

A single thalamic target for deep brain stimulation to treat hemi-body pain syndrome

A. Rezaei Haddad^{1,2} · I. Ughratdar¹ · K. Ashkan¹

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Abstract

Background Patients experiencing hemi-body pain represent a difficult problem when using the thalamus as a DBS target given its anatomical topology.

Methods A 50-year-old HIV positive male underwent a right unilateral thalamic DBS to treat his severe left hemi-body central post-stroke pain following years of unsuccessful medication therapy.

Results The final active contact of the electrode corresponded to stimulation of the nucleus ventrocaudalis parvocellularis internis, which has provided prolonged pain relief.

Conclusion To our knowledge this was the first time this pattern of pain was treated by a single thalamic DBS electrode, suggesting stimulation in this region may be a feasible target for achieving relief from chronic severe hemi-body pain.

Keywords Hemi-body pain · DBS · Central post-stroke pain

Introduction

Deep brain stimulation (DBS) has been well established as an effective treatment for movement disorders such as Parkinson's disease and essential tremor [7, 8]. Modern

functional neurosurgical intervention for chronic pain syndromes dates back to the mid-1960s when Mazars et al., as a result of their pioneering research on stimulation of the thalamic relay nucleus, paved the way for chronic stimulation in patients by the early 1970s [21, 22]. However results from two trials in the 1970s revealed only as few as 18 % of the patients with initial favourable response maintained pain relief at 2 years [5]. As a result, skepticism about the efficacy of DBS hindered further research and uptake of this intervention. In the last decade however there has been a resurgence of the technique following a number of reports that have confirmed a good response to DBS in carefully selected patients [26].

Various DBS targets, including the ventroposterior (VP) thalamus, septal area, periventricular gray matter (PVG) and periaqueductal gray matter (PAG), have been utilised [12, 27, 28]. Given the frequent use and experience with the thalamus as a target for movement disorders such as tremor, it remains the preferred choice for many DBS surgeons including in our unit. In the case of thalamic DBS, the underlying mechanisms of action for the analgesic effects is unclear, but stimulation of the thalamocortical pathways, alteration of thalamic activity and interference of the pain relay pathway between the thalamus and cortex are believed to be responsible [18, 26, 31, 33].

Given the topological arrangement in the thalamus, patients suffering from thalamic syndrome with hemi-body pain represent a specific problem. The ventral posterolateral nucleus (VPL) and ventral posteromedial nucleus (VPM) serve as the somatosensory relay nuclei of the thalamus, where the latter is mainly involved with the general sensation of the head and upper extremities, while the former receives sensory input from the dorsal columns and spinothalamic tracts from the lower extremities [13, 20]. Therefore, treating hemi-body pain with a single DBS electrode proves challenging and of course the strategy of inserting multiple electrodes carries the risk of increased surgical morbidity and haemorrhage [37].

✉ A. Rezaei Haddad
ali.rhaddad@me.com

¹ Department of Neurosurgery, Kings College Hospital, Denmark Hill, London SE5 9RS, UK

² Warwick Medical School, The University of Warwick, Gibbet Hill, Coventry CV4 7AL, UK

Here, we describe a 50-year-old HIV positive male who suffered from a series of thalamic strokes and subsequently developed severe hemi-body pain. This case provided the opportunity to identify whether a single DBS target could alleviate the hemi-body pain experienced by the patient.

Case report

History

A 50-year-old male suffered from four episodes of predominantly right hemispheric stroke over a 2-week period in 2004. As an immediate consequence of the cerebrovascular accident, he developed severe left-sided weakness and pain. Although his physical symptoms recovered following 5 months of rehabilitation, his central post-stroke pain (CPSP) persisted despite trialing a variety of medications under several pain management programmes. His pain was dysaesthetic in nature and involved the lower part of his left face, neck and whole of the left trunk including the left arm and leg. Pre-operatively his medications included pregabalin, nitrazepam, nortriptyline, aspirin and dipyridamole. Given his HIV status, he was also on anti-retroviral medication with a steady viral load of 40 copies/ml and a CD4 count of 1145 cells/ μ l. As his pain severity had not improved over a 7-year period, described as 10/10 by the patient despite therapy, and had limited his capacity to perform normal daily tasks, a right-sided unilateral thalamic DBS was offered and undertaken. An MRI brain scan revealed established infarctions predominantly in the right hemisphere involving the right thalamus, right postero-medial temporal and right antero-inferior occipital lobes, left posterior insula and left corona radiata. There was no significant damage to the right VP thalamus (Fig. 1).

Surgical procedure

A right-sided unilateral thalamic DBS was performed in July 2011 under local anaesthetic. Stereotactic MRI images were acquired with a Leksell G frame and surgical planning was performed using the Medtronic Framelink® platform. Due to the nature of the pain, the target was chosen at a point midway between the atlas coordinates of the VPL and VPM. This corresponded to 9.5 mm posterior to the mid-commissural point, 13 mm lateral to the mid-sagittal plane at the level of the inter-commissural line (Fig. 2). Intra-operative testing and final implantation were achieved using a Medtronic 3389 DBS lead. No microelectrode recordings were performed, although dynamic impedance recordings were used to aid targeting.

During the procedure, the anatomical target was refined via test stimulation assessment in the awake state [2]. Test stimulation was initially performed 2 mm above the target and then

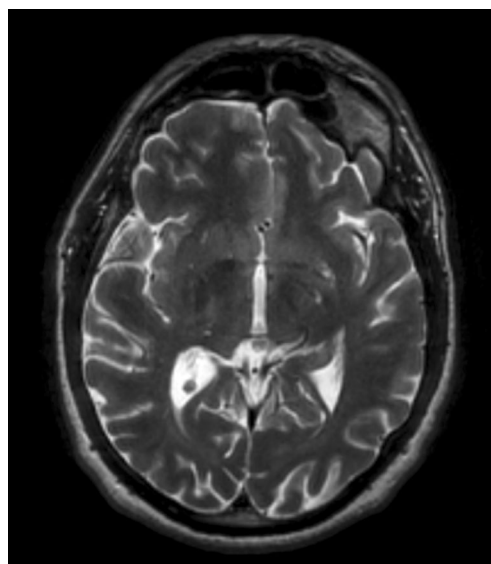


Fig. 1 T2-weighted magnetic resonance imaging showed no significant damage to the right ventroposterior thalamus

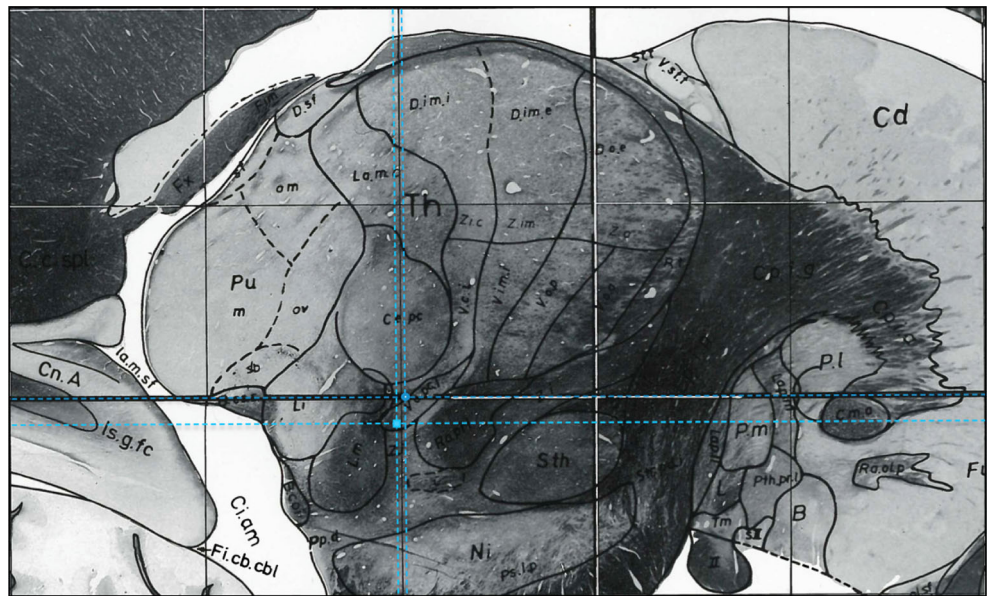
incrementally at 2 mm intervals until 6 mm below the target. The stimulating voltage was increased until pleasant paraesthesia in the distribution of the pain was experienced. The threshold for side effects was verified up to 4.0 V. Optimal results were achieved with stimulation at 4 mm below the inter-commissural line with a voltage of 3.0 V, pulse width of 60 μ s and frequency of 40 Hz. Given the concerns about reducing the infection risk given the patient's HIV status, a Medtronic Soletra battery was implanted in the same operative session and medicated with intravenous prophylactic antibiotics for 5 days post-operatively in line with our previous experience [11].

Image analysis by fusing the post-operative stereotactic CT with the preoperative planning stereotactic MRI [24] confirmed the final position of the centre of the most effective stimulating contact at 11 mm posterior to the mid-commissural point, 12 mm lateral to the mid-sagittal plane and 2.75 mm below the inter-commissural line. Superimposition of this target on the Schaltenbrand-Wahren atlas [29] located the active contact point at the nucleus ventrocaudalis parvocellularis internis (Vcpci) (Fig. 2).

On the second day post-operatively, the battery was switched on to a voltage of 1.0 V, pulse width of 60 μ s and frequency of 40 Hz with the patient reporting pain reduction and comfortable paraesthesia in the distribution of the pain. He was noted to have new mild unsteadiness, left faciolingobrachial paraesthesia and reduced taste intensity in the immediate post-operative phase. However these resolved within a week and were not present on subsequent follow-up visits or when increasing the voltage. He required a further increase in the stimulating voltage over the next 3 months.

At long-term follow-up 38 months later, his stimulation voltage was at 3.0 V. Contact 1 remained as the active contact

Fig. 2 Final position of the active DBS electrode contact. Plate 43, brain LXXVIII, myelin-stained sagittal section 12.0 mm from the midline, with ruled and labelled acetate overlay from the Schaltenbrand and Wahren atlas edited to show the initial target (circular symbol) and the final position of the active contact (square symbol) [29]



(unipolar stimulation). The patient reported that he had discontinued taking his analgesic medications, namely pregabalin, nitrazepam and nortriptyline. He rated his pain as 6/10, a 40 % improvement, and as a consequence, the patient reported that he was able to take part in many daily activities that were not possible prior to surgery such as exercising and shopping.

Discussion

Here, we report marked effects of analgesia following DBS in an HIV-positive patient with severe hemi-body pain caused by a series of strokes. It was estimated that approximately 8 % of patients who suffer from stroke progress to developing CPSP [1]. Further, it is thought that a higher percentage will suffer from this intractable pain if the stroke involves the pain processing and sensory relay pathways, such as the thalamus [15, 16]. The first line of treatment consists of medication therapy [9]. Should these medications fail to alleviate the pain, DBS may be indicated in a selected group of patients [26].

Given the topological arrangement of the thalamus, the pain pattern presented in this case, where the left half of the head, trunk, arm and leg were affected, would be difficult to address by insertion of a single thalamic electrode. Traditionally the VPM (9 mm posterior to the mid-commissural point, 9 mm lateral to the mid-sagittal plane and 0–4 mm below the inter-commissural line) is targeted for facial and upper limb pain whilst the VPL (10 mm posterior to the mid-commissural point, 16 mm lateral to the mid-sagittal plane and 0–4 mm below the inter-commissural line) is targeted for lower limb pain [34]. To our knowledge, this is the first description of a patient with this pattern of severe hemi-body pain treated by a

single electrode targeted at a point halfway between the VPL and VPM corresponding with the active contact located in the region of Vpcpi.

The underlying mechanism may be related to current spread to both the VPL and VPM, although this may also be explained by the modulation of the Vpcpi nucleus, where the final active contact is believed to be located. Potential error introduced as a result of fusing the pre-operative stereotactic MRI, post-operative stereotactic CT and brain atlas should be

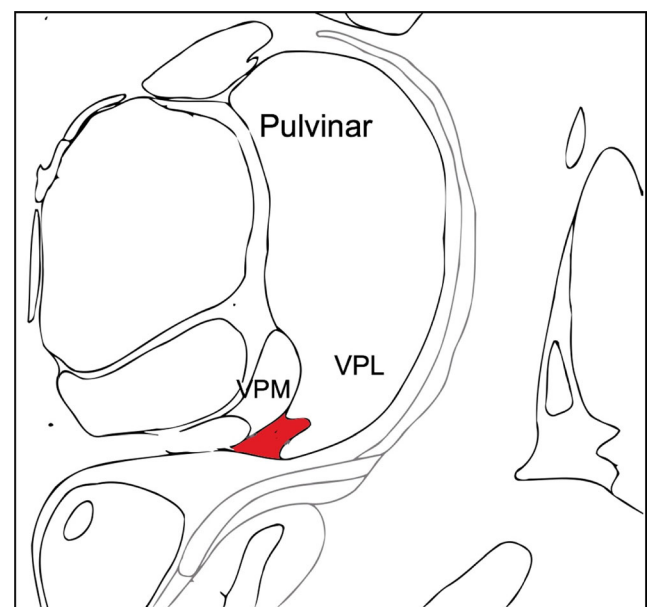


Fig. 3 The position of the ventral posteroinferior nucleus. Drawn coronal section, 11 mm posterior to the mid-commissural plane, based on the Schaltenbrand and Wahren atlas [29], to show the position of the ventral posteroinferior nucleus (shaded area) in relation to the ventral posterolateral and ventral posteromedial nuclei

born in mind when interpreting the results here [24]. Nevertheless, the Vcpai nucleus is believed to be an important structure for gustatory function [17]. The fact that our patient reported altered taste intensity after DBS may hint at the involvement of this nucleus in the mechanism of his pain relief. In fact, a study has reported that strong stimulation of the Vcpai in humans resulted in stimulation of somatic sensation as well, suggesting that gustatory relay pathways convey multiple sensations [17]. No studies to date have looked at the role of Vcpai in pain suppression in humans; however, a link between increased taste sensation and chronic back pain has also been reported, indicating that an interaction between pain and taste pathways may exist [30].

The Vcpai nucleus is situated inferiorly to the ventralis caudalis (VC) nuclei and includes the arcuate nucleus [29]. The lateral part of the Vcpai is known as the ventral posteroinferior nucleus (VPI) and is surrounded by the VPL and VPM (Fig. 3) [29]. The VPI in primates has been reported to contain nociceptive neurons and receive projections from the spinothalamic tract [6]. The arcuate nucleus is a major source of endogenous beta-endorphin, an opioid peptide, in the central nervous system [3], and activity in this nucleus has been shown to be increased in response to chronic pain in rodents [19, 23, 25]. In addition, a few studies have reported that stimulation of the nucleus arcuate was accompanied by the release of beta-endorphin and a reduction of pain sensation in rodents [4, 32, 35, 36]. These results suggest that the arcuate nucleus activity may serve as a secondary mechanism to provide analgesia in response to persistent pain that may partly explain the pain relief noted in our patient following the DBS.

Although DBS for chronic pain has existed for over 6 decades, because of the invasive nature and risks associated with the procedure, it is reserved for when conservative medical treatment has failed. The variable outcomes in the literature warrant further studies and identification of novel surgical targets [10, 14].

Our results support further research to determine the mechanisms responsible for the beneficial effects of Vcpai complex stimulation and to explore whether arcuate nucleus stimulation specifically can have analgesic effects in humans.

Conclusion

We report marked analgesic effects in a patient suffering from post-stroke hemi-body pain following placement of a single thalamic DBS electrode targeted at a point midway between the VPL and VPM with the active contact in the region of Vcpai. To our knowledge this was the first time this pattern of severe hemi-body pain was treated by a single thalamic DBS electrode, suggesting stimulation in this region may be a feasible target for achieving relief from chronic hemi-body

pain. Further studies are required to validate our findings and elucidate the underlying mechanisms of pain relief.

Conflicts of Interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Patient Consent The patient has consented to the submission of the case report for submission to the journal.

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