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Directional stimulation improves stimulation-induced dysgeusia in DBS for essential tremor

1. Introduction

Deep brain stimulation (DBS) targeting the dentatorubrothalamic (DRT) tract is an effective treatment for medication-refractive tremor [1,2]. An altered perception of taste is a disabling and underreported side effect and is assumed to relate to the unintended stimulation of the gustatory pathway [3,4]. In some cases, DBS-induced dysgeusia can be reduced by conventional DBS programming techniques, whereas in others on demand or permanent stimulation discontinuation or surgical repositioning of the electrode(s) is required [3–5]. We present a case demonstrating that stimulation-induced dysgeusia in DRT-DBS can be improved by employing directional DBS.

2. Case description

We report a 71-year-old female with essential tremor (ET) since the age of 65. The tremor involved both hands, severely impaired manual actions and was refractory to medical therapy (*e.g.* propranolol, primidone, and gabapentin). At the age of 70 she underwent bilateral DRT-DBS surgery (Boston Scientific® Vercise™ PC implantable pulse generator with Boston Scientific® Vercise™ Cartesia directional leads). Surgery was DRT tractography-based and performed under general anesthesia.[3] Surgical planning was performed using Brainlab Elements software (Brainlab, Munich, Germany). With postoperative DBS-programming employing omnidirectional stimulation via ventromedial contacts bilaterally (*i.e.* right electrode: C+, (2-3-4)-, 60 μs, 130 Hz, 3.5 mA; left electrode: C+, (2-3-4)-, 60 μs, 130 Hz, 4.5 mA) almost complete tremor suppression was obtained except for a residual mild kinetic tremor of the right hand (*i.e.* TETRAS kinetic arm tremor subscore (right/left): preoperative 3/3, postoperative 2/0). However, since the start of DBS-programming the patient complained of a bitter and sour taste in her mouth, masking the normal taste of food and drinks, leading to decreased oral intake and emotional stress. During outpatient evaluation the left electrode seemed to be responsible. Adapting/lowering the amplitude, pulse width (till 30 μs) or frequency (till 89 Hz) led to tremor exacerbation without dysgeusia improvement. Increasing stimulation frequency (till 179 Hz) or switching to the most ventral contact on the left electrode did not improve dysgeusia. At-home intermittent stimulation discontinuation was not tolerated due to severe tremor exacerbation. Taste did not improve after 30 minutes of inpatient sequential unilaterally switching off the stimulation, however, taste did improve 1 h after bilateral discontinuation (*i.e.* with DBS ON dysgeusia severity was 10 measured on a visual-analogue scale, compared to 2 with DBS OFF). During directional monopolar review, she reported a foul taste and/or electricity and/or pain in the mouth at high amplitudes (from 3.5 mA onwards) at left electrode contacts 3, 5 and 6 exclusively. Hence the left electrode was proposed to be responsible for the dysgeusia. However, only upon bilateral directional stimulation via left electrode contact 4 (*i.e.* ventromedial contact with anterior-medial direction) at 4.0 mA and right electrode contact 5 (*i.e.* dorsomedial contact with anterior direction) at 3.5 mA there was marked improvement of dysgeusia with sufficient tremor suppression. The patient still experienced a mild bitter taste, however not interfering with her oral intake and she no longer experiences emotional stress. In the postoperative phase we used Brainlab Elements software to generate a volume of tissue activated by using anterior directional segments. We expected this to also shift the current away from the more posterior sensory thalamus. In order to visualize both motor and sensory thalamus, we applied probabilistic 7 T MRI segmentation of the thalamus [6]. This evaluation confirmed the initial omnidirectional tissue activation to partially overlap with sensory/gustatory thalamus and the directional tissue activation to be mainly situated in motor thalamus (Fig. 1).

3. Discussion

This case report demonstrates that directional stimulation can be used to improve stimulation-induced dysgeusia and maintaining tremor control in DRT-DBS for ET.

Dysgeusia has been reported in 11 DRT-DBS patients, whereas the prevalence is estimated to be 15% [3–5,7]. Dysgeusia has been described as a foul, metallic, sour, cool and/or tingling taste, with normal sense of smell and absence of oral paresthesias [4,5,7]. Dysgeusia is mild in most cases, but can significantly interfere with eating and drinking [4]. Dysgeusia generally resolves quickly upon stimulation discontinuation whereas it may take up to several hours in some cases [4,7]. Risk of dysgeusia is higher with bilateral electrodes, however in most cases a relation to stimulation through one of the electrodes can be discerned [3–5]. Such dysgeusia-inducing electrodes are generally located more posterior, often in close proximity to or even within the sensory nucleus of the thalamus and/or medial lemniscus [3–5]. These structures contain components of the gustatory pathway, *i.e.* parvicellular portion of the ventral posteromedial nucleus and solitariothalamic tract respectively [4,7,8]. In some instances dysgeusia is resolved by reprogramming (*e.g.* alternative contact) of the respective electrode [5]. In some cases dysgeusia is refractory necessitating stimulation discontinuation, dysgeusia acceptance and sometimes even

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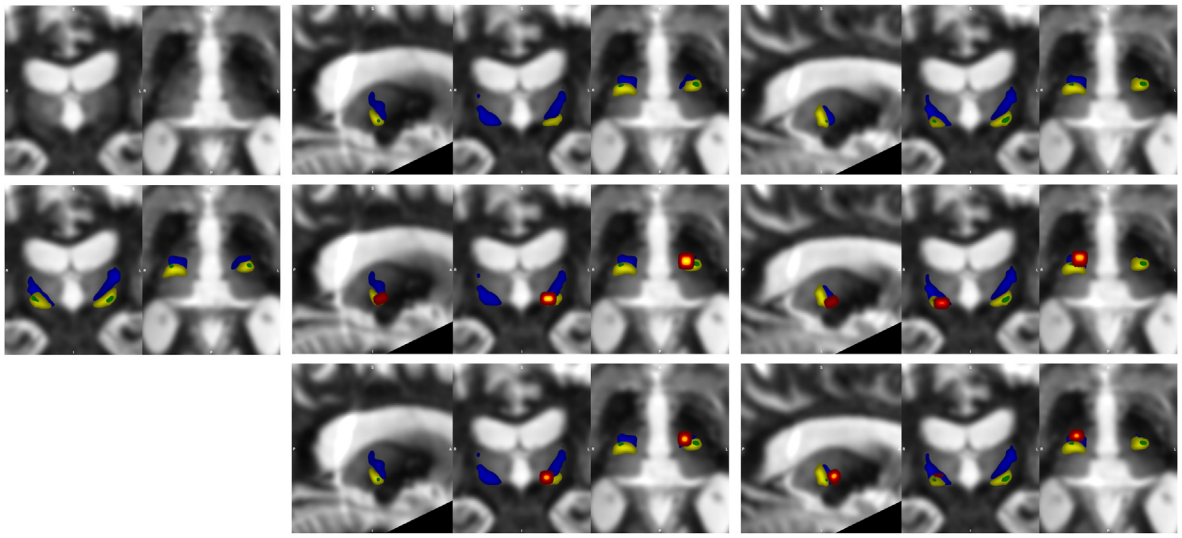

Fig. 1. Relation of omnidirectional and directional stimulation with connectivity-derived thalamic segmentation. The panels show 7T connectivity-derived thalamic segments of the patient, aligned to the commissural line. The blue segment represents the part of the thalamus with mainly motor projections (containing the DRT, to primary motor cortex), the yellow segment represents the part of the thalamus with mainly sensory projections (to primary sensory cortex) and green the part of the thalamus with mainly gustatory projections (to insular cortex and frontal operculum). The left column of panels show the three segments in coronal and axial orientation. The middle column of panels show the location of left omnidirectional (middle row) and directional (lower row) stimulation in sagittal, coronal and axial orientation. The right column of panels show the location of the right omnidirectional (middle row) and directional (lower row) stimulation. By using directional settings the location of stimulation has moved away from sensory/gustatory thalamus and is situated mainly in motor thalamus. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

successful surgical anterior repositioning of the electrode [3,4]. Our case demonstrates directional DBS to be a less invasive solution for refractory cases without loss of therapeutic tremor control or surgical risks.

Of interest, persistent and severe dysgeusia has also been reported in magnetic resonance guided focused ultrasound (MRgFUS) thalamotomy [8,9]. Evidently, in these instances dysgeusia cannot be improved as it concerns lesional surgery. In one case however, dysgeusia was resolved with repeat MRgFUS which was however accompanied by severe neurological deficits [8].

Directional DBS is increasingly employed in DRT-DBS for tremor, both for the management of side effects (*i.e.* muscle contractions, paresthesia, dysarthria, and ataxia) as well as to improve tremor control [10,11]. Our case adds dysgeusia to the indications for directional stimulation in DRT-DBS for tremor. If not for directional stimulation, a surgical electrode revision would have been required to overcome the troublesome dysgeusia. As the gustatory pathway is not visualizable with deterministic tractography used in DBS software for presurgical planning, it cannot be readily avoided [8]. Therefore, in certain instances use of electrodes with segmented contacts when targeting DRT seems advantageous.

4. Conclusion

Dysgeusia is a rare but potentially severe/bothersome stimulation-induced side effect of DRT-DBS probably mediated by unintentional stimulation of the gustatory pathway either at the level of the thalamus or the solitariothalamic tract. Directional steering of stimulation away from the gustatory pathway can overcome this side effect without loss of therapeutic tremor control or surgical risks.

Informed consent

Written informed consent has been obtained from the patient.

Declaration of competing interest

RdB received a research grant from Medtronic paid to the institution. RS is independent consultant for Boston Scientific and Medtronic. The other authors declare that there are no disclosures to report.

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