Epilepsy & Behavior Reports 24 (2023) 100627

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

journal homepage: www.elsevier.com/locate/ebcr

Deep brain stimulation in a patient with progressive myoclonic epilepsy and ataxia due to potassium channel mutation (MEAK). A case report and review of the literature

Michał Sobstyl [a], Nina Kożuch [b], Magdalena Iwaniuk-Gugała [b], Angelika Stapińska-Syniec [a,*], Magdalena Konopko [b], Paweł Jezierski [b]

[a] Department of Neurosurgery, Institute of Psychiatry and Neurology, Sobieskiego 9 Street 02-957, Warsaw, Poland
[b] 1st Department of Neurology, Institute of Psychiatry and Neurology, Sobieskiego 9 Street, 02-957 Warsaw, Poland

ARTICLE INFO

Keywords:
Deep brain stimulation
Progressive myoclonic epilepsy
Myoclonic jerks
Subthalamic nucleus
Substantia nigra pars reticulata

ABSTRACT

Progressive myoclonic epilepsy (PME) is characterized by prominent myoclonus, generalized tonic-clonic seizures, and less often focal, tonic, or absence seizures. The KCNC1 mutation is responsible for specific clinical phenotype of PME which has been defined as myoclonic epilepsy and ataxia due to potassium channel mutation (MEAK). We present a case of a 44 years-old male patient with genetically proven MEAK who underwent subthalamic nucleus/substantia nigra (STN/SNr) deep brain stimulation (DBS) for his pharmacological-refractory myoclonus and drug-resistant epilepsy (DRE). Since the age of 4–5 years, the patient had been suffering from intention tremor, and later the myoclonic jerks, ataxia involving the upper limbs and walking difficulties worsened. The first bilateral tonic-clonic seizure (BTCS) occurred at the age of 22. The patient agreed to staged bilateral implantation of DBS electrodes placed in the STN/SNr region. The follow-up lasts more than 24 months. The myoclonic jerks assessed by Unified Myoclonus Rating Scale (UMRS) were reduced by nearly 70 % and BTCS was completely abolished. The patient's ataxia and dysarthria did not improve. Early diagnosis with genetic testing may significantly help in counseling patients with PME and enables to undertake the surgical approach targeting the STN/SNr.

Introduction

Progressive myoclonic epilepsy (PME) includes a variety of phenotypically similar, but genetically heterogeneous syndromes with common clinical features such as myoclonus, drug-resistant seizures, intention tremor, ataxia, and cognitive impairment [1]. PME syndromes are rare (less than 1 % of all types of epilepsy syndromes) but belong to the most devastating intractable epilepsy syndromes [2]. The etiology and clinical course of PME syndromes may be variable, but the clinical phenotype with intractable myoclonic jerks as first symptoms and thereafter drug-resistant epilepsy appears consistently [1,3,4].

There are several distinct entities of PME which include Unverricht-Lundborg disease (ULD), Lafora disease, myoclonic epilepsy with ragged red fibers, neuronal ceroid lipofuscinosis, sialidosis, and pallido-luysian atrophy [1]. Recently a new subtype of PME has been described [2,5]. This type of PME is caused by a recurrent de nove heterozygous mutation in the KCNC1 (Potassium Channel, Voltage-Gated, Shaw-Related Subfamily, Member 1) gene, which encodes for the Kv3.1 protein (a subunit of the Kx3 subfamily of voltage-gated potassium channels). The loss of Kv3 function disrupts the firing properties of fast-spiking neurons, inhibits neurotransmitter release, and induces cell death [6]. The most affected neurons in progressive myoclonic epilepsy and ataxia due to potassium channel mutation (MEAK) are inhibitory GABAergic interneurons and cerebellar neurons [7].

Patients with MEAK usually have normal early development. The first symptom is the myoclonus. The myoclonus worsens with disease duration and cerebellar signs like ataxia, disturbed gait, intention tremor, and mild cognitive impairment lead to significant reduction of quality of life and loss of patient's autonomy [1–4]. A few patients report bilateral tonic-clonic seizures (BTCS) as an early manifestation but the occurrence of seizures may lead to misdiagnosis [1]. Typical electroencephalographic features include generalized epileptiform discharges (mainly generalized spike-and-wave or polyspike-wave discharges) with photic sensitivity and slowing of background rhythms. Brain imaging

* Corresponding author.
E-mail address: angelika.stapinska@gmail.com (A. Stapińska-Syniec).

https://doi.org/10.1016/j.ebr.2023.100627
Received 23 June 2023; Received in revised form 5 October 2023; Accepted 10 October 2023
Available online 11 October 2023

shows prominent cerebellar atrophy. The early clinical pictures of MEAK may resemble the ULD, but patients with MEAK as a rule present more rapid and severe clinical phenotype [1].

In this case report we present a patient with long-lasting clinical features of PME syndrome who was finally diagnosed with MEAK. Due to disabling myoclonic jerks, intention tremor, and drug-resistant epilepsy, we proceeded with bilateral subthalamic nucleus/pars reticulata of the substantia nigra (STN/SNr) stimulation. To our knowledge, this is the first case report of a patient with genetically confirmed MEAK who was treated with deep brain stimulation (DBS).

Case

The first patient's symptoms appeared at the age of 4–5, reported as a mobility impairment. At that time the patient was evaluated by a pediatric neurologist, who diagnosed cerebellar dysfunction of unknown etiology (head CT and metabolic tests were normal). During early adolescence intention tremor, affecting especially the left upper limb was remarkable, and myoclonic jerks were first described. The latter intensified, which significantly affected the patient's performance in daily activities. Subsequently, ataxia involving the upper limbs and gait difficulties worsened. The patient has been wheelchair-bound since the age of 16. At the age of 22, the patient presented with dysarthria which progressively impaired communication. The first BTCS occurred at the age of 22 and was preceded by prolonged exposure to computer screen and fatigue. EEG showed generalized polyspike-wave discharges with predominance over the right hemisphere. Additionally, there was another kind of seizure observed in this patient (that probably occurred before his first BTCS), manifesting with head deviation, nystagmus, and impaired awareness – focal impaired awareness seizure (FIAS). This FIAS occurred around two years before the first BTCS manifestation. In magnetic resonance imaging, the global symmetrical cerebellar atrophy with enlargement of the fourth ventricle was noticed [Fig. 1].

The patient had extensive genetic testing against spinocerebellar ataxia type SCA1, type SCA2, and SCA 3. All genetic tests for SCA were negative. Fragile X Syndrome as well as myoclonic epilepsy with ragged red fibers (MEFFR) syndrome were excluded. Due to the left-sided intention tremor and myoclonic jerks, the patient underwent a right thalamotomy targeted mainly at the ventral intermediate nucleus (Vim). The thalamotomy effect produced a marked improvement in intention tremor and myoclonic jerks sustained over 2 years. At the age of 28, besides the diagnosis of myoclonic epilepsy, the second misleading diagnosis of secondary generalized dystonia was made. At the age of 36, the patient underwent right-sided posteroventrolateral pallidotomy. The effect of pallidotomy was short lasting reducing only minimally left-sided myoclonic jerks. The myoclonic jerks with intention tremor involved both upper extremities. Ataxia, dysarthria, and mild cognitive impairment greatly reduced the patient's independence. The frequency of FIAS and BCTS also increased.

The therapeutic approach aimed at myoclonus and epileptic seizures included daily doses of topiramate 400 mg, levetiracetam 3000 mg, valproic acid 1000 mg, and clonazepam 4 mg. Additionally, the patient was treated with propranolol 60 mg daily because of the incapacitating intention tremor. The misdiagnosis of secondary generalized dystonia was revisited. Eventually, the suspicion of hereditary PME was raised. The genetic testing revealed the KCNC1 heterozygous mutation c959G > A(p.Arg320His) and ultimately confirmed the diagnosis of myoclonic epilepsy and ataxia due to potassium channel mutation (MEAK). The patient was 41 years old when the final diagnosis was made. The interesting finding is that predominant symptoms were related to cerebellar dysfunction. The FIAS and BTCS appeared relatively late in the course of the disease and probably caused a significant delay in proper diagnosis.

Based on a few promising case reports demonstrating improvements in myoclonus and seizures after DBS in PME, we discussed with the patient this treatment modality. The patient agreed, but with unilateral implantation, and in the case of clinical improvement, implantation of the electrode to the contralateral hemisphere of the brain would be thereafter considered. Due to the left-sided dominance of myoclonic jerks and intention tremor, we have proceeded with the implantation of the DBS system on the right side. DBS electrode implantation was done using a frame-based approach under general anesthesia. The direct targeting was based on stereotactic intraoperative contrast-enhanced computed tomography and image fusion with preoperative contrast-enhanced T1-weighted MPRAGE and non-contrast T2-weighted MRI using Stealthstation software. The planning coordinates of the STN/SNr region relative to the midcommissural point were x= ±11 mm, y = −4 mm, and z = −7 mm. Based on these coordinates, contact 0 of DBS electrode type 3389 was introduced to this tentative target. Implanting the electrode in this manner contact 0 was located in the dorsal part of the SNr, contact 1 at the border between SNr and STN, and contacts 2 and 3 were placed in the STN. No microrecording was used. The DBS electrode 3389 was implanted on the right side with the confirmation of lateral fluoroscopy. The intraprocedural stereotactic CT with the stereotactic head frame was done and merged with preoperative stereotactic CT and MRI sequences to confirm the proper placement of the DBS electrode. Thereafter, the implantable pulse generator (Activa 37603) was implanted in the right subclavicular area. The monopolar survey of the implanted lead was done. The initial stimulation parameters were 2.5 V, 60 microseconds, and 145 Hz. The monopolar stimulation exaggerated dysarthria so the bipolar stimulation mode was utilized. The stimulation was bipolar electrode contact 3 was selected as anode and the remaining three electrode contacts as cathodes. Bipolar stimulation enabled concomitant stimulation of STN, the transitional zone between STN, and SNr. This unilateral simulation produced a marked improvement of myoclonic jerks and intention tremor in the left hemibody. The

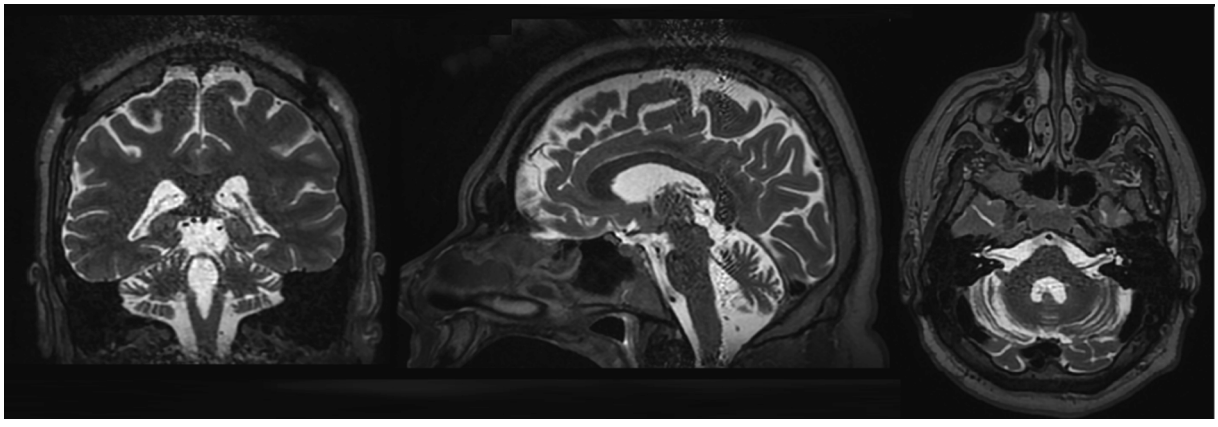

Fig. 1. Marked cerebellar atrophy in magnetic resonance imaging T2 weighted images with enlargement of the fourth ventricle.

opposite DBS procedure was performed after 1 month. Over the follow-up period, the only change was the increase of stimulation voltage on the right side to 4.0 V, and on the left to 4.2 V. The remaining stimulation settings and stimulation mode remained unchanged.

At 24 months of follow-up, the patient was hospitalized for a complex follow-up examination during which formal neurological assessments including video-EEG, neuropsychological, and control brain MRI were done [Fig. 2A–C].

The patient's formal neurological examination after DBS implantation showed mainly features of cerebellar disorder: intention tremor affecting upper limbs, gait ataxia, dysarthria, alternating movement disturbance, and incoordination. Sporadic myoclonic jerks in the extremities were also observed. The myoclonic jerks were reduced by nearly 70 % when compared to the baseline UMRS preoperative scores [Fig. 3]. The patient was able to walk a few steps with assistance. Under bilateral STN/SNr stimulation, BTCS was completely abolished. The FIAS was reduced by around 60–70 %. During 82 h of video-EEG monitoring no clinical or electrographic seizure was registered, EEG showed temporal slow waves, more prominent only on the left side.

The neuropsychological assessment of the patient using standardized neuropsychological methods was impossible because of severe dysarthria, persistent myoclonic jerks, and chronic fatigue. The patient was well auto- and allo-psychically oriented and stayed in logical contact impaired by severe dysarthria. The persistent myoclonic jerks made writing, drawing, and performing motor instructions impossible. In the examination using Mini-Mental State Examination, the patient achieved 24 scores and in the Clock Drawing Test, the patient gained 9 points per 10 (according to Sunderland scoring criteria). Generally, the patient suffered from impaired grapho-motor deficits which were associated with cerebellar dysfunction. Moreover, the patient had deficits in attention, immediate memory, and calculation. The abilities of object naming, writing, and reading were preserved. The postoperative MRI showed the proper placement of both leads (Fig. 2A–C). The preoperative MRI images were fused with intraprocedural CT using the SureTune™ 3 software (Medtronic Minneapolis, Minnesota, USA) which enabled the creation of patient-specific anatomy and DBS lead locations

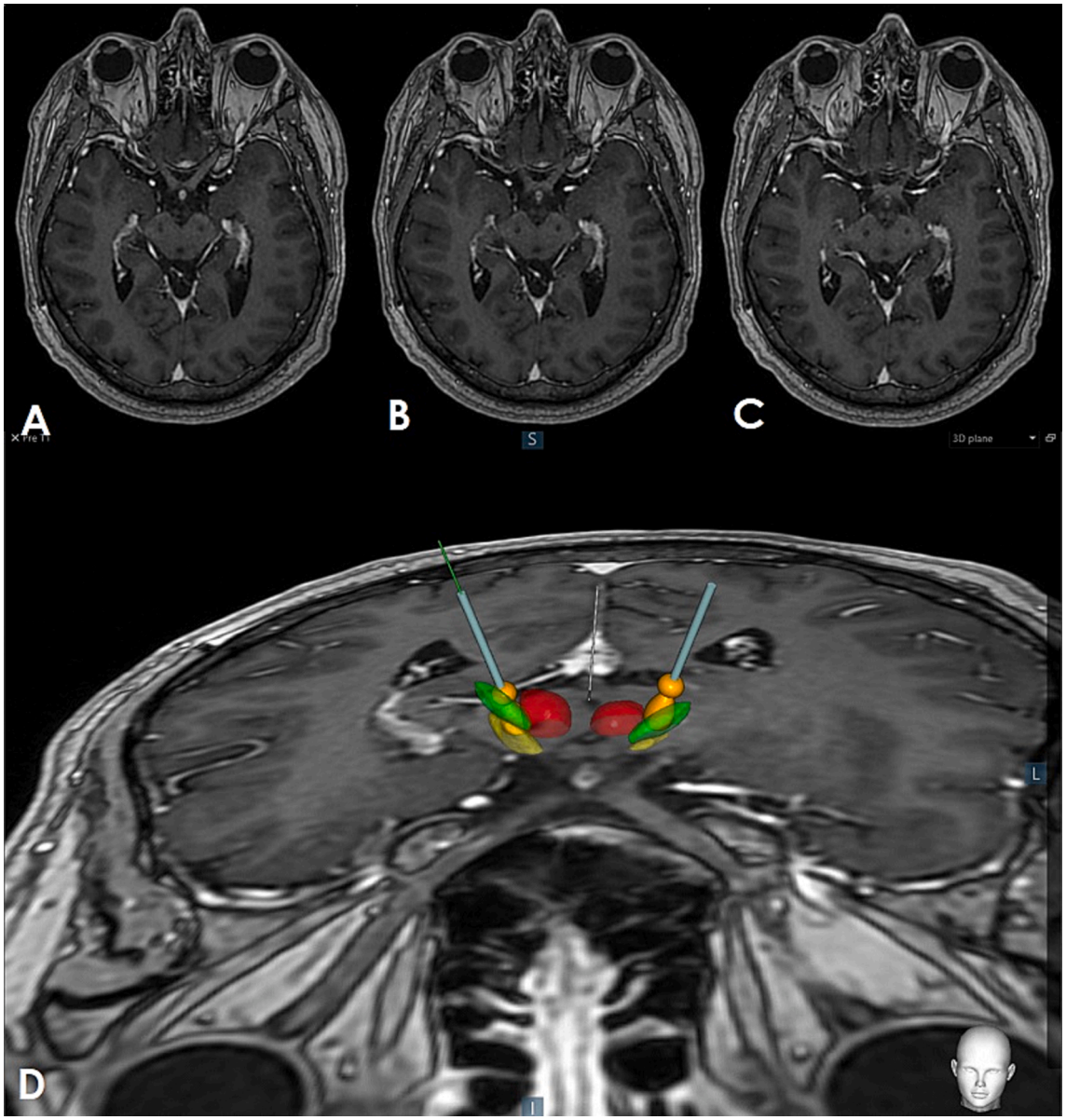

Fig. 2. A–C: T1 weighted images showing the implanted DBS leads in the substantia nigra pars reticulate and subthalamic area. D: Fusion of preoperative MRI images with intraprocedural CT using the SureTune™ 3 software (Medtronic Minneapolis, Minnesota, USA) which enabled the creation of patient-specific anatomy and DBS lead locations in the stimulated area. The patient's specific stimulation settings were used to create the volume of tissue activated (VTA).

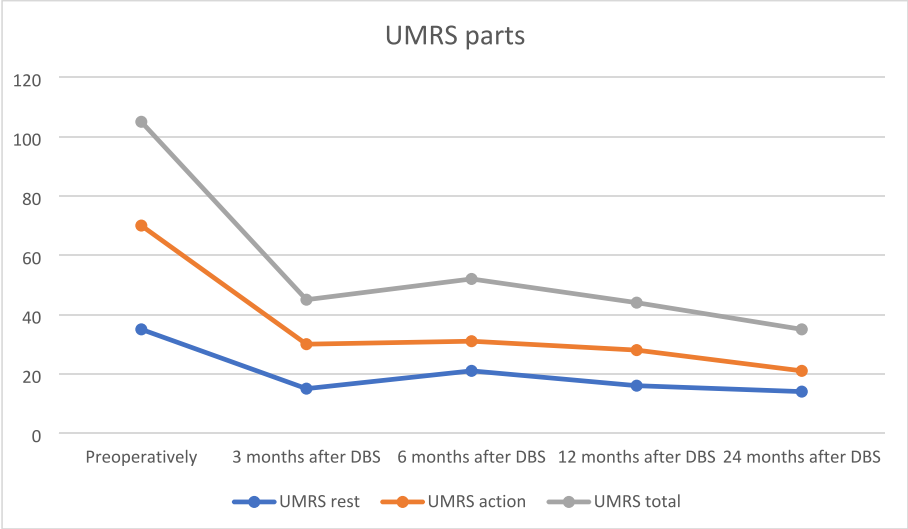

Fig. 3. The rest, action and total Unified Myoclonus Rating scale scores before bilateral STN/SNr DBS and at the scheduled follow-up visits till 24 months postoperatively.

in the stimulated area. The patient's specific stimulation settings were used to create the volume of tissue activated [Fig. 2D]. The functional benefit consists of improvement in some activities of daily living like eating, drinking, and use of the keyboard. Treatment results are satisfactory to the patient and his parents.

Discussion

Consistent with findings of previously published case reports or case series showing the beneficial effects of DBS in PME syndromes, we present a further patient with a genetically established diagnosis of MEAK after bilateral STN/SNr stimulation with long-term follow-up [1,3,4,8,9]. To our knowledge, this is the first reported patient treated by DBS for disabling myoclonus, intention tremor, and drug-resistant epilepsy in the course of MEAK. Further cases will certainly be diagnosed faster as genetic testing becomes more available. The reported cases in the world's literature regarding DBS for different PME syndromes are presented in Table 1 including our case [3,4,8,9].

Different stereotactic targets have been chosen to treat PME syndromes. Vesper et al. were the first to implant DBS electrodes in the STN/SNr in adult PME patients based on earlier promising results in the treatment of focal motor seizures by STN DBS [3,10–14]. Patients with PME syndromes develop highly drug-resistant myoclonic jerks and BTCS. These cardinal disabling symptoms of PME result probably from subcortical and cortical components of abnormal sensorimotor integration and hyperexcitability of the sensory and motor cortex [15]. The STN as well as SNr have broad reciprocal direct and indirect connections with the primary sensorimotor cortex advocating utilization of DBS for intractable PME syndromes [16]. The nigral system remains in a close spatial and functional relationship with the STN and also modulates neuronal transmission in epilepsy [17]. The connections of the STN and SNr to the superior colliculus (dorsal midbrain anticonvulsant zone – DMAZ) represent the rationale for using the STN and SNr as targets for PME syndromes [10,11].

Wille et al. presented the largest case series of patients treated by DBS for PME [4]. These authors found that stimulation of the SNr/STN region reduces myoclonic seizures by 30 % to 100 % [4]. Four patients were additionally implanted in the ventral intermediate nucleus (Vim) with disappointing therapeutic results even triggering myoclonus. The authors found that stimulation of the lowest contacts (contact 0 and 1 negative, case positive) demonstrated adequate suppression of myoclonic seizures, while stimulation of upper contacts (2 and 3 negative, case positive) turned out to be ineffective [4]. Monopolar stimulation of the SNr was more effective than high-frequency stimulation of either the STN or transitional zone between the STN and SNr. The same observation was made in another case report that selective stimulation of SNr efficiently reduced myoclonus [9]. On the contrary, selective stimulation of the motor STN produced a worsening of myoclonus, gait function, and fine motor skills [9]. This observation remains consistent with the concept of subthalamic DBS for movement disorders. STN DBS ameliorates bradykinesia in Parkinson's disease so it is possible that in a patient suffering not from PD, the STN stimulation may produce dyskinesia. The myoclonus as a hyperkinetic symptom may also be worsened by STN DBS [9]. Applying stimulation to the transitional zone between the STN and SNr resulted in the complete disappearance of BTCS and a reduction in myoclonus [9]. As mentioned above selective stimulation of the SNr produced immediate positive effects on myoclonus. This observation may be explained by the fact that SNr DBS in PD worsens bradykinesia explaining the strong positive effect on myoclonus [9]. The SNr stimulation reduced also BTCS. This positive effect of SNr stimulation may be based on a disruption of the pathological hyperactive cortico-subcortical pathway. Di Giacopo et al. chose to stimulate selectively the SNr [9].

In the presented case the clinical phenotype was different than in most patients operated for PME by DBS. The cerebellar deficits prevailed with the relatively late appearance of FIAS and BTCS delaying also the final diagnosis. Taking into account the clinical phenotype of our patient with disabling intention tremor, the myoclonic jerks we have chosen as stereotactic targets in the STN/SNr region. Firstly we have chosen the monopolar stimulation mode by activating contact 0 (SNr) and contact 1 on the border of the SNr and STN as cathodes. The patient reported that even relatively low voltages up to 1.5 Volts produced dizziness and blurred vision. This was the subjective feeling of the patient. Thereafter we have chosen the middle contacts (1 and 2) as cathodes and implantable pulse generator (IPG) as anode. Monopolar stimulation of two middle contacts as cathodes worsened dysarthria and dysphasia. The patient's speech was also affected severely by the disease so this was also another reason to switch to bipolar stimulation mode. These stimulation-induced adverse events disappeared by bipolar stimulation choosing the most distal contacts as cathodes (contacts 0,1,2) and contact 3 as an anode. This stimulation narrowed the stimulation field within the STN and SNr with good clinical effects.

Interestingly, dysphasia worsening was reported in 1 out of 3 patients with genetically proven North Sea PME targeting the caudal zona incerta [8]. In this case series, BTCS frequency was reduced in all patients, a marked reduction in intention tremor and myoclonic jerks was

Table 1
Clinical characteristics of patients operated for progressive myoclonic epilepsy by utilizing deep brain stimulation. Abbreviations: STN – subthalamic nucleus, SNr – substantia nigra pars reticulate, pSTN – posterior subthalamic area, Vim – ventral intermediate nucleus, cZi – caudal Zona Incerta, PME – progressive myoclonic epilepsy, AEDs – anti epileptic drugs, VNS – vagus nerve stimulation, MEAK – myoclonic epilepsy and ataxia due to potassium channel mutation, IPG – implantable pulse generator, NR – not reported.

Authors/ Year of publication	Number of individuals	Gender/ years	Type of progressive myoclonic epilepsy	Side effects of DBS therapy	Stimulation target/electrode type	Stimulation settings	Clinical observation/outcome	Follow-up in months
Vesper et al. 2007 [3]	1	male/39 years	Progressive myoclonic epilepsy		Transitional zone between the STN and the SNr/ Medtronic 3389	Bilateral monopolar 3.0 V 90 us130 Hz	Sustained reduction in the frequency and intensity of myoclonic seizures by 50 %, suppression of generalized tonic-clonic seizures The patient walks few steps without assistance Contacts 0,1 myoclonus suppressionContacts 2.3 turned out to be ineffective	12 months
Wille et al. 2011 [4]	5	Four male/28-39 years median 32 years	Progressive myoclonic epilepsy1 patient diagnosed with Unverricht-Lundborg disease	1 electrode dislocation and cable fracture - reoperation	Transitional zone between the STN and the SNr/Vim Medtronic 3387Vim no therapeutic effects	2.25 V 90 us 110–130 Hz	Sustained or partial reduction in myoclonic seizures (between 30 to 100 %) and seizure frequency. Clinical improvement for standing, walking and fine motor skills	12–42 months (median 24 months)
Anderson et al. 2016 [8]	3	2 Female 1 Male Patient 1 M/9 years Patient 2F/26 years Patient 3F/24 years	North Sea Progressive Myoclonus Epilepsy founder GOSR2 mutation (c.430>T	IPG replacement resulted with sepsis and all DBS hardware removal (patient 2) DBS hardware removal partially due to dysphasia worsening (patient 3)	cZI	Only for patient 1 available 2.1 mA 450 us 130 Hz	In all 3 patients, there was reduction in GTC seizures, 2 patients had reduction in involuntary movements,1 patient had improvement in gait and stance	NR
di Giacopo et al. 2019 [9]	1	Male/32 years	Clinical phenotype of Progressive Myoclonic Epilepsy		Transitional zone between the STN and the SNr/ Medtronic 3389 Stimulation only SNr	Monopolar 2.1 V 90 us 130 Hz	Seizure free for the first six months after implantation BTCS disappeared	24 months
The present case	1	Male/44 years	Progressive myoclonic epilepsy and ataxia due to KCNC1 mulation (MEAK)	Not observed	pSTN/SNr	Bipolar V 3.9 u 60 Hz =145Contacts 0,1,2 (-)Contact 3 (+)	BTCS disappearance, FIAS reduced by 60–70 % In the last 8 month the patient is seizure freeMarked reduction of myoclonus and intention tremor.	24 months

observed in 2 patients, and 1 patient had an improvement in gait and stance [8]. In the study by Anderson et al., two patients had their DBS hardware removed in one case due to septic infection after implantable pulse generator (IPG) replacement and in the other due to possible worsening of dysphasia [8]. STN including caudal zone incerta with its reciprocal connections with subcortical and cortical structures has been selected as a target in the treatment for intention tremor and intractable focal motor seizures [18].

The DBS for PME syndromes is very rarely utilized. The most interesting findings may be derived from these case series and case reports that stimulation of the SNr may produce the strongest positive effects on myoclonus, gait, and the disappearance of BTCS. Moreover, stimulation in the STN or caudal zona incerta may be also effective for intention tremor, myoclonic jerks, and drug-resistant epilepsy. There are obvious limitations to these observations due to the small number of treated patients with PME by DBS so far. Moreover, most observations are based on retrospective unblinded assessments. Further studies are warranted to evaluate these stereotactic targets to validate above mentioned incidental observations. In the presented patient with the diagnosis of disabling MEAK, any improvement could make a difference to the patient's level of functioning.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

None.

References

[1] Barot N, Margiotta M, Nei M, Skidmore C. Progressive myoclonic epilepsy: myoclonic epilepsy and ataxia due to KCNC1 mutation (MEAK): a case report and review of the literature. Epileptic Disord 2020 Oct 1;22(5):654–8. https://doi.org/10.1684/epd.2020.1197.

[2] Nascimento FA, Andrade DM. Myoclonus epilepsy and ataxia due to potassium channel mutation (MEAK) is caused by heterozygous KCNC1 mutations. Epileptic Disord 2016 Sep 1;18(S2):135–8. https://doi.org/10.1684/epd.2016.0859.

[3] Vesper J, Steinhoff B, Rona S, Wille C, Bilic S, Nikkhah G, et al. Chronic high-frequency deep brain stimulation of the STN/SNr for progressive myoclonic epilepsy. Epilepsia 2007 Oct;48(10):1984–9. https://doi.org/10.1111/j.1528-1167.2007.01166.x. Epub 2007 Jun 11.

[4] Wille C, Steinhoff BJ, Altenmüller DM, Staack AM, Bilic S, Nikkhah G, et al. Chronic high-frequency deep-brain stimulation in progressive myoclonic epilepsy in adulthood–report of five cases. Epilepsia 2011 Mar;52(3):489–96. https://doi.org/10.1111/j.1528-1167.2010.02884.x. Epub 2011 Jan 10.
[5] Muona M, Berkovic SF, Dibbens LM, Oliver KL, Maljevic S, Bayly MA. A recurrent de novo mutation in KCNC1 causes progressive myoclonus epilepsy. Nat Genet 2015 Jan;47(1):39–46. https://doi.org/10.1038/ng.3144. Epub 2014 Nov 17.
[6] B. Rudy, C.J. McBain Kv3 channels: voltage-gated K+ channels designed for high-frequency repetitive firing. Trends Neurosci, 24 (September 9) (2001), pp. 517-526.
[7] B.L. Sabatini, W.G. Regehr. Control of neurotransmitter release by presynaptic waveform at the granule cell to Purkinje cell synapse. J Neurosci, 17 (May 10) (1997), pp. 3425-3435.
[8] David G. Anderson, Andrea H. Németh, BSc, MBBS, DPhil (Oxon), FRCP, 3 Katherine A. Fawcett, BSc, PhD, 4 David Sims, BSc, MSc, MRes, PhD, 4 Jack Miller, BSc, PhD, 4 and Amanda Krause, MBBCh, PhD 2 , 5 Deep Brain Stimulation in Three Related Cases of North Sea Progressive Myoclonic Epilepsy from South Africa. Mov Disord Clin Pract. 2017 Mar-Apr; 4(2): 249–253.
[9] di Giacopo A, Baumann CR. Martin Kurthen 2, Francesco Capecchi 1, Oguzkan Sürücü 3, Lukas L Imbach 1 Selective deep brain stimulation in the substantia nigra reduces myoclonus in progressive myoclonic epilepsy: a novel observation and short review of the literature. Epileptic Disord 2019 Jun 1;21(3):283–8. https://doi.org/10.1684/epd.2019.1072.
[10] Benabid AL, Minotti L, Koudsie A, de Saint MA, Hirsch E. Antiepileptic effect of high-frequency stimulation of the subthalamic nucleus (corpus luysi) in a case of medically intractable epilepsy caused by focal dysplasia: a 30-month follow-up: technical case report. Neurosurgery 2002;50:1385–91. https://doi.org/10.1227/00006123-200206000-00037.
[11] Chabardès S, Kahane Ph, Minotti L, Koudsie A, Hirsch E, Benabid AL. Deep brain stimulation in epilepsy with particular reference to the subthalamic nucleus Clinical Trial Epileptic Disord 2002 Dec;4(Suppl 3):S83–93.
[12] Shon YM, Lee KJ, Kim HJ, Chung YA, Ahn KJ, Kim YI, et al. Effect of chronic deep brain stimulation of the subthalamic nucleus for frontal lobe epilepsy: subtraction SPECT analysis. Stereotact Funct Neurosurg 2005;83:84–90. https://doi.org/10.1159/000086867.
[13] Handforth A, DeSalles AA, Krahl SE. Deep brain stimulation of the subthalamic nucleus as adjunct treatment for refractory epilepsy. Epilepsia 2006;47:1239–41. https://doi.org/10.1111/j.1528-1167.2006.00563.x.
[14] Capecci M, Ricciuti RA, Ortenzi A, Paggi A, Durazzi V, Rychlicki F, et al. Chronic bilateral subthalamic stimulation after anterior callosotomy in drugresistant epilepsy: long-term clinical and functional outcome of two cases. Epilepsy Res 2012;98:135–9. https://doi.org/10.1016/j.eplepsyres.2011.08.017.
[15] P Manganotti 1, S Tamburin, G Zanette, A Fiaschi. Hyperexcitable cortical responses in progressive myoclonic epilepsy: a TMS study. Neurology. 2001 Nov 27;57(10):1793-9. doi: 10.1212/wnl.57.10.1793.
[16] Yan H, Ren L, Yu T. Deep brain stimulation of the subthalamic nucleus for epilepsy. Acta Neurologica Scandinavica 2022;146:798–804. https://doi.org/10.1111/ane.13707.
[17] Löscher W, Ebert U, Lehmann H, Rosenthal C, Nikkhah G. Seizure suppression in kindling epilepsy by grafts of fetal GABAergic neurons in rat substantia nigra. J Neurosci Res 1998 Jan 15;51(2):196–209. https://doi.org/10.1002/(SICI)1097-4547(80115)51:2<196::AID-JNR8>3.0.CO;2-8.
[18] Franzini A, Messina G, Marras C, Villani F, Cordella R, Broggi G. Deep brain stimulation of two unconventional targets in refractory non-resectable epilepsy. Stereotact Funct Neurosurg 2008;86(6):373–81. https://doi.org/10.1159/000175800.