

Traitement de la douleur en neurochirurgie

Dr Corentin DAULEAC

Neurochirurgie fonctionnelle, de la moelle épinière et des nerfs périphériques

Service du Pr MERTENS

HCL – Hôpital Neurologique Wertheimer – Lyon

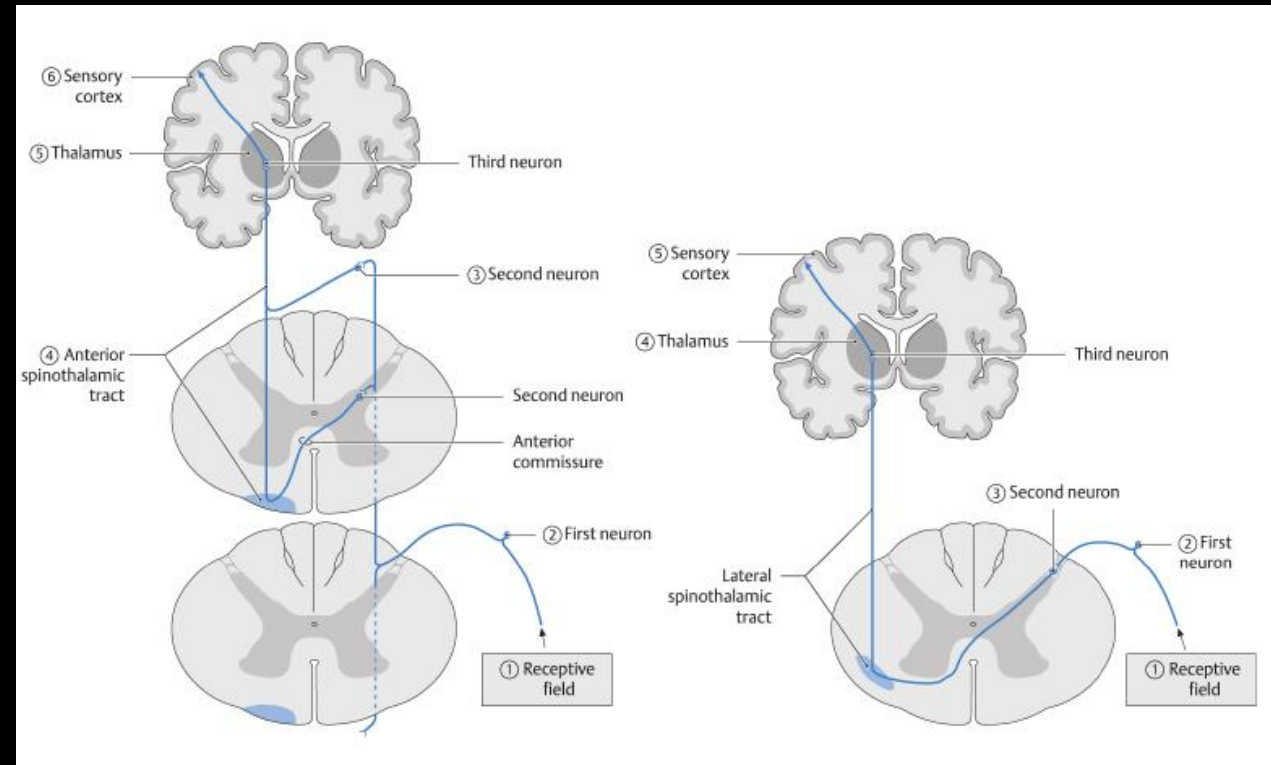
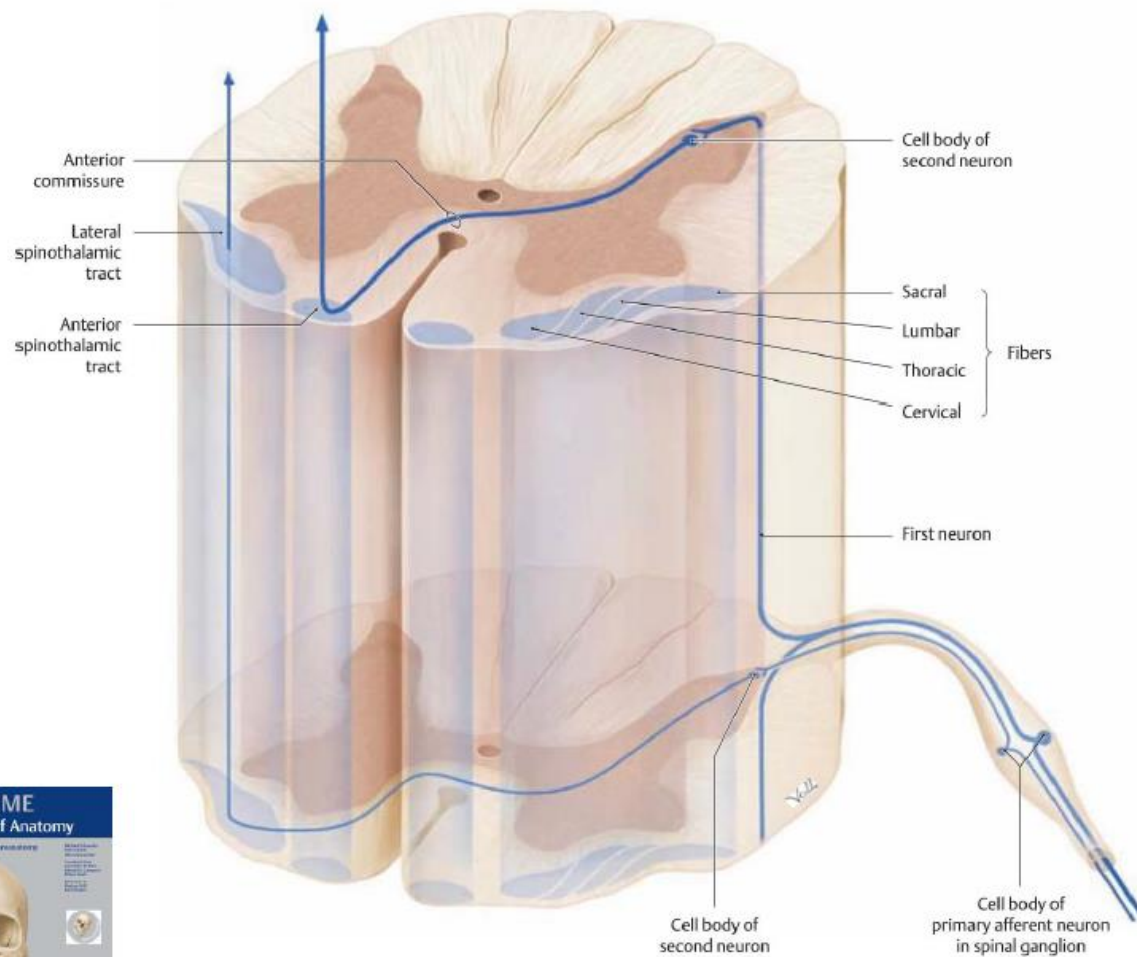
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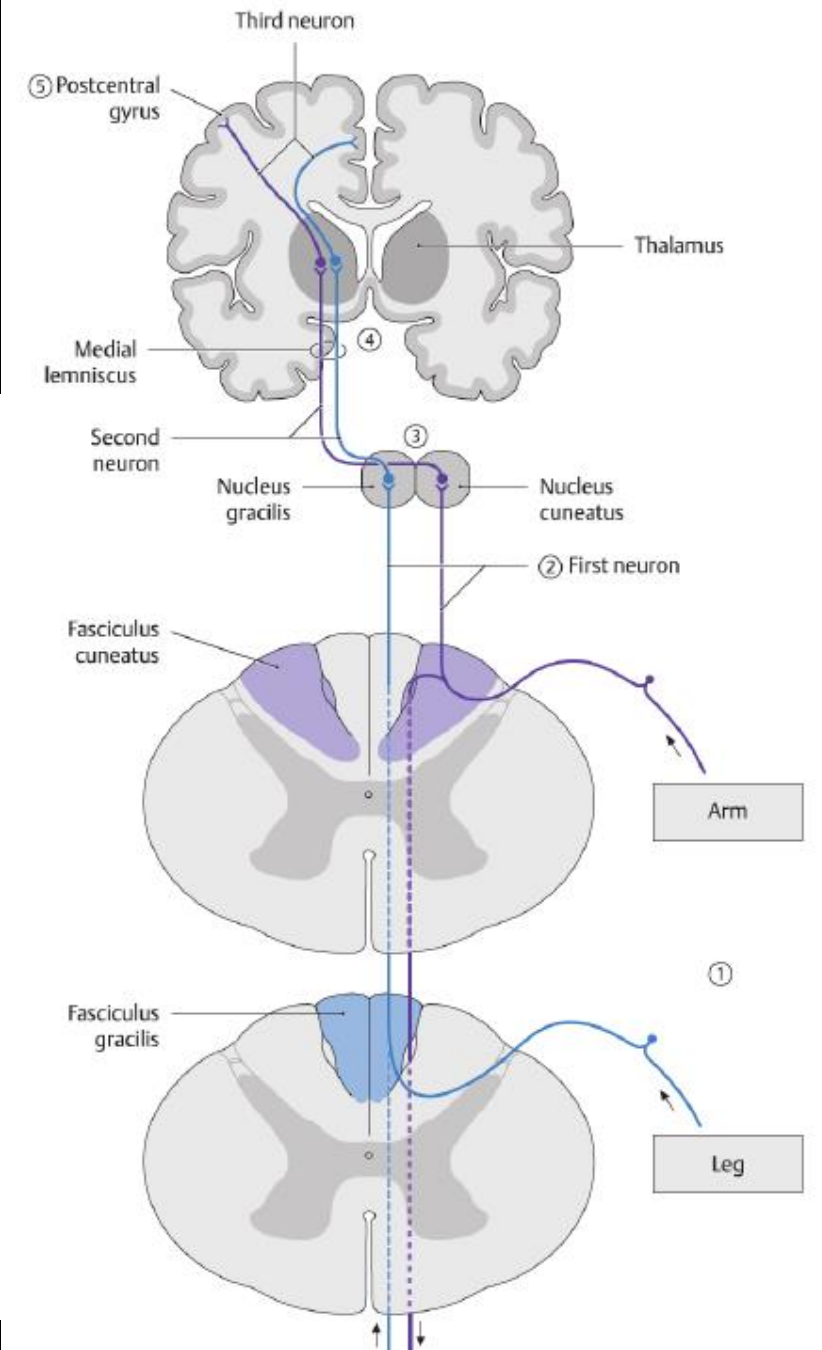
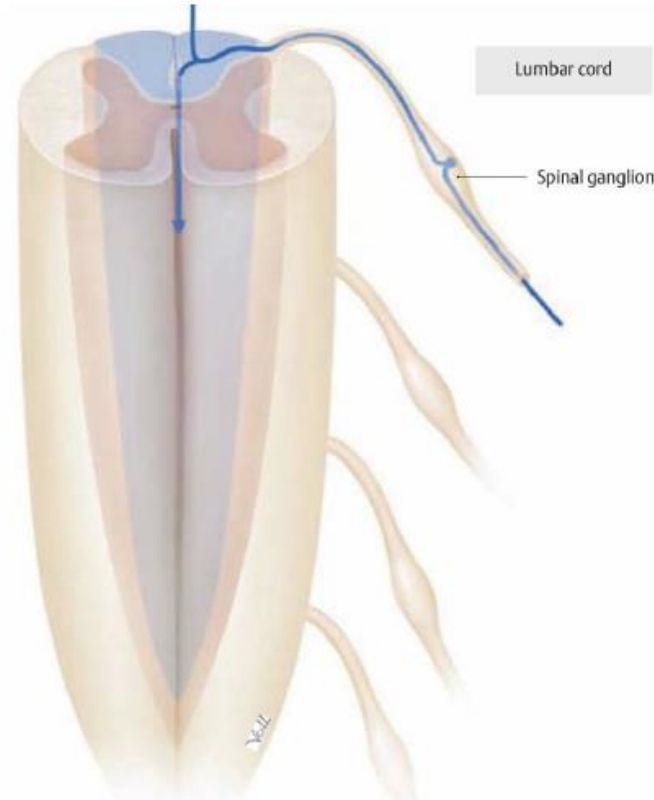
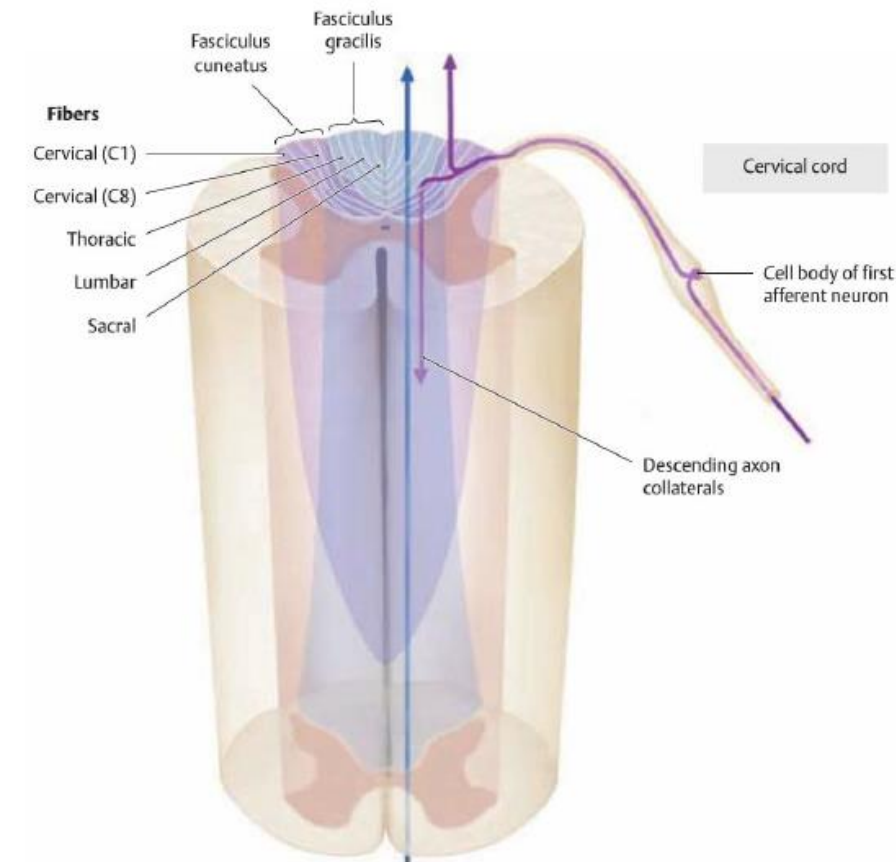
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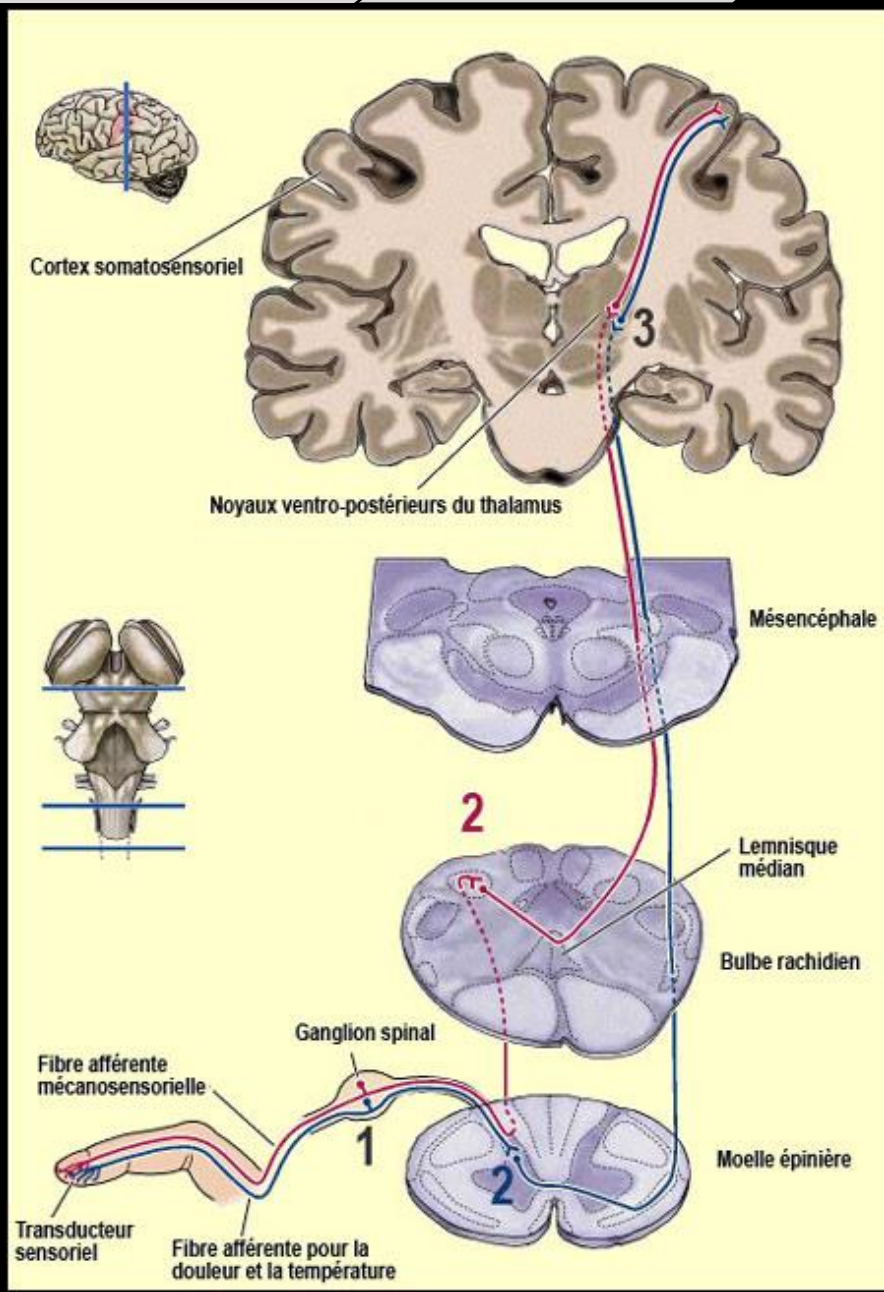
- 1. Anatomie des voies de la douleur
- 2. Théorie du « gate control » et application en neurochirurgie
- 3. Lésion médullaire et plexuelle: application en neurochirurgie
- 4. Thérapies intrathécales

ANATOMIE - Spinothalamic pathway



ANATOMIE - Cordonal pathway



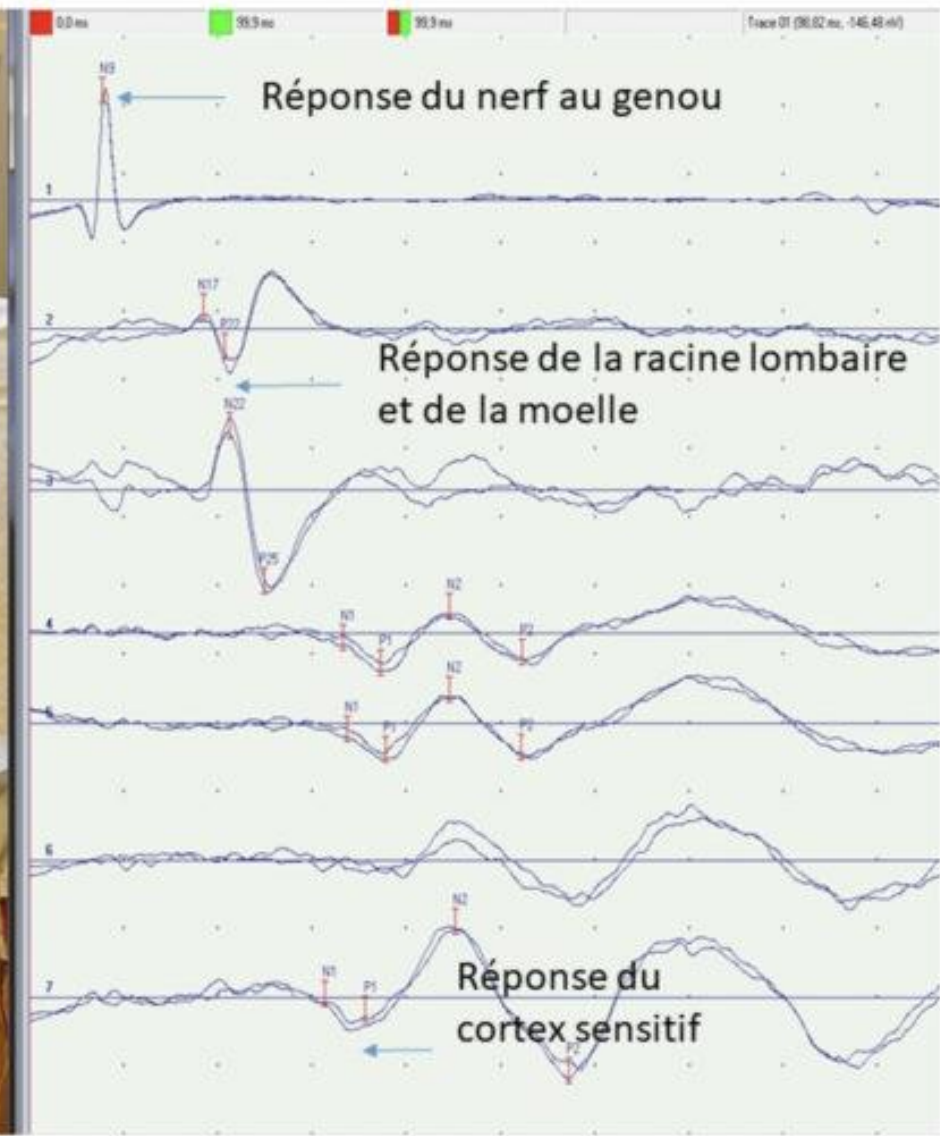


Neuroanatomie de la douleur

- Les fibres C - amyélinisées, vitesse de conduction = 1m/s - sont INEXCITABLES avec des impulsions de durée inférieure à 200 μ s
- Les fibres A δ – myélinisées, faible diamètre, conduction = 20m/s - sont INEXCITABLES aux stimulations d'une durée de moins de 10 μ s
- Les fibres A β RESTENT EXCITABLES avec des impulsions de seulement 2 μ s
- ➔ 2 types de douleur:
 - Lente, lancinante, diffuse
 - Rapide, bien localisée, réflexe de retrait

Axones sensoriels	A α	A β	A δ	C
Axones des fibres sensorielles musculaires	Groupe I	II	III	IV
				
Diamètre (μm)	13 - 20	6 - 12	1 - 5	0.2 - 1.5
Vitesse (m/s)	80 - 120	35 - 75	5 - 30	0.5 - 2
Recepteurs sensoriels	Propriocepteurs des muscles squelettiques	Mécanorecepteurs de la peau	Douleur, température	Température, douleur, démangeaison

PES



Neuropathies sensibles des petites fibres : intérêt des potentiels évoqués laser

Small fiber sensory neuropathies: Contribution of laser evoked potentials

C. Créac'h^{a,*,b}, P. Convers^{a,b}, F. Robert^a, J.-C. Antoine^{a,c}, J.-P. Camdessanche^{a,c}

^a Service de neurologie, CHU Saint-Étienne, hôpital Nord, 42055 Saint-Étienne, France

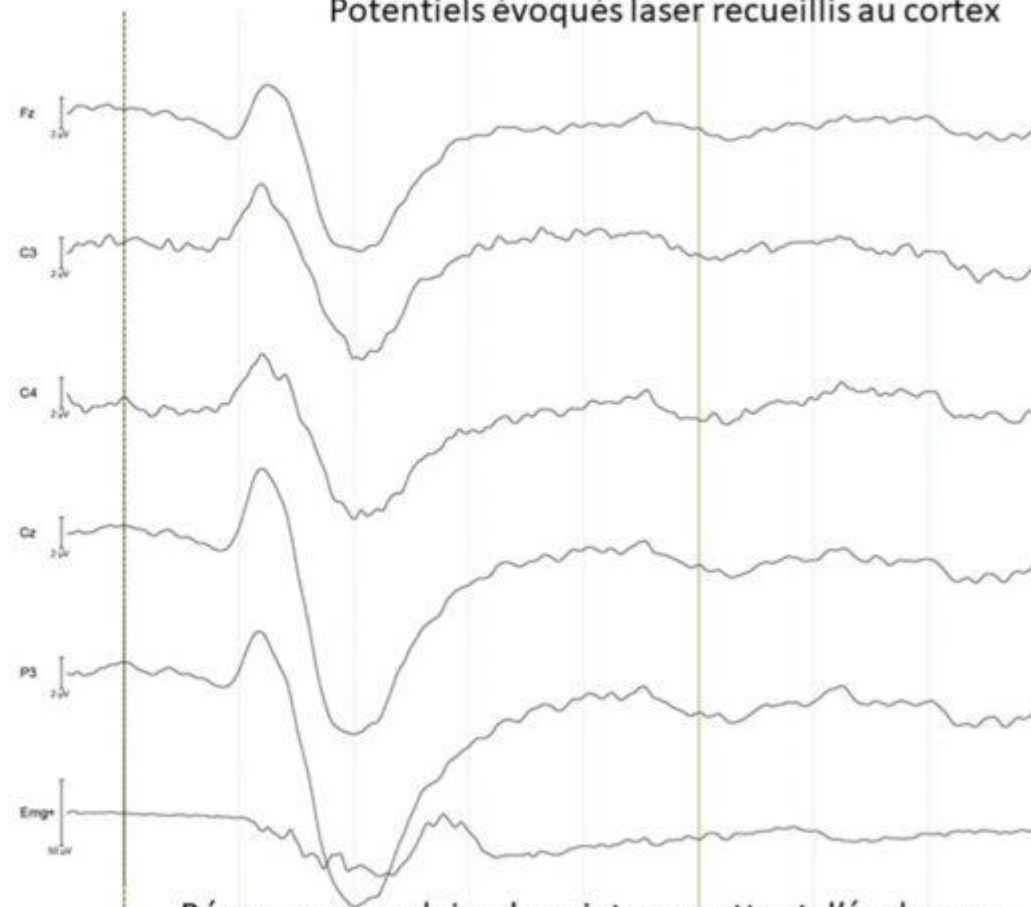
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PEL

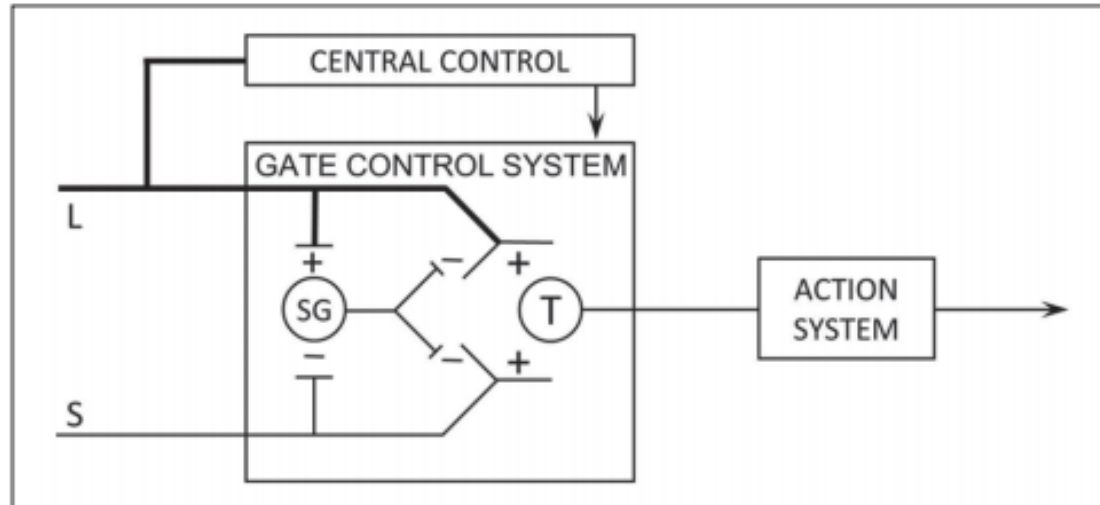


Potentiels évoqués laser recueillis au cortex



Réponse musculaire du sujet permettant d'évaluer sa
capacité à ressentir la chaleur du laser

Contrôle segmentaire - Gate control



- Melzack and Wall, 1965

Figure 1) A schematic illustration of the gate control theory of pain proposed by Melzack and Wall (1), demonstrating how the gating mechanism in the spinal dorsal horn modulates transmission of nerve impulses from afferent fibres to spinal cord transmission cells. The gating mechanism is affected by the relative activity in large- and small-diameter fibres, with the former inhibiting transmission (closing the gate) and the latter facilitating transmission (opening the gate). Notably, the spinal gating mechanism is also modulated by descending nerve impulses from the brain. The authors proposed that the spinal transmission cells activate an action system in the brain comprising regions that underlie the experience and behaviours characteristic of pain. Reproduced with permission from Melzack and Wall (1)

Gate control

- Melzack et Wall ont proposé qu'une « station de transmission dans la moelle épinière influence l'influx nerveux vers le cerveau. Ils ont appelé cette station de transmission « gate ». Pensez-y comme un portail que vous pouvez ouvrir ou fermer pour accéder à votre jardin. La porte peut être ouverte ou fermée de plusieurs façons. Le cerveau peut envoyer des messages électriques le long des tractus pour fermer le portail et bloquer ou réduire l'influx vers le cerveau, ou envoyer des messages qui font exactement le contraire.

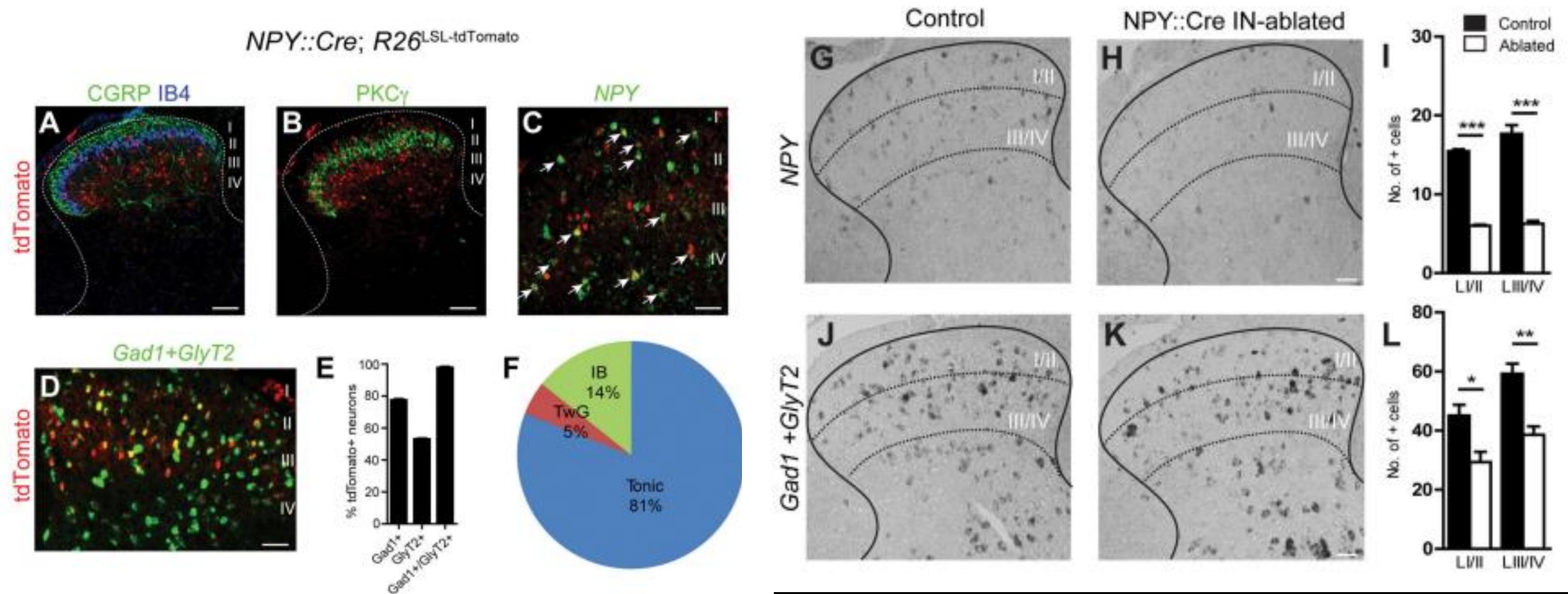
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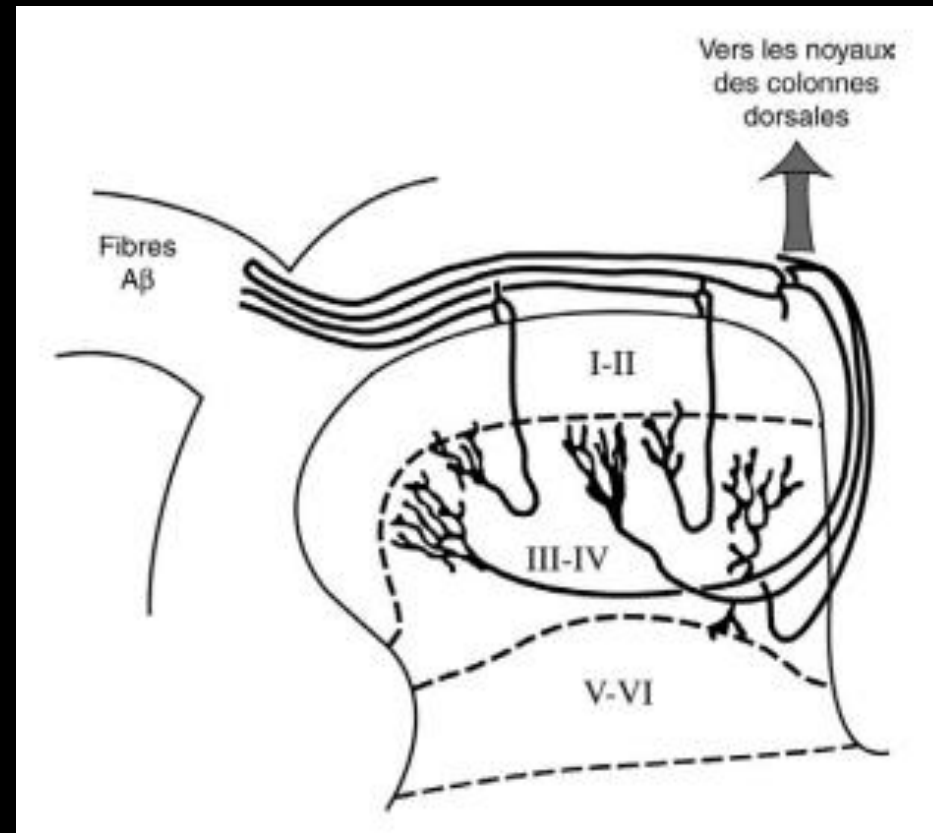
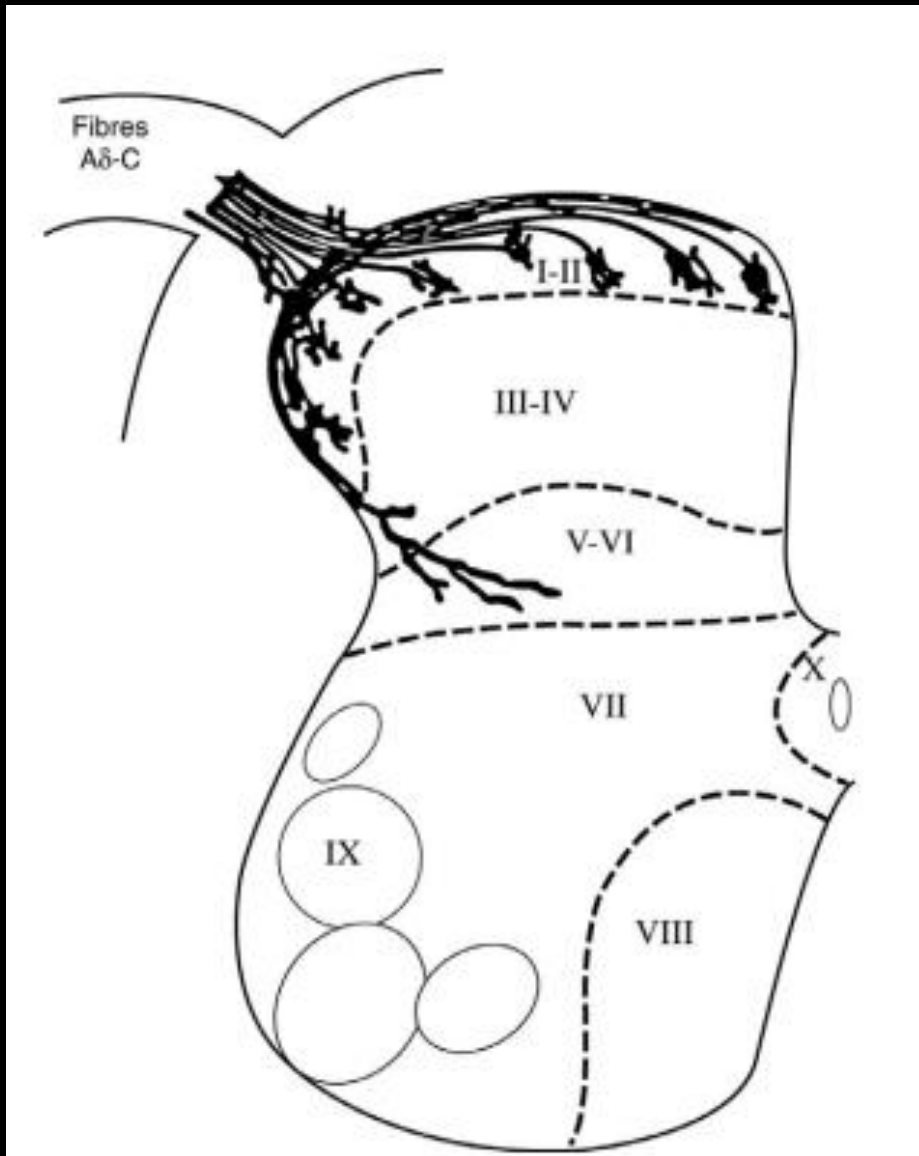
Science. 2015 October 30; 350(6260): 550–554. doi:10.1126/science.aac8653.

Gate control of mechanical itch by a subpopulation of spinal cord interneurons

Steeve Bourane^{1,*}, Bo Duan^{2,*}, Stephanie C. Koch¹, Antoine Dalet¹, Olivier Britz¹, Lidia Garcia-Campmany¹, Euseok Kim³, Longzhen Cheng^{2,4}, Anirvan Ghosh³, Qiufu Ma^{2,#}, and Martyn Goulding^{1,#}

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Le contrôle central de la douleur

Central pain control ◇

Bernard Calvino *, Rose Marie Grilo ¹

Laboratoire de neurobiologie, CNRS UMR 7637, ESPCI, 10, rue Vauquelin, 75231 Paris cedex 05, France

Reçu le 20 septembre 2004 ; accepté le 10 novembre 2004

Disponible sur internet le 19 avril 2005

Gate control

- Rôle inhibiteur des fibres de gros diamètre (tactiles) sur les fibres de petit diamètre (nociceptives) au niveau des cellules convergentes (couche 5) via l'interneurone inhibiteur (SG) situé dans les couches 2 et 3.

Pour conclure

- L'activation des fibres de la sensibilité tactile $A\alpha$, β , en augmentant l'activité des interneurones inhibiteurs, fermerait la « gate » et bloquerait la transmission de l'information nociceptive vers les structures supra-spinales ;
- alors que l'activation des fibres nociceptives $A\delta$ et C, en inhibant l'activité des interneurones inhibiteurs, ouvrirait la « gate » et favoriserait la transmission de l'information nociceptive vers les structures supra-spinales.

Stimulation médullaire

- **Objectifs** :
- Soulager la douleur tout en réduisant la consommation de médicaments et le besoin en ressources de soins de santé
- Améliorer la qualité de vie et augmenter la capacité d'accomplir des actes de la vie quotidienne
- Améliorer les symptômes de la dépression tout en soulageant la douleur

Stimulation médullaire

- **Avantages**
- Procédure réversible
- Minimale ment invasive
- Peut être ajustée et programmée

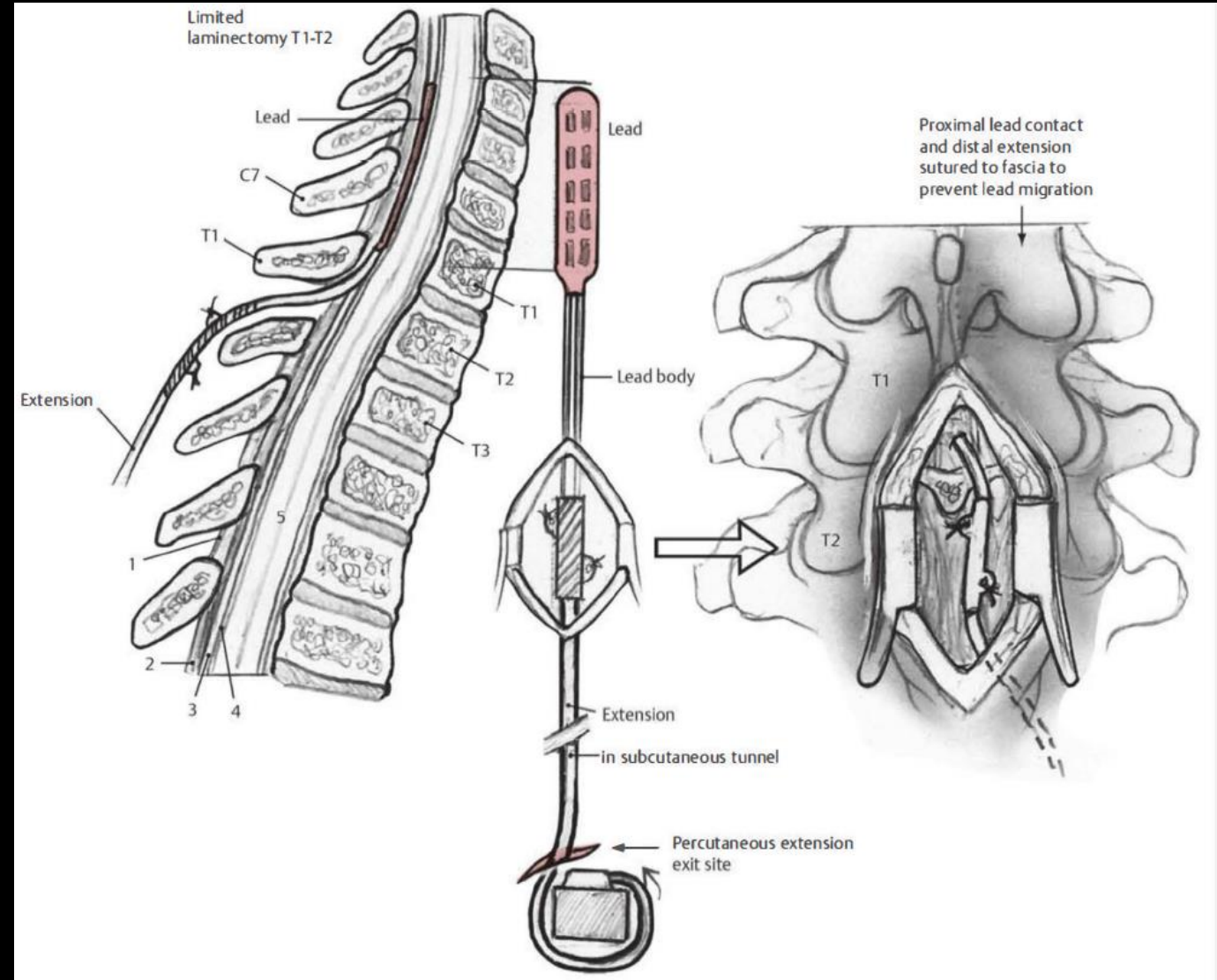
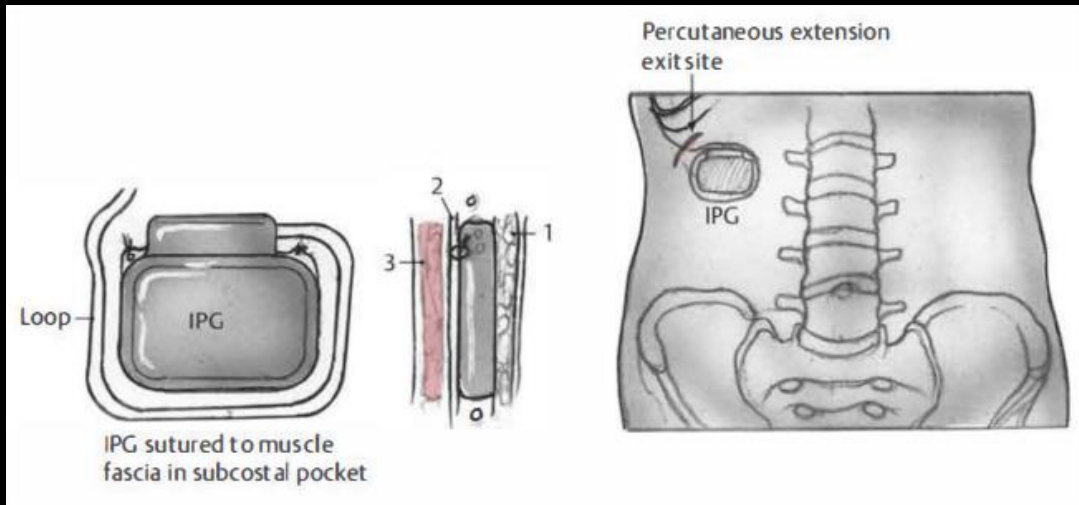
Stimulation médullaire

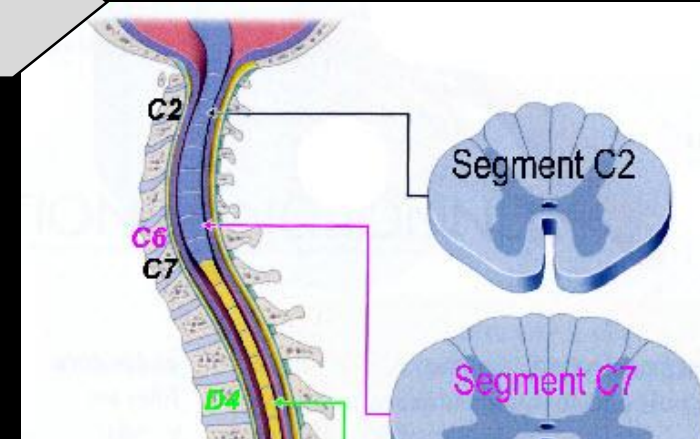
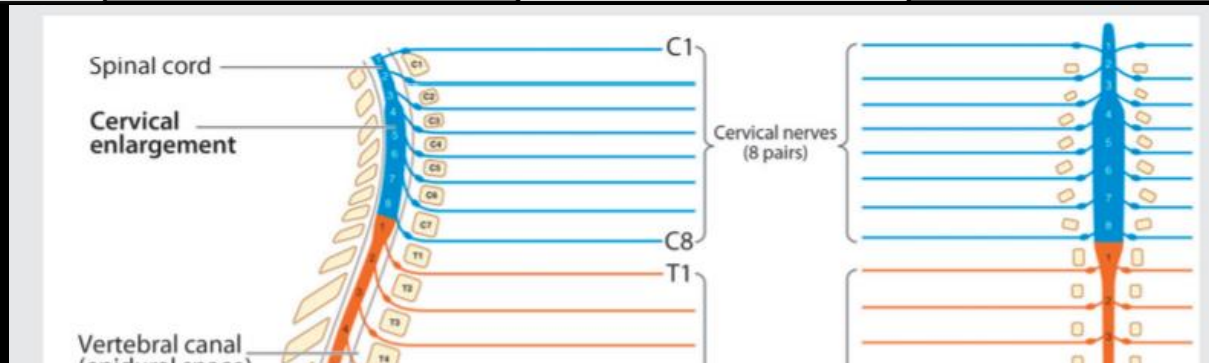
- **Indications:**
- Toute douleur neuropathique avérée
- Sans anomalie de la voie cordonale postérieure
- Chez un patient prêt psychologiquement pour cette PEC
- En échec thérapeutique de ttt précédemment bien conduits

- Failed back surgery syndrome
- Complex regional pain syndrome (CRPS) I and II
- Douleur neuropathique périphérique
- Syndrome du membre fantôme (amputé)
- Névralgie post-herpétique

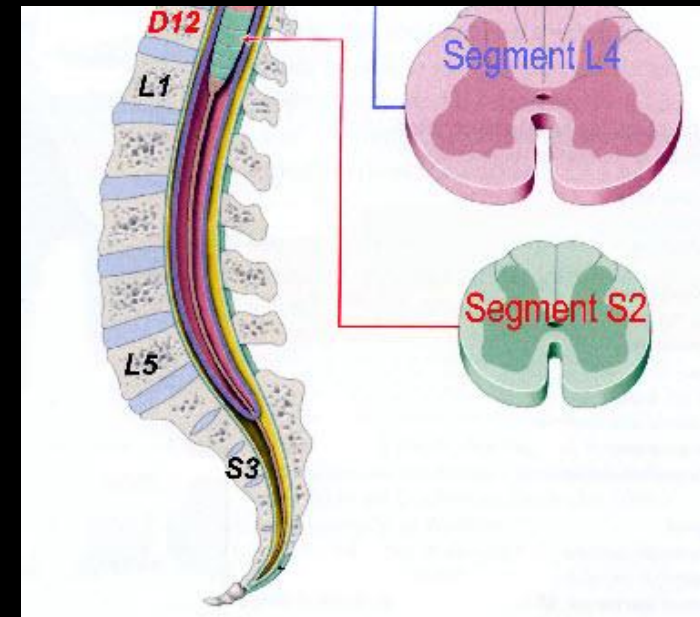
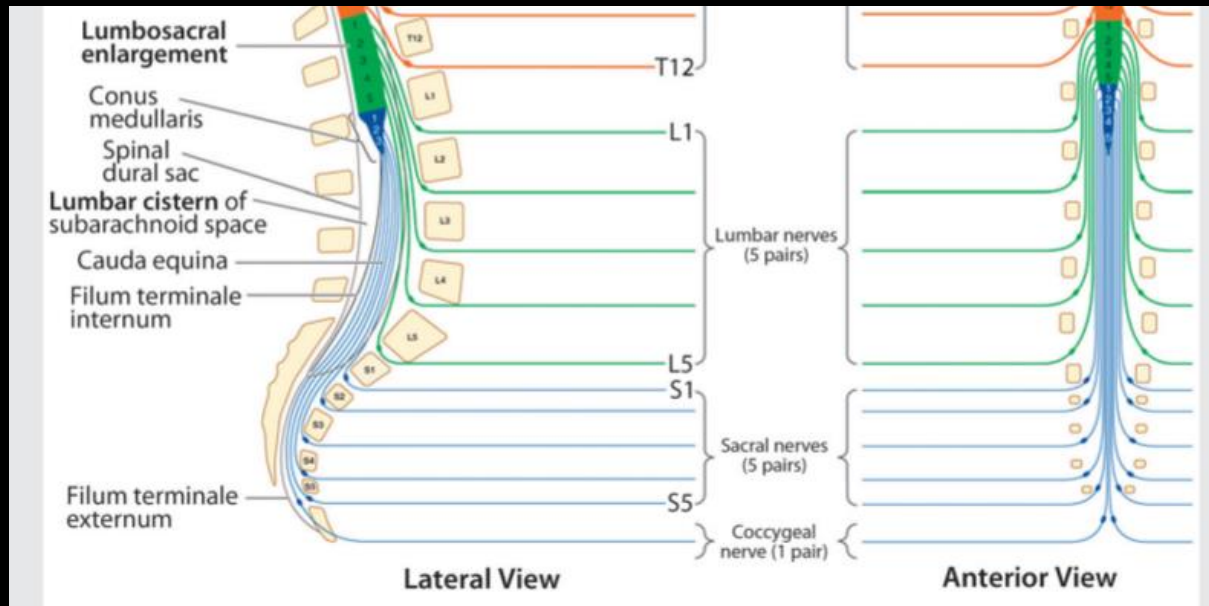
Stimulation médullaire

- Techniques chirurgicales
- open
- Per-cutané





IMPORTANCE DE LA BONNE LOCALISATION DE L'ELECTRODE



Effectiveness of Spinal Cord Stimulation in Chronic Spinal Pain: A Systematic Review

Jay Grider, DO, PhD¹, Laxmaiah Manchikanti, MD², Alexios Carayannopoulos, DO, MPH³, Manohar Lal Sharma, MD, FRCA, FFPMRCA⁴, Carl C. Balog, MD⁵, Michael E. Harned, MD⁶, Vahid Grami, MD, MPH⁷, Rafael Justiz, MD⁸, Kent Nouri, MD⁹, Salim M. Hayek, MD, PhD¹⁰, Ricardo Vallejo, MD, PhD¹¹, and Paul J. Christo, MD¹²

• Résultats

Table 4. Results of published studies of effectiveness of spinal cord stimulation in failed back surgery syndrome.

Study	Study Characteristics	Methodological Quality Scoring	Patients	Pain Relief		Results	
				≤ 12 mos.	> 12 mos.	Short-term ≤ 12 mos.	Long-term > 12 mos.
Kapural et al (38,39)	RA, AC	Cochrane:8/12 IPM-QRB: 34/48	SCS = 81 HF10 = 90	55% vs. 80%	55% vs. 80%	P	P
North et al (13)	RA, AC	Cochrane: 7/12 IPM-QRB: 31/48	SCS = 29 Reoperation = 31	52% vs. 10%	52% vs. 10%	P	P
Kumar et al (18,86)	RA, AC	Cochrane: 9/12 IPM-QRB: 32/48	Total = 100 CMM = 48 SCS = 52	18% vs. 48%	18% vs. 48%	P	P
Schultz et al (77)	RA, AC	Cochrane: 7/12 IPM-QRB: 20/48	Manual = 40 Adaptive = 36 Total = 76	U	NA	U	NA
Perruchoud et al (78)	RA, AC	Cochrane: 7/12 IPM-QRB: 23/48	Total = 33 Sham vs HFSCS = 20	N	NA	N	NA
Schu et al (79)	RA, AC	Cochrane: 9/12 IPM-QRB: 24/48	20	P (burst)	NA	U	NA

RA = randomized; AC = Active-control; SCS = spinal cord stimulation; CMM = conventional medical management; vs = versus; P = positive; N = negative; NA = Not applicable; U = undetermined; HF10 = 10 kHz high frequency therapy; HFSCS = high frequency spinal cord stimulation

Stimulation médullaire - Résultats

Table 1 Selection of SCS literature with focus on back ± lower limb pain studies

Study	Year	Design, cohort, sample size, follow-up	Reported findings	Comments
Barolat et al ²⁸	2001	Prospective, multicenter observational case series n=41 Follow-up: 1 year Cohort: back and leg pain (with predominant pain in back)	Tests SCS systems with paddle electrodes and RF stimulator n=15 at 1 year At 12 months, 88% of patients reported fair-excellent pain relief for leg pain following SCS At 12 months, 68% of the patients reported fair-excellent pain relief for back pain following SCS	Groups pain relief of fair to excellent into one group Three patients dropped from study at 6 months: two due to inadequate pain relief and one classified as technical failure because power required to induce satisfactory paresthesia to control pain was inadequate. This methodology skews the outcome data
Turner et al ^{60,61}	2010	Prospective, controlled cohort study SCS trial, n= 51; multidisciplinary PC n=39; UC, n=68 Follow-up at 6, 12, and 24 months Cohort: workers compensation recipients with FBSS	Tests SCS against UC and a multidisciplinary PC At 6 months, SCS patients had greater improvement in leg pain and function but with concomitant higher rates of opioid use At 12 and 24 months, the groups did not differ in rates of clinically meaningful leg pain of function or in work status	Study among very specific cohort/patient subpopulation Workcover patients could only receive SCS if they joined study SCS > PC and UC (usual care) Baseline pain Baseline Roland-Morris Disability Duration of pain Time in WC claim system

Traitements pharmacologiques et non pharmacologiques de la douleur neuropathique : une synthèse des recommandations françaises

Pharmacological and Non-Pharmacological Treatment for Neuropathic Pain: Short Form French Guidelines

X. Moisset · D. Bouhassira · J. Avez Couturier · H. Alchaar · S. Conradi · M.-H. Delmotte · M. Lantéri-Minet · J.-P. Lefaucheur · G. Mick · V. Piano · G. Pickering · E. Piquet · C. Regis · E. Salvat · N. Attal

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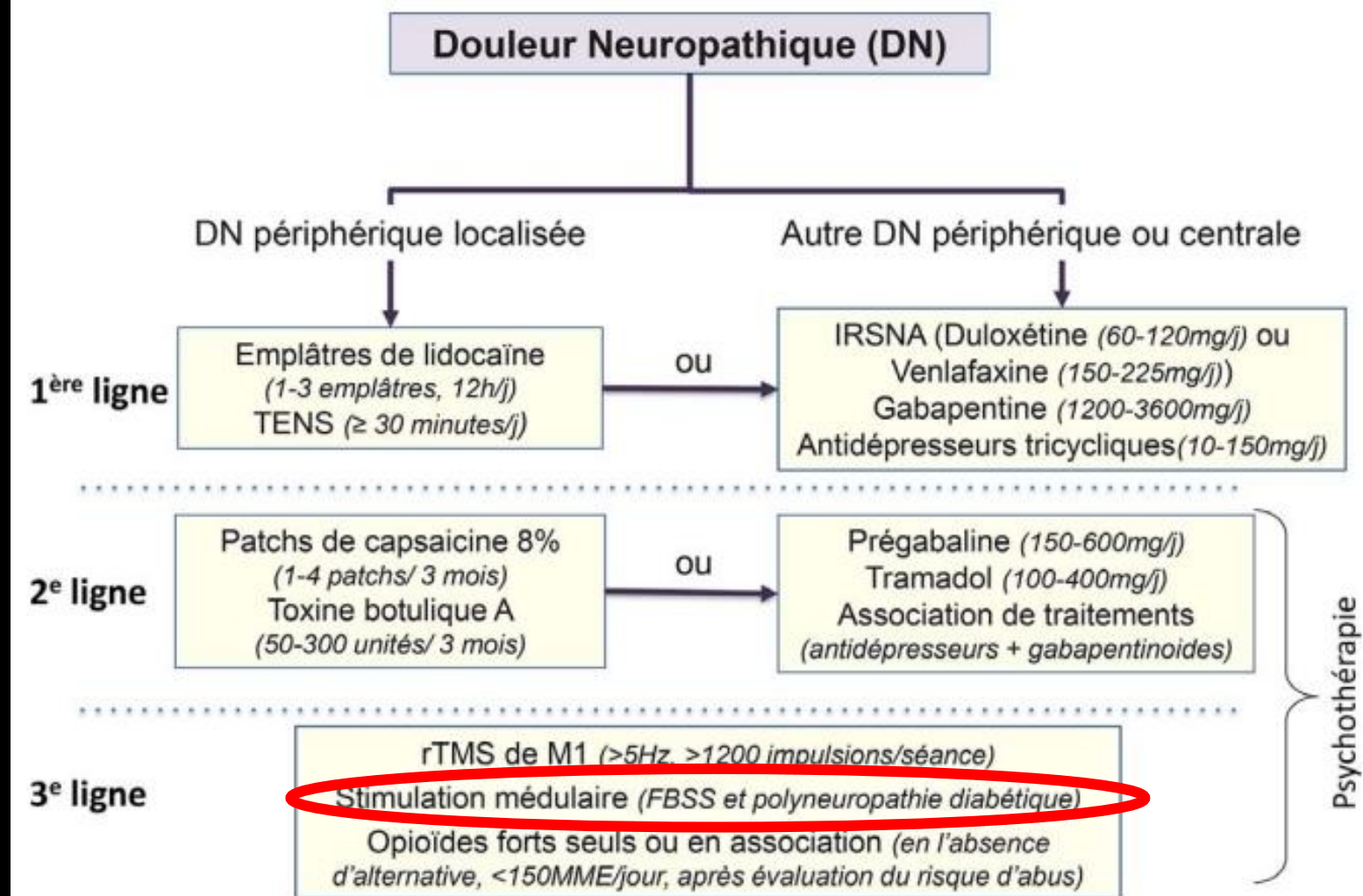
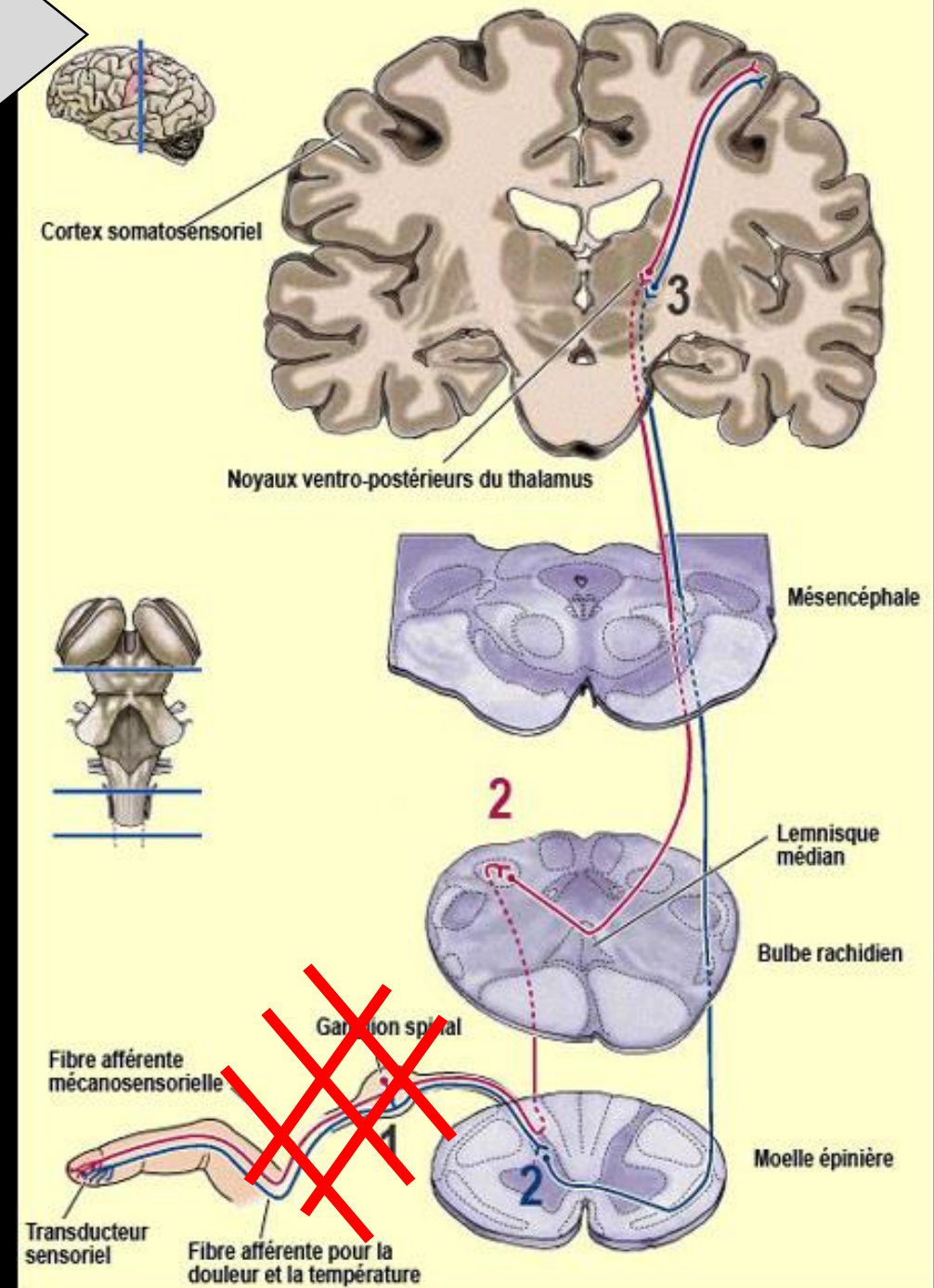
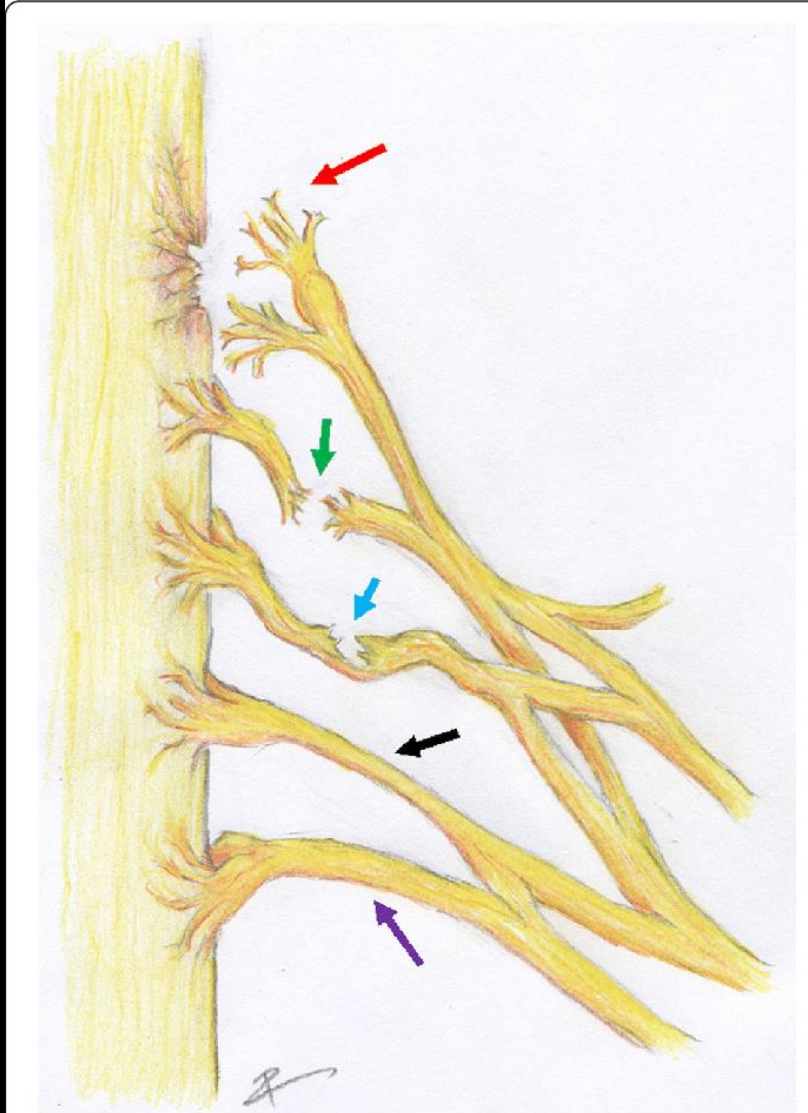


Fig. 1 Algorithme thérapeutique proposé pour la prise en charge de la douleur neuropathique de l'adulte. TENS : *transcutaneous electrical nerve stimulation* ; IRSNA : antidépresseur inhibiteur de recapture de la sérotonine et de la noradrénaline ; rTMS : *repetitive transcranial magnetic stimulation*

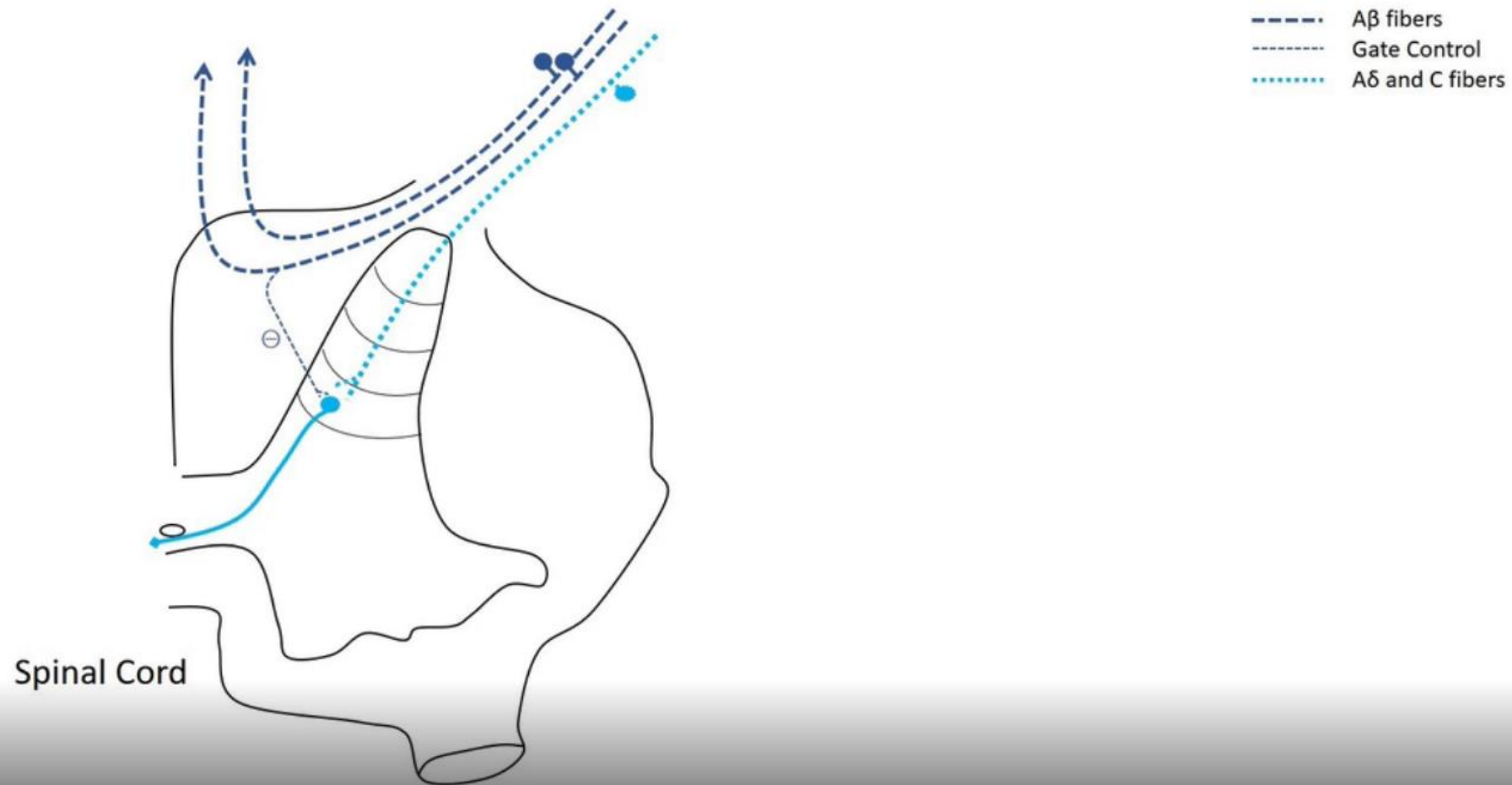
Avulsion plexuelle

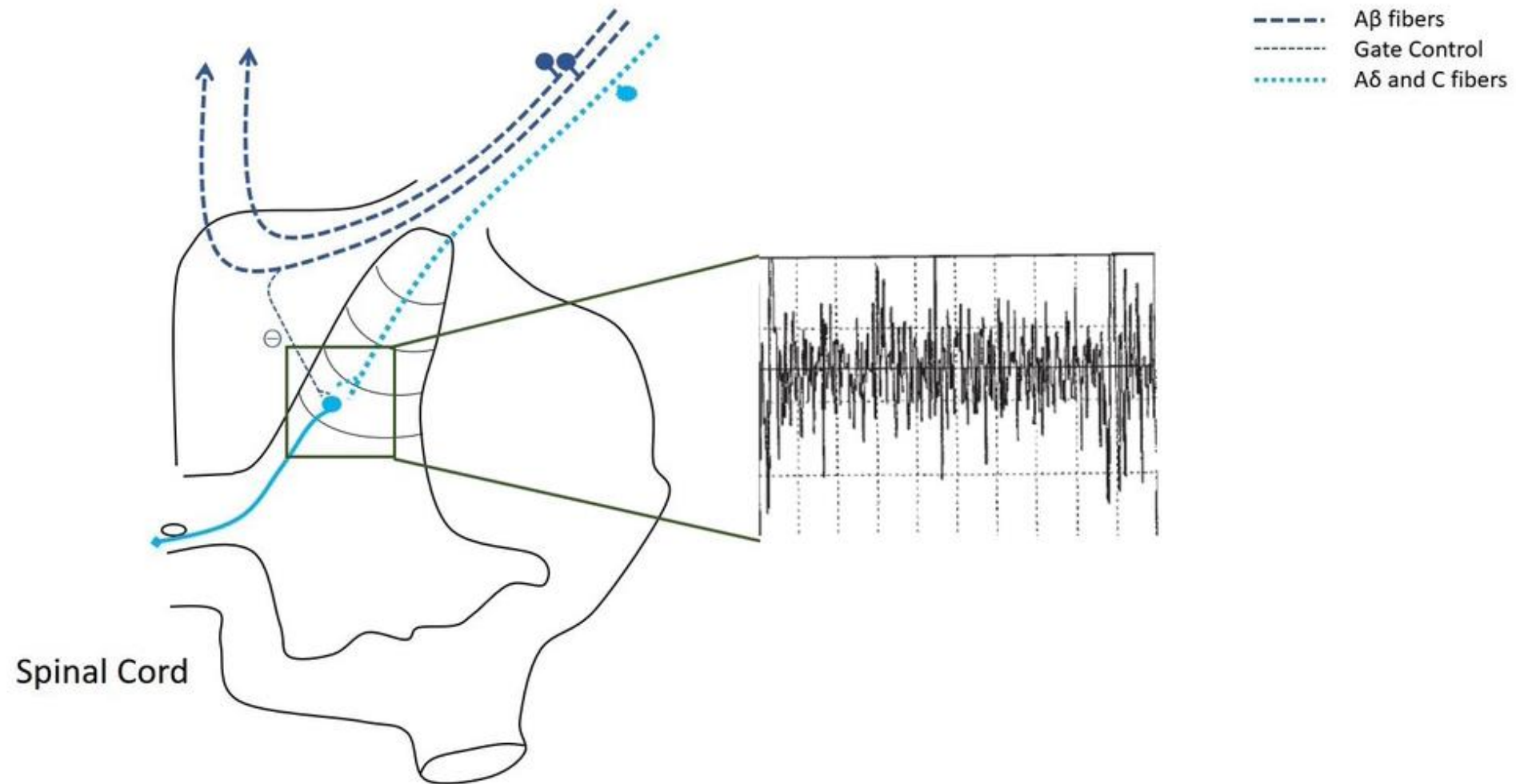


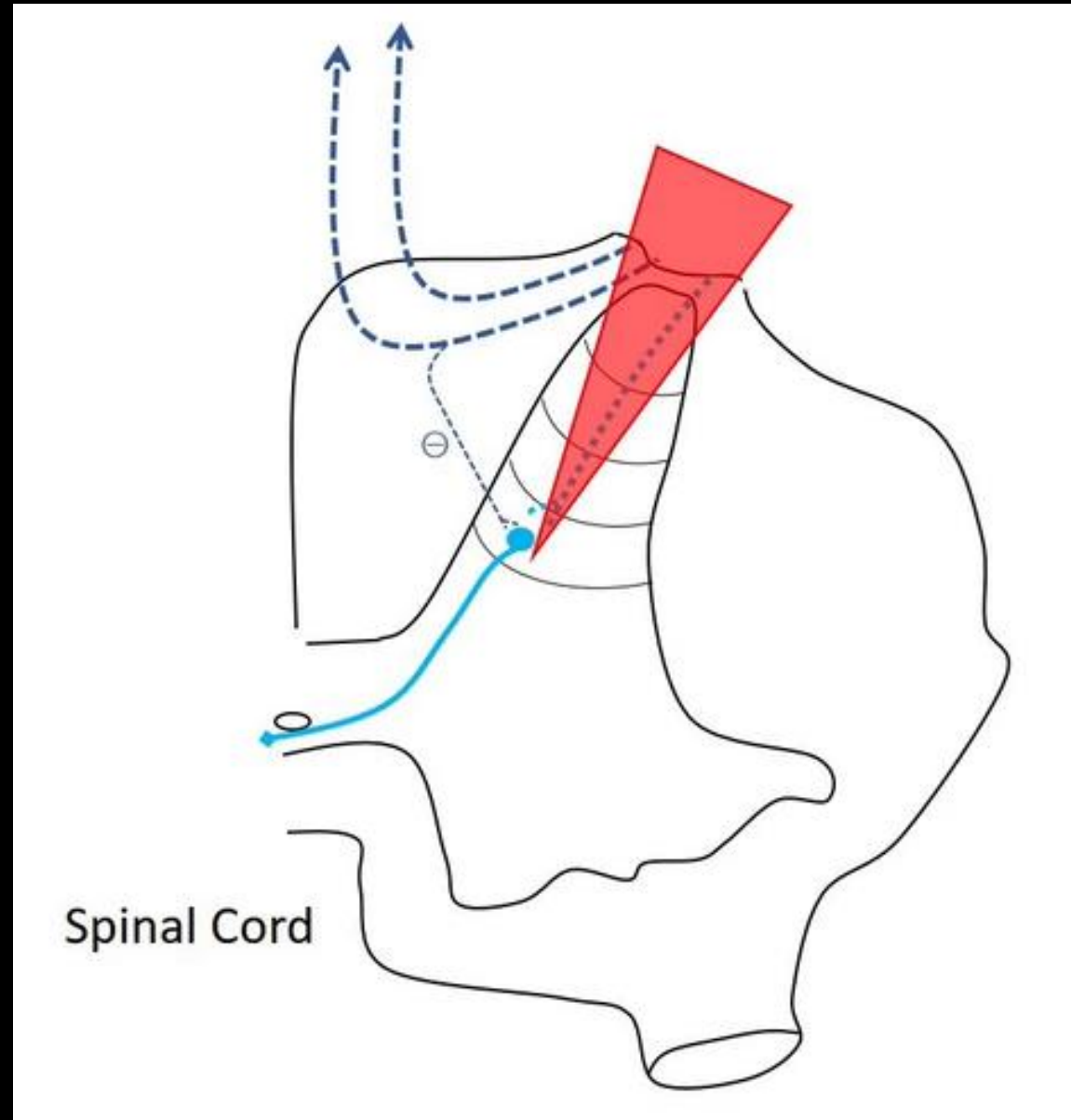
VIDEO ARTICLE

 Check for updates

Microsurgical DREZotomy for Treatment of Brachial Plexus Avulsion Pain

Corentin Dauleac^{1,2}, Andrei Brinzeu^{1,2,5}, Inès Fenniri^{1,2}, Marc Sindou⁴, Patrick Mertens^{1,3}

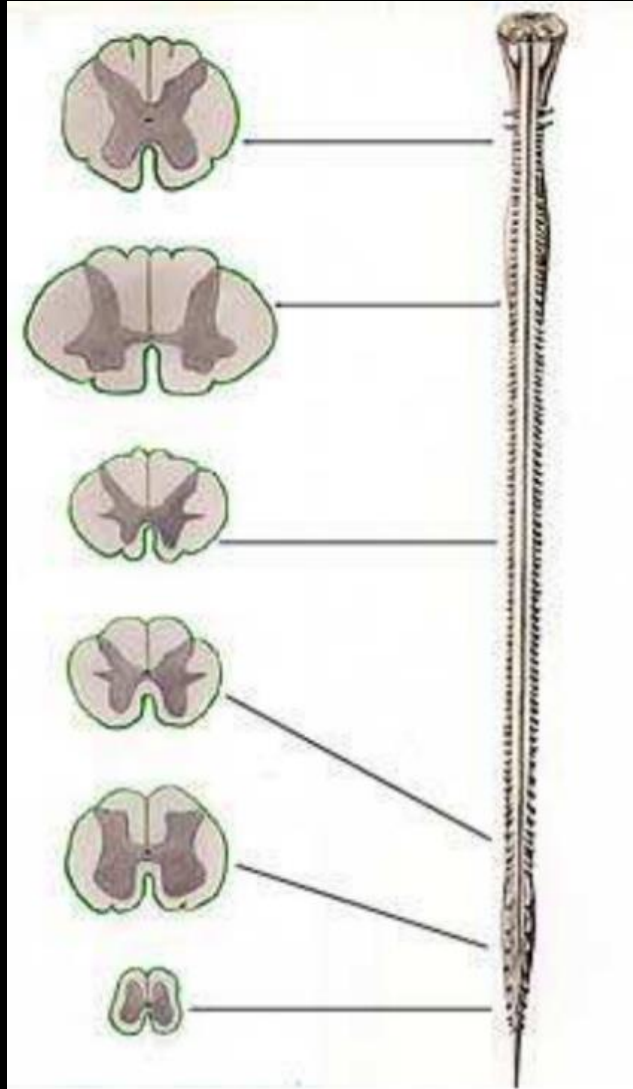




DREZotomie

- **Objectifs :**
- Interrompre préférentiellement les fibres nociceptives tout en préservant dans une certaine mesure les structures inhibitrices de la corne dorsale
- Détruire les neurones anormaux à l'intérieur de la corne dorsale, supposés être responsables de la douleur dite de désafférentation.

Corne dorsale

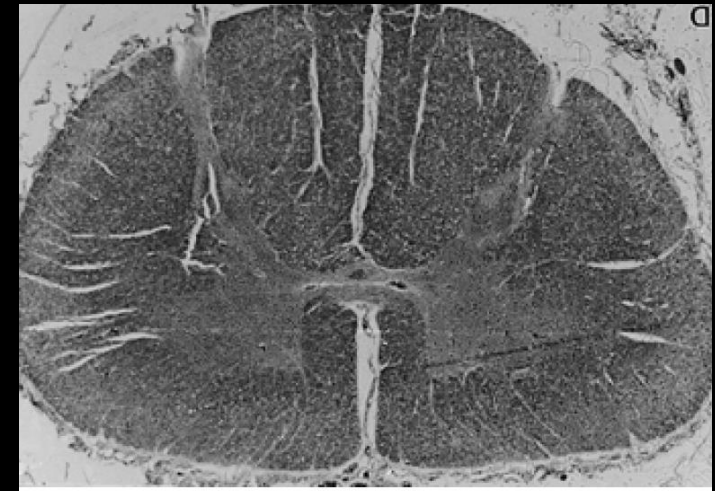
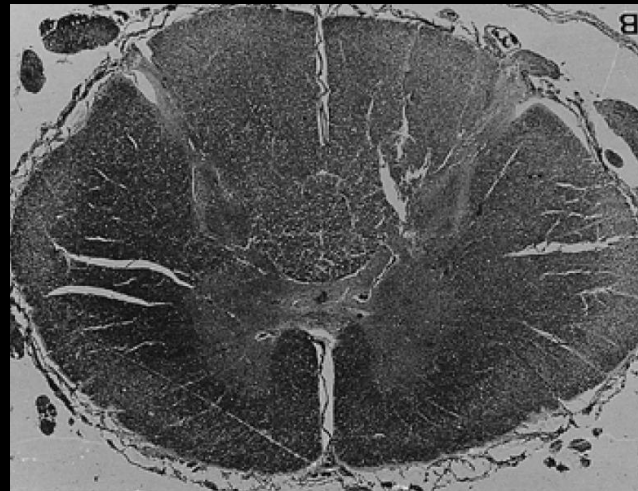


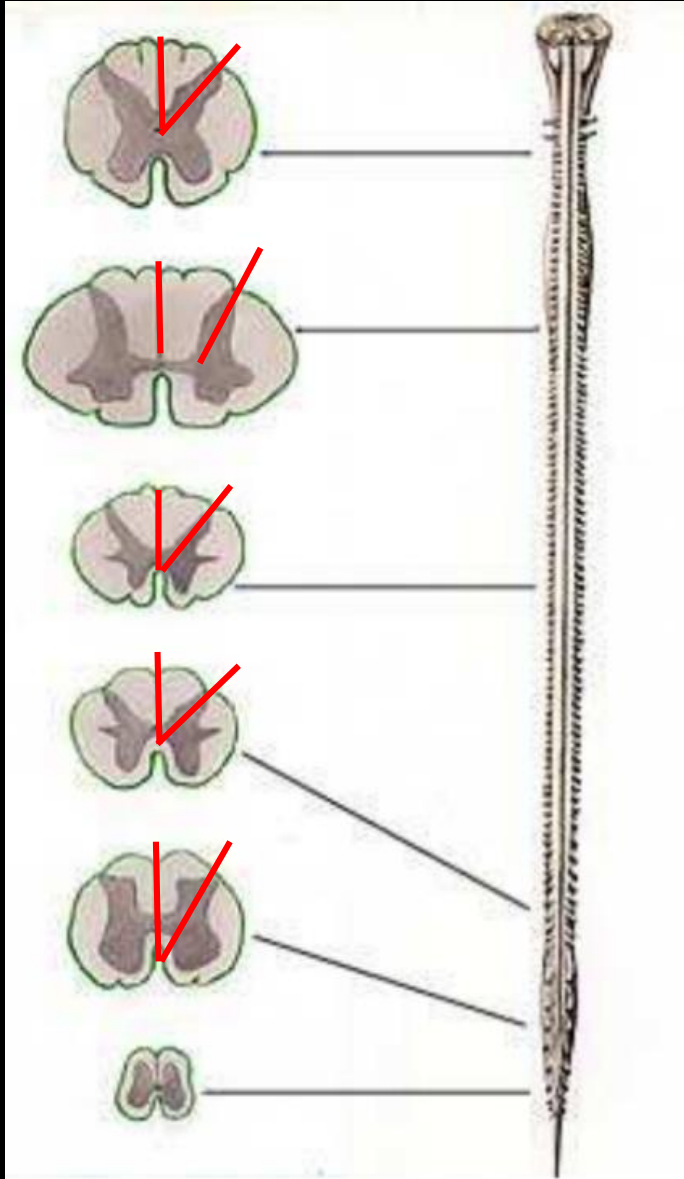
Surg Radiol Anat 22: 81-88
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Radiological anatomy

Radiologic anatomy of the spinal dorsal horn at the cervical level (anatomic-MRI correlations)

P. Mertens¹, M. Guenot⁴, M. Hermier², A. Jouvett³, P. Tournut², J.L. Froment², M. Sindou⁴ and J.P. Carret¹



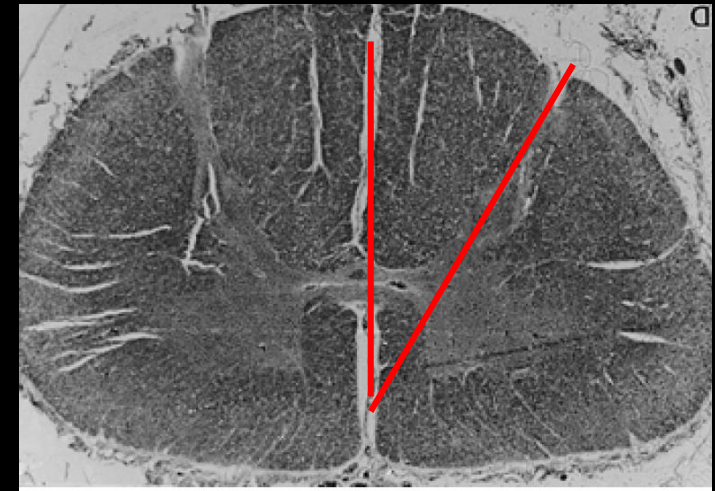
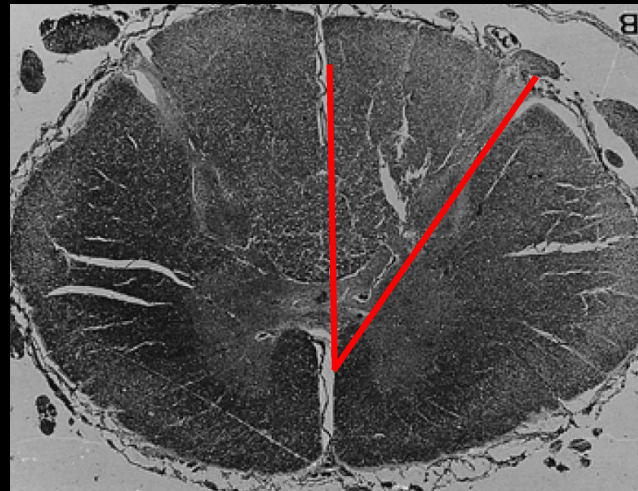


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DREZotomie

VIDEO ARTICLE

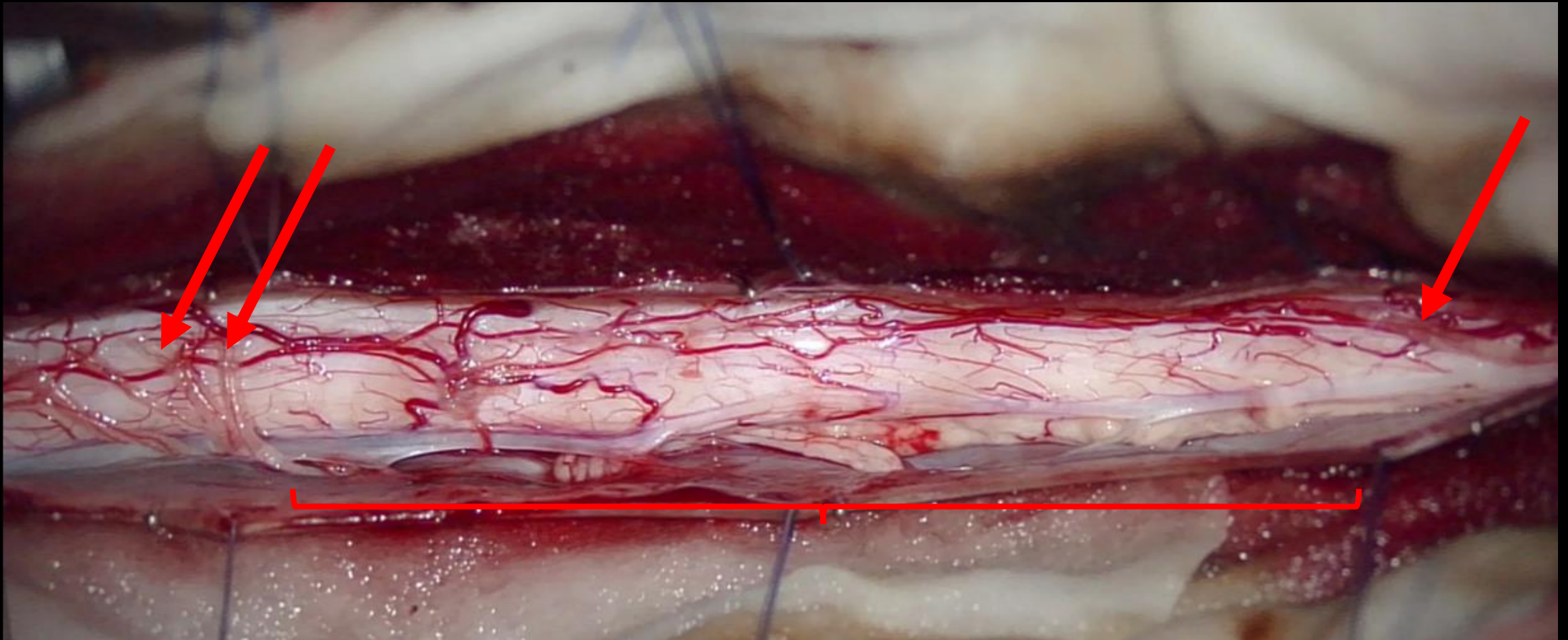
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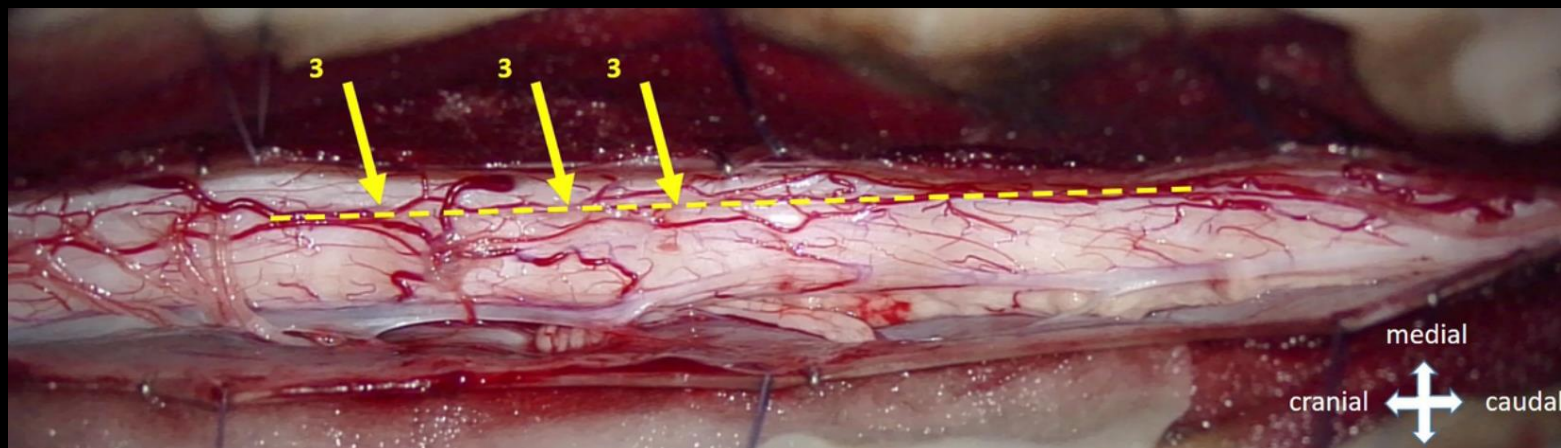
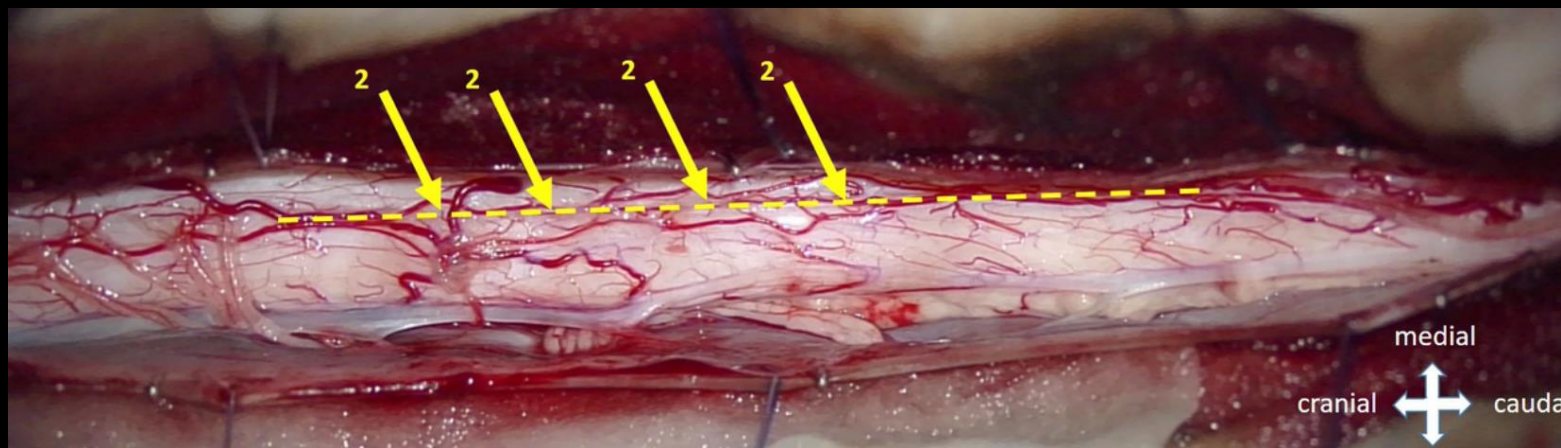
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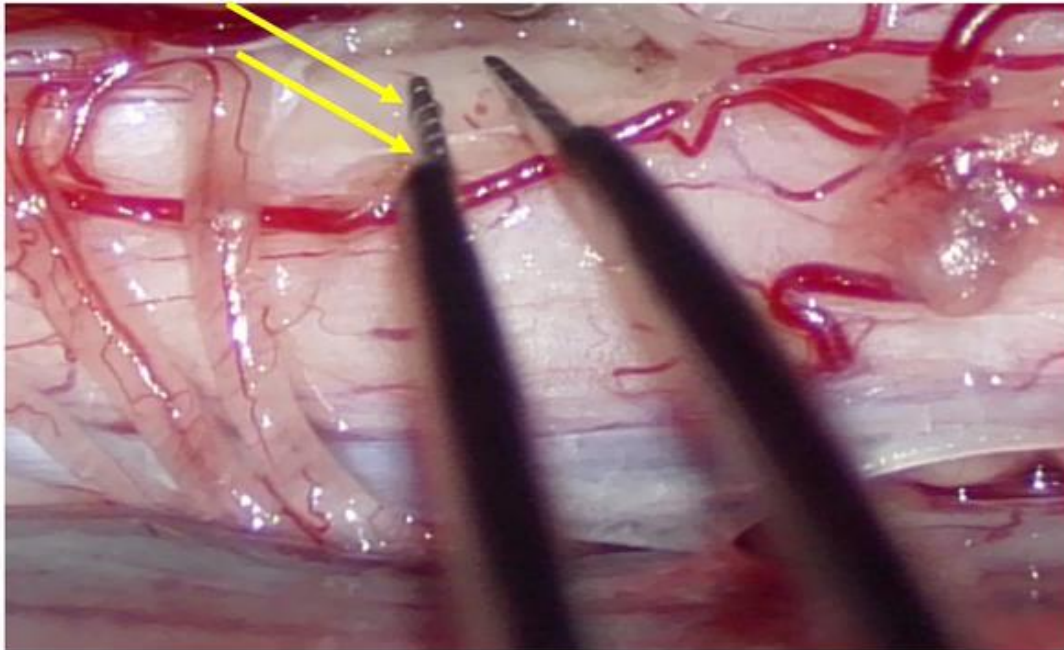


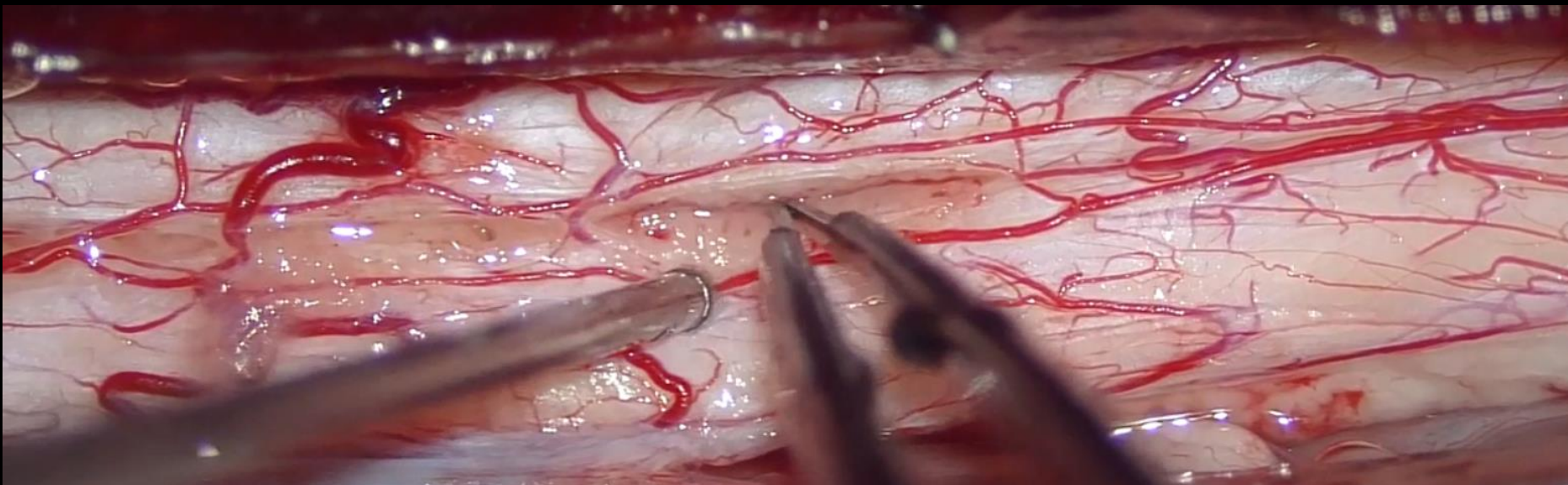
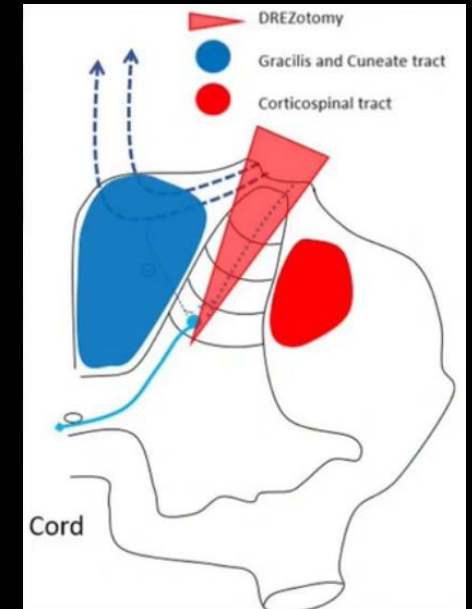
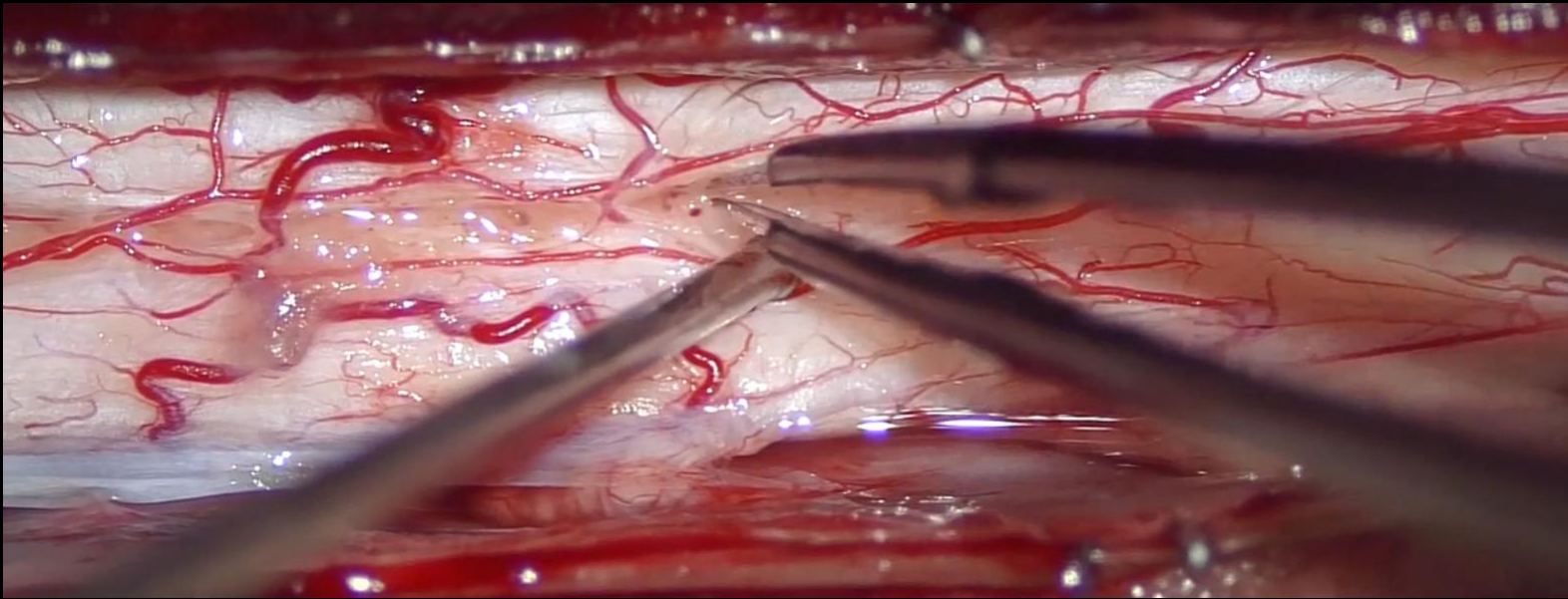
DREZotomie





Micro instruments





DREZotomie

- Indications :

- **lésions du plexus**, notamment l'avulsion, au niveau brachial ou plus rarement lombo-sacré.
- **douleurs segmentaires** après lésions de la moelle épinière (surtout au niveau du conus medullaris). douleurs résultant de lésions des nerfs périphériques, mais uniquement lorsque les principales composantes sont de type paroxystique et/ou allodynique, après échec de la SCS.
- **douleurs circonscrites** dues à une lésion cancéreuse bien limitée topographiquement, comme par exemple dans l'apex thoracique. Syndrome de Pancoast-Tobias
- spasticité invalidante sévère, notamment associée à une à la douleur

DREZotomie

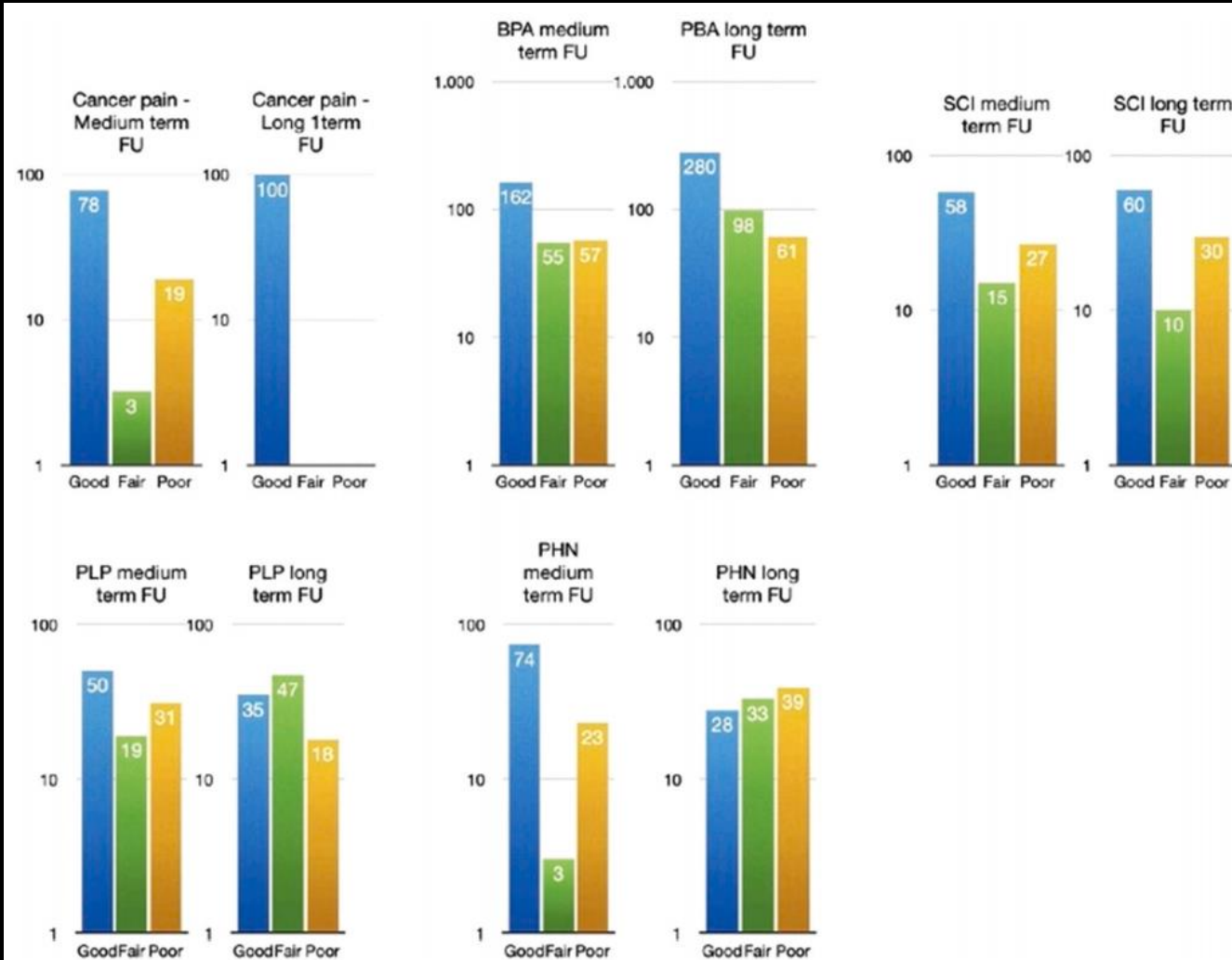
- Résultats

Table 6

Clinical outcome evaluation by Sindou [9].

Outcome	Clinical characteristics and drug intake evaluation
Good	- pain reduction of more than 75%
Fair	- VAS < 3
Poor	- no need of analgesic drugs
	- pain reduction between 75% and 50%
	- VAS < 5
	- residual need of moderate doses of analgesic drugs
	- pain reduction lower than 50%
	- VAS between 3 and 6 with paroxysms higher than 6
	- need of high doses of analgesic drugs

DREZotomie – résultats



Review Article

Long term results of Dorsal Root Entry Zone (DREZ) lesions for the treatment of intractable pain: A systematic review of the literature on 1242 cases

Lorenzo Mongardi^{a,1,*}, Jacopo Visani^{a,1}, Giorgio Mantovani^a, Costanza Vitali^b, Luca Ricciardi^c, Flavio Giordano^d, Michele Alessandro Cavallo^{a,e}, Giorgio Lofrese^f, Marcello D'andrea^f, Paul Roblot^g, Pasquale De Bonis^{a,e}, Alba Scerrati^{a,e}

- Medium term < 3 ans
- Long term > 3 ans

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Lorenzo Mongardi ^{a,1,*}, Jacopo Visani ^{a,1}, Giorgio Mantovani ^a, Costanza Vitali ^b, Luca Ricciardi ^c, Flavio Giordano ^d, Michele Alessandro Cavallo ^{a,e}, Giorgio Lofrese ^f, Marcello D'andrea ^f, Paul Roblot ^g, Pasquale De Bonis ^{a,e}, Alba Scerrati ^{a,e}

DREZ – résultats

Table 7

Clinical outcome for each indication,.

Surgical indication	No. papers	No. patients evaluated	Good Outcome	Fair Outcome	Poor Outcome	Dead/lost during the follow up
Cancer Pain/post radiation	13	130 (10.19%)	98 (75.4%)	4 (3.1%)	24 (18.4%)	4 (3.1%)
Brachial plexus avulsion	25	717 (56,23%)	436 (60,80%)	150 (20,92%)	118 (16,45%)	13 (1,83%)
Spinal cord injury	15	301 (23,61%)	168 (55.8%)	35 (11.6%)	82 (27.3%)	16 (5.3%)
Phantom limb pain	8	49 (3,85%)	22 (44.9%)	14 (28.6%)	13 (26.5%)	–
Post herpetic neuralgia	9	78 (6.12%)	40 (51.2%)	14 (18%)	24 (30.8%)	–
Total	46	1275	764	217	261	33

Table 8

Medium (< 3 years) and long term (> 3 years) follow up outcome evaluation for single indication.

Indication	Medium term follow-up				Long term follow-up			
	Patients	Good	Fair	Poor	Patients	Good	Fair	Poor
Cancer pain	125	97 (77.6%)	4 (3.2%)	24 (19.2%)	1	1 (100%)	0	0
PBA	274	162 (59.1%)	55 (20.1%)	57 (20.8%)	439	280 (63,78%)	98 (22,32%)	61 (13,9%)
SCI	132	76 (57.6%)	20 (15.1%)	36 (27.3%)	153	92 (60.2%)	15 (9.8%)	46 (30%)
PLP	32	16 (50%)	6 (18.7%)	10 (31.3%)	17	6 (35.3%)	8 (47%)	3 (17.7%)
PHN	39	29 (74.4%)	1 (2.6%)	9 (23%)	39	11 (28.2%)	13 (33.3%)	15 (38.5%)
TOT	602				649			

DREZ – résultats



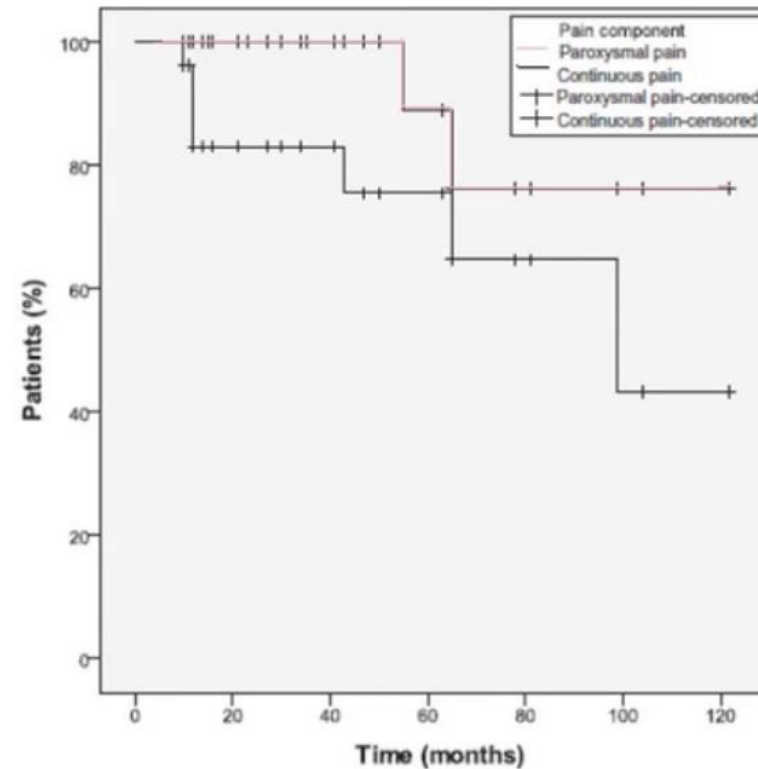
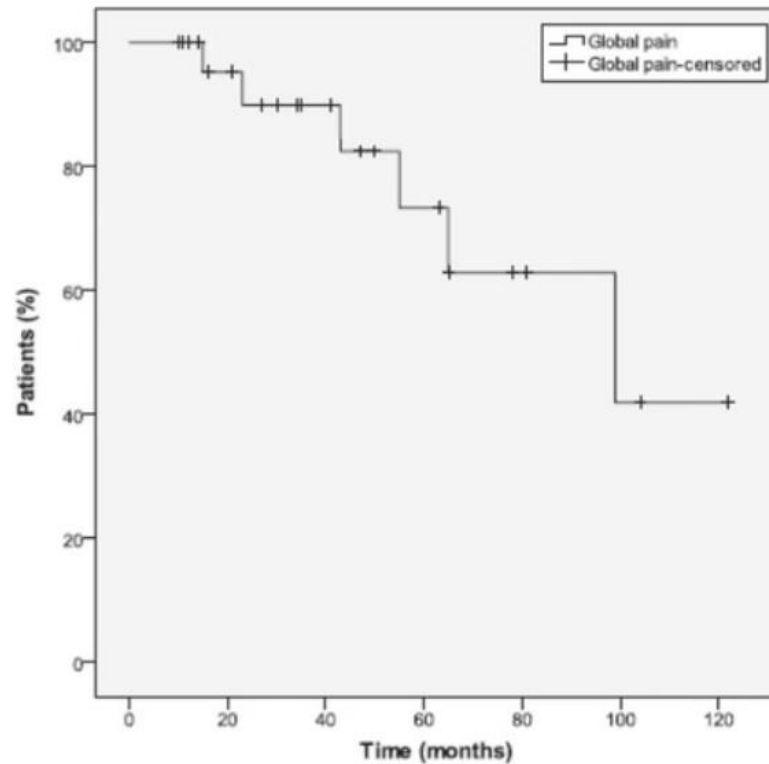
Clinical note

Dorsal root entry zone lesioning for pain after brachial plexus avulsion: Results with special emphasis on differential effects on the paroxysmal versus the continuous components. A prospective study in a 29-patient consecutive series

Faycal Aichaoui^{a,*}, Patrick Mertens^{a,b}, Marc Sindou^a

^a Department of Neurosurgery, P. Wertheimer Neurological Hospital, Hospices Civils de Lyon, Université Lyon 1, Lyon, France

^b Institut National de la Santé et de la Recherche Médicale (INSERM U8), Lyon, France

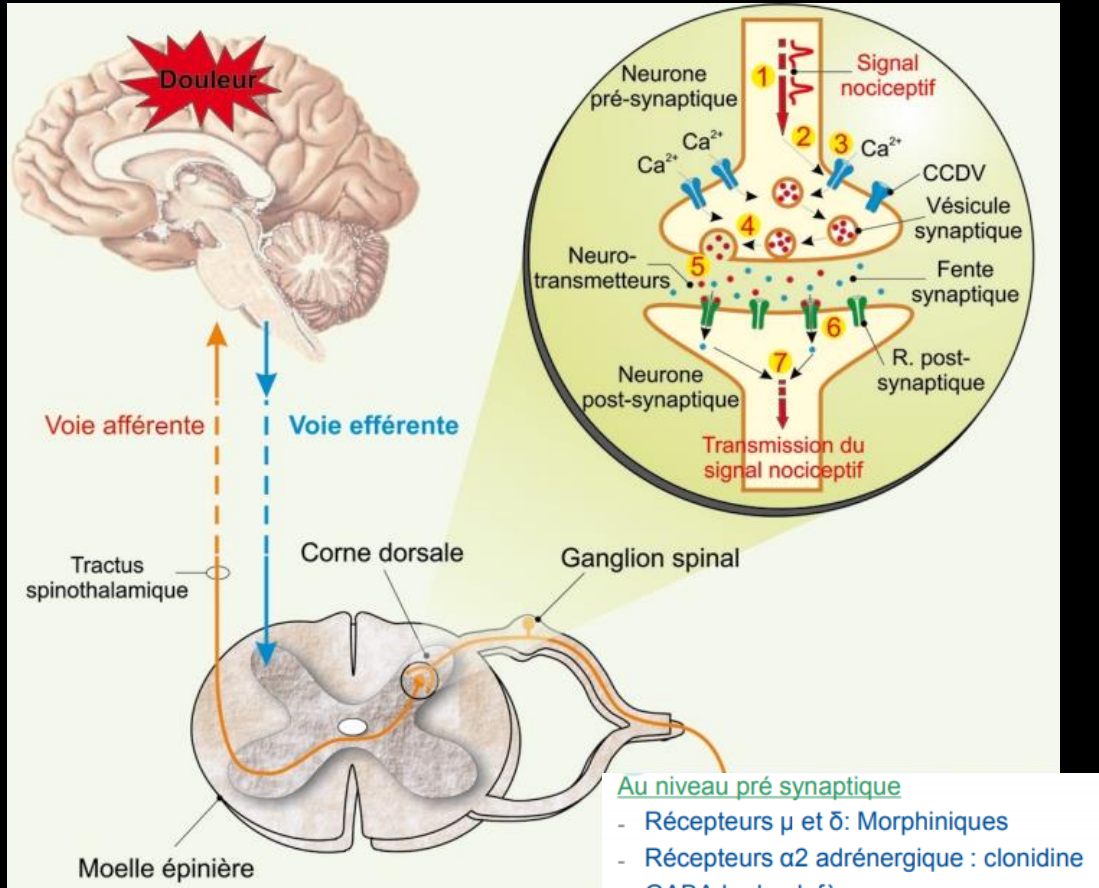


Pain was controlled with or without any additional nonopioid drugs in 75-80%

Aichaoui et al. Pain, 2011.

Médications intrathécales

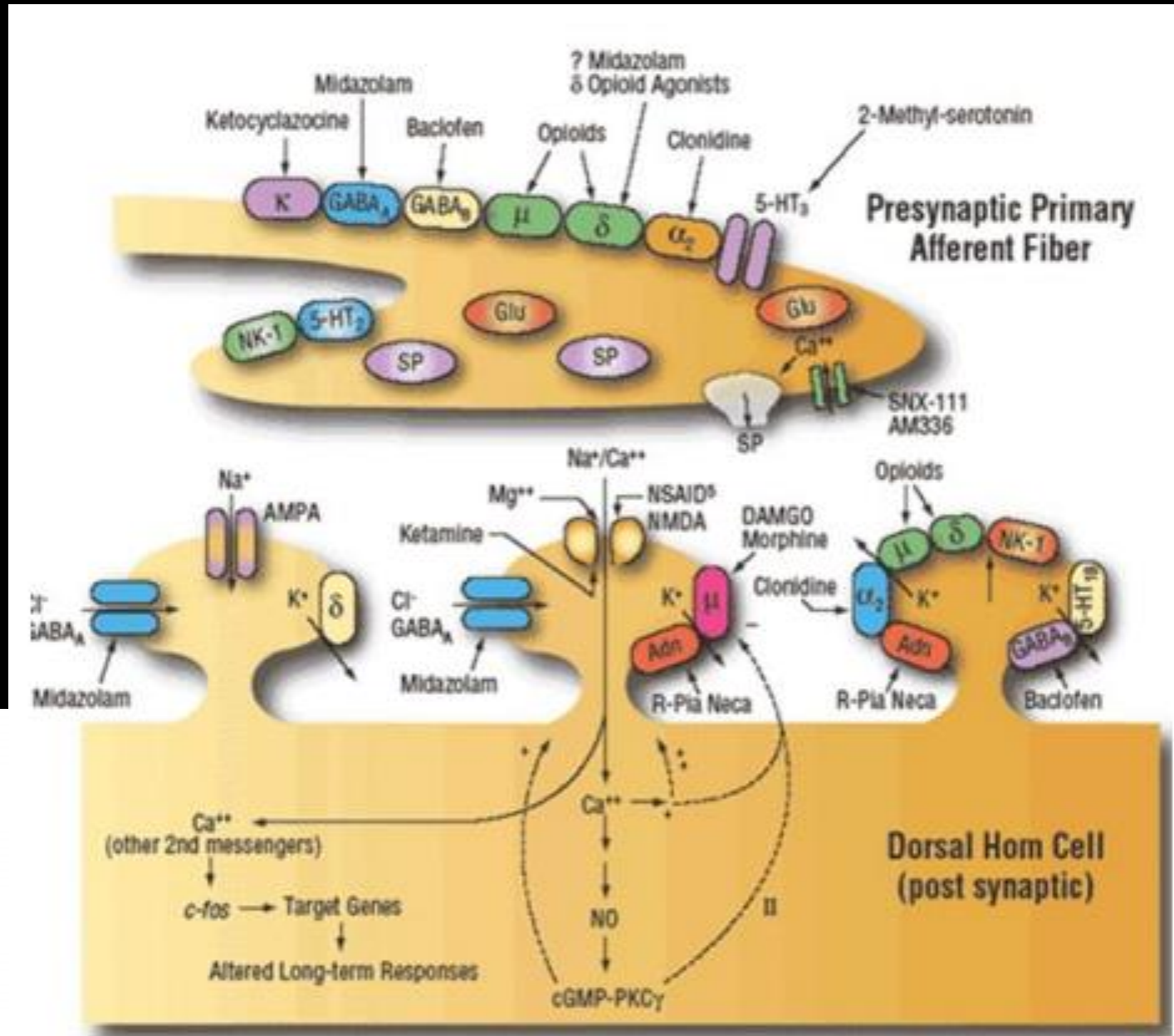
- **Principe**
- Distribuer les antalgiques au plus près des récepteurs médullaires pour :
 - diminuer les doses des analgésiques administrés par voie systémique (per os : 300mg → Iv : 100mg → péridural : 10 mg → IT : 1mg)
 - diminuer les effets secondaires liés aux traitements par voie systémique

Au niveau pré synaptique

- Récepteurs μ et δ : Morphiniques
- Récepteurs α_2 adrénergique : clonidine
- GABA b : baclofène
- Canaux calciques : ziconotide

Au niveau post synaptique

- Récepteurs μ et δ : Morphiniques
- Récepteurs α_2 adrénergique : clonidine
- NMDA : kétamine
- Canaux sodiques : Anesthésiques Locaux



Narrative review of intrathecal drug delivery (IDD): indications, devices and potential complications

Michele Antonio Capozza, Silvia Triarico, Stefano Mastrangelo, Giorgio Attinà, Palma Maurizi, Antonio Ruggiero

Médications intrathécales

- **Indications:**
- Avant tout : validation en RCP +++
- Douleurs nociceptives de cancer (EdV > 3 mois)
 - Chroniques, réfractaires
- Douleurs neuropathiques secondaires à un traumatisme médullaire, avec atteinte des cordons postérieurs

Table 1 Disease indications for IDD (modified by PACC) (2)

Axial neck or back pain (not a surgical candidate)

Multiple compression fractures

Discogenic pain

Spinal stenosis

Diffuse multiple-level spondylosis

Failed back surgery syndrome

Abdominal/pelvic pain

Visceral

Somatic

Extremity pain

Radicular pain

Joint pain

Complex regional pain syndrome

Trunk pain

Postherpetic neuralgia

Post-thoracotomy syndromes

Cancer pain, direct invasion and chemotherapy-related

Analgesic efficacy with systemic opioid delivery complicated by intolerable side effects

IDD, intrathecal drug delivery; PACC, Polyanalgesic Consensus Conference.

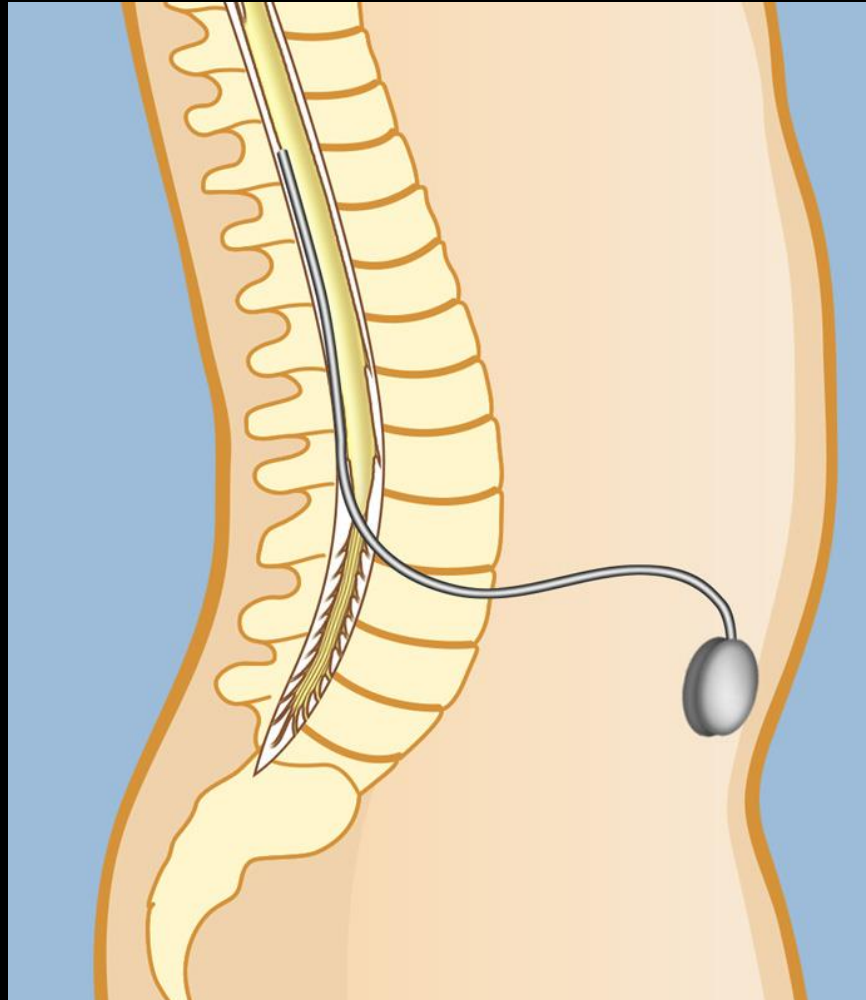
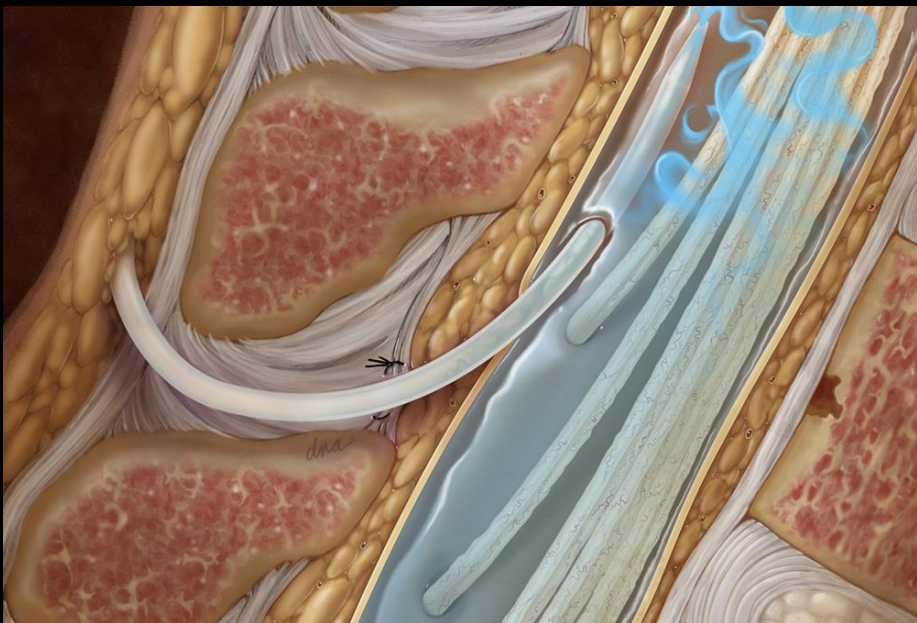
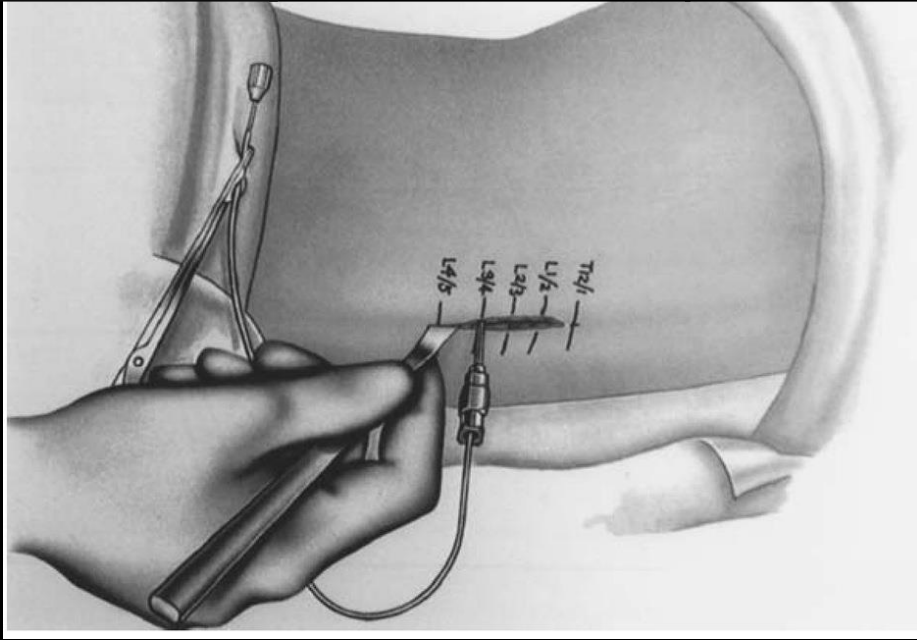
Anatomie

Stimulation
médullaire

DREZotomie

INTRATHÉCAL

Technique chirurgicale



Morphine

- Actif sur les canaux μ et delta pré et post synaptiques
- Dépresseur respiratoire
- Mais antidote (Naloxone)
- Effets stables dans le temps (1/2 vie IT : 73 et 140 min)
- Effet en 5-10 min
- Mais dépendance
- Et risque de diminution de l'effet antalgique avec le temps
- Surveillance de l'apparition d'effets secondaires

REVIEW



A safety review of approved intrathecal analgesics for chronic pain management

Alan Chalil^{a,*}, Michael D. Staudt^{b,c,*}, Tessa A. Harland^{d,*}, Elizabeth M. Leimer^e, Ravneet Bhullar^f and Charles E. Argoff^g

^aDepartment of Clinical Neurological Sciences, London Health Sciences Centre, Western University, London, Ontario, Canada; ^bDepartment of Neurosurgery, Oakland University William Beaumont School of Medicine, Rochester, Michigan, USA; ^cMichigan Head and Spine Institute, Southfield, Michigan, USA; ^dDepartment of Neurosurgery, Albany Medical College, Albany, New York, USA; ^eDepartment of Anesthesiology & Perioperative Medicine, Oregon Health and Science University, Portland, Oregon, USA; ^fDepartment of Anesthesiology, Albany Medical College, Albany, New York, USA; ^gDepartment of Neurology, Albany Medical College, Albany, New York

Table 1. Drug summary: morphine.

Drug Name	Morphine
Phase	FDA Approved
Indication	Chronic refractory cancer and non-cancer pain
Mechanism of action	μ -opioid receptor agonist
Routes of administration	Intrathecal
Chemical Structure	$C_{17}H_{19}NO_3$
Randomized Controlled Trials	Smith TJ et al. Randomized clinical trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain: impact on pain, drug-related toxicity, and survival. <i>J Clin Oncol.</i> 1 October 2002;20 [19]:4040–9. Raphael JH et al. Randomized, double-blind controlled trial by dose reduction of implanted intrathecal morphine delivery in chronic non-cancer pain. <i>BMJ Open.</i> 31 July 2013;3 [7]:e003061.

ZICONOTIDE (Prialt)

- Actif sur les canaux calciques
- Non dépresseur respiratoire
- Effets stables dans le temps
- Demi vie 4h30, pic de perfusion à 5 h
- Pas de toxicité à long terme connue
- Degradé par les peptidases
- Début à 0,5µg/jour et réadaptation en fonction de l'efficacité et des effets secondaires.
- La dose peut être augmentée par paliers de 0,5µg tous les 3 à 15 jours jusqu'à une dose palier de 1,5 à 2,1µg/j (dose maximale 21µg/j).
- Surveillance de l'apparition d'effets secondaires (Neuro psychiatriques essentiellement)
- L'augmentation lente par posologies faibles a permis de réduire de manière significative les effets secondaires importants et fréquents (89%) observés dans les débuts d'utilisation.

Table 2. Drug summary: ziconotide.

Drug Name	Ziconotide
Phase	FDA Approved
Indication	Chronic refractory cancer and non-cancer pain
Mechanism of action	Non-opioid calcium channel antagonist
Routes of administration	Intrathecal
Chemical Structure	$C_{102}H_{172}N_{36}O_{32}S_7$
Randomized Controlled Trials	Staats PS et al. Intrathecal ziconotide in the treatment of refractory pain in patients with cancer or AIDS: a randomized controlled trial. <i>JAMA</i> . 7 January 2004;291 [1]:63–70 Wallace MS et al. Intrathecal ziconotide in the treatment of chronic nonmalignant pain: a randomized, double-blind, placebo-controlled clinical trial. <i>Neuromodulation</i> . 2006 Apr;9 [2]:75–86. Rauck RL et al. A randomized, double-blind, placebo-controlled study of intrathecal ziconotide in adults with severe chronic pain. <i>J Pain Symptom Manage</i> . 2006 May;31 [5]:393–406.

	Morphine	Ropivacaïne Bupivacaïne	Ziconotide
Posologie initiale	Entre 1/50 et 1/100 par rapport à l'IV en mg/jour	6 à 8 mg/jour	0,25 à 0,50 µg/jour
Effets secondaires	• Détresse respiratoire • Rétention Aigue Urinaire : RAU • Œdèmes MI	• RAU • hypoTA • peu de bloc moteur • si bloc ou clonie des membres inférieurs: augmentation trop brutale	• Neuropsych: vertiges, hallucinations, confusion, syndrome dépressif, agressivité
Incrémentation	Quotidienne	Quotidienne	Toutes les 48 à 72H
Stabilité à 30 jours	excellente	excellente	-1%/ jour

Intrathecal Therapy for Chronic Pain: A Review of Morphine and Ziconotide as Firstline Options

Timothy R. Deer, MD,* Jason E. Pope, MD,† Michael C. Hanes, MD,‡ and Gladstone C. McDowell II, MD§

**The Center for Pain Relief, Spine and Nerve Centers of The Virginias, Charleston, West Virginia; †Thrive Clinic, Santa Rosa, California; ‡Jacksonville Spine Center, Jacksonville, Florida; §Integrated Pain Solutions, Columbus, Ohio, USA*

Correspondence to: Timothy R. Deer, MD, The Center for Pain Relief, The Spine and Nerve Center of the Virginias, 400 Court Street, Ste 100, Charleston, WV, USA 25301. Tel: 304-347-6120; Fax: 304-347-6126; E-mail: doctdeer@aol.com.

Table 6. Advantages and disadvantages/considerations for IT morphine and ziconotide

	Morphine	Ziconotide
Advantages	Extensive safety and efficacy profile for systemic administration Tolerability likely in oral opioid-experienced patients	Efficacy demonstrated in randomized placebo-controlled studies No tolerance or withdrawal; may be discontinued abruptly No harmful effects of overdose No reported cases of granulomas
Disadvantages/considerations	Risk of serious AEs (e.g., respiratory depression, granulomas) Tolerance may necessitate dose increases; should not be withdrawn abruptly Development of opioid-induced hyperalgesia	Contraindicated in patients with a history of psychosis Risk of neurologic AEs (e.g., dizziness, confused state) May cause elevations in creatinine kinase

AE = adverse event; CNS = central nervous system; IT = intrathecal.

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Table 2. PACC 2016 recommendations for use of IT opioids and ziconotide in cancer and noncancer pain [9,40]

Statement	USPSTF Evidence Level*	USPSTF Recommendation Grade†	PACC Consensus Level‡
IT therapy with opioids should be utilized for active cancer-related pain	I	A	Strong
IT therapy with ziconotide should be utilized for active cancer-related pain	I	A	Strong
IT therapy with opioids should be utilized for active noncancer pain	III	B	Strong
IT therapy with ziconotide should be utilized for active noncancer pain	I	A	Strong

Figure adapted with permission from: Deer et al, The Polyanalgesic Consensus Conference (PACC): Recommendations on intrathecal drug infusion systems best practices and guidelines. *Neuromodulation* 2017;20(2):96–132 [9]. Additional data reprinted from: Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: A review of the process. *Am J Prev Med* 2001;20(3 Suppl):21–35 [40].

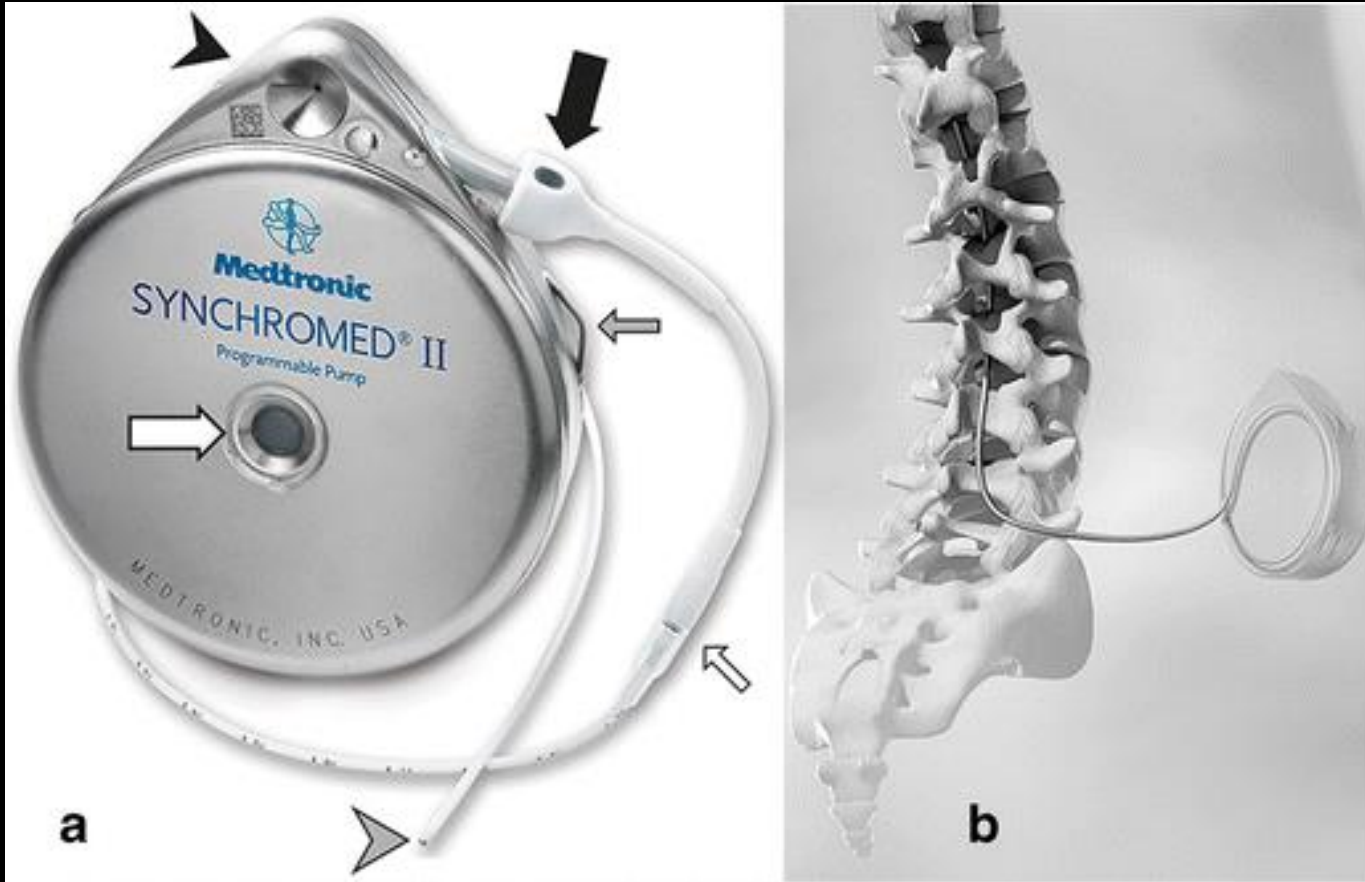
IT = intrathecal; PACC = Polyanalgesic Consensus Conference; USPSTF = United States Preventive Services Task Force.

*Evidence grades: I, at least one controlled and randomized clinical trial, properly designed; II-1, well-designed, controlled, nonrandomized clinical trials; II-2, cohort or case studies and well-designed controls, preferably multicenter; II-3, multiple series compared over time, with or without intervention and surprising results in noncontrolled experiences; III, clinical experience-based opinions, descriptive studies, clinical observations, or reports of expert committees.

†Recommendation grades: A, extremely recommendable (good evidence that the measure is effective and benefits outweigh the harms); B, recommendable (at least moderate evidence that the measure is effective and benefits exceed harms); C, neither recommendable nor inadvisable (at least moderate evidence that the measure is effective, but benefits are similar to harms and a general recommendation cannot be justified); D, inadvisable (at least moderate evidence that the measure is ineffective or that the harms exceed the benefits); I, insufficient, low-quality, or contradictory evidence (the balance between benefit and harms cannot be determined).

‡Level of consensus among members of the PACC: strong, >80% consensus; moderate, 50% to 79% consensus; weak, <49% consensus.

Complications



- 1. Mécaniques
- 2. Médicamenteuses
 - Sur-dosage
 - Sous dosage
- 3. Infectieuses

Résultats

- D'après les recommandations SFAR-SFETD,
- « toutes les études rapportent des résultats positifs, avec une réduction des scores de douleurs.
- 4 études sur 13 montrent une amélioration de la qualité de vie,
- 4 une amélioration fonctionnelle,
- 8 la diminution des traitements systémiques
- 2 une diminution du nombre des consultations ».

Résultats : Pain and Cancer (morphine IT)

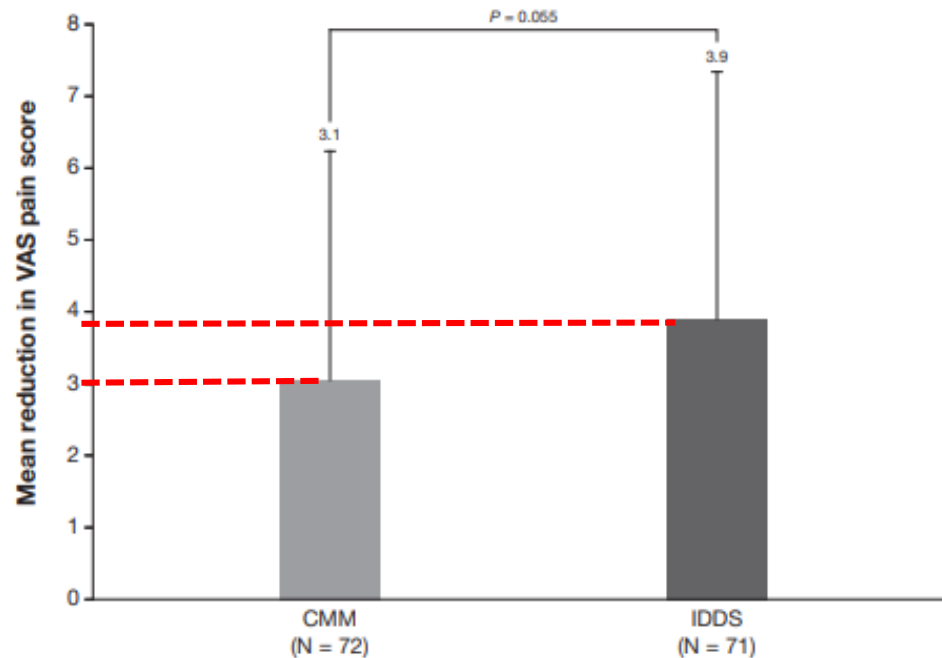


Figure 1. Pain reduction with intrathecal (IT) opioids as the first agent in pump in patients with cancer pain [29]. Patients with cancer pain received comprehensive medical management (CMM; all pain therapy except spinally administered medications, cordotomy, or other similar neurosurgical interventions) or IT morphine or hydromorphone therapy for four weeks. After four weeks of treatment, patients who received IT opioids had a nonsignificantly greater reduction in pain, as measured on a continuous visual analog scale ranging from 0 (no pain) to 10 (worst pain imaginable), than those who received CMM. Figure created with data from: Smith TJ, Staats PS, Deer T, et al. Randomized clinical trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain: Impact on pain, drug-related toxicity, and survival. *J Clin Oncol* 2002;20(19):4040–9 [29]. CMM = comprehensive medical management; IDDS = implantable drug delivery system; VAS = visual analog scale.

Intrathecal Therapy for Chronic Pain: A Review of Morphine and Ziconotide as Firstline Options

Timothy R. Deer, MD,* Jason E. Pope, MD,[†] Michael C. Hanes, MD,[‡] and Gladstone C. McDowell II, MD[§]

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Résultats (morphine)

- Depuis les premiers essais cliniques chez l'homme à la fin des années 1970, de nombreux travaux ont été publiés pour évaluer l'analgésie intrathécale en cancérologie.
- Un seul essai multicentrique randomisé a mis en évidence une diminution de plus de 20 % de la douleur à un mois chez 84,5% des patients dans le groupe traité par un dispositif intrathécal contre 70 % dans le groupe témoin. Cette étude retrouve également une diminution de 50 % de l'indice de toxicité du traitement antalgique dans le groupe intrathécal par rapport au groupe témoin.

Résultats (Prialt)



REVIEW ARTICLE

Ziconotide Monotherapy: A Systematic Review of Randomised Controlled Trials

Morag E. Brookes^{a,c,*}, Sam Eldabe^a and Alan Batterham^b

Table 1. Study characteristics.

Author/ Year	Funding	Target Population	Sample Size	Number of Centres	Average Number Per Centre	Age Range	Randomisation Ratio	Study Group (n)	Control Group (n)	Primary Outcome Measure
Staats, 2004 [39]	*Neurex/ Élan Pharma Inc. and †Medtronic	Cancer and AIDS	111	32 in USA, Australia, Netherlands	3-4	24-85 yrs.	2:1 2- Ziconotide 1- placebo	68	40	VASPI
Wallace, 2006 [40]	Élan Pharma Inc.	Chronic non- malignant pain	255	43 in USA, Belgium, Australia, Austria, Switzerland	5-6	18yrs +	2:1 2 - Ziconotide 1- Placebo	169	86	VASPI
Rauck, 2006 [41]	Élan Pharma Inc.	Severe Chronic Pain	220	39 in USA	5-6	No specific age mentioned. Mean (SD)	1:1 1- Ziconotide 1- Placebo	112	108	VASPI

*Neurex merged with Élan Pharmaceuticals Inc. which then merged with Eisai. These companies manufacture ziconotide (Prialt™)

†Medtronic manufacture the Intrathecal Drug Delivery Systems – SynchroMed pumps that administer the ziconotide or other drugs.

Résultats (Prialt)

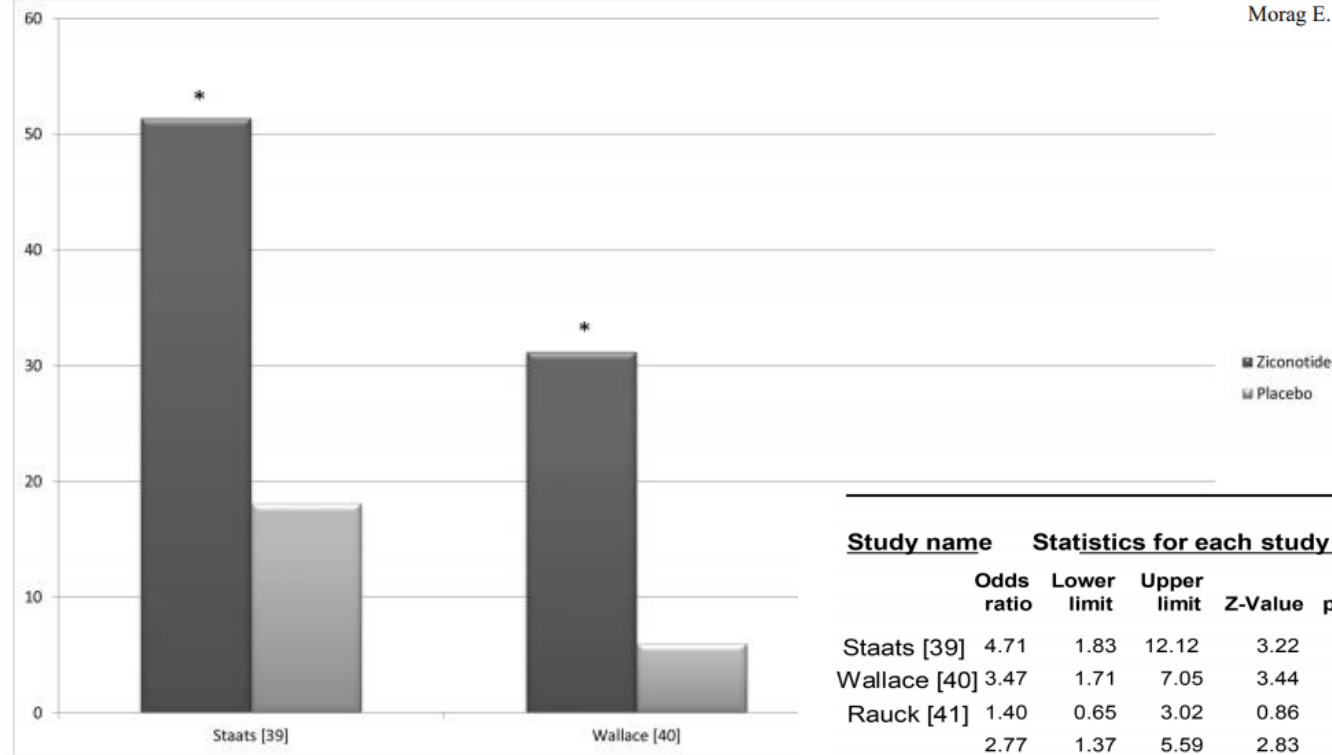
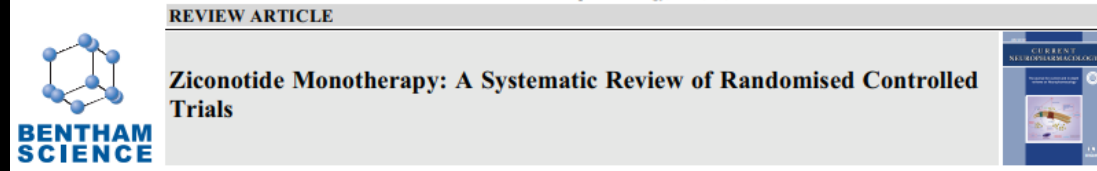


Fig. (7). Percentage change in VASPI score from baseline to end of titration p



Morag E. Brookes^{a,c,*}, Sam Eldabe^a and Alan Batterham^b

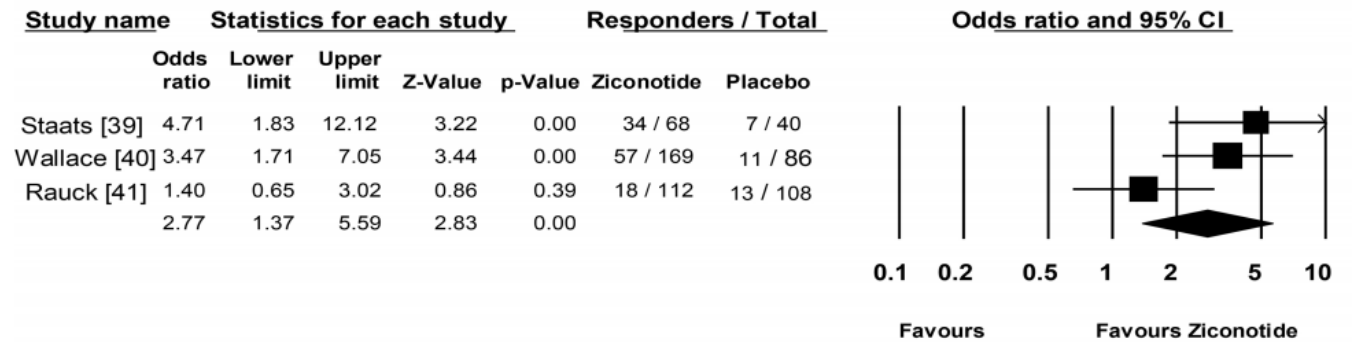


Fig. (8). Forest plot from a random effects meta-analysis of the effect of ziconotide on neuropathic pain.

Si l'on résume ...

- **1. Après échec des techniques médicales bien tenues**
- Douleurs lombaires + radiculaires post arthrodèse : SCS
- Douleurs radiculaires : SCS
- Douleurs sur SC injury (ischémie médullaire) : SCS, DREZ, Ziconotide IT
- Douleurs du membre fantôme : SCS, DREZ
- Douleurs sur Avulsion plexus : DREZ
- Douleurs post-zostériennes : SCS, DREZ
- Douleurs cancéreuses localisées (Pancoast Tobias) : DREZ
- Douleurs cancéreuses diffuses : Morphine IT
- Douleurs AIDS : Ziconotide IT



Intérêt des
PES +++