Seizure (2005) **14**, 354—361

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Unusual ipsilateral hyperkinetic automatisms in SMA seizures

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KEYWORDS
SMA;
Epilepsy surgery;
Automatisms;
Ictal semiology

Summary

Purpose: To describe repetitive movements of the right arm possibly originating from the ipsilateral SMA area in two drug-resistant epileptic patients.
Methods: Two epileptic patients (one female, one male, 35 and 36 years old, respectively) were submitted to pre-surgical evaluation including history, neurological examination, long-term video-EEG monitoring, interictal and ictal SPET, MRI and fMRI, neuropsychological assessment. Invasive recordings (stereoelectroencephalography) were also performed.
Results: In both patients ictal semiology was characterized by very stereotyped repetitive right arm movements, i.e. tapping towards the thorax (movement rate of 6—7 Hz and 3—4 Hz for the two subjects, respectively). Seizures in the first patient, whose epilepsy was cryptogenetic, originated from the right pre-SMA area, which was surgically removed. She is seizure free 2 years after the operation. In the second patient, in whom a right pre-frontal post-abscess porencephaly was disclosed, the epileptogenic zone included the lesion and surrounding areas, while the SMA area was involved less consistently.
Conclusions: Even if, according to literature, SMA epilepsy is predominantly characterized by postural manifestations, ipsilateral repetitive movements could be a relevant sign in this kind of epilepsy, as showed in our first patient. The presence of similar semiology in the second patient, might suggest that the symptomatogenic zone involved SMA area.

Introduction

Frontal lobe epilepsy represents the most frequent extratemporal epilepsy in surgical series.[1] Frontal epilepsy semiology may be hard to clarify due to the complexity of correlations between clinical symptoms and the anatomo-physiological organization of ictal discharges. Ictal signs and symptoms are often related not to the area of primary epileptogenesis but to the electric spread of the discharge to the ipsilateral, contralateral or deep structures and to the complex networking to other cortical lobes.[2] Different classifications have tried to distinguish

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1059-1311/$ — see front matter
doi:10.1016/j.seizure.2005.04.011

specific ictal patterns of frontal lobe epilepsy by referring to data acquired during SEEG explorations[3,4] or based on surgical series.[5,6] More recently, three categories of frontal lobe semiology have been described: focal motor, complex partial and SMA seizures.[7] Complex partial seizures have been suggested to be specifically characterized by motor automatisms in contrast to the postural manifestations of SMA seizures.[8] Conversely, Bleasel[9] concluded that complex partial seizures with vigorous and sometimes bizarre automatisms might be associated to mesial frontal lobe epilepsy.

In this study we describe two drug-resistant epileptic patients who showed repetitive movements of the right arm possibly originating from the ipsilateral SMA area as assessed by both non-invasive and invasive pre-surgical evaluations.

Patients (Table 1)

Patient 1

This patient was a 35-year-old, right-handed female. Neurological examination was fully normal. Family history was negative for epilepsy. Delivery and psychomotor development were carried out normally. No febrile convulsions were described in infancy. Seizures began at the age of 6 years old; their frequency was daily, diurnal and nocturnal. Different AED were only effective in reducing the number of diurnal episodes. Seizure semiology (Fig. 1) was very stereotyped: incapability of speech, rhythmic tapping movements of the right arm towards thorax at a frequency of 6—7 Hz, vocalizations. Seizures lasted around 30 s and were followed by post-ictal laughter and/or crying. There was an immediate recovery of language, without any post-ictal deficits. Apparently, there was a partial loss of contact since the patient was able to remember what happened during seizures. She felt auras only before diurnal seizures: a sensation of ''emptiness'' not well localized and cephalic confusion.

On her first visit to our department she took oxcarbazepine, topiramate and phenobarbitale and showed four to five seizures per night. She had never generalized.

Pre-surgical evaluation protocol included: history, neurological examination, neuro-psycological assessment, prolonged video-EEG monitoring, high-resolution MRI and fMRI, PET scan, Technetium-99m Ethyl Cysteinate dimer (99mTc-ECD) interictal and ictal SPET (the latter obtained during seizures pharmacologically provoked with pentylenetetrazol, a central and respiratory stimulant).

MRI and PETwere fully normal. Neuropsycological assessment disclosed slight mental retardation with a verbal memory deficit. Wada test and fMRI demonstrated left dominance for language. Interictal SPET showed a slight right temporal hypoperfusion while provoked ictal SPET disclosed a clear right fronto-basal hyperperfusion.

Scalp interictal EEG was characterized by bilateral fronto-tempo-central sharp and slow waves, sometimes with right prevalence. Ictal EEG showed bi-fronto-temporal rhythmic spikes and slow waves with slight right prevalence. EMG recordings (biceps) performed during ictal automatisms revealed very stereotyped repetitive motor activity at 6—7 Hz.

In order to define the epileptogenic zone in this cryptogenetic case, invasive recordings were also performed. On the basis of electro-clinical correlations we decided to perform Stereoelectroencephalography (SEEG) by implanting eleven electrodes

Table 1 Clinical features of the two patients

	Patient 1	Patient 2
Sex	Female	Male
Age (years)	35	36
Age at first seizure (years)	6	23
Neurological examination	Normal	Normal
Seizure frequency	Daily	Weekly
Clusters	Yes	Yes
MRI examination	Negative	Post-abscess lesion
Scalp EEG	Frontal bilateral	Right fronto-temporal
Ictal SPET	Right frontal	Right frontal
Therapy	OxC, TPM, PB	CBZ, TPM, TGB, BDZ
Epileptogenic zone	Right pre-SMA	Right pre-frontal
Corticectomy	Right frontal	Right frontal
Outcome	Ia	Ia

OxC: oxcarbamazepine; CBZ: carbamazepina; TPM: topiramate; PB: Phenobarbital; BDZ: benzodiazepine; and TGB: tiagabine.

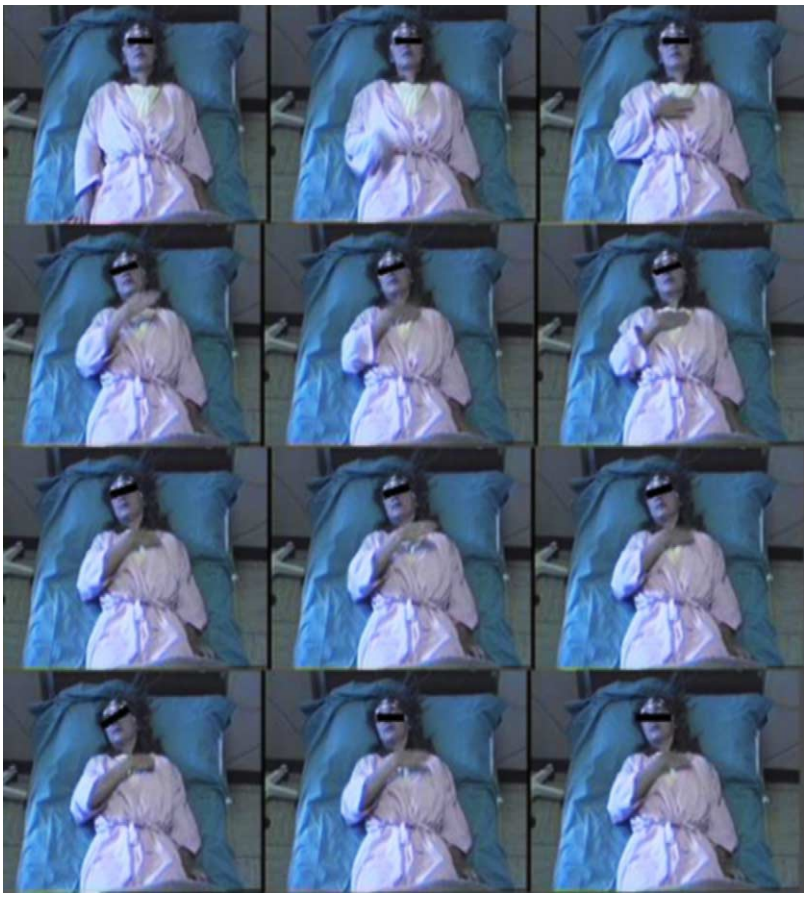

Figure 1 In our first patient seizure semiology was characterized by repetitive movements of the right arm at a frequency rate of 6—7 Hz.

divided between the frontal lobes (six in the right and three in the left) and the right temporal lobe (two electrodes) (Fig. 2). Particularly the left pre-SMA, right pre-SMA and SMA-proper (electrode F and S, respectively) were investigated. The location of each electrode was tailored using lateral and postero-anterior skull films, taken during stereotactic procedures and transferred into Talairach space using angiographic and ventriculographic landmarks.[10] Furthermore, electrode coordinates were superimposed on the high-resolution Talairach-transformed anatomical images obtained from a high resolution MR structural volume (3D MPRAGE sequence) (Fig. 2). The VCA plane was taken as the

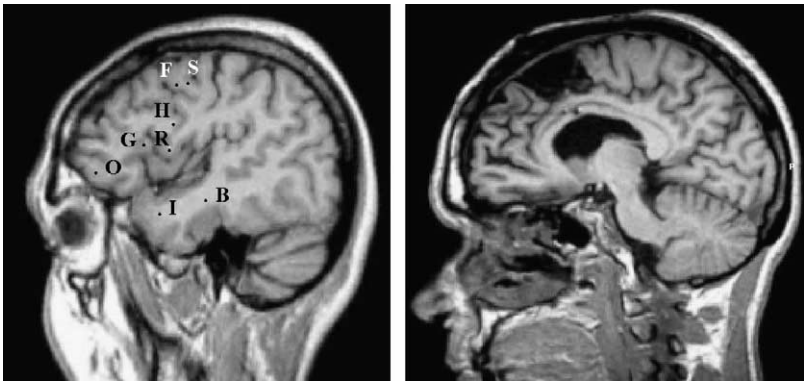

Figure 2 *Left side*: Electrodes implanted in the right fronto-temporal region of patient 1. Note that electrode S and F were located in right SMA-proper and pre-SMA, respectively. *Right side*: Post-operative MRI showing the area of resection in the same patient.

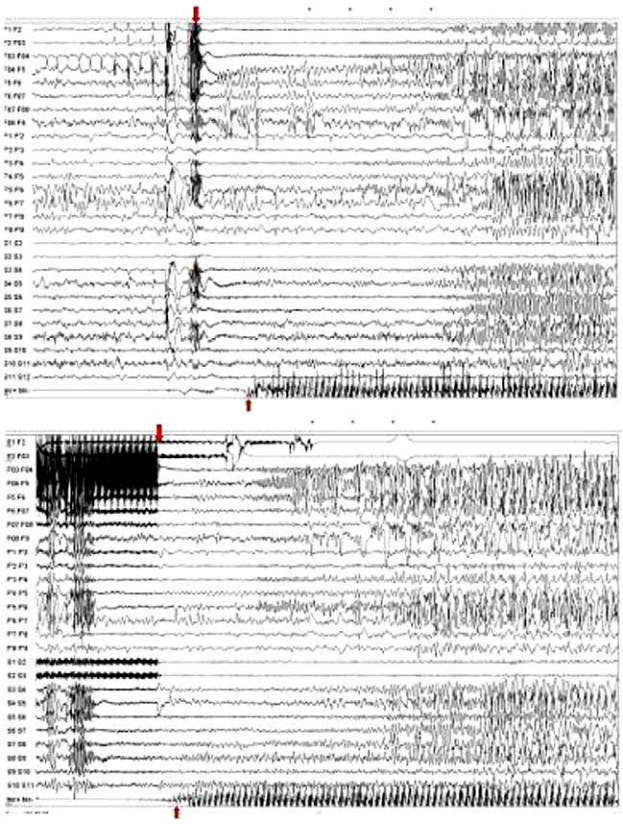

Figure 3 Ictal SEEG in patient 1. Some of the electrodes implanted in the patient are included in figure (for each electrode contact 1 was the deepest one). EMG recordings are showed at the last line. Red arrows indicate the beginning of the ictal discharge at electrode F followed by the muscular rhythmic activity. Upper traces: spontaneous seizure; lower traces: seizure provoked by cortical electrical stimulation. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

border between pre-SMA and SMA-proper, in accordance with literature.[11] Interictal SEEG showed subcontinuous spikes and slow waves at the deepest two contacts of the electrode F implanted in the right pre-SMA, spreading to the two deepest contacts of electrode S implanted in the SMA-proper. Three spontaneous seizures were recorded: in all of which a rapid, low amplitude discharge involved the same contacts of electrodes F and S (see above), with a more tonic involvement of electrode F (Fig. 3). There was only a slight and late involvement of left electrodes. EMG recordings (biceps) performed during ictal automatisms, revealed the same repetitive motor activity at 6—7 Hz described for scalp recordings, beginning 3 s after the ictal electric discharge.

Cortical electrical stimulations were also performed (two frequencies: 1 Hz and 50 Hz, maximum amplitude 3 mA). Two seizures were provoked by high-frequency stimulations (50 Hz, 0.8 mA) at the first two contacts of electrode F (implanted in right pre-SMA). Both of them were very similar to spontaneous seizures, as assessed by both SEEG and EMG recordings (Fig. 3). Right SMA-proper stimulations showed complex flexo-extension movements of the left hand while no clinical response was obtained by stimulating the left pre-SMA.

A right frontal lobe corticectomy involving area 6 and pre-SMA was performed (Fig. 2). No post-operative deficit was observed. Post-operative fMRI with motor task showed a normal activation of the right primary motor area. The patient is seizure-free at 2 years follow-up.

Patient 2

Patient 2 was a 36-year-old, right-handed male. Neurological examination was fully normal. Family history was negative for epilepsy. Delivery and psychomotor development were carried out without problems. At 18 years of age he was submitted to surgery for a right frontal cerebral abscess. Five years after the operation he began to present complex partial seizures, characterized by rapid loss of contact and repetitive movements of the right arm, preceded or followed by ipsilateral simple automatisms of the right fingers (Fig. 4). A post-ictal amnesia was observed, without speech disturbances. The

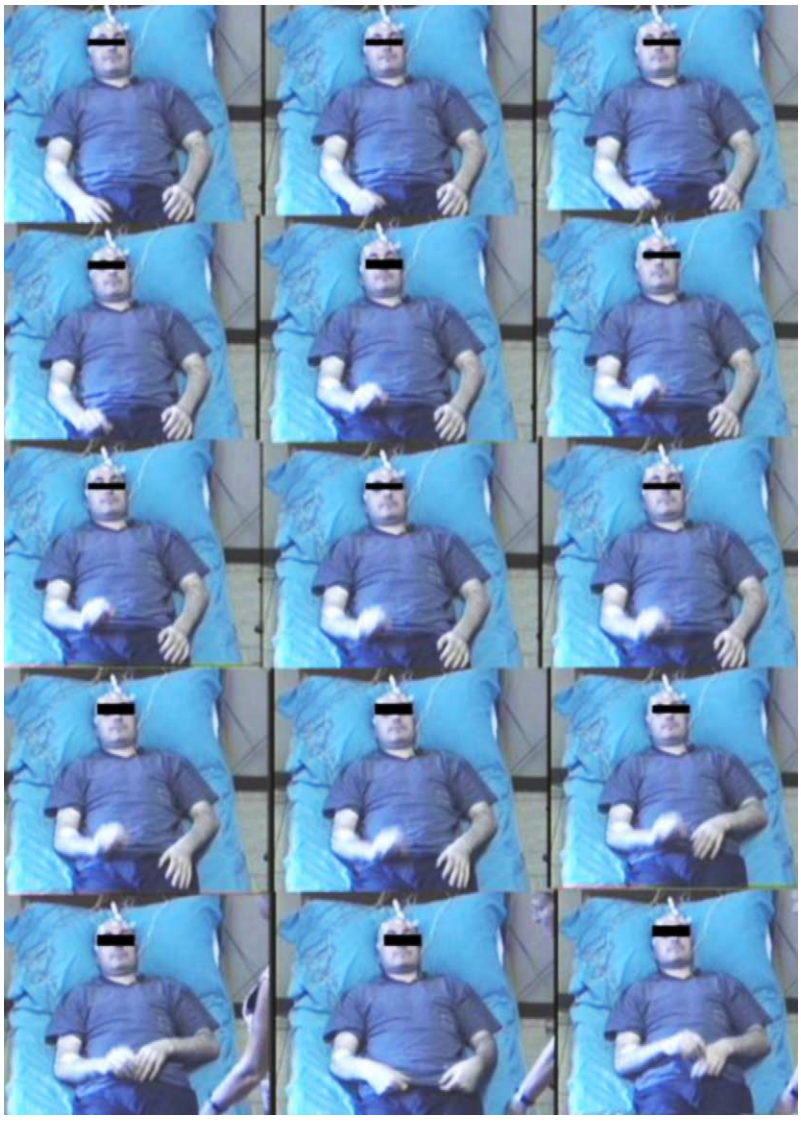

Figure 4 In our second patient seizure semiology was characterized by repetitive movements of the right arm at a frequency rate of 3—4 Hz.

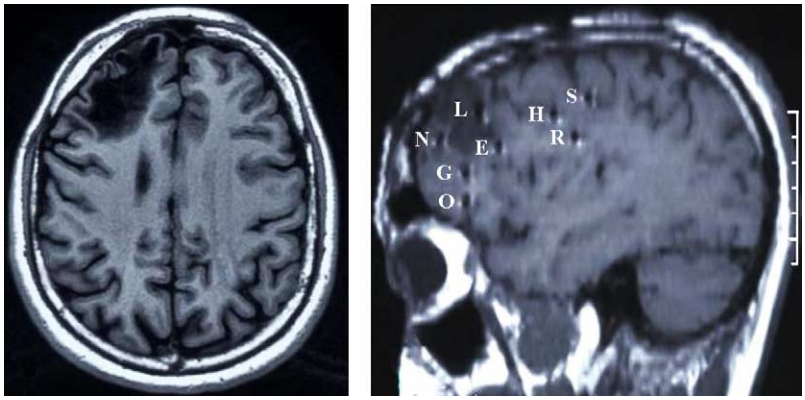

Figure 5 *Left side*: Pre-operative MRI showing the right frontal post-abscess. *Right side*: Electrodes implanted in the right frontal region of patient 2. Note that electrode S was located in right SMA-proper.

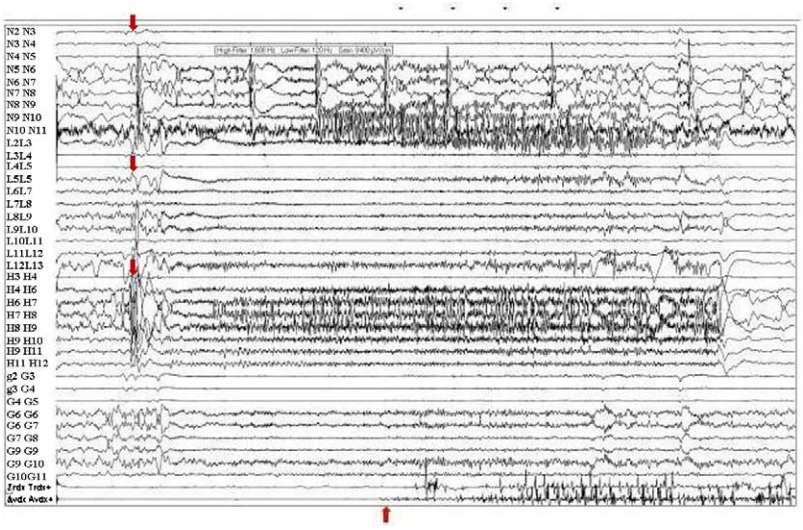

Figure 6 Ictal SEEG in patient 2. Some of the electrodes implanted in the patient are included in figure (for each electrode contact 1 was the deepest one). EMG recordings are showed at the two last lines. Red arrows indicate the beginning of the ictal discharge at electrodes N, L, G, H followed by the muscular rhythmic activity. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

patient described no aura. Seizures were brief (20—30 s) weekly, diurnal, often in clusters. He never generalized. Various AED were not effective.

Pre-surgical evaluation protocol included: history, neurological examination, neuro-psycological assessment, prolonged video-EEG monitoring, high-resolution MRI and fMRI, Technetium-99 m Ethyl Cysteinate dimer (99mTc-ECD) interictal and ictal SPET, the latter obtained during both spontaneous and pharmacologically provoked seizures.

MRI disclosed the previous right frontal corticectomy and ipsilateral ventricular dilatation (Fig. 5). Wada test and fMRI demonstrated left dominance for language. Neuropsycological assessment showed a slight mental retardation. Interictal SPET disclosed right frontal hypoperfusion while spontaneous ictal SPET revealed hyperperfusion in the same region.

Interictal scalp EEG showed bilateral fronto-centro-temporal spikes and slow waves, clearly predominant on the right hemisphere. At ictal scalp EEG, a steep interruption of interictal abnormalities followed by low-amplitude recruiting activity at right fronto-temporal electrodes was observed. EMG (triceps, biceps) indicated repetitive motor activity at 3—4 Hz during right arm automatisms.

Invasive recordings were performed to define the correlation of the lesion to the epileptogenic zone. On the basis of electro-clinical correlations we decided to perform SEEG by implanting eight electrodes in the right frontal lobe, including the lesion (electrodes N and L) and surrounding areas. In this patient, only the SMA-proper was implanted (electrode S) for technical reasons. The exact position of each contact was assessed on individual MRI performed just after implantation (Fig. 5). Interictal SEEG showed very frequent high-voltage spikes, sometimes in clusters, at electrodes N and L, both located in the lesion. Two spontaneous seizures and a number of subclinical paroxystic discharges were recorded. Ictal discharges (Fig. 6) were characterized by low voltage rapid activity involving the lesion (electrodes N, L, G) and surrounding areas until cingulate and F2 gyri (electrode G). The SMA area was less consistently involved. EMG recordings (triceps, biceps) revealed the same repetitive motor activity at 3—4 Hz described for scalp recordings, beginning 6—7 s after the ictal electric discharge.

Cortical electrical stimulations did not provoke any seizure. A sensation of ''someone pushing down'' on the left hand was induced by stimulation of the right SMA-proper.

A provoked ictal SPET was performed during SEEG and confirmed data obtained in previous spontaneous SPET.

A right frontal corticectomy was performed involving the lesion and surrounding areas, extending to the cingulate gyrus (electrodes N, L, G and H). The patient is seizure free at 1-year follow-up.

Discussion

In our two patients with right frontal lobe epilepsy, ictal semiology was characterized by repetitive movements of the ipsilateral upper extremity. According to the ILAE Report[12] we considered these

repetitive movements to be hyperkinetic automatisms. Simple motor automatisms such as tapping or kicking, and complex motor automatisms such as rubbing, thrashing and picking, have been described in previous series of frontal lobe epilepsies.[13–16] However, we failed to find a description of vigorous, rhythmical and stereotyped frontal ictal automatisms similar to those showed by our patients.

Early repetitive movements (RMAs) occurring within 32 s of EEG onset and lasting 35 s or less, were supposed, by Riggio and Harner[2] to originate from the frontal lobe, even if no consistent electro-clinical correlation to a specific frontal area was found. In our first patient there was a clear demonstration that seizures originated from the right SMA and, particularly, the right pre-SMA. In fact, even if the surgical resection involved both pre-SMA and area 6 because of the rapid spreading of seizures, in invasive recordings interictal sub-continuous spikes and ictal discharge onset were localized at the two deepest contacts implanted in pre-SMA. Electrical cortical stimulation was able to induce seizures identical to spontaneous ones only at these two contacts, as assessed by both SEEG and EMG recordings. Finally, surgery determined seizure suppression.

In the second patient SMA area was less consistently involved by ictal discharges and spared in surgical resection. Furthermore, only the most posterior part of this area was implanted. However, the presence of very similar hyperkinetic automatisms might indicate that the symptomatogenic area included this area.

According to ILAE classification, SMA seizures are characterized by classic tonic posturing of the upper extremity and adversive head and eye deviation, speech arrest and vocalizations. Penfield and Jasper[17] first described the so-called 'fencing posture' in SMA seizures. Bancaud and Talairach[3] described four patients with SMA epilepsy characterized by speech arrest, vocalization, palilalia, abduction and lifting of the contralateral upper limb, and adversive movement of the head and eyes to the side of the limb elevation. Ajmone-Marsan and Ralston,[18] Chauvel et al.[4,19] reported a predominance of seizures with complex postural manifestations and bilateral motor activity in patients with ictal involvement of the SMA. A clear definition of SMA seizures has not been simple however, due to their often bizarre appearance and rapid propagation of ictal discharges.[20] Recently,[9] various clinical manifestations, such as tonic posturing, frenetic and bizarre automatisms and motionless staring, have been associated with mesial frontal lobe epilepsy. Our report suggests that not only predominant postural manifestations but also hyperkinetic ictal automatisms could be associated with the SMA area.

Ikeda et al.[21] distinguished SMA ''epilepsy'', in which the epileptogenic zone was located in the SMA, from SMA ''seizures'' (ILAE), seizures originating from or involving the SMA. In this latter case SMA could be preserved in surgical resection. Bleasel and Morris[22] outlined that patients may have an ictal onset distant from, but spreading to the SMA, with initial clinical semiology identical to that of seizures arising within this area. It was, therefore, suggested that imaging data and/or intracranial recordings were necessary for localization of the epileptogenic zone.[23] According to these reports our first patient should be diagnosed as having SMA epilepsy, whilst for our second, a secondary involvement of the area would be suggested.

Both patients showed ipsilateral hyperkinetic automatisms. fMRI studies[24] found a significant preponderance of the ipsilateral over the contralateral response in human pre-SMA particularly for sequential movements. Unilateral cortical electrical stimulation of the SMA could determine bilateral responses and unilateral SMA lesions determine a decrease in bimanual coordination.[25] Most ipsilateral and bilateral responses were elicited by stimulation of the right SMA, thus raising the possibility of a more significant control of the non-dominant SMA in bilateral movements. Chauvel et al.[26] described bilateral upper limb movements after electrical stimulation of the SMA by depth electrodes; occasional bilateral responses have been also described by other authors.[27]

The repetitive character of right arm movements in our patients could be explained by fMRI studies[28] suggesting an important role of both dorsolateral and medial premotor regions in programming trains of repetitive responses.

Conclusions

Due to the various challenges associated with SMA ''epilepsy'', the knowledge of the physiological role of the SMA could help in understanding the clinical semiology of seizures arising from and/or involving this area. The description of unusual patterns might be helpful in localizing the epileptogenic zone particularly in cases of cryptogenetic epilepsies.

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