Brief report: Microvascular Decompression or Neuromodulation in Patients with SUNCT and Trigeminal Neurovascular Conflict?

Journal:	*Cephalalgia*
Manuscript ID	CHA-00385-FT-2017.R1
Manuscript Type:	Article for Fast Track Review
Date Submitted by the Author:	n/a
Complete List of Authors:	Hassan, Samih; University College London Hospitals NHS Foundation Trust, Victor Horsley department of Neurosurgery Lagrata, Susie; 2. Headache Group, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG, UK, Neurology Levy, Andrew; 2. Headache Group, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG, UK , Neurologuy Matharu, Manjit; 2. Headache Group, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG, UK , Neurology Zrinzo, Ludvic; Unit of Functional Neurosurgery, Box 146, Institute of Neurology and National Hospital for Neurology and Neurosurgery, 33 Queen Square, London, WC1N 3BG, UK , Unit of Functional Neurosurgery
Key Words:	Trigeminal nerve

Brief report: Microvascular Decompression or Neuromodulation in Patients with SUNCT and Trigeminal Neurovascular Conflict?

Authors:

Samih Hassan MBBS MRCS FRCS (SN) [1], Susie Lagrata BSc [2], Andrew Levy BChD MSc [2], Manjit Matharu PhD FRCP* [2], Ludvic Zrinzo MD PhD FRCS (Neuro.Surg)* [1,3]

* Both senior authors have equal contribution to the paper

Affiliations:

1. Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG, UK
2. Headache Group, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG, UK
3. Unit of Functional Neurosurgery, Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, University College London, Queen Square, London, WC1N 3BG, UK

Corresponding Author:

Ludvic Zrinzo MD PhD FRCSEd (Neuro.Surg)

Unit of Functional Neurosurgery, Box 146, Institute of Neurology and National Hospital for Neurology and Neurosurgery, 33 Queen Square, London, WC1N 3BG, UK

Email: l.zrinzo@ucl.ac.uk

Fax: +44 (0) 20 3108 0142

Tel: +44 (0) 20 3108 0026

ABSTRACT:

Objectives: To assess the ~~relative~~ effectiveness of neuromodulation and trigeminal microvascular decompression (MVD) in patients with medically intractable short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT).

Methods: Two patients with medically refractory SUNCT underwent MVD following beneficial but incomplete response to neuromodulation (occipital nerve stimulation and deep brain stimulation). MRI confirmed neurovascular conflict with the ipsilateral trigeminal nerve in both patients.

Results: Although neuromodulation provided significant benefit, it did not deliver complete relief from pain and management required numerous postoperative visits with adjustment of medication and stimulation parameters. Conversely, MVD was successful in eliminating symptoms of SUNCT in both patients with no need for further medical treatment or neuromodulation.

Conclusion: Neuromodulation requires expensive hardware and lifelong follow up and maintenance. These case reports highlight that microvascular decompression may be preferable to neuromodulation in the subset of SUNCT patients with ipsilateral neurovascular conflict.

Keywords: SUNCT, neuromodulation, trigeminal nerve, microvascular decompression

Word count: 1503 words (limit 1500)

Abstract: 145 words (limit 150)

References: 1~~9~~7 (limit 12) references added to address reviewer comments

Tables: 1

Figures: 1 (allowed 2)

List of all abbreviations used

CISS	constructive interference in steady state
DBS	deep brain stimulation
ONS	occipital nerve stimulation
MRI	magnetic resonance imaging
MVD	microvascular decompression
SUNA	short-lasting unilateral neuralgiform headache attacks with cranial autonomic features
SUNCT	short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing
SUNHA	short-lasting unilateral neuralgiform headache attacks
TACs	trigeminal autonomic cephalalgias
TN	trigeminal neuralgia
VTA	ventral tegmental area
V2	2nd division of trigeminal nerve

INTRODUCTION

Short-lasting unilateral neuralgiform headache attacks (SUNHA) are a rare primary headache disorder characterised by moderate or severe, strictly unilateral, stabbing or saw-tooth attacks lasting seconds to minutes. Attacks occur at least once a day and are associated with ipsilateral cranial autonomic symptoms or signs.[1] Incidence is 1.2/100,000, and around 58% will respond to medical therapy. When autonomic features include both conjunctival injection and lacrimation (tearing), the disorder is subclassified as short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT). When autonomic symptoms include only one or neither of these ocular symptoms they are referred to as short-lasting unilateral neuralgiform headache attacks with cranial autonomic features (SUNA).[1]

Functional neuroimaging studies in SUNHA and other trigeminal autonomic cephalalgias (TACs) have demonstrated involvement of the posterior hypothalamic region during attacks.[2] Moreover, as with trigeminal neuralgia (TN), a significant proportion of SUNHA patients display neurovascular conflict with the trigeminal nerve ipsilateral to the attacks.[3] This has led to the concept of a pathophysiological overlap between SUNHA, other TACs and TN.[4]

Treatment options in medically refractory SUNHA patients are difficult to evaluate in a systematic fashion due to the severity and rarity of the condition combined with the paucity of reports in the literature. Over the last decade, peripheral and central neuromodulation as well as trigeminal microvascular decompression have emerged as efficacious treatments. [5-7] Reported outcomes after surgical interventions are currently limited to case reports or series. [5-8] Ablative interventions have been successfully used but have fallen out of favour because of their inconsistent results

and tendency to cause adverse effects, including possible anaesthesia dolorosa.[9,10]~~[5,6]~~

As with other TACs, peripheral neuromodulation has emerged as an option. Eight of nine patients receiving occipital nerve stimulation (ONS) for SUNHA were improved with four being rendered pain free.[5]~~[7]~~ Supraorbital and supratrochlear stimulation is limited to a single case report with reported benefit, albeit complicated by skin erosion and infection.[11]~~[8]~~

Central neuromodulation, purported to be posterior hypothalamic deep brain stimulation (DBS) and now understood to be in the ventral tegmental area (VTA), has provided substantial relief in three reported patients.[12-15]~~[9-12]~~ The experience from our centre is that 9 of 11 medically refractory SUNHA patients responded to DBS (defined as ≥ 50% reduction in headache frequency) with four patients rendered pain free ~~(manuscript accepted for publication)~~.[4]

However, in a subset of patients with SUNHA and documented neurovascular conflict with the trigeminal nerve, 15 of 23 reported patients undergoing microvascular decompression (MVD) experienced complete resolution of pain.[7,16-18]~~[13-16]~~

Here, we present two patients with medically refractory SUNCT who underwent MVD after a beneficial, but incomplete, response to neuromodulation. The aim of our report is to describe the response to MVD post neuromodulation in patients with medically intractable SUNCT to help practitioners consider the place for these surgical interventions in the treatment pathway.

CASE SERIES

Patient 1

An 80-year-old male presented with a 13-year history of SUNCT. Initially episodic, symptoms became chronic after the first 3-years.

The SUNCT attacks were strictly right-sided, centred over the infra-orbital region with radiation to the forehead and the temple. The attack frequency varied considerably, ranging from 10 to 100 daily. The attacks lasted 2-5 minutes and were excruciating in intensity. The attacks were accompanied by ipsilateral lacrimation, conjunctival injection, ptosis, rhinorrhoea, bilateral facial sweating and facial redness as well as nausea, photophobia and restlessness. Attacks were both spontaneous and triggered by eating and drinking, swallowing, talking, touching, wind and shaving. There was no refractory period. MRI confirmed ipsilateral arterial conflict with the trigeminal nerve (figure 1A). The patient failed to respond to numerous trials of preventive treatments, including a trial of indomethacin (table 1).

ONS was implanted 7-years after symptom onset with a patient estimate of 80% improvement from baseline with reduction in severity, frequency and duration of attacks (previously reported in {Lambru:2014vx}). Over the years, SUNCT attacks gradually became more frequent and severe, although never reaching pre-ONS levels. Despite improvement from baseline, following ONS the patient still required an average of 1.2 hospital admissions and 4 outpatient consultations per year. A surgical opinion was again sought during an inpatient admission, when the patient had a severe exacerbation that proved difficult to manage with intravenous lidocaine. MVD was proposed and performed during the same admission. Branches of the superior cerebellar artery were found running between the fibres of the trigeminal

nerve and compressing the superior aspect of the nerve. Neural decompression was achieved by splitting the fascicles of the trigeminal nerve lengthwise, mobilising the offending vessels and placing Teflon felt between the offending arteries and nerve (Figure 1). Following the MVD, he became pain free immediately. Apart from temporal V2 numbness which has resolved, he remains pain and autonomic symptoms free 33-months following surgery. He stopped all medications for SUNCT and switched off the ONS device within a few weeks of MVD. He has not required hospital admission and attends out-patient clinic once-a-year to ensure follow-up.

Patient 2

This 67-year-old gentleman presented with a 26-year history of right-sided SUNCT. Initially episodic, symptoms became chronic after the first 5-years. The attacks were strictly unilateral on right, centred on supra-orbital ridge and the temple. He had 50-200 attacks daily, with each attack lasting between 10 seconds and 10 minutes. The pain was excruciating and accompanied by lacrimation, conjunctival injection, nasal blockage and rhinorrhoea. Attacks could be triggered by cutaneous touch, wind on the face, shouting, chewing and hair-combing. There was no refractory period. The combination of oxcarbazepine and lamotrigine was partially beneficial but the patient had significant side effects including unsteadiness, double vision, and tremor. He failed to respond to numerous other medications (see Table 1). MRI confirmed ipsilateral arterial conflict with the trigeminal nerve (Figure1C).

21 years after symptoms started, VTA DBS was performed at age of 62 years. Following DBS, the patient reported an estimated 90% improvement in SUNCT symptoms with reduction in severity, frequency and duration of attacks (previously reported in {Miller:2016ix}. However, this was only achieved in combination with

continued oxcarbazepine and lamotrigine provoking side effects including unsteadiness, double vision and tremor. Multiple attempts to reduce medication caused significant SUNCT pain recurrence. Despite improvement following DBS, an average of 1.3 hospital admissions and 2 outpatient clinic consultations a year were required. After surgical review in our multidisciplinary facial pain clinic, MVD was proposed and performed. He became pain free immediately following surgery. Twenty-three-months after MVD surgery he remains pain free with no autonomic symptoms; there is a small area of reduced sensation to pinprick in V2 with corneal sensation intact. He no longer takes any medications for SUNCT and the DBS system has been switched off. He has not required hospital admission and attends out-patient clinic once-a-year to ensure follow-up.

DISCUSSION

~~Surgical treatment of medically intractable SUNHA is challenging because of the severity and rarity of the condition combined with the paucity of reports of effective treatments in the literature.~~ Severe, medically intractable SUNHA is rare and there is a paucity of reports of effective surgical treatments in the literature. Ablative interventions have been successfully used but they have fallen out of favour because of their inconsistent results and tendency to cause adverse effects, including possible anaesthesia dolorosa. Over the last decade, neuromodulation and MVD have been reported as being efficacious but a ~~head-to-head~~"within patient" comparison has not previously been ~~reported~~ available in the literature.

Here we report on two patients with medically intractable SUNCT who obtained beneficial but incomplete response to peripheral or central neuromodulation with

ONS and DBS respectively. Repeat outpatient visits were required to optimise medical therapy and neuromodulation settings. However, both patients became pain free of SUNCT symptoms following trigeminal MVD. Both patients were able to stop medication and deactivate the neurostimulators. Moreover, there was no further need for hospital admission or numerous follow up appointments. One could argue that numbness following surgery points to ablation as the mechanism of action, However, the transient nature of this in one patient and the small area affected, outside the formerly painful area in the other patient, suggest that this is not the mechanism of action. Although the length of follow up is relatively short (23- and 33-months) we are encouraged by extrapolation from the literature on MVD for TN where recurrence rates 10-years after successful MVD are remarkably low (around 10-20%).[19][~~17~~]

~~We hesitate to suggest "guidelines" for the management of medically refractory SUNA and SUNCT on such a small worldwide, and even smaller local, experience.~~ ~~However~~B, ~~b~~ased on the available evidence, we propose that all SUNA and SUNCT patients undergo high quality MR imaging of the prepontine cistern to rule out pathological processes in the region as well as to examine for neurovascular conflict.

We now offer MVD as a first procedure to those patients with neurovascular conflict who remain symptomatic or suffer from significant side-effects despite optimal medical management. As with every neurosurgical procedure, MVD carries risks including cerebrospinal fluid leak, neurological deficit or death. Nevertheless, in experienced centres, the risk of serious harm is <1% and MVD in such patients is the closest that we can offer to a symptomatic "cure". We reserve neuromodulation for patients without MRI evidence of trigeminal neurovascular conflict or for those with

conflict who have not responded to MVD. In these patients, we offer ONS, reserving DBS for when ONS is not available or has failed to provide sufficient benefit.

CONCLUSION

In patients with medically intractable SUNCT and evidence of neurovascular conflict on MR imaging, MVD may be considered before offering neuromodulation procedures.

Conflict of Interest Statement

Manjit Matharu serves on the advisory board for Allergan, St Jude Medical and Medtronic, and has received payment for the development of educational presentations from Allergan, Merck Sharpe and Dohme Ltd, Medtronic and electroCore.

Ludvic Zrinzo has received payment for the development of educational presentations from Medtronic, St Jude Medical, Boston Scientific, Elekta and Autonomic Technologies.

Samih Hassan, Susie Lagrata and Andrew Levy have no conflicts of interest to declare in relation to this manuscript.

Acknowledgements

The Unit of Functional Neurosurgery, UCL Institute of Neurology, Queen Square, London is supported by the Parkinson's Appeal and the Sainsbury Monument Trust.

Clinical Implications

Microvascular decompression is a valid treatment option for SUNCT

Table 1. Medication History (NT, not tried; NK, not known)

Drug	Patient 1		Patient 2	
	Daily Dose	Effect	Daily Dose	Effect
Lamotrigine	225mg	Partially effective; severe confusion	700mg	Partially effective; marked drowsiness and poor memory
Carbamazepine	NK	Ineffective	800mg	Partially effective; severe dizziness, double vision and tremor.
Oxcarbazepine	NT		600mg	Partially effective; tremor, dizziness and unsteadiness.
Topiramate	175mg	Ineffective; cognitive slowing, nausea and weight loss	400mg	Ineffective.
Gabapentin	4500mg	Ineffective	NK	Ineffective
Pregabalin	500mg	Ineffective	NT	
Baclofen	NT		NK	Ineffective
Phenytoin	NT		250mg	ineffective
Melatonin	12mg	Ineffective	9mg	Ineffective
Lidocaine patches	5% patch for 12 hours daily	Mild benefit; confusion	5% patch for 12 hours daily	Ineffective
Intravenous lidocaine	1- 4mg/min for 7 days	No attacks during infusion with rapid recurrence when infusion discontinued; developed sinus tachycardia	1- 4mg/min for 7 days	No attacks during infusion with rapid recurrence when infusion discontinued
Greater occipital		Partially beneficial for 3 days		Ineffective

nerve block				
Amitriptyline	NK	Ineffective	NT	
Lithium	NK	Ineffective	NK	ineffective
Prednisolone	NK	Ineffective	NT	
Indomethacin	150mg	Ineffective	150mg	Ineffective
Subcutaneous Sumatriptan	6mgs as needed	Ineffective	6mgs as needed	Ineffective
High flow oxygen	100% at 12 litres/min	Ineffective	NT	

Figure 1

Left column: Patient 1 with right sided SUNCT. **A:** High resolution axial CISS 1.5 MRI sequences confirming neurovascular conflict with the right trigeminal nerve. **B: Intraoperative microscope images:** A leash of arterial vessels can be seen in conflict with the right trigeminal nerve in the first image. After retraction of the intervening petrosal vein, one of the offending arteries is clearly seen passing between the fascicles of the trigeminal nerve in the second image. After mobilisation of the offending vessels and splitting of the trigeminal fascicles, Teflon felt has been placed between the most superficial vessel and the surrounding trigeminal fibres in the third image. Further Teflon pieces were placed between the offending vessels and trigeminal nerve prior to surgical closure (not shown).

Right column: Patient 2 with left-sided SUNCT. **C:** High resolution axial CISS 1.5 MRI sequences confirming neurovascular conflict with the left trigeminal nerve. **D: Intraoperative microscope photos:** In the top image, thick arachnoid membranes can be seen matting a loop of the superior cerebellar artery to the superior and medial aspect of the left trigeminal nerve. After division of the arachnoid membranes and mobilisation of the offending vessel, the second image gives a clearer view of the underlying anatomy. The thin white band of the fourth cranial nerve can be seen coursing around the midbrain in the hiatus between petrosal vein and tentorium. The lowest image documents the bright white Teflon felt placed between offending vessel and trigeminal nerve.

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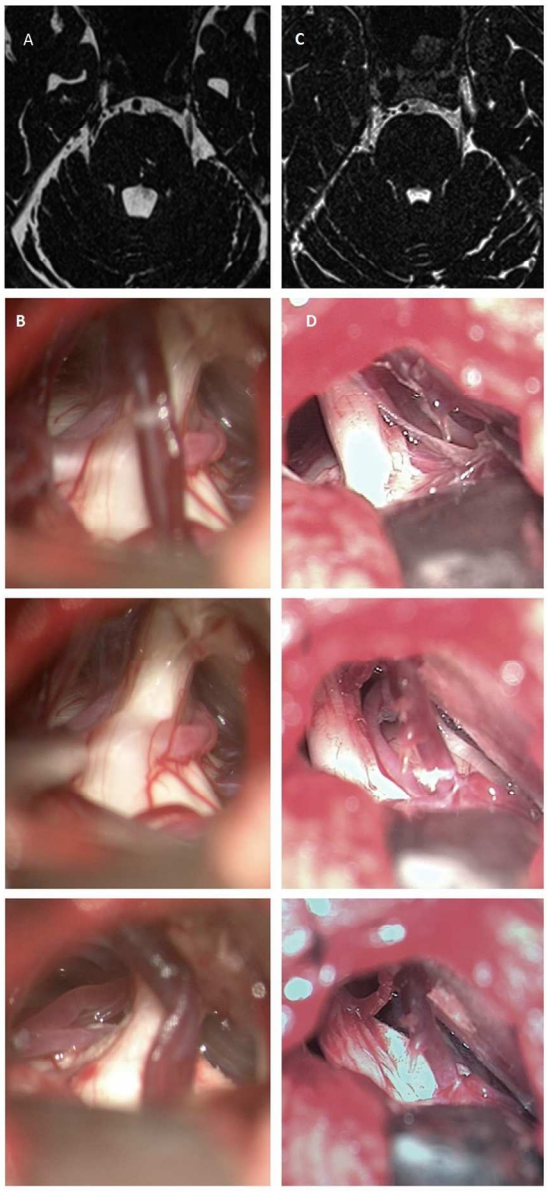
High flow oxygen	100% at 12 litres/min	Ineffective	NT	

NT, not tried; NK, not known



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Right column: Patient 2 with left-sided SUNCT. C: High resolution axial CISS 1.5 MRI sequences confirming neurovascular conflict with the left trigeminal nerve. D:Intraoperative microscope photos: In the top image, thick arachnoid membranes can be seen matting a loop of the superior cerebellar artery to the superior and medial aspect of the left trigeminal nerve. After division of the arachnoid membranes and mobilisation of the offending vessel, the second image gives a clearer view of the underlying anatomy. The thin white band of

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203x334mm (144 x 144 DPI)

CARE Checklist (2013) of information to include when writing a case report

Topic	Item	Checklist item description	Reported on Page
Title	**1**	The words "case report" should be in the title along with what is of greatest interest in this case	**1**
Key Words	**2**	The key elements of this case in 2 to 5 key words	**3**
Abstract	**3a**	Introduction—What is unique about this case? What does it add to the medical literature?	**2**
	3b	The main symptoms of the patient and the important clinical findings	**2**
	3c	The main diagnoses, therapeutics interventions, and outcomes	**2**
	3d	Conclusion—What are the main "take-away" lessons from this case?	**2**
Introduction	**4**	Brief background summary of this case referencing the relevant medical literature	**5-6**
Patient Information	**5a**	Demographic information (such as age, gender, ethnicity, occupation)	**7-8**
	5b	Main symptoms of the patient (his or her chief complaints)	**7-8**
	5c	Medical, family, and psychosocial history including co-morbidities, and relevan t genetic information . .	**7-8**
	5d	Relevant past interventions and their outcomes	**7-8**
Clinical Findings	**6**	Describe the relevant physical examination (PE) findings.	
Timeline	**7**	Depict important milestones related to your diagnoses and interventions (table or figure)	**attched**
Diagnostic Assessment	**8a**	Diagnostic methods (such as PE, laboratory testing, imaging, questionnaires).	**7-8, Figure1**
	8b	Diagnostic challenges (such as financial, language, or cultural)	
	8c	Diagnostic reasoning including other diagnoses considered	
	8d	Prognostic characteristics (such as staging in oncology) where applicable	
Therapeutic Intervention	**9a**	Types of intervention (such as pharmacologic, surgical, preventive, self-care)	**7-8**
	9b	Administration of intervention (such as dosage, strength, duration)	**Table 1**
	9c	Changes in intervention (with rationale)	
Follow-up and Outcomes	**10a**	Clinician-assessed outcomes and when appropriate patient-assessed outcomes.	
	10b	Important follow-up test results	**7-8**
	10c	Intervention adherence and tolerability (How was this assessed?)	
	10d	Adverse and unanticipated events	**7-9**
Discussion	**11a**	Discussion of the strengths and limitations in the management of this case	**9-10**
	11b	Discussion of the relevant medical literature.	**9-10**
	11c	The rationale for conclusions (including assessment of possible causes)	**10**
	11d	The main "take-away" lessons of this case report	**10**
Patient Perspective	**12**	Did the patient share his or her perspective or experience? (Include when appropriate)	
Informed Consent	**13**	Did the patient give informed consent? Please provide if requested	**Yes**

Microvascular Decompression or Neuromodulation in Patients with SUNCT and Trigeminal Neurovascular Conflict? 2 case reports

Authors:

Samih Hassan MBBS MRCS FRCS (SN) [1], Susie Lagrata BSc [2], Andrew Levy BChD MSc [2], Manjit Matharu PhD FRCP* [2], Ludvic Zrinzo MD PhD FRCS (Neuro.Surg)* [1,3]

* Both senior authors have equal contribution to the paper

Affiliations:

1. Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG, UK
2. Headache Group, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, Queen Square, London, WC1N 3BG, UK
3. Unit of Functional Neurosurgery, Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, University College London, Queen Square, London, WC1N 3BG, UK

Corresponding Author:

Ludvic Zrinzo MD PhD FRCSEd (Neuro.Surg)

Unit of Functional Neurosurgery, Box 146, Institute of Neurology and National Hospital for Neurology and Neurosurgery, 33 Queen Square, London, WC1N 3BG, UK

Email:

lidvic.zrinzo@uclh.nhs.ul

Fax: +44 (0) 20 3108 0142

Tel: +44 (0) 20 3108 0026

ABSTRACT:

Objectives: To assess the relative effectiveness of neuromodulation and trigeminal microvascular decompression in patients with medically intractable short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing.

Methods: Two patients with medically refractory short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing underwent trigeminal microvascular decompression following beneficial but incomplete response to neuromodulation (occipital nerve stimulation and deep brain stimulation). MRI confirmed neurovascular conflict with the ipsilateral trigeminal nerve in both patients.

Results: Although neuromodulation provided significant benefit, it did not deliver complete relief from pain. Conversely, trigeminal microvascular decompression was successful in eliminating symptoms in both patients with no need for further medical treatment or neuromodulation.

Conclusion: Neuromodulation requires expensive hardware and lifelong follow up and maintenance. These case reports highlight that microvascular decompression may be preferable to neuromodulation in the subset of short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing patients with ipsilateral neurovascular conflict.

Keywords: SUNCT, neuromodulation, trigeminal nerve, microvascular decompression

Word count: 1496 words (limit 1500)

Abstract: 150 words (limit 150)

References: 18 (limit 12, explained in the covering letter)

Tables: 1

Figures: 1 (allowed 2)

List of all abbreviations used

CISS	constructive interference in steady state
DBS	deep brain stimulation
ONS	occipital nerve stimulation
MRI	magnetic resonance imaging
MVD	microvascular decompression
SUNA	short-lasting unilateral neuralgiform headache attacks with cranial autonomic features
SUNCT	short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing
SUNHA	short-lasting unilateral neuralgiform headache attacks
TACs	trigeminal autonomic cephalalgias
TN	trigeminal neuralgia
VTA	ventral tegmental area
V2	2nd division of trigeminal nerve

INTRODUCTION

Short-lasting unilateral neuralgiform headache attacks (SUNHA) are a rare primary headache disorder characterised by moderate or severe, strictly unilateral, stabbing or saw-tooth attacks lasting seconds to minutes. Attacks occur at least once a day and are associated with ipsilateral cranial autonomic symptoms or signs.[1] Incidence is 1.2/100,000. When autonomic features include both conjunctival injection and lacrimation (tearing), the disorder is sub-classified as short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT). When autonomic symptoms include only one or neither of these ocular symptoms they are referred to as short-lasting unilateral neuralgiform headache attacks with cranial autonomic features (SUNA).[1]

Functional neuroimaging studies in SUNHA and other trigeminal autonomic cephalalgias (TACs) have demonstrated involvement of the posterior hypothalamic region during attacks.[2] Moreover, as with trigeminal neuralgia (TN), a significant proportion of SUNHA patients display neurovascular conflict with the trigeminal nerve ipsilateral to the attacks.[3] This has led to the concept of a pathophysiological overlap between SUNHA and TN.[4]

A significant proportion of SUNHA patients fail to respond to medical treatments. Treatment options in these medically refractory patients are difficult to evaluate in a systematic fashion due to the severity and rarity of the condition combined with the paucity of reports in the literature. Over the last decade, peripheral and central neuromodulation as well as trigeminal microvascular decompression have emerged as efficacious treatments. Reported outcomes after surgical interventions are currently limited to case reports or series. Ablative interventions have been successfully used but have fallen out of favour because of their inconsistent results and tendency to cause adverse effects, including possible anaesthesia dolorosa.[5,6]

As with other TACs, peripheral neuromodulation has emerged as an option. Eight of nine patients receiving occipital nerve stimulation (ONS) for SUNHA were improved with four being rendered pain free.[7] Supraorbital and supratrochlear stimulation is limited to a single case report with reported benefit, albeit complicated by skin erosion and infection.[8]

Central neuromodulation, purported to be posterior hypothalamic deep brain stimulation (DBS) and now understood to be in the ventral tegmental area (VTA), has provided substantial relief in three reported patients.[9-12] The experience from our centre is that 9 of 11 medically refractory SUNHA patients responded to DBS (defined as ≥ 50% reduction in headache frequency) with four patients rendered pain free.[4,13]

However, in a subset of patients with SUNHA and documented neurovascular conflict with the trigeminal nerve, 15 of 23 reported patients undergoing microvascular decompression (MVD) experienced complete resolution of pain.[14-17]

Here, we present two patients with medically refractory SUNCT who underwent MVD after a beneficial, but incomplete, response to neuromodulation. The aim of our report is to describe the response to MVD post-neuromodulation in patients with medically intractable SUNCT to help practitioners consider the place for these surgical interventions in the treatment pathway.

CASE SERIES

Patient 1

An 80-year-old male presented with a 13-year history of SUNCT. Initially episodic, symptoms became chronic after the first 3-years.

The SUNCT attacks were strictly right-sided, centred over the infra-orbital region with radiation to the forehead and the temple. The attack frequency varied considerably, ranging from 10 to 100 daily. The attacks lasted 2-5 minutes and were excruciating in intensity. The attacks were accompanied by ipsilateral lacrimation, conjunctival injection, ptosis, rhinorrhoea, bilateral facial sweating and facial redness as well as nausea, photophobia and restlessness. Attacks were both spontaneous and triggered by eating and drinking, swallowing, talking, touching, wind and shaving. There was no refractory period. MRI confirmed ipsilateral arterial conflict with the trigeminal nerve (figure 1A). The patient failed to respond to numerous trials of preventive treatments (table 1).

ONS was implanted 7-years after symptom onset with a patient estimate of 80% improvement from baseline. Over the years, SUNCT attacks gradually became more frequent and severe, although never reaching pre-ONS levels. Despite improvement from baseline, following ONS the patient still required an average of 1.2 hospital admissions and 4 outpatient consultations per year. A surgical opinion was again sought during an inpatient admission, when the patient had a severe exacerbation that proved difficult to manage with intravenous lidocaine. MVD was proposed and performed during the same admission. Branches of the superior cerebellar artery were found running between the fibres of the trigeminal nerve and compressing the superior aspect of the nerve. Neural decompression was achieved by splitting the fascicles of the trigeminal nerve lengthwise, mobilising the offending vessels and placing Teflon felt between the offending arteries and nerve (Figure 1). Following the MVD, he became pain free immediately. Apart from temporal V2 numbness which has resolved, he remains free of pain and autonomic symptoms 33-months following surgery. He stopped all medications for SUNCT and switched off the ONS device within a

few weeks of MVD. He has not required hospital admission and attends out-patient clinic once-a-year to ensure follow-up.

Patient 2

This 67-year-old gentleman presented with a 26-year history of right-sided SUNCT. Initially episodic, symptoms became chronic after the first 5-years. The attacks were strictly unilateral on right, centred on the forehead and the temple. He had 50-200 attacks daily, with each attack lasting between 10 seconds and 10 minutes. The pain was excruciating and accompanied by lacrimation, conjunctival injection, nasal blockage and rhinorrhoea. Attacks could be triggered by cutaneous touch, wind on the face, shouting, chewing and hair-combing. There was no refractory period. The combination of oxcarbazepine and lamotrigine was partially beneficial but the patient had significant side effects including unsteadiness, double vision, and tremor. He failed to respond to numerous other medications (see Table 1). MRI confirmed ipsilateral arterial conflict with the trigeminal nerve (Figure1C).

Twenty-one years after the symptoms started, VTA DBS was performed at age of 62 years. Following DBS, the patient reported an estimated 90% improvement in SUNCT symptoms. However, this was only achieved in combination with continued oxcarbazepine and lamotrigine, which continued to cause the side effects outlined above. Multiple attempts to reduce medication caused marked worsening of the SUNCT attacks. Despite improvement following DBS, an average of 1.3 hospital admissions and 2 outpatient clinic consultations a year were required. After surgical review in our multidisciplinary facial pain clinic, MVD was proposed and performed. He became pain free immediately following surgery. Twenty-three months after MVD surgery he remains pain free with no autonomic symptoms; there is a small area of reduced sensation to pinprick in V2 with corneal sensation intact. He no longer takes any medications for SUNCT and the DBS system has been switched off. He has

not required hospital admission and attends out-patient clinic once-a-year to ensure follow-up.

DISCUSSION

Surgical treatment of medically intractable SUNHA is challenging because of the severity and rarity of the condition combined with the paucity of reports of effective treatments in the literature. Ablative interventions have been successfully used but they have fallen out of favour because of their inconsistent results and tendency to cause adverse effects, including possible anaesthesia dolorosa. Over the last decade, neuromodulation and MVD have been reported as being efficacious but a head-to-head comparison has not previously been reported in the literature.

Here we report on two patients with medically intractable SUNCT who obtained beneficial but incomplete response to peripheral or central neuromodulation with ONS and DBS, respectively. Repeat outpatient visits were required to optimise medical therapy and neuromodulation settings. However, both patients became pain free following trigeminal MVD. Both patients could stop medications and deactivate the neurostimulators. Moreover, there was no further need for hospital admission or numerous follow up appointments. One could argue that numbness following surgery points to ablation as the mechanism of action, However, the transient nature of this in one patient and the small area affected, outside the formerly painful area in the other patient, suggest that this is not the mechanism of action. Although the length of follow up is relatively short (23- and 33-months) we are encouraged by extrapolation from the literature on MVD for TN where recurrence rates 10-years after successful MVD are remarkably low (around 10-20%).[18]

We hesitate to suggest "guidelines" for the management of medically refractory SUNA and SUNCT on such a small worldwide, and even smaller local, experience. However, based on the available evidence, we propose that all SUNA and SUNCT patients undergo high quality MR imaging of the prepontine cistern to rule out pathological processes in the region as well as to examine for neurovascular conflict.

We now offer MVD as a first procedure to those patients with neurovascular conflict. As with every neurosurgical procedure, MVD carries risks including cerebrospinal fluid leak, neurological deficit or death. Nevertheless, in experienced centres, the risk of serious harm is <1% and MVD in such patients is the closest that we can offer to a symptomatic "cure". We reserve neuromodulation for patients without MRI evidence of trigeminal neurovascular conflict or for those with conflict who have not responded to MVD. In these patients, we offer ONS, reserving DBS for when ONS is not available or has failed to provide sufficient benefit.

CONCLUSION

In patients with medically intractable SUNCT and evidence of neurovascular conflict on MR imaging, MVD may be considered before offering neuromodulation procedures.

Conflict of Interest Statement

Manjit Matharu serves on the advisory board for Allergan, St Jude Medical and Medtronic, and has received payment for the development of educational presentations from Allergan, Merck Sharpe and Dohme Ltd, Medtronic and electroCore.

Ludvic Zrinzo has received payment for the development of educational presentations from Medtronic, St Jude Medical, Boston Scientific, Elekta and Autonomic Technologies.

Samih Hassan, Susie Lagrata and Andrew Levy have no conflicts of interest to declare in relation to this manuscript.

Ethics:

Both patients have given written consent for the publication of case report.

ACKNOWLEDGEMENTS

The Unit of Functional Neurosurgery, UCL Institute of Neurology, Queen Square, London is supported by the Parkinson's Appeal and the Sainsbury Monument Trust.

Clinical Implications

Microvascular decompression is a valid treatment option for short-lasting unilateral neuralgiform headache attacks with autonomic symptoms

Please insert table 1.

Please inset figure 1

Figure 1: Left column: Patient 1 with right sided SUNCT. **A:** High resolution axial CISS 1.5 MRI sequences confirming neurovascular conflict with the right trigeminal nerve. **B:Intraoperative microscope images:** A leash of arterial vessels can be seen in conflict with the right trigeminal nerve in the first image. After retraction of the intervening petrosal vein, one of the offending arteries is clearly seen passing between the fascicles of the trigeminal nerve in the second image. After mobilisation of the offending vessels and splitting of the trigeminal fascicles, Teflon felt has been placed between the most superficial vessel and the surrounding trigeminal fibres in the third image. Further Teflon pieces were placed between the offending vessels and trigeminal nerve prior to surgical closure (not shown).

Right column: Patient 2 with left-sided SUNCT. **C:** High resolution axial CISS 1.5 MRI sequences confirming neurovascular conflict with the left trigeminal nerve. **D:Intraoperative microscope photos:** In the top image, thick arachnoid membranes can be seen matting a loop of the superior cerebellar artery to the superior and medial aspect of the left trigeminal nerve. After division of the arachnoid membranes and mobilisation of the offending vessel, the second image gives a clearer view of the underlying anatomy. The thin white band of the fourth cranial nerve can be seen coursing around the midbrain in the hiatus between petrosal vein and tentorium. The lowest image documents the bright white Teflon felt placed between offending vessel and trigeminal nerve.

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