



2023 FPA VIRTUAL
CONFERENCE
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Update on Medical Treatment of Trigeminal Nerve Pain and Other Nerve Pain - Craniofacial Pain Disorders

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Professor of Neurology (Adjunct Professor)

Department of Neurology

Duke University, Durham NC - USA



Professor of Dentistry (Adjunct Professor)

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Conflict-of-Interest Statement and Qualifier.

Dr Wolfgang Liedtke is a full-term executive employee of Regeneron Pharmaceuticals (Tarrytown NY, USA), since April 2021.

He continues to hold Adjunct Faculty status, at the rank of Professor, with Duke University, Department of Neurology, and New York University College of Dentistry.

The content of this presentation does not represent the views of Regeneron Pharmaceuticals, neither the views of Duke University or New York University.

In 2017, Dr Liedtke co-founded TRPblue, a biotechnology startup company that aims for commercialization of patented small molecules out of the former Liedtke-Lab for topical treatment to skin for pain and chronic itch.

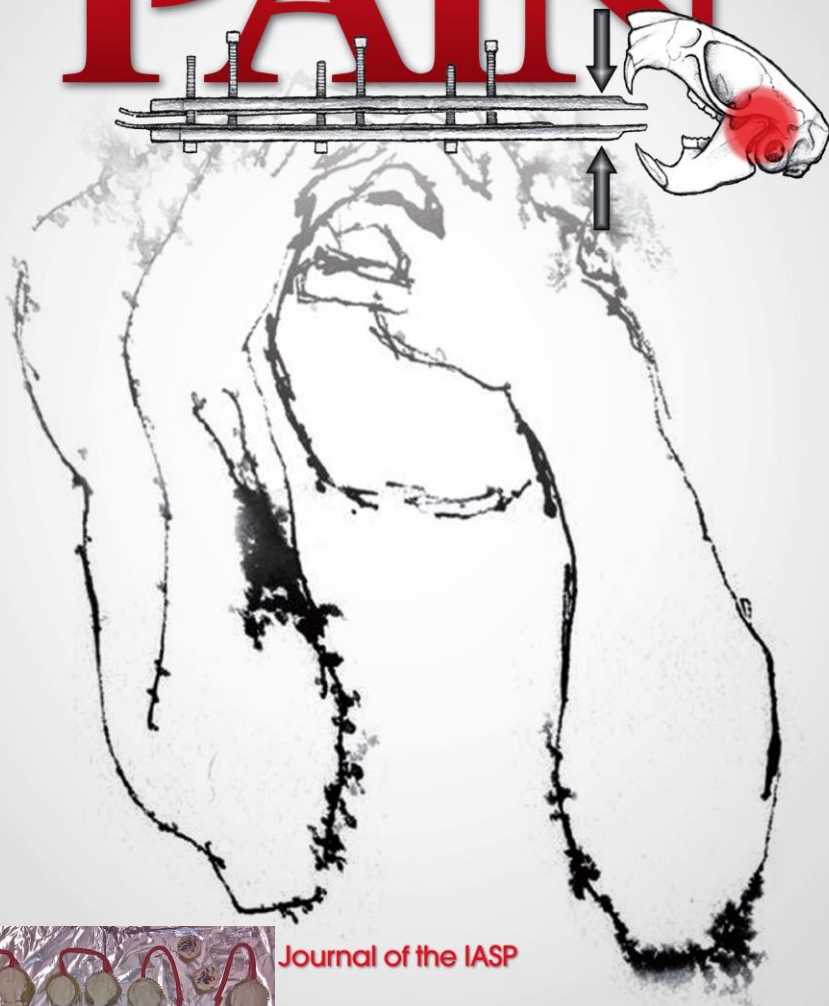
Dr Liedtke is presenting here an informational overview on head-face pain.

The presentation is educational-scholarly in nature.

It also showcases Dr Liedtke's own insights, views and opinions, which are not corporate view of Regeneron, neither do they represent the views of Duke University or New York University.

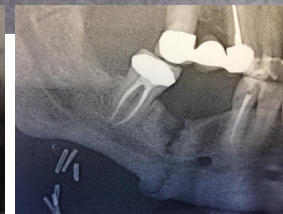
This presentation does not suggest concrete medical measures to be taken against human disease.

PAIN®



Journal of the IASP

clinically- **laboratory-** **based-investigator**



➔ biotech-pharma exec
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Medications for Facial Pain

fast-acting as-needed medications for attacks / episodic worsening
attack / episodic worsening needs to announce itself

legend

bold – compounding pharmacy

blue – controlled substance

italics – approval hurdles/ expensive

- sodium channel blocking anti-neuralgics
 - chewable carbamazepine 50-200 mg
 - liquid oxcarbazepine 50-200 mg
- **GABA-A-receptor enhancing benzodiazepine**
 - orally-dissolving clonazepam 0.125-0.25 mg**
 - liquid, 100-300 mg
- liquid gabapentin
- *orally dissolving –gepant*
- *–gepant nasal spray*
- **ketamine nasal spray**
 - rimegepant 75mg (anti-CGRP repurposing – fast onset !)
 - zavegepant 10mg (anti-CGRP repurposing – fast onset !)
 - 100-150mg/mL**
 - 280mg/mL S-ketamine (Spravato)*
 - 240IU/mL (great safety)**
- **oxytocin nasal spray**
- lidocaine jelly, spray

blood pressure: need to lower attack/ episodic worsening associated hypertension which can further aggravate pain

- fastest acting tablets: captopril 25 mg, clonidine 0.1 mg – joint management with family physician, cardio, hypertension
15-30 min
- **[clonidine nasal drops or nasal spray – fast-acting, but inconsistent absorption]**
- for adjunct sedation: **orally-dissolving clonazepam, liquid lorazepam**

Medication for Facial Pain

regular meds I – tablet taken by mouth in regular intervals

sodium channel inhibiting compounds

carbamazepine 200-400mg 2-3x/d

regular tablet – extended release

oxcarbazepine 300-600mg 2-3x/d

regular tablet – extended release

eslicarbazepine 400mg 2x/d

MoA beyond carba - oxcarba

lacosamide 100-200mg 2x/d

most potent sodium channel inhibitor, best safety - TME

zonisamide 25-100mg 2-4x/d

not as potent, but no effect on body weight

lacosamide, zonisamide suitable in case of SIADH (low sodium) caused by carbamazepine, oxcarba

gabapentinoids

gabapentin 300-800mg and higher, 2-4x/d

regular tablet – extended release

pregabalin 150-450mg and higher, 2-4x/d

(weight)

lamotrigine

100mg 2-4x/d and higher dose

need slow dosing in

Medication for Facial Pain

regular meds II – tablet taken by mouth in regular intervals

analgesic SSRI/SNRI

duloxetine	30-60 mg 1-2x/d	combination w gabapentinoids and/or sodium channel inhibitors capsules 20 mg lowest dose
venlafaxine	25-75mg 1-3x/d	can formulate lower dose; often works when duloxetine does not
vortioxetine	10-30mg/d	sometimes more punch than duloxetine
mirtazepine	15-30mg/d	can enhance weight; normalizes sleep
milnacipran	12.5-25mg 2-4/d	step-up vs duloxetine in comorbid fibromyalgia
bupropion	150-300mg/d	for mental health co-morbidities, NDRI rather than SNRI/SSRI

cannabinoids

marinol	2.5-20 2-3x/d	slow dose-in; cannabinoid effects – can be helpful 3 rd line agent
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anti-inflammatories

indomethacine	25-50mg 2-3x/d	potent pan-COX-i (unwanted effects) – indicative of paroxysmal hemicrania in case there is striking effectiveness
meloxicam	7.5-15mg 1x/d	for treatment of inflammatory co-morbidities in case long-term tx needed

Medication for Facial Pain

regular meds III – tablet taken by mouth in regular intervals // nasal sprays

low-dose naltrexone

unique treatment/prevention medicine // in combination with a well-balanced standard regimen
superb safety profile

in my hands, has changed MANY lives

1-4.5(-6) mg/d better taken before bed

MoA: 1 = kick on endogenous opioid system, in sync w circadian rhythm

2 = gliotropic effect (via TLR-receptors on glial cells), also in sync w circadian rhythm

compound medication

ultra low-dose naltrexone 0.1-0.75 mg/d

for pts who do not tolerate regular ldNtx (comorbidity ?)

suggestion: ldNtx post-MVD, post-stereotactic radiosurgery → prolong relapse interval ?

need clin study to address that question

nasal sprays containing oxytocin (24IU 2x/d) and ketamine (20mg 2-3x/d) can be tried (see treatment of attacks)

compound medications

Medication for Facial Pain

regular meds IV – anti-CGRP medications for subcutaneous self-injection

self-injected anti-CGRP monoclonal antibodies (subcutaneous self-injection)

galcanezumab	120 mg/monthly
fremanezumab	240 mg/monthly
erenumab	140 mg/monthly

these are chronic migraine-appropriate dosing regimens – higher dose more appropriate for trigeminal pain ?
(as for galcanezumab and cluster headache (?) - 300 mg helps more than 120 mg)

[Future: classic hypodermic needles might in the future be replaced with skin patch systems (microneedles)]

Medication for Facial Pain

regular meds V – opioids

low-potency opioids

hydrocodon, oxycodon, tramadol

¶ if helpful, can be used under the appropriate guiding principles

BUT

• when taking low-potency opioids, treatment with low-dose naltrexone becomes non-feasible

- aim for "drug holidays" to maintain susceptibility
- aim for "opioid rotation" to maintain susceptibility

BUT ALSO

- across-the-board phobia for combined treatment of low-potency opioids with orally-dissolving clonazepam not justified

In case low-potency opioids appear essential, but also still left w significant pain

- longer-term management with

¶ methadone (tablets, can also do liquid ((ultra-)low dose possible), odd doses possible; inexpensive, available)

¶ butorphanole

¶ levorphanole (possible difficulties in supply/coverage/\$\$\$)

¶ fentanyl patches

opioid rotation to maintain feasibility

¶ fentanyl lozenges - for as-needed palliation

The multifunctional peptide DN-9 produced peripherally acting antinociception in inflammatory and neuropathic pain via μ - and κ -opioid receptors

future:

Biao Xu, Mengna Zhang, Xuerui Shi, Run Zhang, Dan Chen, Yong Chen, Zilong Wang, Yu Qiu, Ting Zhang, Kangtai Xu, Xiaoyu Zhang, Wolfgang Liedtke, Rui Wang, Quan Fang ... See fewer authors ^ 2019

Medication for Facial Pain

regular meds VI

hypertension

migraine; other headache; TMJD

occipital/neck/vertebrogenic pain

occipital nerve injections

MS; neuromyelitis optica

fingolimod, S1P modulators

rituximab (anti-CD20)

sinus disease & upper respiratory allergies

allergic/chronic irritation (dupilumab)

infectious

dental-oral issues

teeth needing root canals

RC-treated teeth w peri-apicitis

periodontitis

chronic recurring herpes

oral lichen

fibromyalgia

insomnia

brain fog

modafinil; memantine; low-dose ritalin; pitolisant

chronic inflammatory disorders

LongNeuro-COVID

rhA, IBD

OBESITY

semaglutide // tirzepatide // bariatric surgery

low-dose naltrexone

facial skin-skalp issues

atopic dermatitis (dupilumab); rosacea; psoriasis; lupus

head-neck-face malignancies

cemiplimab and other checkpoint inhibitor+ co-treatments

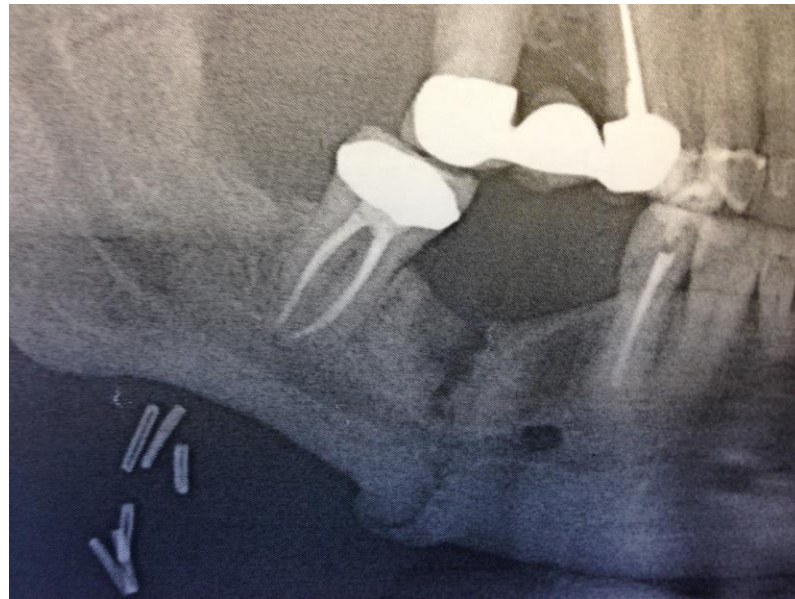
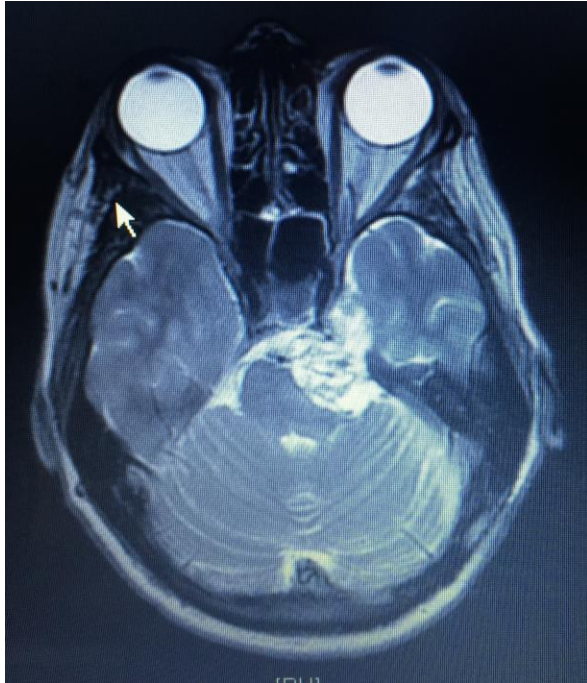
orbital/ eye disease

VIGOROUSLY FIGHT



CO-MORBIDITIES

exemplary case from my clinics – **CO-MORBIDITIES ! FIX THEM !!!**



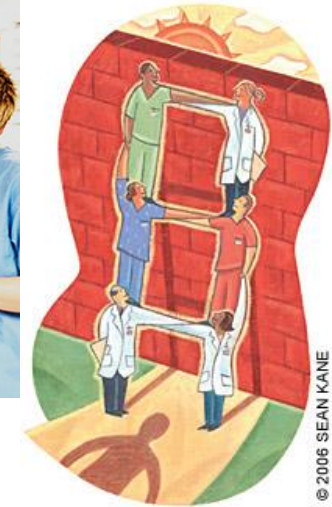
Medication for Facial Pain

meds VII – intravenous

- lidocaine 1.5-3 mg/kg bw (max 4.5) over 1h
EKG-monitoring needed
can be repeated as narrow interval as 1 week – every 10-20 days
tox – pre-med with anti-seizure (no need for benzodiazepine if covered by antineurals, benzo standby)
- phenytoin 15 mg/kg bw over 2h
EKG monitoring needed
anti-flare in urgent care/ ER in case other options have not taken hold (**also control blood pressure !!!**)
important: iv access needs to be 100%, otherwise tissue necrosis at site of paravenous mis-infusion
comtemp alternative: lacosamide (Vimpat) iv: 200-300 mg over 1h
- corticosteroids methyl-prednisolone 500-1000 mg intravenous, 3-5 consecutive days (Mo-Wed-Fri)
great co-med clonazepam 1 mg 2x pre-infusion ("roid" antsiness ...)
can be repeated monthly for 1/2y, then every 6-8 weeks
MoA: wipe-out anti-inflammatory, DIRECT EFFECT ON TRIGEMINAL PAIN SYSTEM
- meloxicam intravenous anti-inflammatory (no iv aspirin in the US), 30-60 mg short-term infusion over 20 min
co-morbid headache/migraine, other inflammatory conditions w flare-up
- eptinezumab intravenous anti-CGRP therapeutic mAb; 100 – 300 mg: I would go for 300 mg if feasible
new; attractive: urgent care/ ER use; interval use for improved pain control (monthly)

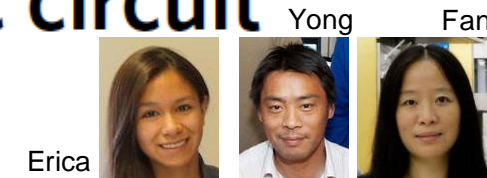
Care needs to build teams with colleagues **who are open to working across disciplinary boundaries** with dedicated focus on a challenging clinical entity:

- orofacial pain-dentistry
- dentistry: endodontics
- dentistry: oral surgery, maxillofacial surgery
- physical therapy – head/neck/face focused
- pain-nursing
- alternative medicine providers / acupuncturists
- anesthesiology/pain
- neurology/headache – trigeminal pain
- neurosurgery – pain neurosurgery
- plastic/facial surgery
- pain clinical immunologists/ allergologists
- pharmacists
- pain-psychiatry
- pain-geronto
- ENT
- ophthalmology
- ob-gyn
- oncology
- pain-admin; pain-lawyer; pain-PR

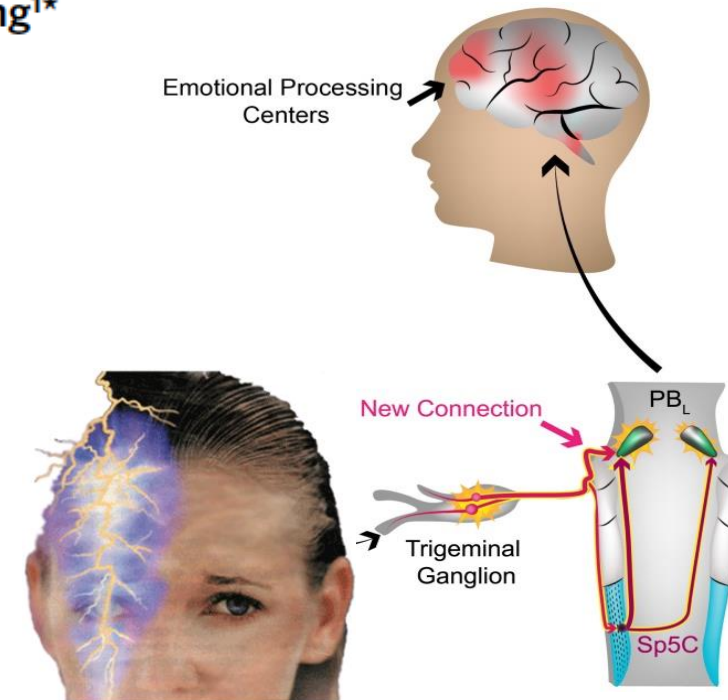
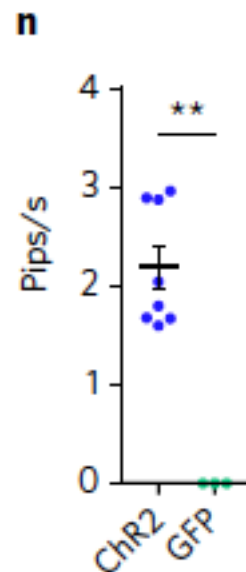


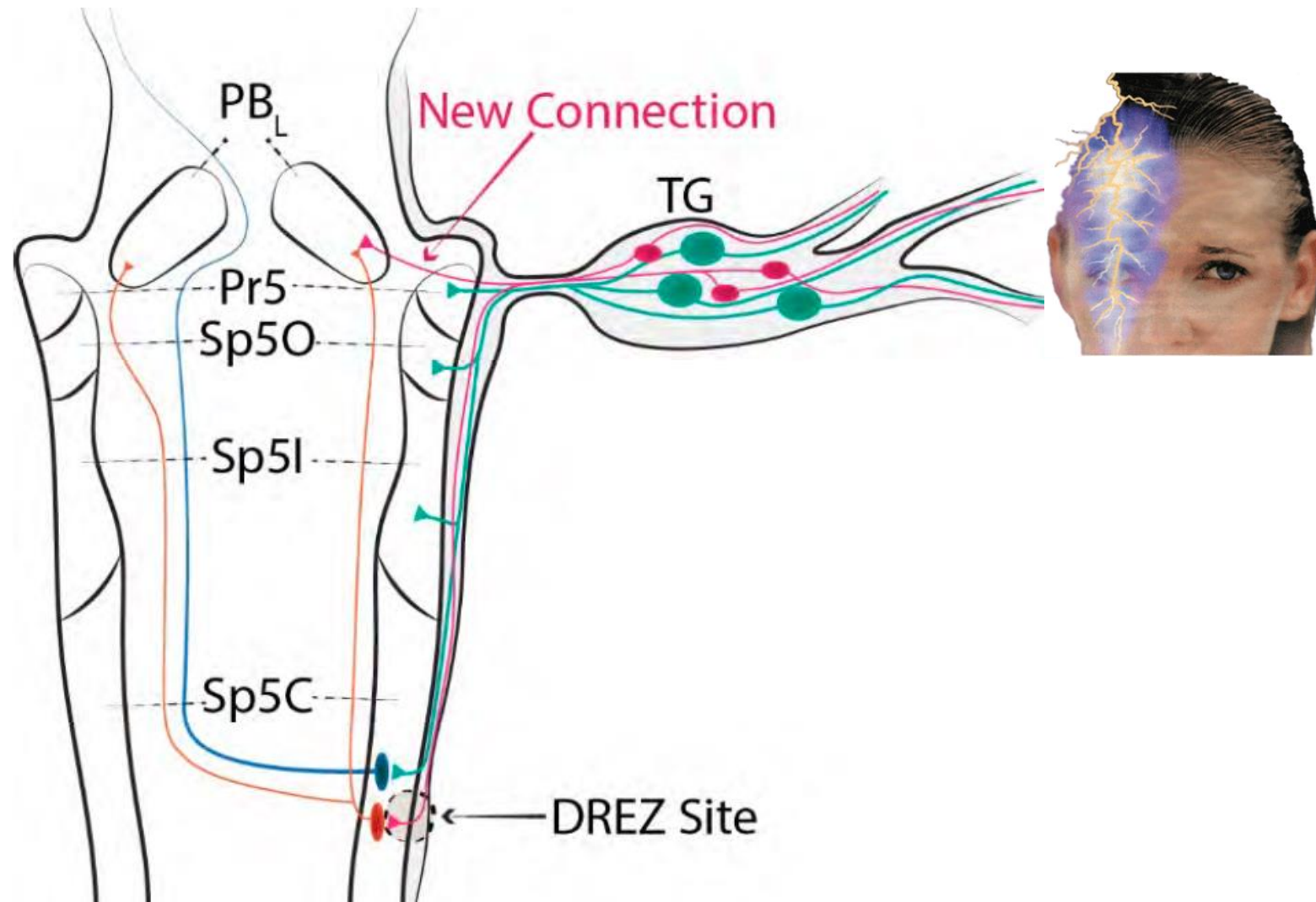
NOBODY owns trigeminally-mediated pain
she/he who suffers should NEVER land between the chairs

A craniofacial-specific monosynaptic circuit enables heightened affective pain



Erica Rodriguez¹, Katsuyasu Sakurai¹, Jennie Xu¹, Yong Chen², Koji Toda³, Shengli Zhao¹, Bao-Xia Han¹, David Ryu¹, Henry Yin³, Wolfgang Liedtke² and Fan Wang^{1*}





**2022 → in need of new type of DREZ
(or 21st Century version thereof)**

NEVER give in !!!

<https://youtube.com/shorts/Dnvs-EMBEE8?feature=share>



be Spock



you're not alone



~~Facial Pain:~~ We've got your number.

