rTMS et douleurs neuropathiques

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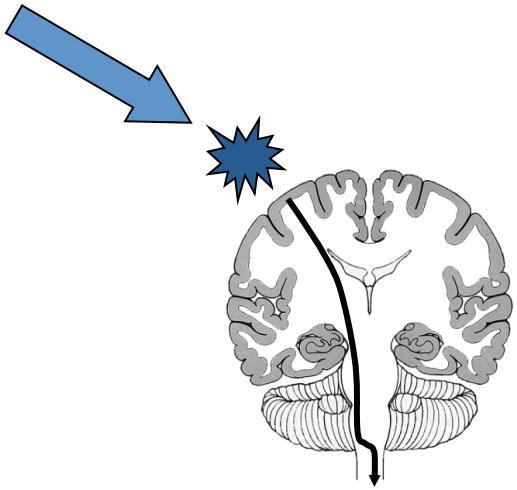
COMMENT ÇA MARCHE LA RTMS ET LES AUTRES NIBS?

TMS: Transcranial Magnetic Stimulation
Principe



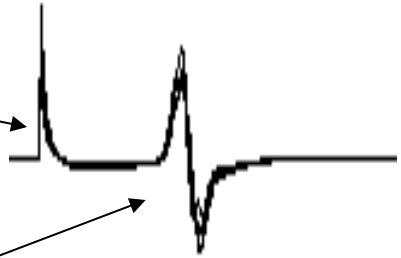
Bobine de stimulation

stimulateur

Recueil du PEM à l'aide d'électrode
(EMG: électromyographie)

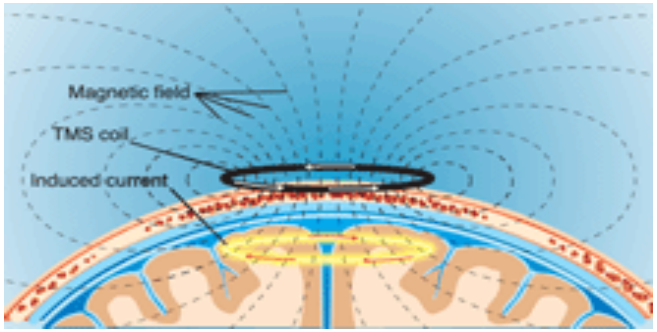
Activation
Voie cortico-spinale

Artefact de stimulation



PEM: potentiel évoqué moteur reflète l'activité musculaire induite par la stimulation corticale

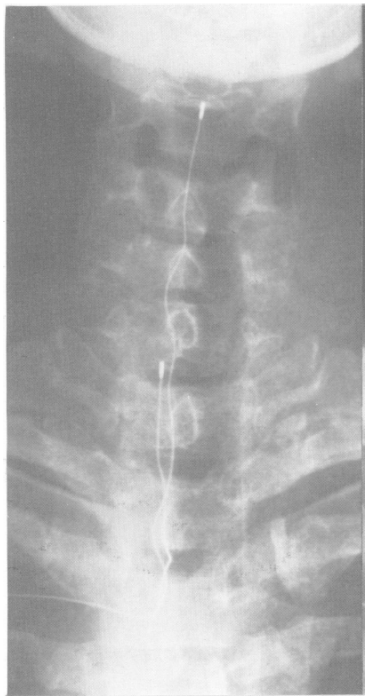
TMS active sélectivement les neurones à orientation horizontale



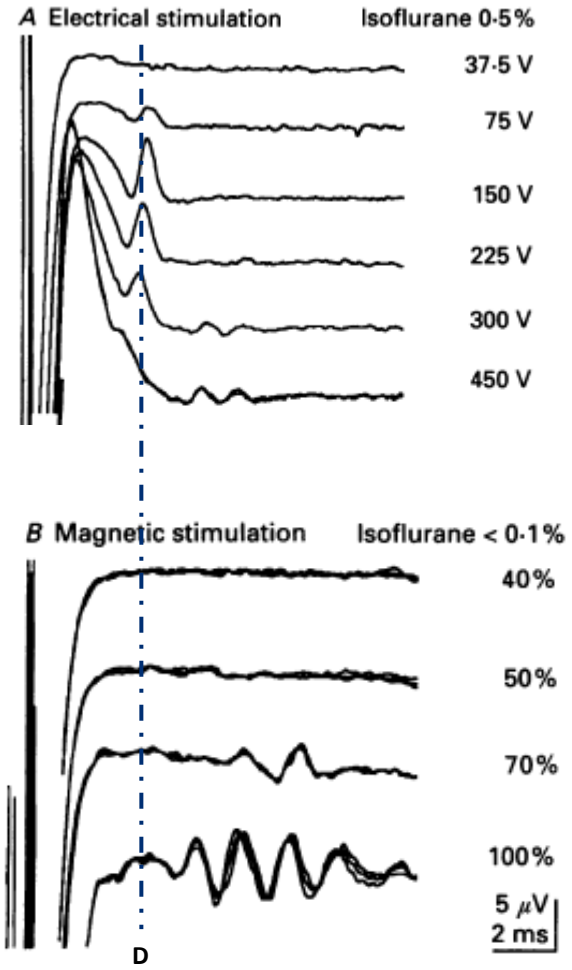
TMS permet de stimuler à travers (« trans ») le crâne
et « mime » les stimulations corticales (ICMS) chez l'animal

Volées corticospinales induites par TMS

Enregistrements épiduraux



Volées corticospinales induites



Burke *al*. *Journal of Physiology* (1993) 470: 383-393

Différentes formes de sonde TMS

Sonde circulaire 50 mm

Sonde circulaire70 mm

Sonde circulaire 90 mm

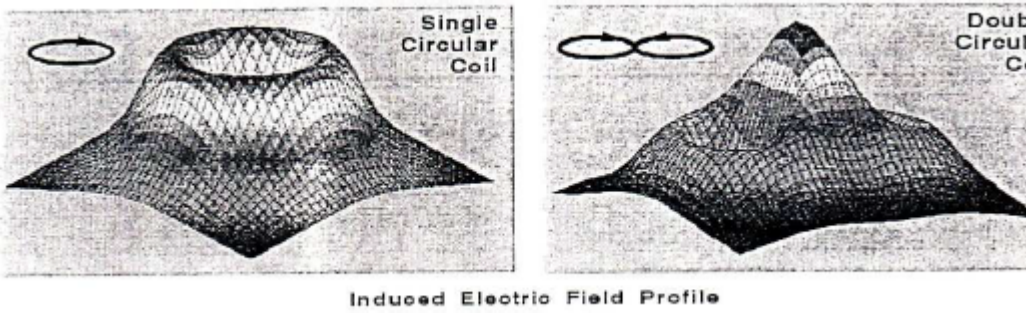
Sonde papillon 25 mm

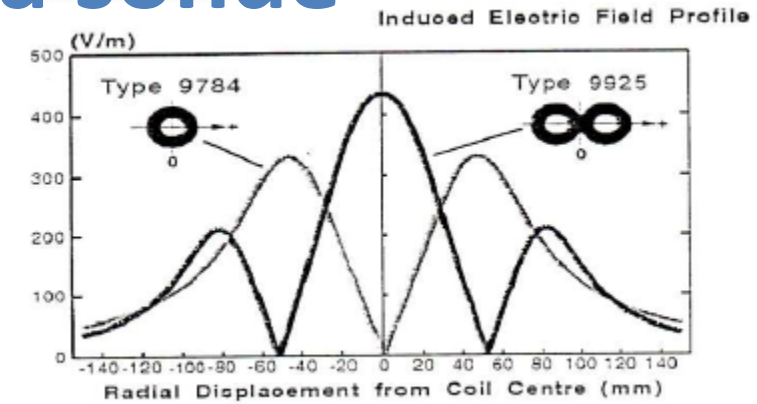
Sonde papillon 70 mm

Sonde double cône

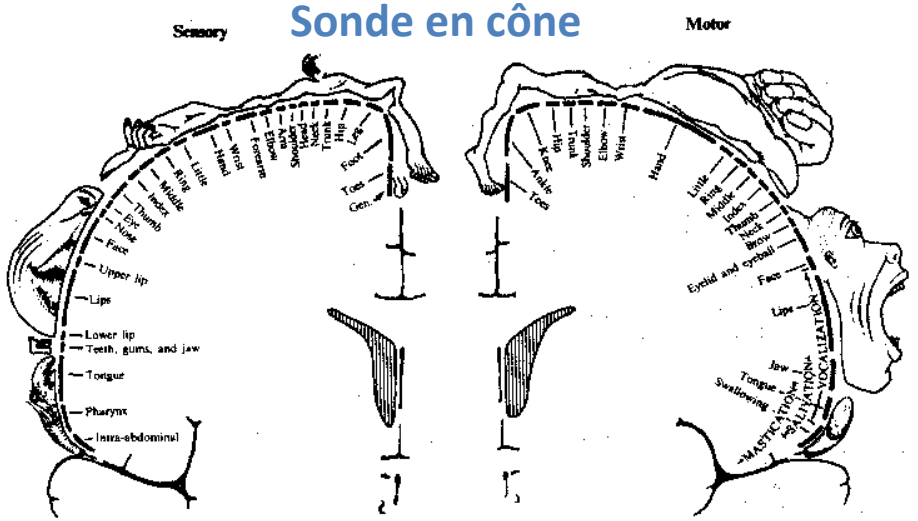
Sonde double cône
70 mm réfrigérée

Champ électrique induit en fonction de la forme de la sonde





Sonde en cône

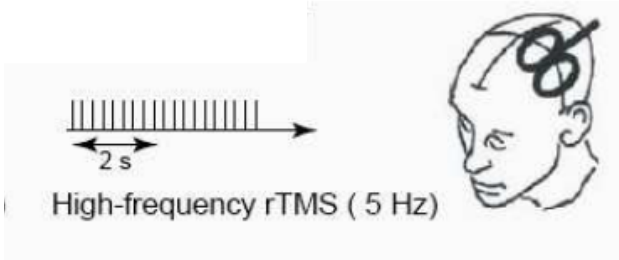


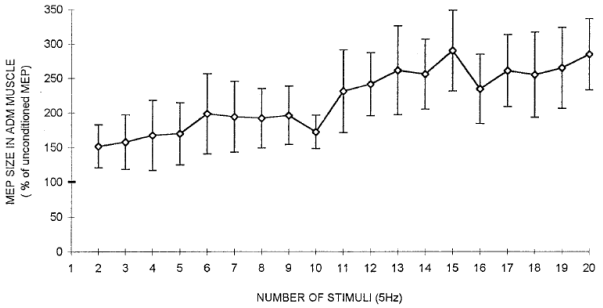
Sonde en papillon
Sonde circulaire

rTMS

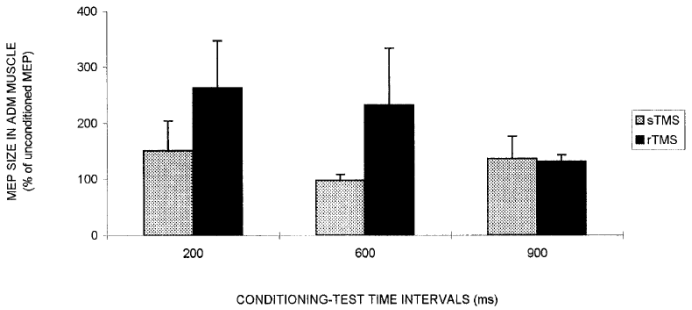
rTMS haute fréquence 5Hz

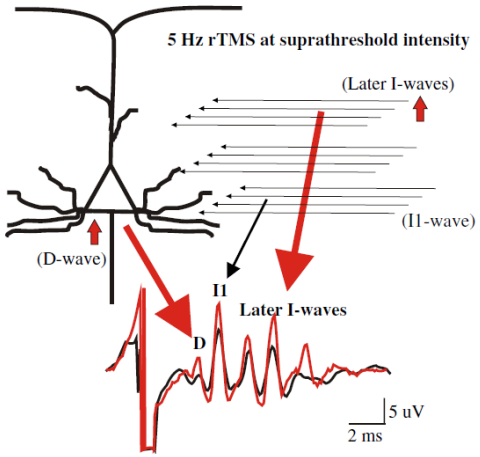
Le PEM ⬆ avec le nb de stimuli



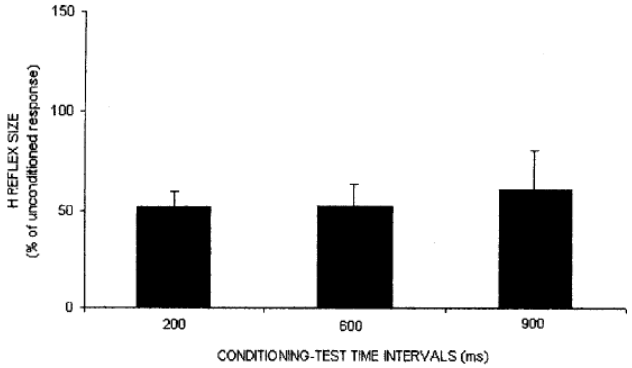


ISI 200 et 600





Pas d'effet sur le H aux ISI 200 et 600



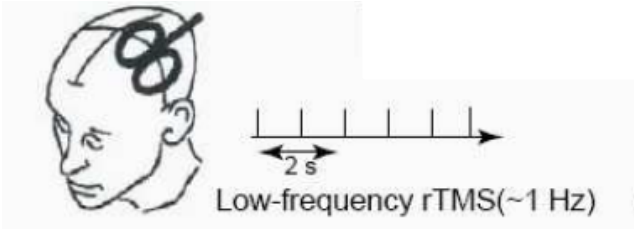
Di Lazzaro et *al*. *Clinical Neurophysiology (*2010) 121:464-573c

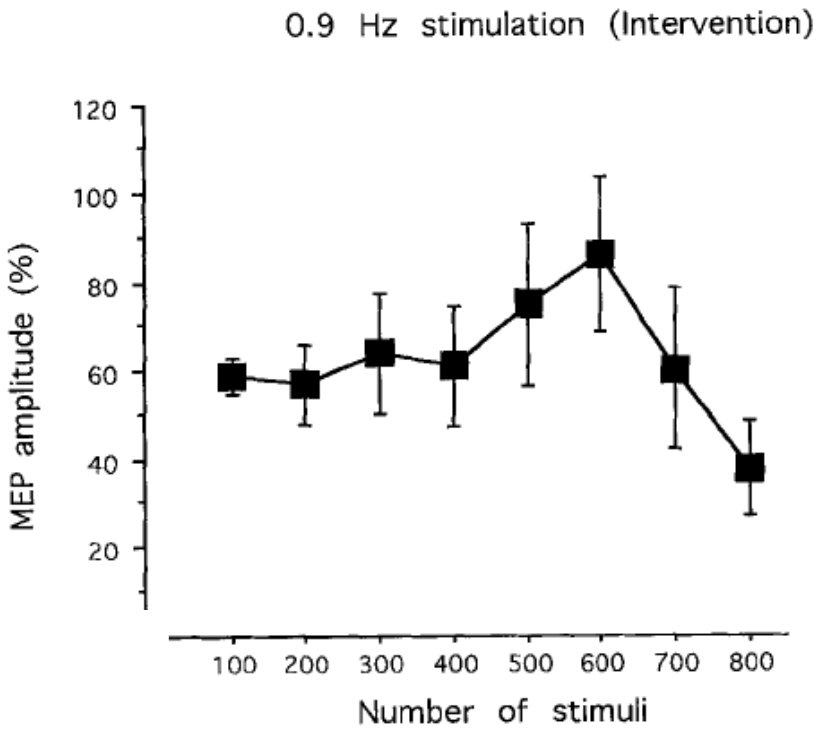
Berardelli et *al*.Experimental Brain Research *(*1998) 122:79-84

rTMS

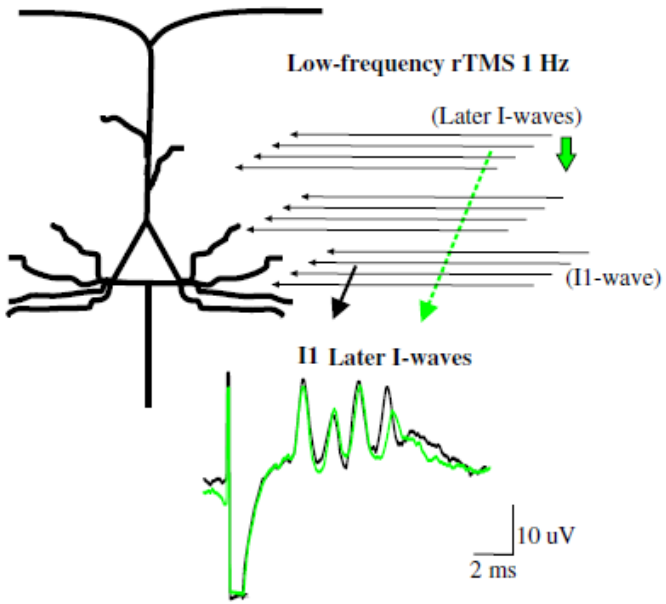
rTMS basse fréquence 1Hz

15 min de stimulation
TMS =115% RMT



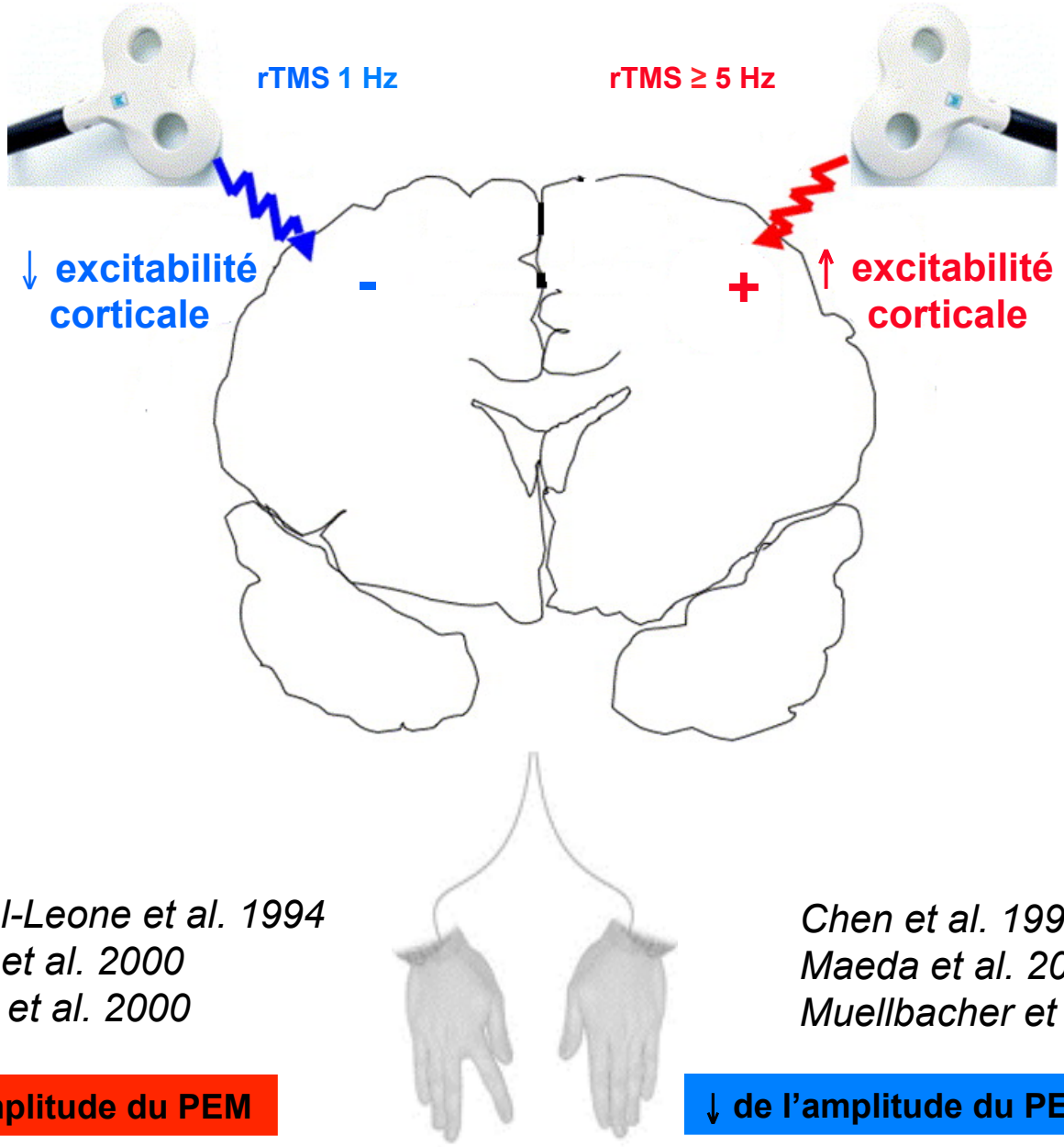


Chen et *al*.Neurology *(*1997) 48:1398 -1403c



Di Lazzaro et *al*. *Clinical Neurophysiology (*2010) 121:464-573c

rTMS et Cortex moteur : rôle de la fréquence



Pascual-Leone et al. 1994
Maeda et al. 2000
Romeo et al. 2000

↑de l'amplitude du PEM

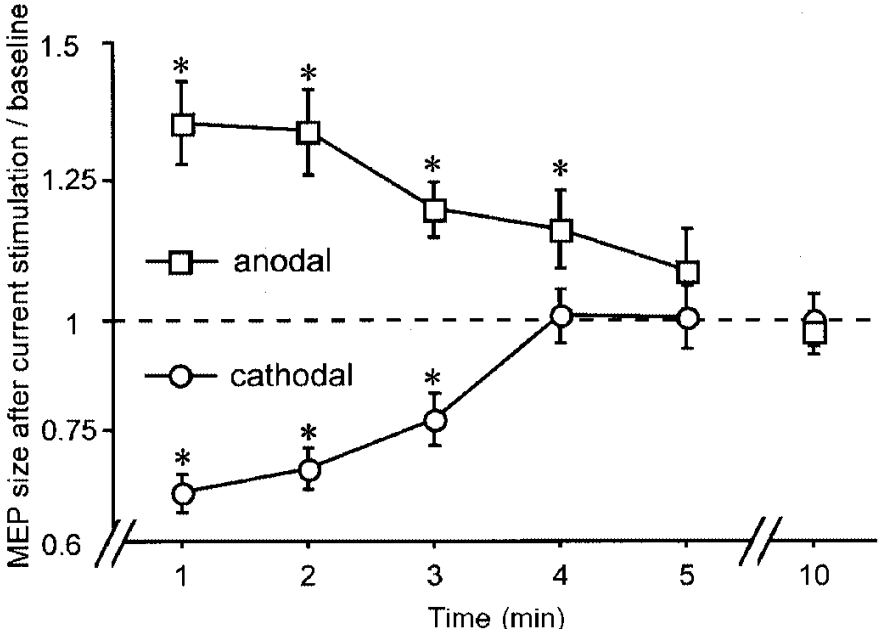
Chen et al. 1997
Maeda et al. 2000
Muellbacher et al. 2000

↓ de l'amplitude du PEM

Courants galvaniques :

tDCS (transcranial Direct Current Stimulation)

- Stimulation anodale: excitation
- Stimulation cathodale : Inhibition



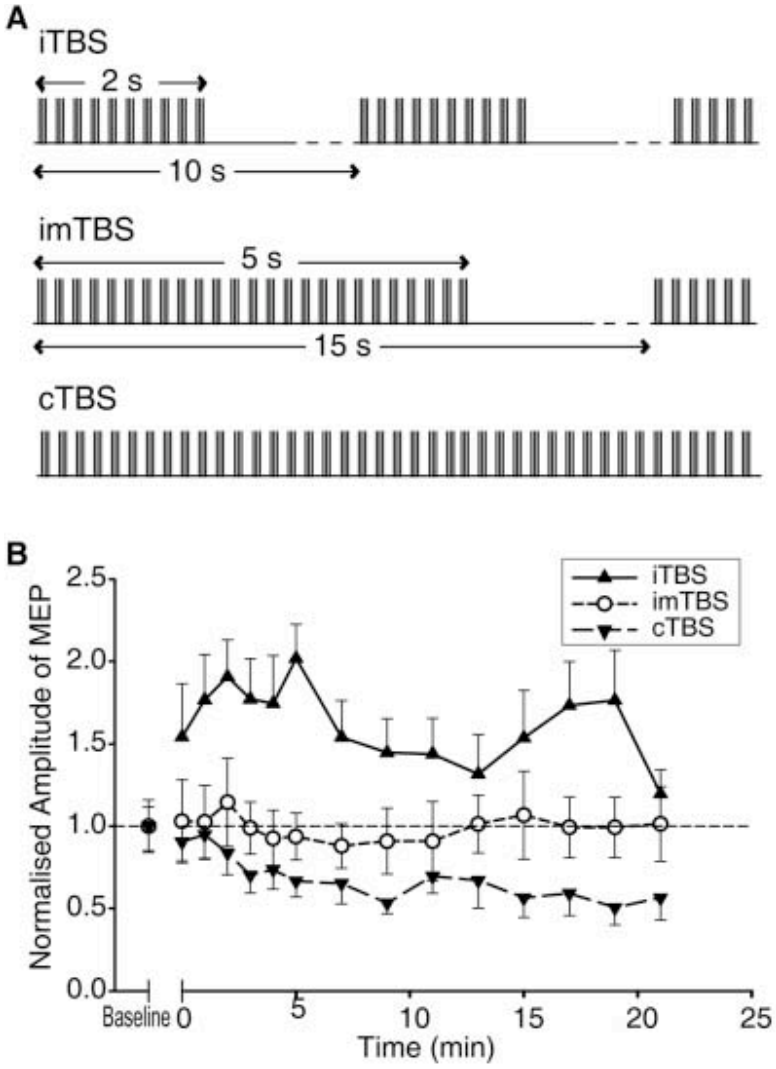
✧ Stimulation placebo

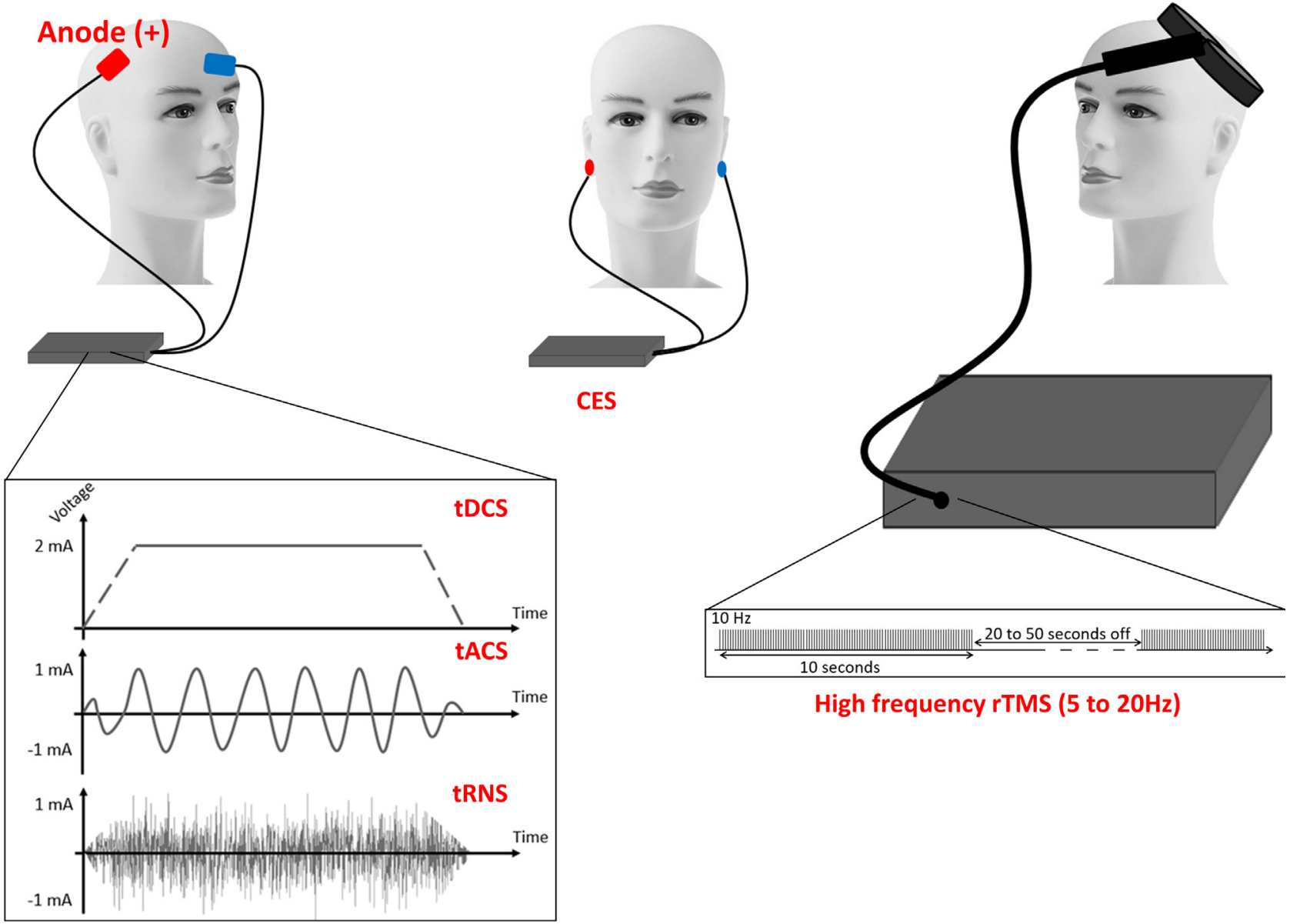
Nitsche et al. 2000

Theta burst Stimulation (TBS)

- Train de 3 coups
- fréquence 50Hz
- toutes les 200 ms (5Hz)
- 80% seuil moteur
- Post-effets + longs pour durée stim très courte < 60 sec (600 pulses (sur M1))

  Huang et al. 2005





D'après Moisset et Lefaucheur

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EST-CE EFFICACE SUR LES DOULEURS NEUROPATHIQUES?

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journal homepage: www.elsevier.com/locate/clinph

Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS)

Jean-Pascal Lefaucheur [a,b,*], Nathalie André-Obadia [c,d], Andrea Antal [e], Samar S. Ayache [a,b], Chris Baeken [f,g], David H. Benninger [h], Roberto M. Cantello [i], Massimo Cincotta [j], Mamede de Carvalho [k], Dirk De Ridder [l,m], Hervé Devanne [n,o], Vincenzo Di Lazzaro [p], Saša R. Filipović [q], Friedhelm C. Hummel [r], Satu K. Jääskeläinen [s], Vasilios K. Kimiskidis [t], Giacomo Koch [u], Berthold Langguth [v], Thomas Nyffeler [w], Antonio Oliviero [x], Frank Padberg [y], Emmanuel Poulet [z,aa], Simone Rossi [ab], Paolo Maria Rossini [ac,ad], John C. Rothwell [ae], Carlos Schönfeldt-Lecuona [af], Hartwig R. Siebner [ag,ah], Christina W. Slotema [ai], Charlotte J. Stagg [aj], Josep Valls-Sole [ak], Ulf Ziemann [al], Walter Paulus [e,1], Luis Garcia-Larrea [d,am,1]

Table 1
rTMS studies in chronic neuropathic pain (target: primary motor cortex).

Articles	Number of patients	Target, coil type	Control condition	Stimulation frequency and intensity	Number of pulses/session and number of sessions	Results	Class of the study
LF rTMS of M1 contralateral to pain side							
Lefaucheur et al. (2001a)	18	M1, F8c	Sham coil	0.5 Hz, 80% RMT	1000 pulses, 1 session	Non-significant pain relief (4% responders)	III
André-Obadia et al. (2006)	12	M1, F8c	Tilted coil	1 Hz, 90% RMT	1600 pulses, 1 session	Non-significant pain relief (0% responders)	III
Irlbacher et al. (2006)	27 (active: 20; control: 18)	M1, F8c	Sham coil (2 Hz)	1 Hz, 95% RMT	500 pulses, 5 sessions	Non-significant pain relief (6% responders)	III
Lefaucheur et al. (2006a)	22	M1, F8c	Sham coil	1 Hz, 90% RMT	1200 pulses, 1 session	Non-significant pain relief (14% responders)	II
Saitoh et al. (2007)	13	M1, F8c	Tilted coil	1 Hz, 90% RMT	500 pulses, 1 session	Non-significant pain relief (unknown % responders)	III
Lefaucheur et al. (2008b)	46	M1, F8c	Sham coil	1 Hz, 90% RMT	1200 pulses, 1 session	Non-significant pain relief (9% responders)	II
Recommendation: LF rTMS of M1 contralateral to pain side is probably ineffective in neuropathic pain (Level B)							
HF rTMS of M1 contralateral to pain side							
Lefaucheur et al. (2001a)	18	M1, F8c	Sham coil	10 Hz, 80% RMT	1000 pulses, 1 session	Significant pain relief (39% responders)	III
Lefaucheur et al. (2001b)	14	M1, F8c	Sham coil	10 Hz, 80% RMT	1000 pulses, 1 session	Significant pain relief (57% responders)	III
Lefaucheur et al. (2004b)	60	M1, F8c	Sham coil	10 Hz, 80% RMT	1000 pulses, 1 session	Significant pain relief (37% responders and 23% improvement)	II
Khedr et al. (2005b)	48 (active: 28; control: 20)	M1, F8c	Tilted coil	20 Hz, 80% RMT	2000 pulses, 5 sessions	Significant pain relief (79% responders)	I
André-Obadia et al. (2006)	12	M1, F8c	Tilted coil	20 Hz, 90% RMT	1600 pulses, 1 session	Non-significant pain relief (36% responders and 11% improvement)	III
Hirayama et al. (2006)	20	M1, F8c	Tilted coil	5 Hz, 90% RMT	500 pulses, 1 session	Significant pain relief (50% responders)	II
Irlbacher et al. (2006)	27 (active: 19; control: 18)	M1, F8c	Sham coil (2 Hz)	5 Hz, 95% RMT	500 pulses, 5 sessions	Non-significant pain relief (7% responders)	III
Lefaucheur et al. (2006a)	22	M1, F8c	Sham coil	10 Hz, 90% RMT	1200 pulses, 1 session	Significant pain relief (55% responders)	II
Saitoh et al. (2007)	13	M1, F8c	Tilted coil	5–10 Hz, 90% RMT	500 pulses, 1 session	Significant pain relief (50% responders)	III
André-Obadia et al. (2008)	28	M1, F8c	Sham coil	20 Hz, 90% RMT	1600 pulses, 1 session	Significant pain relief only with posteroanterior orientation of the coil (13% improvement)	II
Lefaucheur et al. (2008b)	46	M1, F8c	Sham coil	10 Hz, 90% RMT	1200 pulses, 1 session	Significant pain relief (43% responders)	II
Kang et al. (2009)	11 (spinal cord injury)	M1, F8c	Tilted coil	10 Hz, 80% RMT	1000 pulses, 5 sessions	Non-significant pain relief (14% improvement)	III
Ahmed et al. (2011)	27 (active: 17; control: 10)	M1, F8c	Tilted coil	20 Hz, 80% RMT	2000 pulses, 5 sessions	Significant pain relief (up to 2 months after rTMS)	II
André-Obadia et al. (2011)	45	M1, F8c	Sham coil	20 Hz, 90% RMT	1600 pulses, 1 session	Significant pain relief (10% improvement)	II
Lefaucheur et al. (2011b)	59	M1, F8c	Sham coil	10 Hz, 90% RMT	2000 pulses, 1 session	Significant pain relief (36% responders and 22% improvement for "active-sham" condition)	II
Hosomi et al. (2013)	64	M1, F8c	Active coil placed over inactive coil combined with electrical scalp stimulation	5 Hz, 90% RMT	500 pulses, 10 sessions	Significant short-term pain relief (20% responders and 4% improvement for "active-sham" condition), but no significant cumulative improvement	I
Jetté et al. (2013)	16 (spinal cord injury)	M1, F8c	Sham coil	10 Hz, 90% RMT (hand area), 110% RMT (leg area)	2000 pulses, 1 session	Significant pain relief for hand or leg area stimulation for 48 h (about 15% improvement)	III
André-Obadia et al. (2014)	20	M1, F8c	Sham coil	20 Hz, 90% RMT	1600 pulses, 1 session	Significant pain relief (15% improvement), predictive of subsequent positive outcome of implanted chronic motor cortex stimulation	III
Recommendation: definite analgesic effect of HF rTMS of M1 contralateral to pain side in neuropathic pain (Level A)							

Table 2
rTMS studies in complex regional pain syndrome type I (target: primary motor cortex).

Articles	Number of patients	Target, coil type	Control condition	Stimulation frequency and intensity	Number of pulses/session and number of sessions	Results	Class of the study
Complex regional pain syndrome of type I							
Pleger et al. (2004)	10	M1, F8c	Tilted coil	10 Hz, 110% RMT	1200 pulses, 1 session	Significant pain relief (70% responders, but short-lasting effect, <1 h)	III
Picarelli et al. (2010)	22 (active: 11; control: 11)	M1, F8c	Sham coil	10 Hz, 100% RMT	2500 pulses, 10 sessions	Significant pain relief (51% improvement, mostly for affective component of pain)	II
Recommendation: possible analgesic effect of HF rTMS of M1 contralateral to pain in complex regional pain syndrome type I (Level C)							

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Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): An update (2014–2018)

Jean-Pascal Lefaucheur [a,b,*], André Aleman [c], Chris Baeken [d,e,f], David H. Benninger [g], Jérôme Brunelin [h], Vincenzo Di Lazzaro [i], Saša R. Filipović [j], Christian Grefkes [k,l], Alkomiet Hasan [m], Friedhelm C. Hummel [n,o,p], Satu K. Jääskeläinen [q], Berthold Langguth [r], Letizia Leocani [s], Alain Londero [t], Raffaele Nardone [u,v,w], Jean-Paul Nguyen [x,y], Thomas Nyffeler [z,aa,ab], Albino J. Oliveira-Maia [ac,ad,ae], Antonio Oliviero [af], Frank Padberg [m], Ulrich Palm [m,ag], Walter Paulus [ah], Emmanuel Poulet [h,ai], Angelo Quartarone [aj], Fady Rachid [ak], Irena Rektorová [al,am], Simone Rossi [an], Hanna Sahlsten [ao], Martin Schecklmann [r], David Szekely [ap], Ulf Ziemann [aq]

Table 1
HF-rTMS of M1 contralateral to pain region in neuropathic pain.

Articles	Number of patients	Target, coil type	Control condition	Stimulation frequency and intensity	Number of pulses/ session and number of sessions	Significant clinical effects of real versus sham condition	Class of the study
Khedr et al. (2015)	30 patients with malignant neuropathic pain (real: 15; sham: 15)	Hand M1 contralateral to pain, F8c (anteroposterior orientation)	Tilted coil	20 Hz, 80% RMT	2000 pulses, 10 sessions	Reduction of pain score at the end of rTMS protocol (49% on VRS and 37% on VAS), up to 2 weeks after the last session (46% on VRS and 36% on VAS); 87–80% responders (>30% pain relief)	II
Ma et al. (2015)	40 patients with postherpetic neuralgia (real: 20; sham: 20)	Homotopic M1 contralateral to pain region, F8c (anteroposterior orientation)	Tilted coil	10 Hz, 80% RMT	1500 pulses, 10 sessions	Reduction of pain score (17% on VAS), up to 3 months after the last session; 50% responders (>50% pain relief)	II
Attal et al., 2016	32 patients with neuropathic lumbar radicular pain (real: 21; sham: 11)	Hand M1 contralateral to pain, F8c (anteroposterior orientation)	Sham coil	10 Hz, 80% RMT	3000 pulses, 3 sessions	Reduction of pain score at the end of rTMS protocol (#60% on VAS), up to 5 days after the last session (#25% on VAS); 43% responders (>30% pain relief)	II
Nurmikko et al. (2016)	27 patients with neuropathic pain of various origins (crossover)	Homotopic M1 contralateral to pain region or an adjacent motor region, F8c (perpendicular to central sulcus)	Occipital stimulation	10 Hz, 90% RMT	2000 pulses, 5 sessions	Reduction of pain score compared to control condition one week after the last session (9–11% on VAS); 30% responders (>30% pain relief)	II

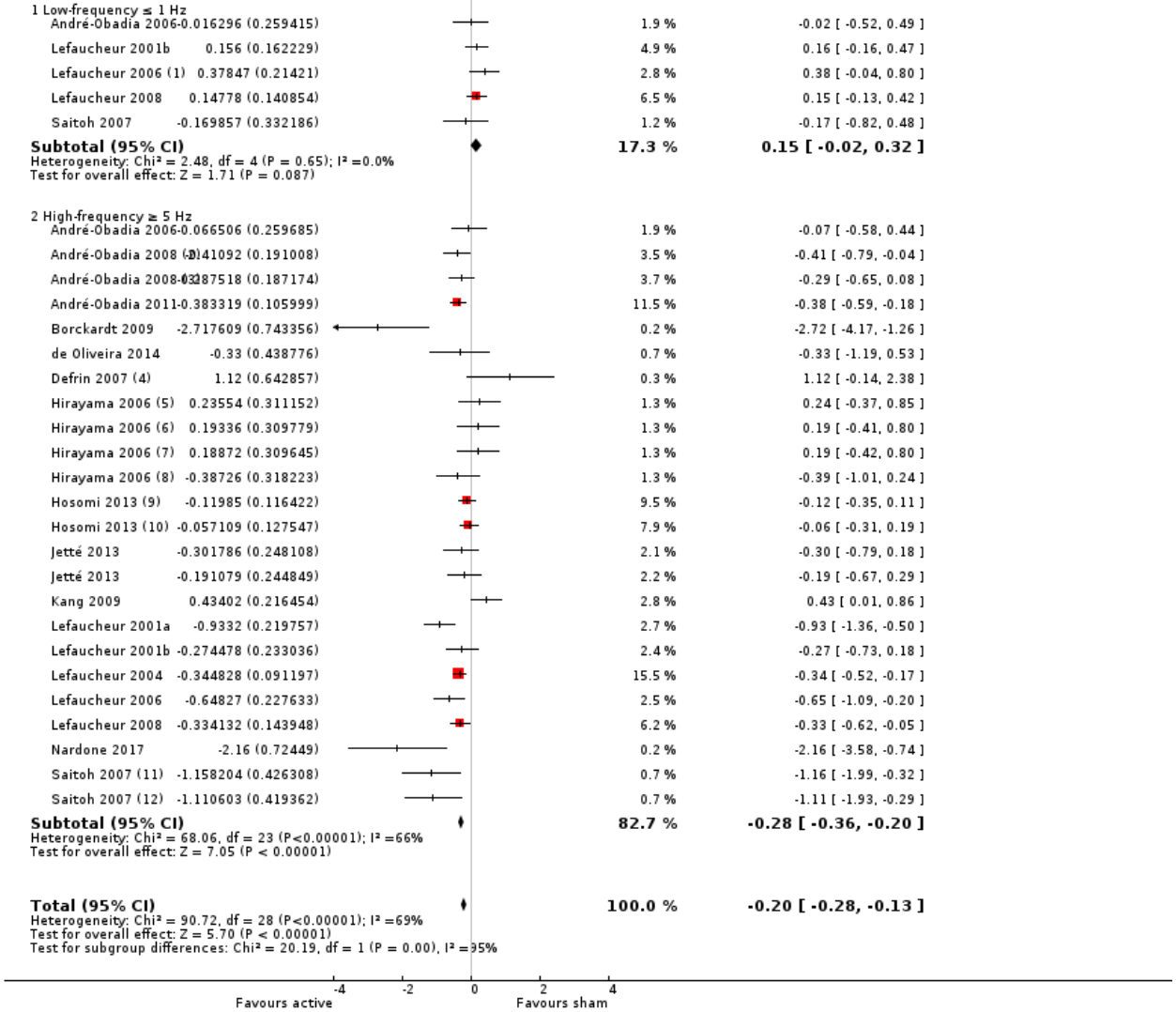
Cochrane Library

Cochrane Database of Systematic Reviews

Non-invasive brain stimulation techniques for chronic pain (Review)

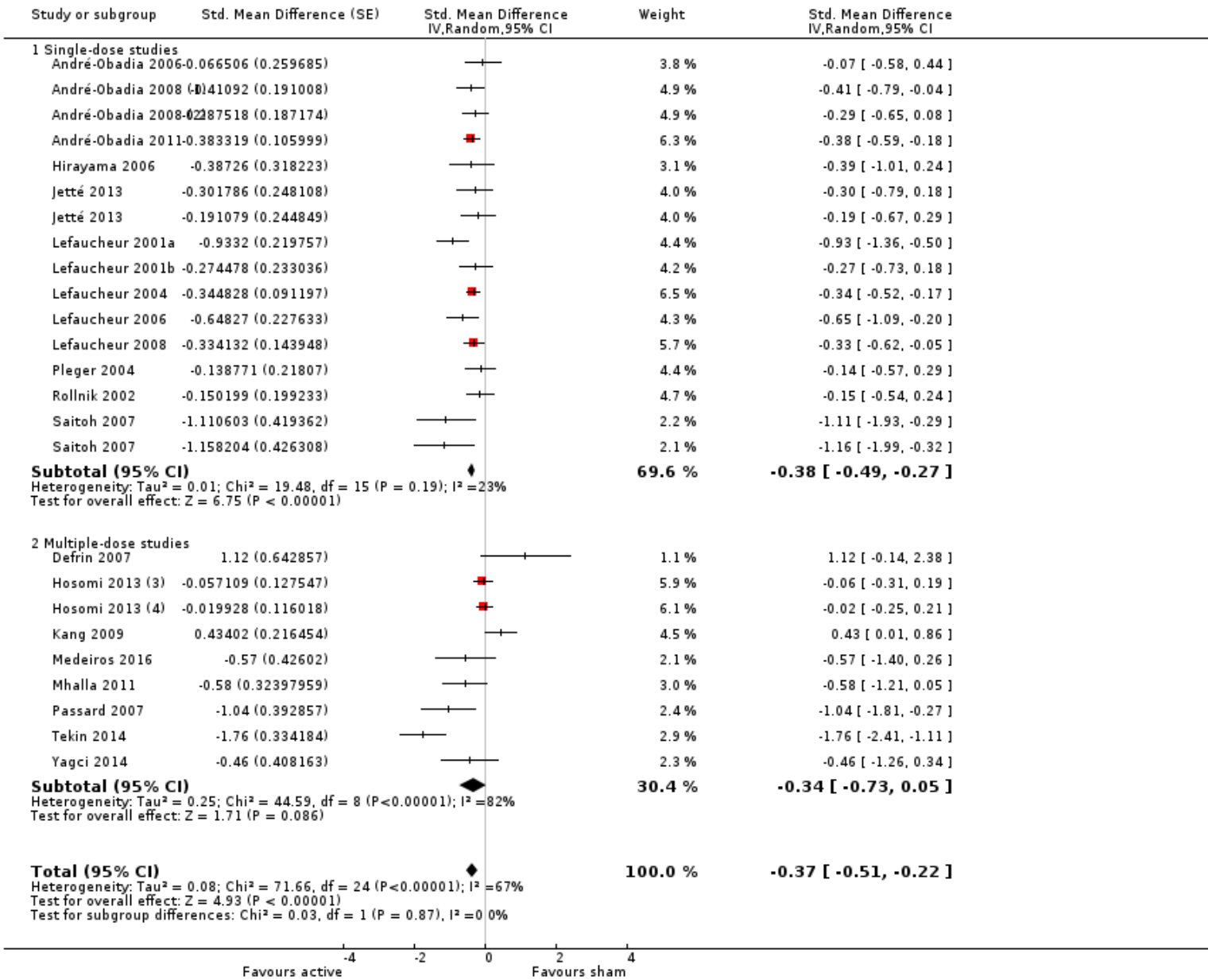
O'Connell NE, Marston L, Spencer S, DeSouza LH, Wand BM

Review: Non-invasive brain stimulation techniques for chronic pain
Comparison: 1 Repetitive transcranial magnetic stimulation (rTMS)
Outcome: 3 Pain: short-term follow-up, subgroup analysis, neuropathic pain participants only



(1) 1Hz
(2) antero-posterior coil orientation
(3) medial-lateral coil orientation
(4) Pain score higher at baseline in active stim group
(5) S1
(6) PMA
(7) SMA
(8) M1
(9) M1 Group B (sham followed by real)
(10) M1 Group A (real followed by sham)
(11) 5Hz
(12) 10 Hz

Review: Non-invasive brain stimulation techniques for chronic pain
Comparison: 1 Repetitive transcranial magnetic stimulation (rTMS)
Outcome: 5 Pain: short-term follow-up, subgroup analysis: motor cortex studies only, low-frequency studies excluded



(1) antero-posterior coil orientation
(2) medial-lateral coil orientation
(3) Group B sham followed by real
(4) Group A real followed by sham

Summary of findings for the main comparison. Repetitive transcranial magnetic stimulation (rTMS) compared with sham for chronic pain

rTMS compared with sham for chronic pain

Patient or population: adults with chronic pain

Settings: laboratory/ clinic

Intervention: active rTMS

Comparison: sham rTMS

Outcomes	Effect size	Relative and absolute effect **(average % improvement (reduction) in pain (95% CIs) in relation to post-treatment score from sham group)*** ***Where 95%CIs do not cross the line of no effect.**	No of participants (studies)	Quality of the evidence (GRADE)
Pain intensity (0 to < 1 week postintervention) measured using visual analogue scales or numerical rating scales	SMD -0.22 (-0.29 to -0.16)	This equates to a 7% (95% CI 5% to 9%) reduction in pain intensity, or a 0.40 (95% CI 0.53 to 0.32) point reduction on a 0 to 10 pain intensity scale.	655 (27)	⊕⊕⊖⊖ **low**[1]
Disability (0 to < 1 week postintervention) measured using self-reported disability/pain interference scales	SMD -0.29, 95% CI -0.87 to 0.29	-	119 (5)	⊕⊖⊖⊖ **very low**[2]
Quality of life (0 to < 1 week postintervention) measured using Fibromyalgia Impact Questionnaire	MD -10.80, 95% CI -15.04 to -6.55	-	105 (4)	⊕⊕⊖⊖ **low**[3]

CI: confidence interval; **MD**: mean difference; **rTMS**: repetitive transcranial magnetic stimulation; **SMD**: standardised mean difference

Summary of findings 3. Transcranial direct current stimulation (tDCS) compared with sham for chronic pain

tDCS compared with sham for chronic pain

Patient or population: adults with chronic pain

Settings: laboratory/ clinic

Intervention: active tDCS

Comparison: sham tDCS

Outcomes	Effect size	Relative effect **(average % improvement (reduction) in pain (95% CIs) in relation to post-treatment score from sham group)*** ***Where 95%CIs do not cross the line of no effect.**	No of participants (studies)	Quality of the evidence (GRADE)
Pain intensity (0 to < 1 week postintervention) measured using visual analogue scales or numerical rating scales	SMD -0.43 (-0.63 to -0.22)	This equates to a 17% (95% CI 9% to 25%) reduction in pain intensity or a 0.82 (95% CI 0.42 to 1.2) point reduction on a 0 to 10 pain intensity scale.	747 (27)	⊕⊖⊖⊖ **very low**[1]
Disability (0 to < 1 week postintervention) measured using self-reported disability/pain interference scales	SMD -0.01, (95% CI -0.28 to 0.26)	-	212 (4)	⊕⊕⊖⊖ **low**[2]
Quality of life (0 to < 1 week postintervention) measured using different scales across studies	SMD 0.66, 95% CI 0.21 to 1.11	-	82 (4)	⊕⊕⊖⊖ **low**[2]

CI: confidence interval; **MD**: mean difference; **SMD**: standardised mean difference; **tDCS**: transcranial direct current stimulation

Est-ce efficace?

- Recommandation de grade A pour la rTMS dans les douleurs neuropathiques
- Niveau C pour le tDCS et le thetaburst
- Pas de recommandations pour les autres techniques

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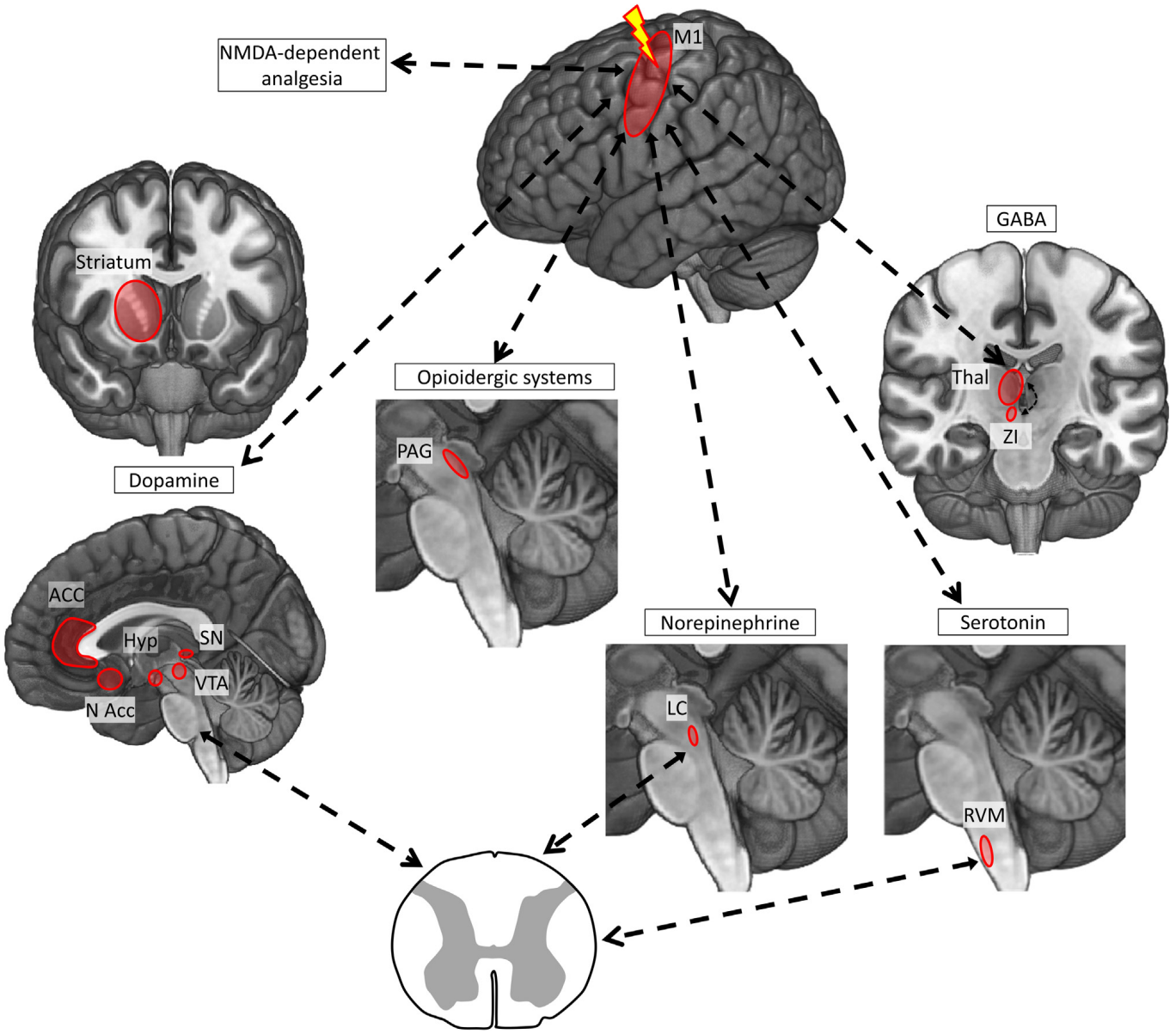
MÉCANISMES D'ACTION



D'après Moisset et Lefaucheur

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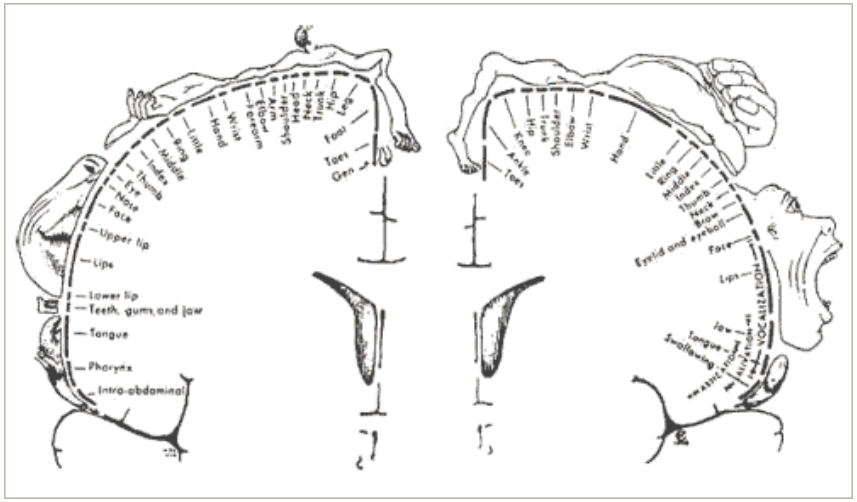
MODALITÉS PRATIQUES

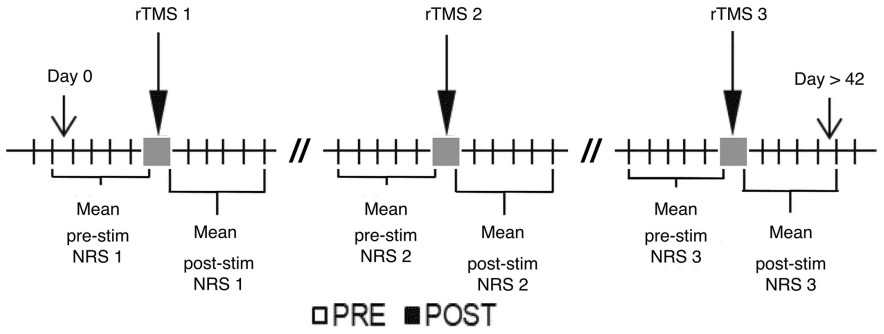
Où stimuler?

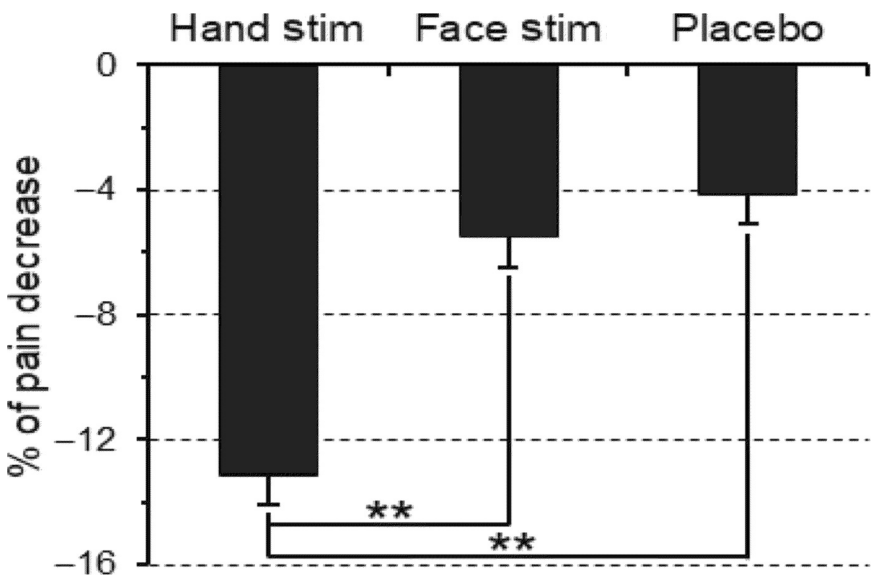
- Cortex moteur primaire :
  - recommandations grade A
- Autres sites :
  - Préfrontal
  - S1 et S2
  - Trop peu d'études pas de recommandations

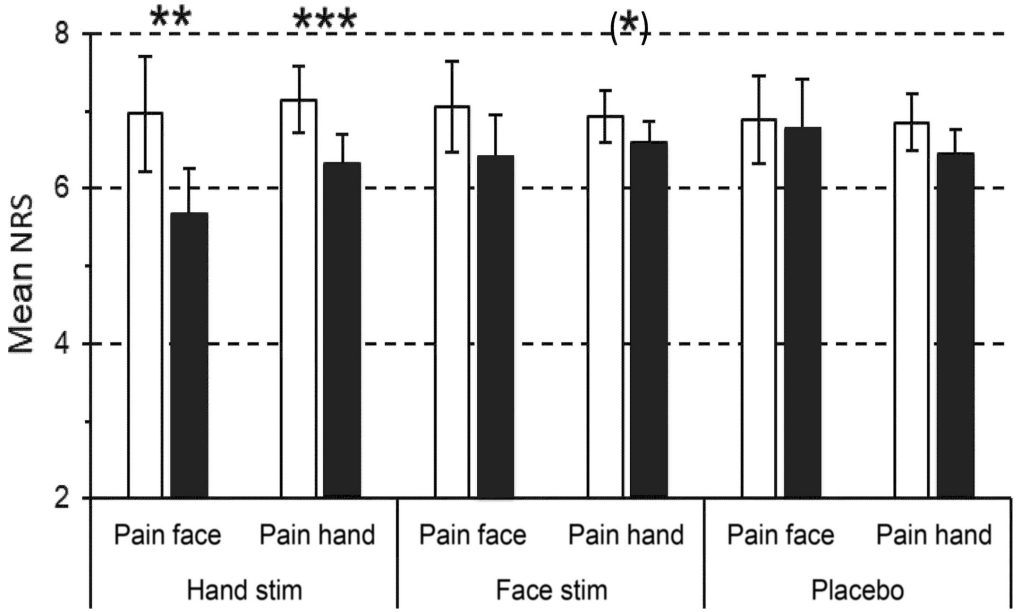


Où stimuler?

- Pas de somatotopie
- Recommandation : l'aire de la main







European Journal of Pain, Volume: 22, Issue: 4, Pages: 707-715, First published: 01 December 2017, DOI: (10.1002/ejp.1156)

Quel programme?

- Haute fréquence >5 Hz : 10Hz, 20 Hz
- Nombre de coups : 1200 à 2000 pulses par session
- 80% du seuil moteur
- Des trains de 5 à 10s
- Des repos de 20 à 60 s
- 1 à 5 sessions
- Tous les 1 à 6 mois

Combien de temps ça marche?

- 1 session :
  - Début d’effet 1 à 3 jours
  - Durée 5 à 7 jours
- 5 sessions :
  - Jusqu’à 1 mois d’efficacité

Les effets indésirables

- Crise d'épilepsie :
  - Cf recommandations européenne
- Migraine
- maux de tête
- Trouble de l'attention
- Acouphènes, phosphènes

- Tous transitoires

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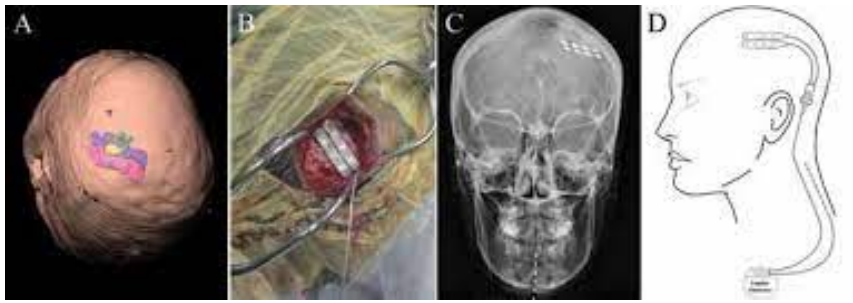
QUELLE PLACE DANS LE TRAITEMENT DES DOULEURS NEUROPATHIQUES?

Test pré-implantatoire?

- Essai d'une session
- Si efficace :
  - Diminution 50% douleurs dans les 1 à 3 j
- Implantation électrodes épidurales sur le cortex moteur



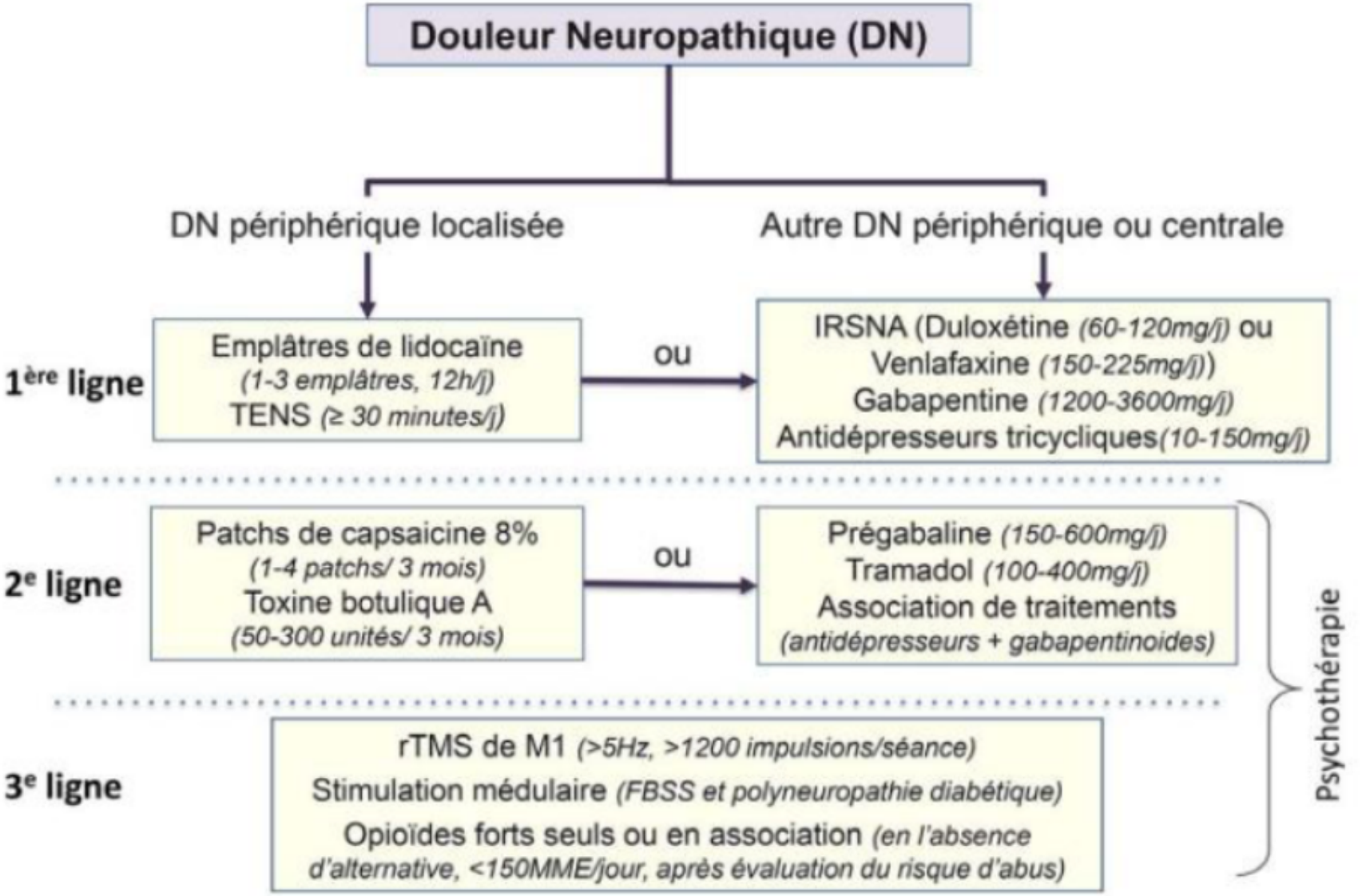


Fig. 1 Algorithme thérapeutique proposé pour la prise en charge de la douleur neuropathique de l'adulte. TENS : *transcutaneous electrical nerve stimulation* ; IRSNA : antidépresseur inhibiteur de recapture de la sérotonine et de la noradrénaline ; rTMS : *repetitive transcranial magnetic stimulation*

NOTRE EXPERIENCE

Methods

71 patients were included (December 2014-2017)
Adults
DN4 > 4
No contra indication to rTMS

rTMS +
motor imagery and mirror therapy

1 Day

rTMS +
motor imagery and mirror therapy

5 Days

rTMS
10 Hz 20 min
Contralateral motor cortex to pain
- *(Jin Y, Pain Physician. 2015)*

motor imagery and mirror therapy

By a physiotherapist 2/ day

Methods

BPI score

→ 1st session
1 day
- Before
- 48 hours later

→ 2nd session
5 days
- Before
- At the end of 5 days

→ Follow up
- M1, M3, M6

Patient characteristics	
No. of patients	**71**
Sex (male/female)	**43/28**
Mean age	**56,3**
Pain duration mean (years)	**6,5**
< 2 years	**38**
> 2 years	**33**
Pathology	
Stroke	**32**
Multiple sclerosis	**6**
Spinal cord injuries	**31**
Head trauma	**2**
Pain Location	
Arm (unilateral / both side)	**16/2**
Leg (unialtearl / both side)	**19/8**
Hemibody	**18**
4 members	**7**

Results

- Day 0 : n= 71
- 48 H: n= 39
- D1: n=
- D5: n=
- M1: n= 47
- M3: n= 46
- M6: n= 33

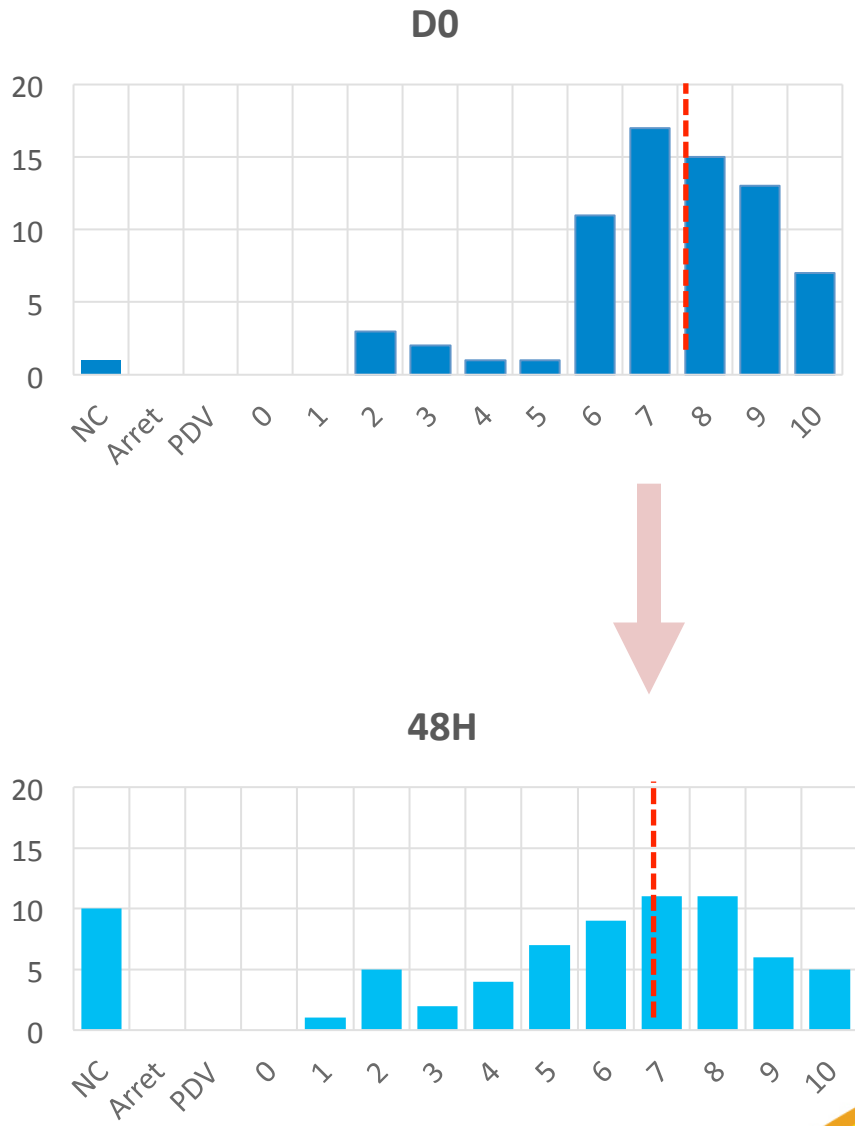
(Results)

- Primary outcome = decreasing of the most intense pain of two points
- Responders
  - 30,5% at 48 hours (n= 39)
  - 25,5% at M1 (n= 47)
  - 28,2% at M3 (n= 46)
  - 33,3% at M6 (n= 33)

Results

Most intense pain evolution

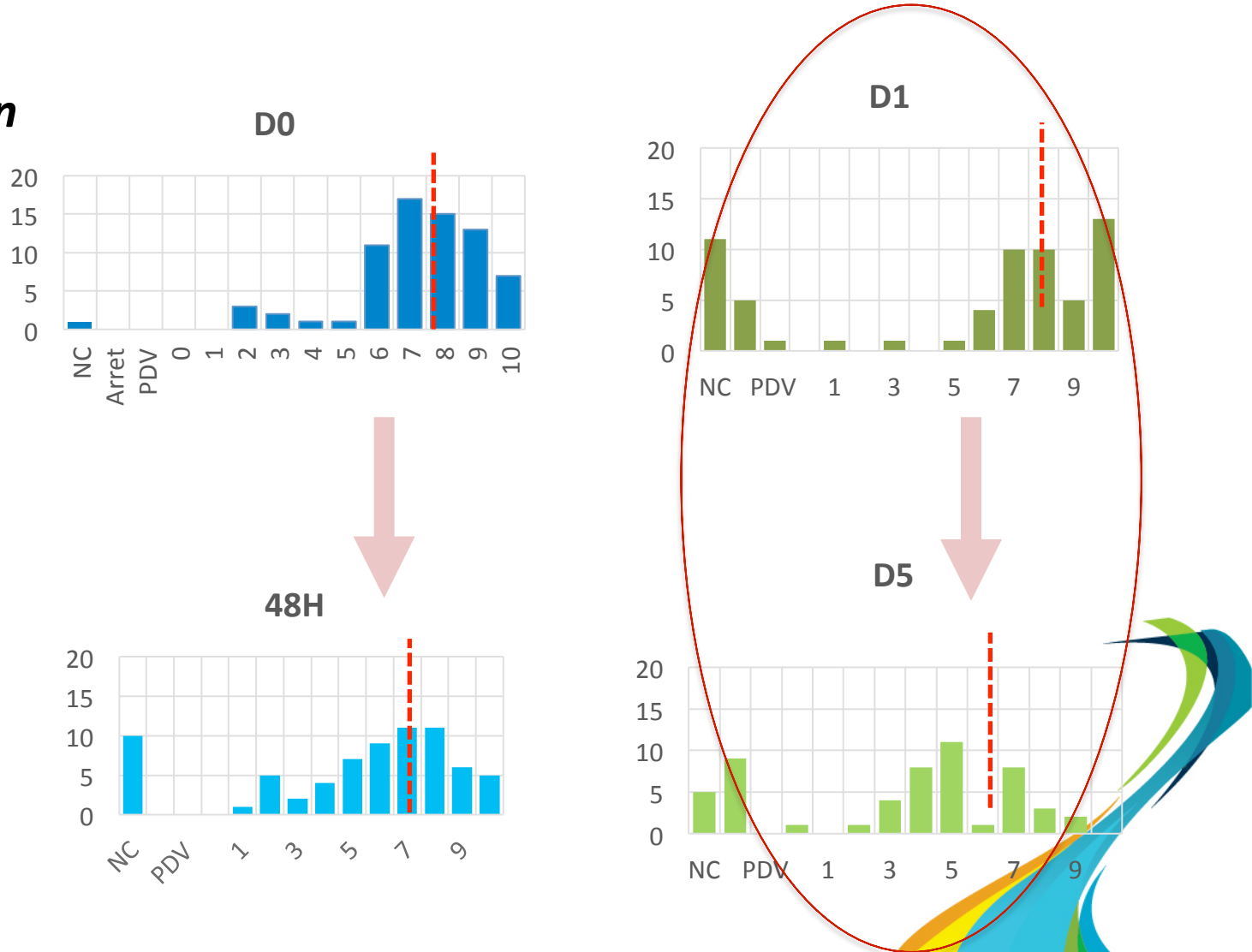
Significant improvement p<0,05



- - - - median

Results

Most intense pain evolution



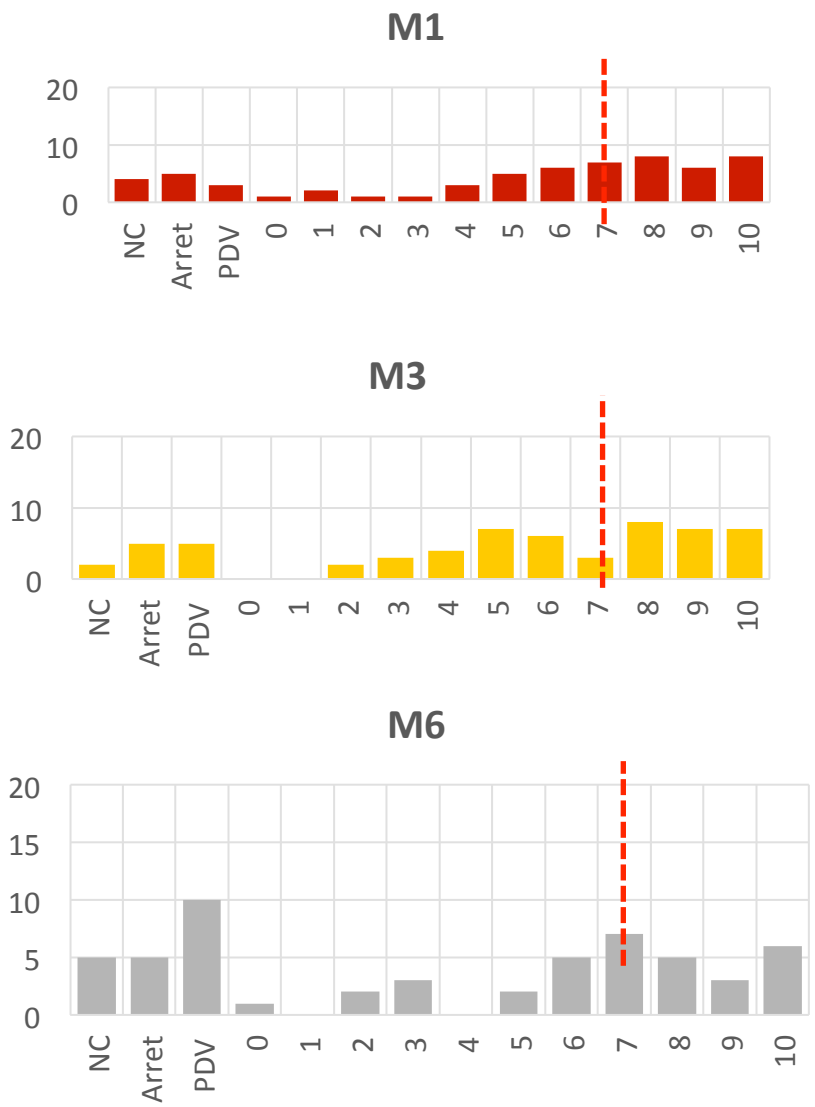
Significant improvement $p<0,05$

- - - - median

Results

Most intense pain evolution

Significant improvement
p<0,05

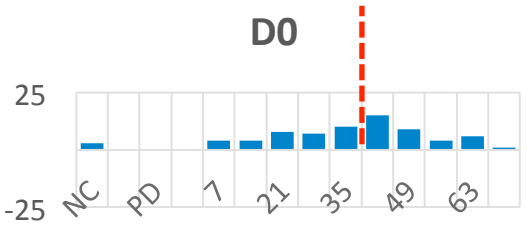


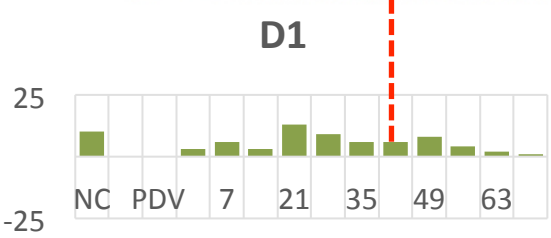
- - - - median

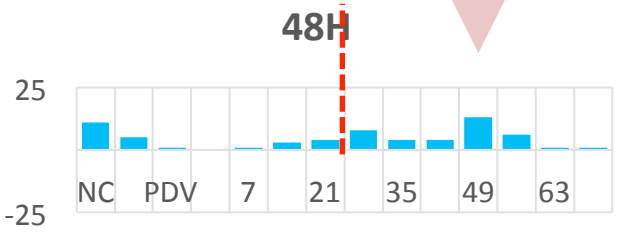
Results

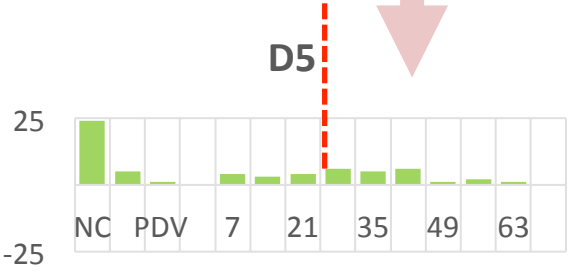
Pain impact evolution

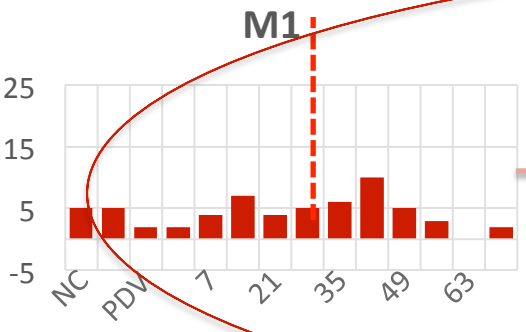
Significant improvement p<0,05

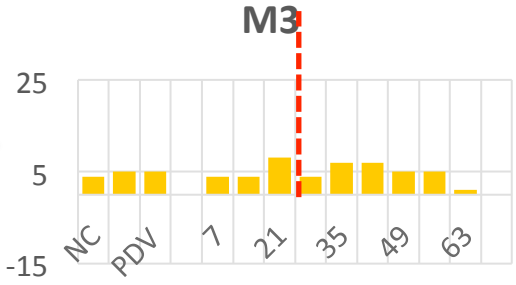


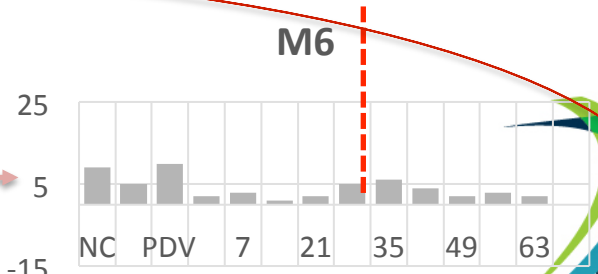












www.isprm2018.com

- - - - median

Conclusion

- rTMS et douleurs neuropathiques : grade A , effet temporaire
- Répétitions de sessions de rTMS et/ou techniques complémentaires (imagerie en miroir ou imagination du mouvement) augmentent la durée d'efficacité
- Il existe de bons répondeurs : 30% dans notre série
- Si bonne réponse mais courte (<1mois) = test préimplantatoire d'une stimulation épidurale du cortex moteur
- Traitement de 3^{ième} ligne des douleurs neuropathiques