Epileptic Disord 2016; 18 (1): 73-6

Electrophysiological findings in Rasmussen's syndrome

Ayşegül Gündüz, Meral E. Kızıltan, Tülin Coşkun, Şakir Delil, Naz Yeni, Çiğdem Özkara

Department of Neurology, Cerrahpasa School of Medicine, Istanbul University, Istanbul, Turkey

Received May 10, 2015; Accepted January 16, 2016

ABSTRACT – *Background*. Rasmussen syndrome is a rare, inflammatory and probably autoimmune disease presenting with epilepsia partialis continua which is generally in the form of myoclonic jerks and involves the upper extremities with or without head involvement. We sought to demonstrate the electrophysiological features in patients with Rasmussen syndrome.
Methods. We performed continuous electrophysiological recordings of involuntary movement, as well as recordings of startle responses and long latency reflex in three patients with a diagnosis of Rasmussen syndrome.
Results. Positive and negative myoclonus were recorded. Startle responses were found to be suppressed. However, long latency reflexes were high in amplitude and one patient even had a C reflex.
Conclusion. Stimulus-sensitive positive and negative cortical myoclonus are typical in epilepsia partialis continua of Rasmussen syndrome and degeneration of brainstem and reticulospinal pathways may develop in Rasmussen syndrome.

Key words: Rasmussen syndrome, epilepsia partialis continua, myoclonus, startle response, long latency reflex

Rasmussen syndrome (RS) is a rare, inflammatory and probably autoimmune disease presenting with epilepsia partialis continua (EPC), recurrent status epilepticus, progressive neurological findings, and unilateral cerebral hemisphere atrophy (Granata and Andermann, 2013). It typically affects children and onset during adolescence or adulthood is defined as late-onset. EPC is generally in the form of myoclonic jerks and involves the upper extremities with or without head involvement (Bien and Elger, 2008).

Neuroimaging shows unilateral focal cortical atrophy with high intensity signal changes of grey or white matter and basal ganglia (Granata and Andermann, 2013).

Although there are extensive neuroimaging studies in RS, data is lacking related to the integrity of corticospinal, basal ganglia and other brainstem pathways. Blink reflex (BR) is characteristically elicited after supraorbital electrical stimulation. Two components of BR, ipsilateral R1 and bilateral R2, have central generators in the brainstem and are modulated by supratentorial and basal ganglia structures (Esteban, 1999). Startle responses which are evoked by sudden stimulation are under the control of the brainstem and can be

Correspondence:
Department of Neurology,
Cerrahpasa School of Medicine,
Istanbul University,
34098 K.M.Pasa,
Istanbul, Turkey
<draysegulgunduz@yahoo.com>

doi:10.1684/epd.2016.0804

recorded by electrophysiological methods (Brown *et al*., 1991).
Therefore, we sought to demonstrate changes of brainstem pathways in patients with RS using the electrophysiological methods.

Patients and methods

Three patients with a diagnosis of RS followed in our epilepsy outpatient clinic were studied.
All patients were diagnosed with RS according to European consensus criteria (Bien *et al*., 2005), meeting either all three criteria of Part A or two out of three criteria of Part B:

– Part A
  • (1) Clinical: focal seizures (with or without epilepsia partialis continua) and unilateral cortical deficit(s).
  • (2) EEG: unihemispheric slowing with or without epileptiform activity and unilateral seizure onset.
  • (3) MRI: unihemispheric focal cortical atrophy and at least one of the following:
  - grey or white matter T2/FLAIR hyperintense signal;
  - hyperintense signal or atrophy of the ipsilateral caudate head.

– Part B
  • (1) Clinical: epilepsia partialis continua or progressive unilateral cortical deficit(s).
  • (2) MRI: progressive unihemispheric focal cortical atrophy.
  • (3) Histopathology: T cell dominated encephalitis with activated microglial cells (typically, but not necessarily forming nodules) and reactive astrogliosis. Numerous parenchymal macrophages, B cells or plasma cells, or viral inclusion bodies exclude the diagnosis of RE.

The study was approved by the local ethical committee and all participants and their family members gave informed consent.
Unilateral orbicularis oculi, masseter, sternocleidomastoid, biceps brachii, abductor policis brevis, and anterior tibial muscles were targeted for electrophysiological recordings using surface silver-silver chloride electrodes and Neuropack Sigma MEB-5504k, Nihon Kohden Medical, Tokyo, Japan. The first step was continuous recording of involuntary movements during rest, posture, action and weight bearing. Second, we performed brainstem reflex recordings by applying supraorbital electrical stimulation (0.2 m, 6-12 mA) for BR, auditory stimulation (binaural 105 dB) for auditory startle response (ASR), and electrical stimulation over the wrist (15-25 mA, 0.2 m) for startle response to somatosensory inputs (SSS). The third step was to obtain segmental reflex (SR) and long latency reflex (LLR) after electrical stimulation of median nerve at the wrist (15-25 mA, 0.2 m). Responses with latencies of 45-65 were defined as LLR II.

Results

A total of three patients (mean age: 20.3±3.8 years; two males) were identified in the study period. Clinical features are summarized in *table 1*. Investigations for autoimmune encephalitis and metabolic/mitochondrial disease were negative in all patients. EPCs were in the form of myoclonic jerks which involved unilateral facial, upper extremity and lower extremity muscles. However, myoclonus exhibited higher amplitude on the distal parts of the upper extremities (*figure 1A, B*) and were sensitive to action or posture. Duration of myoclonus (burst duration) was shorter than 50 ms in all patients. All patients also

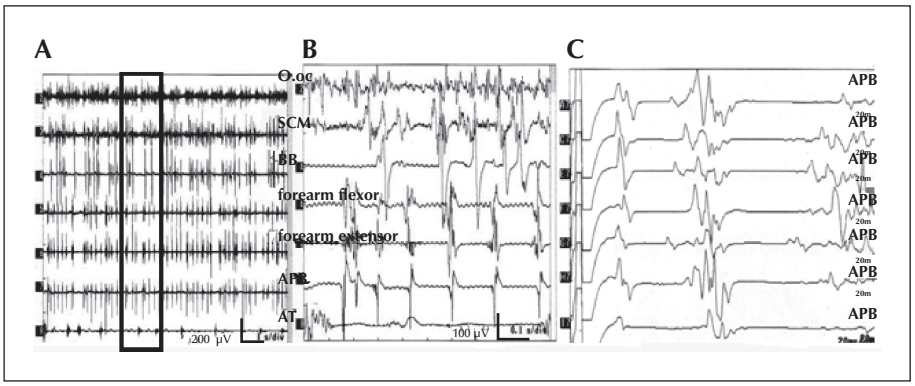

Figure 1. (A, B) Continuous analysis of involuntary movements showing positive and negative myoclonic jerks in a 23-year-old female patient (Patient 1). The sweep speed in (A) is faster than that in (B) based on a particular part of the EMG that has been enlarged to analyse the characteristics of each burst. (C) High-amplitude LLR II over APB after median stimulation at the wrist in a 22-year-old male patient (Patient 2). (O.oc: orbicularis oculi; SCM: sternocleidomastoid; BB: biceps brachii; APB: abductor policis brevis; AT: anterior tibial; sensitivity: 200 µV).

Table 1. Clinical and electrophysiological features.

	Patient 1	Patient 2	Patient 3
Age, years	23	22	16
Gender	Female	Male	Male
Age at onset, years	16	10	15
Clinical features	Myoclonic jerks of right upper and lower extremities, GTCS, CPS, mild right-sided hemiparesis	Myoclonic jerks of left upper and lower extremities, left-sided hemiconvulsions, GTCS, left-sided pyramidal findings	Myoclonic jerks of left upper and lower extremities, GTCS, mild right-sided hemiparesis
Medications	Levetiracetam, carbamazepine, clonazepam	Levetiracetam, oxcarbazepine, phenobarbital, clobazam	Carbamazepine, valproate, levetiracetam, clobazam,
EEG	Left centro-parietal disorganisation and epileptiform activity	Generalised disorganisation and bilateral frontal epileptiform activity	Right centro-parietal disorganisation and epileptiform activity
MRI	Atrophy of left frontal cortex and multiple focal hyperintensities in frontal and parietal lobes	Right fronto-temporal atrophy and gliosis	Left fronto-temporal atrophy and gliosis
BR R1/R2, ms Normal value	9.6/44.4 R1: 10.3±0.9, R2: 31.6±3.4	11.6/47.2	9.6/58.8
ASR, probability,% Normal value	0 33.7±8.7	25	15.6
SSS, presence rate,% Normal value	0 39.5	0	0
SR, latency, ms Normal value	29.4 25.7±2.4	25.0	25.0
C reflex, latency, ms Normal value	55 Absent	Absent	Absent
LLR II, amplitude, μV Normal value	3000 995.1±924.7	1500	3000
SR/LLR II amplitude	0.33	0.33	0.2

BR: blink reflex; ASR: auditory startle response; SSS: startle response to somatosensory inputs; LLR: long latency reflex; SR: segmental reflex. Normal values are presented as mean±SD and were calculated from a group of 18 healthy subjects (mean age: 23.1±5.9 years; males: 44.4%).

had negative myoclonus. Other types of involuntary movements were not observed. R1 components of BR were normal whereas mean latencies of R2 component were delayed (50.1±7.6 m; normal value: 31.6±3.4 m). Probabilities of ASR were low and latencies were long; one patient did not even have a response. SSS was not obtained in any of the patients (*table 1*). Latency and persistency of SR was normal. There was a

C reflex with 55 ms of latency in one patient (Patient 1). LLR II during active contraction was high in amplitude (*figure 1C*).

Discussion

Positive and negative myoclonus were common in RS. Presence of short duration myoclonus, C reflex or high-amplitude LLR II suggest cortical or corticosubcortical myoclonus in RS. This type of myoclonus is typical of myoclonic epilepsies such as progressive myoclonic epilepsy or juvenile myoclonic epilepsy, reflecting high excitability of the sensori-motor cortex or corticospinal pathway (Tobimatsu *et al.,* 1985). Clinical findings of EPC may suggest clonic convulsions. However, the characteristics of each burst, with short burst duration, high amplitude, and very short rising time, suggested myoclonus.

Abnormally delayed BR R2 in the presence of normal R1 suggests abnormal transmission in the central BR pathways, probably due to increased inhibition. Startle reflex is generated in the brainstem, the pedunculopontine nucleus (PPN), and is under the modulatory control of basal ganglia, specifically the dopaminergic system. The efferent pathway is the reticulospinal system. Loss or suppression of reflex suggests inhibition or degeneration of PPN or the reticulospinal system (Williams *et al.*, 2008), whereas, in the case of cortical or basal ganglia lesions, such as RS, exaggeration of startle responses would be expected. Among RS cases, there are few case reports with cranial nerve involvement and unilateral midbrain and pontine involvement on neuroimaging (Quesada *et al.*, 2009). Our results may support involvement of central pathways of BR and reticulospinal pathways in the brainstem even without development of symptoms attributed to the brainstem or neuroimaging findings.

In conclusion, stimulus-sensitive positive and negative cortical myoclonus are typical in EPC of RS and degeneration of brainstem and reticulospinal pathways may develop in RS. □

Acknowledgements and disclosures.
There were no funding sources for this study.
The authors have no conflict of interest to disclose.

References

Bien CG, Elger CE. Epilepsia partialis continua: semiology and differential diagnoses. *Epileptic Disord* 2008; 10(1): 3-7.

Bien CG, Granata T, Antozzi C, *et al*. Pathogenesis, diagnosis and treatment of Rasmussen encephalitis: a European consensus statement. *Brain* 2005; 128(3): 454-71.

Brown P, Rothwell JC, Thompson PD, Britton TC, Day BL, Marsden CD. New observations on the normal auditory startle reflex in man. *Brain* 1991; 114(4): 1891-902.

Esteban A. A neurophysiological approach to brainstem reflexes. Blink reflex. *Neurophysiol Clin* 1999; 29(1): 7-38.

Granata T, Andermann F. Rasmussen encephalitis. *Handb Clin Neurol* 2013; 111: 511-9.

Quesada CM, Urbach H, Elger CE, Bien CG. Rasmussen encephalitis with ipsilateral brain stem involvement in an adult patient. *BMJ Case Rep* 2009. doi: 10.1136/bcr.08.2008.0648.

Tobimatsu S, Fukui R, Shibasaki H, Kato M, Kuroiwa Y. Electrophysiological studies of myoclonus in sialidosis type 2. *Electroencephalogr Clin Neurophysiol* 1985; 60(1): 16-22.

Williams DR, Doyle LM, Lees AJ, Brown P. The auditory startle response in parkinsonism may reveal the extent but not type of pathology. *J Neurol* 2008; 255(5): 628-32.