonic muscular activity can be observed. Autonomic changes, such as modifications of heart and respiration rate, vasomotor phenomena, mydriasis, and positive electrodermogram responses are additional features of tonic seizures [18].

16.3.3 Myoclonic Absences

The distinguishing features of myoclonic absences are (a) appearance of a generalized 3 c/s spike-and-wave discharge lasting up to several seconds and (b) myoclonic jerks associated with spike-wave complexes, particularly evident in the upper limbs that, a few seconds after the onset of the EEG epileptic activity, are superimposed to a progressively increasing tonic muscular contraction, maximal at the shoulders that clinically results in the abduction and elevation of the arms (Fig. 16.5) [20, 21]. Detailed analysis of the EEG-EMG correlations has shown that the positive transient of the 3 c/s spike-and-wave complex is time-locked to the appearance of the myoclonic jerks. The myoclonic bursts are followed by a brief (60–120 ms) silent period that fragments the tonic contraction [21, 22].

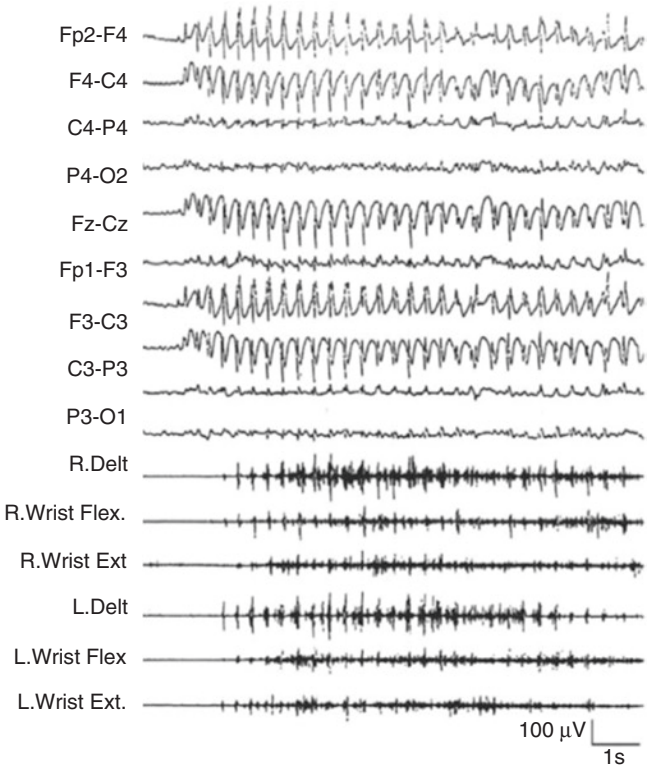


Fig. 16.5 Myoclonic absence seizure. The main feature of this seizure type are (a) generalized 3 c/s spike-and-wave discharge lasting up to several seconds; (b) myoclonic jerks time-locked to the spike-wave complexes, more prominent in the upper limbs that, a few seconds after the onset of the EEG epileptic activity, are superimposed to a progressively increasing tonic muscular contraction, maximal at the shoulders that clinically results in the abduction and elevation of the arms. *R.* right, *Delt* deltoid, *Wrist Flex* wrist flexor, *Wrist Ext* wrist extensor

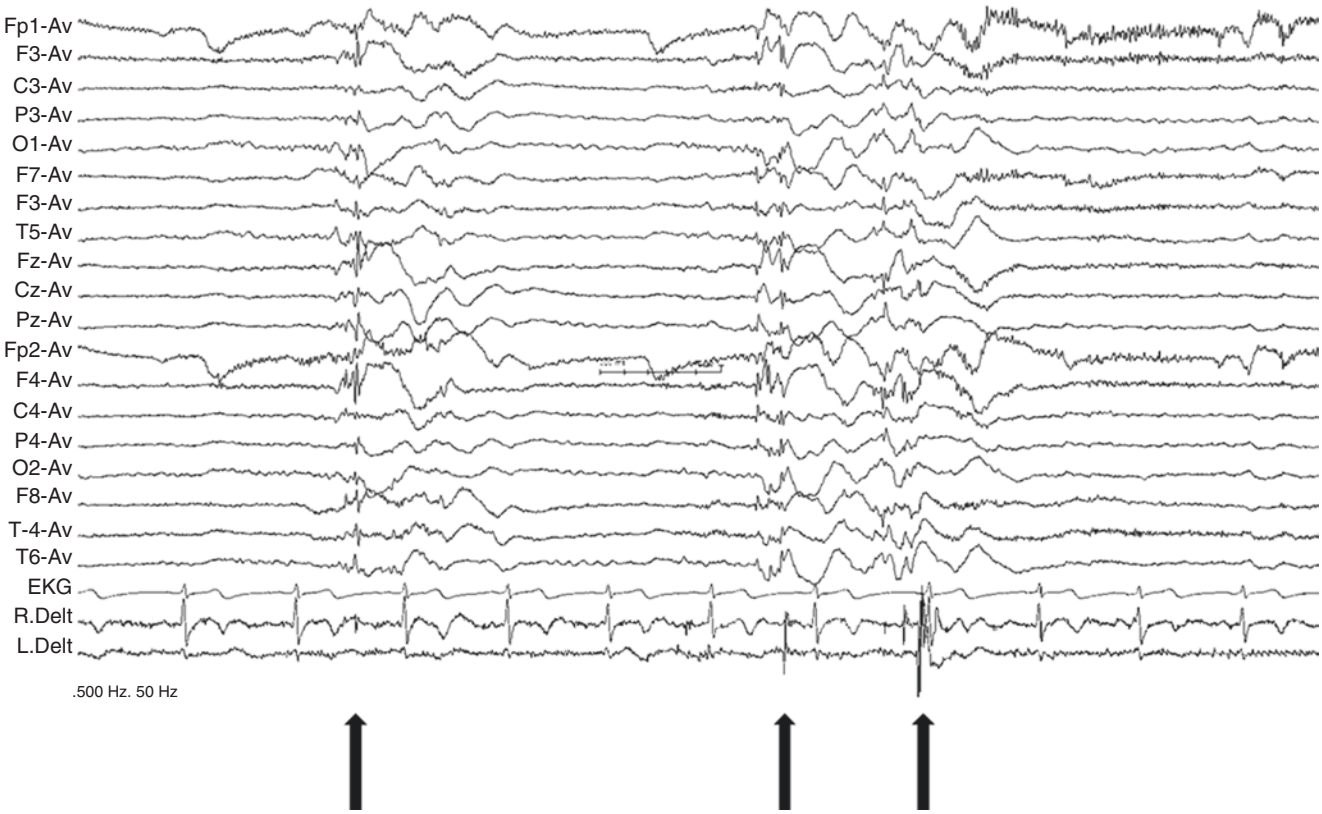


Fig. 16.6 Myoclonic jerks in juvenile myoclonic epilepsy. The myoclonic jerks, indicated by the arrows, are associated with a generalized polyspike-wave discharge. *R.* right, *L.* left, *Delt* deltoid

16.3.4 Juvenile Myoclonic Epilepsy

The polygraphic signature of juvenile myoclonic epilepsy are short bursts of myoclonic jerks—particularly at the upper limbs—associated with polyspike-and-wave complexes at a frequency of 3–3.5 c/s (Fig. 16.6) [23]. Computerized analysis of the polygraphic signal has demonstrated that the myoclonic bursts are correlated to a cortical positive potential encompassed in the polyspike rhythm of the polyspike-wave complex [24].

16.3.5 Epilepsia Partialis Continua

PI in epilepsia partialis continua has shown more or less rhythmic myoclonic EMG potentials whose EEG correlate can be variable, such as slow focal abnormalities, focal paroxysmal discharges, or no evident paroxysmal activity [25]. In some patients, a clinical picture resembling epilepsia partialis continua, characterized by frequent, subcontinuous jerks, evident when the patient maintains a posture or a tonic contraction, can be caused by subcontinuous epileptic negative myoclonia (i.e., brief lapses of the muscular activity time-locked to paroxysmal EEG activity). In these cases, PI are crucial for the correct diagnosis.

16.3.6 Progresive Myoclonus Epilepsies

Progressive myoclonus epilepsies (PMEs) are a group of rare inherited diseases featuring a combination of myoclonus, seizures, and variable degrees of neurological and cognitive impairment. Despite extensive investigations, a large number of PMEs remain undiagnosed. PI can be helpful in the diagnostic process either in the initial phase for differential diagnosis or to detect distinguishing features in the different forms of PMEs.

The main polygraphic feature of progresive myoclonus epilepsies is myoclonus, either at rest or during action that is characterized by EMG potentials of short duration (20–30 ms), which are synchronous on agonist and antagonist muscles (Fig. 16.7) [27]. At rest, erratic myoclonic twitches can occur asynchronously in different muscular groups. In action myoclonus the EMG potentials are of high amplitude and are followed by an EMG silent period lasting 40–120 ms (rarely up to 300 ms). The myoclonic EMG bursts and the silent periods are inconstantly related to EEG spike-and-waves and polyspike-and-waves (Fig. 16.7). In Unverricht-Lundborg disease, myoclonic seizures are characterized by generalized myoclonia, predominant proximally in the upper limbs, with varying rhythm and associated with generalized, symmetrical polyspikes or polyspike-and-waves [28, 29].

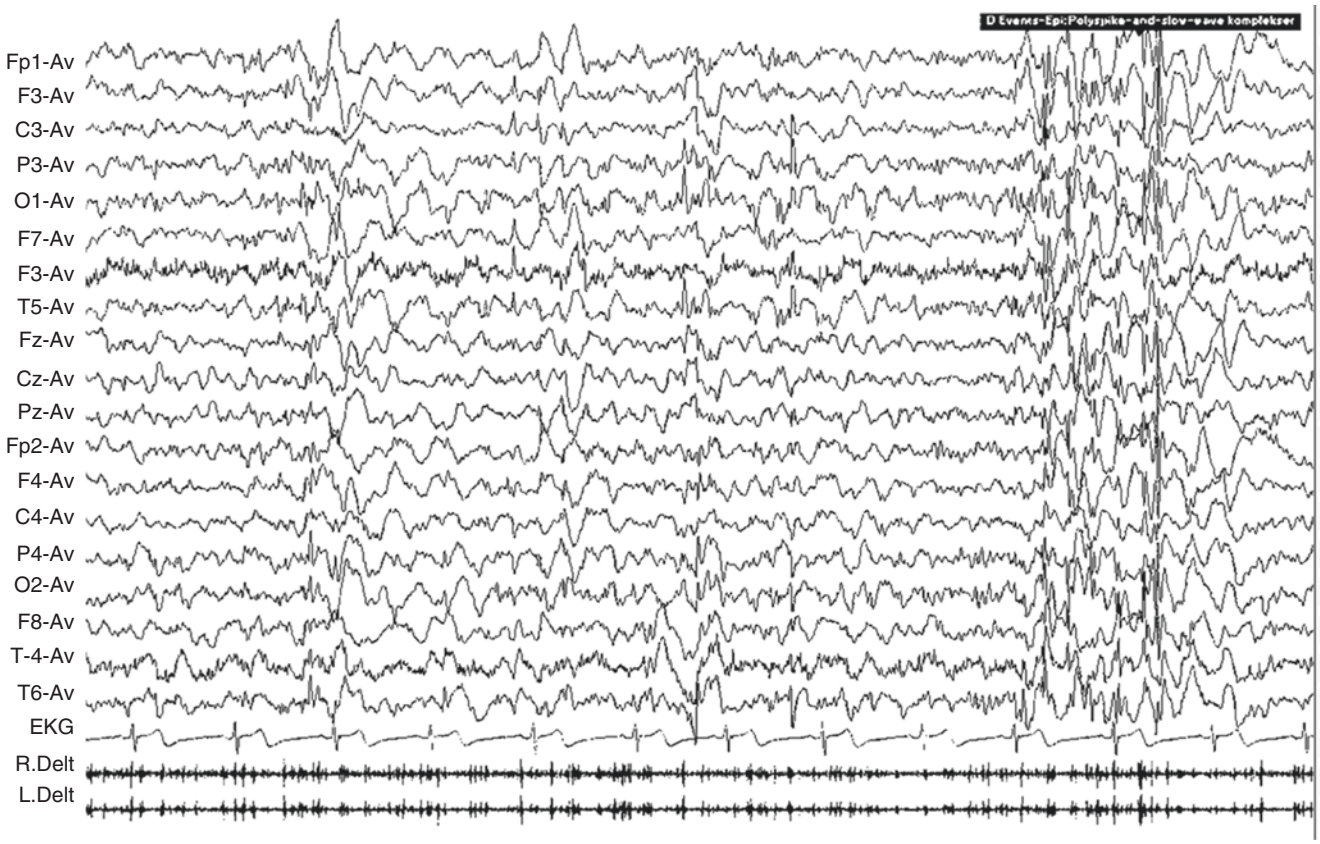


Fig. 16.7 Polygraphic tracing in progressive myoclonus epilepsy with *KCNC1* mutation [26]. The recording at rest shows subcontinuous myoclonic potentials, intermingled with negative myoclonia in both deltoids. The myoclonic EMG bursts and the silent periods are inconstantly related to EEG spike-and-waves and polyspike-and-waves. *R.* right, *L.* left, *Delt.* deltoid

PIs in Lafora disease show abundant, asymmetrical, asynchronous, subtle myoclonia at rest, diffuse to all muscular groups, usually without an EEG correlate [27, 30, 31]. Rarer forms of PMEs, such as sialidosis [32]; ceroid neuronal lipofuscinosis [33]; PMEs associated with *SCARB2* mutations [34], with ASAH1 mutations [35], and with *GOSR2* mutations [36, 37]; and rhythmic myoclonia, clinically resembling a tremor, i.e., "cortical tremor" [38], have been shown, by means of computerized technique of the EEG-EMG signals, to be associated with a rhythmic cortical potential at the same frequency of the myoclonus in the contralateral central regions [39, 40]. In PMEs, visual stimuli and intermittent photic stimulation can be extremely effective in eliciting fast polyspikes and polyspike-and-waves associated with massive myoclonic jerks, i.e., "photic reflex myoclonus" (Fig. 16.8) or even in precipitating myoclonic seizures [41].

16.4 Some Reflections on EEG-EMG Correlations in Epileptic Seizures

The relationships between the features of the epileptic EEG discharges and the associated EMG event can indeed be variable. In fact, based on polygraphic recordings, we can recognize:

1. Seizure types in which there is a strict, time-locked association between the EEG paroxysmal event and the related clinical/EMG phenomenon, such as juvenile myoclonic epilepsy [24], positive and negative myoclonus of epileptic nature [6, 42], photic-induced myoclonus [41], and certain epileptic action myoclonus [27, 43]. In these conditions, a proper analysis, supported by computerized techniques, can show a very precise correlation between the EEG epileptic abnormality, or even to some component of it, and the EMG manifestations.
2. Seizure types in which similar EEG patterns can result in different clinical phenomena. Examples are "tonic" and "atonic" seizures which both can feature rhythmically repeated spikes in the EEG (Figs. 16.3 and 16.4). Similarly with positive and negative myoclonus, we can speculate that "tonic" and "atonic" seizures with apparently "similar" expression on the EEG are indeed related to different positive or negative components of the EEG discharge possibly reflecting different functional and anatomical networks.
3. Seizure types in which the ictal EEG features and the motor event are concomitant but without a strict temporal correlation. Examples of this possibility are represented by tonic seizures (Fig. 16.4), spasms (Fig. 16.2), or even the complex albeit stereotyped motor patterns that can be observed

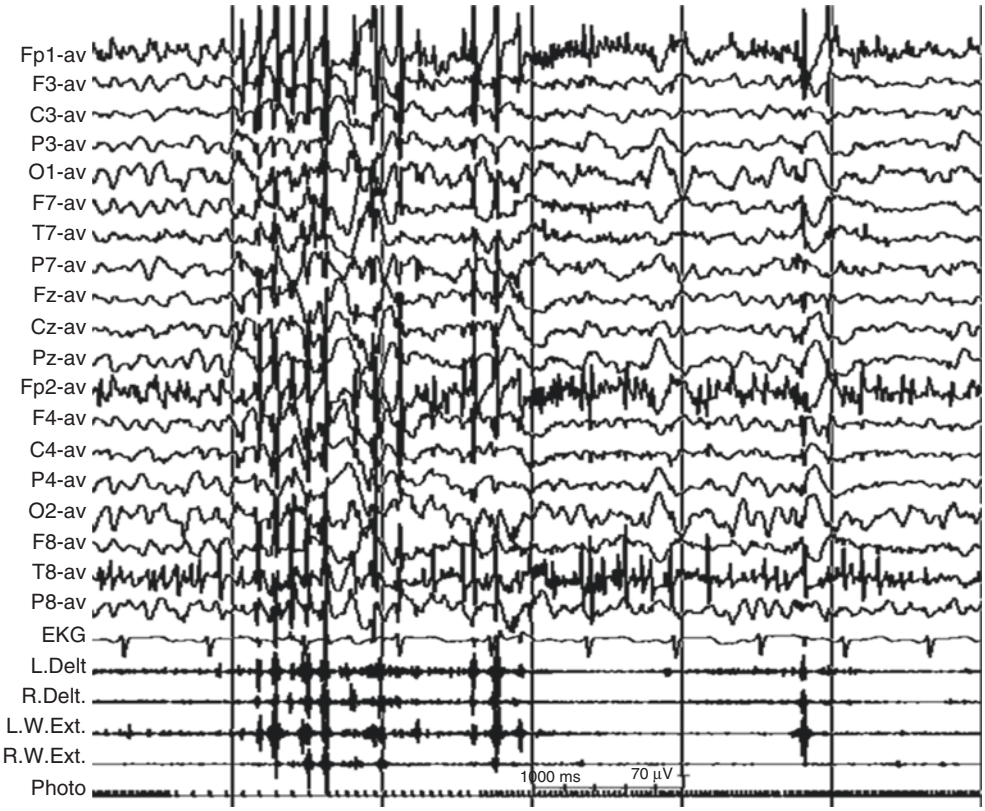


Fig. 16.8 Photic reflex myoclonus in a photosensitive patient. Intermittent photic stimulation elicits generalized spike-wave discharges associated with myoclonic jerks in the upper limbs. *L.* left, *R.* right, *EKG* electrocardiogram, *Photo* intermittent photic stimulation, *Delt.* deltoid, *Wrist Ext.* wrist extensor

in some focal epilepsies. In these instances, the epileptic event in the cortex represents the "trigger" that releases a cascade of motor sequences. In fact, in both tonic seizures and spasms, the muscular manifestations outlast the end of the EEG discharge and encompass some "archaic" motor patterns, such as a startle reaction in tonic seizures [44]. These observations have led to the hypothesis that in certain seizures, the motor semiology results from the activation of genetically determined archaic functional motor systems, such as the central pattern generators [45].

4. Seizure types that seem to result from the combination of different seizures. The best example are myoclonic absences which are characterized by (1) 3 c/s spike-and-wave discharges, almost undistinguishable from the pattern of Childhood Absence Epilepsy; (2) a positive transient encompassed in the spike-wave complex that is associated with rhythmic myoclonias; and (3) a tonic contraction as in tonic seizures (as described by [46]).

16.5 Back-Averaging Techniques Applied to the Analysis of Polygraphic Signals

The introduction of computer-assisted techniques for the collection and the processing of the polygraphic signal has increased the yield of PI. In epilepsy, these techniques have been applied in particular to the analysis of EEG and EMG signals, simultaneously collected, to extract information not obtainable with standard PI. One of the most widespread techniques is back-averaging of the EEG activity triggered by a muscular event.

Back-averaging techniques have been introduced mainly to detect eventual brain electrical potentials associated with an involuntary movement and to study their temporal correlation and their topographic distribution over the scalp. The first description of a temporal correlation between a paroxysmal EEG abnormality and a myoclonic contraction dates back to Grinker [47]. However, by commenting on these data, Dawson [48] recognized that although the two phenomena (EEG abnormality and myoclonic contraction) appeared closely related, their exact temporal relationship could not be determined. It was Shibasaki and Kuroiwa [49] who introduced a method based on the technique of "summation" of neurophysiological signals introduced by Dawson [50]. By using this approach, it was possible to identify cortical events, hidden in the background activity, associated with a muscular phenomenon, to determine their spatial distribution over the scalp, and to establish the temporal relations between the two events. These techniques were called "back-averaging" or "jerk-locked averaging" methods, as they used as trigger for the summation or "averaging" procedure of the related EEG activity, the muscle potential associated with a positive myoclonia (myoclonic jerk) (Fig. 16.9). Later on, techniques that use as trigger an abrupt interruption of muscle contraction, i.e., a negative myoclonus, such as in asterixis, have been introduced (Fig. 16.9). These latter methods have been

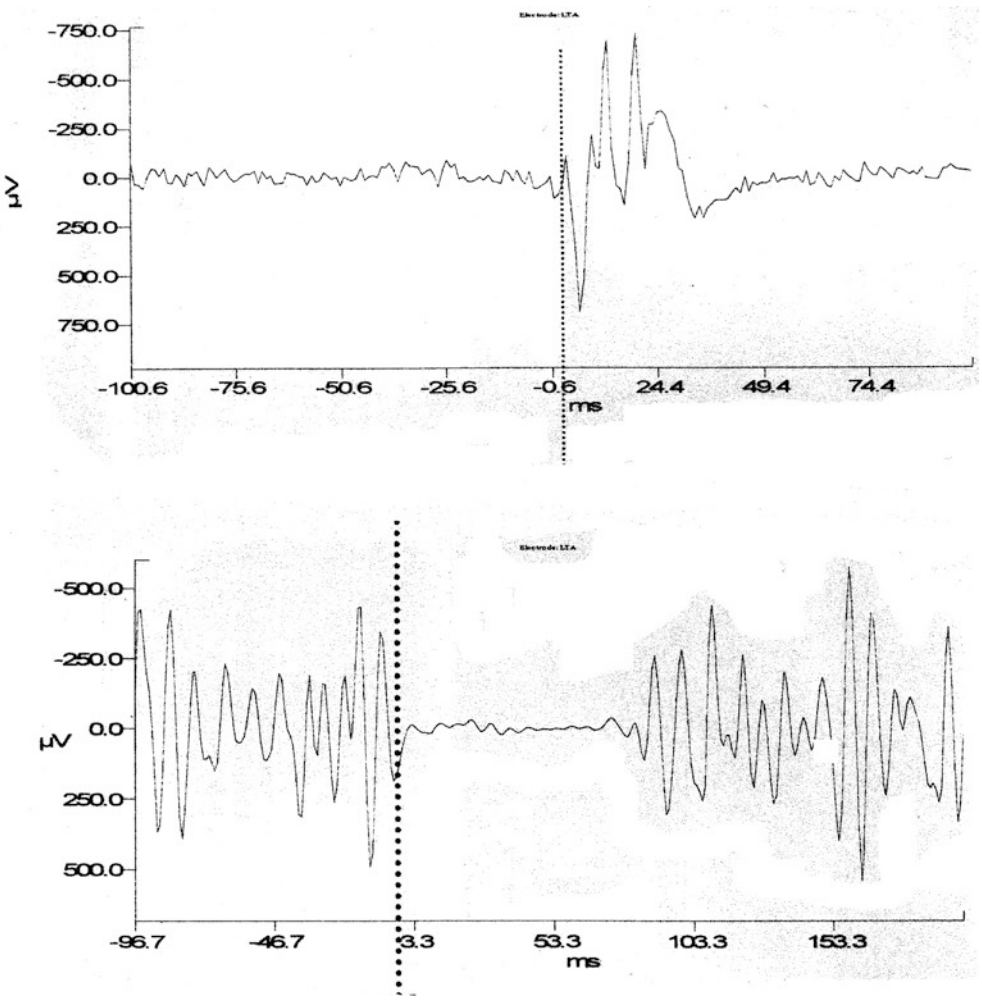


Fig. 16.9 Back-averaging applied to the study of positive and negative myoclonus. Upper trace: In positive myoclonus, the marker (vertical line) for the triggering of the averaging procedure is positioned at the onset of the myoclonic burst. Lower trace: In negative myoclonus, the marker (vertical line) for the averaging procedure is positioned at the onset of the muscular silent period

labelled as "silent period-locked averaging," i.e., summation procedures related to the silent period [51].

The fundamental principle on which the back-averaging techniques of EEG-EMG activity are based is that the electric activity due to "noise" or unrelated to the muscular phenomenon progressively cancels out until it approaches to zero with the process of averaging. On the contrary, the electric brain activities related to the muscular phenomenon add up to a constant latency and will appear, after the process of averaging, as a well-defined signal, distinct from the underlying activity. An important requirement for the muscular phenomenon to act as a "trigger" is that this phenomenon has a rapid and well-defined onset (Fig. 16.9) [52]. Therefore the motor disturbances that are best suitable for this type of analysis and that have been more extensively investigated with these techniques are the myoclonic phenomena.

16.5.1 Back-Averaging Applications to the Study of Myoclonus

By using "jerk-locked averaging," Shibasaki and Kuroiwa [49] were able to demonstrate the existence of a premyoclonic EEG potential, not identifiable by visual inspection of the polygraphic tracing. Moreover, this procedure proved equally effective in defining the temporal relationships between the cortical potential and the myoclonic event even when a paroxysmal activity associated with myoclonus was already evident in the polygraphy. The demonstration of an EEG activity temporally correlated with the myoclonic phenomenon is considered one of the main criteria in the definition of cortical myoclonus, either positive or negative [6]. Therefore, the "jerk-locked averaging" as well as the "silent period-locked averaging" methods can be extremely useful in demonstrating a cortical origin of a myoclonic event.

In this section, we illustrate the EEG and EMG features associated with the different types of myoclonus and the yields provided by computer-assisted techniques.

16.5.1.1 EMG correlates of Positive and Negative Myoclonus

The EMG features of positive cortical myoclonus can be variable. Myoclonic potentials consist of short burst ($\leq$50 ms) of EMG activity, usually synchronous in agonist and antagonist muscles. This EMG activity can be focal, affecting a single muscle, but more often it involves many adjacent muscles.

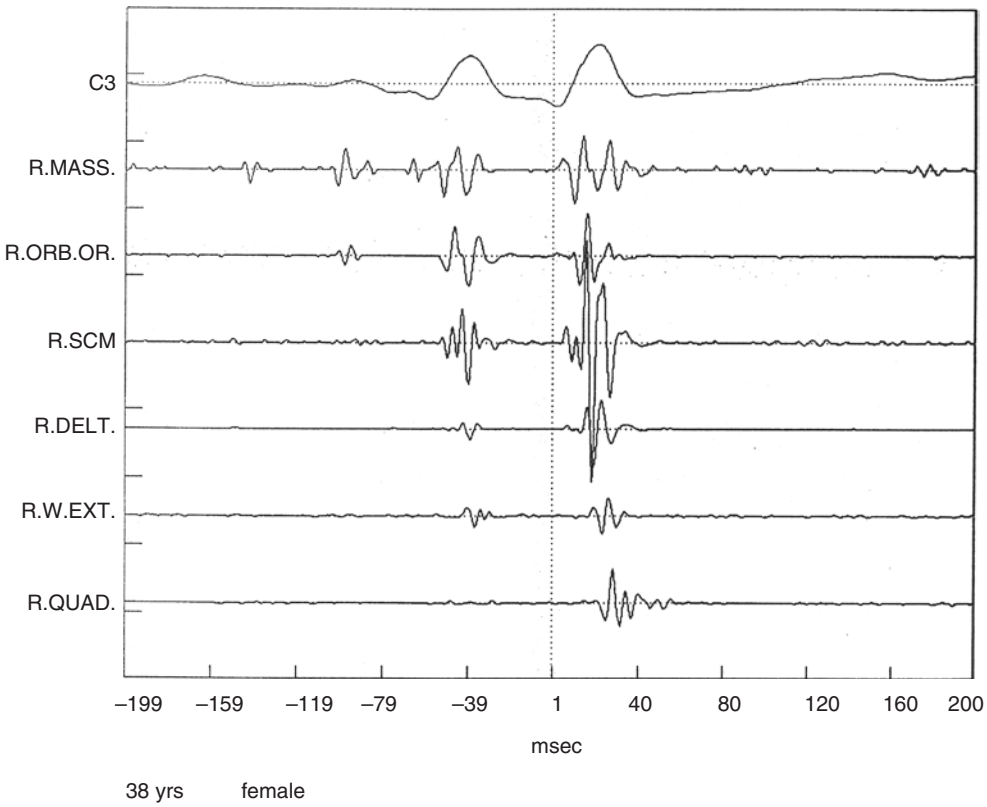


Fig. 16.10 Myoclonic bursts in photic reflex myoclonus. The myoclonic jerks in the right side of the body are related to low-amplitude EEG potentials in the left central region (C3). The different muscles are activated according to a rostro-caudal pattern, and the latency of activation of the different muscles from the EEG potential is consistent with a propagation according to fast-conducting corticospinal pathways. *R.* right, *Mass* masseter, *Orb. Or.* orbicularis oris, *SCM* sternocleidomastoideus, *Delt.* deltoid, *Wrist Ext.* wrist extensor, *Quad.* quadriceps

PI can also show that this type of myoclonus is propagated to different muscle groups with a rostro-caudal pattern and the speed of propagation corresponds to that of the large myelinated motor axons (Fig. 16.10) [6, 53, 54]. Cortical myoclonus can be irregular as well as rhythmic or pseudorhythmic, such as in the so-called cortical tremor or familial cortical tremor with epilepsy and sometimes also in corticobasal degeneration [38, 55, 56]. Frequently, the cortical myoclonus is sensitive to stimuli of various kinds, such as tendon stretching or other somatosensory stimulations, such as maintaining a posture, or active or passive movement. In epileptic positive myoclonus, such as in epilepsia partialis continua, the EMG potentials may be very short and with a very abrupt onset (less than 50 ms) (Fig. 16.11). Myoclonic activities observed in myoclonic absence seizures have peculiar features, as already outlined, such as rhythmic EMG potentials at the same frequency of the spike-wave discharge, superimposed to a tonic activity of progressively increasing amplitude (Fig. 16.5) [21]. This tonic contraction can mask the myoclonus and make the clinical manifestation complex. Each myoclonus is followed by a silent period, with a duration ranging from 60 to 120 ms, which interrupts the tonic EMG activity.

Subcortical positive myoclonus sometimes can be difficult to distinguish from cortical positive myoclonus. Common neurophysiological features of the subcortical myoclonus are a less abrupt onset and often a longer duration. For example, myoclonus of Creutzfeldt-Jakob disease is generally not stimulus-sensitive and occurs subcontinuously and quasi-periodically, with intervals varying between 0.6 and 1.5 s. It is often associated with postures or dystonic movements in the affected limb. The duration of each EMG phenomenon is similar or slightly longer than that of cortical myoclonus. It should be noted that, in more advanced stages of the disease, patients may also show a myoclonus undistinguishable from the typical reflex cortical myoclonus. In some cases of subcortical reflex myoclonus, the pattern of muscular recruitment indicates an initial activation of the muscles related to the nuclei of the VII and XI cranial nerves, and then the myoclonic bursts spread rostrally and caudally. This has led to the hypothesis of the existence of a generator of myoclonic activity at the level of the reticular formation of the brain stem, subserved by fast-conducting reticulospinal pathways [57]. Myoclonia featuring these characteristics is labelled as reflex reticular myoclonias.

The EMG correlates of negative myoclonic phenomena can be variable as well. To identify such phenomena, it is necessary that the subject maintains a tonic contraction in the affected muscular districts. The interruption of the interferential EMG activity due to the negative myoclonus is expressed clinically by a sudden cessation of the muscle contraction, causing a postural lapse or interfering with the execution of a motor task [58]. The longer the duration of the EMG silent period, the more clinically evident and disturbing will be the negative myoclonus. A form of stimulus-sensitive cortical negative myoclonus has been described [59].

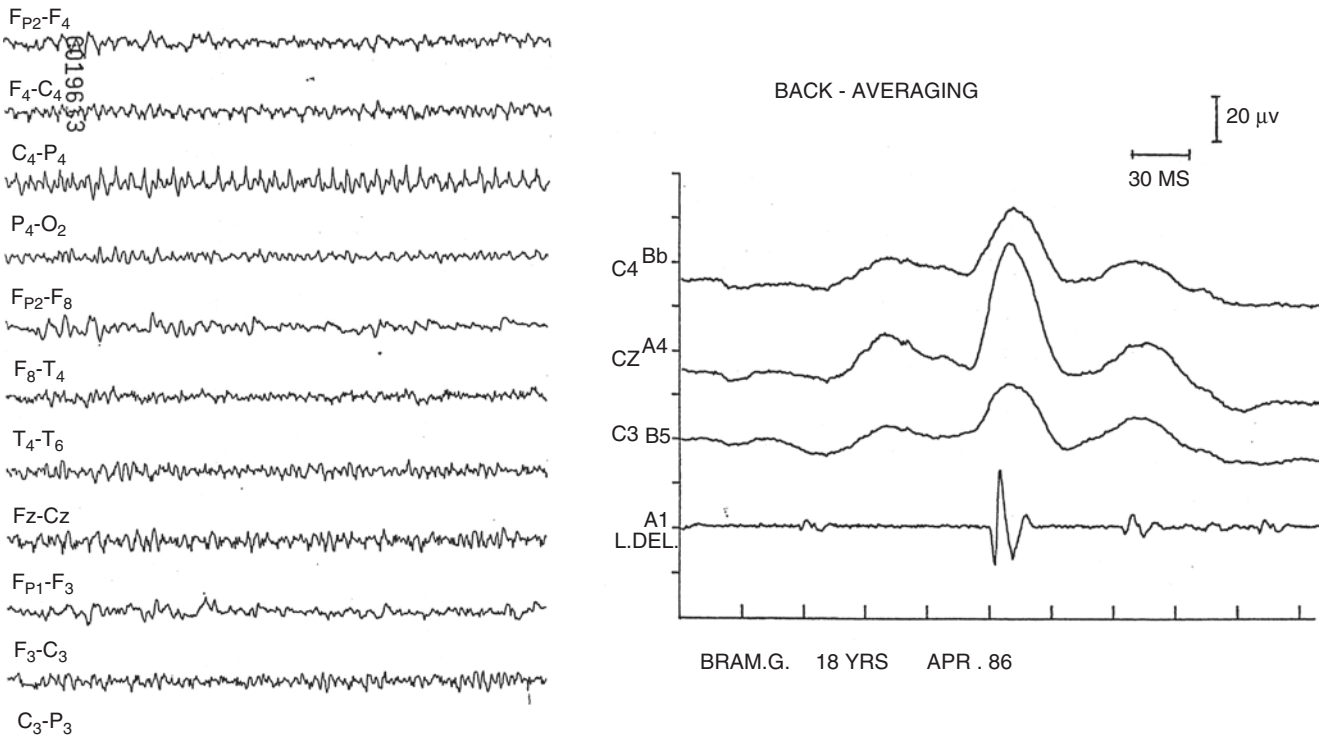


Fig. 16.11 Left: EEG tracing of a patient with epilepsia partialis continua with rhythmic myoclonia at the left upper limb. The EEG shows rhythmic spikes in the right centroparietal leads. Right: back-average of 20 myoclonic jerks in the left deltoid showing a time-locked correlation between the muscular bursts and the EEG potential (that has higher amplitude over Cz). *Delt.* deltoid, *L.* left

Epileptic negative myoclonus (ENM) is characterized by the occurrence of a silent period both on the agonist and antagonist muscle, without being preceded by a positive myoclonia, time-locked to an EEG epileptic discharge [9]. ENM duration can be extremely variable (up to 400 ms).

The subcortical negative myoclonus tends to be rhythmic, and if bilateral, often synchronous between the two sides. Also in this type of negative myoclonus, the EMG silent period is detectable both on agonist and antagonist [60]. Asterixis, probably the most common type of subcortical negative myoclonus, can be relatively rhythmic at a frequency of 6–11 Hz, with silent periods lasting from 50 to 200 ms.

Finally, there are conditions, such as postanoxic myoclonus and progresive myoclonus epilepsies, in which action myoclonus is characterized by a variable combination of positive and negative myoclonic phenomena, inconstantly associated with an EEG correlate (Fig. 16.7) [43].

16.5.1.2 EEG Correlates of Positive and Negative Myoclonus

The demonstration of an EEG potential time-locked to the myoclonic phenomenon is one of the main criteria for the definition of cortical myoclonus. In some epileptic conditions, polygraphic recording can show a clear correlation between an EEG paroxysmal activity and the myoclonic EMG burst. Typical examples are myoclonic absences, where myoclonias are related to the positive transient encompassed in the spike-wave complex. The latencies between the positive transient and the onset of myoclonus is about 15–40 ms, for the most proximal muscles, and of 50–70 ms, for the most distal muscles ([21, 22]). In juvenile myoclonic epilepsy, there is a clear association between the polyspike rhythm of the polyspike-wave complex and the myoclonic jerk (Fig. 16.12). The analysis of this correlation showed a predominantly frontal distribution of the myoclonus-related EEG potential; the myoclonic volley propagates to various muscular segments with a rostrocaudal pattern via fast corticospinal pathways (Fig. 16.12) [24]. In conditions with cortical myoclonus in which standard PIs do not show an overt myoclonus-related EEG event, jerk-locked averaging can unveil the cortical correlate and can provide a measure of the latency between the EEG potential and the EMG myoclonic burst, which ranges between 20 and 40 ms for the muscles of the hand and of the lower limbs, respectively (Fig. 16.13) [61]. It has also been shown that the topography of the premyoclonic potential on the scalp may vary in relation to the muscle affected by myoclonus, respecting the somatotopia of the motor homunculus [53, 61].

In the study of photic reflex myoclonus (Fig. 16.8), a peculiar form of reflex myoclonus induced by visual stimuli,

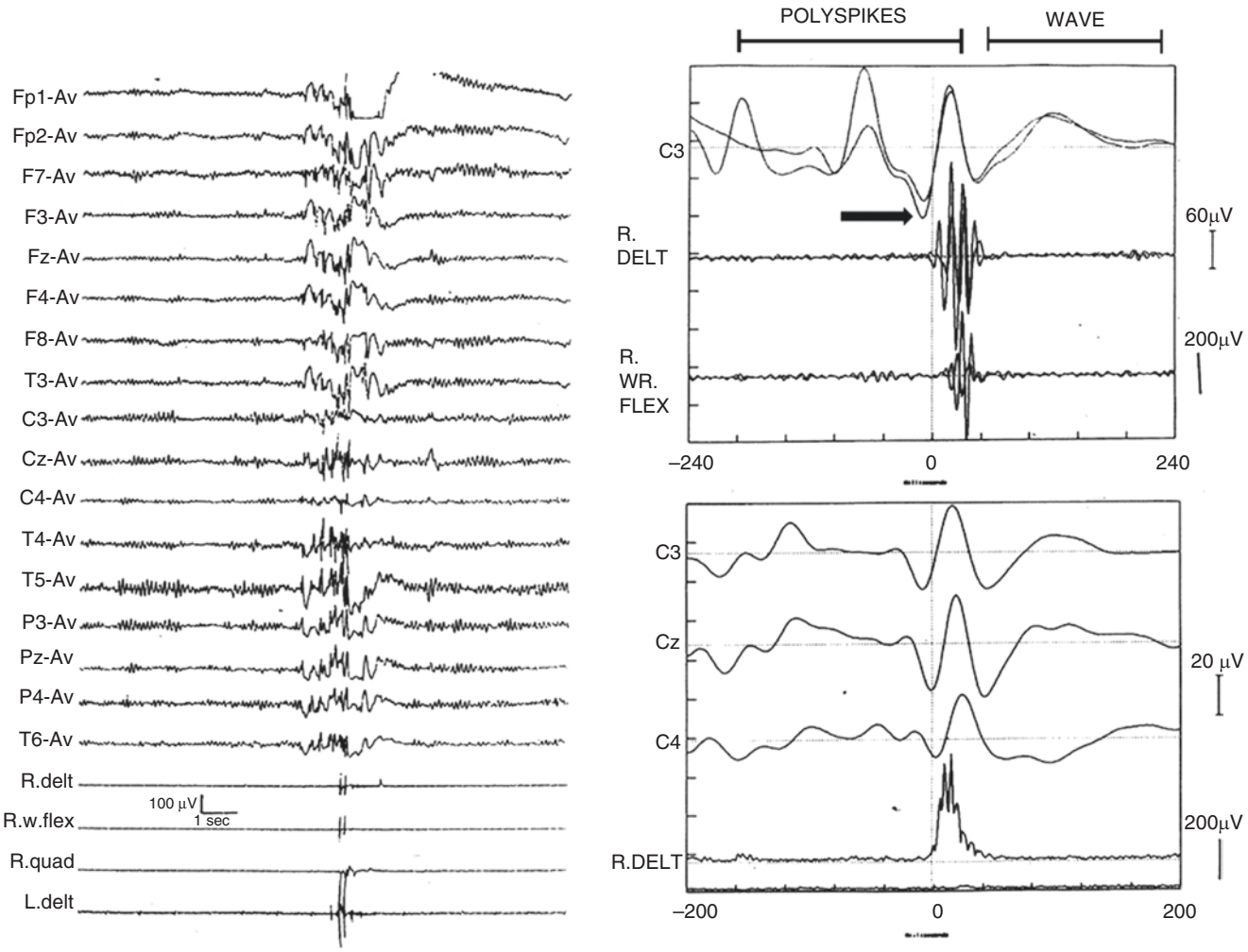


Fig. 16.12 Left: polygraphic recording of a myoclonic jerk in a patient with juvenile myoclonic epilepsy. Right, upper panel: the relationship between the positive transient (arrow) encompassed in the polyspike discharge (indicated by a horizontal line above the figure) and the myoclonus in the muscles of the right upper limb is shown. Right, lower panel: jerk-locked average of 20 myoclonias showing the relationship between the EEG potential and the myoclonic event. The EEG potential in C3 (related to the myoclonia in the right deltoid) anticipated of about 10 ms, the EEG potential in C4. *Delt* deltoid, *Wrist Flex* wrist flexor, *R* right

jerk-locked averaging of the EEG-EMG signals has shown that the visual stimulus activates first the visual cortex and then the cortical excitation propagates (with a latency of about 10 ms), probably via occipito-frontal pathways, to the motor cortex, where a myoclonic volley originates recruiting various muscular districts, according to a rostro-caudal pattern, with latency of recruitment compatible with direct, fast-conducting corticospinal pathways, as observed in other forms of cortical myoclonus (Fig. 16.10) [41, 62]. In action myoclonus [53], photic reflex myoclonus [41], and juvenile myoclonus epilepsy [24], the analysis of bilateral, apparently synchronous, myoclonic jerks showed that there is a brief interval, of about 10 ms, between the myoclonia of the two sides, corresponding to a similar interval between the respective EEG correlates (Fig. 16.12). This data suggests that the cortical myoclonic activity originates in one hemisphere and spreads, probably via transcallosal fibers, to the contralateral one.

The "jerk-locked averaging" techniques can also be very useful in demonstrating either the absence of a myoclonus-related EEG potential or the absence of a temporal relationship between the muscular and the EEG event [57]. These aspects, associated with somatosensory evoked potentials of normal amplitude, are compatible with a subcortical myoclonus.

16.5.2 Averaging Techniques to Study Negative Motor Phenomena

PI associated with "silent period-locked averaging" techniques are crucial to demonstrate the existence of a negative

muscular phenomenon and to detect possible EEG correlates. Ugawa et al. [51], by using this method, showed that asterixis in the upper limbs may be, in some cases, devoid of a clear cortical potential, whereas in other conditions it may be associated with an EEG potential in the contralateral central regions. In postanoxic myoclonus, Lance and Adams [63] found a relationship between the onset of the EMG silent period and the onset of the slow wave of the spike-wave complex. In ENM, "spike-averaging" techniques, where the average is performed using the peak of ENM-related spike as the trigger, have shown that the EMG silent period is related to the ENM-related spikes (Fig. 16.14) [42, 64] or to the slow wave of a spike-wave complex [65]. Further studies have shown that the negative phenomenon occurs when the epileptic activity spreads to frontal (Fig. 16.15) or parietal (Fig. 16.16) inhibitory areas (Fig. 16.17) [9, 42, 64, 67]. Recent data, obtained by intracerebral electrical stimulation combined with averaging techniques of the EMG signal triggered by the electrical stimulus in patients undergoing presurgical evaluation for drug-resistant epilepsies, showed the differential role of premotor, supplementary motor, primary motor, and parietal areas in producing positive or negative myoclonic phenomena. Interestingly, these investigations demonstrated that, regardless the intensity of the electrical stimulation, primary/premotor cortex originates mainly positive myoclonia, whereas supplementary motor cortex originates only negative myoclonia. Stimulation of the parietal cortex could elicit either positive or negative phenomena depending on the stimulus intensity [66]. These findings are in agreement with evidences showing the existence of negative motor areas encompassed in the supplementary motor cortex and in the inferior frontal gyrus [68, 69].

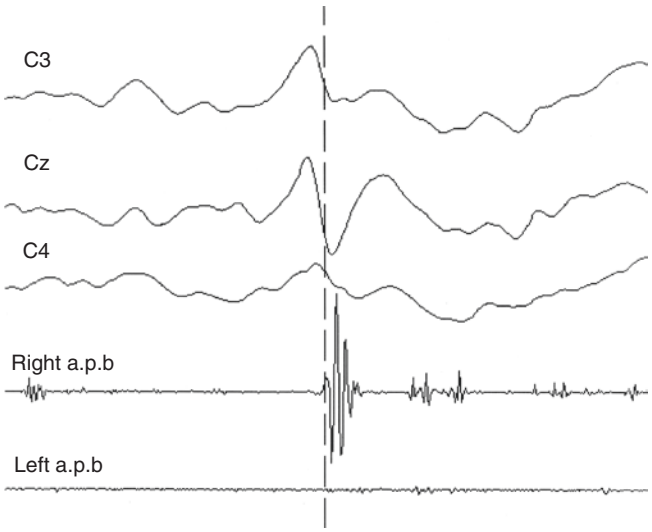


Fig. 16.13 Jerk-locked average of 25 myoclonias in the right abductor pollicis brevis (APB) in a patient with progressive myoclonus epilepsy. A low-amplitude potential in the contralateral central regions, not visible in the polygraphic tracing, is correlated with the myoclonia. *R.* right, *L.* left, *A.P.B.* abductor pollicis brevis

16.6 Conclusions

Back-averaging techniques offer several advantages, such as the possibility to demonstrate a cortical correlate, even of low amplitude, not detectable by visual inspection of the PI,

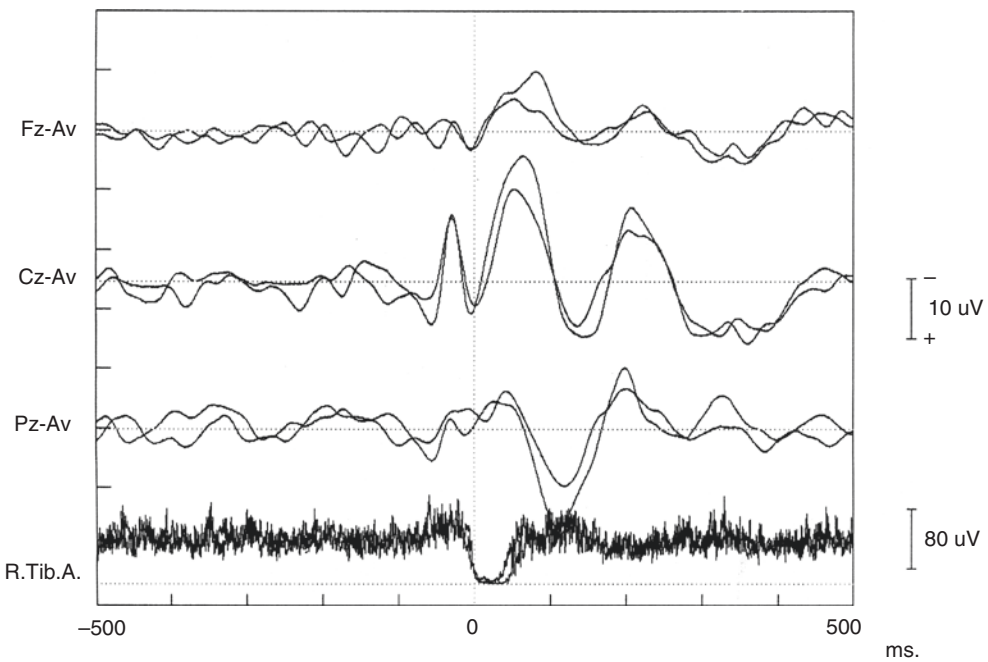


Fig. 16.14 Silent period locked average of 20 epileptic negative myoclonias in the right anterior tibialis (R. Tib. A.—rectified EMG) in a patient with benign partial epilepsy of infancy. The onset of the muscular silent period of the epileptic negative myoclonus is correlated with the peak of spike in Cz, and it precedes the onset of the slow wave

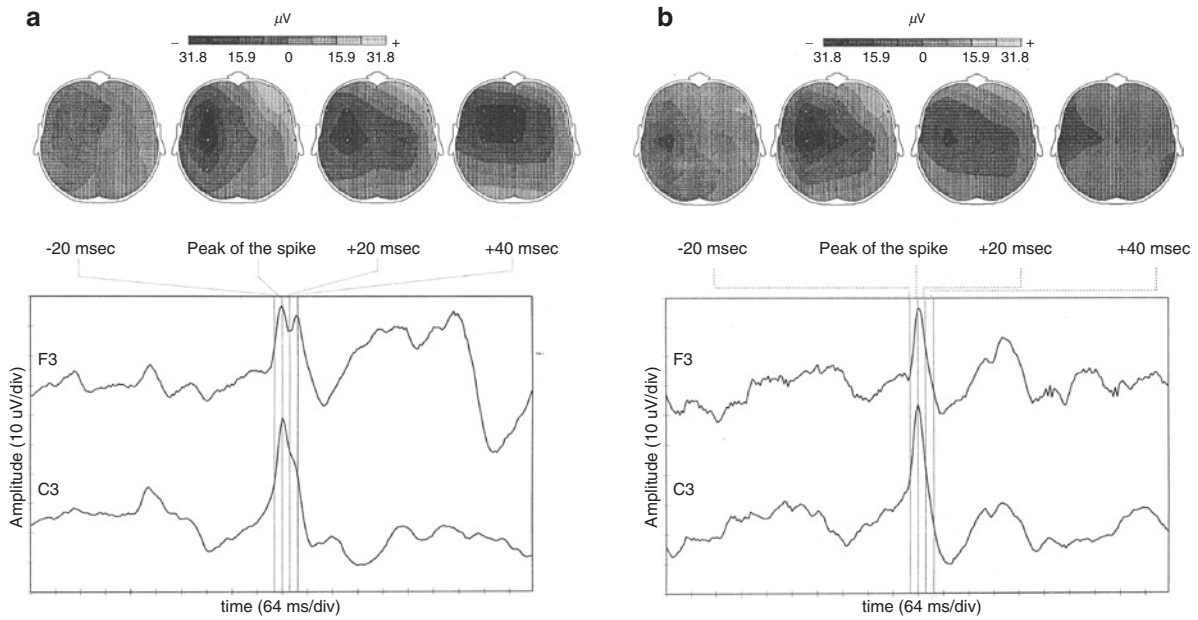


Fig. 16.15 Topographic analysis and spike-averaging of spikes associated with epileptic negative myoclonia (**a**) and spikes nonassociated with epileptic negative myoclonia (**b**). Each averaged spike is the result of the averaging of 20 individual spikes. In (**a**), the averaged spike associated with epileptic negative myoclonus has a second component (evident on F3) distributed over the frontal regions, which is absent in the spike non associated with epileptic negative myoclonus (see also [42])

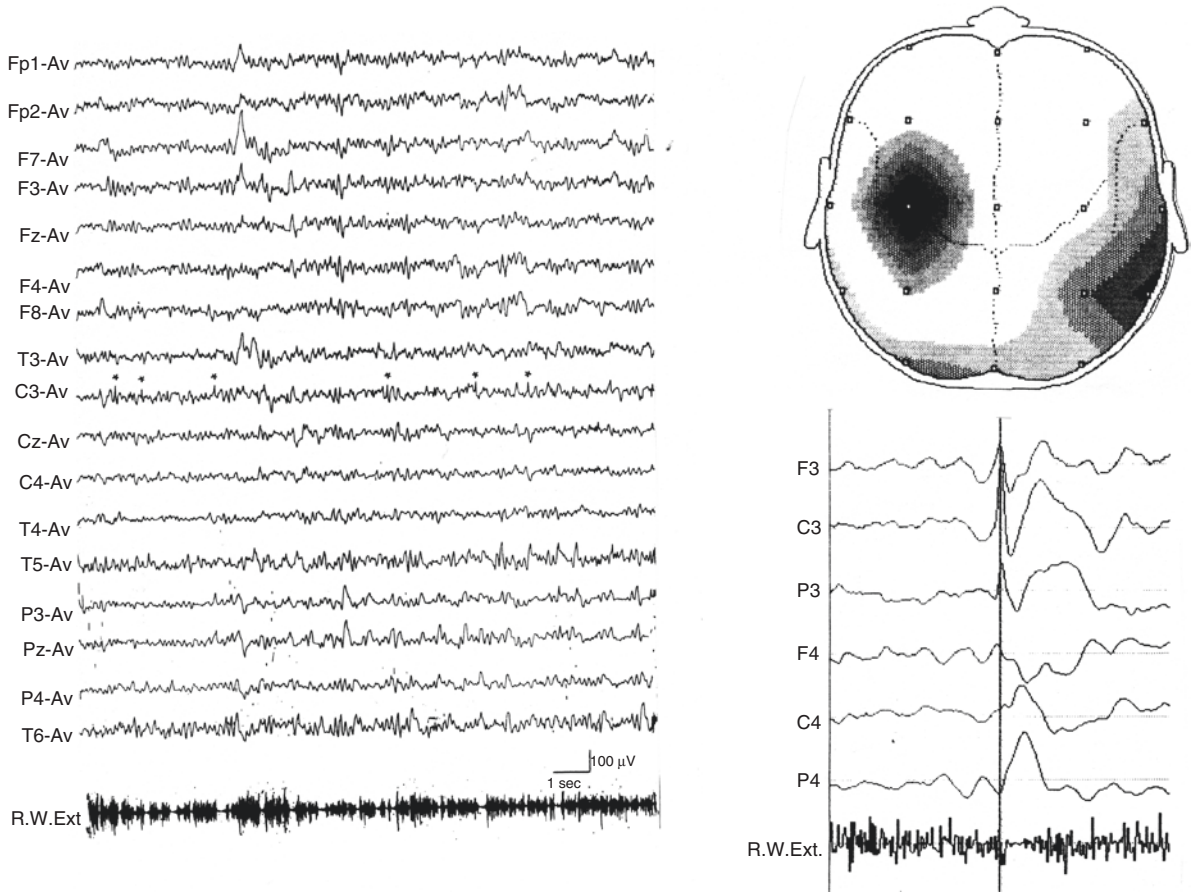
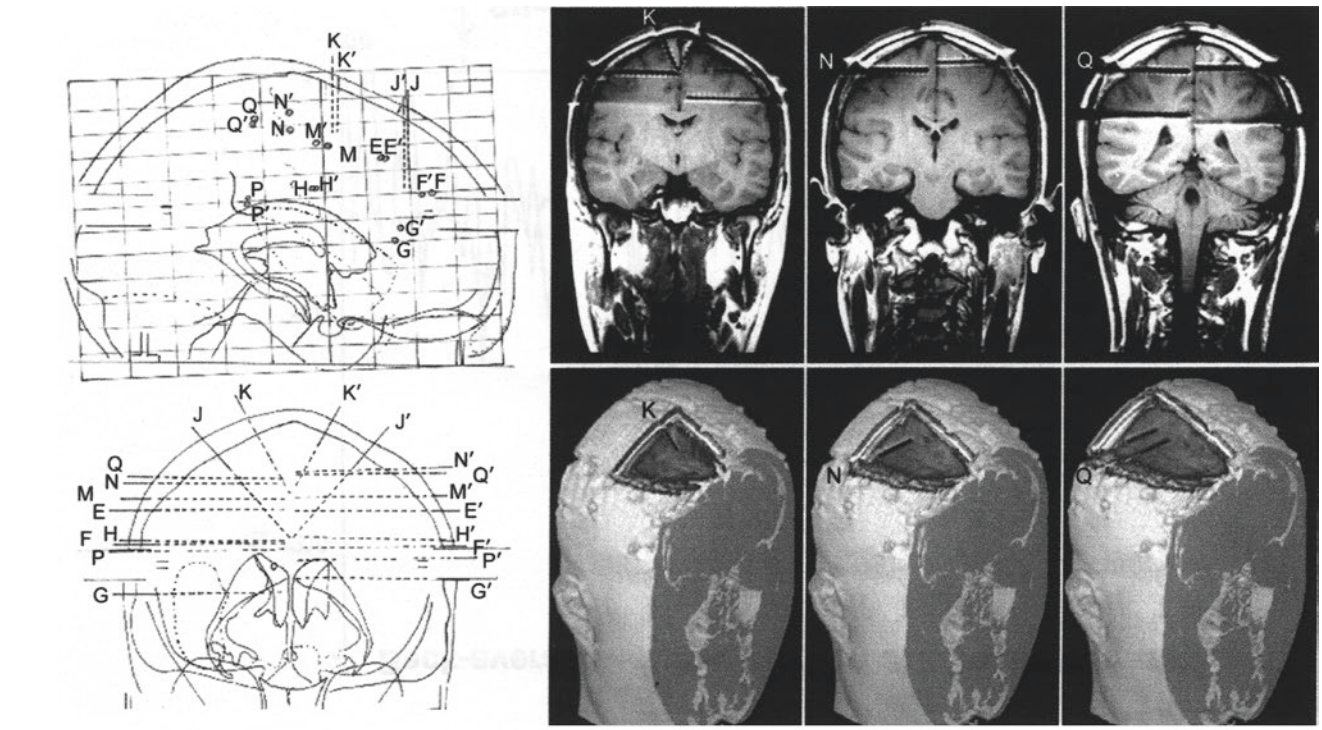


Fig. 16.16 Left: Polygraphic recording in a patient with focal epilepsy associated with left parietal dysplasia and epileptic negative myoclonus in the right wrist extensor (R. Wrist Ext.) The epileptic negative myoclonia is associated with low-amplitude spikes in C3. Right: back-average of 30 epileptic negative myoclonia showing a clear correlation with a low-amplitude sharp spike in C3 (as shown by the topographic map)



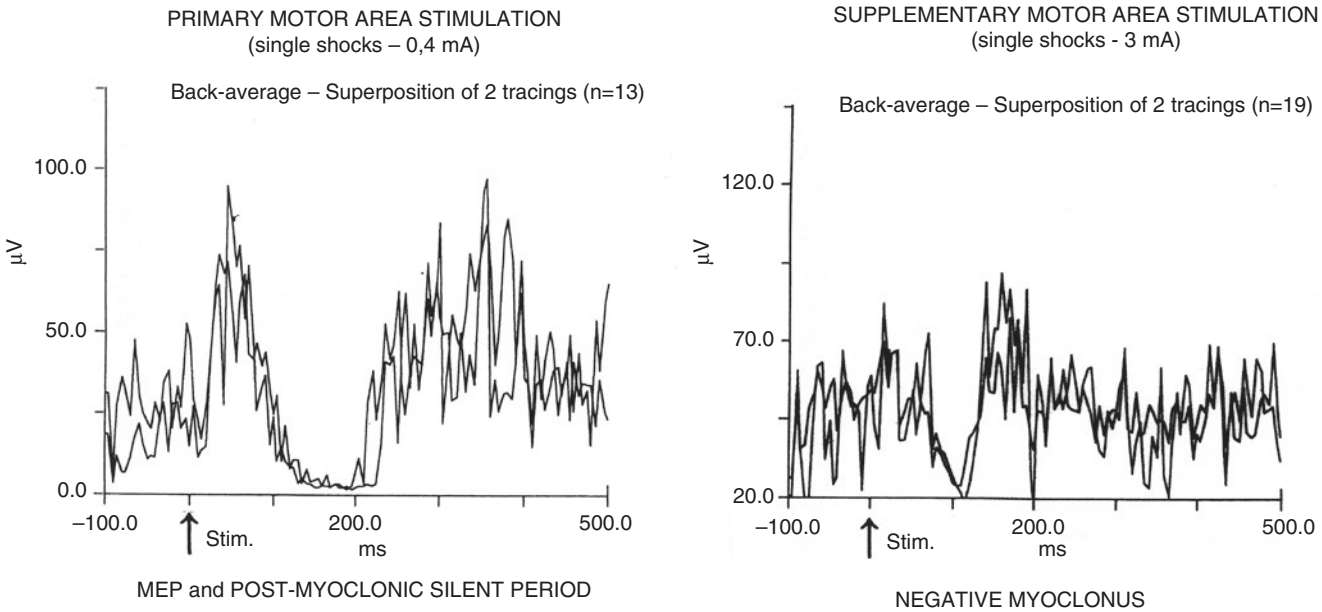


Fig. 16.17 Upper panel: stereo-electroencephalographic scheme (left) and localization of the electrodes in the brain MRI (right). The stereo-EEG electrodes explore the primary motor region (external N electrode), the supplementary motor area (internal electrode K), and parietal cortex (external Q electrode). Lower panel. Left: the electrical stimulation with low-intensity stimuli of the primary motor cortex produces a motor evoked potential (MEP) followed by a post-myoclonic silent period. Right: the electrical stimulation with high-intensity stimuli of the supplementary motor area produces a negative myoclonus. The trigger for the averaging of the EMG signal was the electrical stimulus delivered for intracranial electrical stimulation. EMG tracing rectified from the deltoid muscle contralateral to the electrical stimulation (see also [66])

of a EMG contraction, and to analyze precisely the temporal relationships between the cortical and the muscular phenomena. These techniques have some limits such as a relative arbitrariness in the identification of the onset of the "trigger" event and difficulties in the analysis of rhythmic myoclonic activities, particularly at high frequency. However, if correctly performed and interpreted, they can be useful to investigate the pathophysiological mechanisms of some motor disorders and to orient the diagnostic work-up with possible treatment implications.

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