Journal of Clinical Neuroscience 50 (2018) 242–246

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

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

Technical note

Dysgeusia in deep brain stimulation for essential tremor

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ARTICLE INFO

Article history:
Received 7 November 2017
Accepted 5 January 2018

Keywords:
Taste perception
Deep brain stimulation
Lateral thalamic nuclei
Adverse effects
Essential tremor

ABSTRACT

Dysgeusia, or foul taste, is a rarely reported side effect in patients who have undergone deep brain stimulation (DBS) in the thalamus for essential tremor. This retrospective study evaluated the incidence, nature, neurophysiological and anatomical location of dysgeusia following DBS. Of 52 patients who had undergone DBS for essential tremor, eight (15%) reported dysgeusia, which was described as a "metallic," "sour," "foul," or "cold" taste in the mouth. Dysgeusia was separate and distinguishable from paresthesia. Dysgeusia was more frequently reported with bilateral than unilateral DBS implants (6 of 27 (22%) vs. 2 of 25 (8%) patients, respectively). The anatomical locations of the contacts causing dysgeusia were measured on postoperative MRI, and compared to those from seven control patients who did not experience dysgeusia after receiving bilateral DBS implants. Leads causing dysgeusia were more posterior than non-dysgeusia-associated leads (4.5 ± 1.2 vs. 5.7 ± 1.8 mm anterior to the posterior commissure, respectively, $P < .001$). Intraoperative microelectrode recording indicated that these contacts were in the sensory region of the thalamus. Intraoperative testing found that low sensory threshold for paresthesia predicted the development of dysgeusia postoperatively (1.5 ± 0.5 V vs. 3.3 ± 1.9 V; $P < .05$). These data indicate that taste perception can be altered in the human through DBS, with posterior leads likely within the sensory region of the thalamus. Dysgeusia can be reduced by changing stimulation parameters, or surgical revision of the lead.

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1. Introduction

A patient presenting with severe dysgeusia, in addition to severe paresthesia side effects, was referred to the deep brain stimulation (DBS) program at Sacred Heart Medical Center. Surgical repositioning of the lead resolved dysgeusia as well as paresthesia. This finding led to a careful review of clinic records for reports of dysgeusia among a cohort of patients who received DBS for essential tremor. The following analysis of dysgeusia suggests that DBS lead placement slightly posterior to the standard surgical target may have unmasked inadvertent activation of taste perception within the thalamus.

DBS is highly effective for controlling disabling tremor in patients with essential tremor [1]. The surgical target for implantation of the DBS electrode is in the ventrolateral nucleus of the thalamus, also referred to as the ventrointermedius nucleus (Vim) in the surgical atlas of Schaltenbrand [2]. The optimum surgical target is just anterior to the primary sensory nucleus in the thalamus, the ventroposterolateral (VPL) and ventroposteriormedial (VPM) nuclei, also referred to as the ventrocaudal nucleus (Vc) in the atlas of Schaltenbrand.

DBS often has side effects, even in optimally placed leads. Paresthesia, described as a non-painful tingling, is a common stimulation-induced side effect, and is likely caused by spread of stimulation to the sensory region of the thalamus. Other less common side effects of DBS in the thalamus include dysarthria and dysgeusia. Dysarthria is typically mild, except with misplaced leads, and can be reduced by stimulation adjustment [1,3,4]. Dysarthria in unilateral DBS is associated with activating fibers of the internal capsule [5]. Bilateral thalamic DBS is associated with a high rate of dysarthria [4]. This often occurs with optimally placed leads and cannot be reversed by stimulation adjustment [5]. Dysgeusia is an infrequently reported side effect of DBS in the thalamus [6–8]. However, these limited reports suggest possible activation of taste perception region by DBS in the thalamus.

Conscious taste perception in humans is incompletely understood, and the structures that underlie taste perception are not well mapped. Taste signals originate from taste receptors on the tongue and palate, and primary taste perception is transmitted

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https://doi.org/10.1016/j.jocn.2018.01.013
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through cranial nerves 7, 9, and 10 – largely through the corda tympani – and terminates primarily in the ipsilateral nucleus solitarious in the pons. In primates, and presumably in humans, the nucleus solitarious projects bilaterally to the ventroposteriormedial nucleus of the thalamus pars parvicellularis (VPMpc), the taste sensory relay in the thalamus [9,10]. The VPMpc projects to the human gustatory cortex, which is thought to be located in the insula and parietal operculum, where there is bilateral representation of taste [11,12].

In the primate, the VPMpc is located medial and inferior in the VPM [2]. Thus, the VPMpc lies in a region that DBS could inadvertently activate. Indeed, taste perception has been reported from microstimulation of the medial sensory thalamus [13]. Because these data provide compelling evidence for the existence of a taste perception structure within the vicinity of the surgical target region for DBS, the following retrospective chart review was performed to determine the frequency of dysgeusia in DBS patients, and its relationship to DBS lead placement.

2. Methods

This retrospective chart review was approved by the local Institutional Review Board. Informed consent was waived based on retrospective nature of the study. Research was conducted in compliance with the Declaration of Helsinki.

2.1. Clinical screening for dysgeusia

The medical records of all patients with essential tremor who had DBS surgery in the thalamus over a 15-year period were reviewed (n = 52). This included records from office visits where dysgeusia, paresthesia, and tremor control were evaluated. Data was collected from operative records and charts, which included the nature of dysgeusia, triggers, temporal aspects, and which DBS contacts produced dysgeusia. Control cases (n = 7) with bilateral DBS for essential tremor, but without dysgeusia or sustained paresthesia were collected sequentially, working backwards from present.

2.2. Surgical method

Of the eight patients who reported dysgeusia, six had initial implantation of the DBS system at Sacred Heart Medical Center, and two had DBS lead revisions. Awake microelectrode-guided DBS surgery was performed. Intraoperative CT scans were obtained with the O-arm to confirm lead location, similarly to previously reported methods [14]. Standard microelectrode mapping was performed in all patients, and tremor synchronous neurons were often noted. Sensory testing for the VPL/VPM nuclei was performed by squeezing muscles and brushing the skin of the hand, forearm, bicep, and cheek.

The DBS electrode (either Medtronic 3387 or 3389, Minneapolis, MN, USA) was inserted, then intraoperative bipolar macrostimulation trials were conducted up to 8 V. The therapeutic benefit of bipolar stimulation on tremor was evaluated at the bottom three contacts. Side effects of paresthesia and dysarthria, including the minimum voltage to induce transient and persistent paresthesia, were carefully evaluated at each contact. Stimulation adjustment was performed in a multidisciplinary clinic over years in these patients to optimize tremor control and reduce stimulation side effects.

2.3. Statistical analysis

All patients routinely had postoperative MRI and stereotactic CT within 1 week of implantation. The position of each contact was measured from the mid-anterior commissure-posterior commissure point (MCP) as previously described [14]. Statistical analysis of lead location was performed in Excel v.11 (Microsoft, Redmond, WA, USA). Independent t-tests were used to compare data between patients with dysgeusia and controls. Data are reported as mean ± standard deviation.

3. Results

3.1. Clinical description of dysgeusia

Of the 52 DBS patients with thalamic DBS 8 (15%) reported dysgeusia. Six of 27 (22%) patients with dysgeusia had bilateral thalamic DBS, and of these, three had simultaneous bilateral surgery. Two of 25 (8%) patients had unilateral dominant hemisphere thalamic DBS. Seven control patients with bilateral thalamic DBS without dysgeusia were also studied, three of which had simultaneous bilateral implant.

All of these patients reported a "foul" taste with DBS stimulation. Other descriptions included "metallic taste," "coolness," "tingling taste," or "sour taste." Altered perception of the tongue, which felt enlarged, was also described. All patients could distinguish the foul taste from their normal sense of smell, and the tingling sensation of paresthesia.

Dysgeusia was described as mild in most patients, and did not impact food choices or eating habits. Patients reported that the dysgeusia could be ignored, like a "ringing in the ear that you don't notice unless you think about it." Two patients would turn the DBS system off during meals to avoid the dysgeusia. One patient did develop substantial food aversions, and subsequently had the DBS electrode repositioned.

The onset of dysgeusia was delayed until the first programming session after second lead placement in bilateral staged cases. In no case was dysgeusia reported or perceived in the operating room, in contrast to paresthesia. Rather, the onset of the dysgeusia was immediate following activation of the DBS lead in all patients. Dysgeusia appeared related to stimulation as it quickly resolved in most patients with deactivation of the DBS system. In two patients, dysgeusia dissipated slowly over a one-hour period after stopping stimulation, despite immediate cessation of paresthesia.

In several patients, postoperative programming sessions were successful in identifying a therapeutic contact and adjusting stimulation parameters that would eliminate dysgeusia but maintain tremor suppression. Some patients experienced only temporary relief of dysgeusia after reprogramming, and symptoms reappeared within a few days. Programming eliminated dysgeusia only in the unilateral cases (n = 2). Several patients described dysgeusia at just one or two contacts, but others described dysgeusia at all four contacts. The average programmed voltage was 2.4 V, pulse width 60–90 microseconds (average 72), 145–185 (average 170) Hz.

3.2. Neurophysiological findings related to lead placement

Lead placements associated with dysgeusia were either near, or within the sensory nucleus of the thalamus. Sensory responsive neurons were identified with microelectrode recording in four of six patients with adequate surgical records to make this determination, demonstrating that the lead was in the sensory nucleus. None of the control patients without dysgeusia (n = 7) had sensory responsive neurons in their microelectrode recordings.

Leads associated with dysgeusia all had low transient sensory thresholds compared to controls based on intraoperative macrostimulation on contact 0 (3.3 ± 1.9 V vs. 1.5 ± 0.5 V, $P < .05$). All these leads produced substantial intraoperative relief of tremor; therefore, they were considered adequately placed during surgery.

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