Seizure reduction after deep brain stimulation in a patient with Parkinson disease associated with idiopathic generalized epilepsy

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We report a case of seizure reduction after deep brain stimulation (DBS) of the subthalamic nuclei (STN) in a patient with idiopathic generalized epilepsy and Parkinson disease. A 61-year-old woman had experienced her first seizure at 10 years of age. Generalized tonic-clonic seizures occurred during sleep. Her seizures occurred several times per year while she was taking 800 mg valproate. She also started experiencing bradykinesia and limb tremor at 51 years of age. She was diagnosed with Parkinson disease and received medical treatment. She was finding it difficult to walk; as a result, she was referred to the neurosurgery department for DBS surgery at 54 years of age. Presurgical evaluation revealed no epileptic discharges during long-term electroencephalography monitoring. Valproate was discontinued and STN-DBS was performed uneventfully. Bradykinesia and bilateral tremor improved markedly after DBS. When the estimated electrical current was changed from 31.9 to 12.2 microampere at 5 months after DBS, the first postoperative seizure occurred, and administration of 400 mg valproate was restarted. One year later, when the estimated electrical current was changed from 29.3 to 15.6 microampere, the second and third postoperative seizures occurred. The estimated current was changed from 15.6 to 20.5 microampere and the patient was administered 400 mg of valproate, after which she has remained seizure free for 5.5 years.

(Conclusion) Stimulation current conditions may be responsible for generalized seizure. The comorbidities of idiopathic generalized epilepsy and Parkinson disease showed improvement after STN-DBS. However appropriate stimulation conditions are required for seizure reduction.

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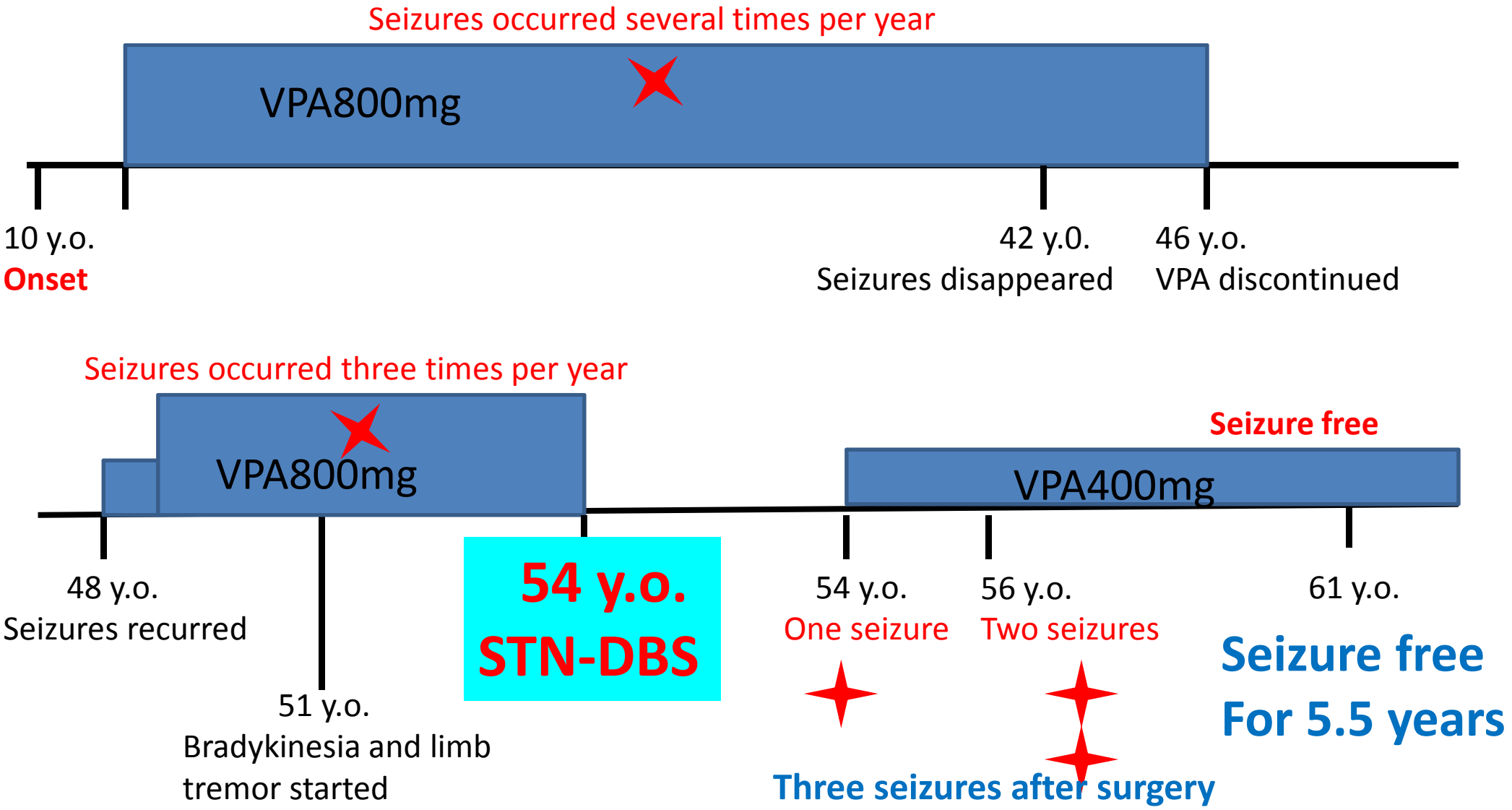
Purpose

- Deep brain stimulation(DBS) has been a possible therapy for epilepsy for more than 30 years, and now it is moving to the point of clinical utility.
- Clinically, an array of sites have been explored, including the cerebellum, anterior nucleus or centromedian nucleus of thalamus, hippocampus, subthalamic nucleus (STN) , brain stem, and corpus callosum.
Direct stimulation of the cortex has also been explored.
- Interest in evaluating these sites for treatment of epilepsy has been enhanced by the success of vagus nerve stimulation (VNS) for epilepsy and DBS for movement disorders [1].
- We report a case of seizure reduction after DBS of the STN in a patient with comorbidities of idiopathic generalized epilepsy and Parkinson's disease (PD).
- We discuss the difference as to the stimulation parameter and mechanism between PD and epilepsy patients.

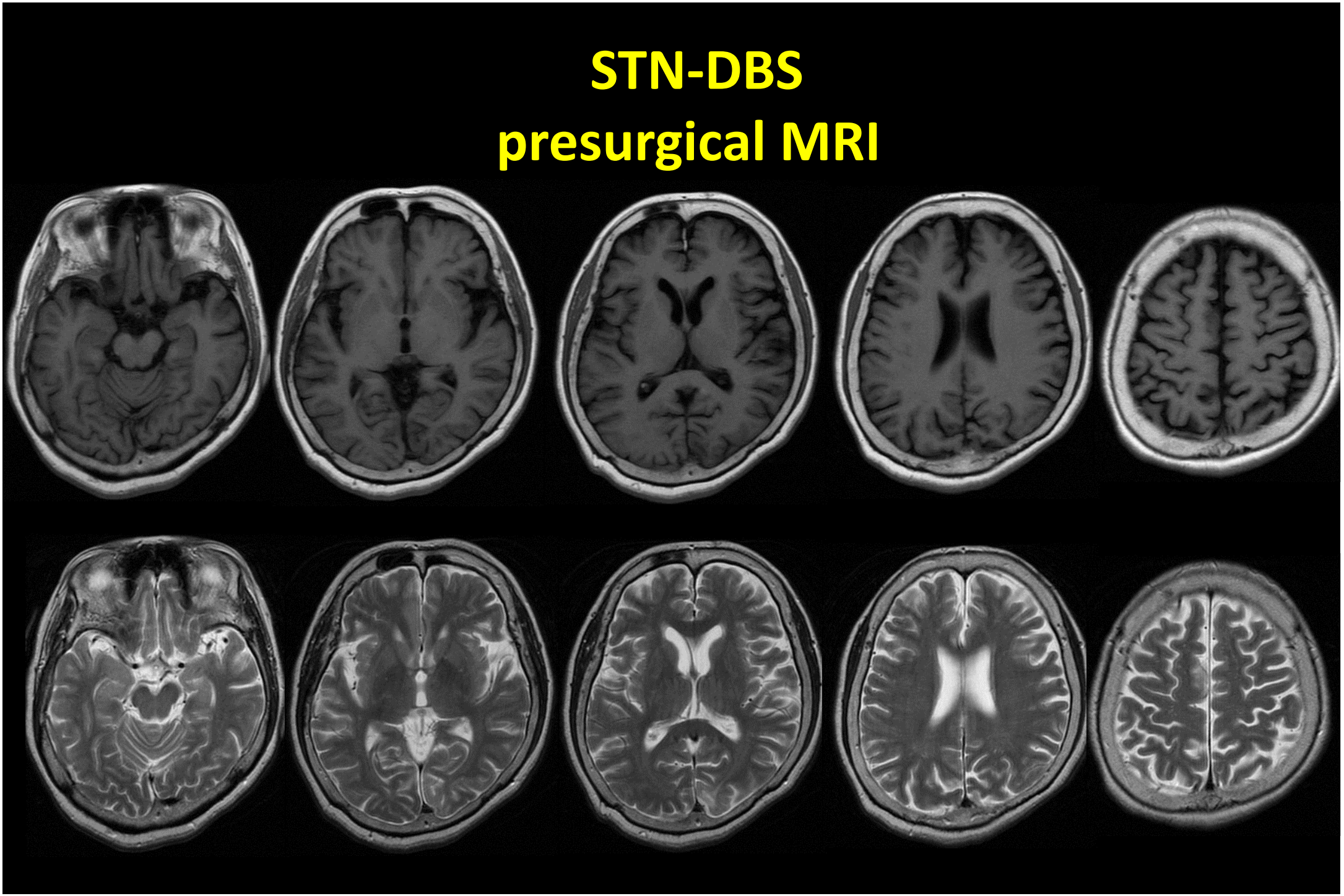
Case presentation

- A 61-year-old woman had experienced her first seizure at 10 years of age. Generalized tonic-clonic seizures occurred during sleep. Her seizures occurred several times per year while she was taking 800 mg valproate.
- She also started experiencing bradykinesia and limb tremor at 51 years of age. She was diagnosed with Parkinson disease and received medical treatment. She was finding it difficult to walk; as a result, she was referred to the neurosurgery department for DBS surgery at 54 years of age.

Clinical Course

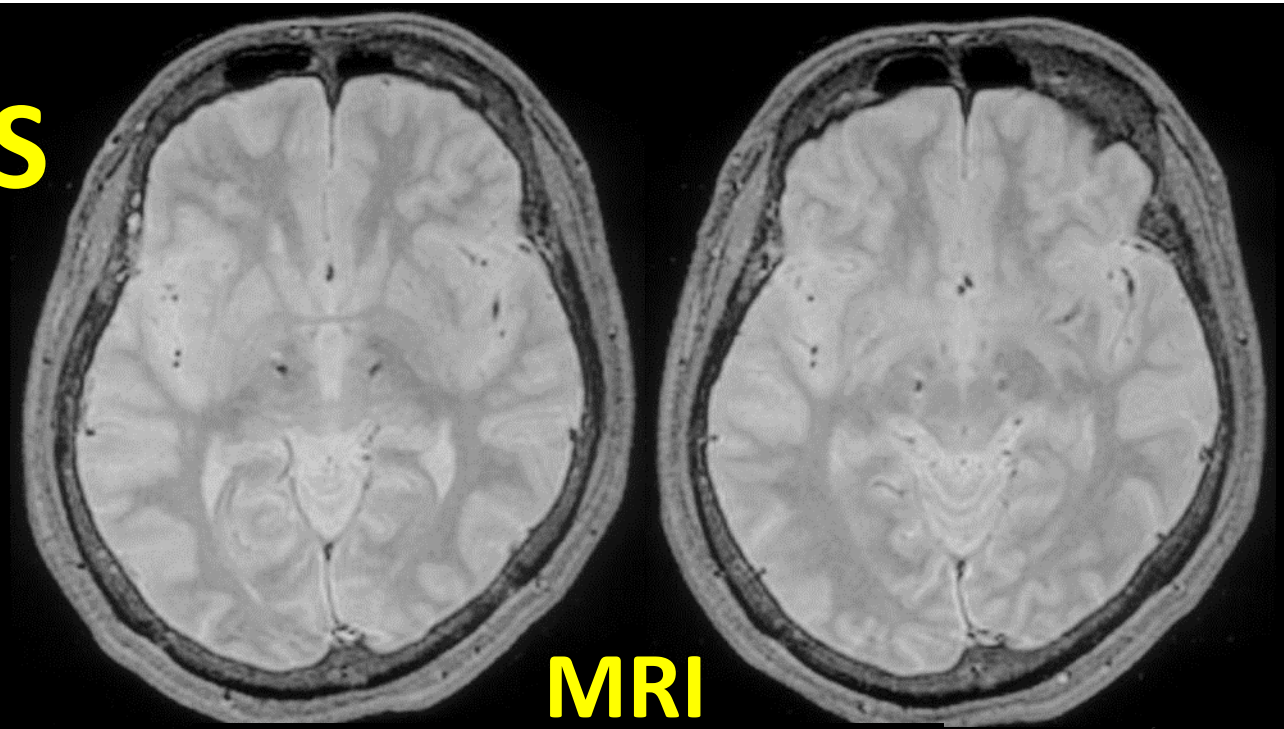


STN-DBS
presurgical MRI



STN-DBS

AC-PC plane
0 mm



AC-PC plane
-4 mm

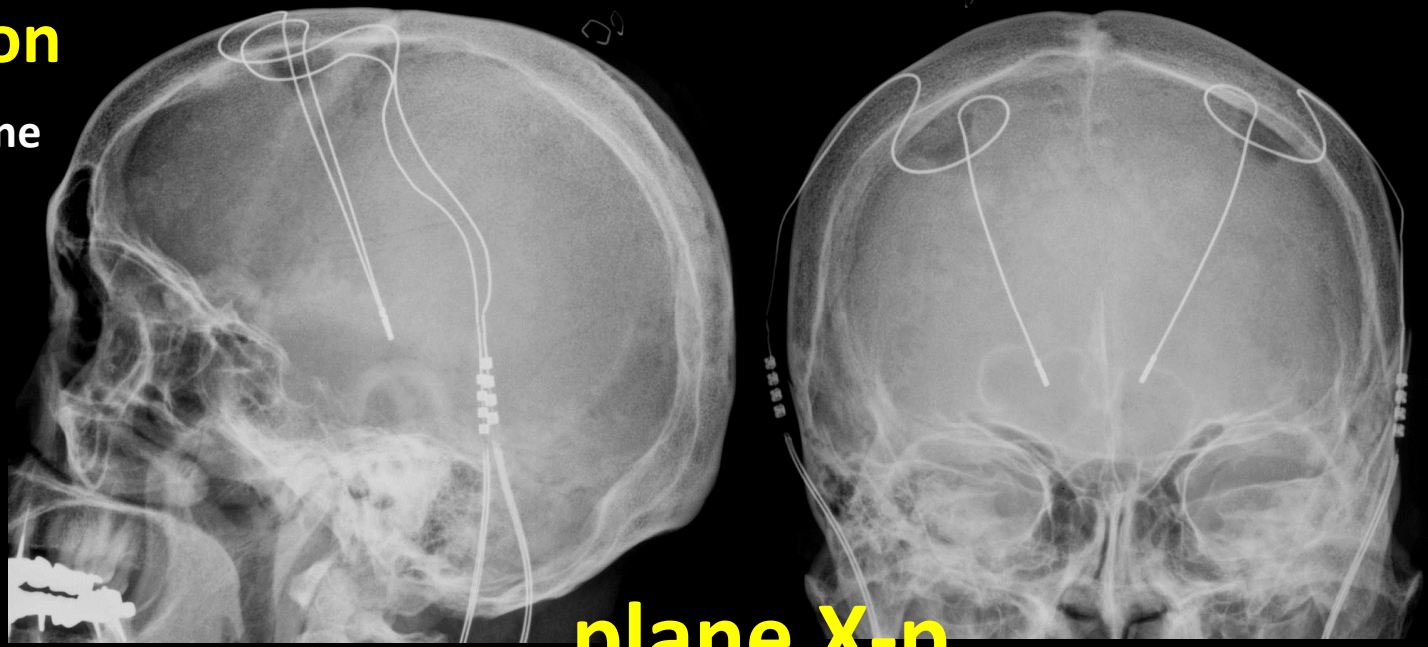
MRI

DBS electrode position

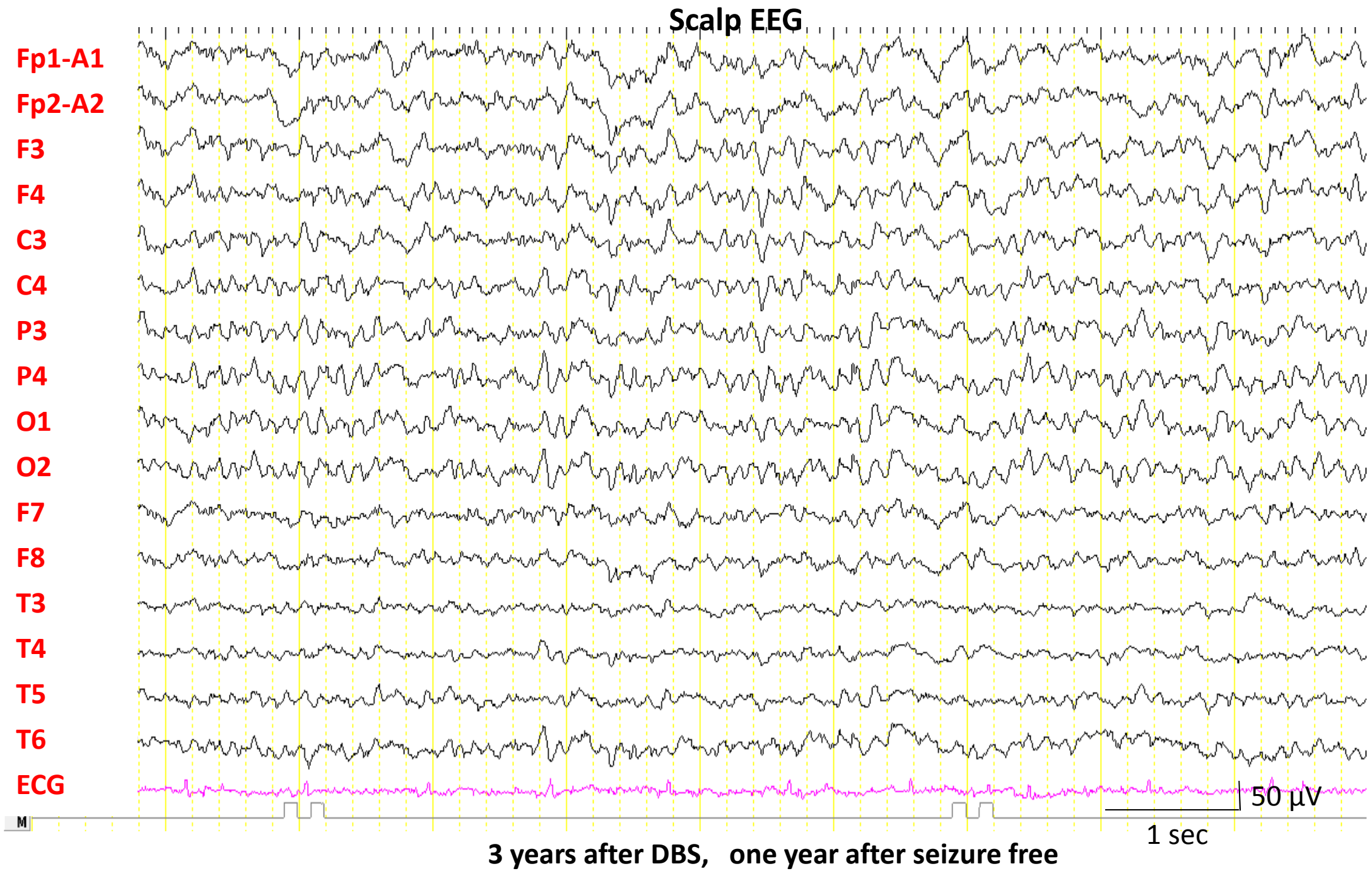
2 mm posterior at mid AC-PC line

4 mm ventral from AC-PC plane

12 mm lateral from midline



plane X-p



3 years after DBS, one year after seizure free

Parameter Review

Para meter / Date	Right			electrode	stimulation	Left			electrode	stimulation
	amplitude	pulse width	rate	negative	positive	amplitude	pulse width	rate	negative	positive
200X.7	STN-DBS									
200X.7	1.1volts	90 μ sec	145 pps	1,2	case	2.0 volts	90 μ sec	130 pps	0	2
200X.8	1.1	90	145	1,2	case	2.1	90	135	0	2
200X.12	1.3	90	145	0,1	case	0.8	90	135	0	2
200X.12	Generalized convulsion									
200X+1.2	1.1	90	145	1,2	case	2.0	90	130	0	2
200X+2.1	1.3	90	145	1,2	case	1.3	60	160	1	case
200X+2.2	Generalized convulsion									
200X+2.3	1.3	90	145	1,2	case	1.4	90	130	1	case
200X+2.9	1.3	90	145	1,2	case	1.4	90	135	1,2	case
200X+2.10	1.3	90	145	1,2	case	1.4	90	135	1,2	case
200X+4.1	1.7	90	135	1	case	1.7	90	145	1	case
200X+4.4	1.8	90	135	1	case	1.7	90	145	1	case
200X+5.12	2.0	90	145	1	case	1.7	90	135	1	case

Parameter Review

- When the estimated electrical current on the left side was changed from 31.9 to 12.2 microampere (μ A) at 5 months after DBS, the first postsurgical seizure occurred, and administration of 400 mg valproate was restarted.
- One year later, when the estimated electrical current on the left side was changed from 29.3 to 15.6 μ A, the second and third postoperative seizures occurred.
- The estimated current was changed from 15.6 to 20.5 μ A and the patient was administered 400 mg of valproate, after which she has remained seizure free for 5.5 years.

$Im=(Pi/Bi)*Pd*Fr*10^3$ Im: mean electrical current, Pi: pulse amplitude, Bi: tissue resistance, usually 800Ω, Pd: pulse width, Fr: pulse per second

DBS Parameters for refractory epilepsy

epilepsy type target (cases) author	stimulation condition amplitude (V)	 pulse width (μsec)	 pulse rate (Hz)
Partial epilepsy STN (2) Handforh A et al 2)	<3.5	60 →90	130 →185
SANTE study AN of thalamus (110) Fisher R et al 3)	5～7	90	145～185
Prog. myoclonic epilepsy SNr/STN (5) Wille C et al 4)	2.25 (1.0～4.0)	90 (60～120)	130 (100～160)

SNr/STN: substantia nigra pars reticulata/subthalamic nucleus

Discussions

- Little is known about mechanism of DBS and optimal stimulation parameters.
- Network effects rely significantly on stimulation parameters and may ultimately result in either excitation or inhibition at sites remote from the local region of stimulation 1).
- No statistically significant difference in the resting STN neuronal discharge rates and in regularity in the discharge pattern between PD and epilepsy patients 5).
- Stimulation parameters for DBS in epilepsy may be same as the condition for DBS in PD patients.
- STN proper may not respond to each pathognomonic change, that is, PD and epilepsy, but have neurophysiologically optimal stimulation parameters and respond the proper parameters.
- DBS in PD usually uses continuous stimulation and DBS in epilepsy uses intermittent one, for example, VNS and SANTE study.

Conclusions

- Stimulation current conditions may be responsible for generalized seizure. The comorbidities of idiopathic generalized epilepsy and Parkinson disease showed improvement after STN-DBS.
- DBS is palliative rather than curative, but this case suggests that DBS-STN for epilepsy may be of benefit to some people with refractory epilepsy.
- From the viewpoint of jamming effect and result of the presented case, continuous stimulation may be better than intermittent one for DBS in epilepsy.
- Establishment of appropriate stimulation parameters are required for seizure reduction.

References
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