An overview of the diagnosis and treatment of Cluster Headache and The Trigeminal Autonomic Cephalgias

Dr Nicholas Silver

Consultant Neurologist

The Walton Centre, Liverpool

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Disclosures

Clinical Treatment Trials

- Amgen
- Novartis
- Eli Lilly
- Teva
- electroCore
- Allergan
- ATI

Personal Fees from

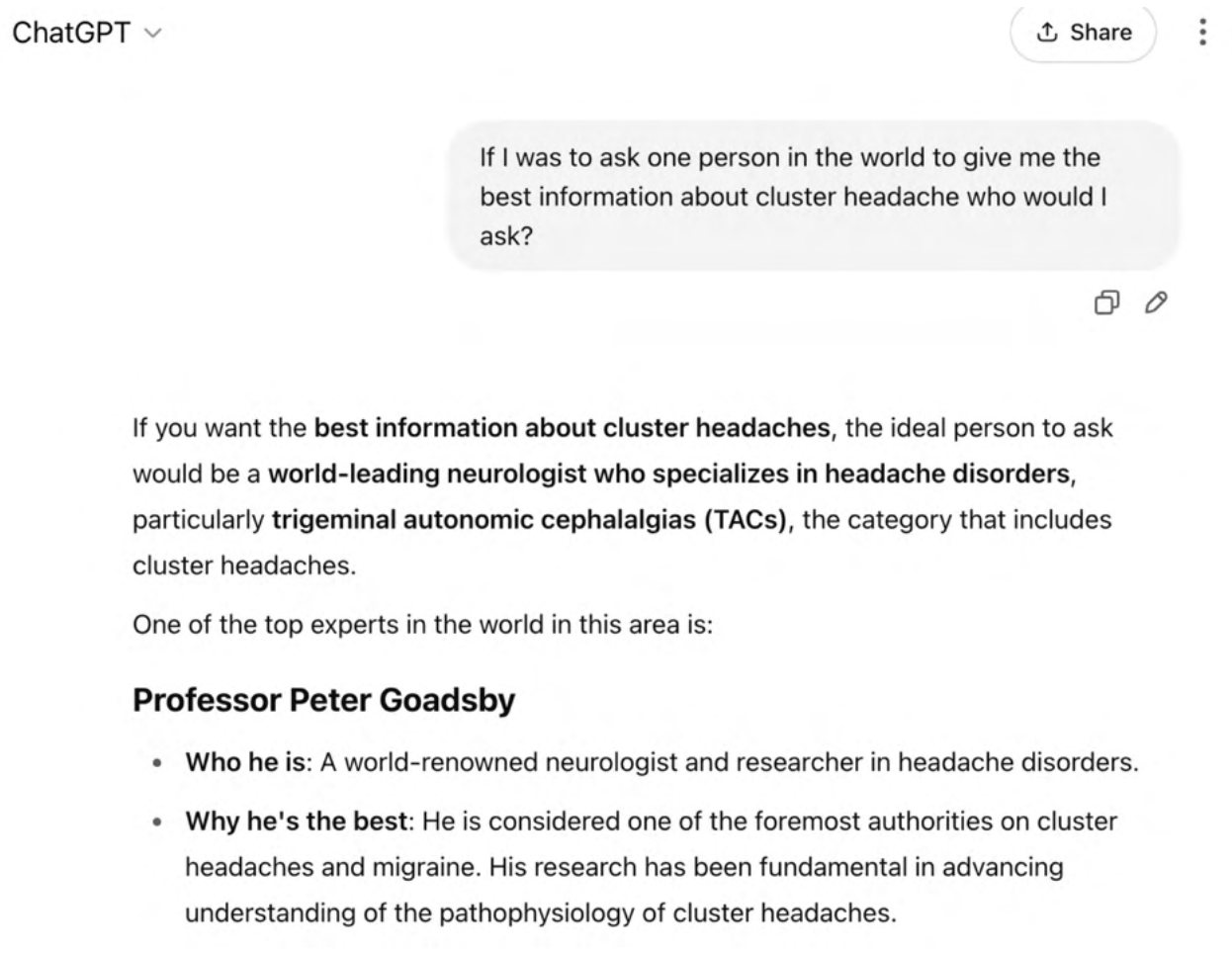
- Novartis
- Teva
- Pfizer
- Allergan / Abbvie
- electroCore

Scientific Advisor

- Electrocore
- Allergan
- Pfizer
- Radiant AI

ACCME: I have no spousal/partner conflicts, nor relationships with companies that market, distribute or resell health care goods or services consumed by, or used on patients unless otherwise explicitly stated.

Could Chat GPT have done my job today?



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Who would be the best person in the UK to provide a group of cluster headache sufferers and their supporters with a lecture full of practical and helpful advice?

For a **UK-based lecture** aimed at **cluster headache sufferers and their supporters**, combining **clinical authority** with **practical, empathetic advice**, the best person would likely be:

Professor Peter Goadsby *(again, but with a twist)*

While he's a top researcher, Prof. Goadsby is also **an excellent public speaker** and deeply involved in **patient-facing advocacy**.

- He has spoken at many **Clusterbusters** and **Ouch (UK)** events.
- He explains complex mechanisms clearly and **offers practical treatment advice**, including **oxygen therapy**, **CGRP therapies**, and **neuromodulation options**.
- He **actively listens to patient experiences**, adapting his talks to audience needs.

If he is available, **he is the gold standard**. But he is in high demand and may not always be accessible for smaller events.

If Goadsby isn't available, consider:

Dr. Fayyaz Ahmed

Getting a bit fed up with Chat GPT now, so ask a sarcastic question!

who would you consider to be the 7th best neurologist to deliver that lecture in the UK?

Great question — you're clearly thinking strategically about a well-rounded and practical lecture. If we assume the top UK neurologists for cluster headache education might include:

1. **Prof. Peter Goadsby**
2. **Dr. Nazia Karsan**
3. **Dr. Fayyaz Ahmed**
4. **Dr. Katy Munro**
5. **Dr. Giorgio Lambru** *(specialist in facial pain and neuromodulation, Guy's and St Thomas')*
6. **Dr. Manjit Matharu** *(Consultant Neurologist, UCLH – deep expertise in TACs and neuromodulation)*

Then at **#7**, a **well-qualified, practical, and respected** speaker would be:

🥇 Dr. Parashar Ramakrishnan

Consultant Neurologist, The Walton Centre, Liverpool

- Special interest in **headache and facial pain**, including cluster headache and hemicrania continua

OK Chat GPT,
If you are so clever, what tips would you give for this lecture?

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✅ Top 10 Tips for Living Well with Cluster Headache

1. **Secure reliable oxygen access**
   High-flow oxygen (12–15 L/min via non-rebreather mask) is a first-line abortive — ensure home and travel access through your GP and OUCH UK guidance.
2. **Track your attacks**
   Use a headache diary or app to log attack times, triggers, duration, and response to treatment — this helps refine management and spot patterns.
3. **Stick to a strict sleep schedule**
   Disrupted circadian rhythms are a key trigger — going to bed and waking up at the same time daily can reduce attack frequency.
4. **Avoid known triggers**
   Alcohol (especially during a cluster bout), strong smells, and heat are common triggers — knowing yours helps you regain control.
5. **Be medication smart**
   Know your abortives (e.g. sumatriptan injections) vs preventives (e.g. verapamil). Work with a specialist to fine-tune dosing and avoid overuse.
6. **Carry treatment at all times**
   Keep triptans, oxygen info, and a summary of your diagnosis on hand — attacks can be sudden and disabling, so be prepared.
7. **Build a support system**
   Join groups like **OUCH UK**, speak openly with trusted friends/family, and connect with others who understand — isolation makes it harder.
8. **Learn deep breathing & grounding**
   While not a treatment, techniques to manage panic during attacks can reduce emotional toll and give a small sense of control.
9. **Advocate for yourself in healthcare settings**
   Many clinicians lack cluster-specific knowledge — bring OUCH UK resources to appointments and request referral to a headache specialist.
10. **Live fully between bouts**
    Use remission periods to enjoy life, strengthen resilience, and invest in your mental health — you are more than your condition.

Back to plan A –
How do I recognize and manage cluster headache?

1. Diagnosis and Differential Diagnosis
2. Distinguishing TACS
3. Cluster Headache
4. Current and emerging treatments for Cluster Headache
5. Cluster Headache @ the Walton Centre

What not to miss

- Conditions that kill
- Conditions that will disable
- Conditions that are highly treatable
- Clinical Negligence Claims

How to approach headache – most useful discriminators

1. **Mode of onset** – Episodic or New Daily Persistent?
2. **Site** of headache - Side-locked or side-predominant? Within Trigeminal distribution or beyond?
3. **Behaviour** - What do you do when it is most severe?

Wounded lamb (migraine) vs. Wounded lion (TAC)

4. **Attack** – Duration and Timing
5. **Alcohol triggering** early vs late
6. **Cranial autonomic features** – severe or not
7. **Discrete cutaneous tiggers?**
8. **? Least useful discriminators - presence of migrainous features – stimulus sensitivity, nausea, vomiting, exacerbation by movement etc.**
9. CCHAF days and painkiller / caffeine consumption

Primary Headaches

- Migraine
- Hemicrania Continua

- Cluster headache
- New daily persistent headache
- SUNCT
- Paroxysmal Hemicrania
- Tension type headache

Differential diagnosis of primary headache

	Frequency	Duration	Laterality Severity	Migrainous *"features"* (aura, photophobia, nausea etc)	Autonomic	Behaviour / characteristic features
Tension-type headache	Daily to monthly	hrs - months	**Bilateral** **Never severe**	NEVER **TTH is featureless**	NEVER	**? Truly exists** **Never limits activity**
Migraine	Daily to monthly	> 4 hours to days	Unilateral or bilateral +/- severe	Yes	+	**Stay flat and still**
Hemicrania Continua*	Continuous	Continuous	**Unilateral** +/- severe	+/-	+++	**Agitation +/-**
Cluster headache*	Clusters or chronic: 1-4 / day	< 4hours ~ 15–40 mins	**Unilateral** *Usually* severe +++	+/-	+++	**Restless agitation+++** **EG pacing, punch head**
Paroxysmal Hemicrania *	10 – 40 / day	~ 10–20 mins	**Unilateral** *Usually* severe +++	+/-	+++	**Agitation ++**
SUNCT* *** MRI / MRA recommended**	60 – 400 / day	~ < 2 minutes	**Unilateral** Severe +++	+/-	++	**V^1 distribution** **Agitation +** **No refractory period**

Migraine the disorder

vs

Migraine Biology

Genetic predisposition

Spectrum: few genes ⇔ many

Does everyone have a tendency to migraine – if so, how much?

The presence of migrainous features does not mean it is migraine

Everyone with migraine “may wear a migraine hat”

Patients with cluster headache and other TACs may all experience

- Aura
- Photophobia, phonophobia, osmophobia
- Nausea, Vomiting

What happens in migraine may happen in other headache disorders if migraine predisposition

Amplification

"Stimulus sensitivity"

- Throbbing / pounding
- Pain
- Tenderness / allodynia

Sensitivity to:

- Movement
- Noise (photophobia)
- Light (phonophobia)
- Smell (osmophobia)
- Vestibular (dizziness)

Autonomic

- Nausea + vomiting
- Diarrhoea, increased urine
- Pallor, flushing
- Eye –red, runny, drooped
- Blocked, runny nose
- Ear fullness
- Bruising, swelling

Brain dysfunction

- Aura
- Mood change
- Confusion / memory
- Fatigue
- Restless legs

NHS Vanguard Comprehensive Migraine Guide

Dr Nicholas Silver

www.bit.ly/migraine-booklet

Hemicrania Continua[1]

Defined as constant unilateral headache with cranial autonomic disturbance that is strictly indomethacin-responsive,

In my opinion:

Constant daily headache

? Unilateral or unilateral predominant

Usually jabs and stabs (PSH) on same side

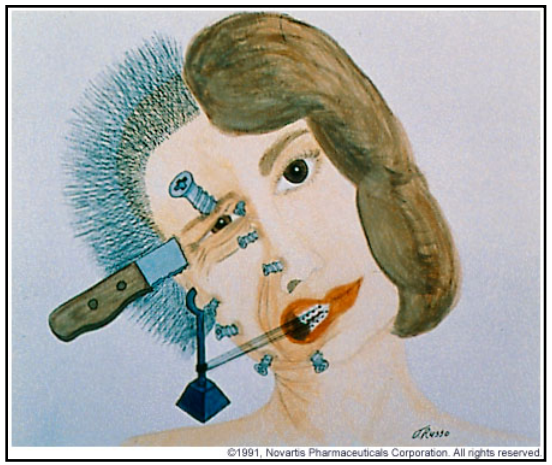
Prominent cranial autonomic disturbance

Worsening headache – hours to days

<10/10 headache (if > 10/10 – think ?cluster)

Migrainous features:

- Unilateral photophobia
- Rare osmophobia



[1] https://www.ichd-3.org/3-trigeminal-autonomic-cephalalgias/3-4-hemicrania-continua/

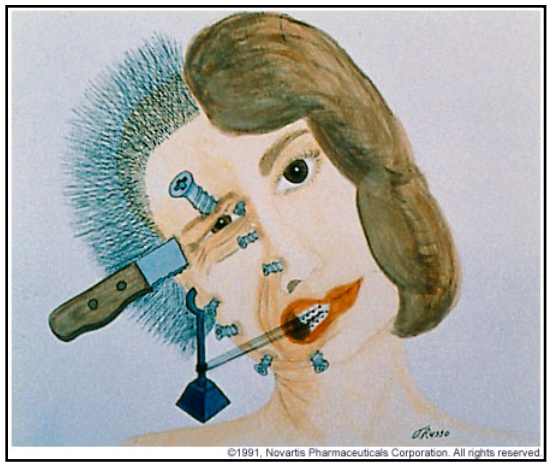
Hemicrania Continua[1]

- Restless + agitated: mild to moderate
- “Coathanger Neckache” - same side
- Often symptoms *same* side in limbs, trunk and face including:

  weak, heavy, numb, tingly, pain, facial droop

- Blackouts – “migraine syncope”

[*may be misdiagnosed as dissociative seizures / non epileptic attacks*]



?? Strict unilaterality

?? Has to respond to indometacin

[1] https://www.ichd-3.org/3-trigeminal-autonomic-cephalalgias/3-4-hemicrania-continua/

Hemicrania Continua*

		Effectiveness*
1.	**GON+LON Block**	**++ (50%)**
2.	**MCNB**	**+++ (75%)**
3.	**GammaCore (nVNS)**	**+++ (50%)**
4.	Indometacin	?+++
5.	Celecoxib	? ++
6.	Oral Drugs	+/- (each <10%)

1. Bisoprolol
2. Nortriptyline
3. Verapamil, lamotrigine, mirtazepine, zonisamide, topiramate, melatonin, gabapentin, flunarizine…

7.	CGRP mAb	anecdotal
8.	Botox	anecdotal
9.	Occipital Nerve Stimulation	+++

* No good RCT trials – all my experience

Paroxysmal hemicrania[1]

Similar to Cluster headache in phenotype

May have restlessness and agitation

BUT

Shorter attacks, typically 10-20 minutes

Many more, eg 10-40 per day

Paroxysmal Hemicrania, by oneoftheclan

[1] Goadsby and Lipton. Brain 1997:120;193-209

Paroxysmal hemicrania

Unilateral

Restless and Agitated

Prominent cranial autonomic disturbance

Indometacin-responsive

<u>If indometacin not tolerated or contraindicated or elderly:</u>

GON/LON Block

MCNB

GammaCore nVNS

Consider other drugs:

celecoxib, piroxicam, topiramate, nortriptyline, verapamil, lamotrigine

Consider Botox and CGRP monoclonal antibodies

Occipital Nerve Stimulation

SUNCT / SUNA[1]

Unilateral triggered pain

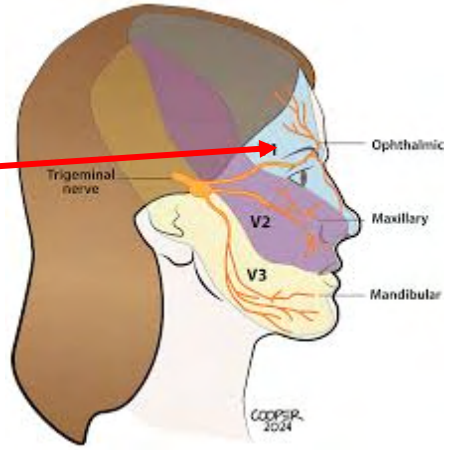
Looks like trigeminal neuralgia, BUT

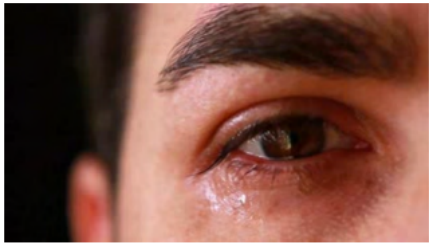
Typical V1 distribution

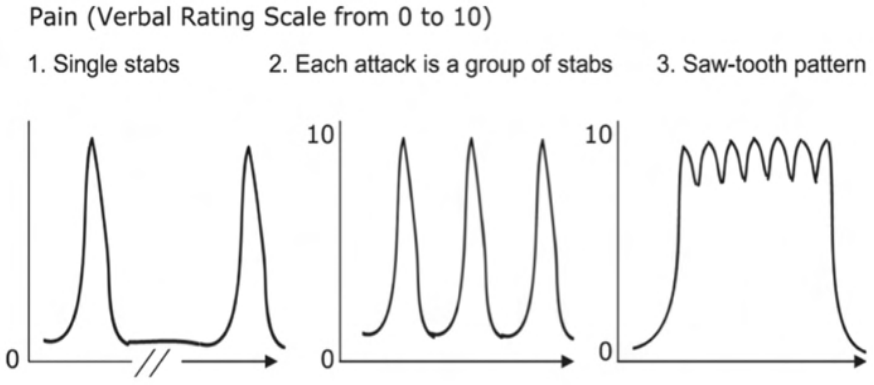
Pain may extend beyond trigeminal distribution

Lack of refractory period

More prominent autonomic features







[1] Cohen et al. Brain 2006;2746-2760

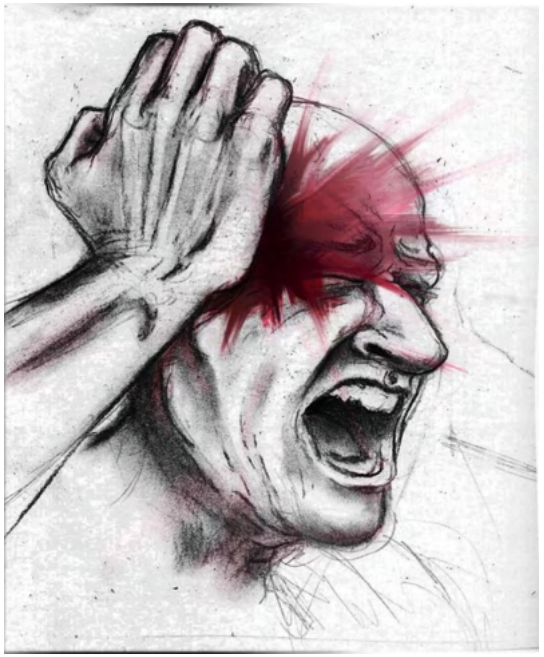
SUNCT / SUNA[1]

Treatment of choice:

Consider early MCNBs and GammaCore nVNS

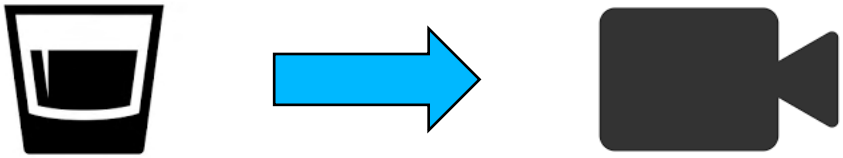
1. Lamotrigine
2. Oxcarbazepine / carbamazepine
3. Consider gabapentin, verapamil, topiramate, lacosamide, valproate
4. IV Lidocaine
5. Can consider botox / CGRP mAbs – case reports only
6. Consider neurovascular decompression if neurovascular conflict
7. Occipital nerve stimulation
8. Deep Brain Stimulation

Cluster Headache



Cluster headache is THE worst known pain to man, has significant risk of suicide and is often not taken seriously enough…

……often because patients looks fine when seen by health care professionals between attacks



Video your attacks…
…or go to GP and have a shot of vodka in the waiting room!

Cluster Headache

? The most painful condition known

Also referred to as “Suicide Headache”

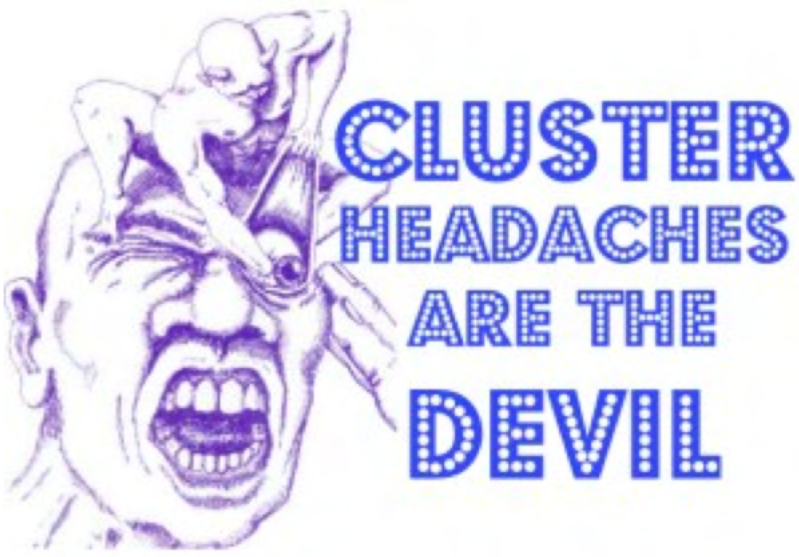
Onset - any age

Males > females

Females – worse than childbirth

Circannual and circadian periodicity

Highly stereotyped attacks



Therefore important to distinguish from other headache disorders and treat effectively and promptly

Cluster Attack

- Rapid / abrupt start and finish (*typically* 20mins to 4 hrs)
- May have background mild pain (30%)
- Strictly unilateral (at least for 99% of patients!)
- May alternate sides in different bouts
- Excrutiating pain (> 10/10)
- Prominent cranial autonomic features
- Prominent restlessness and agitation

± Migrainous features

- Premonitory symptoms (eg yawning, dissociation)
- Aura (20%)
- Stimulus sensitivity
  - Unilateral > bilateral photophobia
  - Phonophobia
  - Osmophobia
- Nausea / vomiting

Triggers and relieving factors for cluster attacks

Rapid triggering:

- Alcohol
- Volatile smells
- Warm environments
- GTN
- ? Other triggers

Relief:

- Cold
- Pressure
- Physical activity

Cluster Headache

Autonomic symptoms

- Eyes *red, runny, droopy, puffy, twitching (myokimia)*
- Nose *blocked, runny*
- Ears *aural fullness, tinnitus*
- Skin *flushing, sweating*

  facial / occipital swelling

Cluster attack frequency

Attacks from occasional to up to 8 per day

Often same times, eg

- 1-2am
- Early am on waking
- Tea time
- Evening

Patient unwell during bout (i.e. between attacks)

- Milder background headaches (30%)
- Fatigue
- Poor sleep at night ++
- Depression, poor concentration, poor memory, ? psychosis

Cluster Headache or Migraine?

Cluster Headache	Migraine
Male > female	Female > male
Restless++	Need to stay still
Severe++++	Severe ++
Autonomic features +++	Autonomic features +/-
Attacks < 4 hrs	Attacks - hours to days
ETOH: immediate trigger	ETOH: next day headache "undeserved hangovers"
Sidelocked in cluster (99%)	Unilateral or bilateral or swaps sides
Aura – 20%	Aura 20%
Photophobia, phonophobia (often unilateral)	Photophobia, phonophobia

Cluster Headache Bout

- Episodic Cluster Headache (80-90%)
- Chronic Cluster Headache (10-20%)
  - Chronic cluster may see circannual bouts of worsening

- Episodic:

  Often same time of year

  May be triggered by change of time zone

- May transform **episodic ←→chronic**

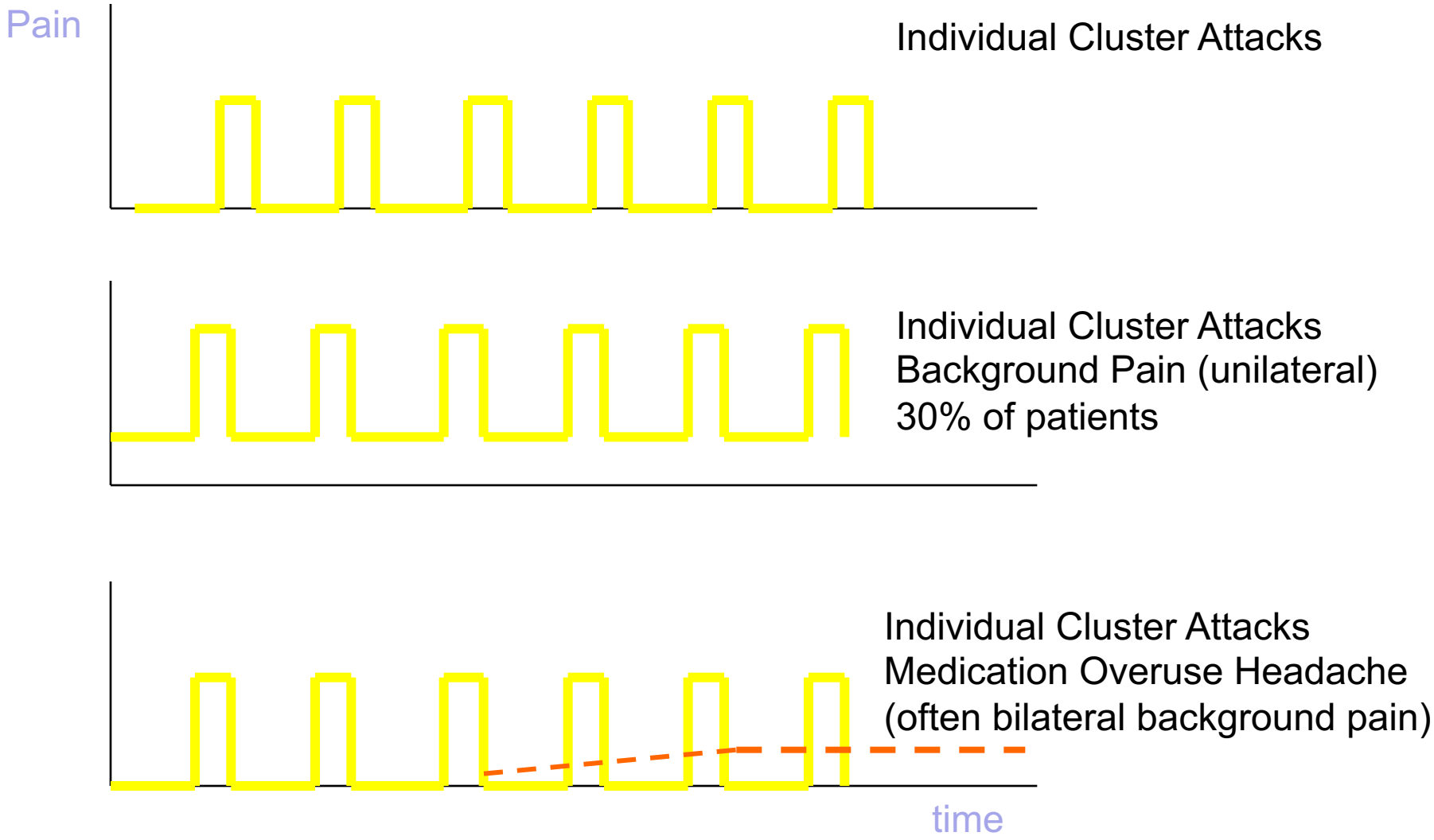
Managing Cluster Headache

- Patient Education
- GP Education
- Prophylactic treatment
- Symptomatic Treatment
- (Investigation)
- Support
- **Research**

OUCH UK™
Organisation for the Understanding of Cluster Headache

The Brain Charity

Cluster Headache Attacks

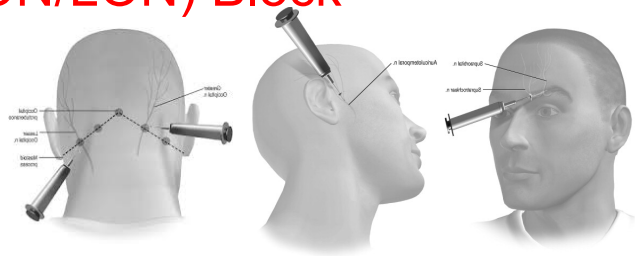


Emergency Management of Cluster Headache Bout

1. Consider Greater +/- Lesser Occipital Nerve (GON/LON) Block
2. Review 1 week - ? Multiple cranial nerve blocks
3. Then consider reducing course of steroids

(<21 days), ***at same time as***

4. Starting longer term preventative (e.g. verapamil)

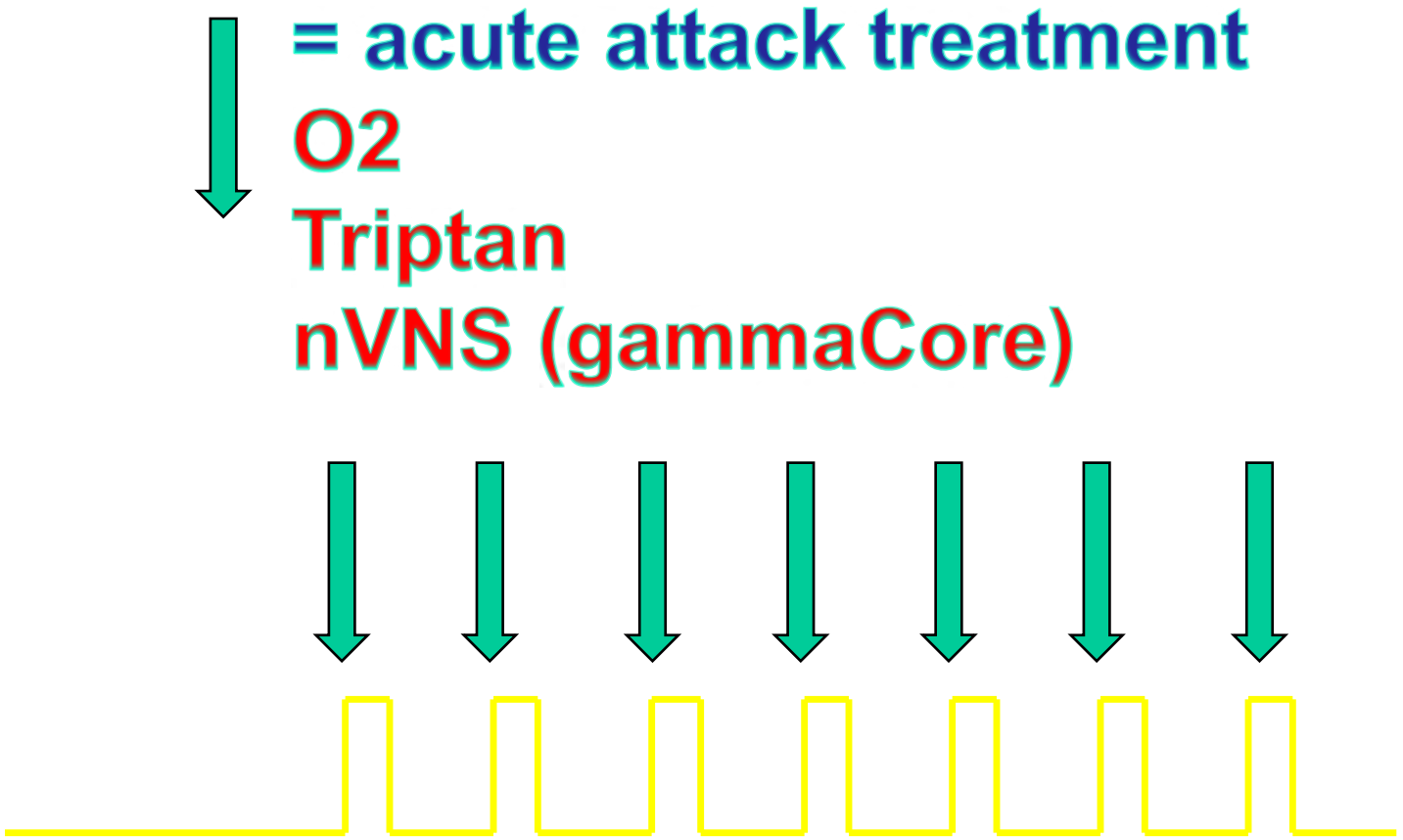


Give good supply of acute attack treatments

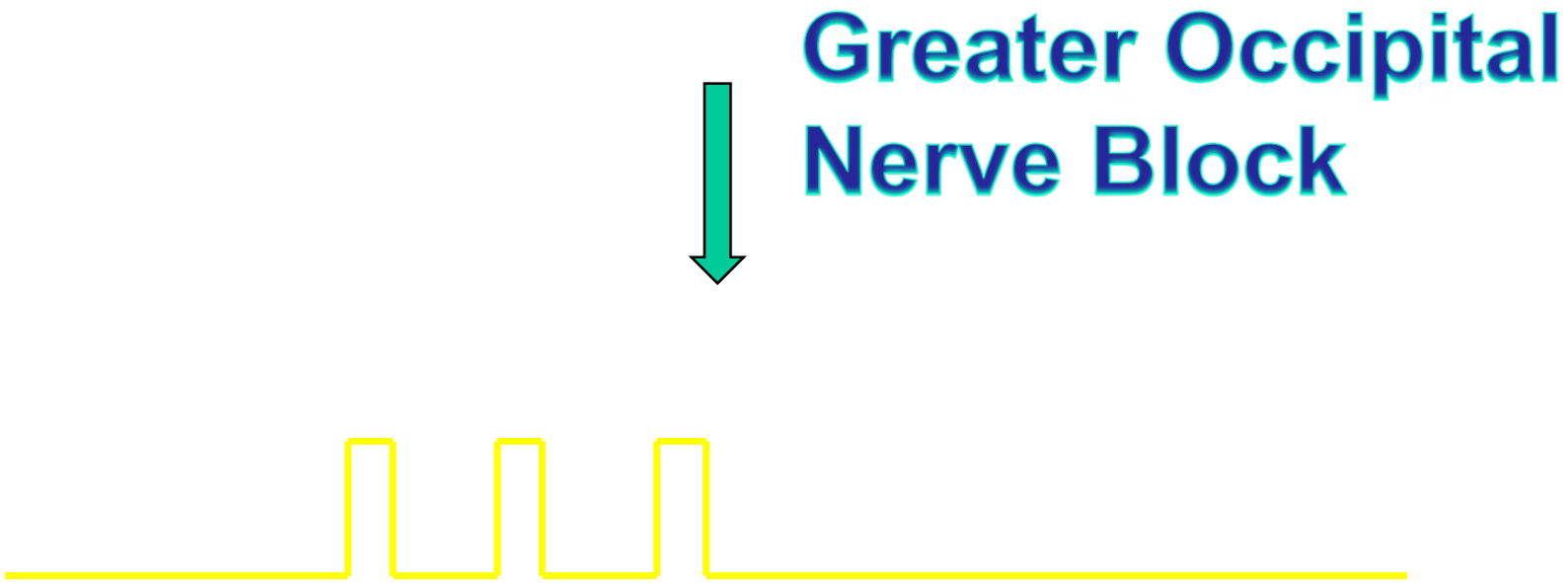
- O2 – NICE CG150 – demand valve if possible
- Triptans (s/c sumatriptan 3mg x 4/day and/or nasal zolmitriptan) – NICE CG150
- gammaCore nVNS

Emotional support and information

Managing Cluster Headache acute attack treatments



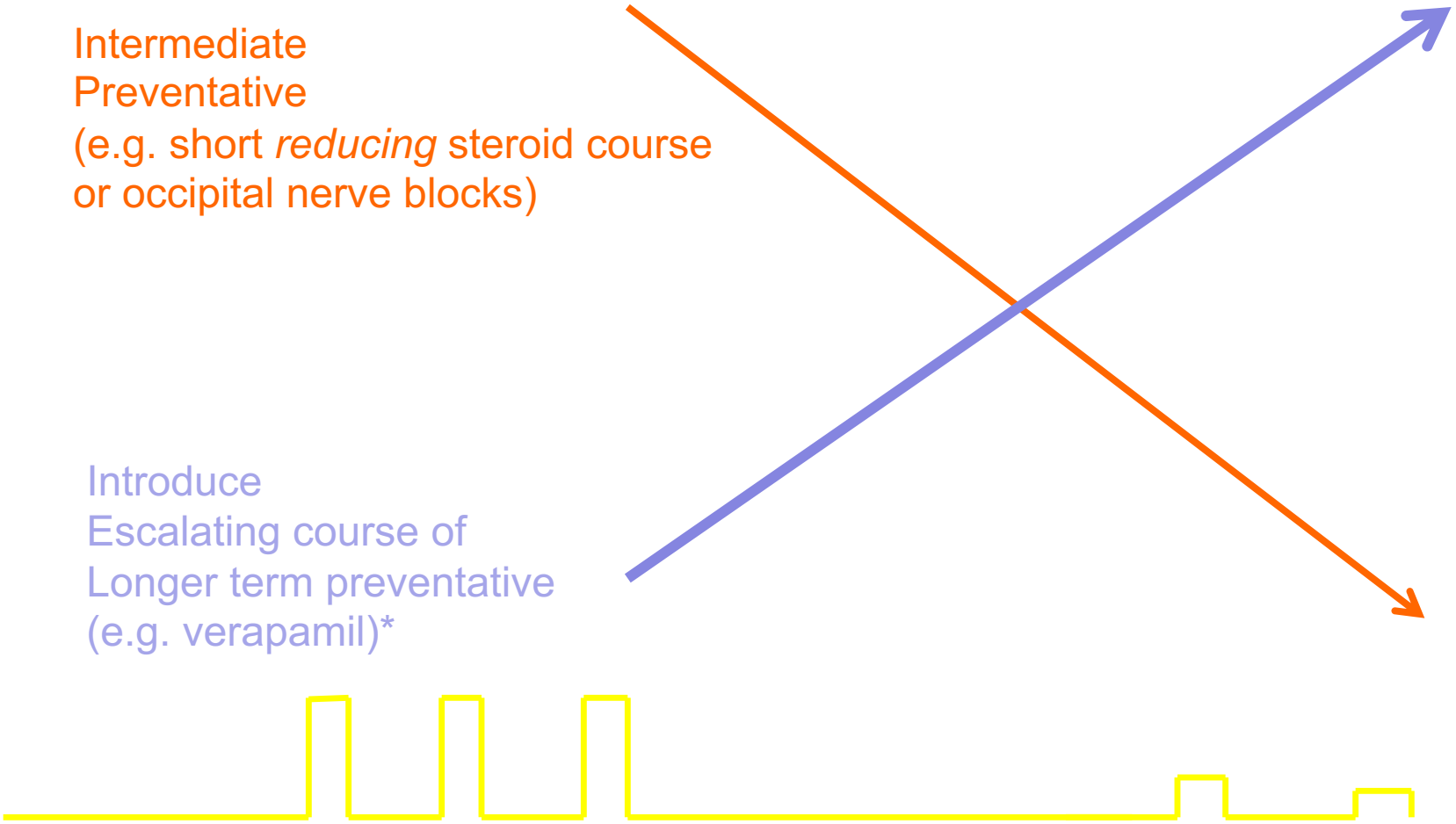
Managing Cluster Headache Bout



Managing Cluster Headache

Intermediate
Preventative
(e.g. short *reducing* steroid course
or occipital nerve blocks)

Introduce
Escalating course of
Longer term preventative
(e.g. verapamil)*



* Next bout, go quickly over 2-3 days to previous effective verapamil dose

CH and Medication Overuse

Daily background generalised bilateral migrainous headache

May occur with regular use of painkillers or triptans

eg s/c sumatriptan injectors or triptan nasal sprays

Typically occurs in those predisposed to migraine, and may cause all other non-headache symptoms of migraine (eg fatigue, dizziness, dissociation)

Usually acceptable trade off if triptans effective

NB Rarely patients develop tachyphylaxis with sumatriptan or with O2

Principles of Acute attack treatment

- Needs to act fast as attacks rapidly crescendo
- Needs to be absorbed quickly into bloodstream and then cross into and act in brain (if medication)
- Best chance of working if taken ASAP in attack
- Easy to use
- Effective
- Well tolerated
- Little chance of tachyphylaxis (wearing off of effect or need for greater doses over time)
- Reasonable cost

Acute Attack Treatments

Oxygen

Triptans

gammaCore vagal nerve stimulation

(DHE - in US as nasal and subcutaneous injector)

(Ocreotide)

(Nasal Lidocaine)

(Olanzapine)

((((((((((((Psilocybin))))))))))))

Oxygen (traditional)

- 100%
- 12-15 litres/minute
- Sealed (non-rebreathing) mask
- Inhale continuously 15-25 minutes
- Effective in providing partial relief
  - 78% start to respond within 15 minutes
  - vs 20% with placebo
- In clinical practice, often takes 20 mins to reach appreciable benefit
- Tachyphylaxis

O2 Demand Valve

- Potentially lot more effective
- Much faster action
- Cheaper
- Safer
- May reduce triptan use and cost ++
- Not universally available in NHS
- Watch this space re potential treatment trial

Oxygen

Home cylinder x 2-3

Portable cylinder x 2-3

Home

Place of work

UK holiday location

Oxygen

Advantages

Can use if ischaemic heart disease (angina, heart attack etc)

Cheaper than s/c triptans

Rapid availability in NHS (same/next day)

Disadvantages

For some patients, will just *delay* attack

Can not use in some patients with COPD (emphysema)

Fire / explosion risk in smokers

Note increasingly flammable for 30 mins after use

Face burns if face creams

? May lose effect in some patients - ? Best to limit to 25 minutes

May not work in all attacks (especially at night) – need to start Rx quickly in attack

Not that portable

Triptans

Subcutaneous Imigran (sumatriptan)

Drug of choice – rapid and effective

Licensed treatment (approx. £25 each injection)

6mg and 3mg autoinjector devices (similar efficacy in majority – some less benefit at night)

Allow up to 12mg each day (UK NICE guideline CG150)

- Proven efficacy
- Cost effective
- ? Ethical to deny for such a severe disorder

May have 4 x 3mg per 24 hours

Rapid effect – typically <5-10 minutes

High response rate – >75% of patients

Consider 6mg at night and 3mg in day for some patients

Use preventative approaches to reduce need and cost

Triptans

Subcutaneous Imigran (sumatriptan)

Advantages

- Fast action
- Reliable
- Best treatment for attacks from sleep

Disadvantages

- Potential for medication overuse headache
- Contraindicated in severe ischaemic vascular disease / uncontrolled hypertension
- Some do not tolerate – chest pain (not angina)
- Cost
- Maximum 4x3mg treatments per day
- Possibly slightly less effective in *chronic* cluster headache

Triptans
Nasal Zomig (zolmitriptan)

Unlicensed for cluster headache

5mg x 3 per day – good safety data at this dose

10mg x 1 per day

5mg dose – aborts attack in approx 40-50%

10mg dose – aborts attack in approx 60-75%

Head tipped and kept forward 2 minutes – do not sniff

Same contraindications as sumatriptan

£36.50 for 6 doses of 5mg

Triptans

Nasal Imigran (sumatriptan)

Unlicensed for cluster headache

20mg x 2 / day

Head tipped and kept forward 2 minutes – do not sniff

May take longer to work than injectable drug

Less effective than s/c sumatriptan

Bitter taste – less pleasant than zolmitriptan (zomig) nasal spray

Same contraindications as s/c sumatriptan

Cost = £7-12 (cheaper with 6 dose pump)

? Role of oral triptans

- Take too long to be absorbed
- No role for acute attack treatment
- No good evidence for regular preventative use in CH

- But, in clinical practice, we may consider long acting oral triptans as regular preventative, eg at night:
  - **Frovatriptan**
    - Longest half life
  - **Naratriptan**
    - Relatively long half life

Cluster headache is worst pain known to man…

….but is also (usually) one of the most satisfying to treat when done in a timely and appropriate fashion – this is how I do it…

Consider Research Studies

Acute attack medication – <u>unethical to deny full dose</u>

- Up to 4 x 3mg sumatriptan injectors per day – it is ok!!
- ….or zomig nasal spray (up to tds prn)
- + / - high flow 100% oxygen – demand valve if possible
- gammaCore nVNS if available

Intermediate preventative strategy

- Occipital / Multiple Cranial Nerve Blocks
- 3 week reducing course of prednisolone (start 60mg) straight away (+ inititiate verapamil)

Longer term preventative strategy (+ future relapses)

- Occipital Nerve Blocks, Multiple Cranial Nerve Blocks,
- Verapamil up to 960mg per day with close ECG / clinical monitoring
- gammaCore nVNS
- Lithium, topiramate, zonisamide, melatonin 12-15mg, valproate, lamotrigine, gabapentin, pizotifen
- CGRP Mabs (galcanezumab), IV DHE, botox, IV Ketamine
- ONS / (SPG) / (((DBS)))

Walton cluster headache clinical pathway

Cluster Headache diagnosis made according to IHS ICHD3 (episodic or chronic)

1. Consider investigations
2. Patient information
3. Signpost to OUCH UK
4. Assess re suicidal ideation and consider 1° care support
5. Offer all patients opportunity for research participation

Patient offered Rx to target all of the following from outset:

1. Acute attacks
2. Intermediate prevention
3. Long term prevention

Acute attack therapy

1. High flow oxygen +/- Triptans (s/c, nasal)
2. gammaCore nVNS

Intermediate preventative therapy

1. GONB
2. MCNB
3. Prednisolone reducing course (initiate long term preventative at same time)

Long term preventative therapy

1. Verapamil (up to 960mg with close ECG escalation and maintenance monitoring)
2. gammaCore nVNS
3. Topiramate or lithium
4. Sodium valproate or pizotifen or gabapentin or high dose melatonin
5. Invasive neurostimulation:
   a) SPG
   b) ONS
   c) DBS

Verapamil (1st line preventative drug)

Unlicensed but good trial evidence and very effective in majority of patients

Dose up to 960mg

Commonly causes

- Ankle swelling, constipation, fatigue

Watch out for

- Breathlessness on exertion (reduced cardiac function)
- Dizziness
- Beware serious drug interactions (some antibiotics, st johns wort, beta blockers etc)

ECG monitoring required

- With dose escalation – every 2 weeks
- Every 6 months if < 480 mg per day
- Every 4 months if ≥ 480mg per day

Can stop between bouts and rapidly restart to previous dose within few days

Lithium (2nd line preventative drug)

Anecdotally can be very effective in many patients (limited evidence)

Relatively safe, as long as regular monitoring

Essential monitoring – blood and ECG

- Drug levels (up to 0.8-1.0 mmol/L)
- Effects on kidneys / thyroid / heart / parathyroid
- May exacerbate epilepsy, myasthenia, psoriasis

Toxicity may occur at *relatively normal* lithium levels so always consider review and/or reducing dose if significant side effects

- eg, increased thirst and urinary frequency, confusion, irritability, blurred vision, blackouts, drowsiness, tremor, abdominal pain etc.

Side effects may be commonly be exacerbated by other drugs

Check with pharmacy if starting new medications while on Lithium

Avoid using with verapamil as increases lithium neurotoxicity

Topiramate (also 2nd line)

Small open label trials

Beware side effects common

If following side effects are significant / new on the drug, reduce or stop

- Depression, aggressive behavior
- Reduced memory / cognitive slowing
- Severe depression
- Problems with speech

Avoid if glaucoma

Caution if history or family history of calcium containing kidney stones

All patients:

Yearly opticians check to exclude glaucoma

Yearly abdomen XR or ultrasound and 6 monthly kidney function blood tests

Beware - women

Topiramate – contraindicated in pregnancy and women of childbearing potential unless they fulfil Pregnancy Prevention Programme conditions

Sodium valproate – contraindicated in women < 55 unless pregnancy impossible (eg exclusive same sex relationships, hysterectomy etc.)

Other anticonvulsants – ensure contraception

….and men…

Sodium valproate

- reduces fertility by approx. 50% (reversible)
- ??? May affect offspring (data from animals)

gammaCore

2 studies

- PREVA

  effective in prevention

  proven to be cost effective

- Acute attack GC-03 Study

  effective acute attack treatment in episodic cluster headache

  (but not chronic cluster headache attacks)

- NHS approval for cluster headache
- I recommend it 3 stimulations x 3 times per day
- If no benefit at 3 months stop
- If some benefit – worth continuing
- May reach maximum effect by 9-12 months

Nerve Blocks - GONB / MCNB

Steroid (eg kenalog)

Long acting local anaesthetic (eg levobupivacaine 0.5%)

Large volume within safe limits

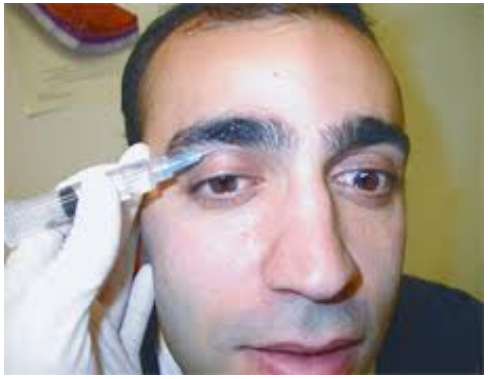
Benefits

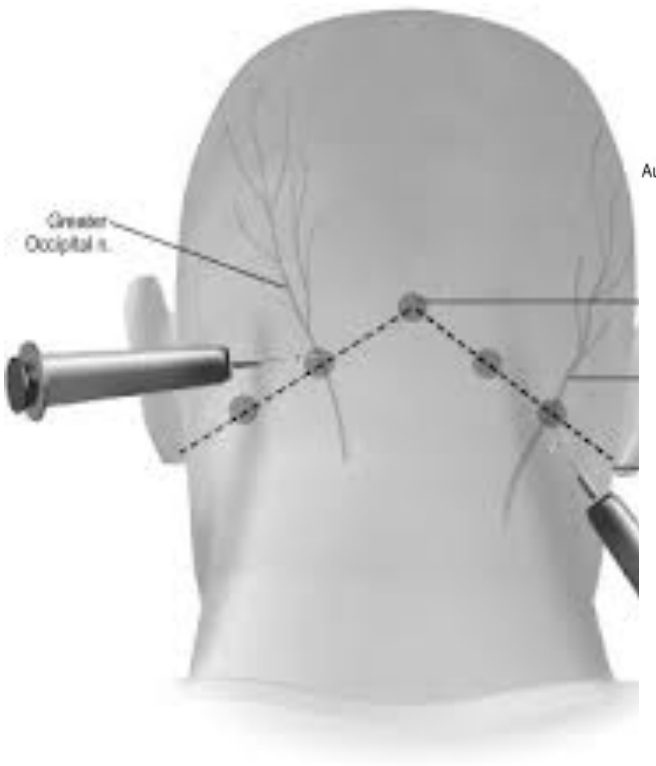
- Easy, rapid onset of action, one off treatment
- Safe
- Pregnancy (and planning), breastfeeding

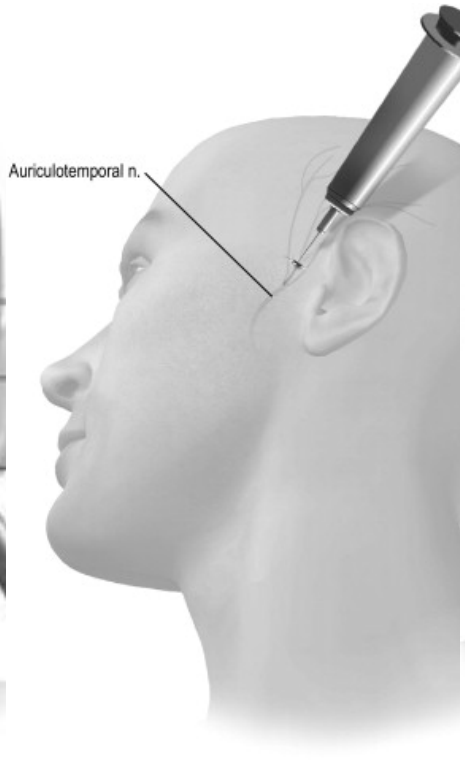
Risks:

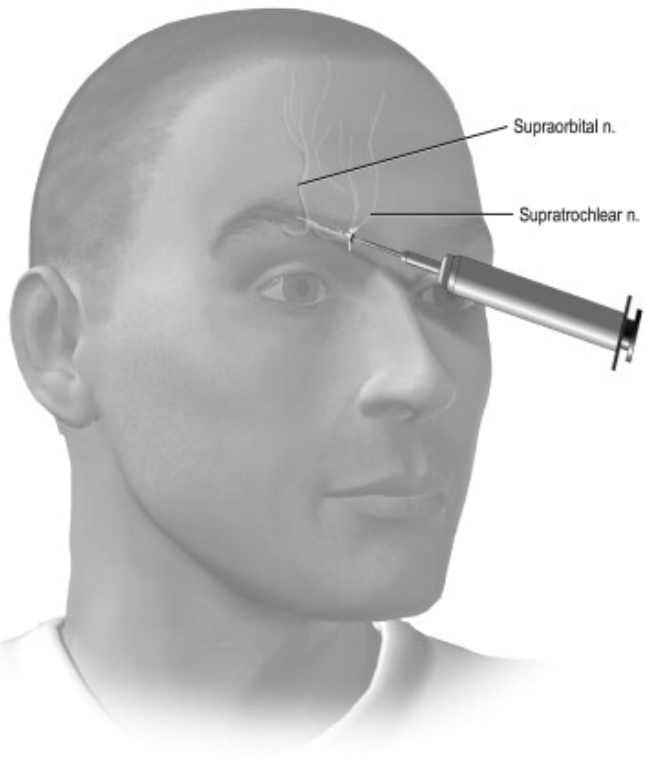
- Skin dimple (fat atrophy)] very rare if use low steroid dose
- Hair loss] (<1 in 150)
- Rare – worse headache
- Very rare - severe mood disturbance for few weeks

Multiple Cranial Nerve Blocks (MCNB)







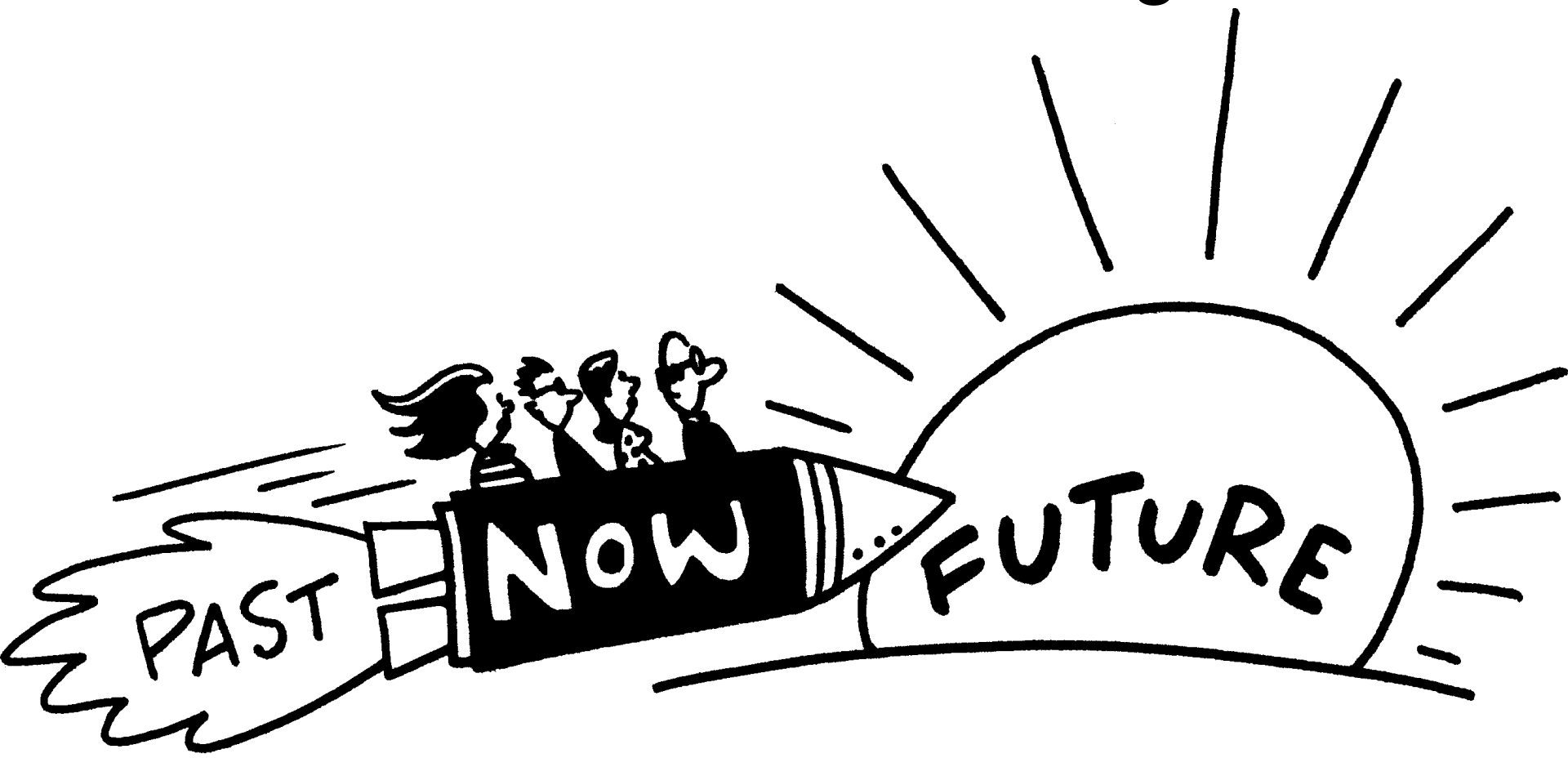


MCNB* – anecdotal experience

Condition	Response	Duration
Chronic migraine	50%	days to months
Hemicrania Continua (HC)	75%	often months
Episodic Cluster (ECH)	75%	usually covers cluster bout
Chronic Cluster (CCH)	50-75%	weeks to months

- Total <20mls of 0.5% levobupivacaine
- 0.25ml Kenalog per each occipital injection

Where have we come and where are we heading?



Headache Prevention

What is the future direction?

Drugs

Vs.

Handheld stimulators

Vs.

Local Injections

Vs.

Systemic Injections

(CGRP Monoclonal Abs)

Efficacy
Safety
Tolerability
Practicality
Compliance
Teratogenicity
Cost
NHS resources

CGRP monoclonal antiobodies

- 4 drugs
  - Fremanezumab - monthly sc
  - Galcanezumab - monthly sc
  - Erenumab - monthly sc
  - Eptinezumab - 3 monthly IV injection

- All have proven benefit in migraine

CGRP monoclonal antiobodies in CH – RCT Trial evidence

Galcanezumab

- Effective in preventing episodic CH – but at **300mg** dose

  (migraine dose = 240mg initial dose then 120mg)

  - Licensed US for episodic cluster headache
  - Not NICE approved in UK for cluster headache
- Not proven effective in preventing chronic CH

Fremanezumab

- Studies to prevent Episodic and Chronic CH negative

Eptinezumab

- Not been found effective in CH to date

CGRP monoclonal antiobodies in CH – RCT Trial evidence

Negative RCT trials:

- Do not exclude treatment having effect in small numbers of patients
- Do not exclude very small benefits in more patients
- Depend on study design and number of patients studied

BUT a negative study suggests we are not looking at a dramatically helpful treatment that will help many patients with the condition

? Wrong target for treatment or wrong dose

Occipital Nerve Stimulation

Varied results – often effective in highly refractory patients

ICON RCT studies have demonstrated benefits

Meta analysis of 45 small studies - pooled response rate of 57%

Need to do bilateral

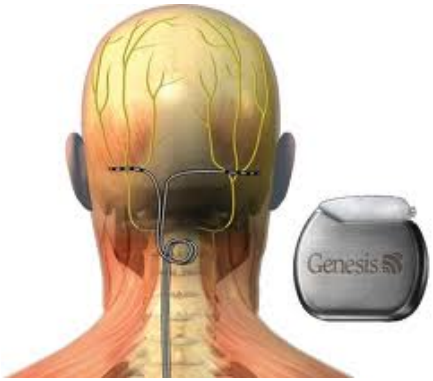
Can take up to 6 months to onset of useful effect

May reduce severity and frequency of CH attacks

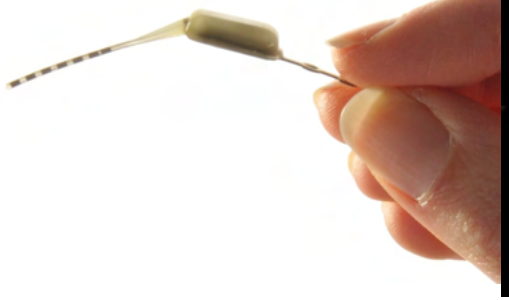
Can be dramatic

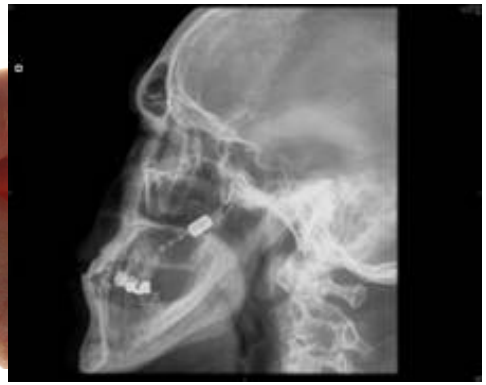
Potential side effects and complications – common

Need to do in experienced centre



SPG stimulation – not currently available Worldwide for CH





- ATI Neurostimulation system

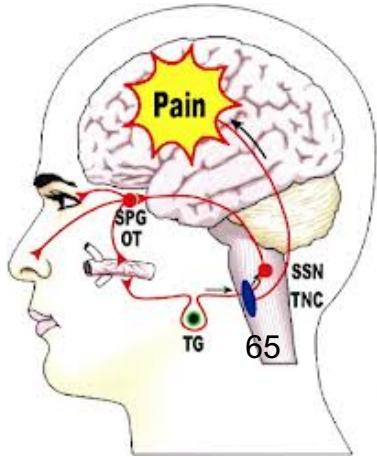
  Abortive > preventative

  67.1% of treated attacks achieved pain relief at 15 minutes, compared to 7.4% of sham treated attacks ($p<0.0001$)

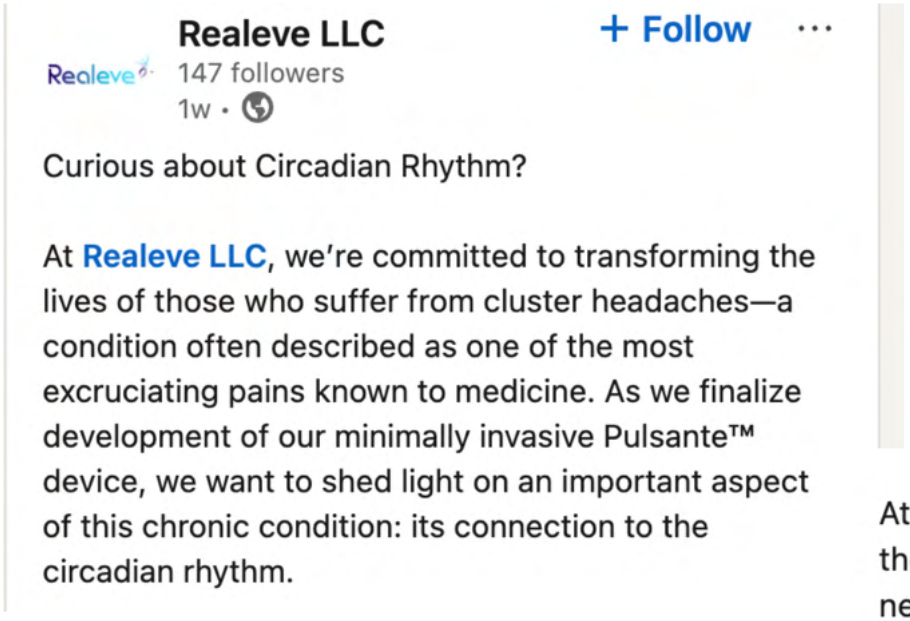
  Average number of cluster attacks per week reduced by 31% ($p=0.005$)

  Meaningful improvements in quality of life

  Cost effective (reduced acute attack medications)



Realeve



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Curious about Circadian Rhythm?

At **Realeve LLC**, we're committed to transforming the lives of those who suffer from cluster headaches—a condition often described as one of the most excruciating pains known to medicine. As we finalize development of our minimally invasive Pulsante™ device, we want to shed light on an important aspect of this chronic condition: its connection to the circadian rhythm.

At Realeve, our mission is to give patients control over their pain. The Pulsante™ device is designed to offer a new level of relief, helping patients reclaim their lives from the grip of cluster headaches.

Stay tuned as we continue to push forward, driven by science, compassion, and the goal of making a real difference.

Learn more about our work at **realeve.net**.

#ClusterHeadache #CircadianRhythm #Innovation #MedTech #Realeve #Pulsante #PatientCare

Psychedelics – LSD and Psilocybin

Anecdotal reports of benefit to abort attacks, extend remissions or reduce attack frequency

- Placebo vs real effect?
- Regression to the mean
- ? Basic science supports mechanism of action
- ? Safety and drug interactions with other medicines

Little clinical trial supportive evidence

- Certainly of interest
- Problem as Class A drugs (legal); can not prescribe in UK
- No medical product (consistency)
- Long term safety data limited (beware share similarities with ergot drugs that may cause significant medical risk in long term use)

Risk of fibrosis

J Psychopharmacol. 2024 Jan 12;38(3):217–224. doi: 10.1177/02698811231225609

Microdosing psychedelics and the risk of cardiac fibrosis and valvulopathy: Comparison to known cardiotoxins

Antonin Rouaud [1], Abigail E Calder [1], Gregor Hasler [1,2,✉]

months or years. Concerningly, both LSD and psilocybin share structural similarities with medications which raise the risk of cardiac fibrosis and valvulopathy when taken regularly, including methysergide, pergolide, and fenfluramine. 3,4-Methylenedioxymethamphetamine, which is also reportedly used for microdosing, is likewise associated with heart valve damage when taken chronically. In this review,

Conclusion and future directions

Taking all this information into consideration, it is possible that chronic microdosing may carry a risk of fibrosis and VHD, which should be assessed in future studies.

Furthermore, potency at 5-HT2BR appears to be the best predictor of potential for drug-induced VHD, and it is possible that even microdoses are indeed large enough to raise the risk of fibrosis when taken regularly (Huang et al., 2009).

Psychedelics – exploratory studies

- Exploratory investigation of a patient-informed low-dose psilocybin pulse regimen in the suppression of cluster headache: Results from a randomized, double-blind, placebo-controlled trial. Schindler et al. Headache 2022.
  - Results from 14 of 16 randomised patients (vs placebo)
  - 3 dose pulse psilocybin (each 5 days apart)
  - Note very low number of attacks per week at outset (approx. 8 / week)
  - Attacks reduced by > 5 per week in active group vs no change in placebo – not statistically significant
  - ? Blinding as patients experienced psychotropic effects
  - No serious / adverse effects reported

"Findings from this initial, exploratory study provide valuable information for the development of larger, more definitive studies. Efficacy outcomes were negative, owing in part to the small number of participants. The separation of acute psychotropic effects and lasting therapeutic effects underscores the need for further investigation into the mechanism(s) of action of psilocybin in headache disorders."

Psychedelics – exploratory studies

- Psilocybin pulse regimen reduces cluster headache attack frequency in the blinded extension phase of a randomized controlled trial. Schindler et al J Neurol Sci 2024
  - 3 dose pulse psilocybin (10mg/70kg, each 5 days apart)
  - Repeated after 6 months
  - Reduced cluster attack frequency by 50% but did not reach statistical significance
  - But – only 10 patients

Ketamine

Systematic review – Neumann et al 2024

- 4 reports, 68 patients
- All uncontrolled data
- Reported outcomes very heterogenous

Limited currently to anecdotal data

Challenging to deliver

Need for anaesthetist provision with close monitoring

(Limited numbers treated so far at Walton Centre, Liverpool)

Psychotic side effects common

Anecdotal cases show benefit

Demand valve O2

Watch this space…

Useful information

OUCH UK

https://ouchuk.org

NHS Vanguard Comprehensive Migraine Guide

www.bit.ly/migraine-booklet

The Brain Charity

https://www.thebraincharity.org.uk/