Nerve stimulation and nerve block in headache (treatment)

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南區頭痛讀書會

Outline:

I. Nerve block: introduction
II. Occipital nerve block in headache treatment
III. Nerve stimulation: introduction
IV. Nerve stimulation in headache treatment

I. Nerve block: introduction

Why nerve block?

- Peripheral nerve block has long been used for headache treatment
- Maybe indicated for: those are resistant or intolerant to pharmacological treatment
- Benefits: rapid relief, safe, ease to perform

What to inject?

Local anesthesia*

- **lidocaine** (1%): onset: 4-8 min, duration: 1-2 hr
- mepivacaine
- **bupivacaine** (0.25-0.5%): onset: 8-12 min, duration: 4-6 hr
- prilocaine

± Steroid

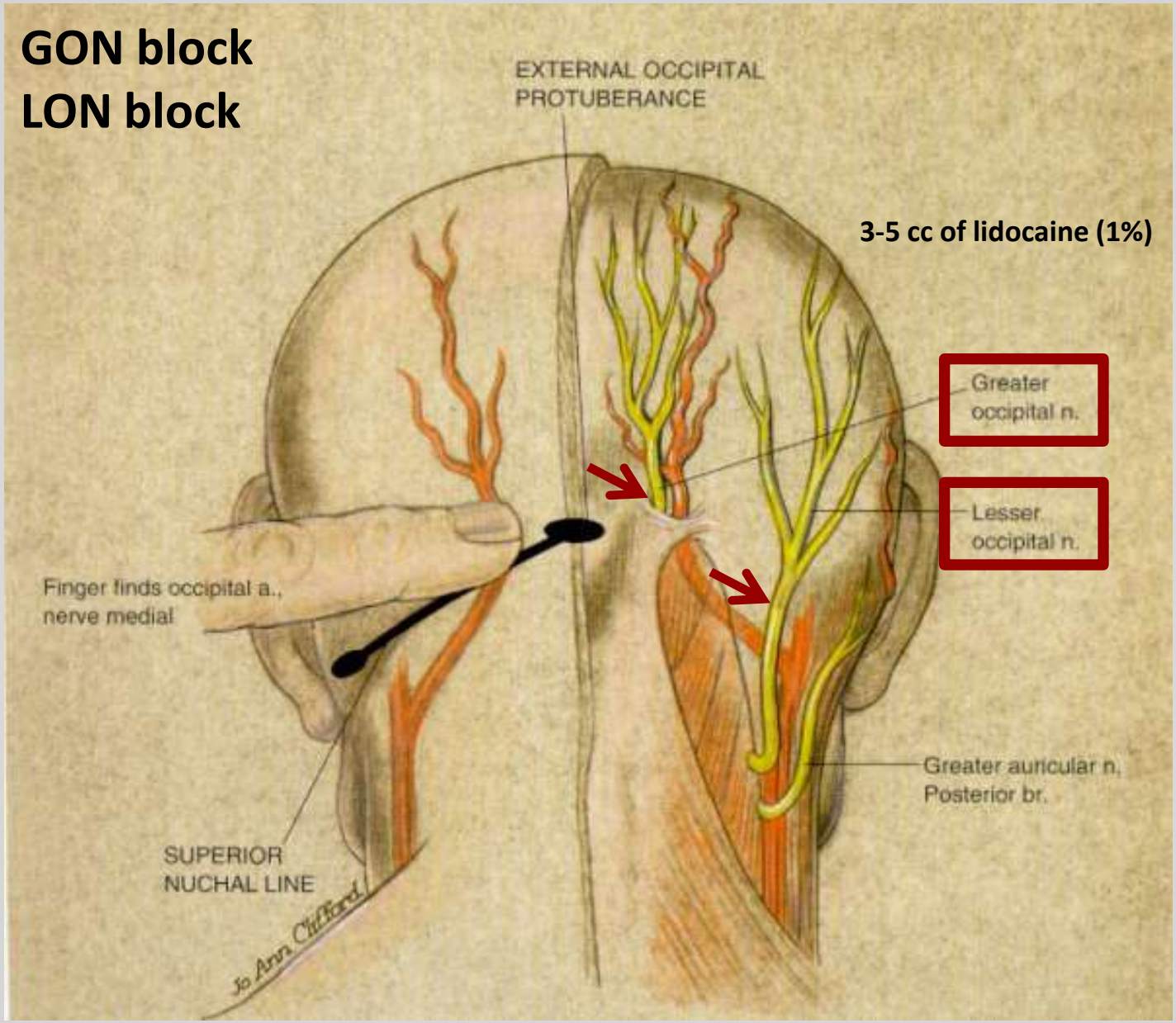
- triamcinolone
- methylprednisolone

* Many choose to combine bupivacaine + lidocaine
* Do not use epinephrine

Where to inject?

Nerves	indications
Greater occipital nerve (GON)	Various headache syndromes
Lesser occipital nerve (LON)	?
Auriculotemporal nerve	?
Supraorbital nerve (SON) Supratrochlear nerve	Supraorbital neuralgia Migraine
Infraorbital nerve	Infraorbital neuralgia Trigeminal neuralgia
Sphenopalatine ganglion	Acute cluster headache

GON block
LON block

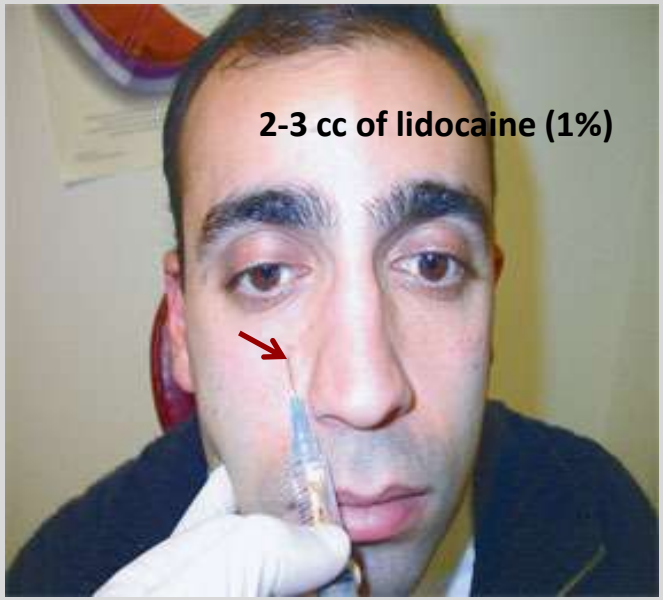


Supraorbital nerve block
Supratrochlear nerve block

- Supraorbital nerve: Insert the needle **toward** the supraorbital foramen

- Supratrochlear nerve: insert the needle along the upper orbital margin, 1 cm medial to the supraorbital foramen

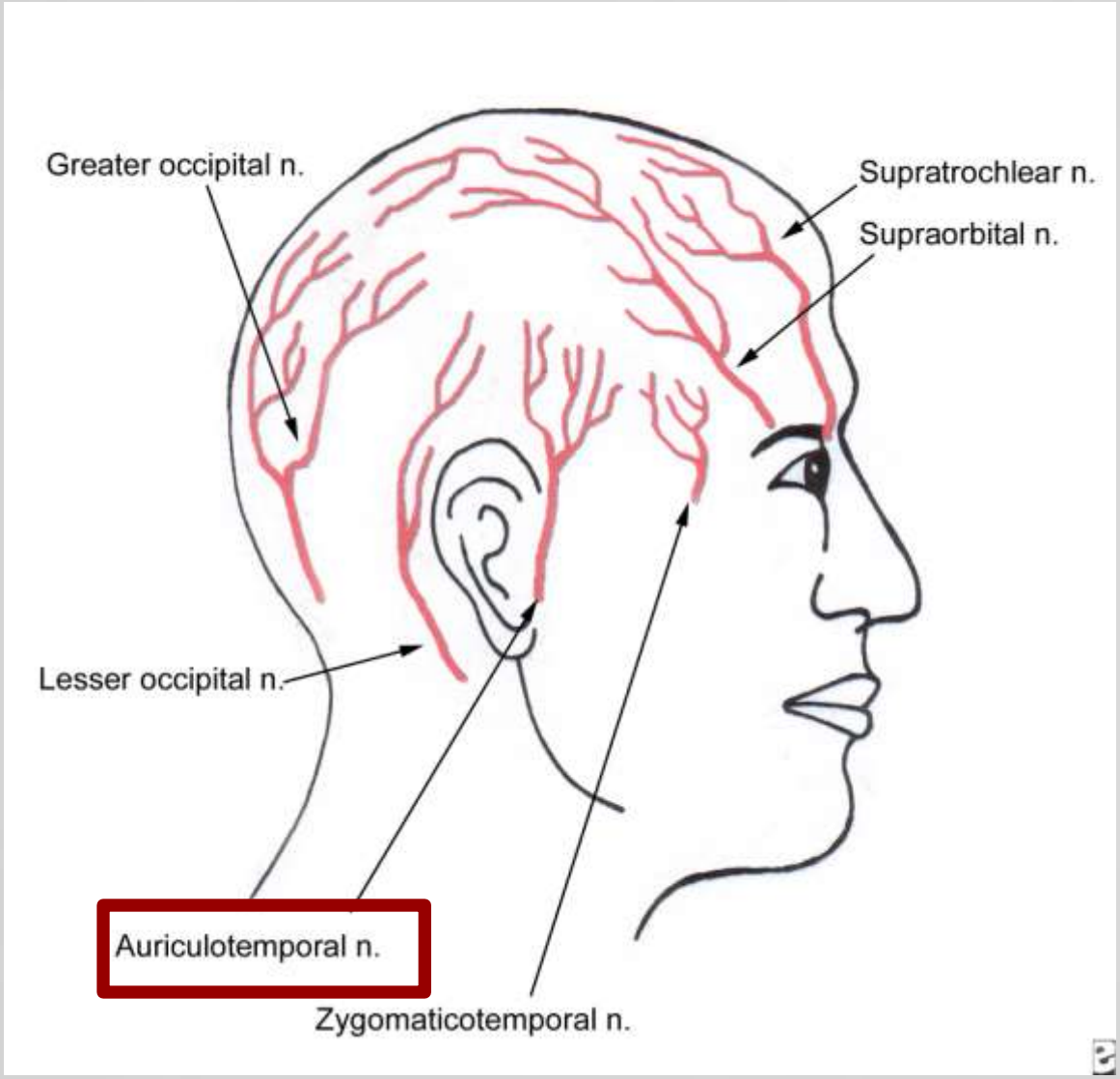
Infraorbital nerve block



- Infraorbital nerve: inser the needle about 1 cm inferior to the infraorbital foramen and advanced upward **toward** the foramen

American family physician 2004; 69: 585-90.

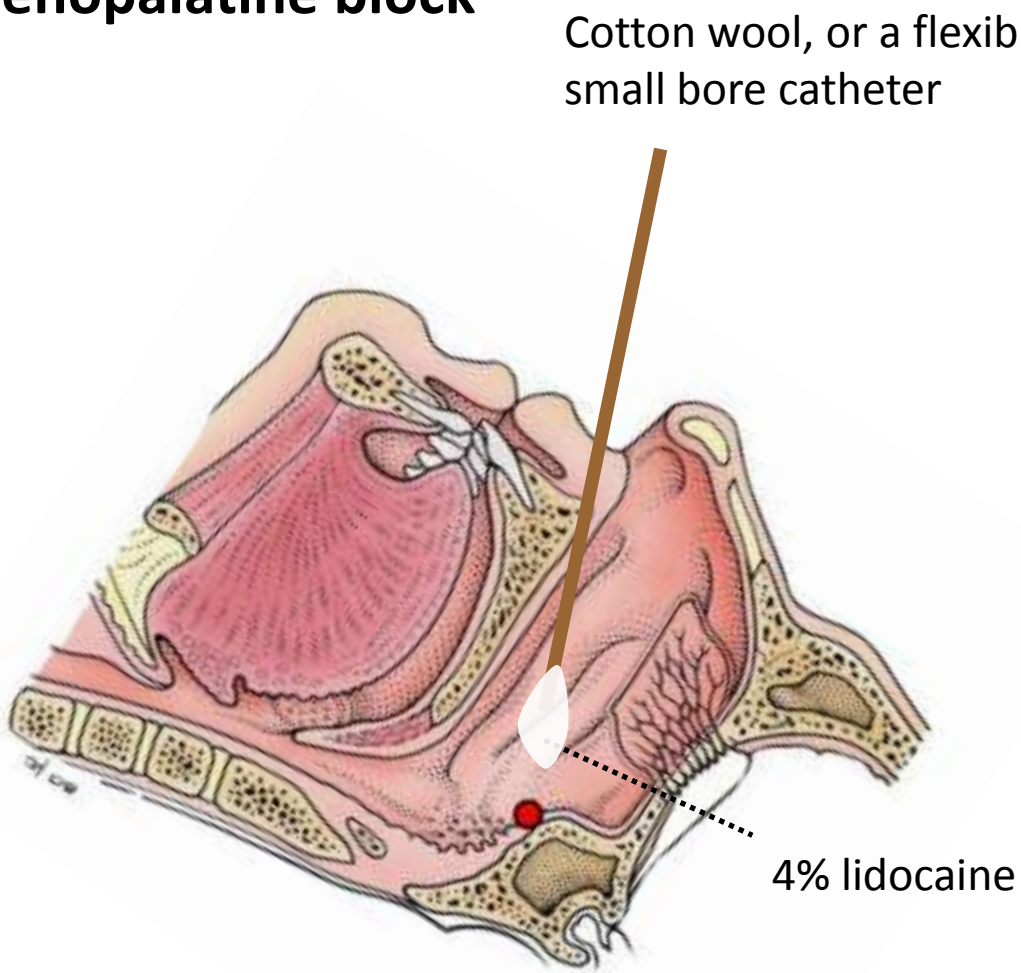
Auriculotemporal nerve block



2-4 cc of lidocaine (1%)

Insert the needle superiorly and anteriorly to the tragus.

Sphenopalatine block



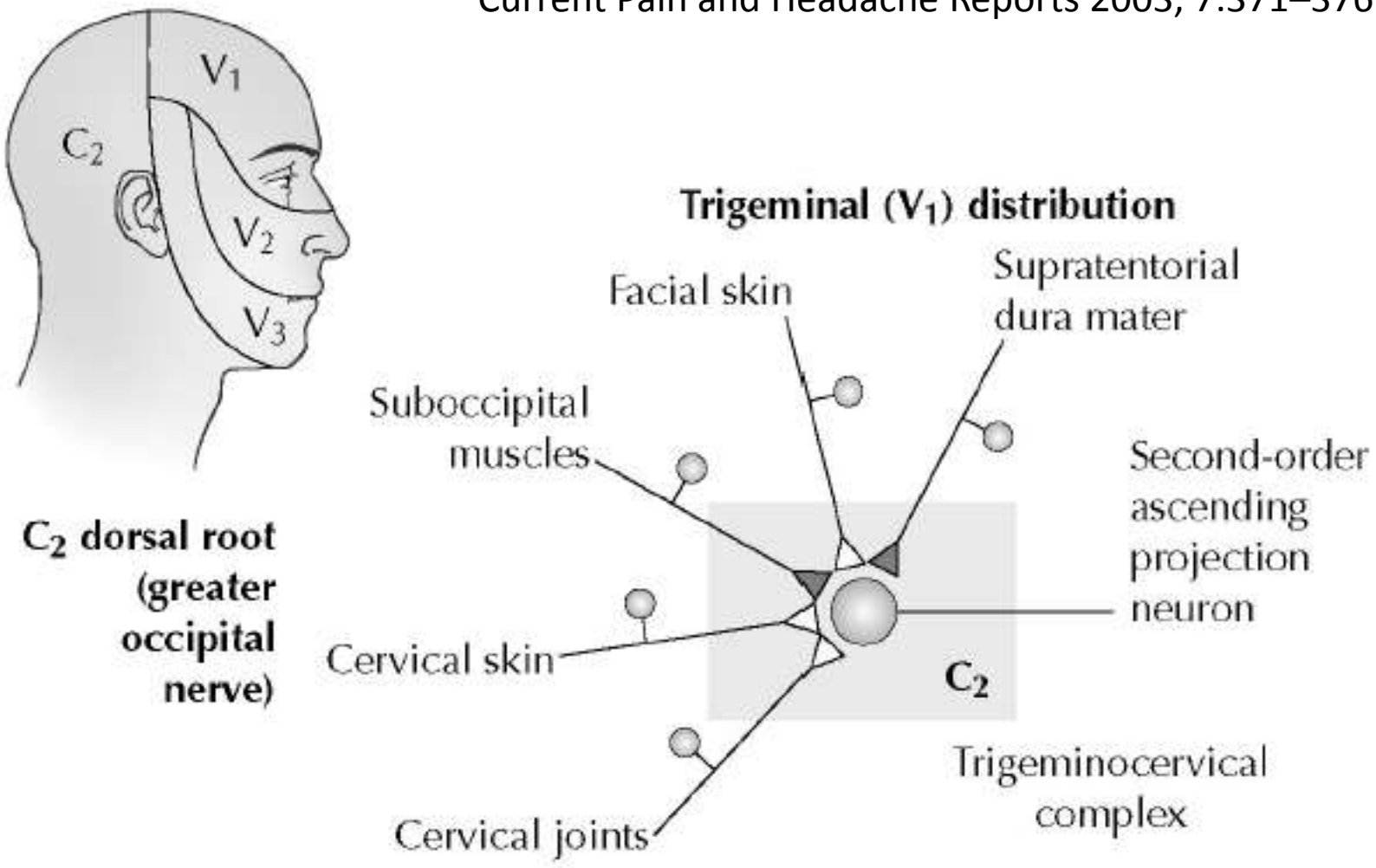
the head is rotated in a reclining position on his back about 45 degrees backwards and 30 ° - 40 ° towards the affected side.

Possible mechanisms of nerve block effects in primary headache

- The mechanisms are still unknown!
  - Primary headaches (esp. migraine) and occipital neuralgia may coexist
  - ↓afferent tone… ↓activity at the first synapse of the trigeminal nociceptive pathway
  - Blocking the meningeal nociceptors outside the skull

- However, it can't explain the long-term improvement of nerve block on headache

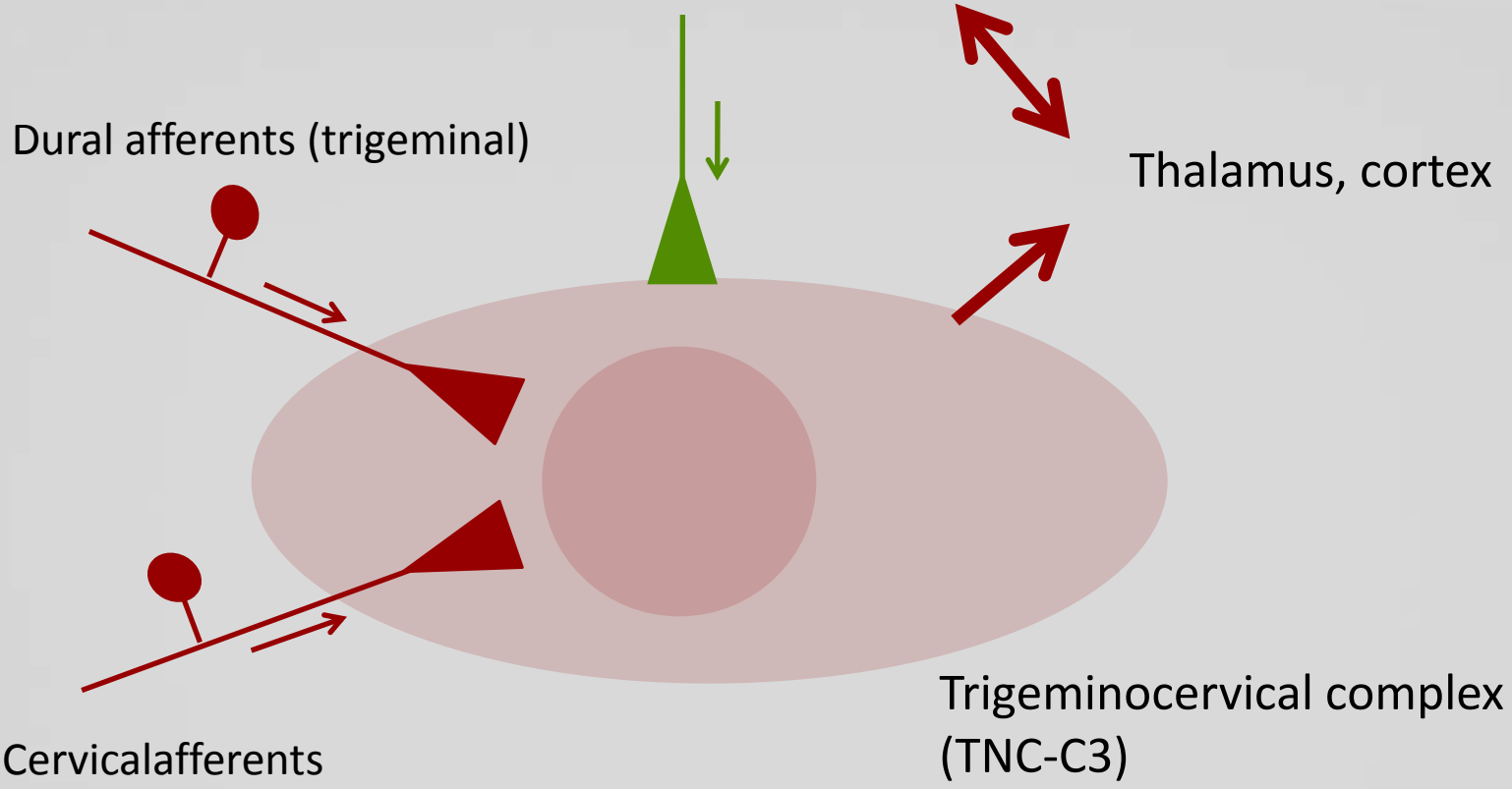
Current Pain and Headache Reports 2003, 7:371–376



The convergence of trigeminal (dura, skin) and cervical (muscle, joints, skin) afferents on to the same nociceptive second-order neuron in the trigeminocervical complex at the level of C2.

Pain modulating system:
PAG, RVM, hypothalamus

Headache 2008; 48: 313-8.



Dural and cervical afferents converge onto the same nociceptive neuron in the trigeminocervical complex (A).
The convergent neuron in the trigeminocervical complex may be sensitized because of an ↑afferent inflow (A) into the spinal cord by strong noxious stimuli. Alternatively, calcium-dependant pain modulatory circuits in the brain stem may contribute to a facilitated processing (B) of nociceptive trigeminal input.

Possible side effect of nerve block

- Local side effect:
  - Local Infection or hematoma
  - nerve damage/neuroma formation
  - Local alopecia
- Systemic side effect:
  - CNS--- **dizziness**, tinnitus, metallic taste, visual disturbance, lip/tongue numbness, LOC, seizure
  - CV--- ↓ventricular contractility & conduction, ↓BP
  - Cushing syndrome (steroid)

II. Occipital nerve block in headache treatment

Occipital nerve block (ONB): proved indications

- Cervicogenic headache
- Occipital neuralgia
- Cluster headache

Headache 2009

Occipital nerve block (ONB): possible indications

- **Migraine**
- Orgasmic headache (?)
- Post-dural puncture headache(?)
- Adjuvant therapy for MOH

Occipital nerve block (ONB): lack of efficacy in the following

- Tension-type headache
- Post-traumatic headache
- Hemicrania continua
- Chronic paroxysmal hemicrania (CPH)

Cervicogenic headache: ICHD-II criteria

- A. Pain referred from the neck and in ≥1 regions of the head or face, fulfilling criteria C & D
- B. Clinical, lab or imaging evidence of a disorder in the C-spine or neck soft tissues known as a valid cause of headache
- C. Evidence that the pain can be attributed to the neck disorder:
  - Clinical signs that implicate a source of pain in the neck, or
  - Abolition of headache following diagnostic blockade of a cervical structure or its nerve supply using placebo- or other adequate controls
- D. Pain resolves in 3 months after successful Tx of the causative disorder

Occipital neuralgia: ICHD-II criteria

- A. Paroxysmal stabbing pain ± persistent aching between paroxysms, in the distribution(s) of the GON, LON, or 3rd occipital nerve
- B. Tenderness over the affected nerve
- C. Pain is eased temporarily by local anesthetic block of the nerve

ONB for cervicogenic headache (1)

	Drugs	Method	Results
Naja `06 (n=32)	LC, LC+epi BP, Fetanyl, clonidine	Unil GON+LOC ± facial n. injection	Time to rescue analgesics: ●Active group: 3.2 d ●Saline group: 1.4 d
Naja `06 (n=47)	As above	Bil injection q2w PRN, if VAS>4 or analgesics >3d/wk	●5.3 (1-13) injections ●96% were pain-free for ≥6 months ●↑Pain-free period with ↑injection no.
Inan `01 (n=28)	LC (Dx) → BP (Tx)	Unil GON qw x2	During 2-month F/U: ●GON block: HA freq ↓90%, severity ↓46% ●C2-3 block: HA freq ↓94%, severity ↓68%
Anthony `00 (n=410)	LC+MP MP LC	Unilateral GON	●LC+MP: 90% had relief for 23.5 d ●MP: 91% had relief for 77 d ●LC during HA: 84% had relief for 1.6-3h

LC = lidocaine, epi = epinephrine, BP = bupivocaine, MP = methylprednisolone

ONB for cervicogenic headache (2)

	Drugs	Method	Results
Vincent `98 (n=41)	LC (Dx) BP (Tx)	Unil GON	●VAS dropped from 3.8 to 2.0
Bovim/Sand `92 (n=24)	LC + epi	Unil GON ± SON	●Tx group: 55% had response after 30 min ●Saline group: no response at all

Conclusion: ONB is effective for cluster headache

Note: different Dx criteria were used among studies… patients with occipital neuralgia may be recruited

ONB for occipital neuralgia

- Occipital neuralgia should respond to ONB by IHS criteria.
- Two published reviews suggests the response rate was around 85% (lower in those w/ MOH).

	Drugs	Method	Results
Anthony `92 (n=86)	LC+MP	Unil GON	●LC: 88% had no headache ●LC+MP: 87% ●Mean headache-free period: 31 d
Tobin/Flitman (unpublished)	BP+MP	Area of tenderness	●w/o medication overuse: 89% responded ●w/ medication overuse: 64% responded ●Duration lasted 1-2 months

ONB for cluster headache

	Drugs	Method	Results
Ambrosini `05 (n=23)	LC+BM	Uni GON	●LC+BM: 85% pain-free for 4 wk- 4 month ●Saline: 0% responded
Peres `02 (n=14)	LC+TC	Unil GON	●Headache-free ≥2 wk: 29% (mean: 42 d) ●Headache-free <2 wk: 36% (mean: 3 d) ●Mean pain-free duration: 13 d
Busch `07 (n=15)	prilocaine	Unil GON	●Minor response: 60% ●No response: 40%
Anthony `00 (n=20, CCH)	LC, MP	Unilateral GON	●LC during HA: 80% had relief for 1.6-3h ●MP (interictal): 100% had relief (mean: 32 d)

Conclusion: ONB is an effective acute (and possible preventive) Tx for cluster headache (response rate 60-85%)

LC = lidocaine, BM = betamethasone, TC = triamcinolone, MP = methylprednisolone

ONB for migraine

- ONB can reduce cutaneous allodynia
- Several observational study support use of ONB for migraine

ONB for migraine

	Drugs	Method	Results
Caputi/Firetto `97 (n=27)	BP	Unil or bil SON ± GON qod x 5-10 times	●Total pain index: ↓69% (1st month) ●Total pain index: ↓84% (6th month) ●Response of SON+GON = SON
Afridi `06 (n=54, **CM**)	Prilocaine, DM, LC	Unil GON	●No headache: 16% (mean: 9 d) ●↓Headache ≥30%: 30% (mean: 61 d)
Ashkenazi `08 (n= 37, **TM**)	LC+BP+TC LC+BP	Bil GON + trigger point injection	●LC**+TC**: no headache 1.0 ± 1.1d partial response 5.5 ± 4.9d ●LC: no headache 2.7 ± 3.8 d partial response 14.3 ± 5.1 d
Anthony `92 (n=50)	LC+MP LC	Unil GON	●LC: 88% headache-free ●LC**+MP**: 88% headache-free ●Mean headache-free period: 32 d

LC = lidocaine, BM = betamethasone, TC = triamcinolone, MP = methylprednisolone

III. Nerve stimulation: an introduction

Neurostimulation in headache

- Scribonius Largus (Roman physician): the use of torpedo fish (electric ray) for Tx of headache
- The 19th century: proposals for electrostimulation for Tx of may illnesses

- 1950s: therapeutic DBS… for drug-resistant disorders (movement disorders, epilepsy, and pain)
- Neurostimulation is increasingly used as a substitute for surgical lesion in chronic neuropathic pain

Fewer studies were performed in headache

For headache:

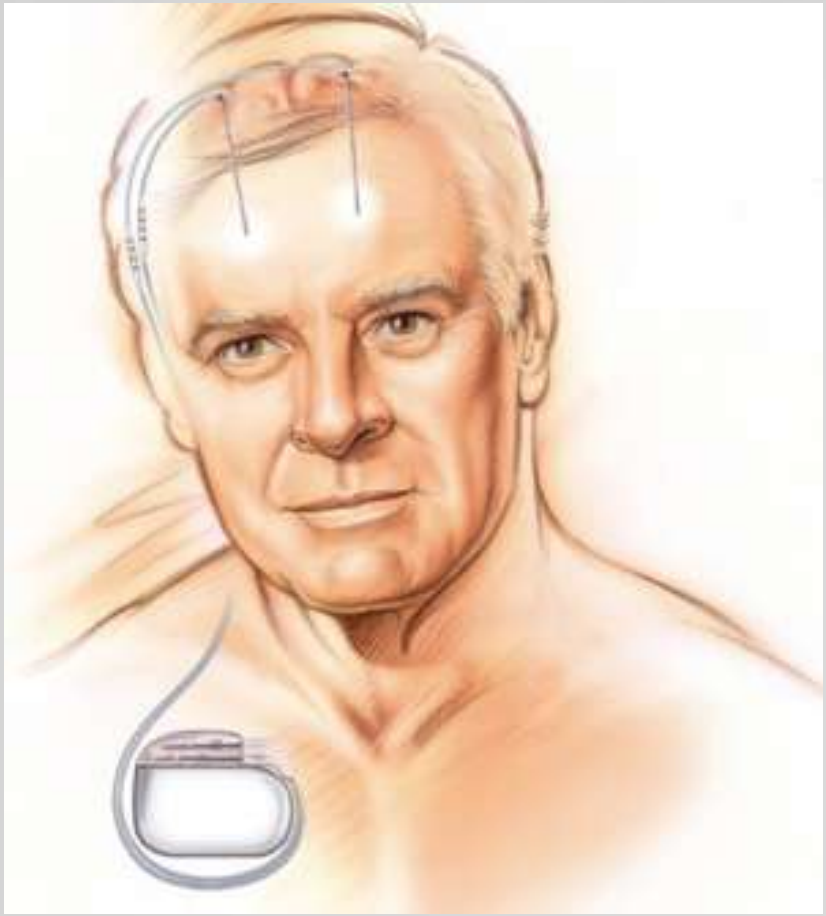
- In earlier studies:
  - TENS/PENS (transcutaneous or percutaneous electrical nerve stimulation) showed mixed results
- More recently:
  - DBS (deep brain stimulation)
  - PNS (peripheral nerve stimulation) w/ implanted subcutaneous electrodes

Types of nerve stimulation used in headache headache

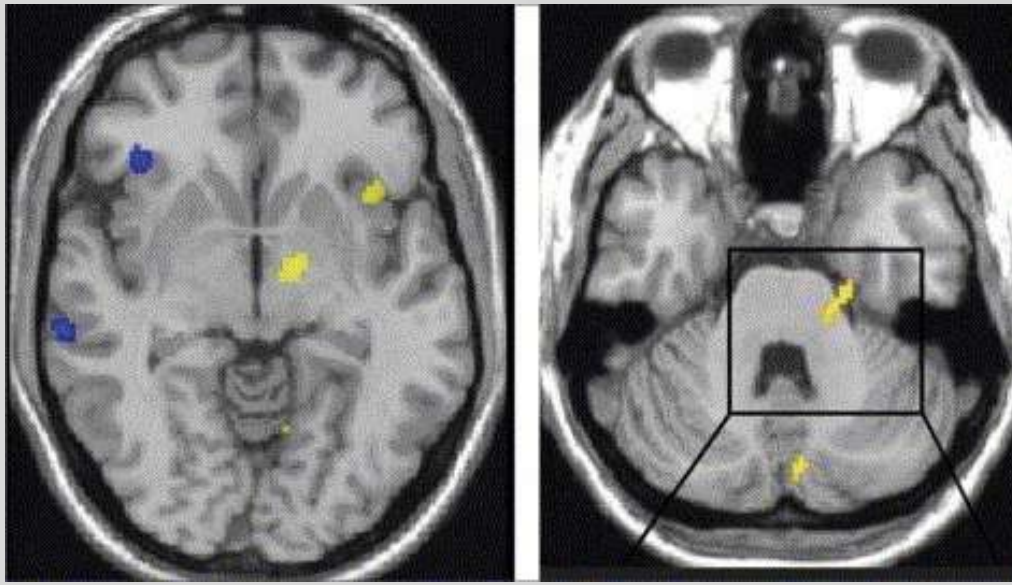
- Hypothalamic deep brain stimulation (hDBS)
- Occipital nerve stimulation (ONS)
- Supraorbital nerve stimulation (SNS)
- Vagus nerve stimulation
- Repetitive transcranial magnetic stimulation (rTMS)

How it works: hypothalamic DBS

- High-frequency DBS has inhibitory effect on local neurons
- Possible mechanisms of DBS:
  - restore hypothalamic modulation of TNC
  - activate several areas of pain neuromatrix in addition to the hypothalamus (PET study)
  - interfere with the modulation or endogenous production of opiods (clinical study)



Images from a $H_2{}^{15}O$-PET study

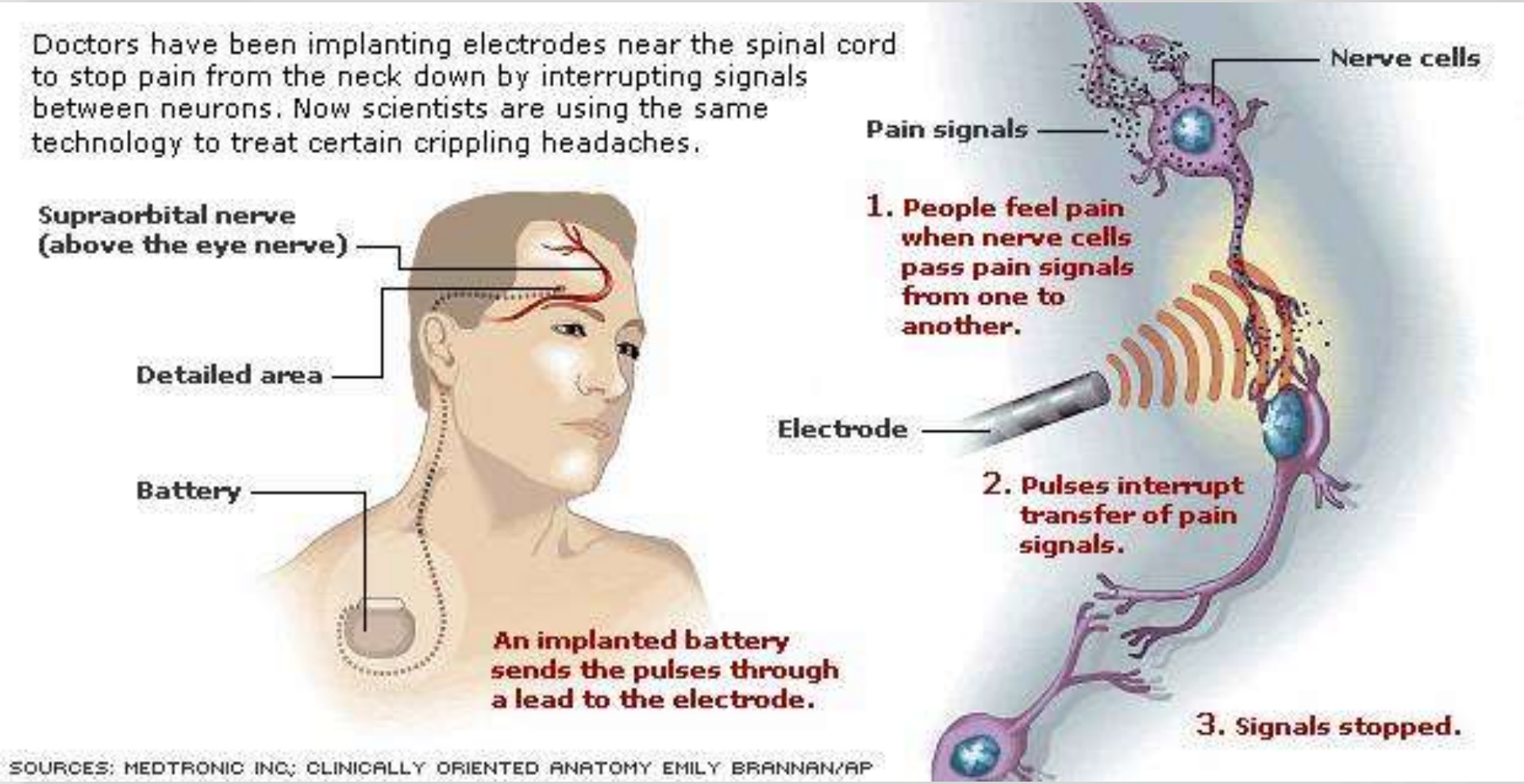


Ipsilateral hypothalamic activation hDBS

Activation of ipsilateral trigeminal nucleus, nerve, and ganglion

J Neurosci 2006; 26: 3589-3593

How it works: PNS



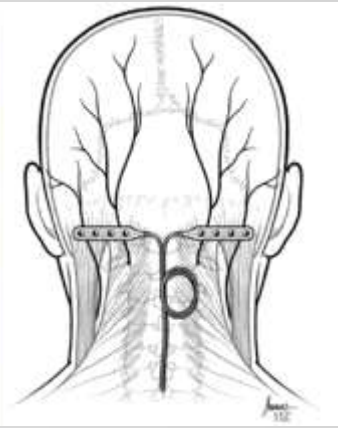
- Animal studies: GON stimulation increased the metabolic rate of TNC & upper C-dorsal horn
- PET study: thalamic change during GON stimulation

- Possible mechanism of PNS:
  - Induction of slow neuromodulatory processes at the level of spinal TNC
  - No change in pain threshold after ONS (no direct analgesic effect)

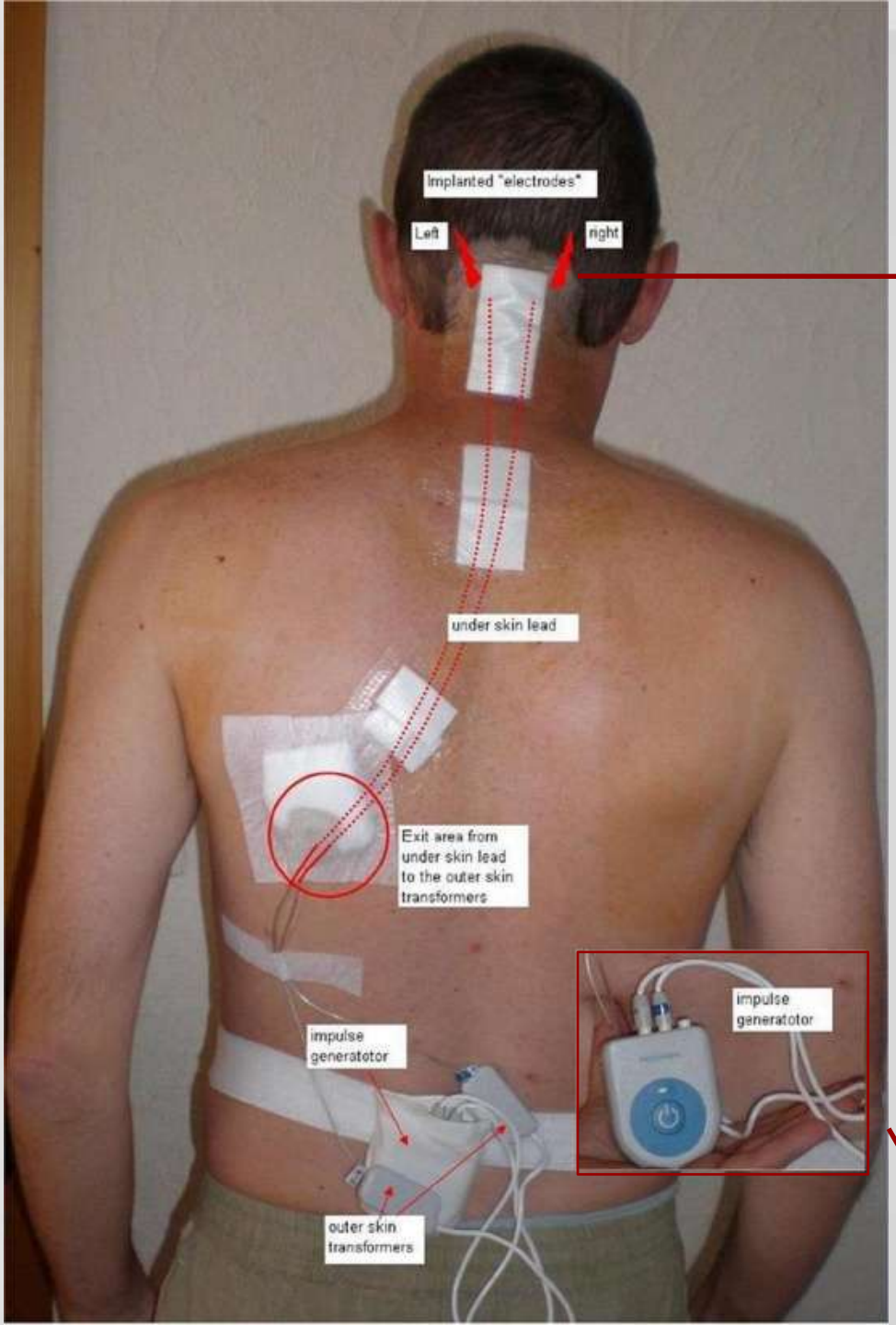
- The influence of PNS may occur at higher levels, which explains its effect at multiple headaches types

Occipital nerve stimulation

Implantable cylindrical or paddle electrodes in the unilateral or bilateral regions of the occipital nerve

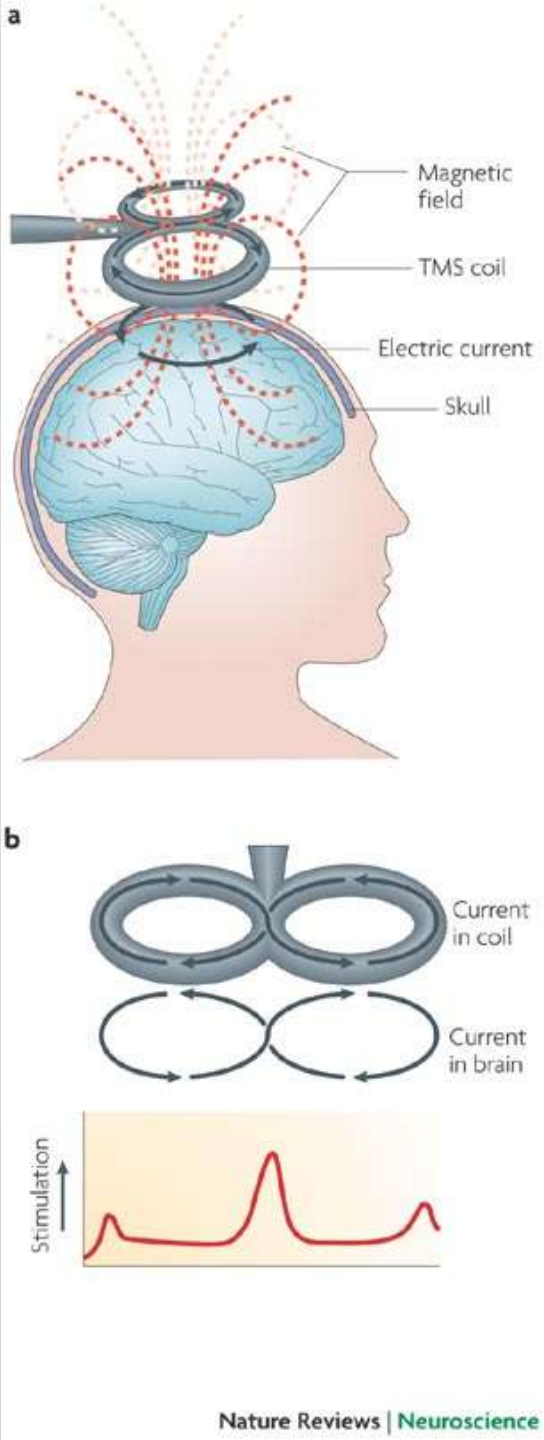


Implantable pulse generator in subclavicular, abdominal or axilla areas



How it works: rTMS

1. Each pulse of transcranial magnetic stimulation (TMS) produces an electrical current in the brain
2. The stimulus activates local neural elements in the cortex or subcortical white matter
3. High-freq rTMS (>5Hz): ↑neural excitability
   Low-freq rTMS (1 HZ): ↓neural excitability



IV. Nerve stimulation in headache treatment

Hypothalamic DBS (hDBS)

- Two studies: ventroposterior hDBS
- Leone: 16 iCCH pateints
  - 13/16: headache-free
    3/16 improved
  - 11/16: stop preventive treatment
  - Overall: 60% had satisfactory improvement
- Schoenen: 6 iCCH
  - 2/6: headache-free
  - 1/6: partial relief
  - 1/6: remission mixed with exacerbation

Head Curr. Cephalalgia, 2008; 28, 789-97. Brain 2005, 128:940-7.

Hypothalamic DBS (hDBS)

- Side effect:
  - Oculomotor disturbance: diplopia, skew deviation, dizziness
  - Panic attack (during electrode placement)
  - Electrode migraine, dysfunction, infection
  - ICH (7.7%)

- No physiological or clinical marker for the right positioning of the stimulating electrode in hDBS (no specific neuronal firing patterns identified)

Occipital nerve stimulation (ONS)

Two open-label trials of ONS for iCCH*

- Burns (`07): n=8
  - 6/8 reported 20-95% improvement
- Magis (`07): n=8
  - Attack frequency: ↓80%; attack intensity: ↓50%
  - 5/8: either pain-free or >90% improvement
  - At long-term F.U.: Attack frequency: ↓54%; attack intensity: ↓47%
  - ↓Prophylactic drug use

* no placebo-controlled trial due to blinding problem

Lancet 2007; 369(9567):1099-1106. Lancet Neurol 2007; 6(4):314-21.

Occipital nerve stimulation (ONS)

- Schwedt (`07): n=12 (8 CM, 3 CCH, 2 PTH, 2 HC)
  - Headache frequency: ↓38%
  - Headache severity: ↓34%
  - MIDAS score: ↓39%
  - BDI: ↓40%
- Schwedt (`06): n=2 (1 CCH, 1 HC)
  - One P't: 70% improvement in attack frequency & intensity
  - The other p't: headache-free

Cephalalgia 2007; 27(2):153-7. Cephalalgia 2006; 26(8):1025-7.

Occipital nerve stimulation (ONS)

- Onset time: several weeks to months
- Unilateral vs. bilateral stimulation?
- Adverse effect: mild & reversible
  - Local discomfort is the most common: neck stiffness, pain at incision or stimulator sites, variable paresthesia in the area of greater occipital nerve
- Short battery life, lead migration
- No know prognostic predictors --- response to occipital nerve block did not predict ONS efficacy

Supraorbital nerve stimulation (SNS)

- A case report: SNS for iCCH
  - No attack after 2 months of continuous stimulation
  - Still pain-free after 12 months, with all preventive medication stopped
  - Switching off: pain recurred in 24h

Headache 2007; 47(7):1100-2.

Vagus nerve stimulation (VNS)

- Improvement of 2 iCCH patients with VNS
  - One patient: ↓cluster attack frequency
  - The other: ↓MIDAS score, but still dependent on fetanyl patches, poor general function
  - Onset time: 2 months
  - Side effect: neck pain
- Improvement in 2 out 4 patients with chronic migraine after VNS

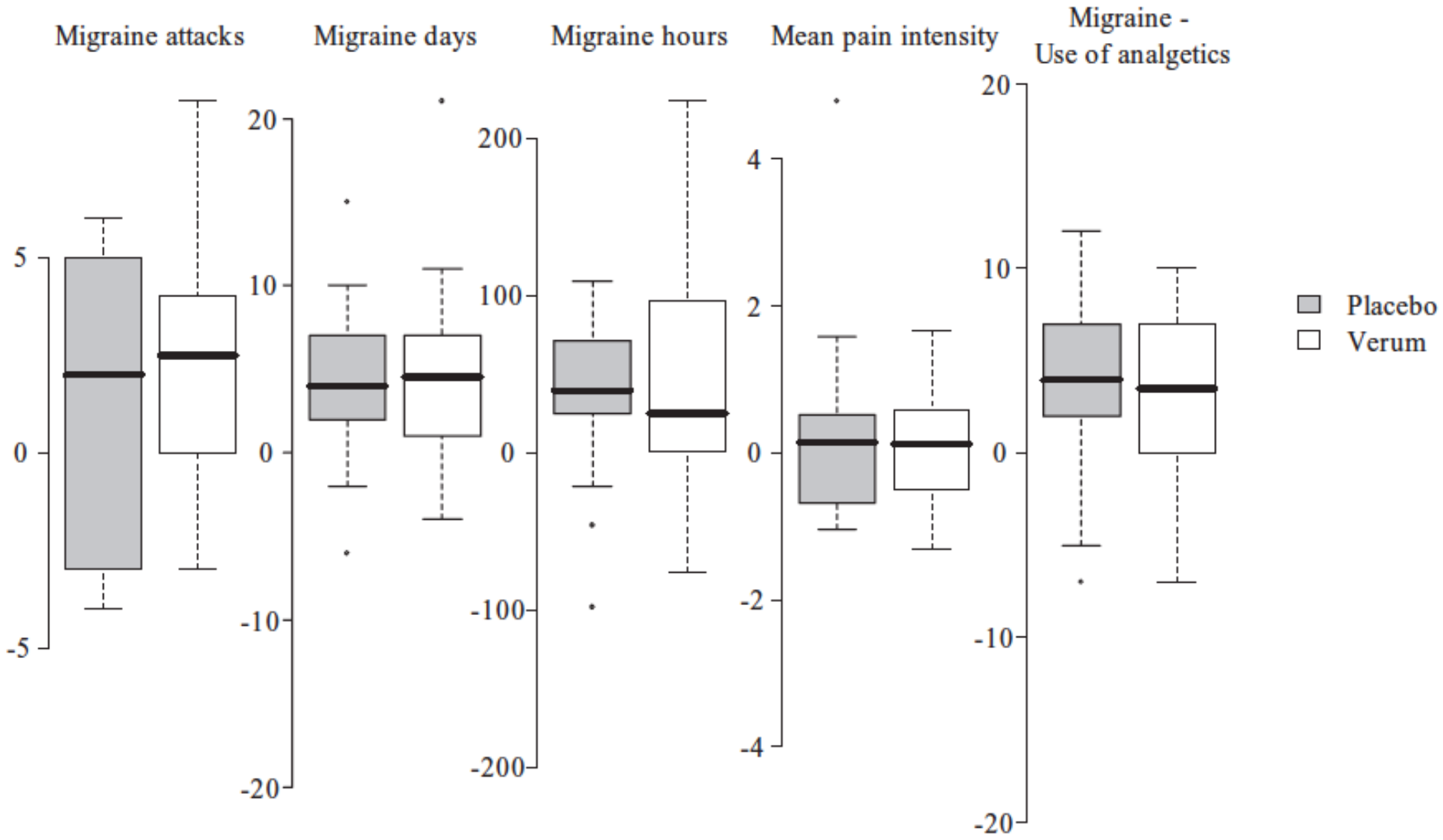
Cephalalgia 2005; 25(2):82-6

Repetitive transcranial magnetic stimulation (rTMS) for migraine prevention

- A placebo-controlled, blinded study
- Two trains of 500 pulses (low freq: 1Hz) applied over the vertex with a round coil for 5 days
- Verum group: n=14
  Placebo group: n=13
- The primary end-point: reduction of migraine attacks compared with placebo
- The procedure was well-tolerated

Cephalalgia. 2009 Jun 8. [Epub ahead of print]

rTMS stimulation over vertex with 1 Hz was not effective in migraine prophylaxis when compared with placebo.



Cephalalgia. 2009 Jun 8. [Epub ahead of print]

Conclusion:

- Occipital nerve block: effective in various headache syndromes
- Other types of nerve block: maybe useful in specific situations
- hDBS: effective for chronic cluster headache
- Occipital nerve stimulation: maybe useful
- rTMS: ??