Procedural Approach in Migraine Treatment

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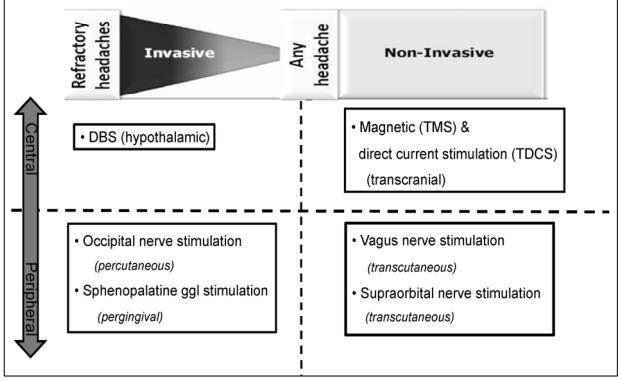
Neuromodulation

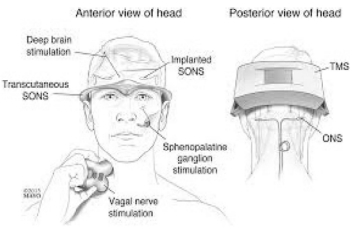
The electric torpedo | The Electreat | ECT | DBS

Nerves can be stimulated with electricity, which can either inhibit or generate neural impulses depending on the stimulation parameters

Classification



Peripheral vs. central stimulation Targets in headache



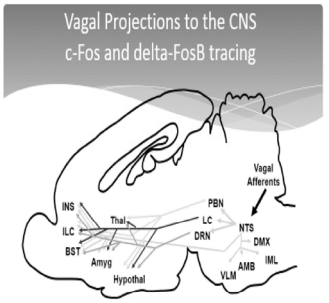
1.Chronic cluster headache (and other TACs)
2.Chronic and episodic migraine

Pain medicine 2015: 16: 1827-1834

VNS in migraine

- Convenient
- Easy to use
- Portable

- Acute treatment of Migraine
- Preventive treatment of CM
- Cluster headache



INS = insular cortex; ILC = infralimbic cortex; PBN = parabrachial nucleus; LC = locus coeruleus; DRN = dorsal raphe; NTS = nucleus tractus solitarius; AMB = nucleus ambiguus; VLM = ventrolateral medulla; IML = intermediolateral cell column

Courtesy of Thomas Cunningham, PhD, University of Texas Health Science Center at San Antonio

Cunningham JT, M. S. (2008). *Neuropsychopharmacology*, Jul;33(8):1884–95.

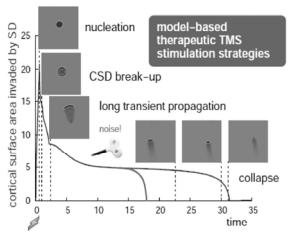
Clinical trial of VNS: Migraine

Study	Principal Investigator	Size (N/attacks)	Format	Status
Acute Treatment				
Acute Migraine	Goadsby	27/80	Open-label	Goadsby P, et al. Effect of noninvasive vagus nerve stimulation on acute migraine: an open-label pilot study. [published online March 7, 2014]. *Cephalalgia*.
Acute Migraine	Grazzi	30/96	Open-label	Grazzi L, et al. Presented at 66th Annual Meeting of the American Academy of Neurology; April 26-May 3, 2014; Philadelphia, PA. Abstract P7.196.
Chronic Migraine	Moscato	22/79	Open-label	Moscato, et al. Presented at 56th Annual Meeting of the American Headache Society; June 26-29, 2014. Abstract LBP 1.
Chronic Migraine/MOH	Rainero	15/362	Open-label	Rainero I, et al. Presented at 66th Annual Meeting of the American Academy of Neurology; April 26-May 3, 2014; Philadelphia, PA. Abstract P1.262.
Preventive Treatment				
Chronic Migraine (M-US-02 [EVENT])	Silberstein	59/-	Double-blind, pilot RCT (inactive sham)	Complete

TMS in migraine

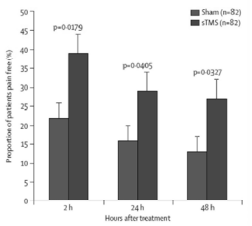
Single-pulse TMS Device: FDA approved for acute treatment of migraine with aura

- sTMS = single pulse
- rTMS = repetitive
- 1Hz=inhibitory, 10Hz=excitatory



sTMS for acute treatment of of MWA

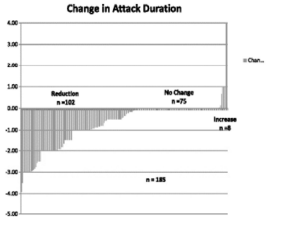
Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham-controlled trial



The LANCET Volume 9, No. 4, p373–380, April 2010

RESEARCH ARTICLE Open Access

Single-pulse transcranial magnetic stimulation (sTMS) for the acute treatment of migraine: evaluation of outcome data for the UK post market pilot program



Bhola et al. The Journal of Headache and Pain 2015

rTMS for migraine prevention

- Low frequency (1Hz): rTMS over the vertex: no superiority vs placebo
- High frequency (>10 Hz) over the prefrontal cortex: conflicting results

Randomized, proof-of-principle clinical trial of active transcranial magnetic stimulation in chronic migraine

Cephalalgia 2014 34: 464-472

High-rate repetitive transcranial magnetic stimulation in migraine prophylaxis: a randomized, placebo-controlled study

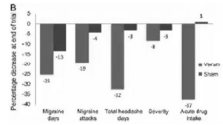
Journal of Neurology 2013:260: 2793-2801

Transcutanous supraorbital nerve stimulation (tSNS) in migraine

Cefaly Migraine Preventing TENS Headband : FDA approved for migraine prevention

Migraine prevention with a supraorbital transcutaneous stimulator

A randomized controlled trial

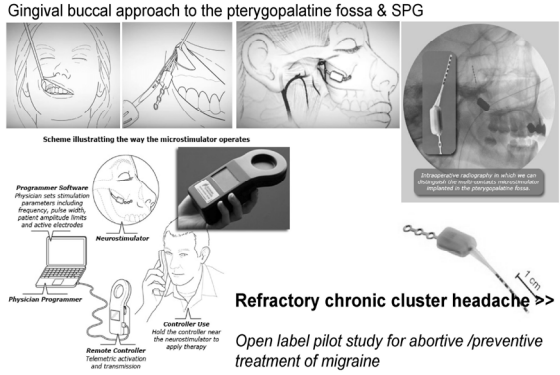


Safety and patients' satisfaction of transcutaneous Supraorbital NeuroStimulation (tSNS) with the Cefaly® device in headache treatment: a survey of 2,313 headache sufferers in the general population

The Journal of Headache and Pain 2013, 14:95

Sphenopalatine Ganglion Stimulation

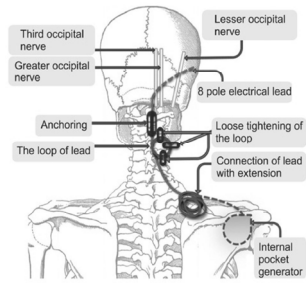
Gingival buccal approach to the pterygopalatine fossa & SPG



Refractory chronic cluster headache >>

Open label pilot study for abortive /preventive treatment of migraine

Occipital nerve stimulation



PRO
- Effect in > 60% of CCH
- Long term F/U data
- Tested in other TACs
- 3 RCTs in CM

CON
- Invasive procedure
- Difficult to blind
- Similar responder in CM
- Paresthesia
- Lead migration and infection in up to 35%

ONS in chronic migraine prevention

	Patients (n)	Follow-up (months)	Main findings	Side-effects
Popeney (2003)[74]	25	18·3	64% of patients improved by at least 50%	Lead migration; infection
Matharu (2004)[75]	8	18	100% of patients improved by at least 50%	Abdominal haematoma; lead migration
Schwedt (2007)[76]	8	19	50% of patients improved by at least 50%	Lead migration
Lipton (2009)*[77]	125	3	No difference *vs* sham	Infection; site pain; sensory symptoms
Marchioretto (2010)*[78]	34	12	Overall 56% frequency reduction	Mild
Saper (2011)[79]	66	3	39% of patients improved by at least 50%	Lead migration; infection
Silberstein (2011)*[80]	157	3	Reduction in headache days by 36%	Infection
Reed (2011)*†[81]	44	13	Overall 57% frequency reduction	..
Narouze (2011)*[82]	12	13	Overall 81% frequency reduction	Slight lead migration
Linder (2011)*†[83]	13	NR	Overall 80% frequency reduction (60% pain free)	..
Total	500	..	About a 56% improvement	..

Combined ONS & SONS

Cephalalgia
International Headache Society
doi:10.1111/j.1468-2982.2009.01996.x

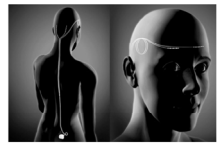
Combined occipital and supraorbital neurostimulation for the treatment of chronic migraine headaches: initial experience

KL Reed[1], SB Black[2], CJ Banta II[3] & KR Will[3]
[1]Department of Anesthesiology, Presbyterian Hospital of Dallas, [2]Medical Director of Neurology, Baylor University Medical Center of Dallas, and [3]Department of Orthopedic Surgery, Presbyterian Hospital of Dallas, Dallas, TX, USA

Dual occipital and supraorbital nerve stimulation for chronic migraine: a single-center experience, review of literature, and surgical considerations

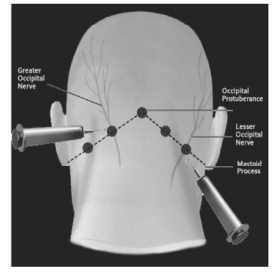
Shannon Hann, M.D., and Ashwini Sharan, M.D.
Department of Neurosurgery, Thomas Jefferson University, Philadelphia, Pennsylvania

Neurosurg Focus 35 (3):E9, 2013

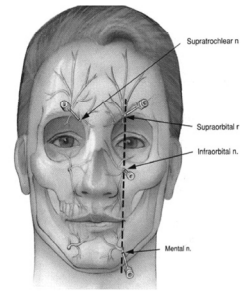


Peripheral Nerve Block in migraine

Greater Occipital nerve



Supraorbital nerve



Peripheral Nerve Block in migraine

Study design	n	Intervention	Results	Reference
Retrospective	97	A single or repeated GON block(s) using lidocaine and methylprednisolone	Headache improvement in 34% of subjects for up to 6 months	Gawel and Rothbart[5]
Retrospective	27	Repeated GON and SON blocks using bupivacaine	Headache improvement in 85% of subjects for up to 6 months	Caputi and Firetto[6]
Retrospective	14	A single GON block with or without SON block using lidocaine and epinephrine	Head pain reduction in 6% of subjects at 30 minutes	Bovim and Sand[3]
Prospective, non-controlled	19	A single GON block using lidocaine and triamcinolone, and TPIs using lidocaine	A significant decrease in head pain in 80% of subjects	Ashkenazi and Young[2]

GON = greater occipital nerve; n = number of subjects; SON = supraorbital nerve; TPI = trigger point injections.

Ashkenazi, Avi, et al. "Peripheral nerve blocks and trigger point injections in headache management–A systematic review and suggestions for future research." Headache: The Journal of Head and Face Pain 50.6 (2010): 943-952.

RCT on GONB for migraine : Different methodologies & results

Acta Neurol Scand. 2015 Oct;132(4):270-7. doi: 10.1111/ane.12393. Epub 2015 Mar 13.

Greater occipital nerve blockade for the treatment of chronic migraine: a randomized, multicenter, double-blind, and placebo-controlled study.

Inan LE[1], Inan N[2], Karadas Ö[3], Gül HI[4], Erdemoğlu AK[5], Türkel Y[6], Akyol A[6].

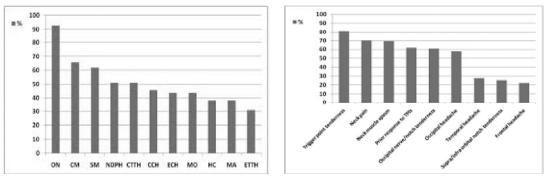
Cephalalgia. 2015 Oct;35(11):959-68. doi: 10.1177/0333102414561872. Epub 2014 Dec 12.

Occipital nerve block for the short-term preventive treatment of migraine: A randomized, double-blinded, placebo-controlled study.

Dilli E[1], Halker R[2], Vargas B[2], Hentz J[2], Radam T[2], Rogers R[2], Dodick D[2].

No universal technique or approaches

Indication for the use of trigger point injection



By headache diagnosis

By Symptoms

Reference	Headache Dx	Study design	Subject	Injection method	Agents	Injection frequency	Outcomes
Ashkenazi and Young	CM /EM	prospective	19	GONB, TPI	Lidocaine + triamcinolone lidocaine	1 single series of injection	89.5% of patients 20 minutes after treatment
Garcia_Leiva et al	CM /EM	prospective	52	TPI	Ropivacaine	1 series of weekly injection over 12 wks	59.6% of patients reported being much or very much improved after 12 week treatment period

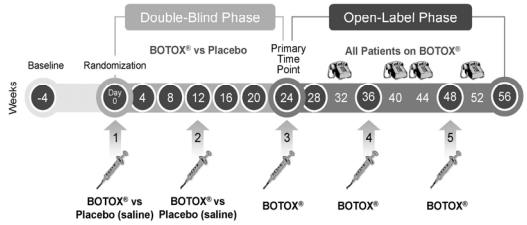
Botulinum Toxin for Chronic Migraine

	Study, Year	Population and Headache Characteristics	Dose and Injection Paradigm[1-3]	Results
CM	Mathew et al, 2005	N = 356; ≥15 headache days/month	3 consecutive identical treatments at 90-day intervals with placebo or BOTOX® 105–260 U; follow-the-pain	Negative
CM	Silberstein et al, 2005	N = 702; ≥15 headache days/month	3 consecutive identical treatments at 90-day intervals with placebo or BOTOX® 75, 150, or 225 U; fixed-site, fixed-dose	Positive
CM	Aurora et al, 2010	N = 679; ≥15 headache days/month, ≥ 50% migraine or probable migraine days	2 injection cycles, 12 weeks apart with placebo or BOTOX® 155 U, maximum dose 195 U; modified follow-the-pain	Positive
CM	Diener et al, 2010	N = 705; ≥15 headache days/month, ≥ 50% migraine or probable migraine days	2 injection cycles, 12 weeks apart with placebo or BOTOX® 155 U, maximum dose 195 U; modified follow-the-pain	Positive

1. Aurora SK. Presented at AHS 2006.
2. Aurora SK, et al. *Cephalalgia*. 2010; Epub ahead of print.
3. Diener HC, et al. *Cephalalgia*. 2010; Epub ahead of print.

PREEMPT Study Design[1]

- 만성 편두통 환자에 대한 대규모 임상 프로그램 (1384명)
  - ✓ 북미와 유럽의 122개 사이트
  - ✓ 24주, 무작위, 이중맹검, 위약 대조, 32주 개방표지 임상시험

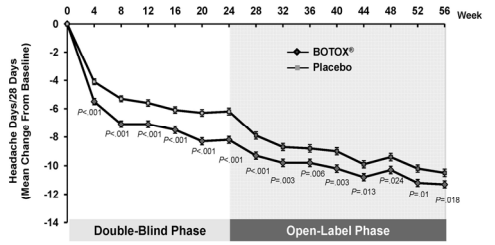


전화 조사 : 두통 증상과 약물복용이 전화 일지로 기록됨
보톡스 주사

1. Dodick DW, et al. *Headache*. 2010;50:921-936.

PREEMPT Pooled Analysis:
보톡스® 를 투여받은 환자에서 편두통 발생일수가 평균적으로 8일 감소되었음

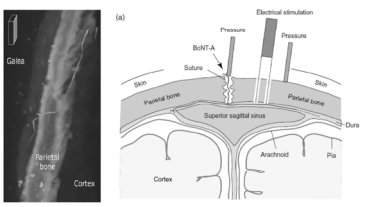
56주 후, 보톡스® 를 투여 받은 환자의 약 **70%**에서, 편두통 발생일수가 **50%** 이상 감소하였습니다.

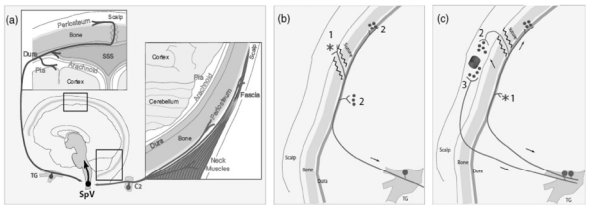


Mean ± standard error.
The double-blind phase included 688 subjects in the BOTOX® group and 696 in the placebo group.
Headache days at baseline: 19.9 BOTOX® group vs 18.9 placebo group, *P*=.328.

1. Aurora SK, et al. Presented at IHC 2009.

Selective inhibition of meningeal nociceptors by BTX





J Comp Neurol. 2009 July 20; 515(3): 331–348

Order of injection and patient position: FSFD

- The anatomic injection sites follow distributions and areas innervated by the trigeminal - cervical nerve complex

Supine

A. Corrugator: 5 U each side
B. Procerus: 5 U (one site)
C. Frontalis: 10 U each side

D. Temporalis: 20 U each side

Sitting

E. Occipitalis: 15 U each side

F. Cervical paraspinal: 10 U each side
G. Trapezius: 15 U each side

0.1 mL = (5 U/site).
Blumenfeld AM et al. Presented at AAN 2010.

Summary

- Invasive neurostimulation for very severe and treatment refractory migraine
- Noninvasive neurostimulation as useful adjuncts to more conventional therapies
- FDA approved: SONS (Migraine prevention) and TMS (migraine with aura)
- Botulnum Toxin for CM, CM with MOH, refractory CM : primary Treatment