What should be the anatomical target in deep brain stimulation in an essential tremor plus rest tremor case? Technical case report of deep brain stimulation

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ABSTRACT

While Deep Brain Stimulation (DBS) of Subthalamic Nucleus (STN) is effective on resting tremors, but its effectiveness on postural and kinetic tremors is limited. DBS of the Ventral Intermediate Nucleus (VIM) is effective on many types of tremors, especially postural and kinetic tremors, but its effect is weak on motor symptoms in Parkinson's disease (PD). Although there is a consensus in the literature about where the anatomical target should be in essential tremor (ET) and PD, there are only case reports about where the anatomical target should be in Essential Tremor Plus Rest Tremor (ET+RT) cases. In this article, we aimed to reveal the effectiveness of STN DBS in a case-diagnosed with ET+RT. The patient had action tremors in both upper extremities for 21 years and developed rest tremors in both upper and lower extremities for the last six years. Rest tremor was effectively controlled with bilateral STN DBS. Postural tremor in the right upper extremity was continued, although it decreased.STN may be an appropriate choice when choosing an anatomical target in DBS in cases of resting, postural, and kinetic tremor.

Keywords: Essential tremor plus rest tremor, deep brain stimulation, subthalamic nucleus

Tremor is defined as rhythmic, involuntary movements seen in body parts. We can categorize tremors under two headings: physiological and pathological tremors. While physiological tremor occurs with excitement and anxiety, pathological tremors can almost always be seen [1].

Essential tremor (ET) is defined as action tremor in the upper extremities that has persisted for at least 3 years. It is one of the most common types of tremors. While the incidence rate in all age groups is 0.4-0.9%, the incidence rate in individuals over 65 years of age is between 4.6-6.3%. ET is considered to be a risk factor for the development of Parkinson's disease (PD) in the future. In some studies, this risk increases up to 4 times [2]. In our country, its prevalence in the group aged 18-60 was calculated at 226,454 per hundred thousand [3]. The International Parkinson and Movement Disorder Society published a new 2-axis

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classification of tremors in 2018. According to this classification, tremor was divided into two isolated tremor syndrome and combined tremor syndrome according to their clinical features in Axis-1.

ET was included in isolated tremor syndromes. In Axis 2, classification was made according to etiology. When resting tremor, dystonic posture, cognitive impairment, or tandem walking difficulty are added to ET, the term ET-plus is used [4]. ET may change over the years and turn into ET-plus. The most common group among ET-plus cases is Essential Tremor Plus Rest Tremor (ET+RT) [5].

While Deep Brain Stimulation (DBS) of Subthalamic Nucleus (STN) is effective on resting tremor its effectiveness on postural and kinetic tremor is limited. DBS of the Ventral Intermediate Nucleus (VIM) is effective on many types of tremors, especially postural and kinetic tremors, but its effect is weak on motor symptoms in PD [6]. Although there is a consensus in the literature about where the anatomical target should be in DBS in ET and PD there are only case-based studies where the anatomical target should be in DBS in ET+RT cases or in cases where ET and Parkinsonism findings overlap [7-12]. STN may be an appropriate choice when choosing an anatomical target in DBS in cases of resting, postural, and kinetic tremor.

CASE REPORT

40-year-old male patient complaints started with slim tremors in both hands at the age of 19. During this period, his complaints were mild; he was able to carry out his daily activities without any problems despite the tremors. He enlisted in the military at the age of 20 and was able to use a gun. His complaints increased over the years that tremors appeared in his head and feet as well as in his hands and that he could not do his daily activities in recent years. He used drugs such as propranolol, primidone, gabapentin, L-dopa, and dopamine agonists in his medical history and did not benefit from them. He could not use the drug at the recommended doses due to the development of involuntary movements approximately 1-2 years after starting levodopa+benserazide. He partially benefited from trihexyphenidyl 8 mg/day among the medications given. Routine blood tests were unremarkable. No pathology was detected in Magnetic Resonance Imaging (MRI). There was no family history of tremor. He had never drunk alcohol in his life, so his response to alcohol was unknown. In his neurological examination, resting, postural and action tremors were observed in both upper extremities. Due to severe tremors, bradykinesia could not be evaluated properly in the finger-tapping test. Upper extremity tremor was accompanied by lower extremity and head tremor. Tremor continued intensely during the walk. There was +2 rigidity in the right upper extremity. L-dopa response was examined, but the response could not be evaluated clearly due to the development of severe dyskinesia after L-dopa. ET+RT was considered in the foreground because the patient's complaints had been present for 21 years, The tremor initially started as a bilateral slim tremor and got worse over the years, and while it was only an action tremor at first, rest tremor was also added over the years.

We applied STN DBS to the patient to suppress resting, postural, and kinetic tremors and to control Parkinsonism findings that are likely to become evident in the future. The most effective response was

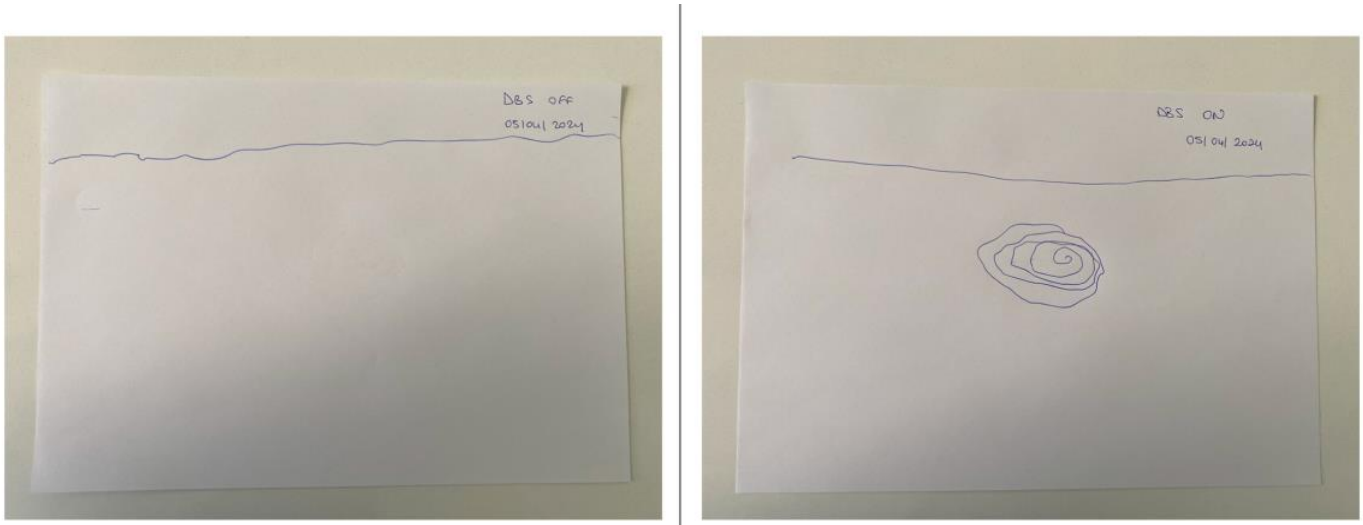

Figure-1. After DBS a significant improvement was observed in the straight line drawing test and spiral drawing test.

obtained at Contact 3. Right STN: amp:5.45 mA, pulse width 60 seconds, frequency 120 Hz. Left STN: amp:6.00 mA, pulse width 60 seconds, frequency 120 Hz. After effective stimulation, we were able to completely control resting tremors in both the upper and lower extremities. İn the right upper extremity, postural and kinetic tremor marked reduced but continued. After DBS, a significant improvement was observed in the straight line drawing test and spiral drawing test (Figure 1). According to the Fahn-Tolosa-Marin tremor rating scale, the score he received after stimulation decreased from 60 to 15.

DISCUSSION

High-flow nasal cannula (HFNC) oxygen therapRetrospective studies have shown that ET-plus cases constitute 53-84% of ET cases and are more common than ET [13-14]. The most common group among ET-plus cases is ET+RT (5). ET+RT has a heterogeneous structure. There are different opinions about how it emerged. First rest tremor may be a late feature in cases of ET that persists for many years. Secondly, ET+RT may represent a separate disease from ET that develops with different pathophysiological mechanisms. Third, the development of rest tremor in ET may define superimposed PD. Fourth, these cases may have been misdiagnosed as ET and have a different disease, such as dystonic tremor [15]. Considering the change in tremor over the past 21 years of disease we thought that our case was ET+RT.

When the literature was examined, it was seen that different points were targeted in DBS in cases where rest tremor and severe kinetic tremor coexisted. These are:

1. Ventral-intermediate nucleus (VIM) [7]
2. Subthalamic nucleus (STN) [8]
3. STN and VIM with two separate electrodes [9]
4. STN and VIM with a single electrode [10,11]
5. STN and Zona incerta (ZI) with a single electrode [12]

In a retrospective study of 44 patients who underwent VIM DBS, no change was observed in Fahn-Tolosa-Marin Tremor scores between ET and ET-plus cases, and VIM DBS was shown to be as effective as ET in ET-plus cases. It was observed that in ET-plus cases, higher stimulation parameters were needed, and the active electrodes were located more dorsally. This study showed that VIM DBS can be used safely to control tremors in ET-plus cases [7]. Symptom control was achieved with left VIM DBS and right STN DBS in the patient who had ET for 30 years and PD for the last 10 years with resting, postural, and kinetic tremors. In this case, motor symptoms of Parkinson's disease were controlled with STN DBS. ET was able to be controlled due to the effect of STN DBS on the cerebellothalamic pathway [8]. In a 79-year-old treatment-resistant tremor-dominant Parkinson's case there was no adequate response with bilateral VIM-DBS. Dual stimulation was later applied by additionally applying STN-DBS to the left side, and tremor control was achieved by simultaneous stimulation of STN and VIM. In this case, simultaneous stimulation of two separate targets and stimulation of the posterior subthalamic area, where ZI is located, by both electrodes were thought to be effective in tremor control [9].

In some studies, two separate electrodes were used to target the STN and VIM, but due to the risk of bleeding, infection, and increase in cost, stimulation of two points with a single electrode was later brought to the agenda. Targeting VIM and STN with a single electrode was found effective and reliable in controlling the symptoms of a tremor-dominant Parkinsonian patient resistant to L-dopa [10]. VIM and STN were targeted with a single electrode in a tremor-dominant case who was followed up with the diagnosis of PD for eight years. Initially, postural tremor was controlled by stimulating VIM, and it was planned to stimulate the STN to control Parkinson's motor symptoms, which are likely to become more pronounced in the future [11]. In the case of a patient who had ET for many years and PD for the last seven years, symptom control was achieved by stimulating STN and ZI with a single electrode. In the first application using 'Monopolar Directional Montage, ' akinesia, rigidity, and rest tremor were taken under control, but kinetic tremor could not be effectively suppressed. Using "Bipolar Directional Montage," STN and the adjacent ZI were activated simultaneously, and thus, kinetic tremor could be controlled [12].

In our case, we were able to control the rest of the tremors in the left upper extremity and both lower extremities after the bilateral STN DBS application. Although we were able to almost completely control

the rest tremor in the right upper extremity, postural tremor and kinetic tremor continued, albeit partially. In this case, STN+VIM could be targeted with a single electrode on the left side to control the right upper extremity rest and postural tremor. By using the "Bipolar Directional Montage" on the left STN, the adjacent ZI can be activated simultaneously. Or after bilateral STN DBS, left VIM DBS could be applied. However, these were not applied because the patient's clinical condition was good, and he was able to perform all daily life activities comfortably.

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Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contribution

Study Conception: NBP, DY; Study Design: NBP, DY; Literature Review: NBP, DY; Critical Review: NBP, DY; Data Collection and/or Processing: NBP, DY; Analysis and/or Data Interpretation: NBP, DY; Manuscript preparing: NBP, DY.

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