Liens d'Intérêt

Pr. Éric VIEL, M.D., PhD.
Centre d'Évaluation et de Traitement de la Douleur
Centre Hospitalier Régional Universitaire Caremeau

Financement recherche : *Merz Pharma (France & global),*
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Air Liquide Santé, Vertex

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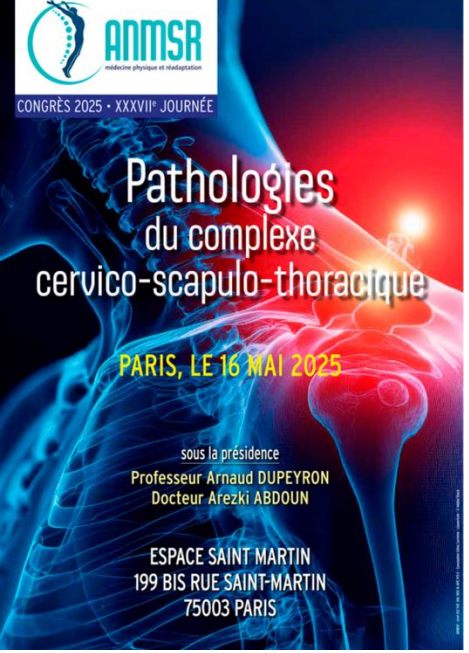
Grünenthal (France / Belgique / Ireland / UK / Mexico / Spain / Portugal / Norway)
Ethypharm, Viatris



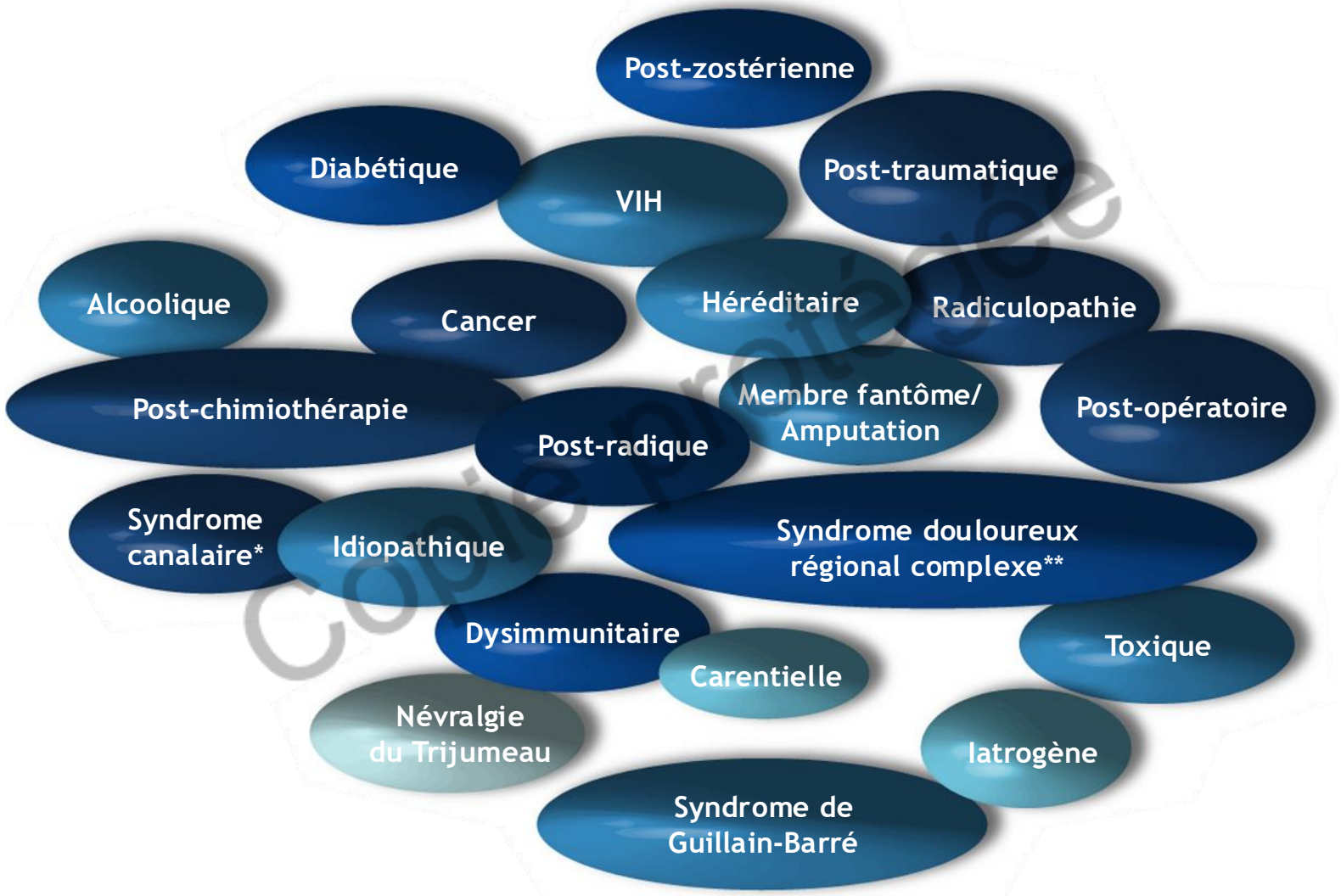
Les traitements topiques des douleurs neuropathiques

Antalgiques d'aujourd'hui ? Antalgiques de demain ?

Pr. Éric VIEL, M.D., PhD.
Centre d'Évaluation et de Traitement de la Douleur
Centre Hospitalier Régional Universitaire Caremeau

MUSE MONTPELLIER UNIVERSITY OF EXCELLENCE
institute for neurosciences montpellier
INSTITUT Analgesia Fondation de recherche sur la douleur
cemd Collège des Enseignants de Médecine de la Douleur
FACULTÉ DE MÉDECINE MONTPELLIER-NÎMES DEPUIS 1220
CHU NIMES
GHT Groupement Hospitalier de Territoire CÉVENNES | GARD | CAMARGUE

Principales étiologies des DNP (1,2)



** Ex. : syndrome du canal carpien, du canal tarsien, etc. - ** Atteintes des nerfs ou plexus d'origine traumatique ou chirurgicale -*

(1) Attal N, Bouhassira D. Neuropathies périphériques douloureuses in Bouche P et al. Neuropathies périphériques. Doin Eds 2004 : 355-79.
(2) Dworkin RH et al. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. Arch Neurol 2003 ; 60 (11) : 1524-34.

THE LANCET

Persistent postsurgical pain: risk factors and prevention

Henrik Kehlet, Troels S Jensen, Clifford J Woolf

Lancet 2006; 367: 1618–25

Acute postoperative pain is followed by persistent pain in 10–50% of individuals after common operations, such as

Wang *L et al Br J Anesth 2020* http://dx.doi.org/10.1016/j.bja.2020.04.088

187 observational studies with **297 612** breast cancer patients. Prevalence of PP**S**P ranged from 2% to 78%, median 37% (inter-quartile range: 22-48%); pooled prevalence was 35% (95% confidence interval [CI]: 32-39%).

Also, the effect of aggressive, early therapy for postoperative pain should be investigated, since the intensity of acute

...e role of genetic factors ...elop chronic pain. Based ...entral nervous system in ...ere, we outline strategies ...nt entity of chronic pain.

Narrative Review

PAIN

ICD-11

The IASP classification of chronic pain for *ICD-11*: chronic postsurgical or posttraumatic pain

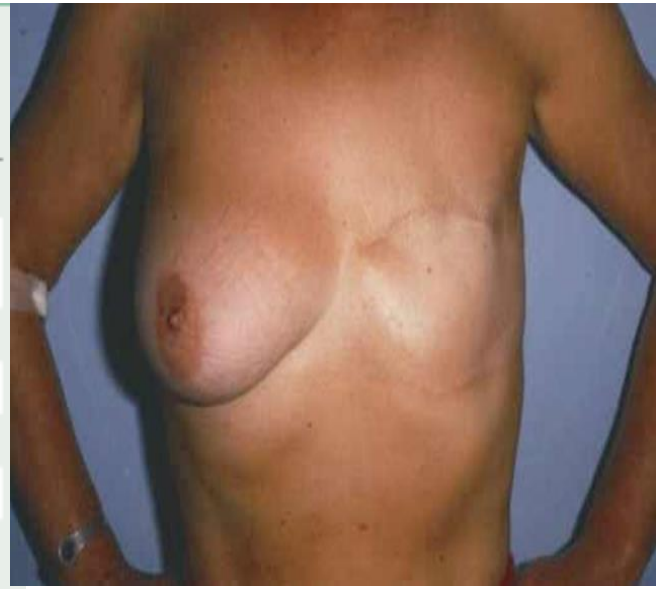
Stephan A. Schug[a], Patricia Lavand'homme[b], Antonia Barke[c], Beatrice Korwisi[c], Winfried Rief[c], Rolf-Detlef Treede[d,*], The IASP Taskforce for the Classification of Chronic Pain

Abstract

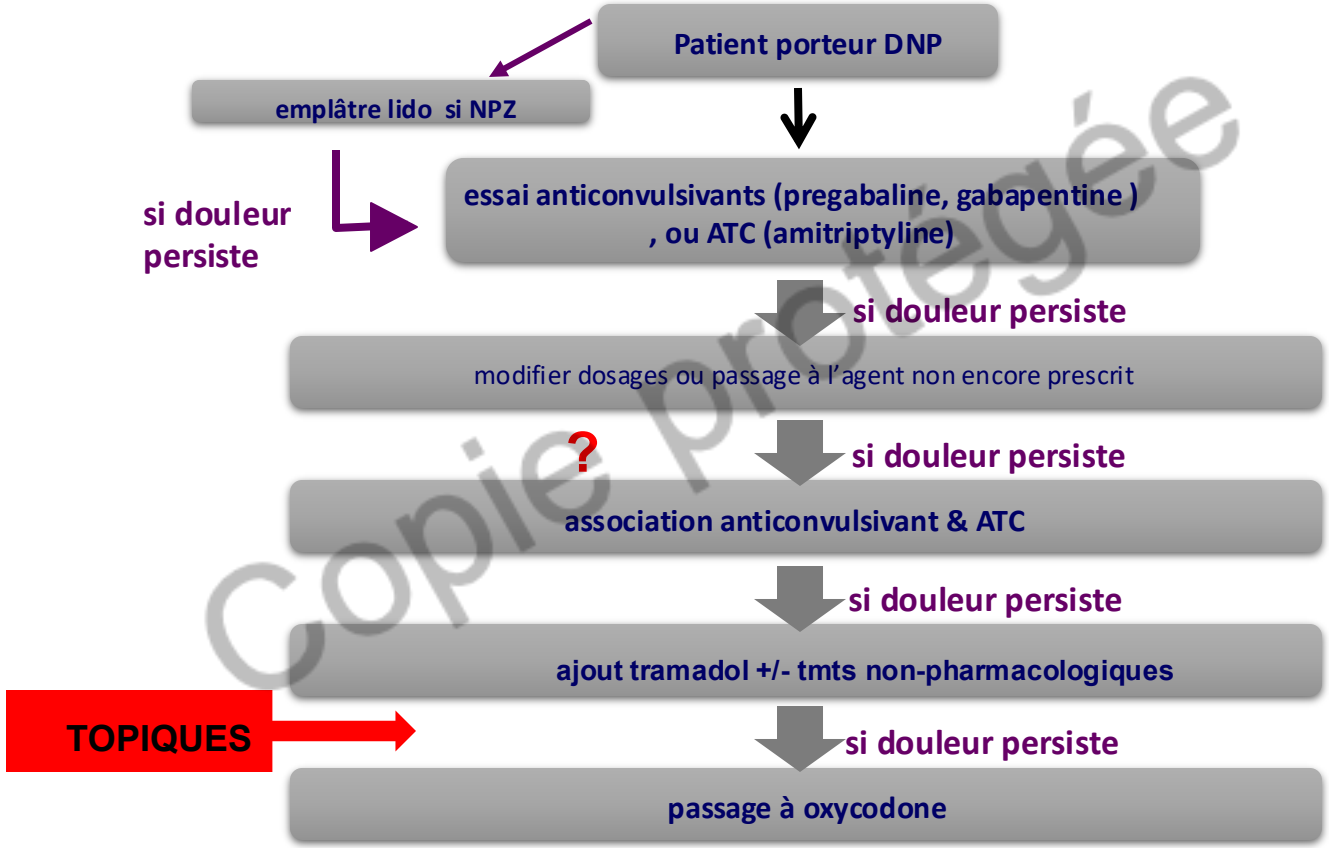
Chronic pain after tissue trauma is frequent and may have a lasting impact on the functioning and quality of life of the affected person. Despite this, chronic postsurgical and posttraumatic pain is underrecognised and, consequently, undertreated. It is not represented in the current *International Classification of Diseases* (*ICD-10*). This article describes the new classification of chronic postsurgical and posttraumatic pain for *ICD-11*. Chronic postsurgical or posttraumatic pain is defined as chronic pain that develops or increases in intensity after a surgical procedure or a tissue injury and persists beyond the healing process, ie, at least 3 months after the surgery or tissue trauma. In the classification, it is distinguished between tissue trauma arising from a controlled procedure in the delivery of health care (surgery) and forms of uncontrolled accidental damage (other traumas). In both sections, the most frequent conditions are included. This provides diagnostic codes for chronic pain conditions that persist after the initial tissue trauma has healed and that require specific treatment and management. It is expected that the representation of chronic postsurgical and posttraumatic pain in *ICD-11* furthers identification, diagnosis, and treatment of these pain states. Even more importantly, it will make the diagnosis of chronic posttraumatic or postsurgical pain statistically visible and, it is hoped, stimulate research into these pain syndromes.

Keywords: Classification, *ICD-11*, Chronic pain, Postsurgical pain, Posttraumatic pain, Injury, Trauma, Surgery, Thoracotomy, Herniotomy, Mastectomy, Breast surgery, Hysterectomy, Arthroplasty, Whiplash, Burns, Amputation

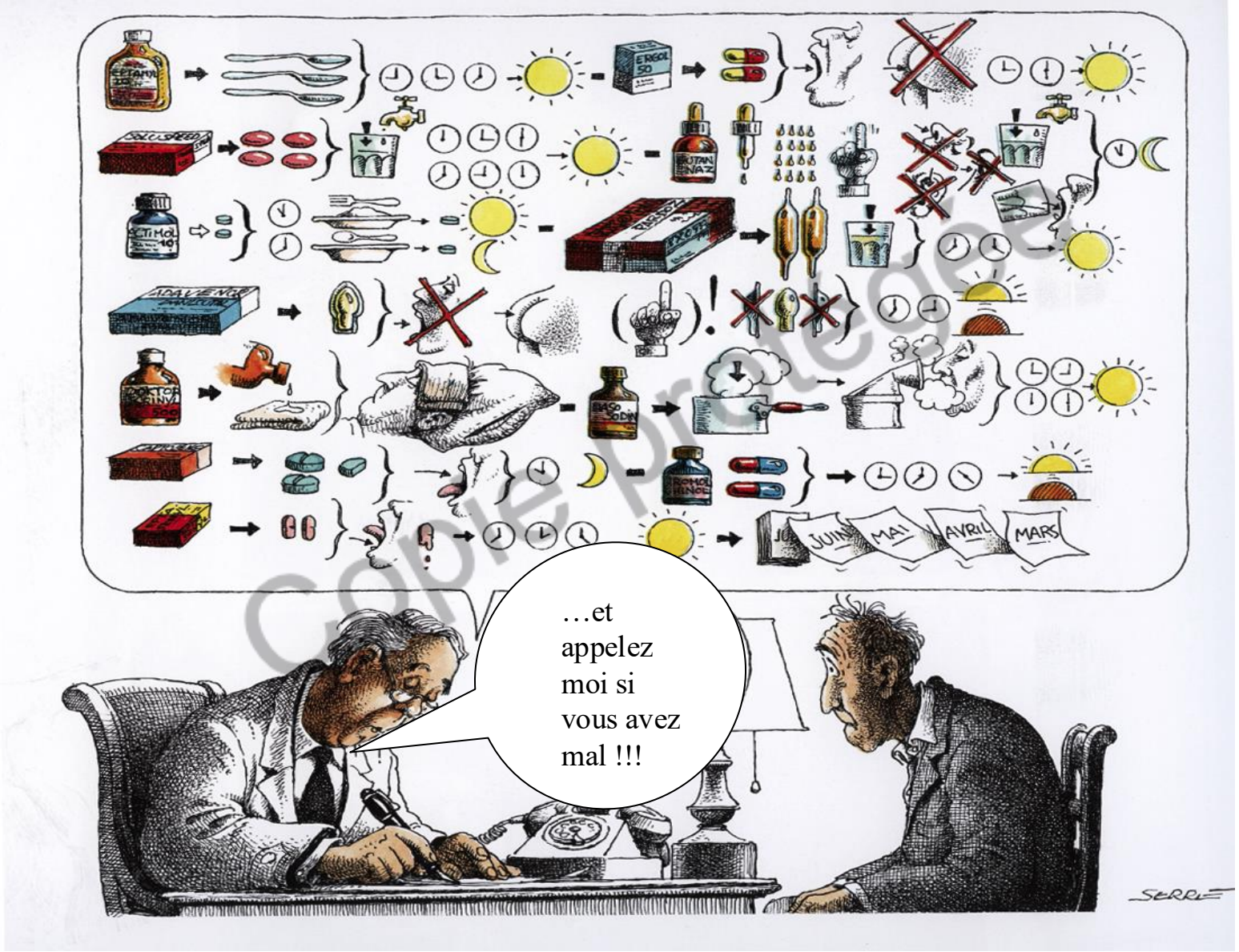
Estimated incidence of chronic postoperative pain and disability after selected surgical procedures



Dans la pratique quotidienne, l'algorithme est de mise en oeuvre complexe et parfois approximative : changements et mille-feuilles sont la norme !!!



des traitements variés, parfois … exotiques



observance thérapeutique ???

Original Article

What Is the Medication Iatrogenic Risk in Elderly Outpatients for Chronic Pain?

Julie Jambon, PharmD, Chloé Choukroun, PharmD,*† Clarisse Roux-Marson, PharmD,*† Éric Viel, MD, PhD,‡ and Géraldine Leguelinel-Blache, PharmD, PhD*†§*

Purpose: Medication iatrogeny is a major public health problem that increases as the population ages. Therapeutic escalation to control pain and associated disorders could increase polypharmacy and iatrogeny. This study aimed to characterize the medication iatrogenic risk of elderly outpatients with chronic pain.

Methods: This was a prospective cohort study recruiting patients 65 years or older with chronic pain. A medication iatrogenic assessment was performed based on the best possible medication history to record risk of adverse drug events (Trivalle score), STOPP (Screening Tool of Older Person's Prescriptions)/START (Screening Tool to Alert doctors to Right Treatment) criteria, and potentially inappropriate medications.

Results: We recruited 100 patients with an average age of 71 years. The median number of medications before pain consultation was 8 (interquartile range = [7;11]). Trivalle score showed that 43% of patients were at moderate or high medication iatrogenic risk. Before consultation, 79% and 75% of patients had at least 1 STOPP or START criterion on their orders, respectively. One-third of orders mentioned benzodiazepine prescribed for more than 4 weeks. At least 1 potentially inappropriate medication was prescribed for 54% of the patients, with a median of 1 per patient (interquartile range = [0;1]). A combination of several anticholinergics was prescribed in 23% of patients.

Conclusion: Elderly patients with chronic pain are at risk of medication iatrogeny. Preventive measures as multidisciplinary medication review could reduce the iatrogenic risk in these outpatients.

This study is registered at clinicaltrials.gov as NCT04006444 on July 3, 2019.

Key Words: chronic pain, drug-related side effects and adverse reactions, elderly, medication safety, potentially inappropriate medications

(*Clin Neuropharm* 2022;45: 65–71)

Clin Neuropharmacol **2022**

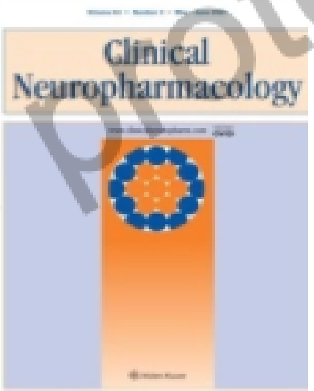


TABLE 4. Characterization of Medication Iatrogeny Before and After a Specialized Medical Consultation on Pain (n = 100)

	Before	After
Trivalle score		
Trivalle score, median (IQR)	1 (1;4)	1 (1;4)
Risk level according to Trivalle score, %		
Low	57	56
Moderate	41	42
High	2	2
STOPP Criteria		
Prescriptions with at least 1 STOPP criterion, %	79	77
STOPP criteria per prescription, median (IQR)	2 (1;4)	2 (1;4)
STOPP criteria per prescription with at least 1 STOPP criterion, median (IQR)	3 (1;5)	3 (1;5)
STOPP criteria found in at least 10% of patients, %		
Medications prescribed beyond the recommended duration	36	36
Benzodiazepines or hypnotics for more than 4 wk	34	34
Opiates as background treatment without concomitant laxative prescription	30	28
Medications prescribed without clinical indication	28	28
Medications that increase the risk of falling = benzodiazepines	23	23
≥2 anticholinergic medications	23	23
Medications that increase the risk of falling = hypnotics	18	18
Duplication of therapeutic class	17	16
START criteria		
Prescriptions with at least 1 START criterion, %	75	75
START criteria per patient, median (IQR)	1 (1;2)	1 (1;2)
START criteria per prescription with at least 1 START criterion, median (IQR)	2 (1;3)	2 (1;3)
START criteria found in at least 10% of patients, %		
Influenza vaccination	43	43
In a person receiving opiates on a regular basis, a laxative treatment	30	28
If home confinement, falls, or osteopenia, vitamin D supplementation	21	21
If persistent major depressive symptoms, a nontricyclic antidepressant	11	10
Potentially inappropriate medication from Laroche list		
Prescriptions with at least 1 PIM, %	54	53
PIM per patient, median (IQR)	1 (0;1)	1 (0;1)
PIM per prescription with at least 1 PIM, median (IQR)	1 (1;2)	1 (1;2)
PIM found in at least 10% of patients, %		
Anticholinergic association	23	23
Benzodiazepines and related drugs with a short or intermediate half-life used at greater than half the dose proposed in young adults	17	17
Benzodiazepines and related derivatives, long half-life	14	14
Association ≥2 psychotropic medications from the same therapeutic class, ≥2 benzodiazepines or related substances, ≥2 neuroleptics, ≥2 antidepressants	10	9

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CHU NÎMES

Revue neurologique
Practice Guideline › Rev Neurol (Paris). 2020 May;176(5):325-352.
doi: 10.1016/j.neurol.2020.01.361. Epub 2020 Apr 7. X Moisset et al

Pharmacological and non-pharmacological treatments for neuropathic pain: Systematic review and French recommendations

French recommendations Nov 2019 annual meeting of French Society for tthe study of Pain

Neuropathic pain

	Focal peripheral NP [2]		Other peripheral or central NP [1]
1st line	Lidocaine plasters TENS	or	Duloxetine Gabapentin Tricyclic antidepressants
2nd line	Capsaicin 8 % patch Botulinum toxin A	or	Pregabalin Venlafaxine Tramadol Combination therapy
3rd line [3]	Pulsed radiofrequency Spinal cord stimulation	or	Strong opioids HF-rTMS of M1

Psychotherapy [4]

Toxine botulique A

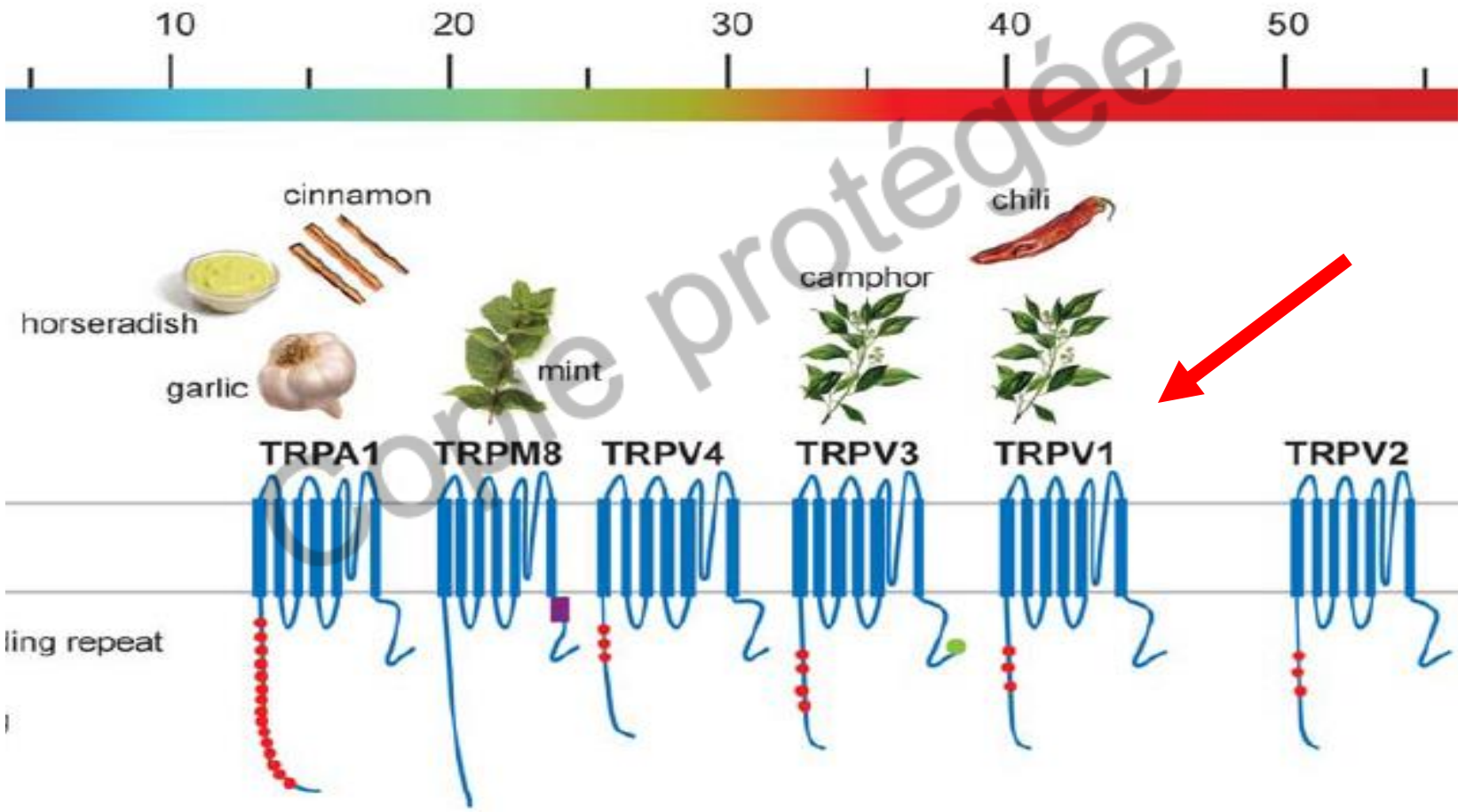
Patch de capsaïcine

Quel rationnel pour l'utilisation topique de la capsaïcine pour traiter la douleur neuropathique périphérique ? Comment çà marche ?

Une vieille histoire … qui commence avec les médecins arabo-andalous *Ibn SIna* et *Ibn Roshd* !
et l'application topique de *felfel soudaniya*

des nocicepteurs spécifiques de ligands naturels des traitements topiques connus…

Thermorégulation

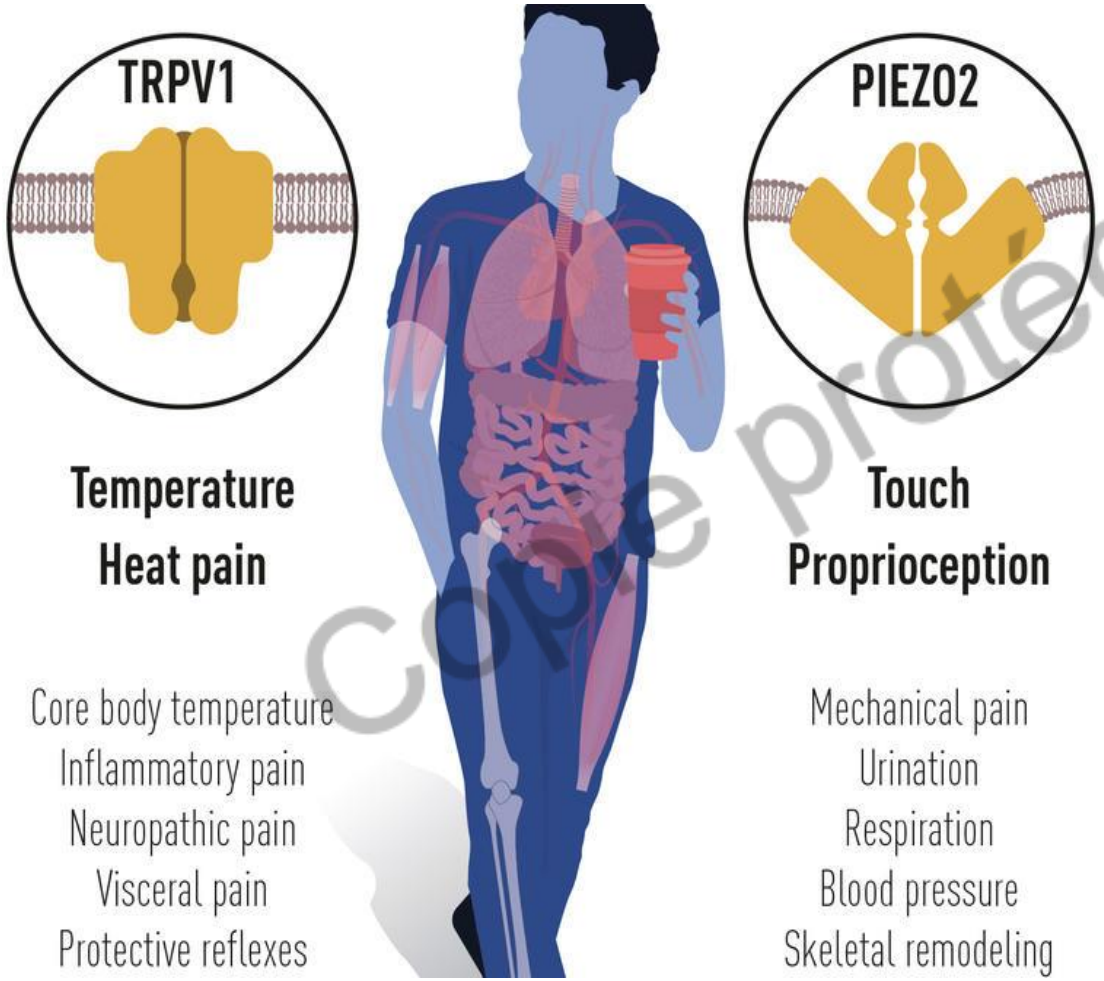


Dhaka (2006) Annu. Rev. Neurosci.

2021 Nobel Prize for the discovery of TRPV1 and PIEZO2 receptors

Prix Nobel 2001 : récepteurs à notre environnement !

PIEZO2 (proprioception) et TRPV1 : température)



Prof. Ardem Patapoutian & Prof. David Julius
USA

THE NOBEL PRIZE

Source: www.nobelprize.org/prizes/medicine/2021

The capsaicin receptor: a heat-activated ion channel in the pain pathway

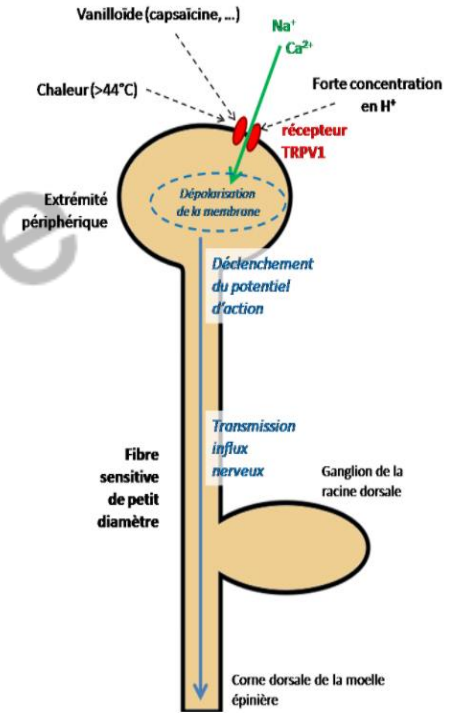
Nature **389**, 816–824 (1997)

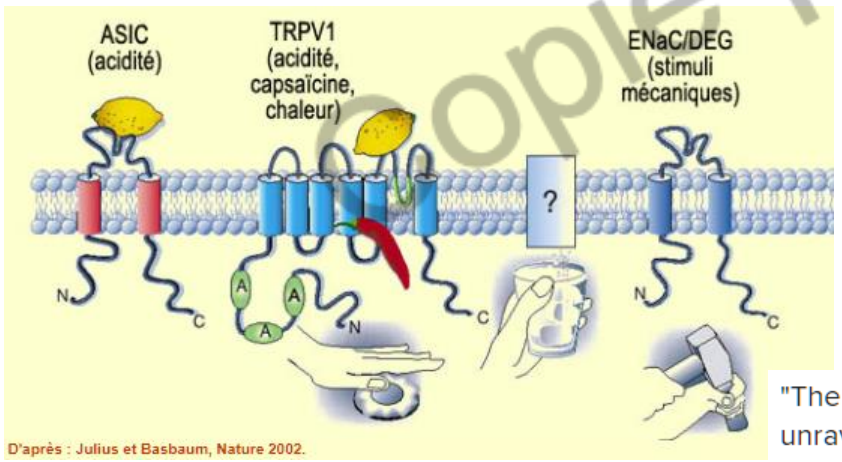
Michael J. Caterina, Mark A. Schumacher, Makoto Tominaga, Tobias A. Rosen, Jon D. Levine & David Julius

The Nobel Assembly at the Karolinska Institute has decided to award the 2021 Nobel Prize in Physiology or Medicine to

DAVID JULIUS
ARDEM PATAPOUTIAN

"for their discoveries of receptors for temperature and touch"

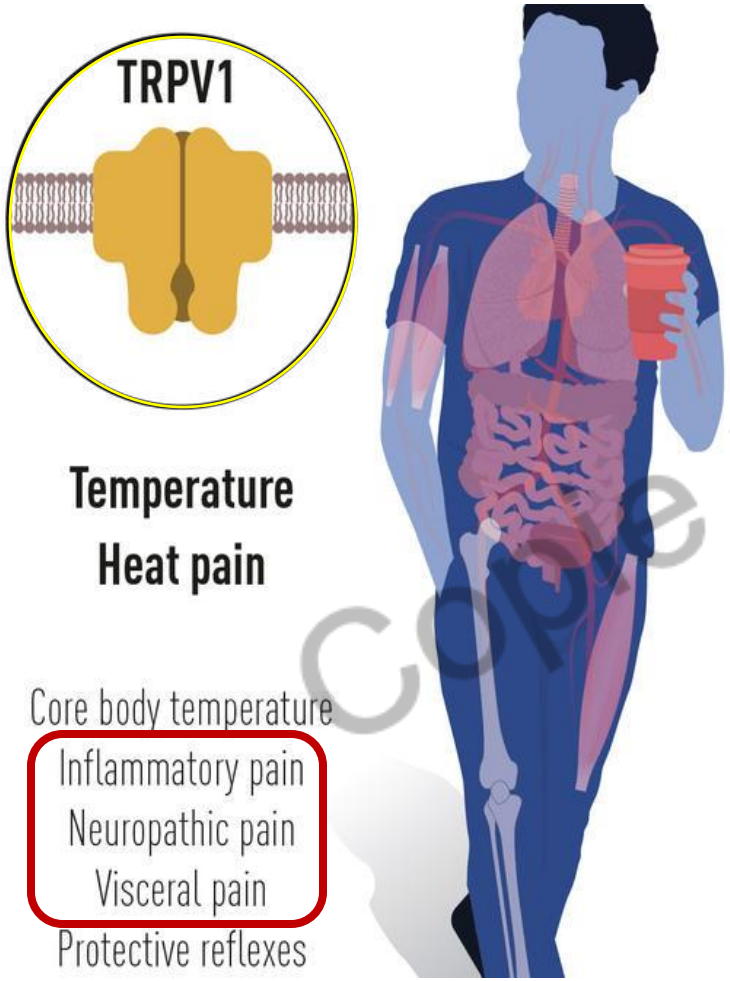




D'après : Julius et Basbaum, Nature 2002.

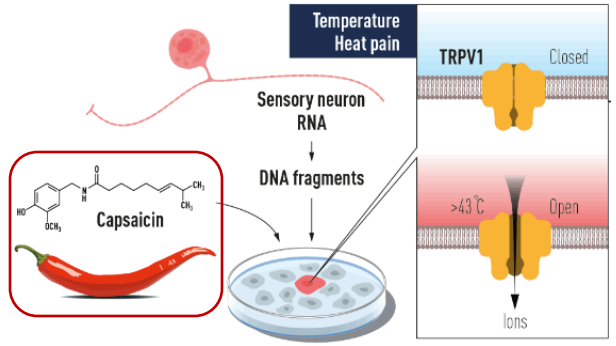
"The discovery of TRPV1 was a major breakthrough leading the way to the unravelling of additional temperature-sensing receptors," the committee said.

2021 Nobel Prize for the discovery of TRPV1 and PIEZO2 receptors



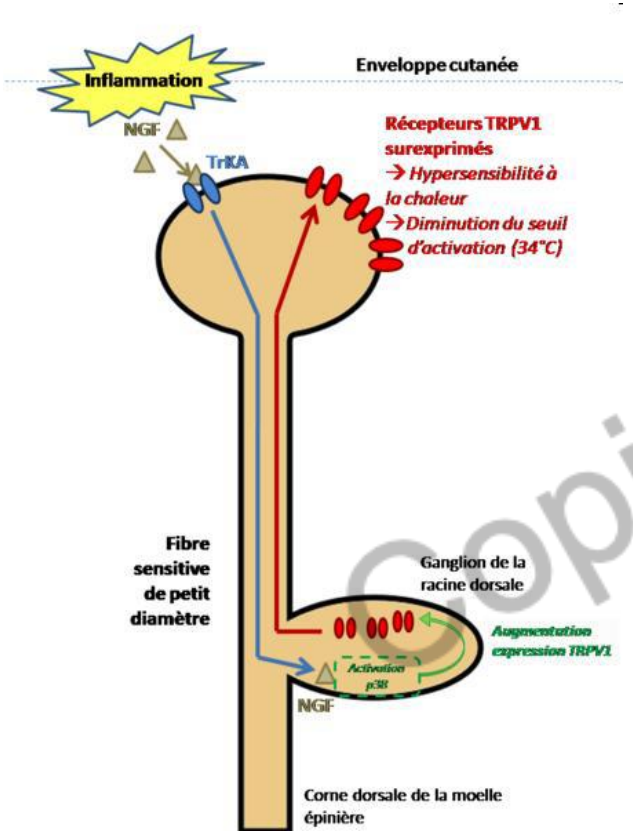
Transient Receptor Potential Vanilloid 1 receptor plays a critical role in pain signalling

TRPV1 discovery has laid the foundation for the development of innovative non-opioid pain therapies



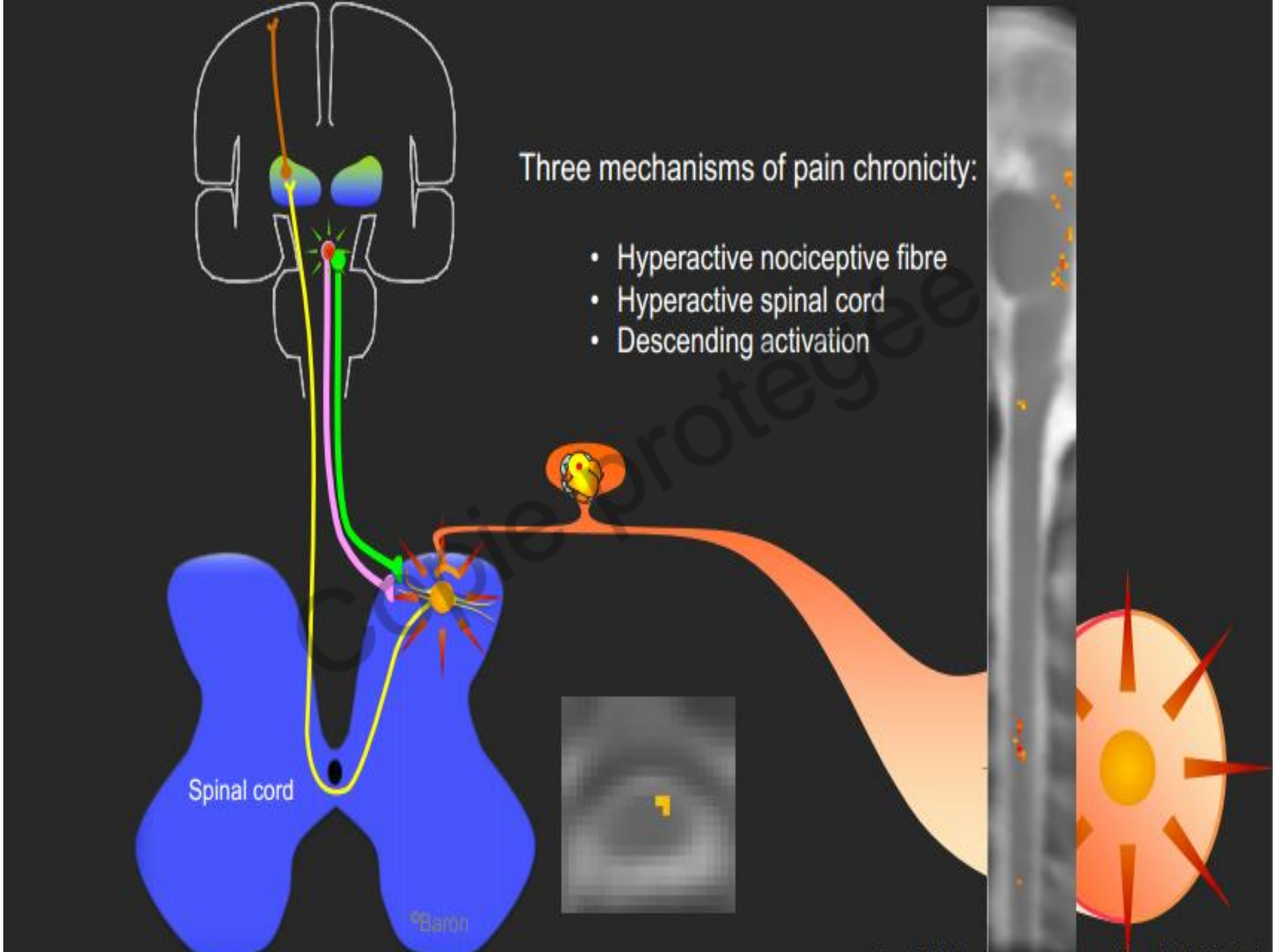
Source: www.nobelprize.org/prizes/medicine/2021

Rôle des des TRPV1

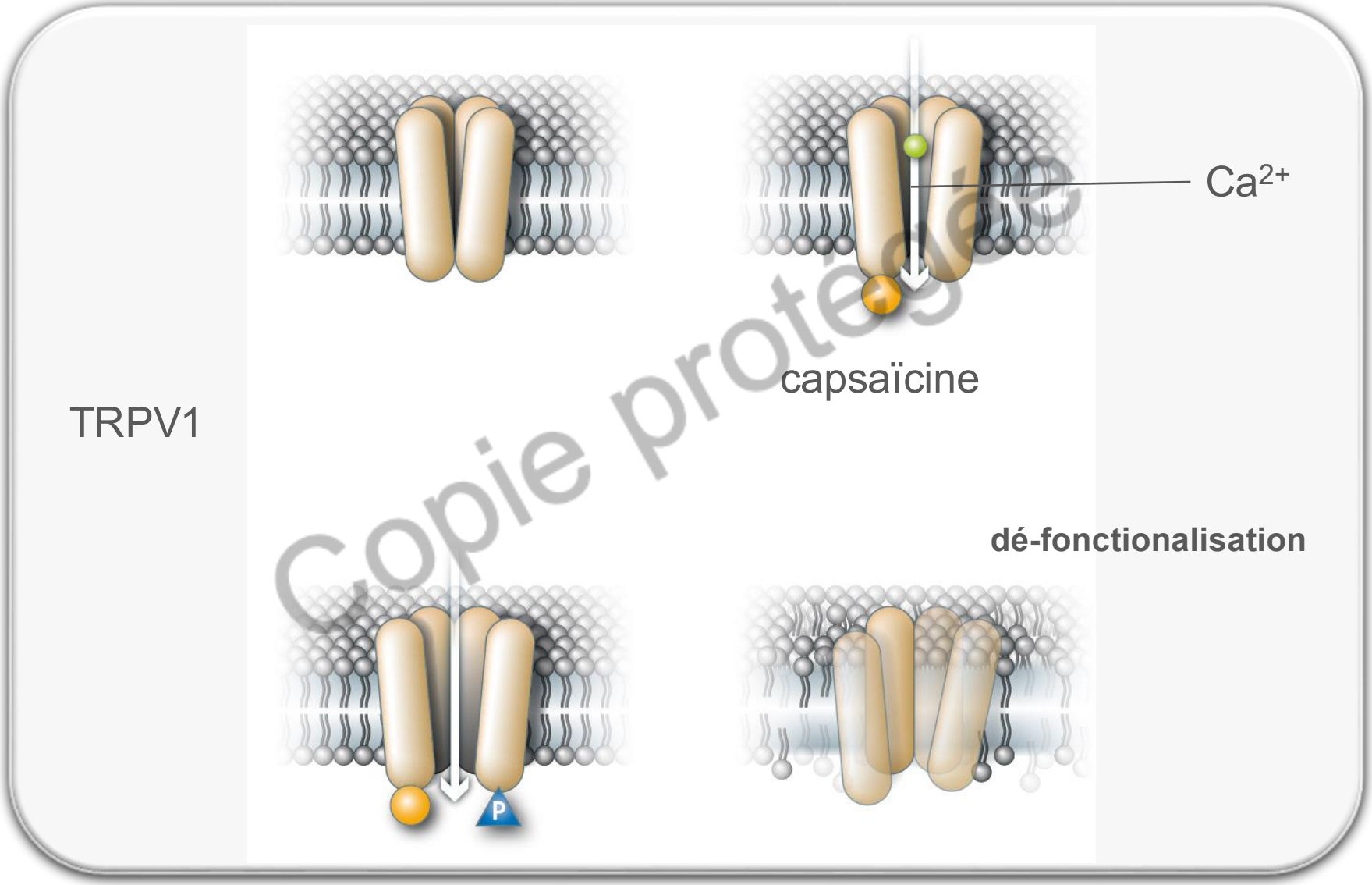


- Rôle clef dans la nociception
- Présents sur les terminaisons des fibres A delta et C
- Activés par la chaleur
- **surexpression de ce récepteur** par les afférences nociceptives dans les douleurs neuropathiques

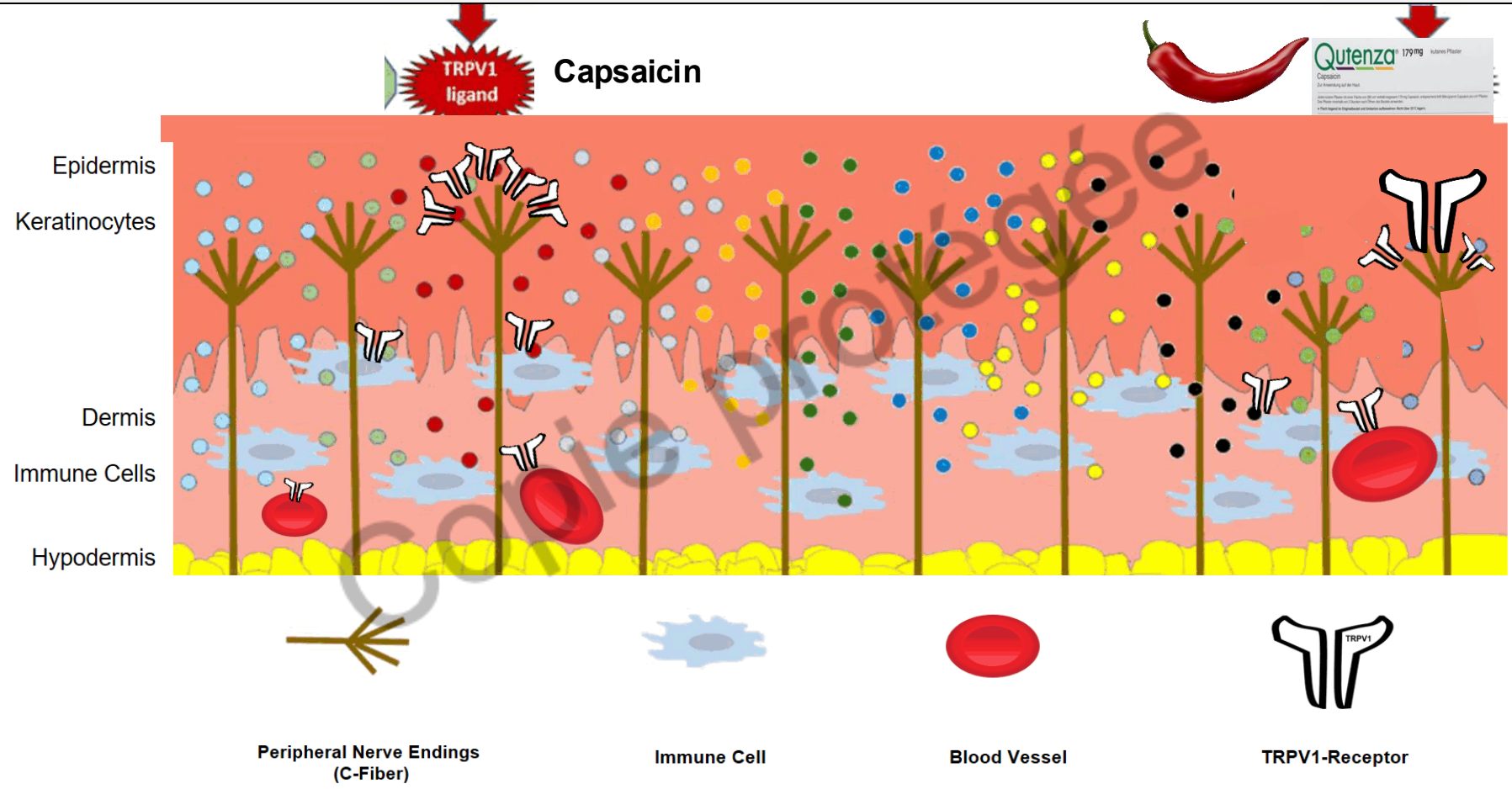
Szallasi A, Cortright DN, Blum CA, Eid SR. The vanilloid receptor TRPV1: 10 years from channel cloning to antagonist proof-of-concept. Nat Rev Drug Discov. 2007;6(5):357-72.


Three mechanisms of pain chronicity:
• Hyperactive nociceptive fibre
• Hyperactive spinal cord
• Descending activation
Spinal cord
©Baron

la capsaïcine est un agoniste des récepteurs TRPV1



Ligands des canaux ioniques, recepteurs, protéines et enzymes sous forme de traitements topiques



Source adapted from: **Aurora V. et al. Pharmacology & Therapeutics 220 (2021)**

Mode d’action de la capsaïcine topique 8%

La capsaïcine appliquée à concentration élevée provoque une **défonctionalisation** par l’intermédiaire d’une **ablation des terminaisons afférentes exprimant** TRPV1, provoquant ainsi une analgésie prolongée.

“défonctionalisation des nocicepteurs”

Hyperactive peptidergic afferents

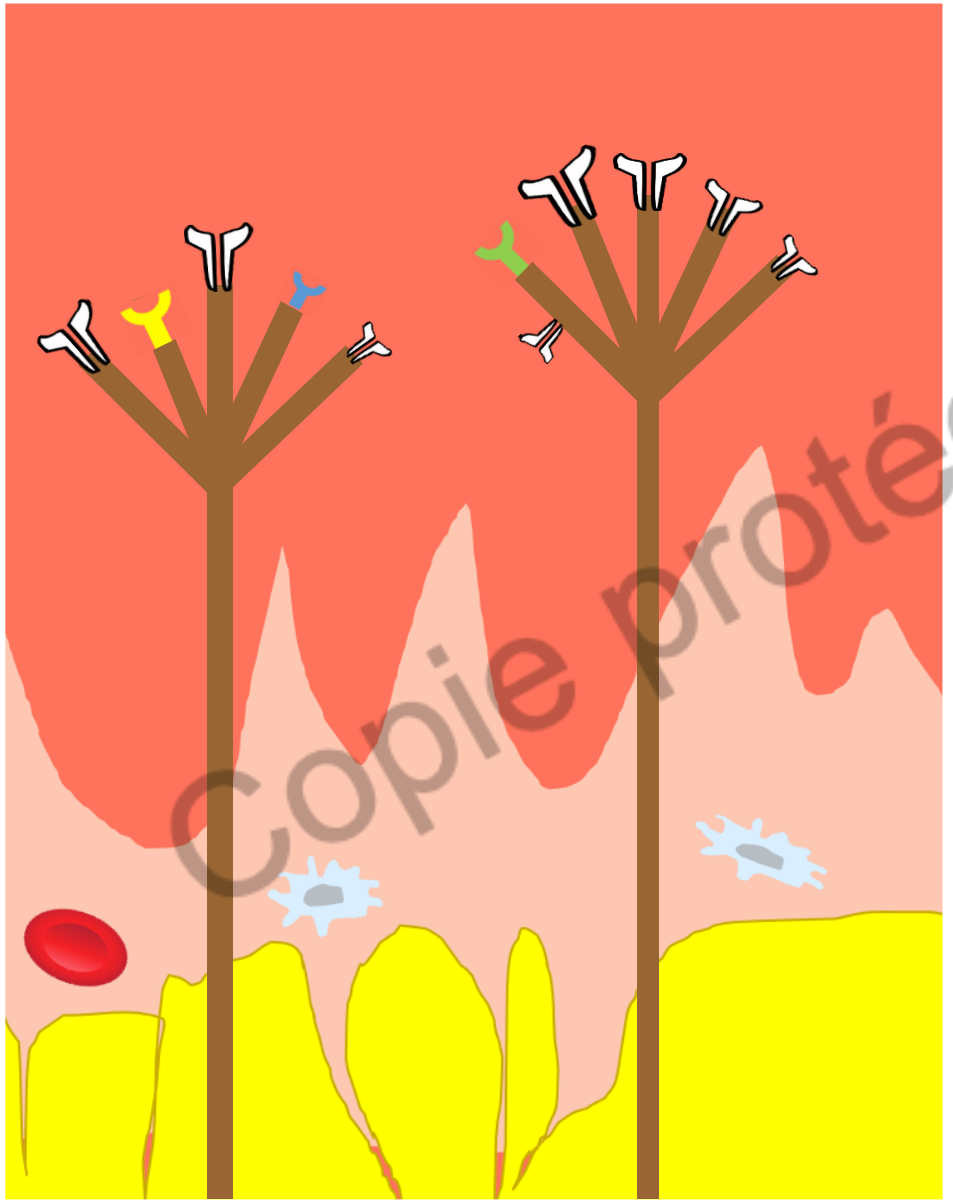
TRPV1 defunctionalization and retraction of aberrant fibres

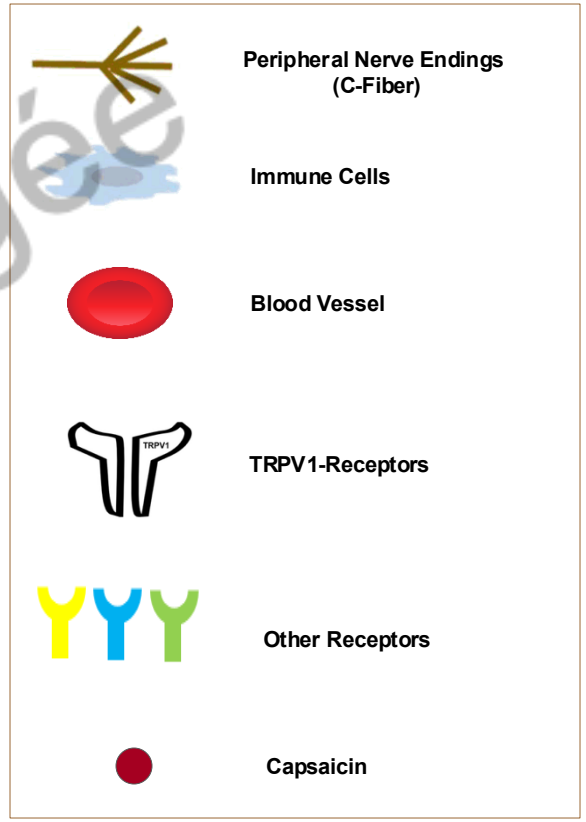
Regeneration and restoration of healthy sensory nerve fiber function

Epidermis

Dermis

Hypodermis





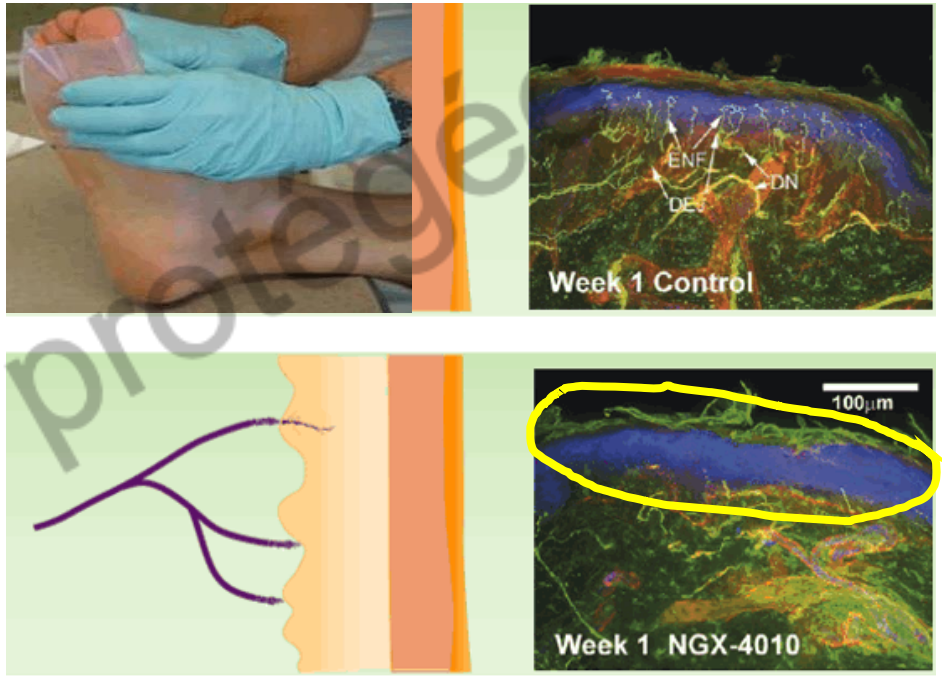
Neuropathic pain returns

Source adapted from: **Aurora V. et al. Pharmacology & Therapeutics 220 (2021)**

défonctionalisation réversible des fibres nerveuses épidermiques sensibilisées

Densité normale

semaine 1: ~80% ablation



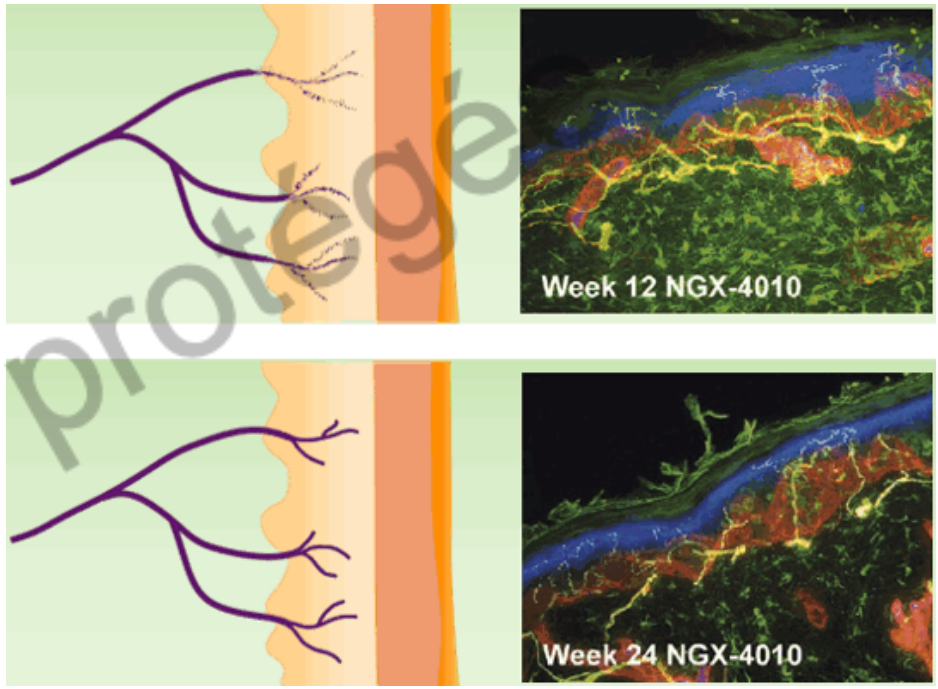
Adapted from: Kennedy WR, et al. J Pain. 2010;11(6):579–87.

Réduction intensité des douleurs neuropathiques

puis régénération de fibres nerveuses épidermiques „*normales*“

semaine 12: ~80% +

semaine 24: >95% +



Adapted from: Kennedy WR, et al. J Pain. 2010;11(6):579–87.

La capsaïcine active les **processus de régéneration** au niveau des fibres afférentes en # 12 à 24 semaines

Local or systemic treatment for Neuropathic Pain? ELEVATE: an open-label, randomized, multicenter, non-inferiority efficacy and tolerability study.

Maija Haanpaa (1), Etienne Ernault (2), Tommaso Siciliano (3)

1. Departments of Anaesthesiology and Neurosurgery, Pain Clinic, Helsinki University Hospital, Helsinki, Finland. 2. Astellas Pharma Europe, BV, The Netherlands. 3. Astellas Pharma Europe, Chertsey, UK

Peripheral Neuropathic Pain (PNP) is highly prevalent in the world. PNP has a devastating impact on patients' lives and it poses a high burden on healthcare resources. Topical high concentration (8%) capsaicin patch (QUTENZA™) and oral Pregabalin are effective treatments for PNP. QUTENZA™ is licensed in Europe for the treatment of NP in non-diabetic adults.

METHODS

568 subjects were randomized to one of two treatment arms: QUTENZA™ (single application of up to 4 patches) or Pregabalin (daily administration at a flexible, optimized dose). All subjects recorded average pain scores for 8 weeks: daily, for the first two and for the last week of treatment, otherwise weekly. The primary efficacy endpoint was the proportion of subjects in each arm who achieved at least a 30% decrease in the average NPRS score from Baseline to Week 8. Safety was assessed by evaluation of adverse events, laboratory tests and vital signs. Hypotheses were tested using odds ratio. A non-inferiority margin of -8.5%, under reasonably conservative assumptions, translated into a margin on the odds ratio (OR) of 0.693. The null hypothesis of inferiority was rejected if the two-sided 95% confidence interval for the odds ratio of QUTENZA™ versus Pregabalin fell completely above 0.693.

568 subjects were randomized to one of two treatment arms: QUTENZA™ (single application of up to 4 patches) or Pregabalin (daily administration at a flexible, optimized dose). All subjects recorded average pain scores for 8 weeks

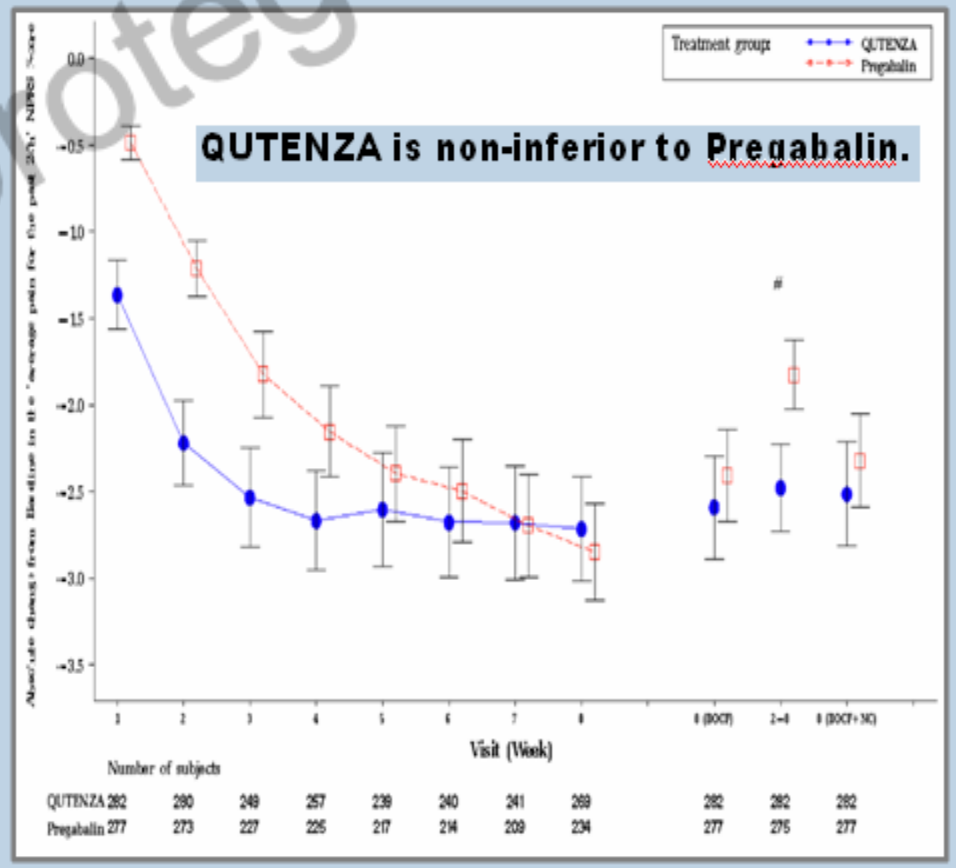
RESULTS

In both the Full Analysis Set (FAS - all randomised subjects who initiated treatment) and the Per Protocol Set (PPS - subset of subjects of the FAS, selected to ensure sensitivity to differences in treatment effects), the lower bound for the 95% confidence interval for the odds ratio of QUTENZA™ versus Pregabalin was greater than 0.693

Difference (QTZ - Pregabalin)	1.2%		0.3%	
95% CI for Difference	[-7.1%, 9.4%]		[-8.3%, 8.9%]	
Achieve Non-inferiority criteria[2]	Yes		Yes	
P-value for superiority test	p=0.860		p=0.875	

95% CI for the difference between Qutenza and Pregabalin was above -8.5%
Results on FAS and PPS demonstrated that QUTENZA is non-inferior to Pregabalin.

Mean Percent Change from Baseline in the Average NPRS Score throughout the Study (FAS)



AACA2014
14th Asian Australasian Congress of Anaesthesiologists

TIME TO ONSET OF PAIN RELIEF IN ELEVATE: AN OPEN-LABEL, RANDOMISED, MULTICENTER NON-INFERIORITY EFFICACY AND TOLERABILITY STUDY

Maija Haanpaa (1), Etienne Ernault (2), Tommaso Siciliano (3)

WIP meeting Maastricht mai 2014

Peripheral Neuropathic Pain (P
devastating impact on patient
poses a high burden on healt
Topical high concentration (8%
(QUTENZA™) and oral pregaba
treatments for PNP.[2,3] ELEVATI
randomised Clinical Trial to co
and tolerability of these drugs
PNP.

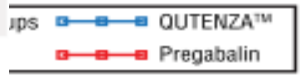
Table 2. Treatment emergent adverse events

Preferred Term (MedDRAV 13.1)	Qutenza™ (N=282)	Pregabalin (N=277)
Application site pain	67 (23.8%)	0
Erythmia	59 (20.9%)	1 (0.4%)
Burning sensation	45 (16.0%)	1 (0.4%)
Headache	38 (13.5%)	51 (18.4%)
Application site erythmia	25 (8.9%)	0
Pain	18 (6.4%)	7 (2.5%)
Pain in extremity	15 (5.3%)	9 (3.2%)
Nausea	14 (5.0%)	35 (12.6%)
Abdominal pain upper	9 (3.2%)	15 (5.4%)
Dizziness	7 (2.5%)	54 (19.5%)
Oedema peripheral	3 (1.1%)	17 (6.1%)
Somnolence	2 (0.7%)	43 (15.5%)
Constipation	2 (0.7%)	14 (5.1%)
Vertigo	1 (0.4%)	14 (5.1%)
Weigth increase	0	17 (6.1%)
Dry mouth	0	15 (5.1%)

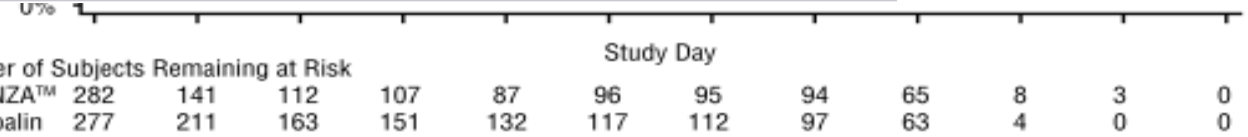
et its primary endpoint,
QUTENZA™ is as effective
n optimised dose of
s with PNP over 8 weeks.
relief was significantly
NZA™ arm.

Median time to pain
(where 50% of subje
had a 30% reductior
in 'average pain for t
past 24 hours') was
days (95% CI 6.0, 10
for QUTENZA™ versu
36 days (95% CI 22.
50.0) for pregabalin.
hazard ratio adjustec
country-gender-NPR
at baseline was 1.68
in favour of QUTENZA™
(95% CI 1.35, 2.08),
p<0.0001.

of pain relief

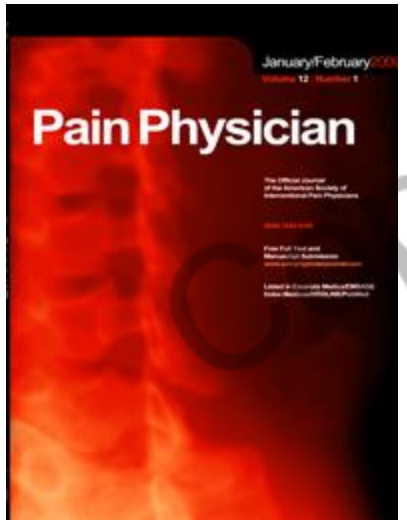


ubjects Without Pain Relief)



HR: Hazard ratio

PERIPHERAL NEUROPATHIC PAIN : Are topical treatments sufficient ?



Pain Physician 2021; 24:453-463 • ISSN 1533-3159

Randomized Trial

Treatment Impact on Patient-Reported Outcomes in Peripheral Neuropathic Pain: Comparing Single Intervention With Topical High-Concentration Capsaicin to Daily Oral Pregabalin

Eric Viel, MD, PhD[1], Mariëlle Eerdekens, MD[2], and Prashanth Kandaswamy, MSc[2]

From: [1]Centre d'Étude et de Traitement de la Douleur, Pôle A.R.D.U., Centre Hospitalier Universitaire, France; [2]Grünenthal GmbH, Aachen, Germany

Address Correspondence: Eric Viel, MD, PhD Chef de Service, Centre d'Étude et de Traitement de la Douleur, Pôle A.R.D.U., Centre Hospitalier Universitaire, 30029 Nîmes cedex 9, France E-mail: eric.viel@chu-nimes.fr

Disclaimer: The study was sponsored by Astellas Pharma Europe Ltd. Medical writing was funded by Astellas Pharma Europe Ltd and then Grünenthal GmbH. Study investigators received clinical study payments from the study sponsor to carry out the study at their centers using fair market value principles to determine study costs.

Conflict of interest: None of the authors received funding or reimbursement for their work on this publication. Eric Viel has been a consultant for Grünenthal GmbH and was one of the investigators in the trial; Mariëlle Eerdekens and Prashanth Kandaswamy are employees of Grünenthal GmbH.

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Accepted for publication: 12-17-2020

Free full manuscript: www.painphysicianjournal.com

Background: Peripheral neuropathic pain (PNP) is a complex, subjective experience affecting both physical and psychological aspects of functioning. Assessing patient-reported outcomes (PROs) beyond pain relief is important and aligns with the recommendations of IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials). Moreover, PRO data are key to clinical decision-making when evaluating treatment options. However, direct comparisons between such options are scarce. High-concentration capsaicin 179 mg (8% w/w) cutaneous patch (HCCP) is applied to the skin at minimum intervals of 90 days under physician supervision; alternative recommended treatments for PNP are mostly orally administered on a daily basis. The ELEVATE study directly compared HCCP with pregabalin and found noninferior efficacy of HCCP to pregabalin in relieving pain after 8 weeks, with a significantly faster onset of action and fewer systemic side effects.

Objectives: The objective of this analysis was to compare PRO outcomes defined as secondary objectives of the ELEVATE study after a single intervention with HCCP to daily oral pregabalin for 8 weeks.

Study Design: ELEVATE was an open-label, randomized (1:1) multicenter study.

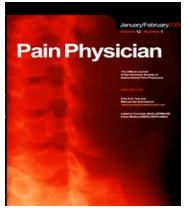
Setting: The study included 92 sites in 22 countries in Europe and Asia.

Methods: Five hundred fifty-nine non-diabetic patients with PNP received a single intervention with HCCP (n = 282; 1-4 patches at baseline) or oral daily pregabalin (n = 277; 150-600 mg, 8 weeks). At baseline (Day 0) and Week 8, patients completed the following PROs in addition to the regular pain assessments: Patient Global Impression of Change (PGIC), Medical Outcomes Study Cognitive Functioning scale (MOS-Cog), Medical Outcomes Study Sleep scale (MOS-Sleep), Treatment Satisfaction Questionnaire for Medication (TSQM), and EuroQol 5-Dimensions 5-levels (EQ-5D-5L) Utility Index (EQ-UI) and Visual Analog Scale (EQ-VAS).

Results: At Week 8, 76% and 75.9% of patients on HCCP and pregabalin, respectively, reported to be very much/much/minimally improved on the PGIC. HCCP application was associated with significant improvements from baseline vs. pregabalin in MOS-Cog (mean difference: 4.28 [95% CI: 2.90-5.66]; $P < 0.001$), EQ-VAS (3.11 [0.30-5.92]; $P = 0.030$), and TSQM global satisfaction (6.74 [2.29-11.20]; $P = 0.029$), particularly the side-effects dimension (21.23 [17.55-24.94]; $P < 0.0001$). No significant differences in improvements were noted for the MOS-Sleep, TSQM convenience, and EQ-UI.

Limitations: The ELEVATE study has an open-label design, with only one comparator (pregabalin); it was limited to 8 weeks. The sample size was determined for the primary endpoint.

Conclusions: A single intervention with HCCP showed benefits vs. daily pregabalin at Week 8 on several PROs. While HCCP has been approved in the United States for PNP treatment in diabetic and PHN patients, these observations provide information on how patients perceive the effects of distinct PNP treatments. They are complementing already existing knowledge on efficacy and safety of different treatment options with data on patient preferences and may help identify the appropriate treatment option in dialogue with the patients and shared decision-making.



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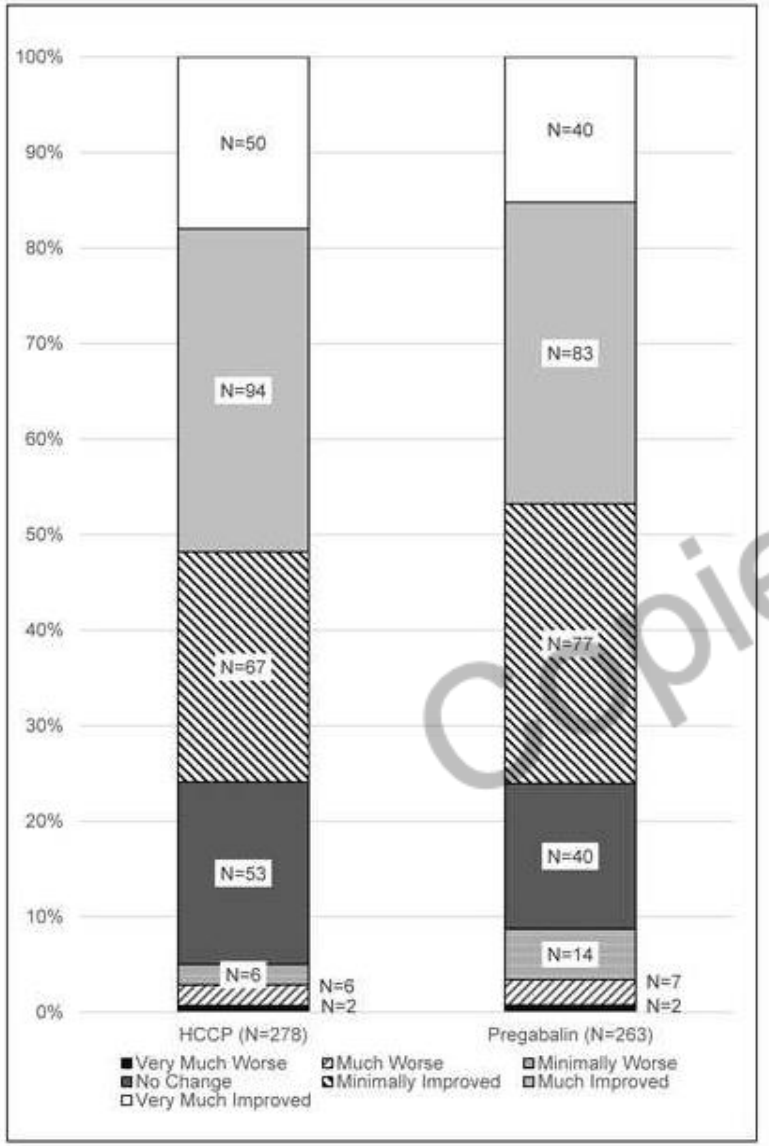
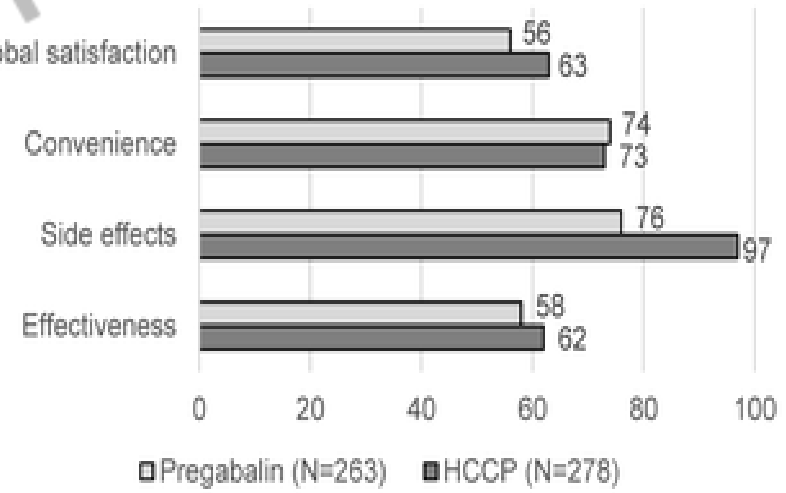
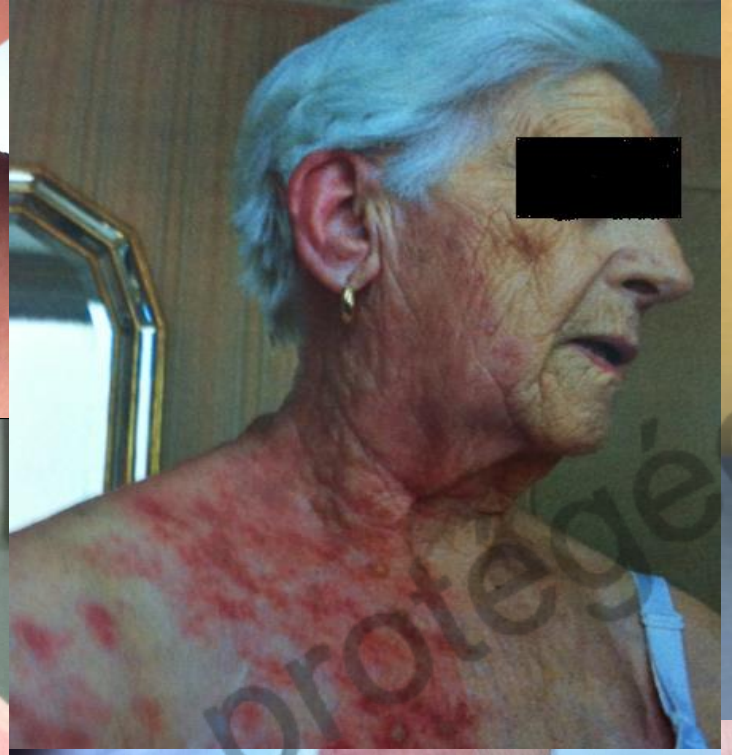
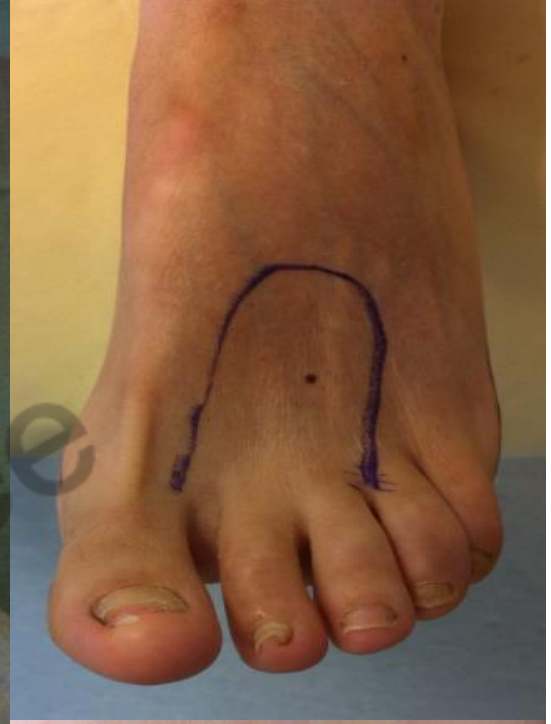
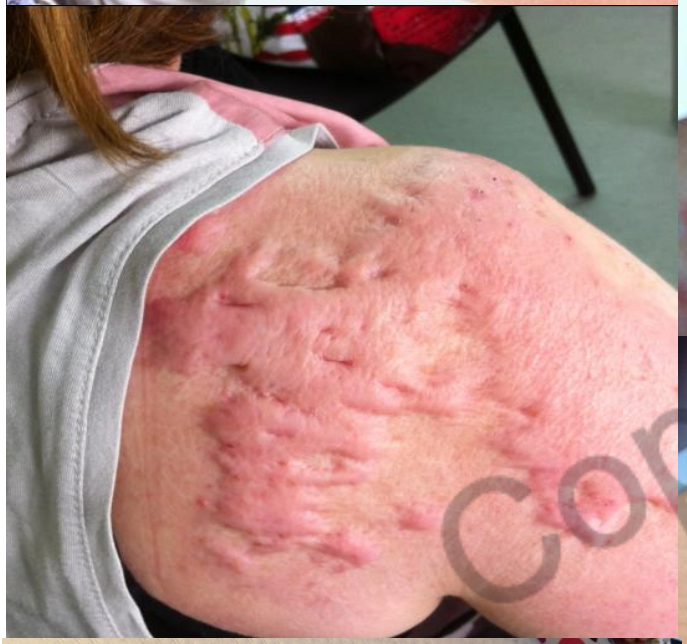
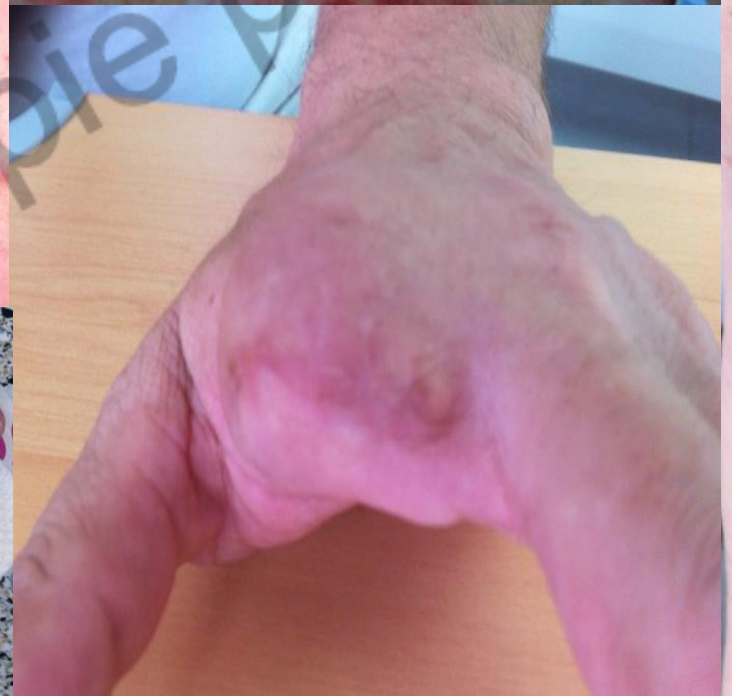
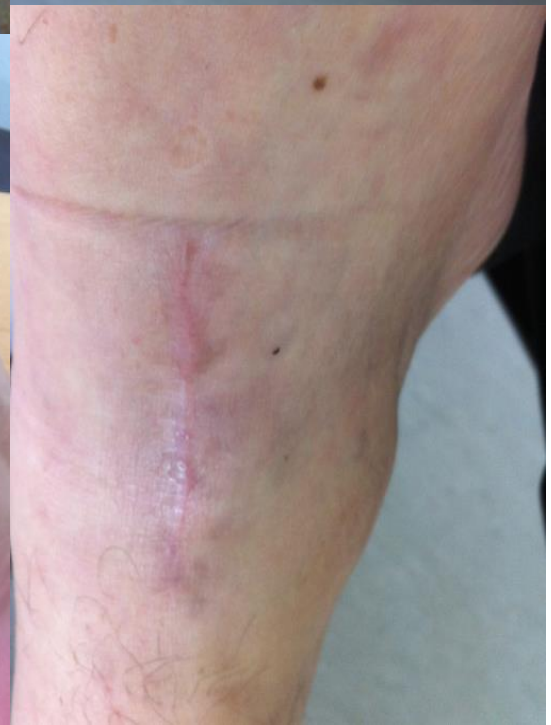
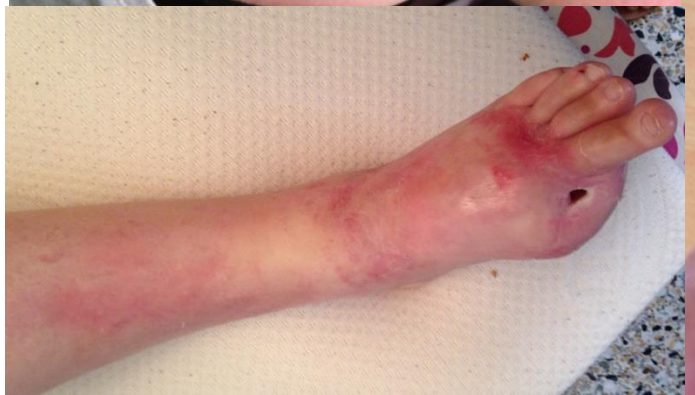




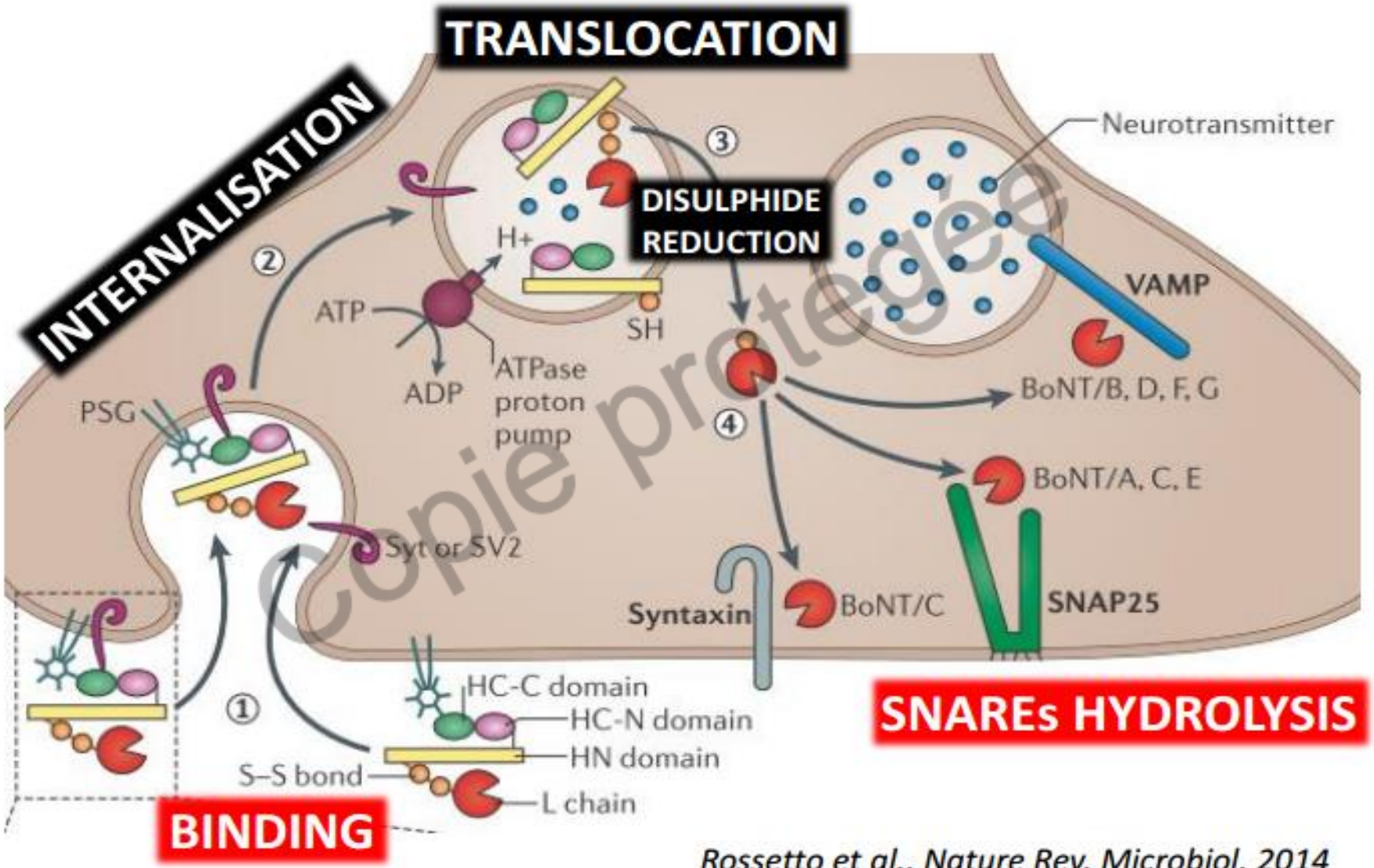








Toxine botulique A

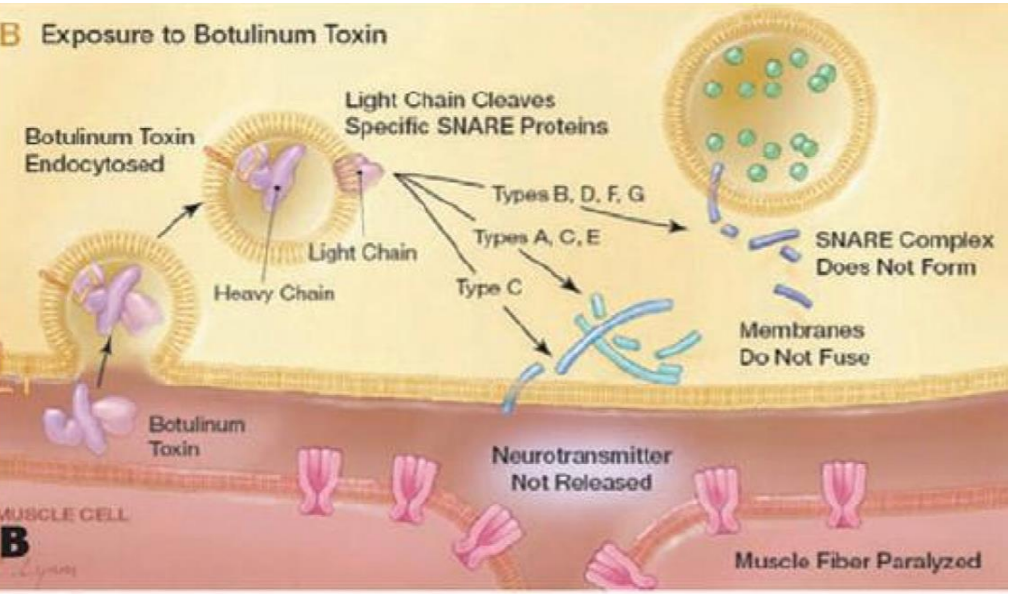
toxins *Toxins* **2015**, *7*, 3127-3154; doi:10.3390/toxins7083127

Botulinum Toxin for Neuropathic Pain: A Review of the Literature

Hyun-Mi Oh and Myung Eun Chung



Rossetto et al., Nature Rev. Microbiol. 2014



La toxine botulique peut agir sur l'exocytose de nombreux neurotransmetteurs au niveau de toute cellule contenant le complexe SNARE et les récepteurs correspondants

- Acétylcholine, AAE (GLU), glycine, sérotonine
- CGRP, substance P

et sur le transport axonal de certains récepteurs dont TRPV1

The Journal of Neuroscience, 2008

Long-Distance Retrograde Effects of Botulinum Neurotoxin A

Flavia Antonucci,[1] Chiara Rossi,[1] Laura Gianfranceschi,[2] Ornella Rossetto,[3] and Matteo Caleo[1]

PLoS Pathog 2012

Botulinum Neurotoxins A and E Undergo Retrograde Axonal Transport in Primary Motor Neurons

Laura Restani[1,2☯], Francesco Giribaldi[1☯¤], Maria Manich[1,3], Kinga Bercsenyi[1], Guillermo Menendez[1], Ornella Rossetto[4], Matteo Caleo[2], Giampietro Schiavo[1*]

PAIN 2014

Botulinum toxin type A selectivity for certain types of pain is associated with capsaicin-sensitive neurons

Ivica Matak [a], Ornella Rossetto [b], Zdravko Lacković [a,*]

d'après Bernard Poulain
CNRS Strasbourg

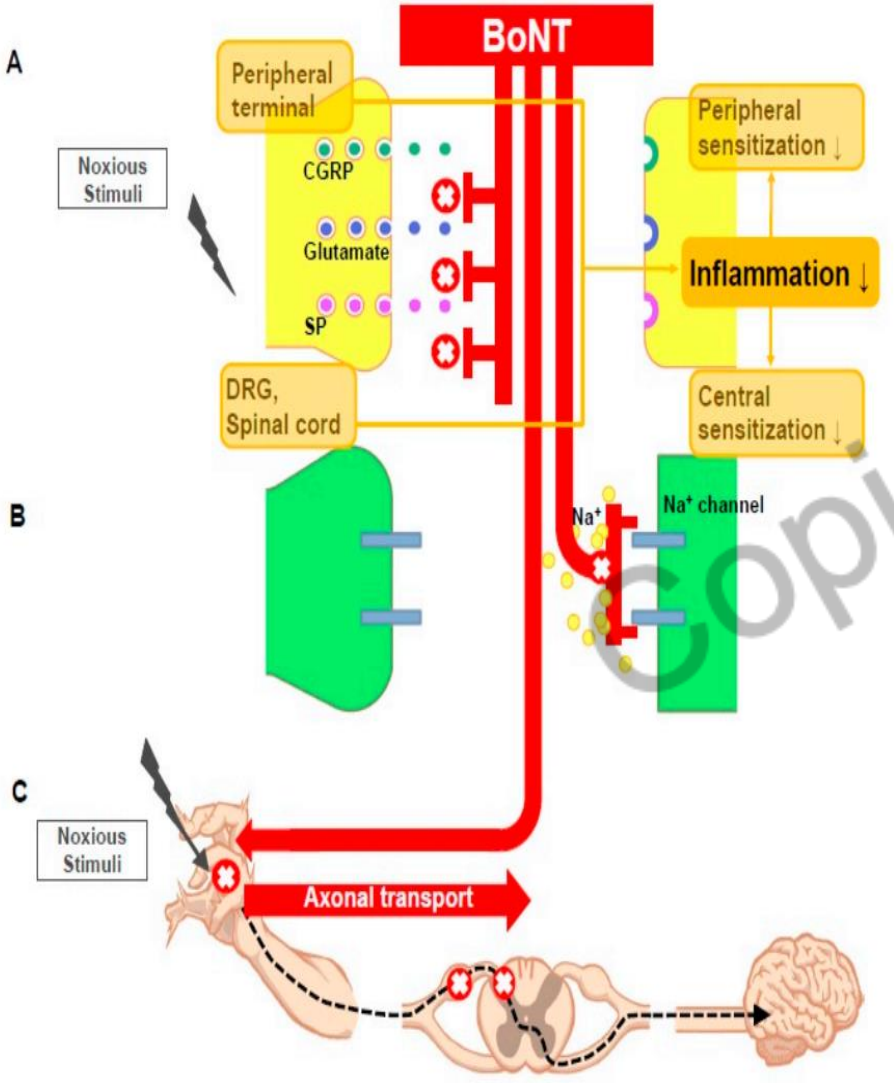
Review

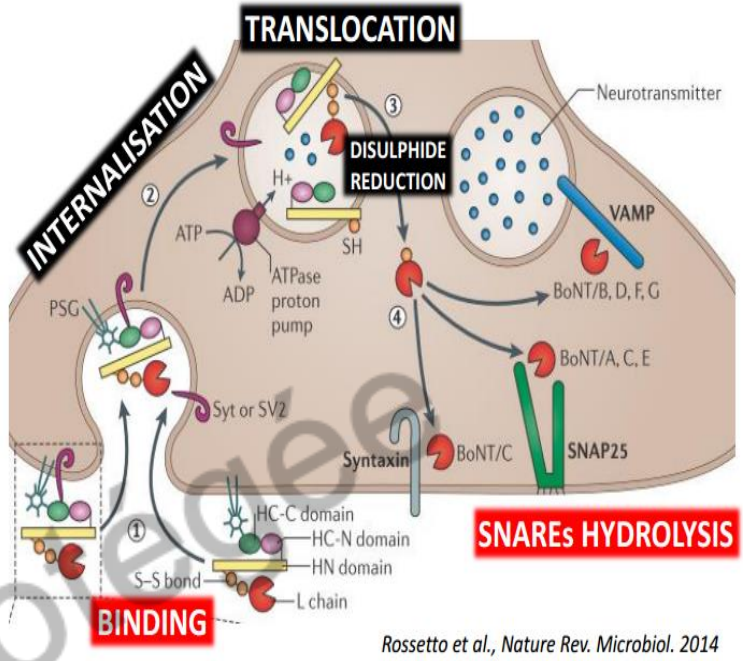
Botulinum Toxin for the Treatment of Neuropathic Pain

toxins

Toxins **2017**, *9*, 260; doi:10.3390/toxins9090260

JungHyun Park [1] and Hue Jung Park [2,*]





Rossetto et al., Nature Rev. Microbiol. 2014

(**A**) Noxious stimuli cause inflammation through the release of neuropeptides and inflammatory mediators, which can cause peripheral sensitization. This action also occurs in DRG, dorsal horn of spinal cord and can lead to central sensitization. Botulinum toxin (BoNT) inhibits the release of pain mediators in peripheral nerve terminal, DRG, and spinal cord neuron, thereby reducing the inflammatory response and preventing the development of peripheral and central sensitization. Symbols; SP, substance P; CGRP, calcitonin gene related protein; DRG, dorsal root ganglion; (**B**) The hyperexcitability and spontaneous action potential mediated by the Na channel in peripheral sensory neuron contribute to the pathophysiology of neuropathic pain. BoNT can control neuropathic pain by blocking the Na channel; (**C**) Some of the BoNT appear to retrograde transport along the axons. SNAP-25 is cleaved in the dorsal horn of the spinal cord and central nuclei after a small amount of BoNT is administered to the periphery, thereby boosting the retrograde transport of BoNT.

La toxine botulique

Cui et al 2004 / Aoki et al 2011/ Wheeler et al 2013

- Inhibe la libération des neurotransmetteurs : terminaisons périphériques / ganglion spinal/ corne postérieure
  CGRP, substance P, monoamines, sérotonine, ac.aminés excitateurs

- Désactive les canaux sodiques : mécanismes différents / AL, TTX, antiépileptiques

- Subit un transport axonal bi-directionnel, notamment rétrograde vers corne postérieure

The Journal of Neuroscience, 2008
Long-Distance Retrograde Effects of Botulinum Neurotoxin A
Flavia Antonucci,[1] Chiara Rossi,[1] Laura Gianfranceschi,[2] Ornella Rossetto,[3] and Matteo Caleo[1]

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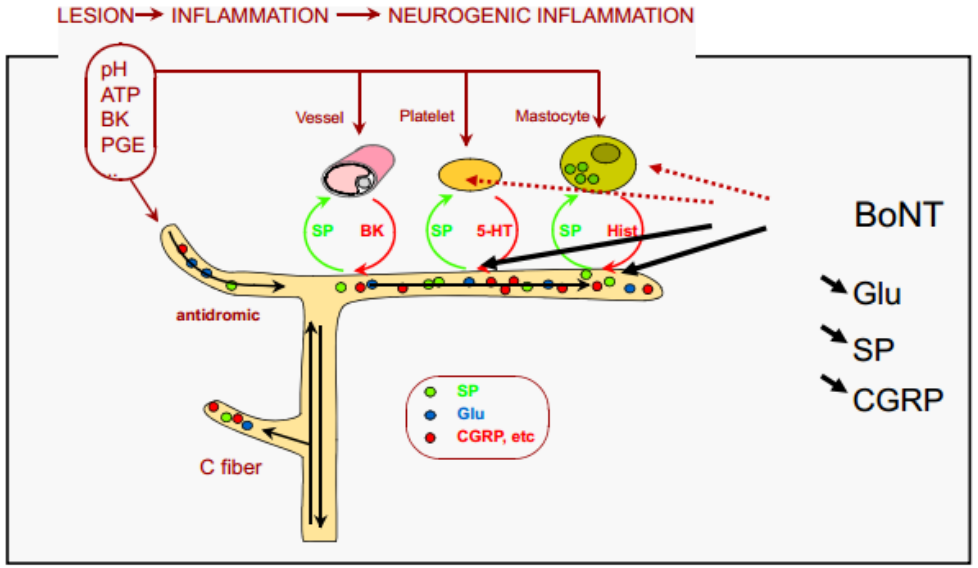
Botulinum Neurotoxins A and E Undergo Retrograde Axonal Transport in Primary Motor Neurons
Laura Restani[1,2¶], Francesco Giribaldi[1¶¤], Maria Manich[1,3], Kinga Bercsenyi[1], Guillermo Menendez[1], Ornella Rossetto[4], Matteo Caleo[2], Giampietro Schiavo[1*]

PAIN 2014
Botulinum toxin type A selectivity for certain types of pain is associated with capsaicin-sensitive neurons
Ivica Matak[a], Ornella Rossetto[b], Zdravko Lacković[a,*]

- Bloque le transport axonal des récepteurs TRPV1

- Exerce un effet anti-inflammatoire local:
  réduit ou inhibe l'expression de COX-2 (enzyme d'adaptation)
  réduit l'inflammation neurogène (locale)

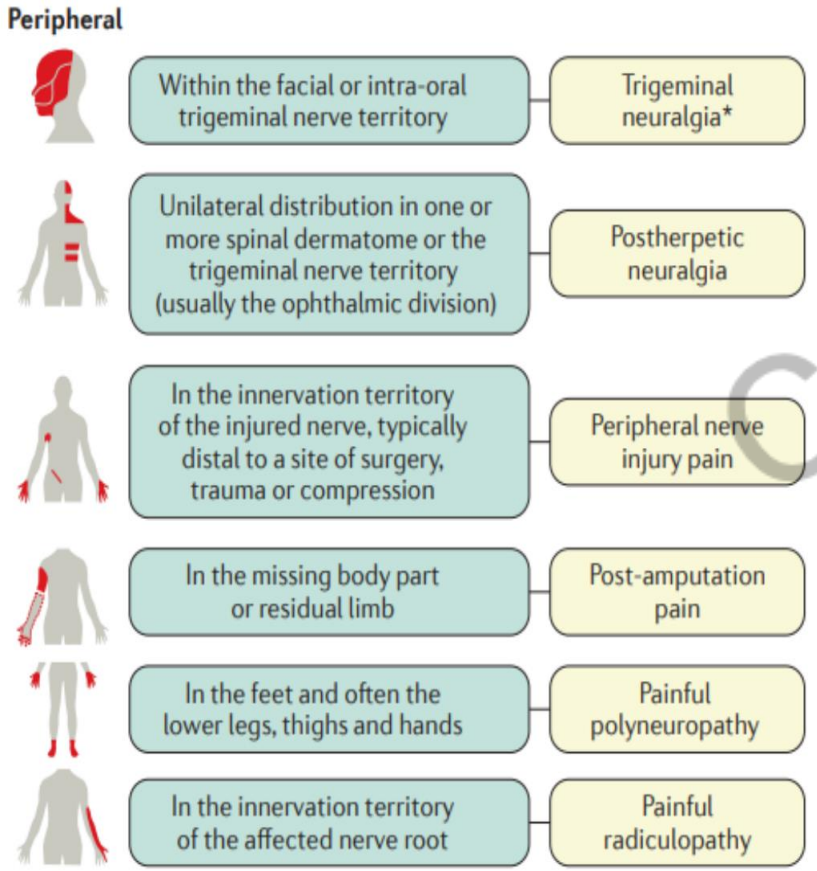
Poulain et al Proc Natl Acad Sci USA 1988 & 55 références

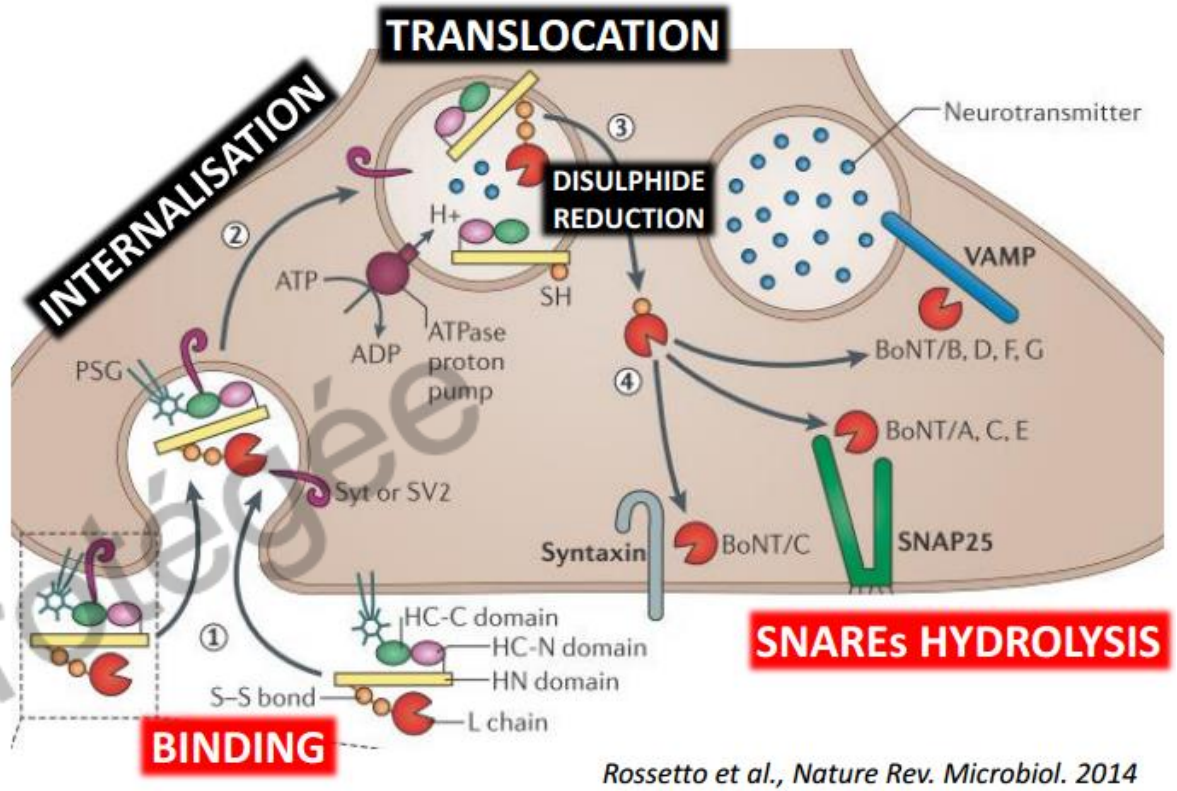


• Les douleurs neuropathiques périphériques sont associées à un lésion ou une maladie du système somatosensoriel

• La prévalence en population générale est estimée à 5 à 10 % selon les étude épidémiologiques

• L'impact sur la qualité de vie et le sommeil est supérieur à celui des douleurs non neuropathiques





Journal of Neural Transmission
https://doi.org/10.1007/s00702-020-02163-5

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - ORIGINAL ARTICLE

Botulinum neurotoxin injections for muscle-based (dystonia and spasticity) and non-muscle-based (neuropathic pain) pain disorders: a meta-analytic study

Paula Ruth L. Siongco[1] · Raymond L. Rosales[1,2] · Austen Peter Moore[3] · Rainer Freynhagen[4,5] · Kimiyoshi Arimura[6] · Petr Kanovsky[7] · Ryuji Kaji[8] · Hubert H. Fernandez[9] · Dirk Dressler[10]

Received: 25 November 2019 / Accepted: 18 February 2020

Douleurs neuropathiques ???

- Modèles animaux : BoNTA → réduisait l'allodynie expérimentale induite par des lésions nerveuses périphériques
- Effet sur les voies nociceptives indépendant de l'effet musculaire

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Quels sont les bons répondeurs au traitement par toxine botulique A ?

RCT Ranoux et al. 2008 et BOTNEP 2016

- → efficacité de BoNTA sur les symptômes neuropathiques évalués le questionnaire Neuropathic Pain Symptom Inventory (NPSI)
- → +++ sur la douleur paroxystique (notamment les décharges électriques),
- → +++ efficacité sur l'allodynie au frottement et à la pression fine mesurée par des tests quantifiés sensoriels
- → Corrélation entre l'efficacité de la BoNT et la préservation de la sensibilité thermique
- → La préservation de la densité en fibres intra-épidermiques au sein de l'aire douloureuse (évaluée par une biopsie cutanée avant le traitement) était associée à une meilleure réponse au traitement par toxine botulique.

Profil particulier de répondeurs à la BoNTA ? « **Les bons répondeurs semblent caractérisés par une préservation relative de la sensibilité thermique et/ou une allodynie mécanique dans la zone douloureuse.** » Attal. et al. 2020 (Bulletin de l'académie de médecine – séance janvier 2020)

Diapositive adaptée de Dr M.Stainmesse 2023

- Injections intra-articulaires
- Blocs péri-nerveux

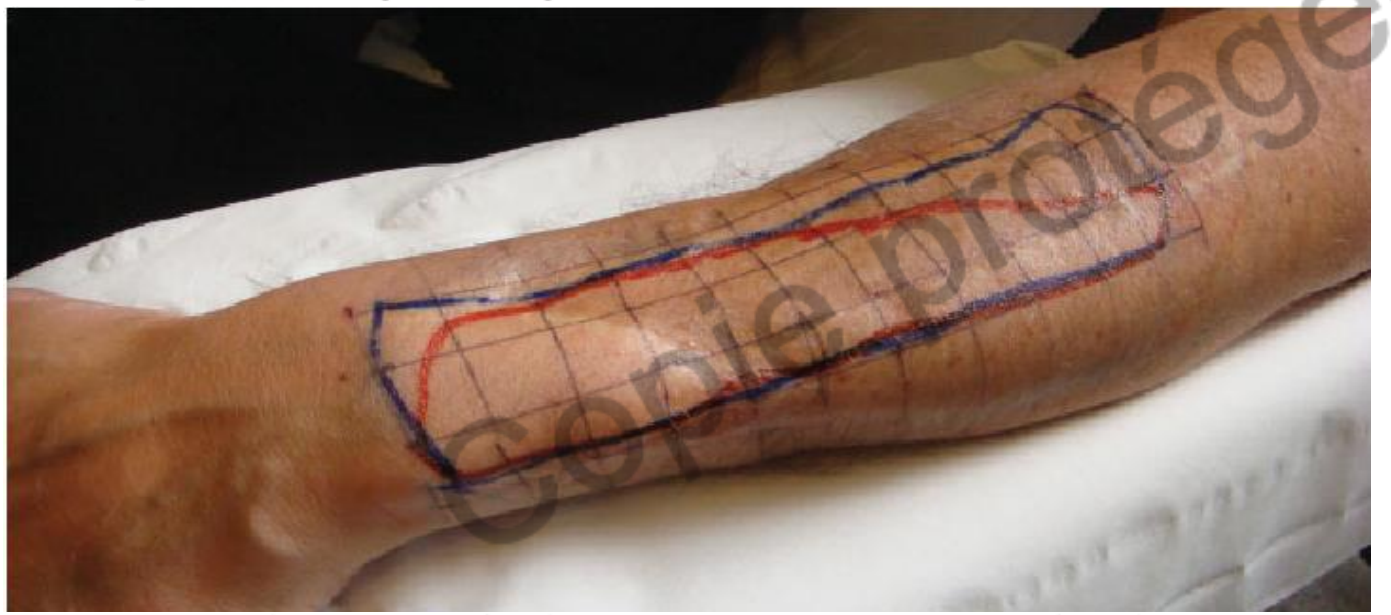
- Douleurs chroniques post-chirurgicales
- Membres fantômes (douloureux) & douleurs de moignon
- SDRC Algodystrophies
- Névralgie post-zostérienne
- Neuropathie diabétique
- Névralgie Gd Occipital (Arnold)
- Douleurs post-lésion médullaire
- Douleurs neuropathiques centrales post-AVC
- Névralgie trigéminale
- Syndromes douloureux chroniques pelviens

Botulinum Toxin Type A Induces Direct Analgesic Effects in Chronic Neuropathic Pain

Ann Neurol 2008;64:274–284

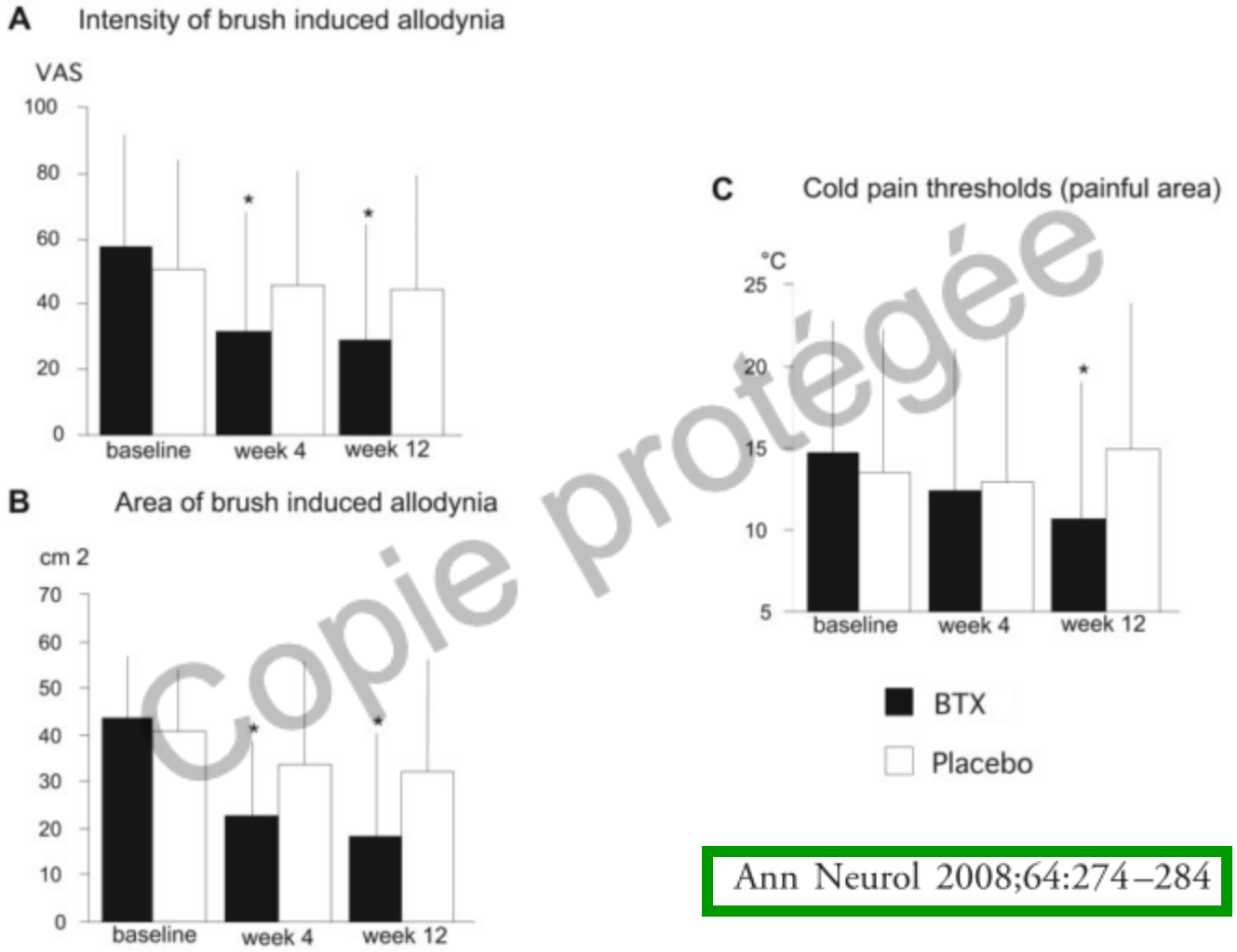
Danièle Ranoux, Nadine Attal, Francoise Morain, D. Bouhassira

Botulinum toxin type A (BTX-A) has been reported to have analgesic effects independent of its action on muscle tone, possibly by acting on neurogenic inflammation. Such a mechanism may be involved in peripheral neuropathic pain.



botulinum toxin type A (BTX-A) intradermal injection technique for the painful area in one male patient with posttraumatic radial nerve lesion just before BTX-A injection. Intradermal injections were performed using equidistant grid lines 1.5cm apart (marked in black) aiming to cover the area of maximal spontaneous pain (in blue) and the whole area of allodynia (in red).

Toxines botuliques / douleurs chroniques



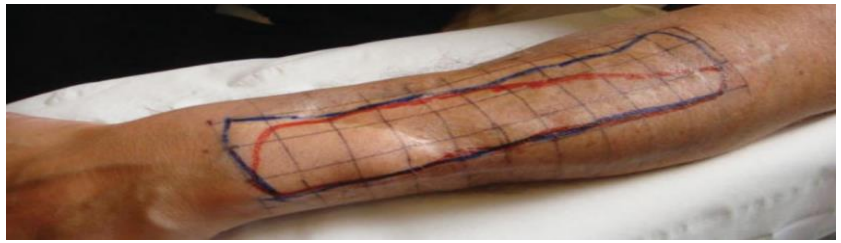
Ann Neurol 2008;64:274–284

Interpretation: These results indicate for the first time that BTX-A may induce direct analgesic effects in patients with chronic neuropathic pain independent of its effects on muscle tone and suggest novel indications for BTX-A in analgesia.

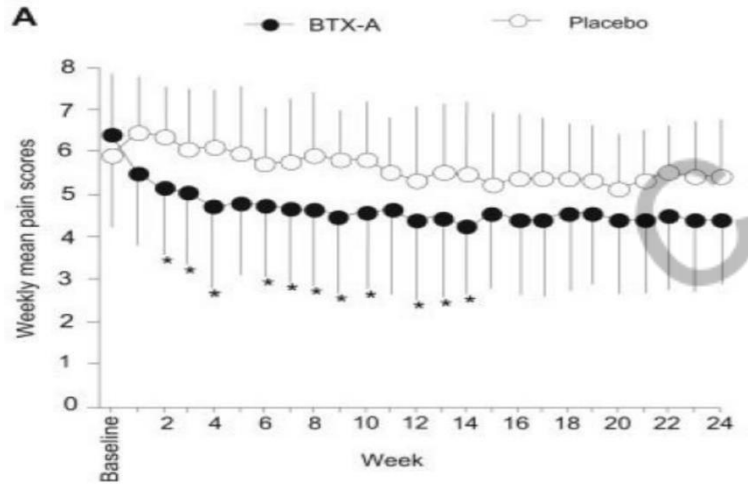
ORIGINAL ARTICLE

Botulinum Toxin Type A Induces Direct Analgesic Effects in Chronic Neuropathic Pain

Danièle Ranoux, MD,[1] Nadine Attal, MD, PhD,[2–4] Francoise Morain, Clinical Research Assistant,[2–4] and D. Bouhassira[2–4]



29 patients BTX *vs.*placebo s.c.
3 à 5 UI / cm^2



Réduction intensité douleur 2ème → 12ème semaine & NNT 50% : 3.3

Ann Neurol 2008;64:274–284

Tableau 1 Études cliniques contrôlées randomisées en double aveugle contre placebo de la toxine botulinique de type A dans les douleurs neuropathiques autres que la névralgie faciale essentielle.

Auteurs	Indication	Doses et modalités	Placebo	Nombre de patients	Méthodologie	Durée de l'essai	Résultats critère primaire	NNT (50 % amélioration douleur)	Autres résultats d'efficacité
Ranoux et al. 2008 [28]	Douleur neuropathique périphérique avec allodynie (trauma, zona)	Injections SC de 50 à 200 U selon l'aire douloureuse	Sérum physiologique	29	Groupes parallèles	24 semaines	Positif sur douleur moyenne/24 h	3,0 (1,6–22)	Effets sur brûlure, allodynie, douleur paroxystique. Effet supérieur si déficit thermique faible
Yuan et al. 2009 [29]	Neuropathie douloureuse du diabète	Injections intradermiques pieds ; dose fixe 50 U	Sérum physiologique	20	« Cross over »	12 semaines	Positif sur douleur moyenne/24 h	2,3 (1,5–4,7)	Effets sur la qualité du sommeil
Xiao et al. 2010 [30]	Douleur post-zostérienne	Injections SC dose unique 5 U/mL	Sérum physiologique et 0,5 % lidocaïne	40/60	Groupes parallèles	12 semaines	Positif sur douleur moyenne/24 h	NA	Effet sur la durée du sommeil
Apalla et al. 2013 [31]	Douleur post-zostérienne	Injections SC dose	Sérum physiologique	30	Groupes parallèles	16 semaines	Positif sur la proportion de répondeurs (50 %)	1,2 (1,0–1,4)	Effet sur l'intensité douleur (EVA), qualité du sommeil
Attal et al. 2016 [19]	Douleur neuropathique périphérique (trauma, zona, neuropathie douloureuse)	2 séries d'injections SC de 50 à 300 U selon aire douloureuse à 3 mois	Sérum physiologique	66	Groupes parallèles	24 semaines	Positif sur douleur moyenne/24 h	7,3 (3,0–16)	Renforcement effet par 2nde injection. Effets sur allodynie, brûlure, douleur paroxystique. Effet supérieur chez patients présentant préservation fonction nociceptive ou allodynie mécanique
Han et al. 2016 [33]	Douleur neuropathique liée à lésion médullaire	Injection SC dose fixe de 200 U dans l'aire de douleur maximum	Sérum physiologique	40	Groupes parallèles	8 semaines	Positif sur douleur moyenne/24 h (EVA)	9,9	Effet sur composante sensorielle/affective de la douleur, douleurs sous lésionnelles, meilleur si lésion médullaire incomplète

NNT : nombre nécessaire à traiter pour obtenir un répondeur au traitement actif et non au placebo ; SC : sous-cutanée.

Effet non lié à effet sur tonus musculaire

Safety and efficacy of repeated injections of botulinum toxin A in peripheral neuropathic pain (BOTNEP): a randomised, double-blind, placebo-controlled trial

Nadine Attal, Daniel C de Andrade, Frédéric Adam, Danièle Ranoux, Manoel J Teixeira, Ricardo Galhardoni, Irina Raicher, Nurcan Üçeyler, Claudia Sommer, Didier Bouhassira

Lancet Neurol 2016; 15: 555–65

Summary

Background Data from previous studies suggest that botulinum toxin A has analgesic effects against peripheral neuropathic pain, but the quality of the evidence is low. We aimed to assess the safety and efficacy of repeated administrations of botulinum toxin A in patients with neuropathic pain.

Methods We did a randomised, double-blind, placebo-controlled trial at two outpatient clinics in France (Clinical Pain Centre, Ambroise Paré Hospital, APHP, Boulogne-Billancourt, and Neurological Centre, Hôpital Dupuytren, Limoges) and one in Brazil (Neurological Department, Hospital das Clínicas da FMUSP, São Paulo). Patients aged 18–85 years with peripheral neuropathic pain were randomly assigned (1:1) by block randomisation, according to a centralised schedule, to receive two subcutaneous administrations of botulinum toxin A (up to 300 units) or placebo, 12 weeks apart. All patients and investigators were masked to treatment assignment. The primary outcome was the efficacy of botulinum toxin A versus placebo, measured as the change from baseline in self-reported mean weekly pain intensity over the course of 24 weeks from the first administration. The primary efficacy analysis was a mixed-model repeated-measures analysis in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, NCT01251211.

Findings Between Oct 2, 2010, and Aug 2, 2013, 152 patients were enrolled, of whom 68 were randomly assigned (34 per group), and 66 (37 [56%] men) were included in the primary analysis (34 in the botulinum toxin A group and 32 in the placebo group). Botulinum toxin A reduced pain intensity over 24 weeks compared with placebo (adjusted effect estimate –0·77, 95% CI –0·95 to –0·59; p<0·0001). Pain on injection was the only adverse effect reported, and occurred in 19 (56%) participants in the botulinum toxin A group and 17 (53%) of those in the placebo group (p=1·0). Severe pain was experienced by ten (29%) participants in the botulinum toxin A group and 11 (34%) in the placebo group (p=0·8).

Interpretation Two administrations of botulinum toxin A, each of which comprised several injections, have a sustained analgesic effect against peripheral neuropathic pain. Several factors, such as the presence of allodynia and a limited thermal deficit, may be useful in predicting treatment response and should be investigated further.

	Botulinum toxin A (n=34)	Placebo (n=32)
Age (years)	51·6 (16·7)	52·3 (15·8)
Sex		
Male	17 (50%)	20 (63%)
Female	17 (50%)	12 (38%)
Pain duration (years)	5·1 (4·7)	6·3 (7·4)
Mean pain intensity*	6·5 (1·6)	6·4 (1·6)
Cause of pain		
Post-traumatic or postsurgical†	25 (74%)	21 (66%)
Polyneuropathy‡	5 (15%)	9 (28%)
Postherpetic neuralgia	4 (12%)	2 (6%)
Area of maximum pain		
Hand or forearm	14 (41%)	16 (50%)
Foot or ankle	12 (35%)	13 (41%)
Thorax or abdomen	6 (18%)	3 (9%)
Shoulder	2 (6%)	0
Concomitant analgesics		
Antidepressants	25 (74%)	28 (88%)
Gabapentin or pregabalin	9 (26%)	11 (34%)
Opioids	17 (50%)	14 (44%)
NSAIDs or paracetamol	12 (35%)	17 (53%)
Other antiepileptics§	6 (18%)	6 (19%)

Data are mean (SD) or number (%). Some percentages do not add up to 100 because of rounding. NSAID=non-steroidal anti-inflammatory drug. *On the numerical rating scale (range 0–10) of the Brief Pain Inventory from pain diaries at baseline. †25 (38%) participants had post-traumatic nerve lesions (14 in the botulinum toxin A group and 11 in the placebo group) and 21 (32%) had postsurgical nerve lesions (ten and 11). Post-traumatic nerve lesions corresponded to work or sports accidents (eg, crush, luxation, or fracture), but not to amputations or scars. ‡Causes were chronic inflammatory demyelinating neuropathy in five patients (two in the botulinum toxin A group and three in the placebo group), diabetes in two (both in the placebo group), idiopathic small fibre neuropathy in four (two in each group), vasculitis in two (one in each group), and leprosy in one (botulinum toxin A group). §Clonazepam, carbamazepine, and lamotrigine.

Table 1: **Demographics and baseline clinical characteristics**

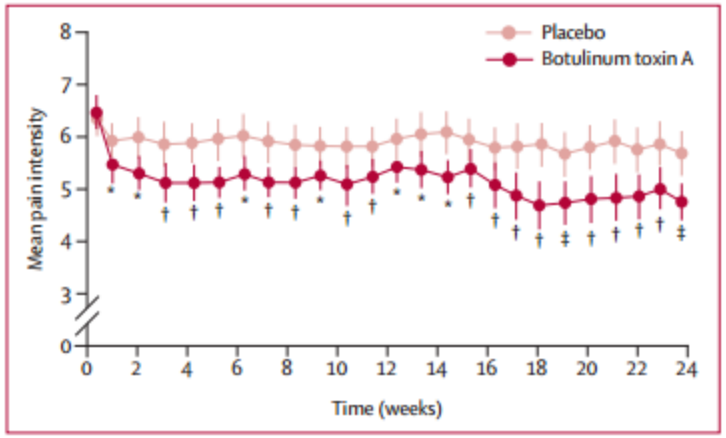


Figure 2: **Effects of botulinum toxin A and placebo on the primary endpoint**
Bars are SE. p values are for the difference between botulinum toxin A and placebo at each timepoint. *p<0·05. †p<0·01. ‡p<0·001.

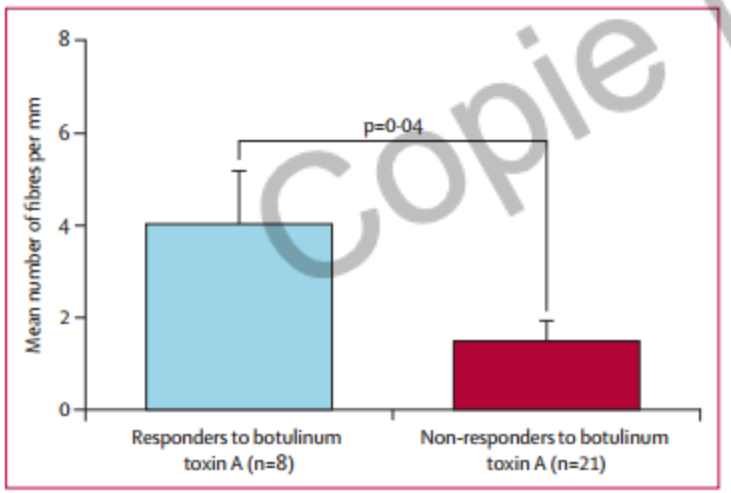


Figure 3: **Intra-epidermal nerve fibre density at baseline**
Bars are SD.

In participants who received at least one administration of botulinum toxin A (n=34), the efficacy of the treatment on mean pain intensity over 24 weeks was greater in participants with allodynia (based on the NPSI) at baseline (n=15) than in those without allodynia (n=19; adjusted effect estimate 0·56 [SE 0·14]; p=0·0003). We noted similar findings when allodynia was defined on the basis of QST (n=59 [29 with allodynia and 30 without]; adjusted effect estimate 0·59 [SE 0·14]; p=0·0002). The response to botulinum toxin A at 24 weeks (≥50% pain relief) was also predicted by the severity of brush-induced allodynia (odds ratio 4·6, 95% CI 1·5–13·7; p=0·007) and pressure hyperalgesia (3·5, 1·03–12·2; p=0·04) on QST. Finally, we noted significant positive or inverse correlations between the efficacy of botulinum toxin A at 24 weeks and baseline warm detection thresholds (Rho –0·49; p=0·03), cold detection thresholds (Rho 0·46; p=0·02), and mechanical pain thresholds (Rho –0·42; p=0·02) on the painful side, showing that less thermal deficits and stronger mechanical allodynia were associated with greater efficacy of botulinum toxin A. No such relations were noted in the placebo group.

Safety and efficacy of repeated injections of botulinum toxin A in peripheral neuropathic pain (BOTNEP): a randomised, double-blind, placebo-controlled trial

Fighting neuropathic pain with botulinum toxin A

Back in the late 1980s, botulinum toxin was incidentally found to attenuate pain in addition to its known spasmolytic effect.[1]

February 29, 2016
http://dx.doi.org/10.1016/S1474-4422(16)00056-9

Ralf Baron, Andreas Binder

In summary, increasing evidence shows that botulinum toxin A is effective in patients with peripheral neuropathic pain, in particular in a subgroup with preserved small fibre innervation.

Gabapent gabapent			gh
SNRI anti			gh
Tricyclic a			derate
Topical lid			w
Topical ca			gh
Tramadol	4–9	4·7 (3·6–6·7)	Low moderate
Strong opioids	4–12	4·3 (3·4–5·8)	Low moderate
Botulinum toxin A (previous studies)	4–24	1·9 (1·5–2·4) in published studies†, but one unpublished study was negative	Low
Botulinum toxin A (this study)	24	7·3 (−3·0 to 16·6)	NA

Previous data from Finnerup and colleagues.[5] NA=not applicable. SNRI=serotonin-norepinephrine reuptake inhibitor. *Calculated as the inverse of the absolute difference between the proportion of responders in the active and placebo treatment groups (based on a 50% decrease in pain). †Risk of bias, inconsistency, and imprecision were high.

Table 5: Treatments for peripheral neuropathic pain and quality of the evidence

International NeuPSIG Guideline for the treatment of neuropathic pain

Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis

Nanna B Finnerup*, Nadine Attal*, Simon Haroutounian, Ewan McNicol, Ralf Baron, Robert H Dworkin, Ian Gilron, Maija Haanpää, Per Hansson, Troels S Jensen, Peter R Kamerman, Karen Lund, Andrew Moore, Srinivasa N Raja, Andrew S C Rice, Michael Rowbotham, Emily Sena, Philip Siddall, Blair H Smith, Mark Wallace

Lancet Neurol 2015; 162-73
Published Online January 7, 2015
http://dx.doi.org/10.1016/S1474-4422(14)70251-0

Summary

Background New drug treatments, clinical trials, and standards of quality for assessment of evidence justify an update of evidence-based recommendations for the pharmacological treatment of neuropathic pain. Using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE), we revised the Special Interest Group on Neuropathic Pain (NeuPSIG) recommendations for the pharmacotherapy of neuropathic pain based on the results of a systematic review and meta-analysis.

www.thelancet.com/neurology Vol 14 February 2015

NEUROPATHIC PAIN | NeuPSIG
IASP Special Interest Group

IASP INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN CELEBRATING | 1974–2024

	First-line drugs			Second-line drugs			Third-line drugs	
	Serotonin-noradrenaline reuptake inhibitors duloxetine and venlafaxine	Tricyclic antidepressants	Pregabalin, gabapentin, gabapentin extended release or enacarbil	Tramadol	Capsaicin 8% patches	Lidocaine patches	Strong opioids	Botulinum toxin A
Quality of evidence	High	Moderate	High	Moderate	High	Low	Moderate	Moderate
Balance between desirable and undesirable effects								
Effect size	Moderate	Moderate	Moderate	Moderate	Low	Unknown	Moderate	Moderate
Tolerability and safety*	Moderate	Low-moderate	Moderate-high	Low-moderate	Moderate-high	High	Low-moderate	High
Values and preferences	Low-moderate	Low-moderate	Low-moderate	Low-moderate	High	High	Low-moderate	High
Cost and resource allocation	Low-moderate	Low	Low-moderate	Low	Moderate-high	Moderate-high	Low-moderate	Moderate-high
Strength of recommendation	Strong	Strong	Strong	Weak	Weak	Weak	Weak	Weak
Neuropathic pain conditions	All	All	All	All	Peripheral	Peripheral	All	Peripheral

Finnerup NB, et al. Lancet Neurol. 2015;14(2):162–73.

Toxicon
Volume 147, 1 June 2018, Pages 120-128

Botulinum toxin treatment of pain syndromes –an evidence based review

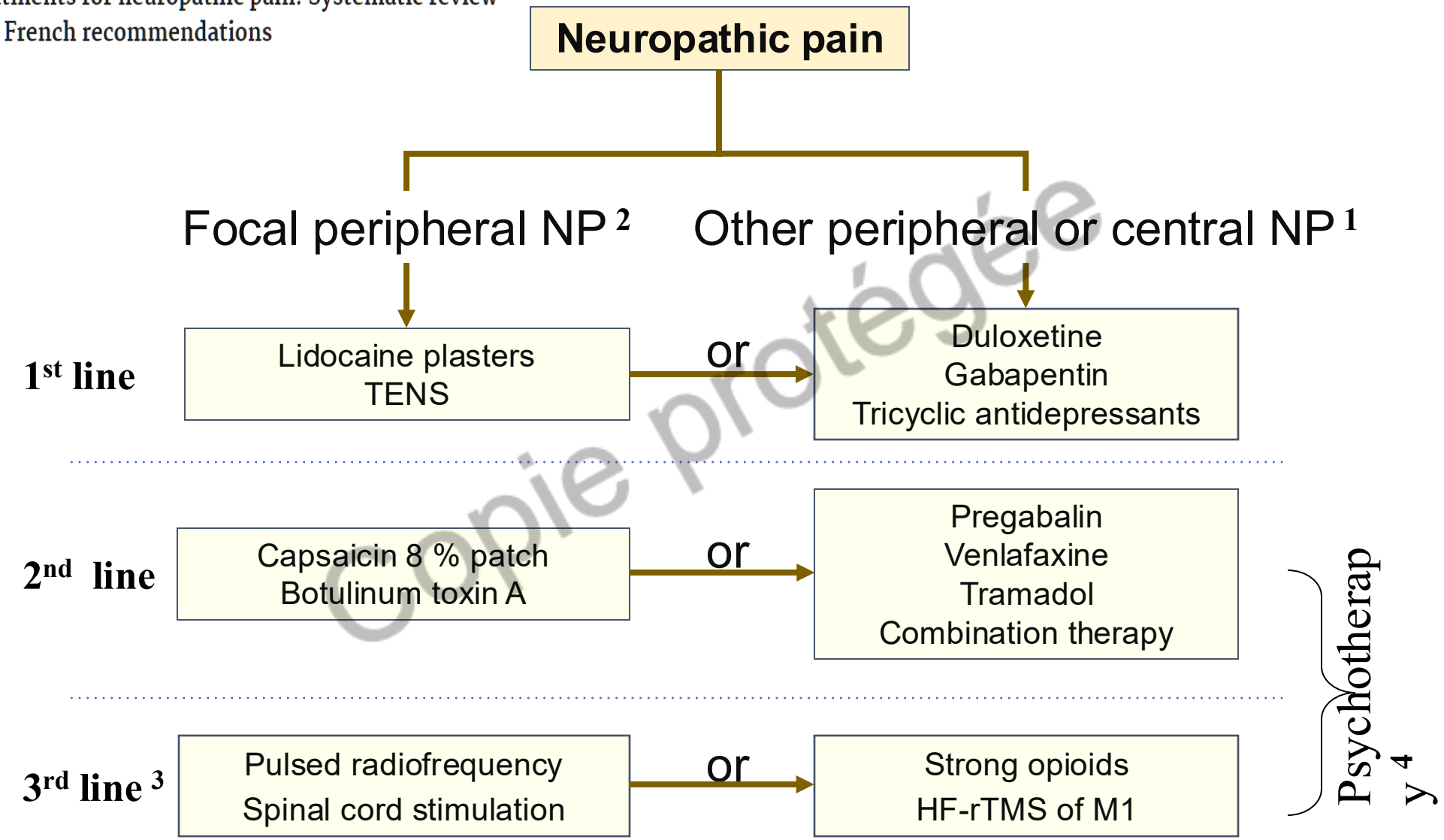
Yasaman Safarpour , Bahman Jabbari

This review evaluates the existing level of evidence for efficacy of BoNTs in different pain syndromes using the recommended efficacy criteria from the Assessment and Therapeutic Subcommittee of the American Academy of Neurology. There is a level A evidence (effective) for BoNT therapy in post-herpetic neuralgia, trigeminal neuralgia, and posttraumatic neuralgia. There is a level B evidence (probably effective) for diabetic neuropathy, plantar fasciitis, piriformis syndrome, pain associated with total knee arthroplasty, male pelvic pain syndrome, chronic low back pain, male pelvic pain, and neuropathic pain secondary to traumatic spinal cord injury. BoNTs are possibly effective (Level C -one class II study) for female pelvic pain, painful knee osteoarthritis, post-operative pain in children with cerebral palsy after adductor release surgery, anterior knee pain with vastus lateralis imbalance. There is a level B evidence (one class I study) that BoNT treatment is probably ineffective in carpal tunnel syndrome. For myofascial pain syndrome, the level of evidence is U (undetermined) due to contradicting results. More high quality (Class I) studies and studies with different types of BoNTs are needed for better understanding of the role of BoNTs in pain syndromes.

Practice Guideline › Rev Neurol (Paris). 2020 May;176(5):325-352.
doi: 10.1016/j.neurol.2020.01.361. Epub 2020 Apr 7. X Moisset et al

Pharmacological and non-pharmacological treatments for neuropathic pain: Systematic review and French recommendations

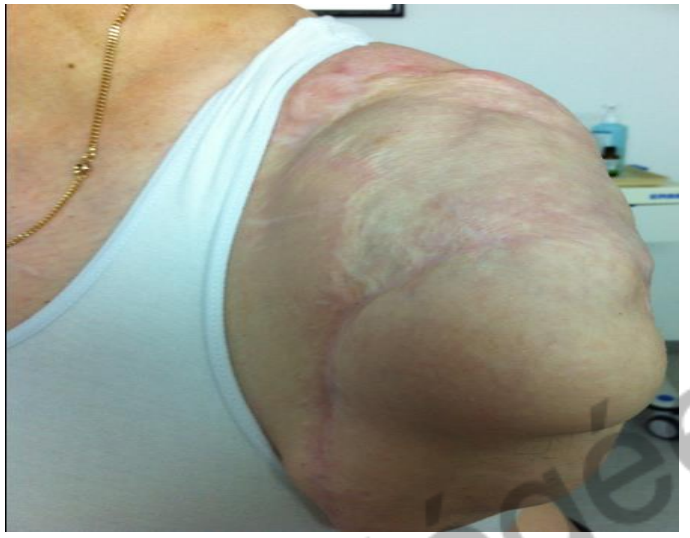
French recommendations Nov 2019 annual meeting of French Society for tthe study of Pain

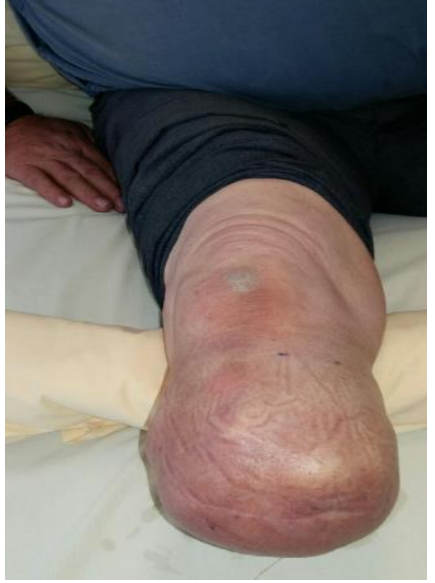


Membres fantômes (douloureux) & douleurs de moignon

Botulinum toxin for phantom limb pain.

Study Design	No. of Patients	Method of Injection (Total Volume)	Result	Reference
Prospective, randomized, double-blind, pilot	14	Intramuscular/cutaneous/subcutaneous/ neuroma (EMG guidance) 50 U per site (250–300 U)	Both groups improved pain and BoNT group had an advantage over pain control during 3–6 months but could not completely change phantom limb pain.	[57]
Case series	3	EMG guidance into points with strong fasciculation (500 U)	Phantom pain, pain medication could be reduced, the gait became more stable and the artificial limb was better tolerated.	[58]





55 ans, AVP bus/ravin dans les Pyrénées
Arrachement MSG/ 27 mois plus tôt

Abandon traitements systémiques (dont opioïdes, prégabaline)

Décision : patch capsaïcine d'emblée
4 applications / 9 mois

Successivement :
→ disparition des ADP
→ réduction surface allodynie et DNP
→ réduction intensité

Injection BoNT sur zones gâchettes cicatrices

Membres fantômes (douloureux)
& douleurs de moignon

Pain Medicine

Pain Medicine 2014; 15: 292–305

Phantom Limb Pain: Systematic Neuroanatomical-Based Review of Pharmacologic Treatment

Zachary McCormick, MD, George Chang-Chien, DO, Benjamin Marshall, DO, Mark Huang, MD, and R. Norman Harden, MD

Results. We found level 2 evidence for gabapentin, both oral (PO) and intravenous (IV) morphine, tramadol, intramuscular (IM) botulinum toxin, IV and epidural Ketamine, level 3 evidence for amitriptyline, dextromethorphan, topiramate, IV calcitonin, PO memantine, continuous perineural catheter analgesia with ropivacaine, and level 4 evidence for methadone, intrathecal (IT) buprenorphine, IT and epidural fentanyl, duloxetine, fluoxetine, mirtazapine, clonazepam, milnacipran, capsaicin, and pregabalin.

The peripheral afferent theory of PLP centers around the neuroma as a generator of pain and potentially a driver of secondary central changes. Neuromas form at the cut end of the nerves in the residual limb. They generate ectopic afferent impulses that may be perceived as pain by the brain.

Botulism toxin injection is commonplace in the treatment of pain syndromes related to tonic muscle spasm and has recently been appreciated to have analgesic properties independent of its effect on neuromuscular transmission Though initial level 4 evidence demonstrated some promise in the treatment of PLP with local botulism toxin injection [71–73], a recent randomized, double-blinded pilot study of 14 patients with chronic PLP found no improvement in pain intensity up to 6 months following local injection.

Membres fantômes (douloureux)
& douleurs de moignon

Intradermal Botulinum Toxin Type A Injection Effectively Reduces Residual Limb Hyperhidrosis in Amputees: A Case Series

Arch Phys Med Rehabil 2008;89:1407-9

Alexandra Charrow, Marc DiFazio, Leslie Foster, Paul F. Pasquina, Jack W. Tsao

Effect of BTX-A Treatment on Residual Limb Hyperhidrosis, Prosthesis Fit and Function, and Pain Levels

Clinical Measure	Before BTX-A Treatment	After BTX-A Treatment	*P*
Degree of hyperhidrosis	7.1±1.9	3.5±1.4	.001
Interference of prosthesis function by hyperhidrosis	7.1±2.1	2.9±1.7	.008
Interference of prosthesis fit by hyperhidrosis	7.2±2.1	2.8±2.3	.028
Severity of phantom limb pain	3.5±2.6	4.0±2.2	.39
Severity of residual limb pain	4.2±2.8	3.8±2.9	.89

NOTE. Values are mean ± SD.

Main Outcome Measure: A 10-cm continuous Likert visual analog scale was used to assess residual limb sweating and pain and prosthesis fit and function before and 3 weeks after BTX-A injections.

Results: Patients reported a significant reduction in sweating and improvement in prosthesis fit and function after treatment. However, residual limb and phantom pain were unaffected by treatment.

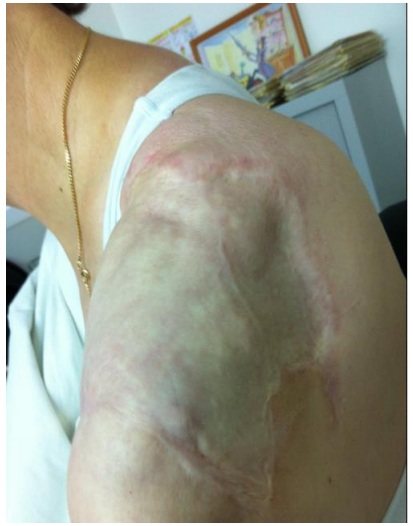
Conclusions: BTX-A may be an effective treatment for residual limb hyperhidrosis, resulting in subjective improvement in prosthesis fit and functioning. BTX-A should be considered as a method to manage excessive sweating in the residual limb of traumatic amputees.

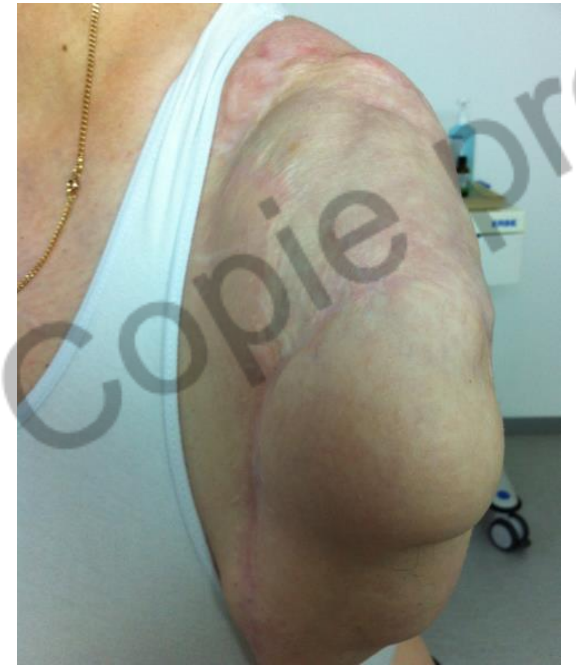
Membres fantômes (douloureux) & douleurs de moignon

A Prospective Randomized Double-blinded Pilot Study to Examine the Effect of Botulinum Toxin Type A Injection Versus Lidocaine/Depomedrol Injection on Residual and Phantom Limb Pain:

Clin J Pain. 2012 February ; 28(2): . doi:10.1097/AJP.0b013e3182264fe9.

Hong Wu, Rizwana Sultana, Kerrey Barton Taylor and **Aniko Szabo**





Pain Medicine Volume 10 • Number 2 • 2009

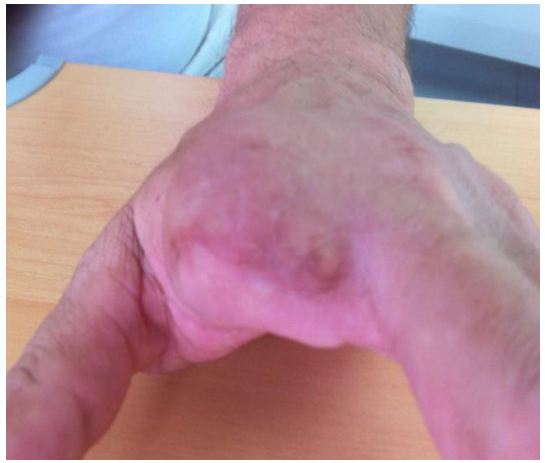
Treatment of Phantom Limb Pain with Botulinum Toxin Type A

Lingjing Jin, Katja Kollewe, Klaus Krampfl, Reinhard Dengler, Bahram Mohammadi

Methods. Three patients who had previously undergone amputation of their leg due to accident (N = 2) or injury by a landmine (N = 1) were treated with BoNT-A (Dysport®). We injected a total dose of up to 500 units (U) BoNT-A under EMG-control. Global clinical improvement was based on a 0–3 scale (0 = no effect; 3 = marked improvement) and on a questionnaire rating pain intensity (based on the visual analog scale), intake of pain medication and phantom limb sensations.

Results. All three patients evaluated the clinical global improvement with 3 (marked improvement). The pain intensity and pain medication was reduced significantly in all three cases. No side effects were reported. The duration of response lasted up to 11 weeks.

Discussion. These three successfully treated phantom and stump pain patients show that therapy with BoNT-A may be worth studying as an effective and safe treatment option for this kind of pain.



Botulinum toxin for complex regional pain syndrome (CRPS).

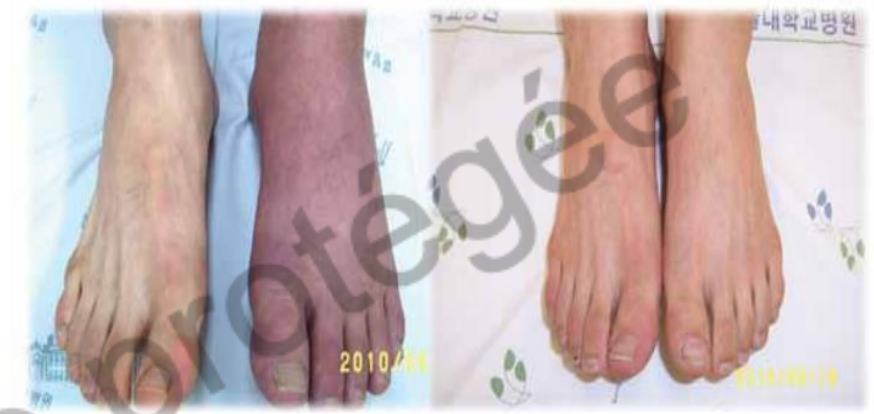
SDRC Algodystrophies

Study Design	Number of Patients	Method of Injection (Total Volume)	Result	Reference
Case series	2	Intramuscular Trigger point 20 U per site	Reduction of CRPS pain and myofascial pain	[52]
Randomized, prospective, double-blind, placebo-controlled, and open-label extension	14 (8 BoNT group, 6 control group)	Intradermal, subcutaneous Allodynia area 5 U per site (40–200 U)	No difference between BoNT group and placebo group, terminated study early.	[53]
Randomized, double-blind, placebo-controlled crossover	9 (18 cases)	Lumbar sympathetic block 75 U BoNT + 0.5% bupivacaine/0.5% bupivacaine	Longer duration of pain reduction (BoNT vs. control/71 days vs. 10 days)	[54]
Case series	2	Lumbar sympathetic block 5000 U BoNT-B + 0.25% levobupivacaine	VAS and CRPS symptoms were reduced.	[12]
Prospective, open case series	11	Affected site, 25–50 U per site (300 U)	All patients had improved VAS, allodynia, hyperalgesia, and skin color after 6 to 12 weeks	[55]
Retrospective, uncontrolled, unblended	37	Affected site, 10–20 U per site (100 U)	The 97% patients reduced pain. (average pain reduction of 43%)	[56]

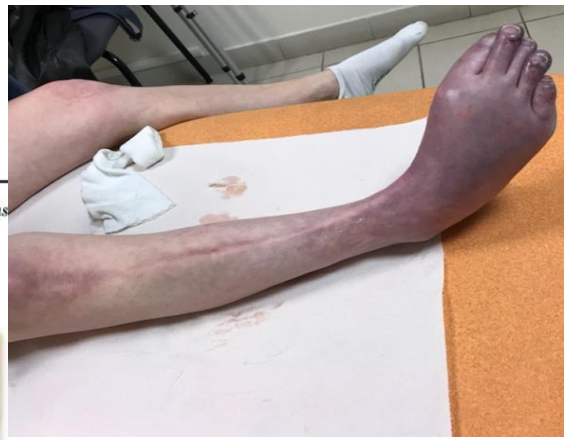
Lumbar Sympathetic Block with Botulinum Toxin Type B for Complex Regional Pain Syndrome: A Case Study

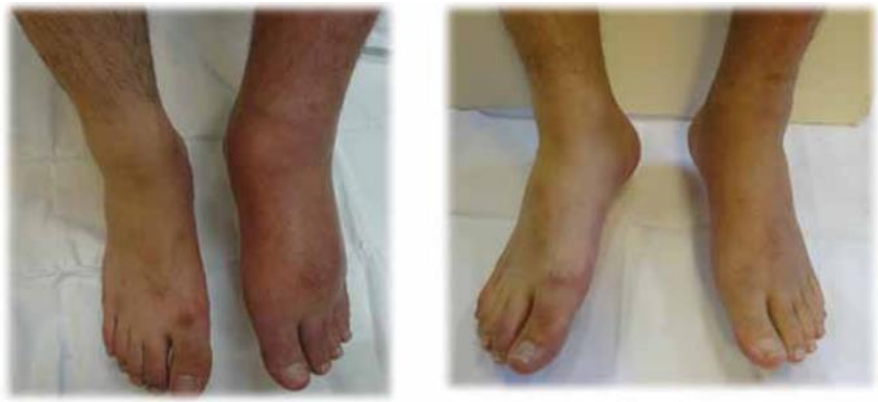
Pain Physician 2015; 18:E911-E916

Eunjoo Choi, Chan Woo Cho, Hye Young Kim, Pyung Bok Lee and Francis Sahngun Nahm



Case 1 Skin color change before the lumbar sympathetic block (LSB) with botulinum toxin type B (BTX-B). Two months after LSB with BTX-B. Skin color and turgor normalized.





Case 2 Skin color change before the lumbar sympathetic block (LSB) with botulinum toxin type B (BTX-B). One month after the second LSB with BTX-B, skin color and turgor normalized.

ANESTHESIOLOGY

Botulinum Toxin Type A for Lumbar Sympathetic Ganglion Block in Complex Regional Pain Syndrome: A Randomized Trial

Yongjae Yoo, M.D., Ph.D., Chang-Soon Lee, M.D., Jungsoo Kim, M.D., Dongwon Jo, M.D., Jee Youn Moon, M.D., Ph.D.

ANESTHESIOLOGY 2022; 136:314–25

Background: The present study was designed to test the hypothesis that botulinum toxin would prolong the duration of a lumbar sympathetic block measured through a sustained increase in skin temperature. The authors performed a randomized, double-blind, controlled trial to investigate the clinical outcome of botulinum toxin type A for lumbar sympathetic ganglion block in patients with complex regional pain syndrome.

Methods: Lumbar sympathetic ganglion block was conducted in patients with lower-extremity complex regional pain syndrome using 75 IU of botulinum toxin type A (botulinum toxin group) and local anesthetic (control group). The primary outcome was the change in the relative temperature difference on the blocked sole compared with the contralateral sole at 1 postoperative month. The secondary outcomes were the 3-month changes in relative temperature differences, as well as the pain intensity changes.

Results: A total of 48 participants (N = 24/group) were randomly assigned. The change in relative temperature increase was higher in the botulinum toxin group than in the control group (1.0°C ± 1.3 *vs.* 0.1°C ± 0.8, respectively; difference: 0.9°C [95% CI, 0.3 to 1.5]; $P = 0.006$), which was maintained at 3 months (1.1°C ± 0.8 *vs.* –0.2°C ± 1.2, respectively; $P = 0.009$). Moreover, pain intensity was greatly reduced in the botulinum toxin group compared with the control group at 1 month (–2.2 ± 1.0 *vs.* –1.0 ± 1.6, respectively; $P = 0.003$) and 3 months (–2.0 ± 1.0 *vs.* –0.6 ± 1.6, respectively; $P = 0.003$). There were no severe adverse events pertinent to botulinum toxin injection.

Conclusions: In patients with complex regional pain syndrome, lumbar sympathetic ganglion block using botulinum toxin type A increased the temperature of the affected foot for 3 months and also reduced the pain.

(ANESTHESIOLOGY 2022; 136:314–25)

Botulinum toxin for spinal cord injury-induced neuropathic pain.

Study Design	Number of Patients	Method of Injection (Total Volume)	Result	Reference
Randomized, double-blind, placebo-controlled	40	Subcutaneous (200 U)	Significantly VAS was decreased at 4 and 8 weeks.	[59]
Randomized, double-blind, placebo-controlled	44	Subcutaneous (200 U) Once daily for 8 weeks	Significantly VAS was decreased at 4 and 8 weeks.	[60]
Case	2	Subcutaneous 5 U of BoNT at 16–20 sites	Significant VAS reduction for more than 3 months	[61]
Case	1	Subcutaneous 20 U of BoNT at 10 sites	VAS decreased from 96 to 23.	[62]

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Case	1	Subcutaneous 20 U of BoNT at 10 sites	VAS decreased from 96 to 23.	[62]

Botulinum toxin for trigeminal neuralgia.

Study Design	Number of Patients	Method of Injection (Total Volume)	Result	Reference
Randomized double-blind, placebo-controlled	42	Intradermal, submucosal (75 U/saline 1.5 mL)	50% VAS reduction 68.8% (Botulinum toxin (BoNT) group) 15% (Control)	[31]
Randomized, double-blind, placebo-controlled	84 (27 BoNT 25 U, 29 BoNT 75 U, 28 control)	Intradermal, submucosal (25 U/75 U/saline 1 mL)	Visual analog scale (VAS) reduction 70.4% (25 U) vs. 86.2% (75 U) vs. 32.1% (Control)	[32]
Randomized, double-blind, placebo-controlled	36 (20 BoNT, 16 control)	Intramuscular (50 U/saline 1 mL)	VAS (BoNT vs. Control) 4.9 vs. 6.63 (2 months) 4.75 vs. 6.94 (3 months)	[33]
Prospective, open, case series	15	Injected at the trigger zones (50–100 U)	All patients improved frequency and severity of pain attacks	[34]
Prospective, open, case series	12	Subcutaneous (20–50 U)	VAS reduced lasting more than 2 months in 10 patients.	[35]
Prospective, open, case series	8	Around zygomatic arch, 1.5–2 cm depth (50 U per point, total 100 U)	Incidence of pain and VAS were reduced in all patients.	[36]

toxins

MDPI

Toxins **2018**, *10*, 224; doi:10.3390/toxins10060224

Douleurs neuropathiques centrales post-AVC

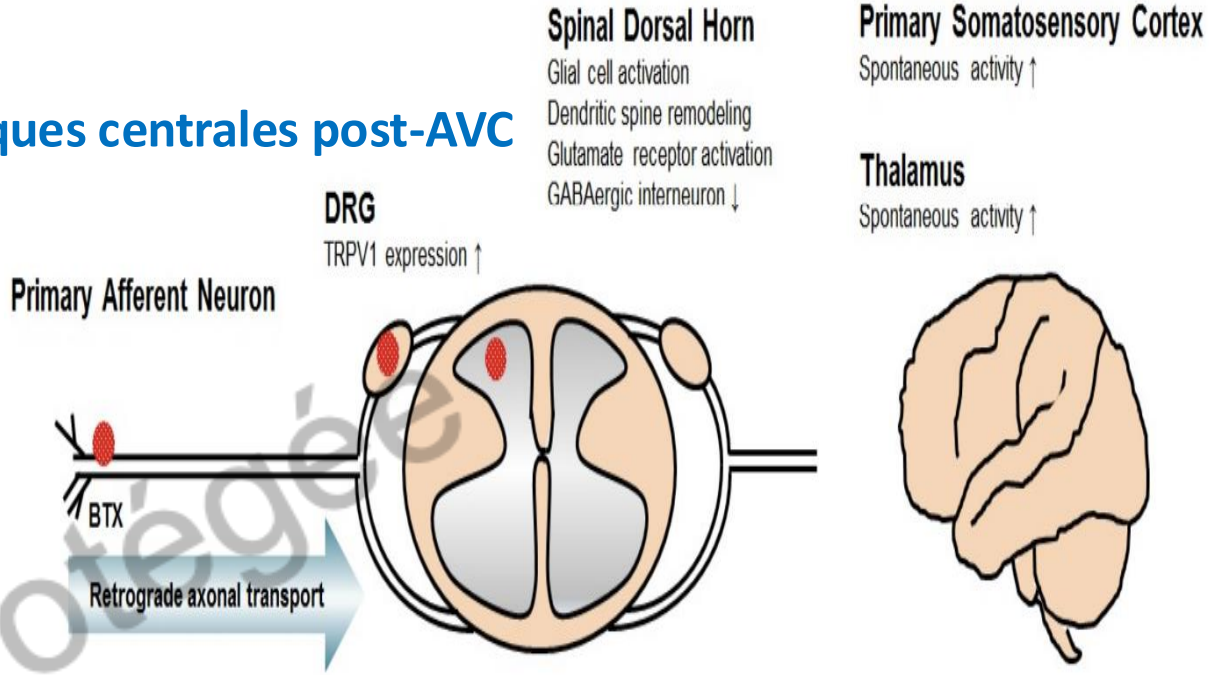
Review

Botulinum Toxin for Central Neuropathic Pain

Jihye Park [1] and Myung Eun Chung [2,*]

Botulinum toxin for central poststroke pain.

Study Design	Number of Patients	Method of Injection (Total Volume)	Result	Reference
Case	1	Intramuscular Biceps Brachii 100 U, Brachialis 75 U and Brachioradialis 25 U	Pain was reduced after 2 days, spasticity was improved after 1 week.	[63]
Case	2	Intramuscular Affected muscle (200 U)	NRS reduction for more than 3 months	[64]
Randomized, double-blind, placebo-controlled	273 (139 BoNT, 134 control)	Intramuscular Dosing was determined by investigator, second injection was performed with an open label and at least 12 weeks after the first injection	Significantly VAS was decreased at 12 weeks and reductions in pain were sustained through Week 52.	[65]



Illustrated mechanism of central neuropathic pain associated with spinal cord injury (SCI). These mechanisms include transient receptor potential vanilloid type 1 (TRPV1) overexpression in dorsal root ganglion (DRG) neurons, glial cell activation, dendritic spine remodeling, glutamate receptor activation and loss of GABAergic interneuron in the spinal dorsal horn, and spontaneous firing of neurons in the thalamus and primary somatosensory cortex. It has been suggested that the antinociceptive mechanism of botulinum toxins (BTXs) applied to the nerve endings not only affects the primary afferent neurons but also acts on the DRG and spinal dorsal horn through retrograde axonal transport.

Summary of studies of botulinum toxin (BTX) for central neuropathic pain.

Author, Year	Study Design	Sample Size (*N*)	Diagnosis	Injection Site/Dose	Follow up	Pain Measure	Results
Jabbari, 2003 [55]	Case series	2	SCI	Subcutaneous injection at the site of allodynia/BTX-A 16–20 U/site		VAS	Pain was decreased; frequency of severe spontaneous pain was reduced
Han, 2014 [56]	Case report	1	SCI	Subcutaneous injection in the painful foot/BTX-A	Week 4	VAS	Pain severity and the frequency of burst was reduced
Han, 2016 [57]	Double-blind, randomized controlled study	40	SCI	Subcutaneous injection/BTX-A 200 U	Week 4, 8	VAS (100 mm), McGill Pain Questionnaire	Pain was reduced significantly in BTX-A treated group
Yelnik, 2007 [58]	Double-blind, randomized controlled study	20	stroke	Subscapularis muscle/BTX-A 500 U/injection + physical therapy	Week 1, 2, 4	verbal scale (10 point)	Pain improvement with BTX-A from first week
Marco, 2007 [59]	Double-blind, randomized controlled study	31	stroke	Pectoralis major muscle/BTX-A 500 U/injection + TENS for 6 weeks	Week 1, 4, 12, 24	VAS (100 mm)	Significantly greater pain improvement from the first week in BTX group
Kong, 2007 [60]	Double-blind, randomized controlled study	17	stroke	Pectoralis major, biceps brachii muscles/BTX-A 500 U	Week 4, 8, 12	VAS (0–10)	No difference in shoulder pain
Lim, 2008 [61]	Double-blind, randomized controlled study	29	stroke	Infraspinatus, pectoralis and subscapularis muscles + IA saline injection; IA triamcinolone (40 mg) injection + saline to the same muscles/BTX-A 100 U	Week 2, 6, 12	NRS	Significantly greater pain improvement in the BTX-A–treated at 12 weeks
Boer, 2008 [62]	Double-blind, randomized controlled study	22	stroke	Subscapular muscle/BTX-A 50 U, twice	Week 6, 12	VAS (vertical 100 mm)	No significant changes in pain
Shaw, 2011 [63]	Double-blind, randomized controlled study	333	stroke	Elbow, wrist and finger flexor muscles/ BTX-A, 4 times/injection + physical therapy 4 weeks	Week 4, 12, 48	verbal scale, NRS	Significant decrease at 12 months in the BTX group
Castiglione, 2011 [8]	Pilot study	5	stroke	IA shoulder joint/BTX-A 500 or 100 units	Week 2, 8	VAS	Decreased pain at 2 and 8 weeks after BTX-A injection

Author, Year	Study Design	Sample Size (*N*)	Diagnosis	Injection Site/Dose	Follow up	Pain Measure	Results
Marciniak, 2012 [64]	Double-blind, randomized controlled study	21	stroke	Pectoralis major ± teres major muscles/BTX-A 140–200 units	Week 2, 4, 12	VAS	Decreased pain scores at 4 weeks
Choi, 2016 [65]	Retrospective, unblinded, uncontrolled study	6	stroke	Subscapularis muscle/BTX-A	Week 1, 2, 4, 8	PI-NRS	Pain improvement with BTX-A injection
Carroll, 2009 [66]	Double-blind, randomized controlled study	18	CRPS	LSB/Bupivacaine 0.5% + 75 units of BTX-A	Week 4	VAS (10 cm)	The rate of pain return was significantly lower after LSB with BTA
Safarpour, 2010 [67]	Double-blind, randomized controlled study Uncontrolled, unblinded, open-label study	14 (6 control)	CRPS	Intradermally and subcutaneously into the allodynic area/ 5 units per site (total 40–200 units)	Week 3, 8	Brief pain inventory, PIQ, McGill pain questionnaire, QST, patients satisfaction scale	No significant response after injection; study terminated prematurely because of intolerance
Kharkar, 2011 [68]	Retrospective, unblinded, uncontolled study	37	CRPS	Upper limb girdle muscles/BTX-A 10–20 units per muscle (total 100 units)	Week 4	Likert scale (11 point)	43% decrease in local pain scores
Safarpour, 2010 [69]	Case series	2	CRPS	Trigger point in the proximal muscle/BTX-A 20 units per site	□	VAS (1–10)	Alleviate both myofascial pain syndrome and the distal allodynia, discoloration and, tissue swelling
Birthi, 2012 [70]	Case report	1	CRPS	Subcutaneous injection on the dorsum of the hand/BTX-A 5 units per site (total 100 units)	weekly, 12 weeks	McGill Pain Questionnaire	Able to decrease daily opioid medication by 20% at 8th week; pain returned to baseline at 12th week
Choi, 2015 [71]	Case series	2	CRPS	Lumbar sympathetic block/levovupivacaine 0.25% + 5000 units of BTX-B	Week 8	VAS, LANSS	Pain intensity and LANSS score were significantly reduced
Buonocore, 2017 [72]	Case report	1	CRPS	TP, FDL, FHL muscles, tibial nerve around the tarsal tunnel/BTX-A 120 units per muscle, twice	Week 36	□	Significant decrease in the frequency of acute dysesthesias

SCI: Spinal cord injury; CRPS: Complex regional pain syndrome; VAS: Visual analog scale; NRS: Numeric rating scale; IA: Intra-articular; LANSS: Leeds assessment of neuropathic symptoms and signs; LSB: Lumbar sympathetic block; TP: Tibialis posterior; FDL: Flexor digitorum longus; FHL: Flexor hallucis longus.

Douleurs myofasciales

toxins

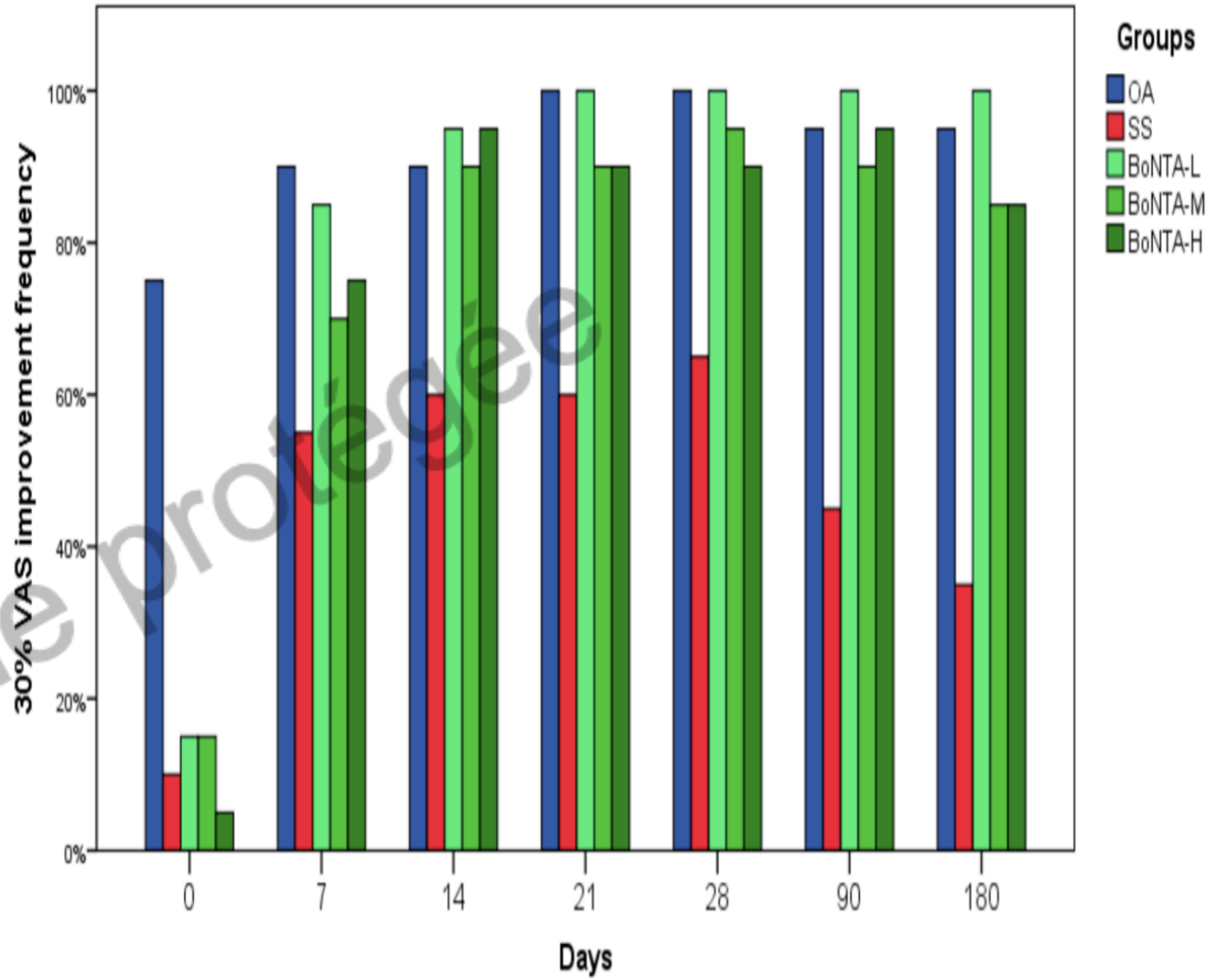
MDPI

Article

Efficacy and Safety of Botulinum Toxin Type A on Persistent Myofascial Pain: A Randomized Clinical Trial

Giancarlo De la Torre Canales [1,*], Natalia Alvarez-Pinzon [1], Victor Ricardo Manuel Muñoz-Lora [1], Leonardo Vieira Peroni [2], Amanda Farias Gomes [2], Alfonso Sánchez-Ayala [3], Francisco Haiter-Neto [2], Daniele Manfredini [4] and Célia Marisa Rizzatti-Barbosa [1]

Toxins **2020**, *12*, 395; doi:10.3390/toxins12060395



Clinical improvement (30%) in subjective pain.

RESEARCH ARTICLE

Efficacy of Botulinum Toxin A for Treating Cramps in Diabetic Neuropathy

Domenico A. Restivo, MD, PhD,[1] Antonino Casabona, PhD,[2] Lucia Frittitta, MD, PhD,[3,4] Antonino Belfiore, MD,[4] Rosario Le Moli, MD,[4] Damiano Gullo, MD,[4] and Riccardo Vigneri, MD[4,5]

J Rheumatol. 2010 November ; 37(11): 2377–2386.

Intraarticular Botulinum Toxin A for Refractory Painful Total Knee Arthroplasty: A Randomized Controlled Trial

Jasvinder A. Singh, **Maren L. Mahowald**, and **Siamak Noorbaloochi**

University of Minnesota, Minneapolis, Minnesota; Departments of Health Sciences Research and Orthopedics, Mayo Clinic School of Medicine, Rochester, Minnesota; Birmingham Veterans Affairs Medical Center and University of Alabama at Birmingham, Birmingham, Alabama, USA.

Toxine intra-articulaire

In this single-center randomized trial, single IA-BoNT/A injection provided clinically meaningful short-term improvements in pain, global assessment, and function in patients with chronic painful TKA. A multicenter trial is needed to confirm these findings.

Objective—To assess short-term efficacy of single intraarticular botulinum toxin (IA-BoNT/A) injection in patients with chronically painful total knee arthroplasty (TKA) in a randomized, placebo-controlled, triple-blind study.

Methods—Patients with chronic TKA pain (pain > 6 on 0–10 scale and > 6 months post-TKA) evaluated in and referred from orthopedic surgery clinics were recruited. The primary outcome, proportion of patients with clinically meaningful decrease of at least 2 points on 0–10 visual analog scale (VAS) for pain, was compared between treatment groups at 2 months using comparison of proportions test and for all efficacy timepoints (2, 3, and 4 months) using generalized estimating equations (GEE). Secondary outcomes of global assessment, function, and quality of life were compared using GEE, duration of pain relief by t-test, and adverse events by chi-square test.

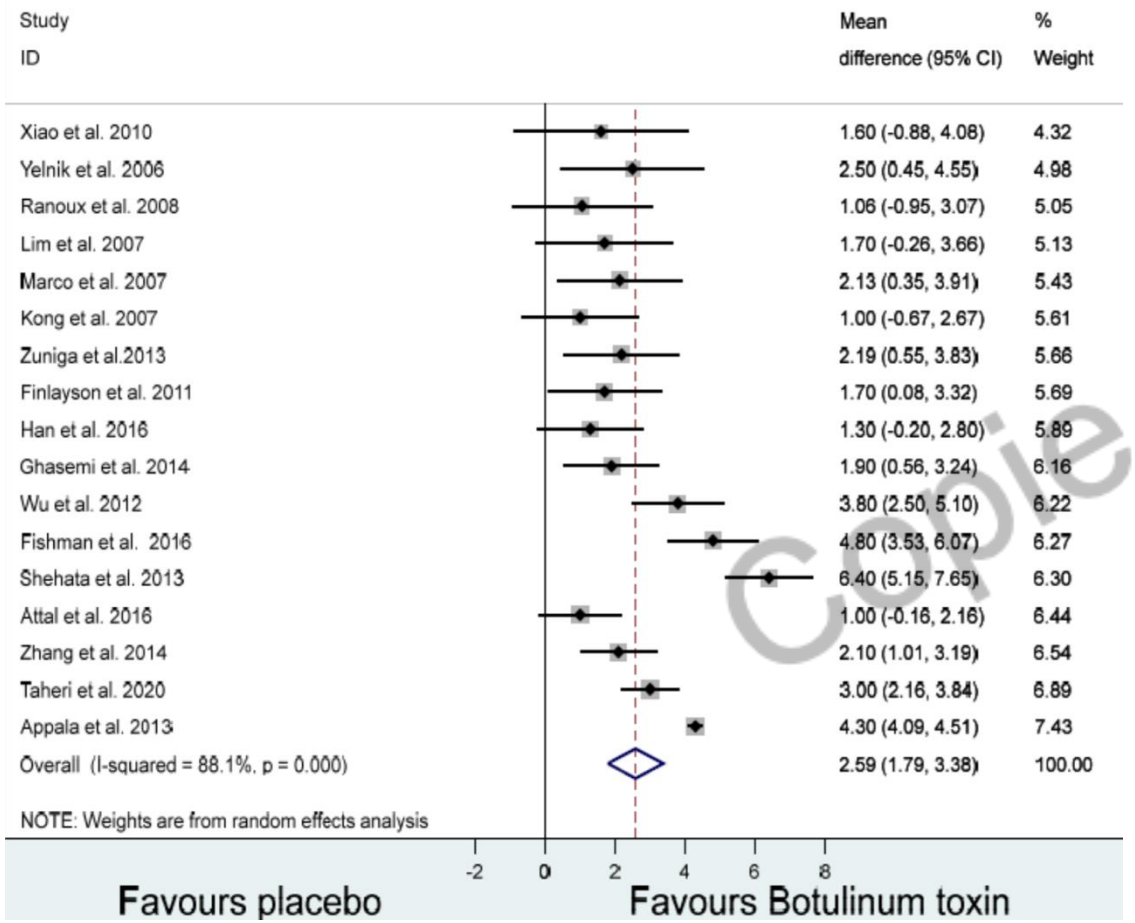
Results—In total, 54 patients with 60 painful TKA were randomized, with main analyses restricted to one TKA per patient (49 TKA in 49 patients). Mean age was 67 years, 84% were men, and mean duration of TKA pain was 4.5 years. A significantly greater proportion of patients (71%) in the IA-BoNT/Agroup compared to IA-placebo (35%) achieved clinically meaningful reduction in VAS pain at 2 months ($p = 0.028$) and at all efficacy timepoints ($p = 0.019$). Duration of meaningful pain relief was significantly greater after IA-BoNT/A, 39.6 days (SD 50.4) compared to IA-placebo, 15.7 days (SD 22.6; $p = 0.045$). Statistically significantly better scores were seen in IA-BoNT/A vs IA-place-bo for all efficacy timepoints for the following outcomes: "very much improved" on physician global assessment of change ($p = 0.003$); Western Ontario McMaster Osteoarthritis Index physical function ($p = 0.026$), stiffness ($p = 0.004$), and total scores ($p = 0.024$); and Short-Form 36 pain subscale score ($p = 0.049$). Number of total and serious adverse events was similar between groups, with no patients in either group with new objective motor or sensory deficits during followup.

toxins

Review

A Systematic Review and Meta-Analysis of Efficacy of Botulinum Toxin A for Neuropathic Pain

Anupam Datta Gupta [1,*], Suzanne Edwards [2], Jessica Smith [1], John Snow [3], Renuka Visvanathan [4], Graeme Tucker [4] and David Wilson [4]



17 études → réduction EVA 3.59 vs. placebo

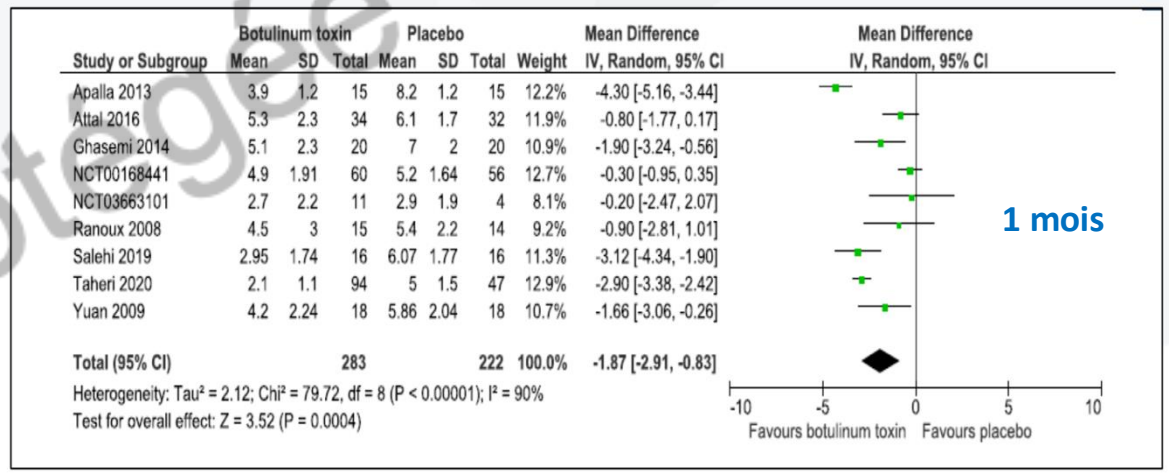
DOI: 10.1002/ejp.1941

REVIEW ARTICLE

2016 EJP

Efficacy and safety of botulinum A toxin for the treatment of chronic peripheral neuropathic pain: A systematic review of randomized controlled trials and meta-analysis

Vincent Hary[1,2] | Sebastien Schitter[2,3] | Valeria Martinez[2,3,4,5]



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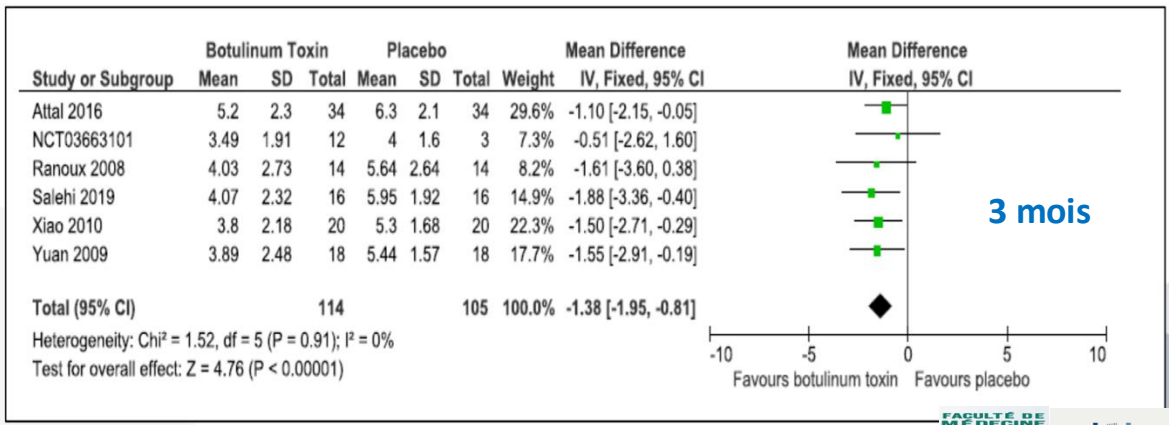

3 mois

toxins 2016 MDPI

Article

Incobotulinum Toxin-A Improves Post-Surgical and Post-Radiation Pain in Cancer Patients

Rezvan Rostami [1], Shivam Om Mittal [2], Reza Radmand [3] and Bahman Jabbari [1,*]

Journal of Personalized Medicine 2020 MDPI

Review

The Safety and Effect of Local Botulinumtoxin A Injections for Long-Term Management of Chronic Pain in Post-Herpetic Neuralgia: Literature Review and Cases Report Treated with Incobotulinumtoxin A

Songjin Ri [1,2,*], Anatol Kivi [3] and Jörg Wissel [1,3]

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Letter to the Editor

Intraoral alveolar submucosal injections of Incobotulinumtoxin A: Relief of therapy-refractory trigeminal neuropathy after tooth extraction

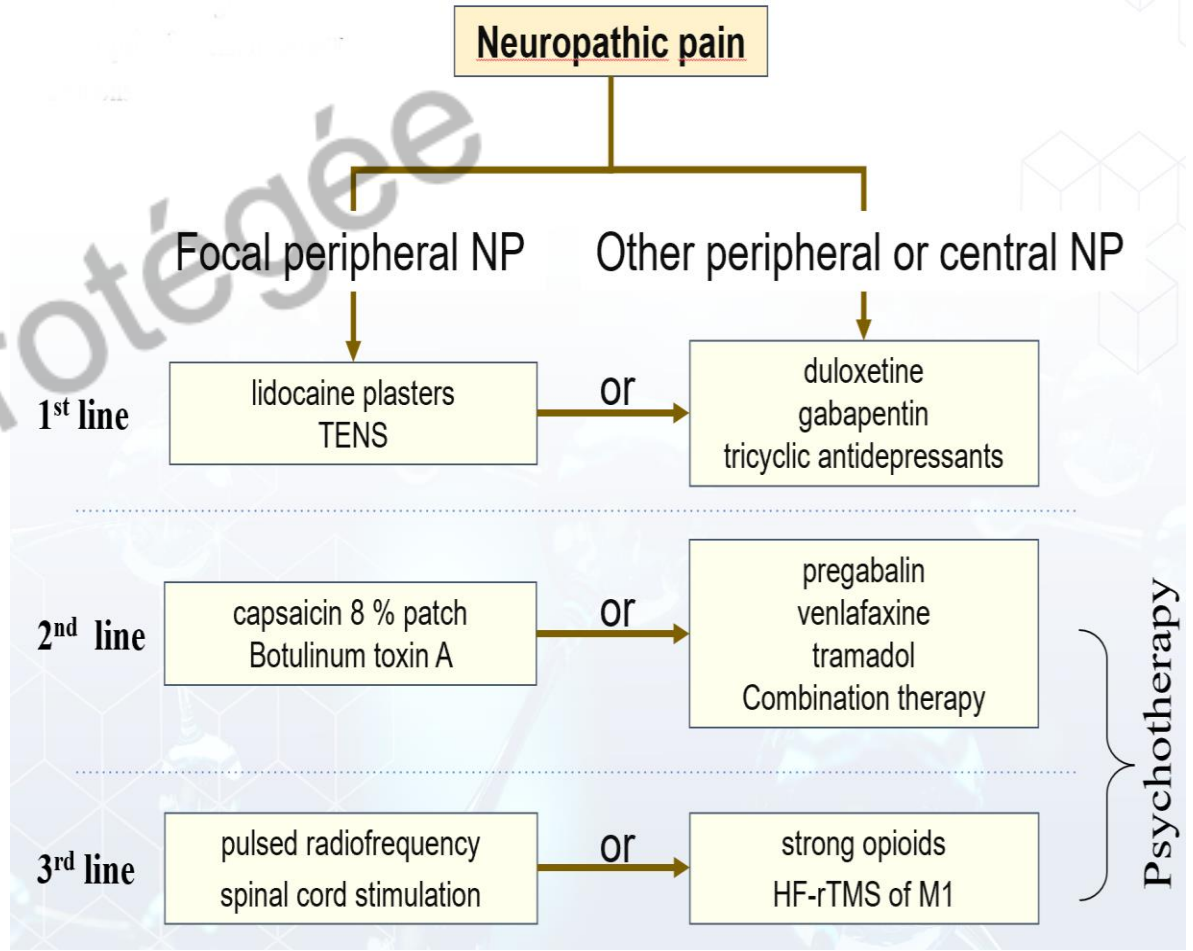
Pain Medicine Case Reports

Perineural Botulinum Toxin Injection for Cancer-related Pain: Case Report of Two Patient

Volume 7, Number 5, pp. 261-264
2023
Yohann Bohren, MD, PhD and Ionut Daniel Timbolschi, MD

Practice Guideline > Rev Neurol (Paris). 2020 May;176(5):325-352.
doi: 10.1016/j.neurol.2020.01.361. Epub 2020 Apr 7. X Moisset et al

Pharmacological and non-pharmacological treatments for neuropathic pain: Systematic review and French recommendations



European Annals of Otorhinolaryngology, Head and Neck diseases (2012) **129**, e6—e10

Botulinum toxin in the treatment of post-radiosurgical neck contracture in head and neck cancer: A novel approach

C.-A. Bach[a,b,*], **I. Wagner**[a], **X. Lachiver**[a], **B. Baujat**[a], **F. Chabolle**[a,b]

[a] *Service de chirurgie ORL et cervicofaciale, hôpital Foch, 40, rue Worth, 92150 Suresnes, France*
[b] *UFR de médecine Paris Ouest Saint-Quentin en Yvelines, université de Versailles—Saint-Quentin en Yvelines, 9, boulevard d'Alembert, 78280 Guyancourt, France*

Table 2 Main patient characteristics. Injection sites and doses.

Patient no.	Age (years)/Gender	End RT (months)	Injection site	Bilateral injection	Number of injection points × dose (mL)	Total units injected (U)
1	65/M	5	PMF	No	5 × 0.1	125
2	54/M	24	PMF	No	5 × 0.1	125
3	73/F	18	PMF	No	4 × 0.2	200
4	68/M	36	SCM	No	4 × 0.1	100
5	64/F	84	SCM	No	3 × 0.2	150
6	58/M	15	SCM	No	5 × 0.1	125
7	54/F	7	SCM	No	6 × 0.2	300
8	52/M	15	SCM	Yes	5 × 0.2 + 5 × 0.2	500
9	60/M	48	SCM	Yes	8 × 0.2 + 8 × 0.2	800

M: male; F: female; PMF: pectoralis major flap; SCM: sternocleidomastoid muscle.

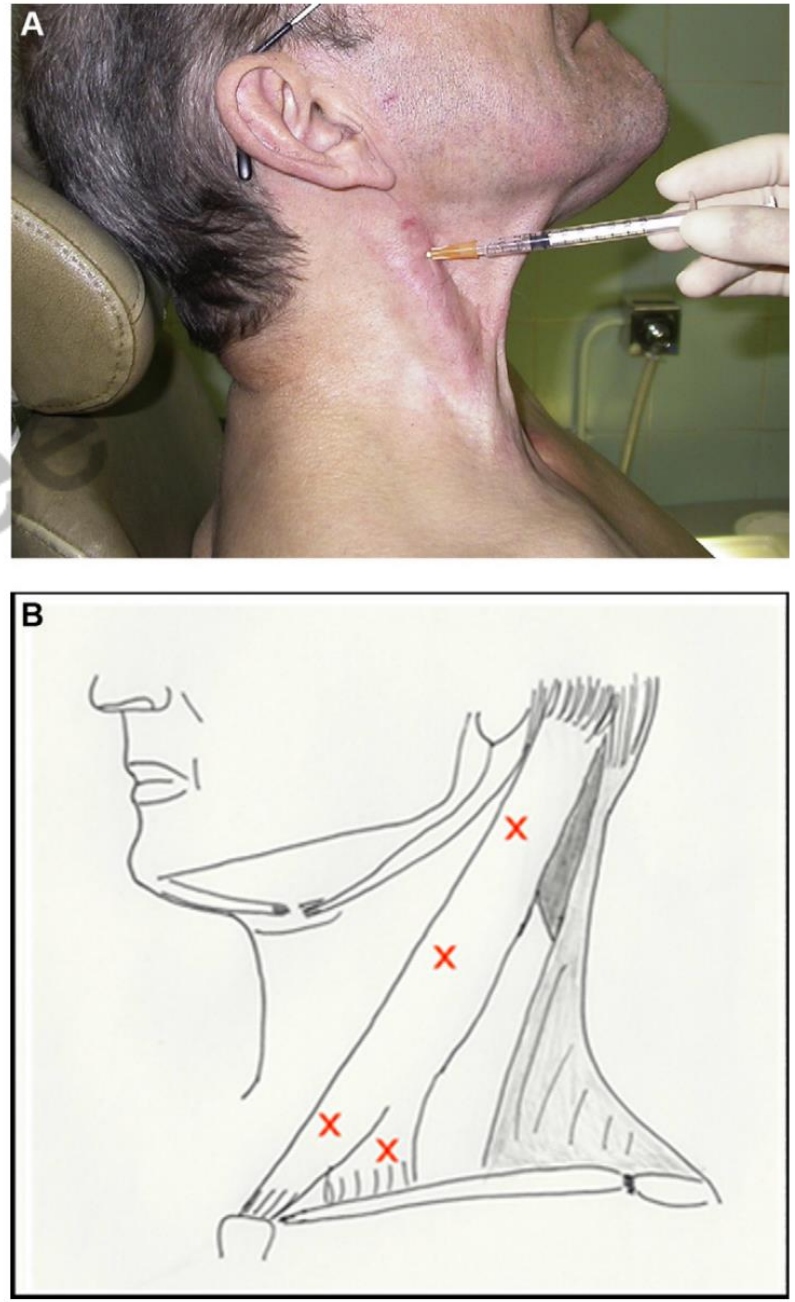


Figure 1 A. Intramuscular sternocleidomastoid injection at a peak contracture point. B. Diagram of potential sternocleidomastoid injection sites.

The patient's demographic information, cancer type, prior treatment, and outcome before and after incobotulinum toxin A injection.

Pt No/Sex/Age	Location/Pathology of Cancer	Treatment and Medication before Botulinumtoxina Injection	Nature/Site of Pain	Sites/Total Dose of Injection (Unit)	Initial VAS/ VAS at 6 Weeks/ VAS at 12 Weeks	PGIC at 6 Weeks/PGIC at 12 Weeks
1/F/56	R-breast/adenocarcinoma	Surgery/Gabapentin, Lidoderm patch, Methocarbamol	Sharp, burning, superficial/R-upper abdomen, below rib cage	Subcutaneous, grid-like/100	10/5/7	Minimally improved/ minimally improved
2/M/60	L-tonsil/squamous cell carcinoma	Surgery/Morphine, Dilaudid	Sharp, superficial with allodynia, muscle spasms and tightness/L-temporal, L-zygomaticus and masseter	Subcutaneous, grid-like/95	10/5/7	Much improved/ much improved
3/M/31	R-frontal lobe/oligo-dendro-glioma	Craniotomy, radiation/Methadone, Depakote, Clonazepam	Sharp, burning, superficial/R-frontotemporal scalp, R-posterior neck, L-frontotemporal scalp, L-posterior neck	Bilateral subcutaneous/100	10/7/8	Much improved/ very much improved
4/F/70	R-breast metastasized to R-jaw/adenocarcinoma	Surgery/Gabapentin, Oxycodone, Ibuprofen	Dull constant/R-masseter, rizorius, zygomaticus	Subcutaneous divided into 5 sites/85	10/5/8	Much improved/ much improved
5/M/56	L-tonsil/squamous cell carcinoma	Surgery, radiation/None *	Severe, painful cramps/bilateral masseter	Subcutaneous both masseter, grid-like/100	10/3/8	Very much improved/ very much improved
6/F/51	R-breast/adenocarcinoma	Surgery, radiation/Gabapentin, Oxycodone	Dull, deep pain and muscle spasms/R-shoulder, arm, hand	Subcutaneous R-pectoralis, trapezius, triceps divided into 4 sites/100	5/3/3	Much improved/ very much improved
7/F/64	L-breast/inflammatory carcinoma	Surgery, radiation/Ibuprofen, Aspirin	Sharp, superficial/L-upper abdomen under L-breast	Subcutaneous, grid-like/100	9/0/0	Very much improved/ very much improved
8/M/53	R-neck/squamous cell carcinoma	Surgery, radiation/None *	Sharp muscle spasms/both masseters upper right, sternocleidomastoid	Subcutaneous divided into different units and sites/80	5/2/1	Very much improved/ very much improved

M: Male, F: Female; * These patient failed multiple medications before but at the time of enrollment were on no medications; VAS = visual analog scale, range from 0 (no pain) to 10 (severe pain); PGIC = Patients' Global Impression of Change scale.

	Study Title
1	Botulinum Toxin for Trigeminal Neuralgia
2	Botulinum Toxin Type A for Neuropathic Pain in Patients With Diabetic Peripheral Polyneuropathy
3	Botulinum Toxin in Peripheral Neuropathic Pain
4	Botulinum Toxin Type A Block of the Sphenopalatine Ganglion in Trigeminal Neuralgia Safety Issues
5	Botulinum Toxin Type A for Treating Allodynic Pain in SCI and MS
6	Neuropathic Pain Study With Botulinum Toxin A in Spinal Cord Injury Patients
7	Efficacy Study of Botox to Treat Neuropathic Pain
8	Botulinum Toxin Injections for Oral Neuropathic Pain
9	A Study of Intradermal Injection of Botulinum Toxin Type A for the Diabetic Neuropathic Foot Pain
10	Injecting Botulinum Toxin A Underneath the Skin to Treat Spinal Cord Pain in Patients With Spinal Cord Injury
11	A Study Evaluating Botulinum Toxin Type A in Subjects With Postherpetic Neuralgia
12	Botulinum Toxin A as Treatment For Chronic Postsurgical Pain Following Lung Cancer Surgery
13	Incobotulinum Toxin for the Treatment of Trigeminal Neuralgia
14	Study to Evaluate the Efficacy of Botulinum Toxin Serotype A Injections for Cervicobrachial Myofascial Syndrome
15	Early Administration of Botox® in Neuropathic Pain Due to Thoracotomy in Thoracotomy
16	Botulinum Toxin Type A for Peripheral Neuropathic Pain in subjects With Carpal Tunnel Syndrome
17	Botulinum Toxin A in Patients With Myofascial Pain Syndrome With and Without Tizanidine Supplementation
18	Support in Post-Surgical Neuralgia
19	Study Mechanisms of Action in Altering the Microglia Environment in Which Pain Fibers Exist
20	An Agonistic Effect of Ten Injection of Botulinum Toxin Type A in the Ganglion Impar in Patients With Chronic Proctalgia
21	A Clinical Trial to Investigate Efficacy and Safety of NT 201 Injections Compared With Placebo Injections in Participants Aged 18 Years and Older With Chronic Nerve Pain After Shingles or Nerve Injury

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ClinicalTrials.gov

Antalgique de demain ???

21 études en cours inscrites sur le site

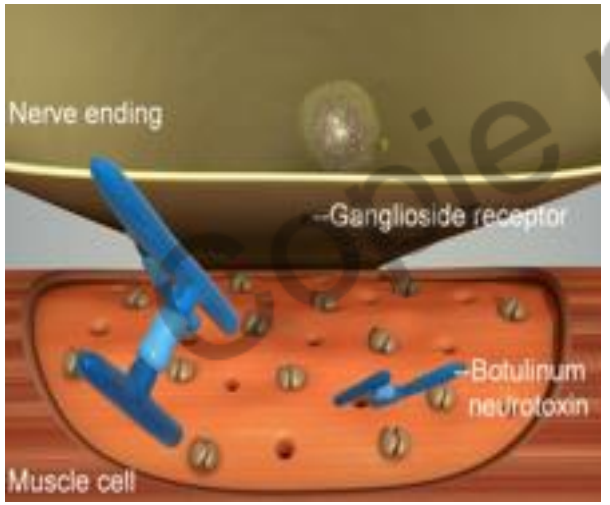
ClinicalTrials.gov

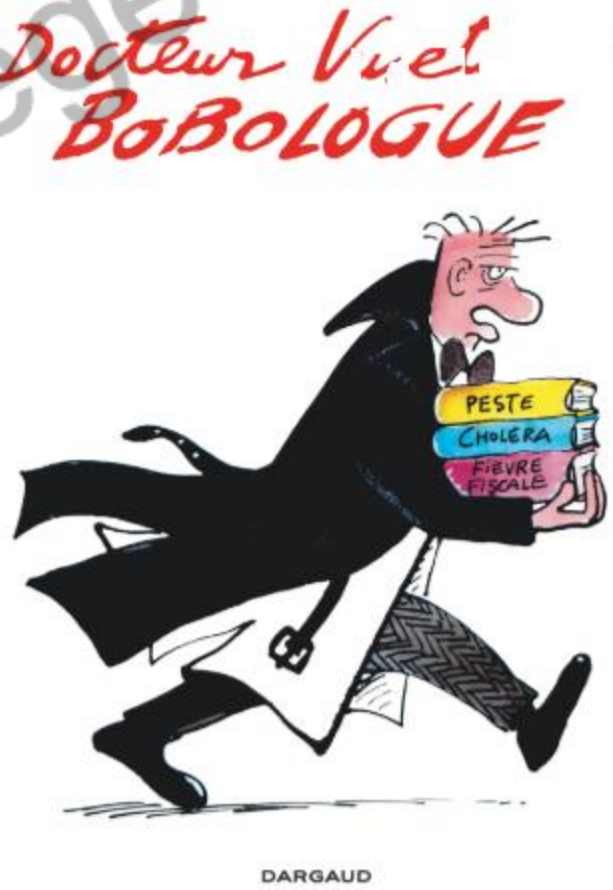
A Clinical Trial to Investigate Efficacy and Safety of NT 201 Injections Compared With Placebo Injections in Participants Aged 18 Years and Older With Chronic Nerve Pain After Shingles or Nerve Injury (PaiNT)

ClinicalTrials.gov ID NCT06091020

Sponsor Merz Therapeutics GmbH

Merci de votre attention





Pr. Éric VIEL, M.D., PhD.
Centre d'Évaluation et de Traitement de la Douleur
Centre Hospitalier Régional Universitaire Caremeau