Movement Disorders
CLINICAL PRACTICE

LETTER: NEUROMODULATION

Rhythmic Eyelid Closure Responsive to STN-DBS: Blepharoclonus, Blepharospasm, Eyelid Opening Apraxia, or Eyelid Tremor?

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Deep brain stimulation (DBS) targeting the subthalamic nucleus (STN) is an effective treatment for the motor complications of Parkinson's disease (PD).[1] People with PD can present with eyelid movement disorders, of which blepharospasm and eyelid opening apraxia (EOA) are well characterized,[2] whereas other eyelid abnormalities—including blepharoclonus and eyelid tremor—have been poorly defined.[3] Here we describe a 58-year-old man with a 10-year history of tremor-dominant PD characterized by involuntary eyelid movements responsive to STN-DBS (Fig. 1A) and provide a brief overview of the differential diagnosis of such phenomenology.

Frequent bilateral rhythmical eyelid movements and bilateral upper-limb resting and postural tremor were noted during the first programming visit in the med-*off* condition. The eyelid movements had been present before surgery and were poorly responsive to levodopa. Notably, after a prolonged forceful eyelid closure, there was no sustained contraction of the orbicularis oculi (OO) or hyperactivation of the frontalis muscle.

To better characterize this phenomenology, electromyography was recorded with surface electrodes over the left biceps, triceps, bilateral extensor carpi radialis, flexor carpi ulnaris, and OO muscles. Arm tremor was also recorded with an accelerometer on the left hand, with arms in resting and outstretched position (Fig. 1B,C). The patient was evaluated in med-*off* condition, DBS-OFF, DBS-left ON, DBS-right ON, and DBS-ON bilaterally (Table S1).

In the DBS-OFF condition, there was a rhythmical bilateral eyelid movement, presenting in bursts with an average frequency of 4.3 Hz (coherence of 0.87 between both eyelids) and a bilateral resting tremor of the left and right arms with an average frequency of 5.5 and 4.5 Hz, respectively (Video 1; Fig. 1C).

There was no coherence in frequency between tremor in both arms nor between arms at rest and OO activity. In the outstretched position, there was a low coherence between OO activity and the ipsilateral arm as well as between OO activity and the contralateral arm (Table S1). These findings were suggestive of different oscillation generators for each arm, a well-known feature of parkinsonian tremor,[4] and different oscillators between the arms and the eyes. Voluntary bilateral rhythmic hand movement elicited no entrainment of eyelid contractions.

With left-DBS ON, there was a reduction in the right-side tremor both postural and at rest. The duration of OO contraction bursts decreased with arms in resting position but not with arms outstretched.

With right-DBS ON, there was nearly complete suppression of the left-arm resting tremor and a significant reduction in the duration of eyelid contraction bursts. With both arms outstretched, a moderate decrease in left-arm postural tremor was observed, accompanied by a slight increase in the duration of the eyelid contraction burst.

With bilateral DBS-ON, there was significant reduction in arm tremor and no more eyelid movements (Video 1). Notably, response of eyelid tremor to bilateral stimulation was superior to unilateral stimulation, aligning with observations for other midline tremors in PD.[5] The lack of coherence between hand and eyelid tremor as well as the rapid effect of DBS even when blindly turned ON or OFF ruled out a possible functional etiology of these tremors.

Apart from tremor, other movement disorders can involve the eyelid. Blepharospasm is caused by hyperactivity of the OO muscles and may initially present with an increased blinking rate that evolves over time into more sustained eyelid closure.[6]

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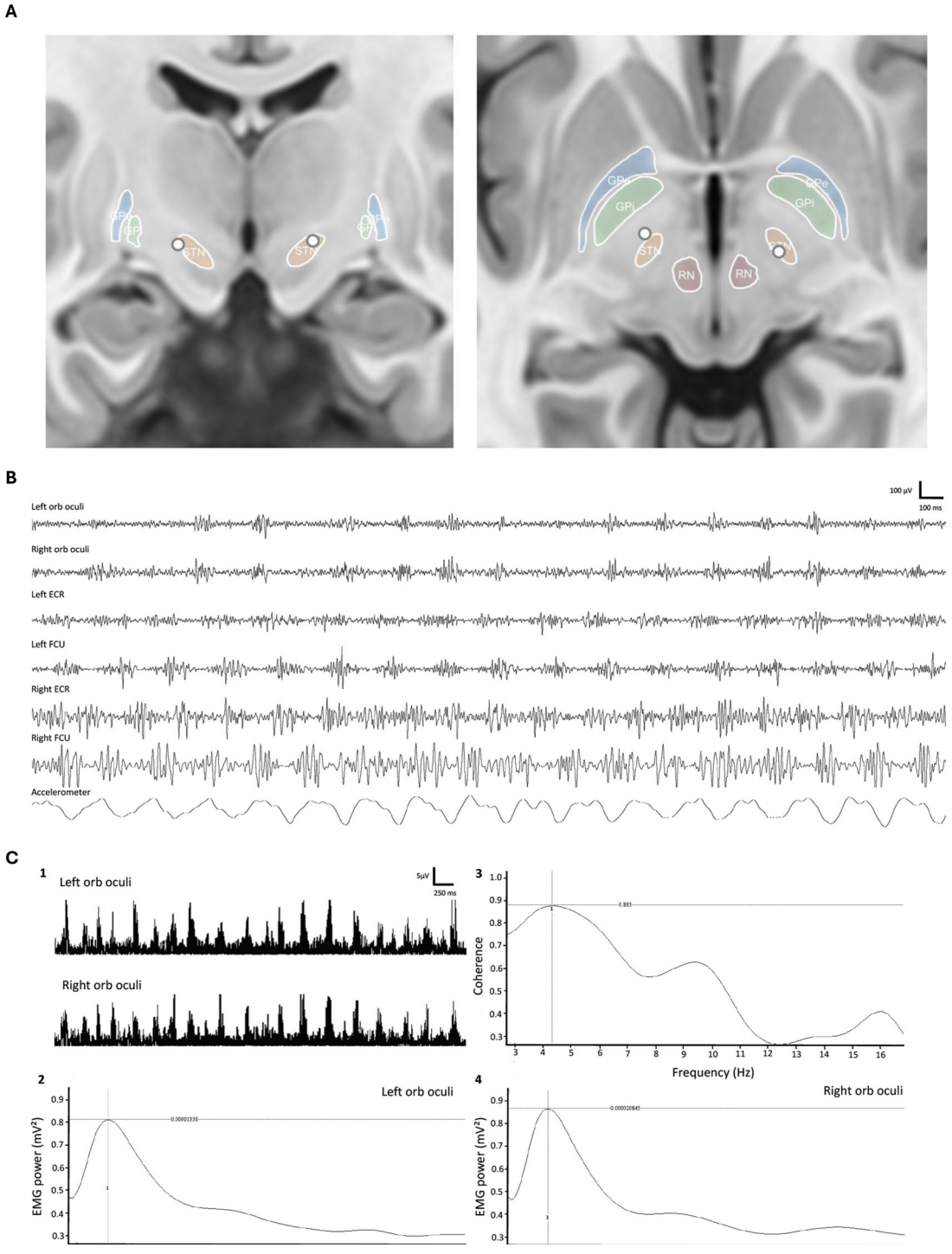
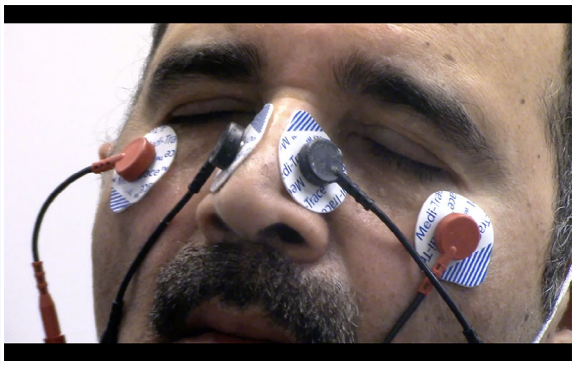


FIG. 1. (**A**) Two-dimensional reconstruction of the electrodes, using Lead DBS version 3.0. The leads are located in the subthalamic nucleus (orange). Other depicted structures are the nucleus ruber (red), the globus pallidus internus (green), and the globus pallidus externus (blue). (**B**) Multichannel surface EMG (top row) and accelerometer (bottom row) recordings during the DBS (deep brain stimulation)–OFF condition. Resting tremor for the upper limbs recorded with both arms at rest shown as rhythmic, alternating EMG bursts with a mean frequency of 4.5 Hz (right wrist flexor and extensor muscles) and 5.5 Hz (left wrist flexor and extensor muscles). A 4.3-Hz rhythmic contraction of both OO muscles is also noted. (**C**) 1: Rectified multichannel surface EMG recordings; 2: power spectrum analysis of the left tremor, with a peak frequency at 4.1 Hz; 3: coherence analysis between right and left OO tremor with a coherence of 0.87 at 4.3 Hz; 4: power spectrum analysis of the right OO tremor, with a peak frequency at 4.1 Hz (all recordings during the DBS-OFF condition). ECR, extensor carpi radialis; EMG, electromyography; FCU, flexor carpi ulnaris; OO, orbicularis oculi.



Video 1. In the DBS-OFF condition (segment 1) a bilateral involuntary rhythmic closure of the eyelids as well as rest and postural tremor of the arms is observed. The mild head tremor is presumably passive transmission of the arm tremor to the trunk and neck. During bilateral DBS-ON condition (segment 2) a significant reduction in eyelid movement and arm tremor is observed.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.70030

EOA, defined as the patient's inability to voluntarily initiate the opening of the eyelids without a visible contraction of the OO, rarely occurs in PD, typically during the later stages of the disease or after STN-DBS.[7] Blepharoclonus was defined by Obeso et al. as an "inappropriate, brief, repetitive and clonic contraction of the orbicularis oculi," usually preceding or associated to blepharospasm.[8] Subsequently, the term "blepharoclonus" has been used to describe a clonic OO activation elicited during voluntary gentle eye closure,[9] an observation relatively common in PD.[3]

Based on the rhythmic and oscillating nature of the eyelid movements (Fig. 1B,C) and the presence of a single peak in the frequency spectral analysis, we argue that the eyelid involuntary movement in our patient is consistent with tremor. Although a grade I blepharospasm may manifest only with an increased blink rate, the frequencies described in such a condition (blinking ranges 17–131 per min) are lower than those recorded in our patient.[10] Our patient had no difficulty in initiating the opening of the eyes, thus ruling out EOA.

Finally, the involuntary eyelid movement of our patient was not provoked by the attempt to close his eyelids but occurred during normal visual fixation. Therefore, we believe that blepharoclonus can be ruled out as well.

Eyelid tremor is a rare, and probably underrecognized, type of parkinsonian tremor. A proper clinical examination and a neurophysiological assessment can be helpful in distinguishing it from its main mimics. Further studies are needed to better understand the prevalence, pathophysiology, and treatment response of this condition.

Author Roles

All authors had full access to all the data and accept responsibility to submit for publication. 1. Research project: A. Conception, B. Organization, C. Execution; 2. Statistical analysis: A. Design, B. Execution, C. Review and critique; 3. Manuscript preparation: A. Writing of the first draft, B. Review and critique.

G.G.: 1B, 1C, 3A
A.B.: 1B, 1C, 3A
T.G.: 1C, 3A
R.Ci.: 1B, 3B
R.E.: 1B, 3B
R.Ch.: 1B, 3B
A.F.: 1A, 3B

Disclosures

Ethical Compliance Statement: RBD number: 24-5180—Clinical progression of patients with movement disorders. Informed consent was obtained from the subject described in this letter. We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Supporting Information

Supporting information may be found in the online version of this article.

Table S1. Electrophysiological findings depending on arm position and STN-DBS condition.