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Non-invasive Neuromodulation

Rachel Pickering- Clinical Nurse Specialist

Headache and Facial Pain Group

The National Hospital for Neurology and Neurosurgery London, UK

Disclosures

I have received funding from Teva for providing educational sessions

Transcranial Magnetic Stimulation (TMS)	Non-invasive vagal nerve stimulation (VGS) – gammaCore	Non-invasive supraorbital nerve stimulation – Cefaly	Trigeminal and occipital nerve stimulation - Relivion	Remote electrical neuromodulation (REN) – Nerivio
FDA and NICE approved 2014	FDA approved 2017 NICE approved 2019	– Cefaly FDA approved 2014, (Recent) evaluation by NICE update 2022 – recognized as acute but not routinely funded	FDA approved 2021	FDA approved 2023
Approved for abortive and preventative treatment	Approved for abortive and preventative treatment	Approved for abortive and preventative treatment	Approved for acute treatment	Approved for acute and preventative treatment

Non-Invasive Neuromodulation:
Transcutaneous supra-orbital nerve stimulation (tSNS)

Non-Invasive Neuromodulation: Transcutaneous supra-orbital nerve stimulation (tSNS)

Cefaly device-

100 Hz for 60 min for acute treatment

60 Hz for 20 min daily for preventive treatment

Impulses can be increased in intensity

Cost: £378 for device £320 refund if sent back within 60days

Purchased through the cefaly website (include link to website)

Should try for 2-3 months.

Side effects: rare, skin reaction to electrode, fatigue during and after session and headache after the session

CI with pacemaker, electrical device

Non-Invasive Neuromodulation: Transcutaneous supra-orbital nerve stimulation (tSNS)- evidence

Study	Number	Treatment	Outcome
Single pilot study open label[1]	10 episodic migraine patients	Acute treatment	13% pain freedom during attack
Double blind, sham controlled, parallel group study of eTNS vs sham [2]	106 episodic migraine patients	Acute treatment	59% reduction in pain vs 39% at 1hr* Significant reduction in VAS 1,2 + 24hrs
Prospective, randomized, sham controlled, double blinded, multicentre[3]	67 episodic migraine patients	3 months, preventative	Monthly migraine days were reduced by 30% in treatment group but only 5% in sham (p=0.054). 50% responder rate: eTNS 38.1%, Sham 12.1% (p = 0.023
Prospective, multicentre, open label data[4]	19 patients with chronic migraine	4 months, preventative	Mean decrease migraine days 31% Mean decrease acute medication use 49.6% MO not appear influence response
prospective, multi-center clinical study. Open label [5]	27 patients with EM or CM completed	3 month, preventative	Significant reduction monthly headache days, moderate to severe headache days and use of analgesia

1) Gerardy et al. Cephalalgia 2009;29:134
2) Chou DE et al. Cephalalgia. 2019;39(1):3-14
3) Schoenen et al. Neurology 2013;80:697-704
4) Di Fiore et al. Neurol Sci 2017:38(S1):S201-206
5) Vikelis et al. BMC Neurol 2017;17:97

Single-pulse transcranial magnetic stimulation (sTMS)

Single-pulse transcranial magnetic stimulation (sTMS)

- Portable and rechargeable- activated every 3 months with prescription
- Device placed at the back of the head which delivers a brief magnetic pulse
- For acute treatment- 2-4 pulses
- For preventatives treatment- 4 pulses twice daily

Cost= free 3 month trial

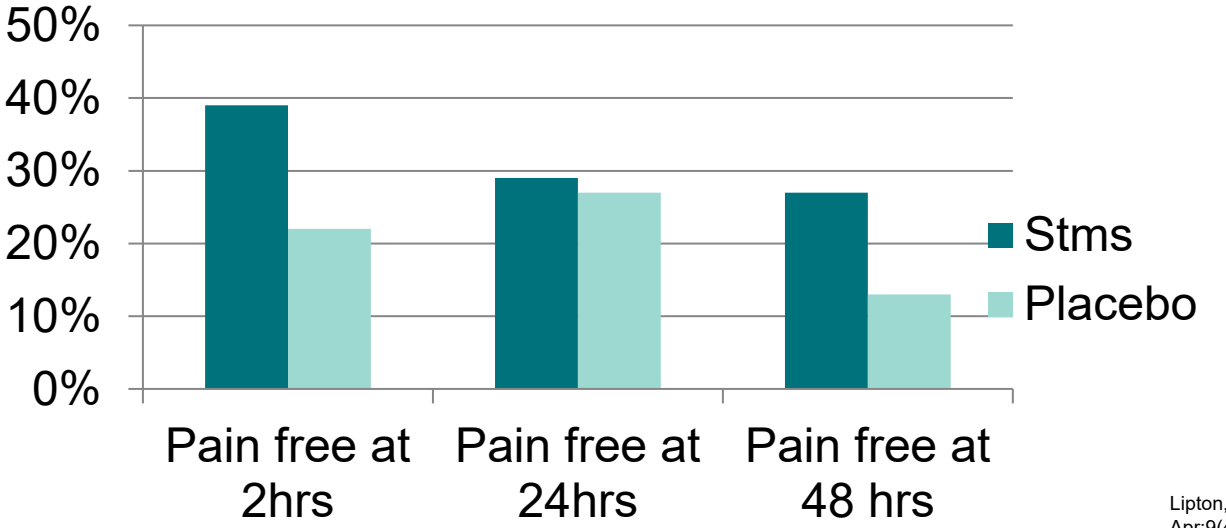
£185 per month thereafter

- NICE approved in 2014 for acute and preventative treatment of migraine. Not available on the NHS, available via private prescription
- Side effects can include scalp discomfort at site of stimulation, tingling, light headedness, transient tinnitus
- Contra indicated for patients with pacemaker, shunt, spinal cord stimulator

Single-pulse transcranial magnetic stimulation (sTMS)- evidence

ACUTE

Lipton et al (2010)- randomised sham-controlled trial for acute treatment for patients with migraine with aura



Lipton, R (2010) Lancet neurology. Apr;9(4):373-80

Single-pulse transcranial magnetic stimulation (sTMS)- evidence

Prevenative

EPOUSE study (Starling et al 2018)

Multicenter, prospective, single-arm, open-label observational study in the US.

Included episodic and chronic migraine patients (4-25 headache days/ month)

1 month of baseline and 3 months of treatment

	sTMS	Placebo
Mean reduction in headache days per month	-2.75 (from 9.1 baseline)	-0.63
≥50% responder rate	46%	~20% (placebo benchmark

Starling AJ, et al Cephalalgia. 2018;38(6):1038-48.

Non-invasive Transcutaenous Vagal Nerve Stimulator (gammacore)

Non-invasive Transcutaenous Vagal Nerve Stimulator (gammacore)

Handheld portable device that delivers mild electrical stimulation to the cervical branch of the vagus nerve via the skin of the neck

- Provided free of charge for 1st 3 months (93 days)
- Subsequent costs £625 for 93 days (excluding VAT)
- Approved by NICE 2019 for Cluster headaches
- Not available on NHS for migraine

Side effects include stiff neck, application site discomfort, sore throat, dizziness
Contraindications include active devices near the site of stimulation (such as pacemakers, defibrillators), as well as carotid atherosclerosis, history of cervical vagotomy, significant hypertension, hypotension, bradycardia, or tachycardia.

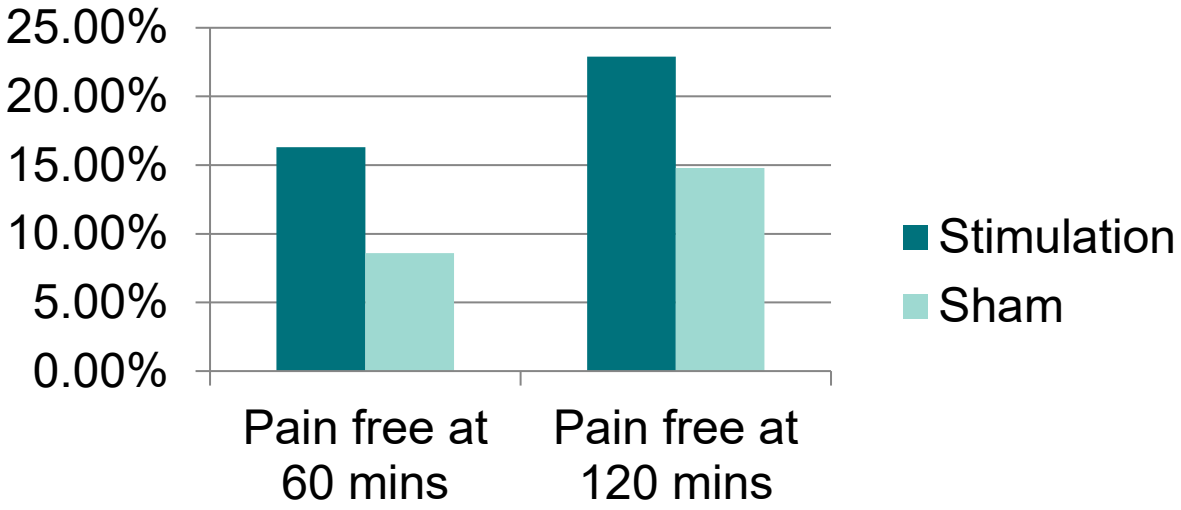
Non-invasive Transcutaenous Vagal Nerve Stimulator (gammacore) for migraine

For acute attacks of migraine, treatment consists of up to two stimulations applied at headache onset, followed by two more after 20 min and after 2hr if needed.

Prophylaxis of migraine consists of two stimulations (each 2 min long) TDS.

Non-invasive Transcutaenous Vagal Nerve Stimulator (gammacore) for migraine

PRESTO study (Tassorelli et al, 2018)- large randomised sham-controlled trial of GammaCore for the acute treatment of migraine attacks



Non-invasive Transcutaenous Vagal Nerve Stimulator (gammacore) for cluster headache

Acute

- Apply gel before each stimulation
- Use 1 application and if it doesn't help you can try again after 10-20mins up to TDS
- After two minutes GammaCore will beep twice and automatically turnoff. The device should remain off for ten seconds after each stimulation Stimulations can be performed on the same side of the neck, or you can switch sides, if preferred.

Preventative

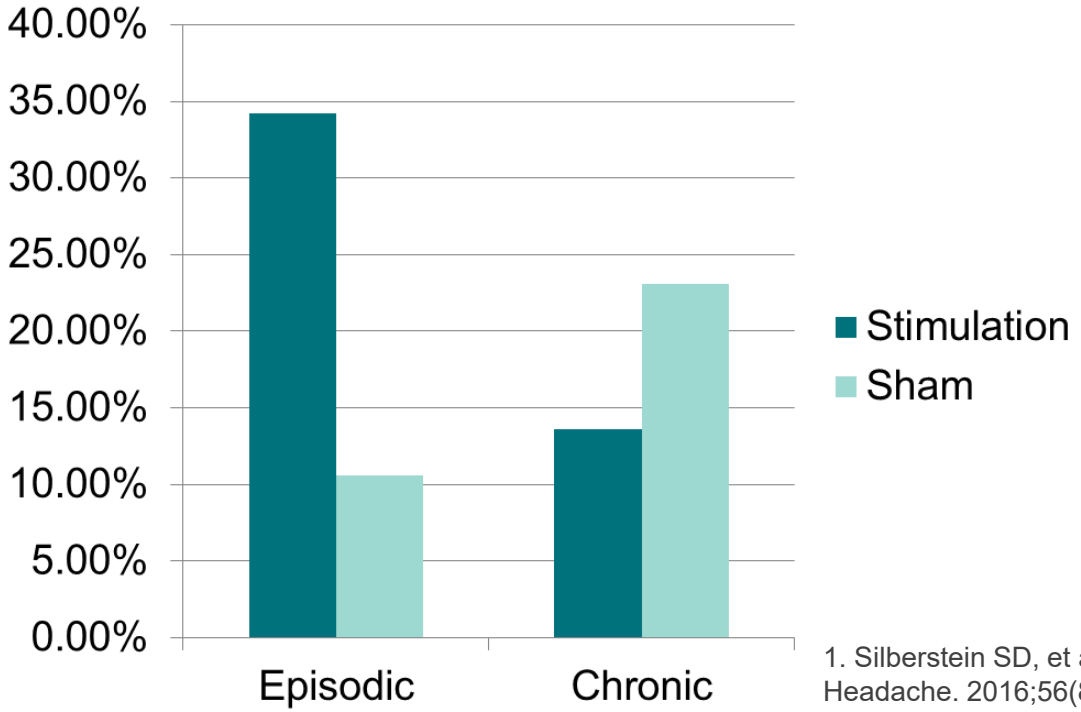
- Used B2 applications TDS

- GammaCore can deliver up to 30 stimulations per day

Non-invasive Transcutaenous Vagal Nerve Stimulator (gammacore) for cluster headache

ACT 1[1] and ACT2[2] trials (double-blind, randomised sham controlled trials) studied devices use in adults with episodic (101 patients) and chronic cluster headache (49 patients)

Primary endpoint for ACT 1: Percentage of patients reporting "mild pain" or "no pain" 15 minutes after treating their first attack



1. Silberstein SD, et al. Headache. 2016;56(8):
2. Goadsby PJ, et al. *Cephalalgia*. 2018;38(5):959-969

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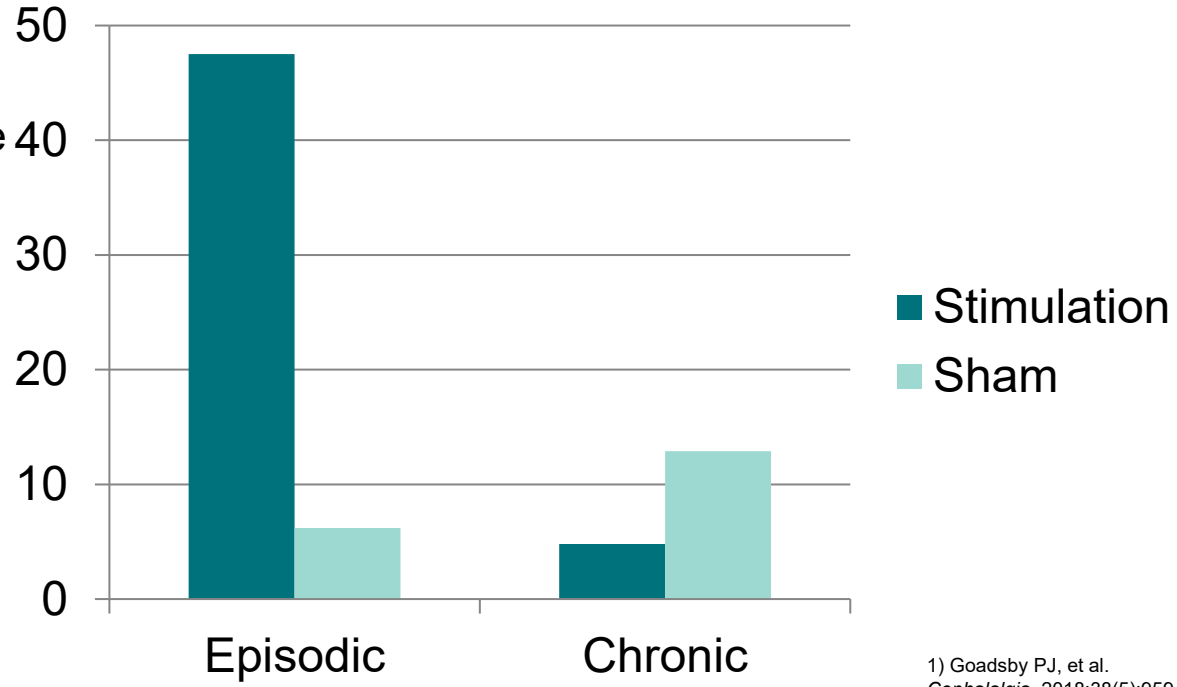
Non-invasive Transcutaenous Vagal Nerve Stimulator (gammacore) for cluster headache

Primary endpoint for ACT 2[1]: Percentage of total attacks that were pain-free at 15 minutes after initiation of treatment



1) Goadsby PJ, et al. *Cephalalgia*. 2018;38(5):959-969

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Non-invasive Transcutaenous Vagal Nerve Stimulator (gammacore) for cluster headache

Prevention and Acute Treatment of Chronic Cluster Headache (PREVA) Study [1] (Gual et al 2015)

Prospective open-label, randomised study that compared adjunctive prophylactic n-VNS with standard of care alone

Higher response rates were observed in the nVNS group, with more patients achieving ≥50% and ≥75% reductions in attack frequency

N-VNS group showed reduced use of subcutaneous sumatriptan and high flow oxygen use

1. Gaul, C *et al*. Cephalalgia. 2016 May;36(6):534-46

Remote Electrical Neuromodulation (REN) – Nerivio device

Remote Electrical Neuromodulation (REN) – Nerivio device

Stimulates upper arm peripheral nerves (Adelta and C fibres) to induce conditioned pain modulation (CPM)

Smartphone-controlled wireless device applied for 30-45 minutes on the upper arm within 1 hour of attack onset

Preventative used every other day for 45 mins

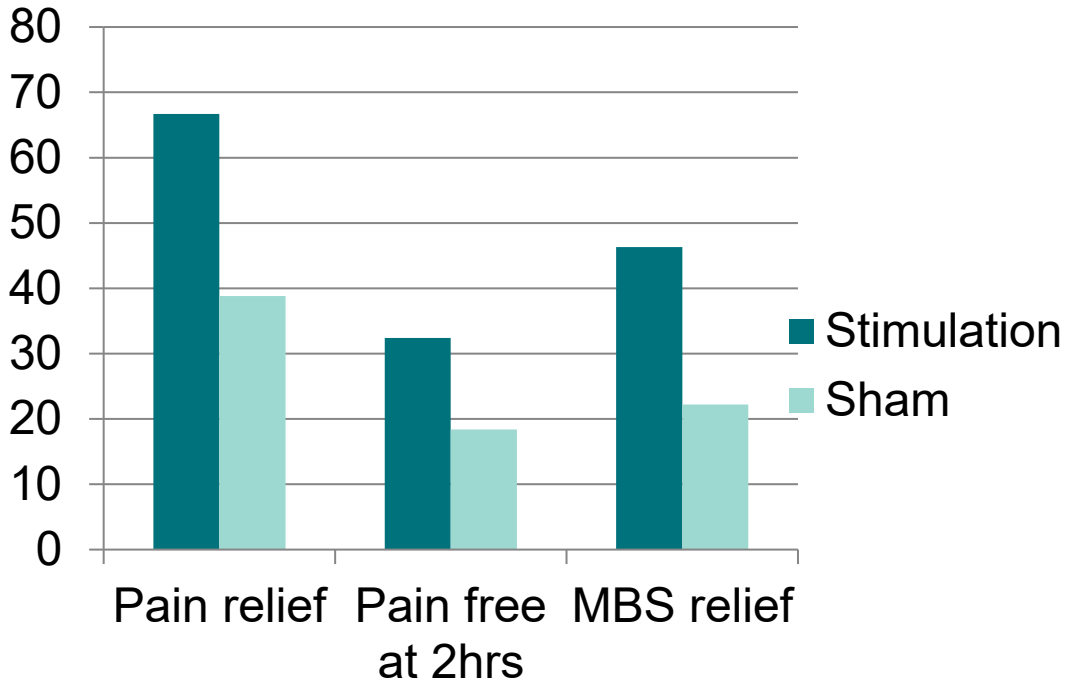
Side effects mainly related to topical peripheral sensations of warmth, itching, arm pain, redness and numbness

£249/unit (18 treatments)

Remote Electrical Neuromodulation (REN) – Nerivio device

Randomised double-blind, sham-controlled multicenter study looked at the Nerivio device for the acute treatment of episodic migraine

Active stimulation was better than sham in achieving pain relief [1]



1. Yarnitsky D et al. Headache. 2019;59(8):1240-52

Remote Electrical Neuromodulation (REN) – Nerivio device

Preventative treatment [1]

Double blinded study demonstrated that using Nerivio every other day resulted in a significant reduction of 3.97 migraine days per month, compared to 1.28 days in the sham group.

- The device also reduced the number of moderate/severe headache days and acute medication usage

1. Tepper SJ, et al. Headache. 2023 Mar;63(3):377-389

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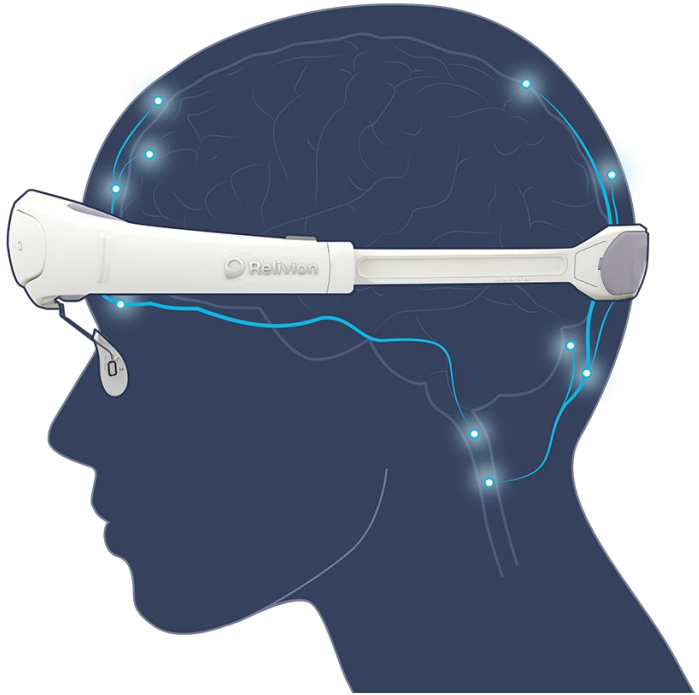
Combined Trigeminal and Occipital Nerve Stimulation (CTONS)- Relivion Device



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Combined Trigeminal and Occipital Nerve Stimulation (CTONS)- Relivion Device

For acute treatment of migraine

Multi-centre, double blind, sham controlled, parallel group study

55 episodic and chronic patients (27 active treatment; 28 sham)

60 +/- 20min home treatment within 45mins of migraine episode onset.

	Neurostimulation	Sham
Pain freedom 2 hrs	41.7%	20%
Pain relief 2 hrs	76.2%	31.6%
>50% VAS reduction	66.7%	32%

14 subjects (6 active, 8 sham) had mild adverse events; headache (n=2), numbness/paraesthesia (n=2), skin irritation (n=1), nausea (n=1), and itching scalp

Daniel O, et al. Pain Ther. 2022;11(3):907-22

Advantages

Safe and well tolerated

Reduces risk of medication overuse headache

Can be used at home by the patient- increased independence, reduced hospital visits

Self-management strategy

Some patients want alternatives to pharmacological treatments

Co-morbities that preclude pharmacological

Based on speakers experience

Limitations & Challenges

Cost/ insurance coverage

Access to treatment is limited

Small evidence base compared to more established pharmaceutical treatments

Correct use is critical- application technique and frequency of use

Headache diaries must be kept for objective outcome measure

Ensuring regular and frequent follow up- demand vs capacity

Based on speakers experience

The Future…

Digital healthcare- use of apps to track usage and outcomes

Wearable devices

New waveforms and types of neuromodulation

Based on speakers experience