

SUNCT, SUNA and Trigeminal Neuralgia

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SUNCT, SUNA: an historical note

1978 Multiple, neuralgiform, unilateral headache attacks associated with conjunctival injection and appearing in clusters. A nosological problem.

1989: Short-lasting, unilateral neuralgiform headache attacks with conjunctival injection, tearing, sweating and rhinorrhea.

2004: SUNCT and SUNA (Appendix)

2013: SUNHA (Short-lasting Neuralgiform Headache Attacks)

2018: SUNHA (Short-lasting Neuralgiform Headache Attacks)

2019: SUNA (Short-lasting Neuralgiform Headache Attacks with Autonomic features)

SUNCT and SUNA: Terminology

Short-lasting

Unilateral

Neuralgiform attacks with

Conjunctival injection and

Tearing



Pain associated with BOTH

- Conjunctival injection
- Lacrimation

Short-lasting

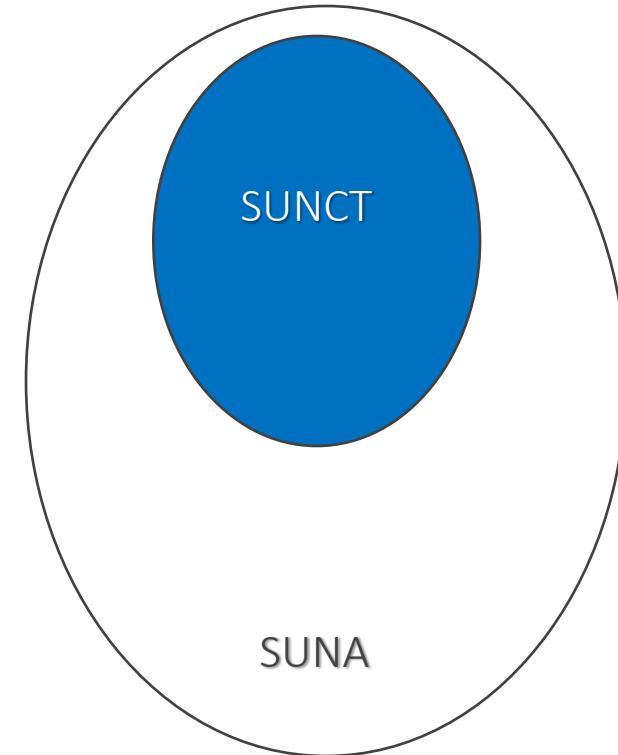
Unilateral

Neuralgiform attacks with

Autonomic symptoms



Pain associated with at least one cranial autonomic feature



SUNCT, SUNA and Trigeminal neuralgia

DEMOGRAPHIC AND CLINICAL OVERLAP

SUNCT and SUNA: ICHD-3 diagnostic criteria

SHORT-LASTING UNILATERAL NEURALGIFORM HEADACHE ATTACKS

Laterality and site:	• Unilateral: V1-V2-V3
Pain severity:	• Moderate - severe
Attacks duration:	• 1-600 seconds
Attack pattern:	• Single stab – groups - serrated
Cranial autonomic features:	• ≥ 1 (SUN ^{CT} and SUN ^A)
Attack frequency:	• ≥ 1 /day (when the disorder is active)

Further sub-classified as:

- Chronic SUNCT/SUNA
- Episodic SUNCT/SUNA

- Cutaneous triggers (74%)
- No refractory periods

A prospective comparative study and analysis of predictors of SUNA and SUNCT

Giorgio Lambru, MD, Khadija Rantell, PhD, Andrew Levy, MD, and Manjit S. Matharu, MBChB, FRCP, PhD

Neurology® 2019;93:1-11. doi:10.1212/WNL.00000000000008134

Prospective detailed demographic and clinical description of a series of SUNCT=70 and SUNA=63 patients

Detailed the phenotype of SUNCT and first detailed description of SUNA

Comparison of demographic and clinical characteristics between SUNA & SUNCT

SUNCT and SUNA: demographics and clinical phenotype

	SUNCT=70	SUNA=63
Gender	F = 71.4%	F = 54.3%
Site of pain	V1: 90% V2: 73% V3: 28.6%	V1: 81% V2: 77.8% V3: 36.5%
Pain character	- Stabbing - Sharp - Electrck-shock like	- Stabbing - Sharp - Electrck-shock like
Pain duration	162.4 ± 194.5 seconds	158.5 ± 200.5 seconds
Pain frequency	Median: 30 (IQR 10–55)	Median: 20 (IQR 8–53) Mean frequency of >100 attacks: 7-11%
Cranial autonomic symptoms	>> Ptosis and rhinorrhoea >> severe lacrimation	<< ptosis and rhinorrhoea < severe lacrimation

SUNCT and SUNA: demographics and clinical phenotype

	SUNCT=70	SUNA=63
Triggered/ spontaneous attacks	S+T: 63% S only: 33% T only: 4.3% 91%: cutaneous triggers Alcohol was not a trigger	S+T: 49% S only: 47.6% T only: 3.2% 88%: cutaneous attacks Alcohol was not a trigger
Refractory period	7%	7%
Behaviour during pain	No restlessness: 70%	No restlessness: 69%
Background pain	53%	43%
Migraine features	45% (at least 1 migraine symptom)	33% (at least 1 migraine symptom)
Temporal pattern	Chronic: 87%	Chronic: 92%

SUNA and SUNCT comparison and new proposed diagnostic criteria

The comparison between SUNA and SUNCT phenotypes showed no significant clinical differences except that SUNCT is characterized by more prominent cranial autonomic features and triggerability compared to SUNA.

- Significant association between ipsilateral ptosis and SUNCT
(OR 3.79, 95% CI 1.64–8.77, $p = 0.002$)
- Significant association between ipsilateral rhinorrhoea and SUNCT
(OR 2.46, 95% CI 1.09, 5.59, $p = 0.031$).
- Spontaneous attacks only was found to be a predictor of SUNA
(OR 2.58, 95% CI 1.10, 6.05, $p = 0.029$).

SUNCT and SUNA should be considered one clinical entity

SUNCT and SUNA: Differential diagnosis

Short-lasting headache and facial pain syndromes

PRIMARY HEADACHE SYNDROMES

Trigeminal autonomic cephalalgias

- Cluster headache
- Paroxysmal hemicrania
- Hemicrania continua

Other rare syndromes

- Primary stabbing headache

NEUROPATHIC SYNDROMES

Paroxysmal (Cranial neuralgias)

- Trigeminal neuralgia
- Glossopharyngeal neuralgia
- Nervus intermedius neuralgia
- Terminal branch neuralgias

Continuous

- Trigeminal neuropathy

TRIGEMINAL NEURALGIA: ICHD-3 diagnostic criteria

Disorder characterised by recurrent, short-lived very severe pain paroxysms limited to the distribution of one or more sensory divisions of the trigeminal nerve

Classical TN, purely paroxysmal

Laterality and site:

- Unilateral: V1-V2-V3

Pain severity:

- Severe

Attacks duration:

- 1-120 seconds

Pain quality:

- Electric shock-like, stabbing

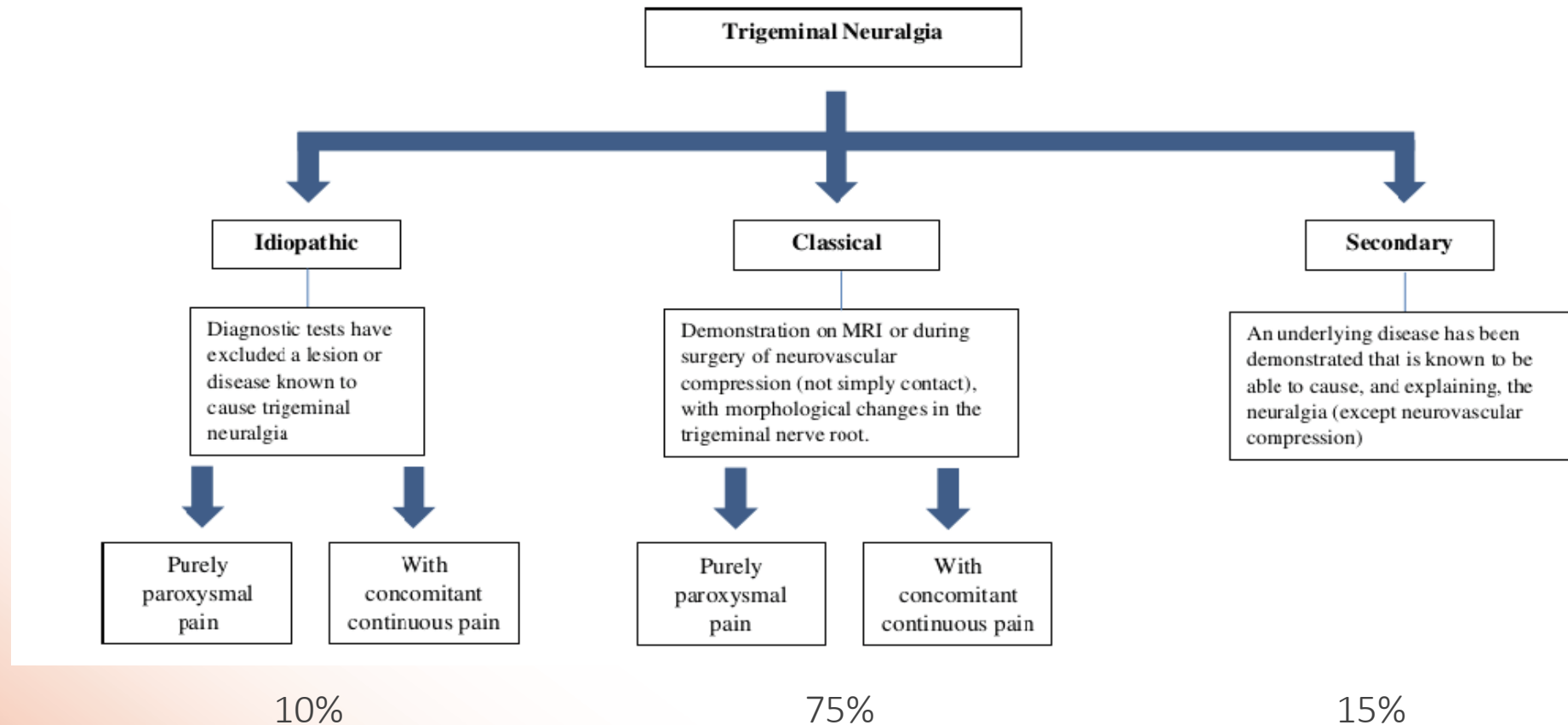
Attack frequency:

- Precipitated by innocuous stimuli of the affected side of the face

Classical TN with concomitant persistent facial pain

TRIGEMINAL NEURALGIA: ICHD-3 diagnostic criteria

MRI brain with trigeminal sequences (CISS/FIESTA) is part of the diagnostic work-up



SUNCT and SUNA: Differential diagnosis – TN

	SUNCT/SUNA	Trigeminal neuralgia
Site of pain	V1-V2-v3	V2-V3-v1
Duration	≤10 minutes	≤2 minutes
Severity	Moderate-severe	Severe
Pain quality	Stabbing	Stabbing
Attacks frequency	≥1/day	1-hundreds
Cranial autonomic features	C+T or ≥1	None
Cutaneous triggers	YES	YES
Refractory period	ABSENT	PRESENT
Response to CBZ	PARTIAL	COMPLETE

SUNCT and SUNA and Trigeminal neuralgia

- Clinical differences -

SITE OF THE PAIN

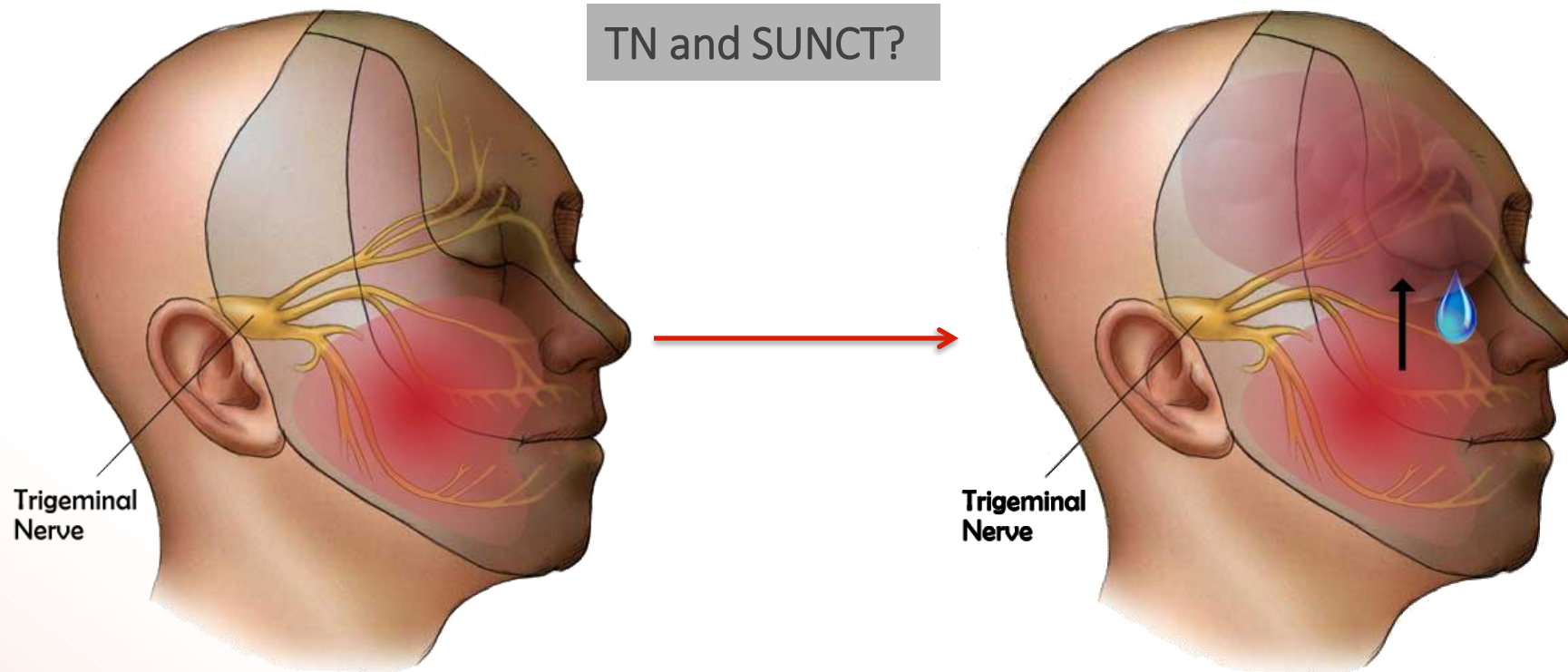
- When pain in V2-V3, patients are rarely asked about cranial autonomic signs and symptoms

CRANIAL AUTONOMIC FEATURES

- Sjaastad et al (1997): 8/19 patients with V1 TN (42%); mainly lacrimation and conjunctival injection
- Pareja et al (2002): 21/26 attacks of V1 TN (81%): lacrimation (mild/moderate)
- Simms et al, 2011: 62/92 TN patients (67%) 1 autonomic symptom (not only V1 TN): correlation between site and type of symptom

SUNCT and SUNA and Trigeminal neuralgia

- Clinical scenario-



Short-lasting attacks:

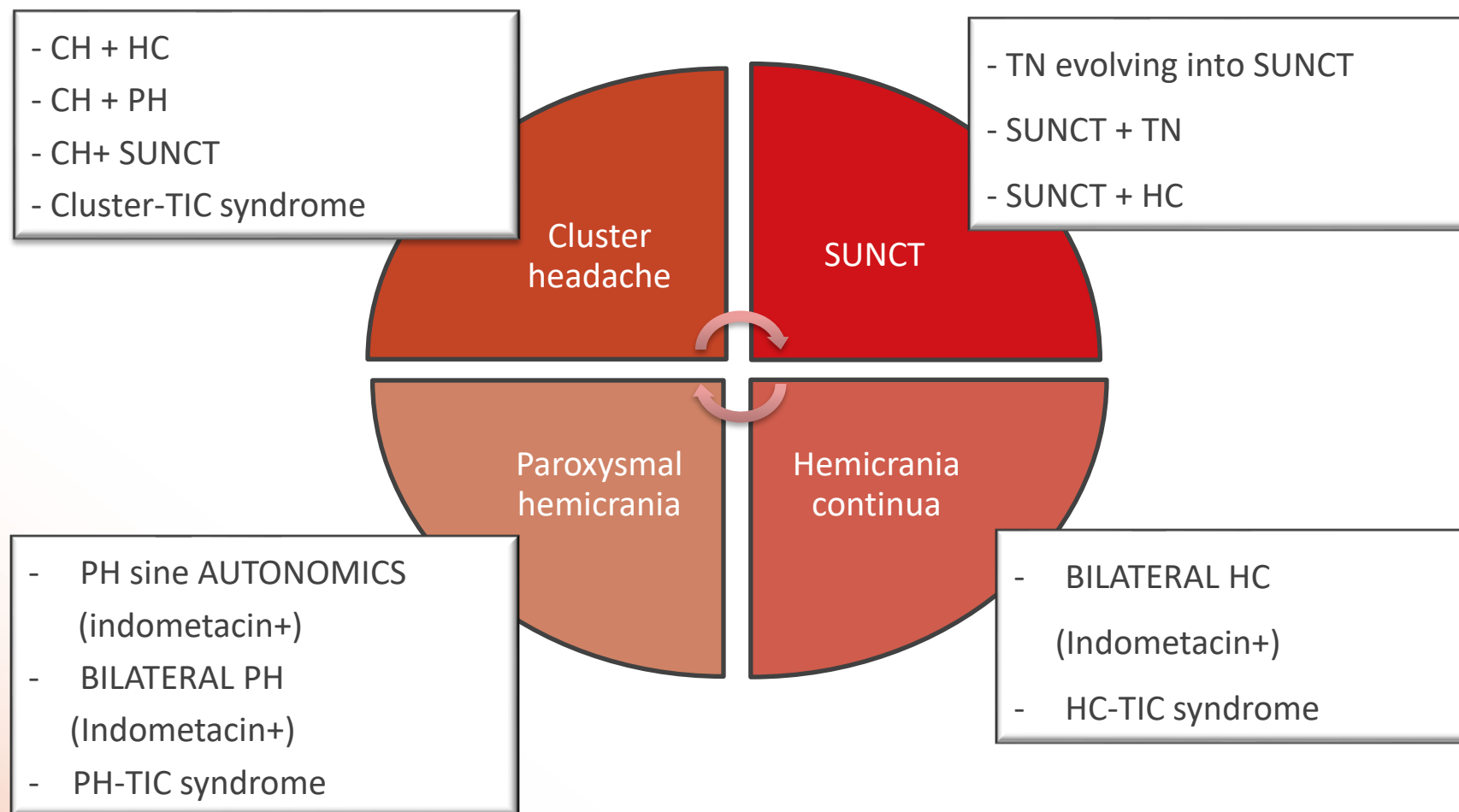
- Featureless in V2-V3

Longer-lasting attacks:

- V1 radiation and CAF

TRIGEMINAL AUTONOMIC CEPHALALGIAS

Coexistence of multiple TACs

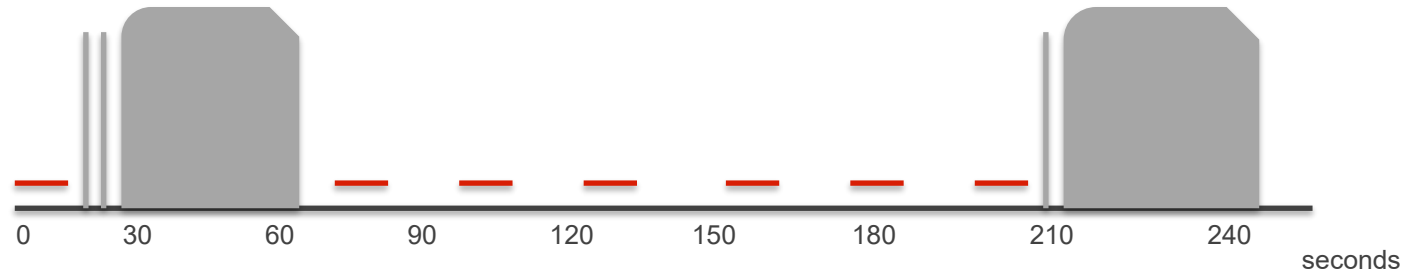


SUNCT, SUNA and TRIGEMINAL NEURALGIA

Refractory period

DEFINITION

Period (2-3 minutes) after a paroxysmal attack where new attacks cannot be elicited



DATA

- Lambru *et al* (2019): 7% of SUNCT and SUNA had a refractory period
- Paliwal *et al* (2012): 3 SUNCT cases with refractory periods
- Exact proportion of TN patients with refractory period is unknown

CLINICAL RELEVANCE

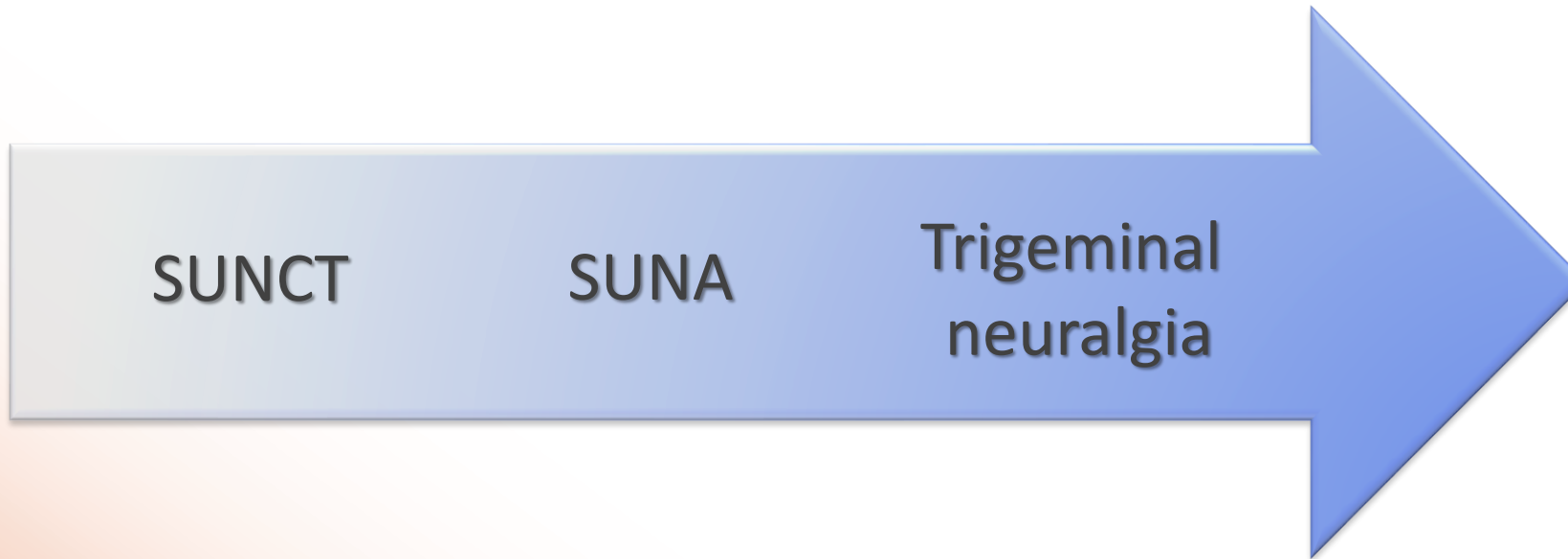
- Most patients struggle to remember or never dare triggering another attack
- May be useful in differentiating between TN and SUNCT/SUNA

SUNCT, SUNA and Trigeminal neuralgia



SUNCT, SUNA and trigeminal neuralgia: different disorders or variants of the same disorder?

Giorgio Lambru^a and Manjit S. Matharu^{a,b}



SUNCT and SUNA and Trigeminal neuralgia

- Demographic and clinical continuum -

SUNCT	SUNA	Trigeminal neuralgia
F > M	F > M	F > M
Mainly V1-V2	Also V2-V3	Mainly V2-V3
Pronounced and numerous CAF	Less pronounced and numerous CAF	Mild or no CAF
Spontaneous/triggered attacks	Spontaneous/triggered attacks	Triggered/spontaneous attacks
Refractory period (No=93%)	Refractory period (No=93%)	Refractory period (Yes=100%?)
Background pain (53%)	Background pain (43%)	Atypical TN (49%)

SUNCT, SUNA and Trigeminal neuralgia

AETIOLOGICAL OVERLAP

SUNCT and SUNA and Trigeminal neuralgia

- Aetiology-

POSTERIOR FOSSA ABNORMALITIES

- Ipsilateral cerebellopontine arteriovenous malformation
- Carotid artery aneurism
- Ischaemic cerebellar infarction
- Multiple sclerosis with lesions in the midbrain and pons
- Epidermoid tumor in the cerebellopontine angle

PITUITARY ADENOMAS

- Macro- and micro-prolactinomas
- Macro-micro adenomas
- Adenoma GH-secreting

SUNCT and SUNA and Trigeminal neuralgia

Trigeminal neurovascular conflict

COMPRESSION OF THE TRIGEMINAL SENSORY ROOT



- In TRIGEMINAL NEURALGIA (n=135 pts): severe neurovascular contact was highly prevalent on the symptomatic compared to the asymptomatic side [53% versus 13%, odds ratio = 11.6 (4.7–28.9), $P < 0.001$].
- In SUNCT/SUNA (N=159 pts): severe neurovascular contact were considerably more prevalent on the symptomatic side (61.4%), compared to the asymptomatic side (31.0%) (OR 4.16, 95% CI 2.46-7.05; $P < 0.0001$).

Severe (with morphological changes) trigeminal NVC is involved in the aetiology of Trigeminal neuralgia and SUNCT/SUNA

SUNCT and SUNA and TRIGEMINAL NEURALGIA

Demographic, clinical and aetiological continuum

SUNCT	SUNA	Trigeminal neuralgia
F > M	F > M	F > M
Mainly V1-V2	Also V2-V3	Mainly V2-V3
Pronounced and numerous CAF	Less pronounced and numerous CAF	Mild or no CAF
Spontaneous/triggered attacks	Spontaneous/triggered attacks	Triggered/spontaneous attacks
Neurovascular conflict (61%)	Neurovascular conflict (61%)	Neurovascular conflict (53%)

SUNCT, SUNA and Trigeminal neuralgia

MEDICAL AND SURGICAL TREATMENTS' OVERLAP

SUNCT and SUNA treatment

Original research

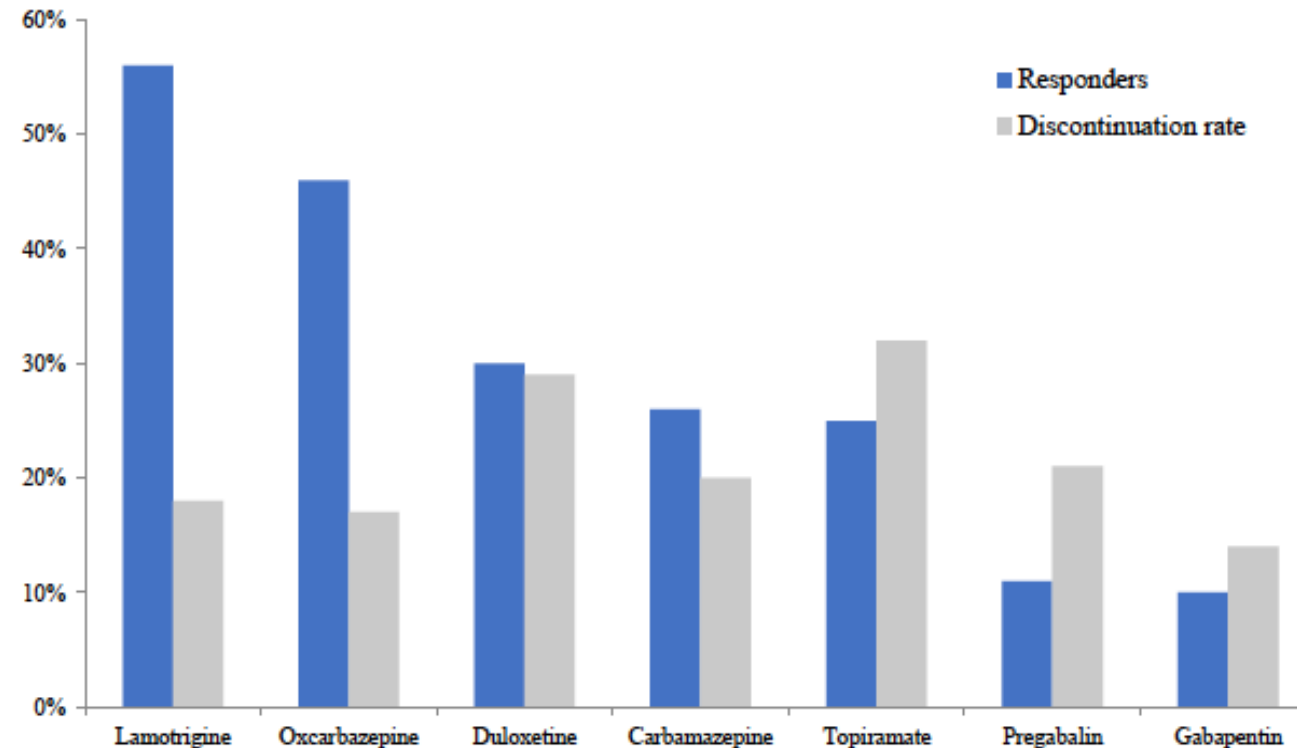
Medical treatment of SUNCT and SUNA: a prospective open-label study including single-arm meta-analysis

Giorgio Lambru,¹ Anker Stubberud,^{2,3} Khadija Rantell,⁴ Susie Lagrata,^{1,5}
Erling Tronvik,^{2,3} Manjit Singh Matharu ^{1,5}

Prospective open-label single centre study and single-arm meta-analysis

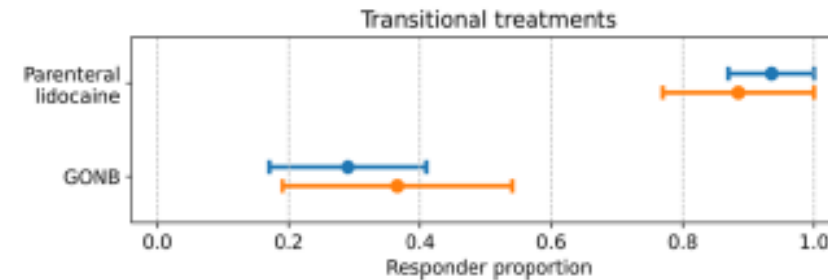
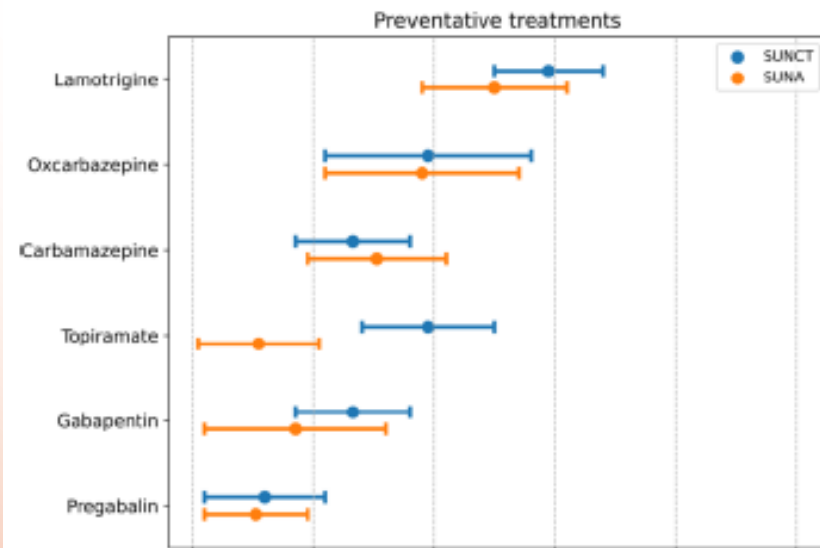
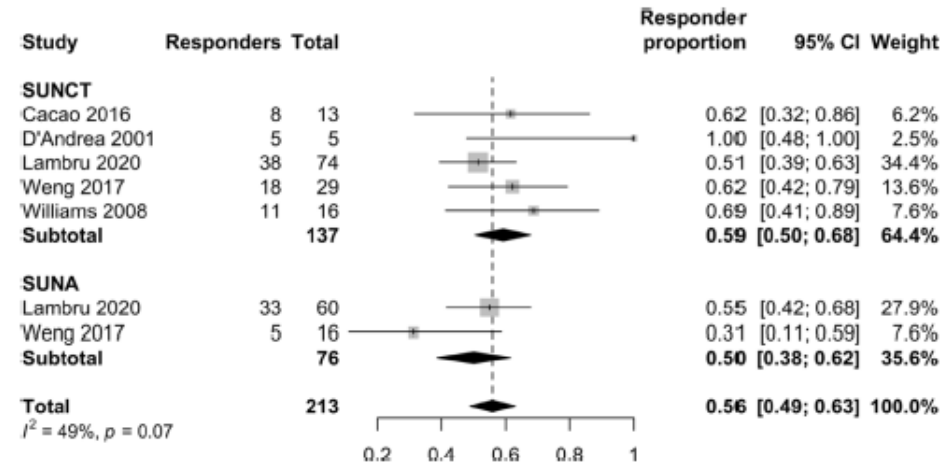
➤ N= 161 patients

SUNCT and SUNA treatment



- GONBs: 37% of patients responded for a mean of 38.4 ± 34.7 days
- IV Lidocaine: 90% of patients responded for a mean of 22.1 days (3–90 days)

SUNCT and SUNA treatment: meta-analysis



SUNCT and SUNA treatment

- Lamotrigine and oxcarbazepine seem to be the most effective treatments.
- No significant differences emerged in our study from the comparison of oral and parenteral treatments between SUNCT/SUNA
- Sumatriptan, oxygen, verapamil and indometacin are not effective in SUNCT/SUNA

Medications (maximum dose)	
First-line treatment	▶ Lamotrigine (up to 700 mg/day)
Second-line treatments	▶ Oxcarbazepine (up to 2400 mg/day)
	▶ Duloxetine (up to 120 mg/day)
	▶ Carbamazepine (up to 1600 mg/day)
	▶ Topiramate (up to 800 mg/day)
Third-line treatments	▶ Gabapentin (up to 4800 mg/day)
	▶ Pregabalin (up to 600 mg/day)
	▶ Lacosamide (up to 400 mg/day)
	▶ Mexiletine (up to 1200 mg/day)

Trigeminal Neuralgia

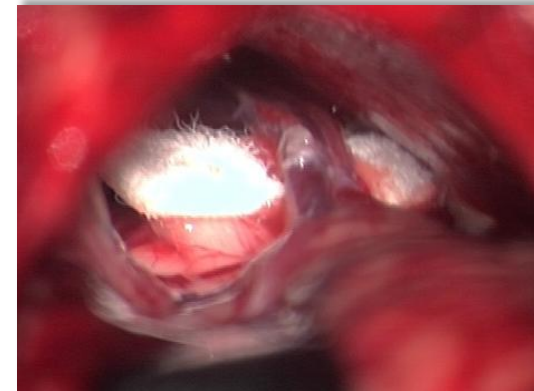
- Medical management -

	Evidence	Dose	Responders	Tolerability
Carbamazepine	Class I	800-1200 mg/d	88% NNT: 1.7	Poor (NNH: 3.4)
Oxcarbazepine	Class II	600-1800 mg/d	88%	Better than CBZ Less drug interaction
Lamotrigine	Class II	200-400 mg/d	- 84.6% - 62%	Better than CBZ
Baclofen	Class II	30-60 mg/d	70%	1 drop out
Tizanidine	Class III	12 mg/d	80% (6/10 efficacy wore off)	3/10 dropped out
Pregabalin	Class IV	150-600 mg/d	74% (25% pain-free)	42% had side effects
Gabapentin	-	1800-3600 mg/d	Similar to CBZ	Better than CBZ



Trigeminal microvascular decompression for short-lasting unilateral neuralgiform headache attacks

Giorgio Lambru, Susie Lagrata, Andrew Levy, Sanjay Cheema, Indran Davagnanan, Khadija Rantell, Neil Kitchen, Ludvic Zrinzo, Manjit Matharu



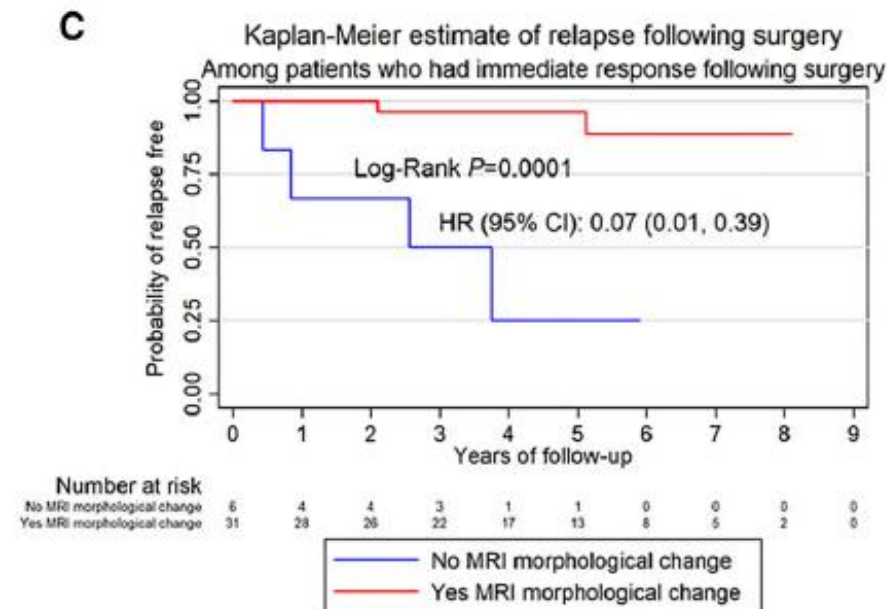
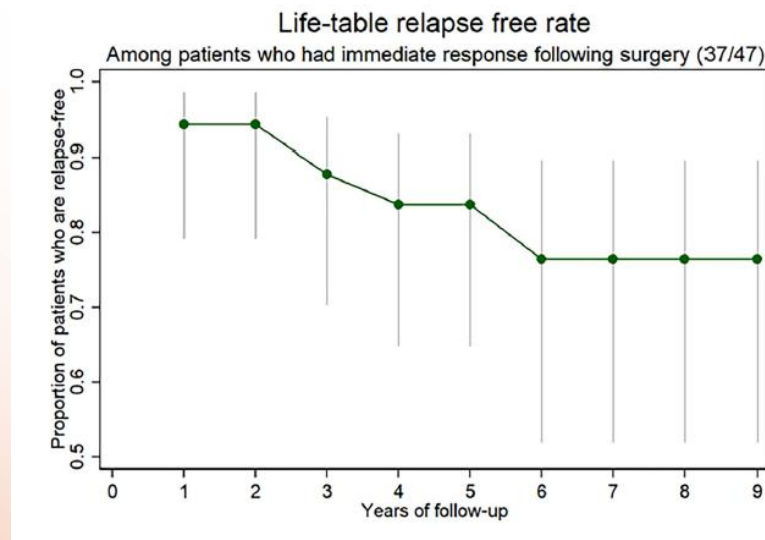
Prospective single-centre uncontrolled study

47 medically refractory patients (SUNCT = 31; SUNA = 16)

SUNCT and SUNA: trigeminal MVD

- N=47 patients
- Mean post-surgery follow-up was 57.4 ± 24.3 months (range 11-96 months)
- Post-op responders: 79%; responders at final FU: 66%

The annual risk of recurrence at year 1 was 5.6%, at year 3 was 12.3%, at year 4 it was 16.3% and at year 5 it was 23.4%.



TRIGEMINAL NEURALGIA and SUNCT/SUNA

- Surgical management -

MICROVASCULAR DECOMPRESSION OF THE TRIGEMINAL NERVE

	COHORT	FOLLOW-UP	RESPONDERS
Barker et al, (1996)	1155 TN patients	10 years	70% of patients
Lambru et al (2022)	47 SUNCT/A patients	5 years	66% of patients

- Trigeminal MVD is an established surgical treatment option for refractory TN
- Emerging evidence suggest its role also in the management of refractory SUNCT/A patients

SUNCT and SUNA and TRIGEMINAL NEURALGIA

Demographic, clinical, aetiological, therapeutic continuum

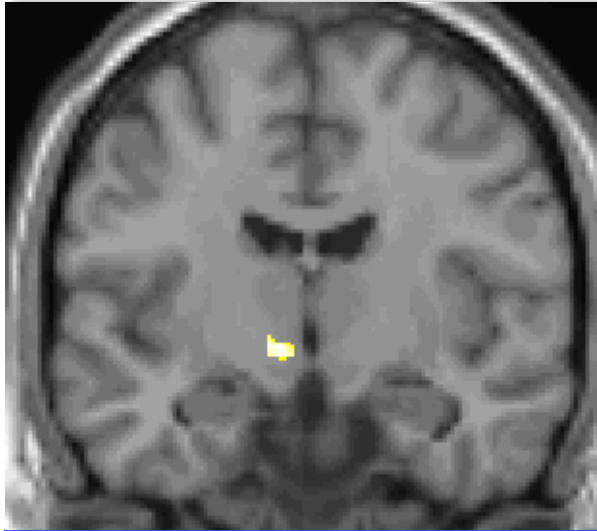
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Spontaneous/triggered attacks	Spontaneous/triggered attacks	Triggered/spontaneous attacks
Neurovascular conflict (61%)	Neurovascular conflict (61%)	Neurovascular conflict (53%)
Sodium channels block	Sodium channels block	Sodium channels block
MVD: 66 %	MVD: 66%	MVD: 70%

SUNCT, SUNA and Trigeminal neuralgia

CONCLUSIONS

SUNCT and SUNA

- Pathophysiology -

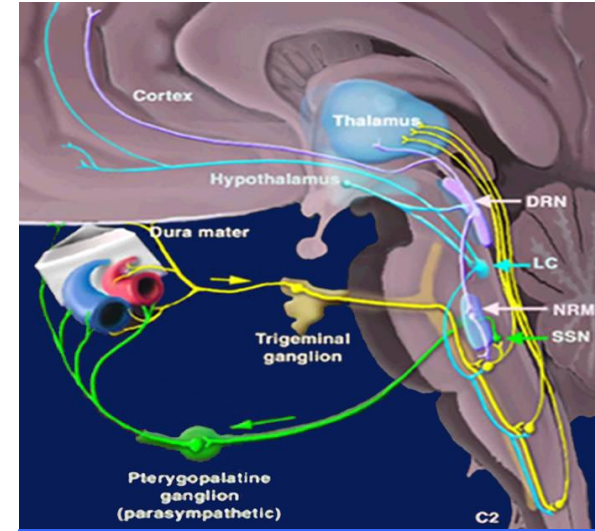


DYSFUNCTION OF THE
POSTERIOR HYPOTHALAMUS

Lack of modulation
of the activity of the
Trigeminal nucleus
caudalis

→

Central disinhibition
of the Trigemino-autonomic
reflex



TRIGEMINO-AUTONOMIC
REFLEX

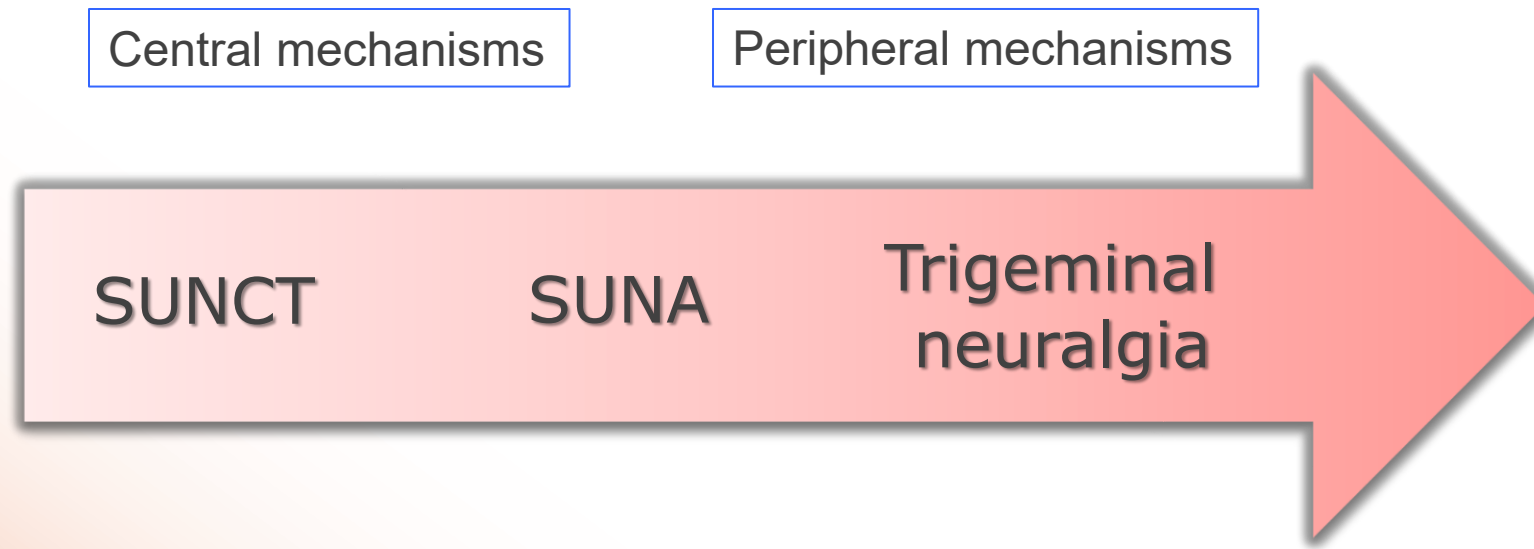


- Short-lasting paroxysms
- Cutaneous triggers
- Absence of refractory period
- Response to Na channel blockers

SUNCT-SUNA-TRIGEMINAL NEURALGIA

- Pathophysiological model -

SUNCT, SUNA and trigeminal neuralgia may recognise a complex interaction and degree of involvement of similar central and more peripheral mechanisms.



SUNCT, SUNA and Trigeminal Neuralgia:

Different entities or a continuum of the same disorder?

SUNCT and SUNA are considered TACs:

- Unilateral mainly V1 pain and the presence of CAF
- Posterior hypothalamic activation during attacks

SUNCT, SUNA and TN display a remarkable overlap in:

- Demographic data and clinical phenotype
- Radiological findings
- Outcome of medical and surgical treatments

SUNCT, SUNA and TN may constitute a continuum and may be lumped together under the same diagnostic category

