Neuromodulation centrale, médullaire et cérébrale : pour quels bénéfices en MPR

JB Thiébaut

service de neurochirurgie - CETD - Fondation Rothschild - Paris

service de MPR - Hôpital Raymond Poincaré - Garches

Pas de conflit d'intérêt pour ce travail

A Joint Meeting

www.neuromodec.com/nycnans2018

2018 NYC Neuromodulation Conference & NANS Summer Series

August 23–26, 2018 | New York City

Sheraton New York Times Square Hotel

The joint meeting of the 2018 NYC Neuromodulation Conference and NANS Summer Series is produced by neuromodec.com and the North American Neuromodulation Society (NANS).

Jointly provided by the Congress of Neurological Surgeons and the North American Neuromodulation Society

Daily Morning Guided Meditation with Optional E-Meditation

August 24 - 26, 2018

7:30 AM - 8:20 AM

Description:

Baron Short MD and Bashar Badran PhD will be offering tDCS-enhanced meditation (E-Meditation) to start your day. tDCS will be optionally included for the first 10 individuals. The group will be led through a beginner-level guided meditation, which will help kick start your day by quieting your mind. tDCS is optional and this meditation will be provided both with and without stimulation. No prior meditation experience required.

Amping up Brain Function with tDCS

tDCS – augmenter ses performances cognitives

- *Hunter 2018 Mindfulness-based training with tDCS modulates neuronal resource allocation in working memory*

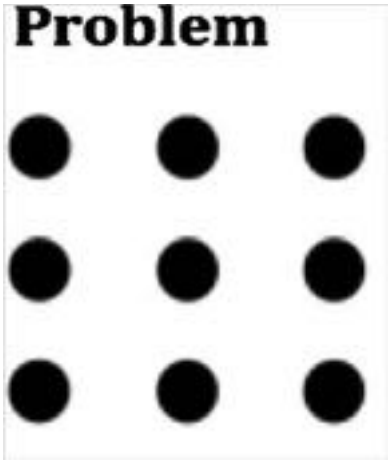
Evidence for the potential compatibility of using eMBT to modulate WM capacity through the allocation of attention

- *Chi 2012 Brain stimulation enables the solution of an inherently difficult problem: atypical protocol enabled the solution of a problem that was previously unsolvable*

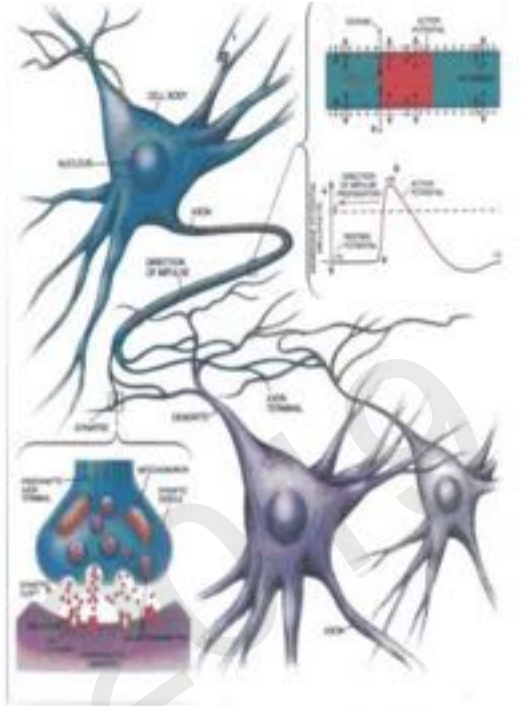
The 9-dot problem

- Relier les 9 points avec 4 lignes droites sans lever la plume de la feuille ni retracer une ligne
- Difficile de résoudre rapidement le problème pour la majorité des participants

  Après 10min de tDCS latéral, > 40% des participants réussissent



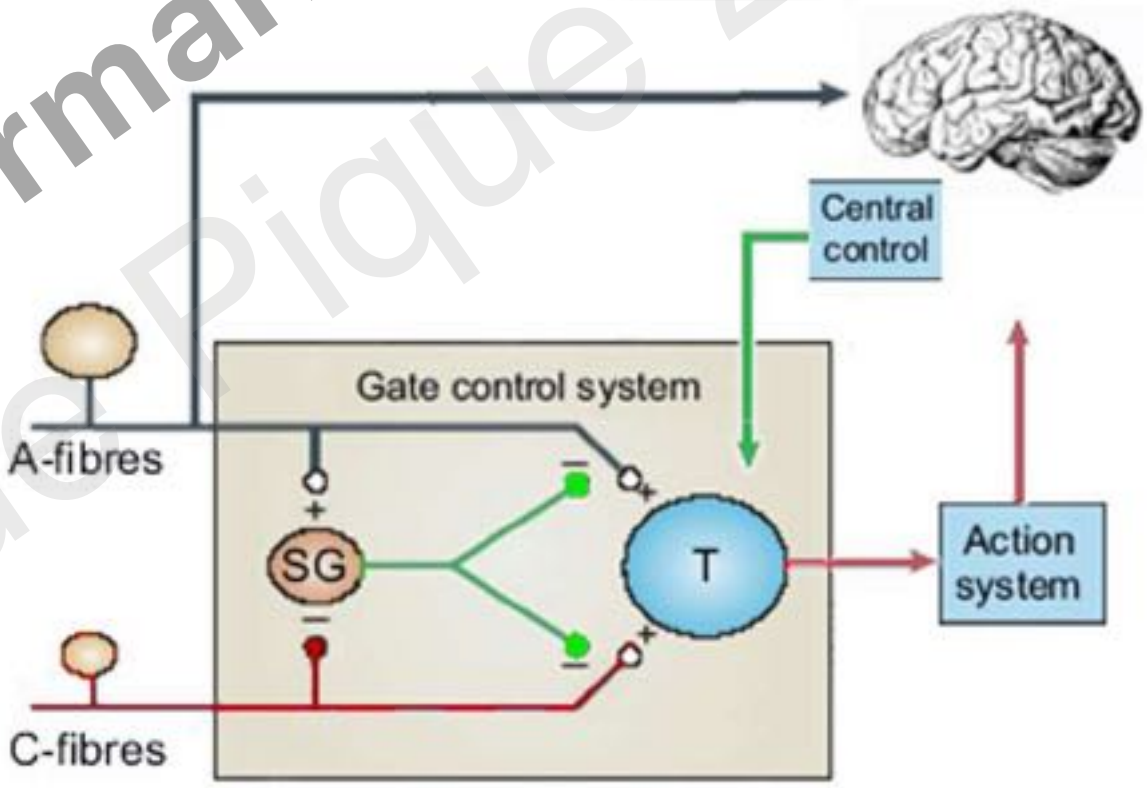
Neuromodulation



- **Modifier le fonctionnement du système nerveux**
  en agissant au niveau des neurones ou des synapses
  par des stimulations électriques ou autres (excitabilité)
  par administration de neurotransmetteurs (récepteurs membrane)

  Ne remplace pas une structure détruite

- Travaux de Melzack et Wall 1965
  Inhibition présynaptique
  Gate control theory
- Domaines d'applications
  douleur
  moteur (SCI – mvts anormaux)
  cognitif
- Cibles
  médullaires (SCS)
  cérébrales (DBS – SCM- NTBS)
- Méthodes
  invasives ou non invasives



Stimulation médullaire (SCS)

Shealy 1967

•Traitement de la douleur – *troubles moteurs*

douleurs séquellaires de lombosciatique

douleurs neuropathiques

SDRC

•Principe

Stimulation des fibres afférentes de gros diamètre entraîne une inhibition des fibres de petit diamètre au niveau de la corne postérieure de la moelle

•Prérequis

La stimulation entraîne des paresthésies dans le territoire douloureux

• Cible

cordons postérieurs de la moelle en para médian

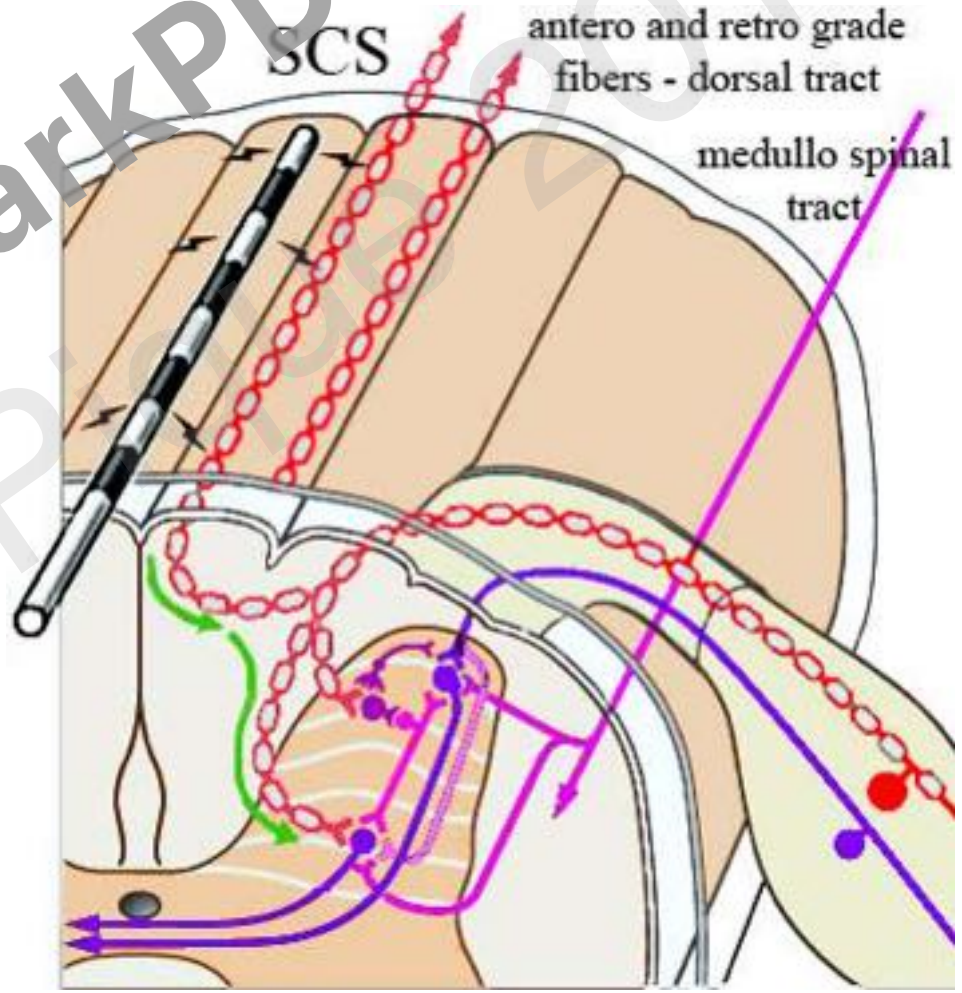
Mécanisme précis non déterminé

•Limites

Stimulation radiculaire f (LCS)

Traitement des lombalgies

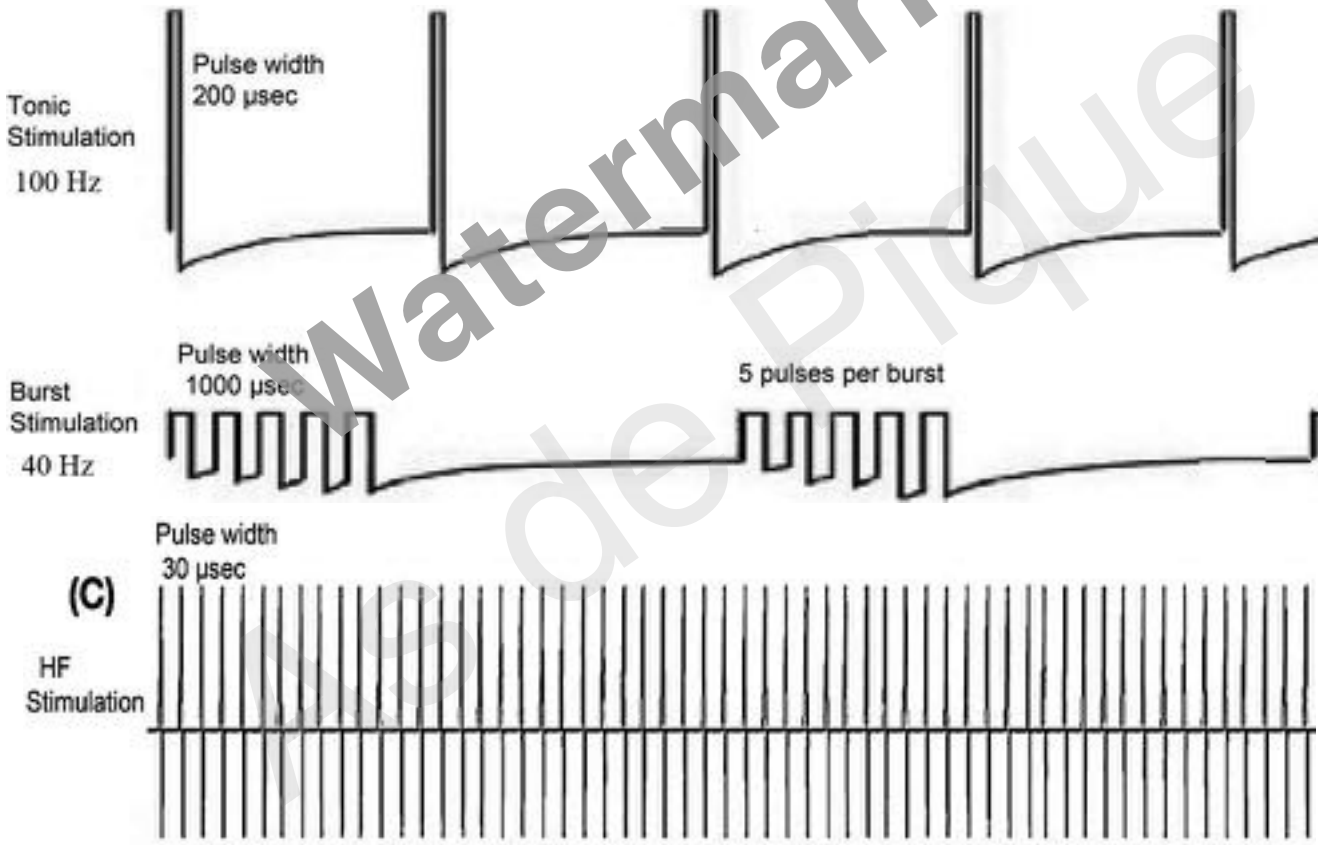
Etat des fibres stimulées

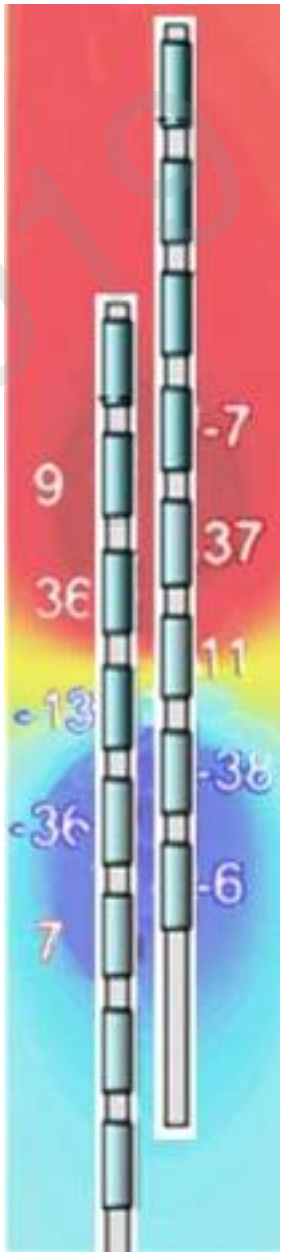


Stimulation médullaire (SCS)

Evolution du matériel

- Sondes multi plots avec alimentation indépendante de chaque contact
  paramètres f (anatomie probabiliste des segments médullaires fonctionnels)
- Stimulation du ganglion rachidien
- Nouvelles gammes de fréquence avec possibilité de choix
  BurstDR et très haute fréquence (10kH)
  absence de paresthésies évoquées
  possibilité de test en aveugle



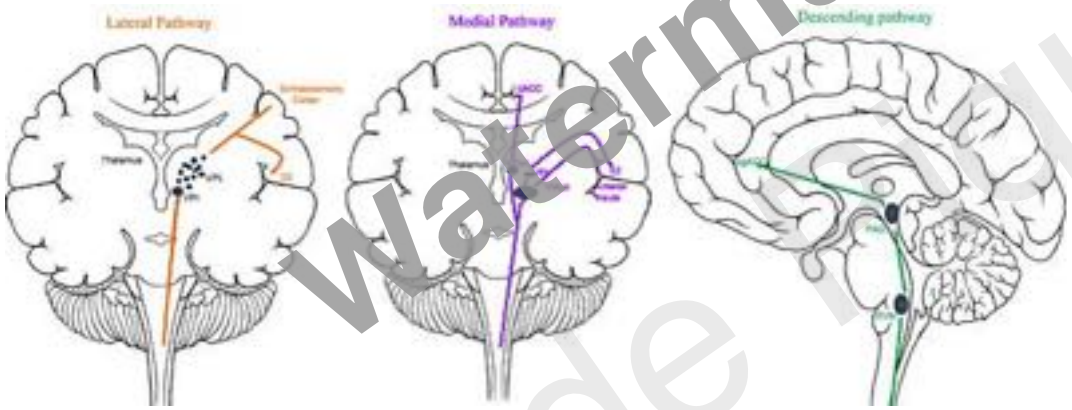


Stimulation en BurstDR

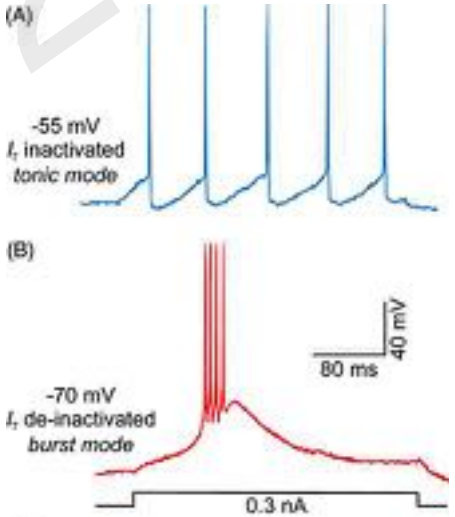
BDR Faible amplitude et longue durée de largeur de pulsation (pw = 1 ms)
active les dendrites des fibres Abeta plus que les axones des codons post
rompt l'activité synchronisée des fibres c

•BDR / HF : charge/pulse > 0.654 / 0.11 µC
Meuwissen 2017 charge/sec <130.8 / 480 µC/s
•BDR / stimulation Tonique :

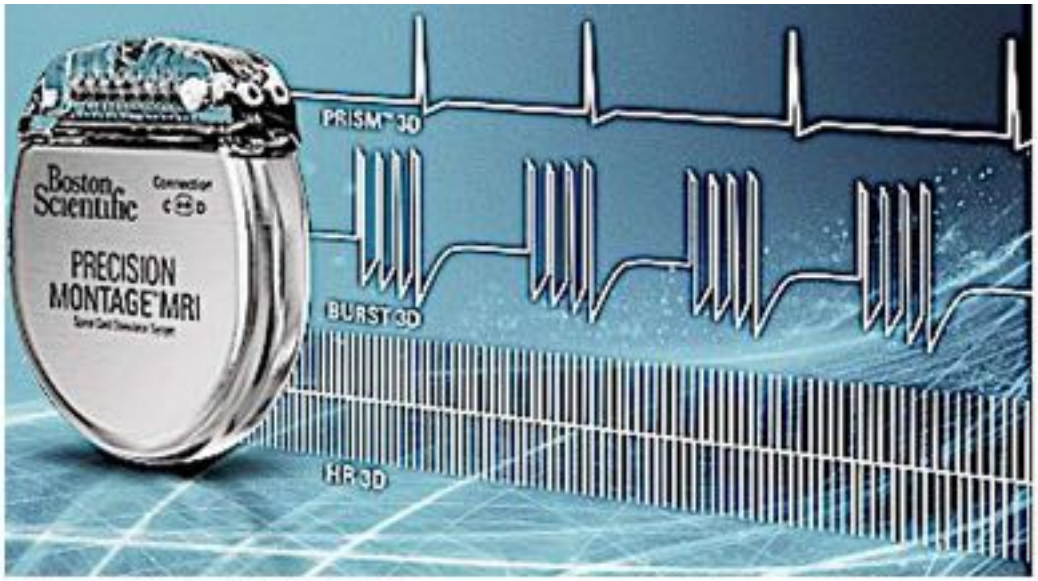
- activité EEG alpha > cingulum ant et post, dorsolateral PFC, M1
- fIRM : contrôle les aires médianes de la douleur

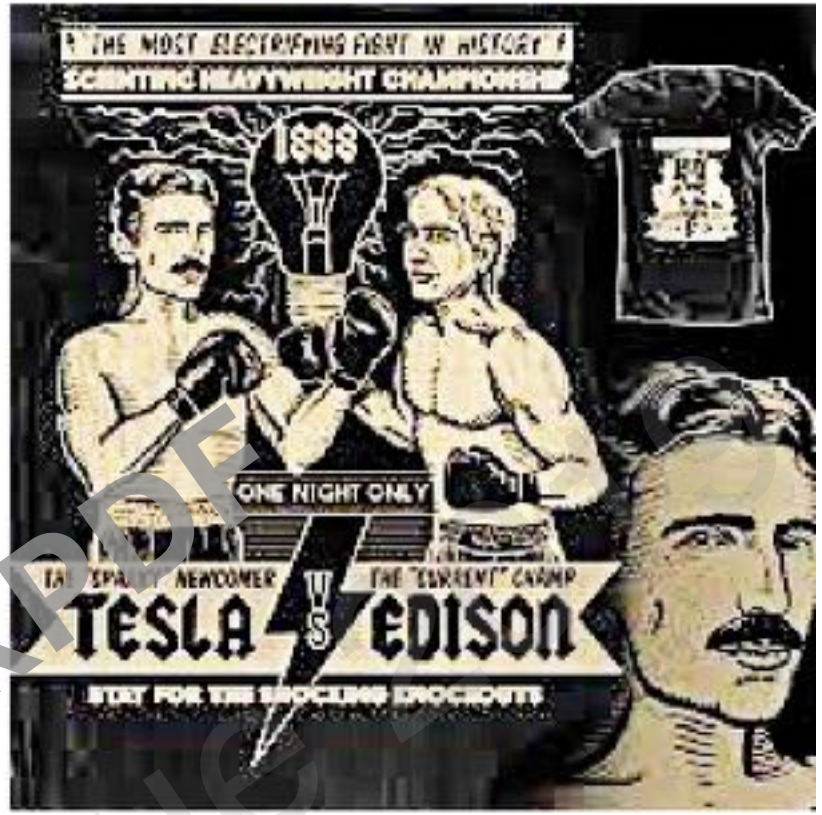


Shermann

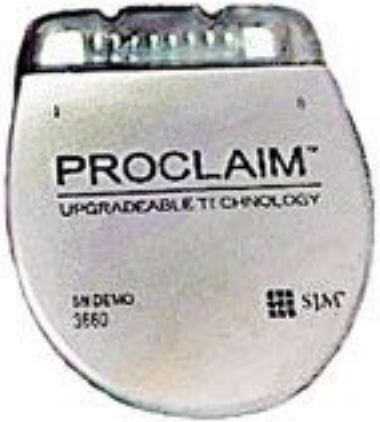


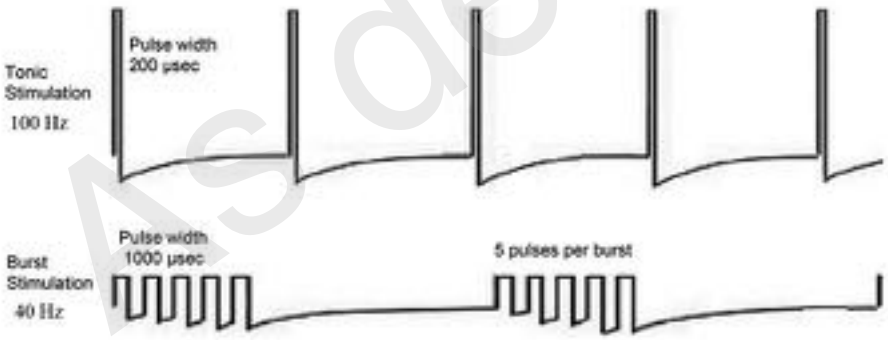
- *Deer 2017* Success using neuromodulation with Burst (SUNBURST) Results from a prospective, randomized controlled trial
- *Shermann 2017* Functioning of Circuits Connecting Thalamus and Cortex *BDR est physiologique*





Controverses





DeRidder

SCS et blessés médullaires (SCI)

Dimitrijevic *1980* Study of sensation and muscle twitch responses to spinal cord stimulation

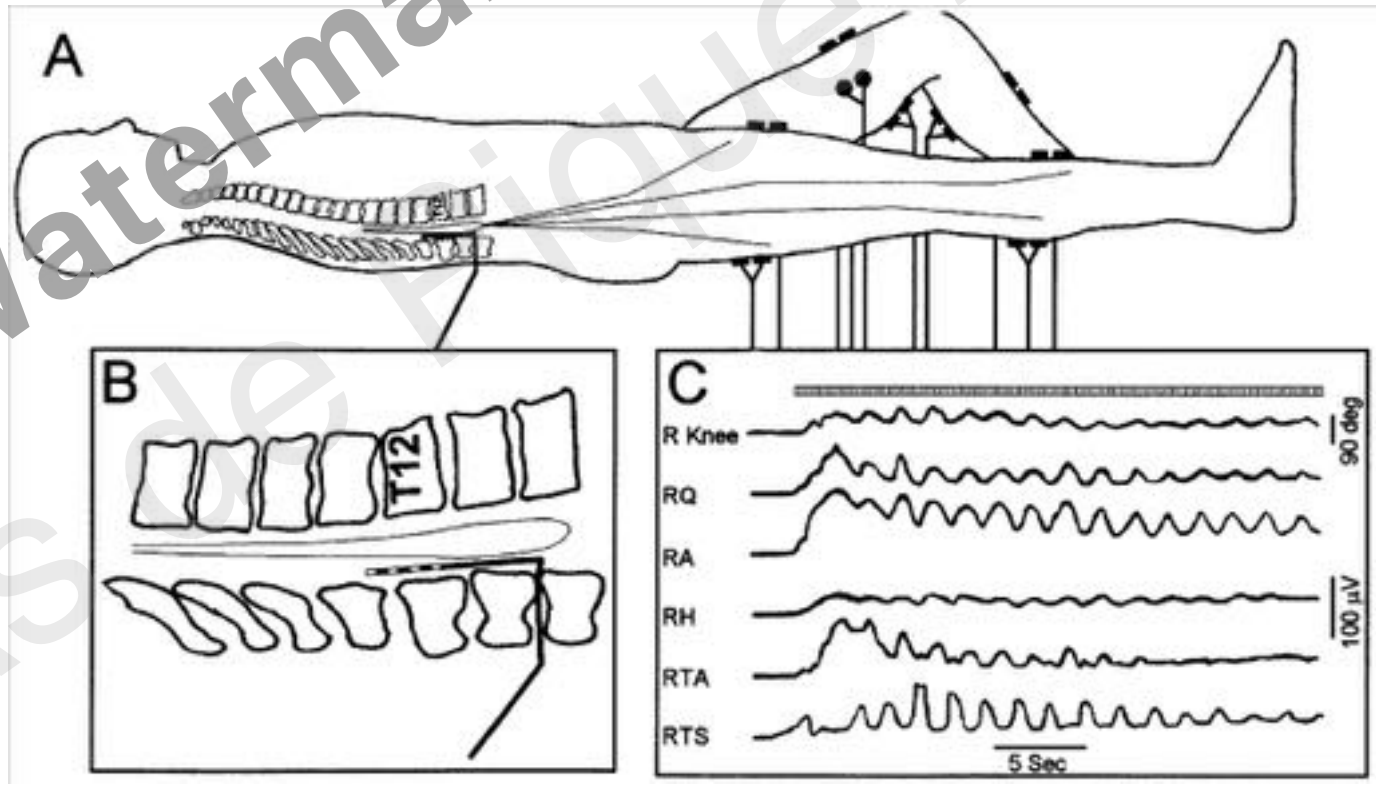
Barbeau 1987 Recovery of locomotion after chronic spinalization in the adutt cat

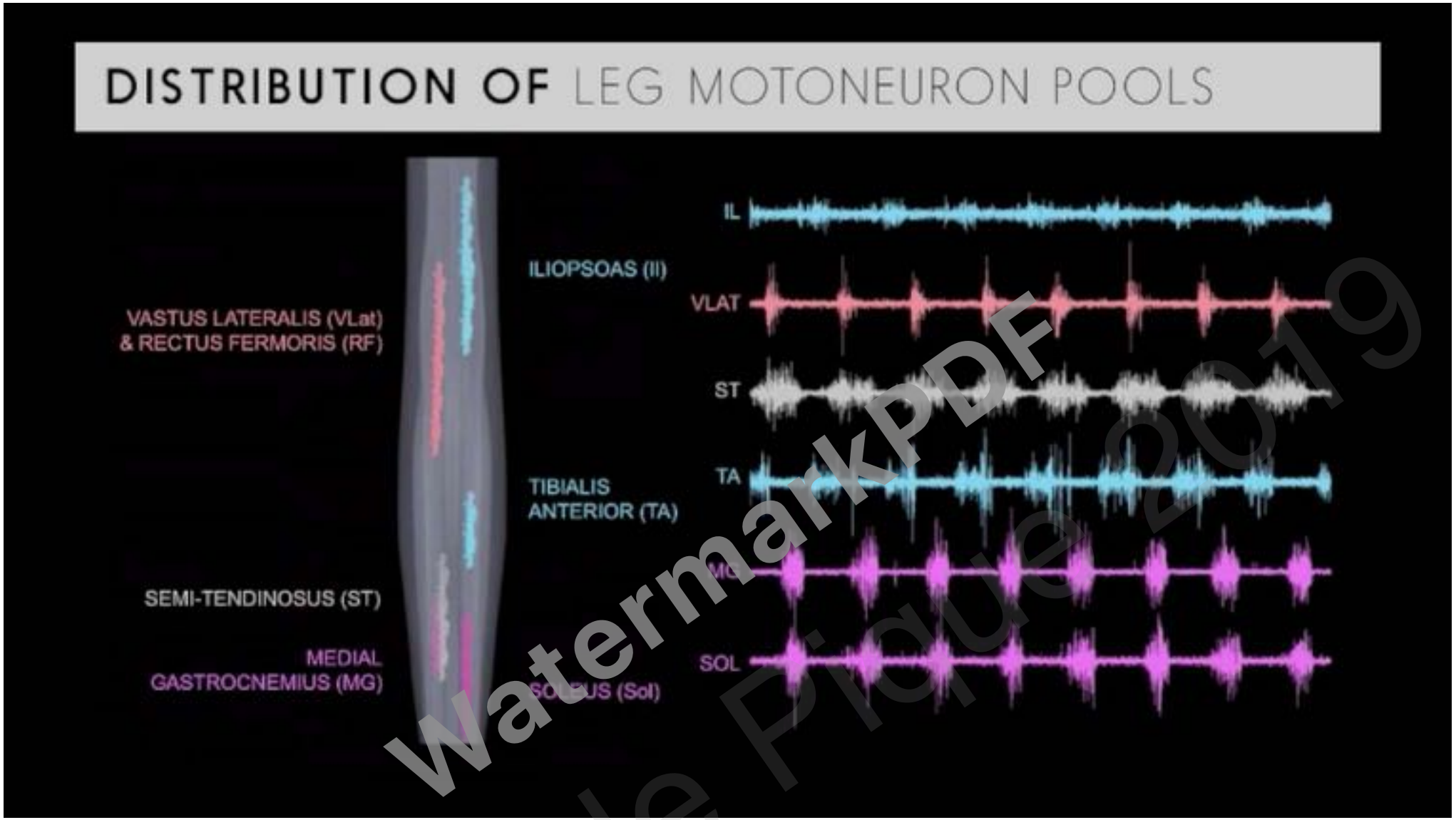
Bussel 1989 Late Flexion Reflex in Paraplegic Patients. Evidence for a Spinal Stepping Generator

Dimitrijevic Evidence for a Spinal Central Pattern Generator in Humans

Gerasimenko 2000 Mechanisms of Locomotor activity generation under epidural cord stimulation

Harkema 2011 Effect of Epidural stimulation of the lumbosacral spinal cord
on voluntary movement, standing, and assisted stepping after motor complete paraplegia

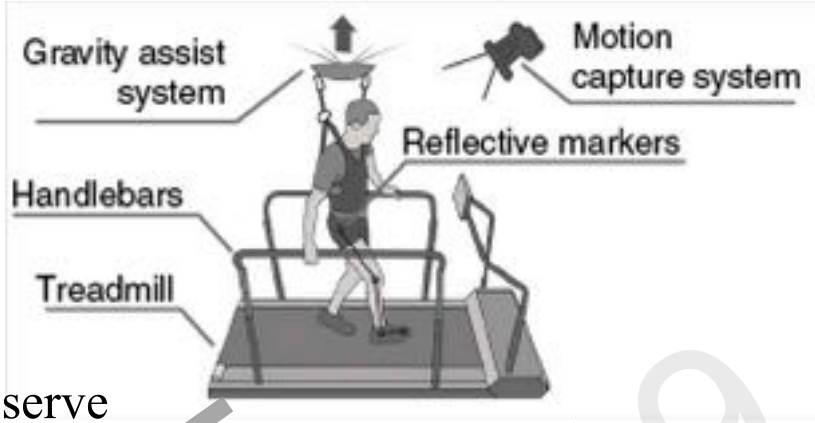




Rééducations
Place de l'électrode
Paramètres de stimulation
Contrôle cortical

Lésion
Evolution temporelle après SCS
Récupération d'un mvt volontaire

SCS - SCI

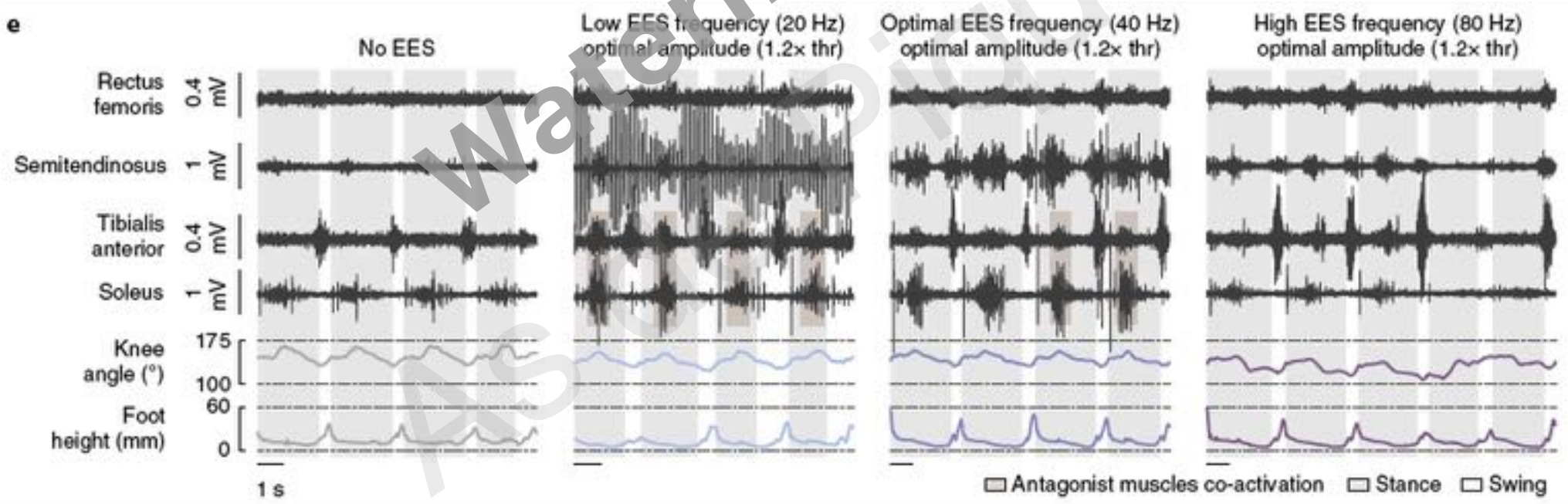


Wagner 2018 **Targeted neurotechnology restores walking in humans with spinal cord injury**

Formento 2018 Electrical spinal cord stimulation must preserve proprioception to enable locomotion in humans with spinal cord injury

Gill 2018 Neuromodulation of lumbosacral spinal networks enables independent stepping after complete paraplegia

Angely 2018 Recovery of Over-Ground Walking after Chronic Motor Complete Spinal Cord Injury



Mrs L. S - born on 6 June 1932

May 2007 Off simulation

November 2017 Off simulation

Mrs L. S - born on 6 June 1932

May 2007 On simulation

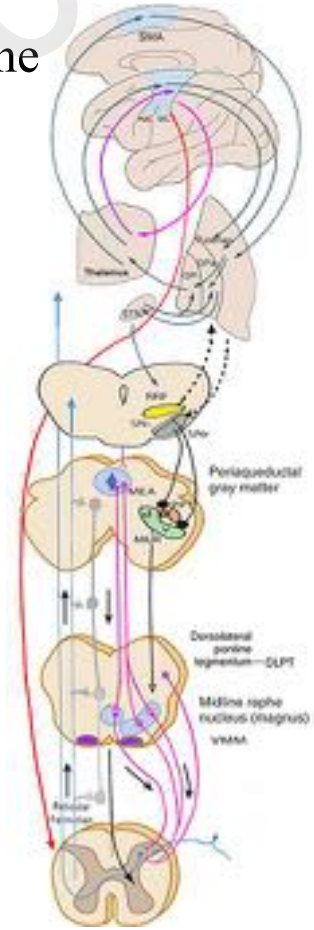
November 2017 On simulation

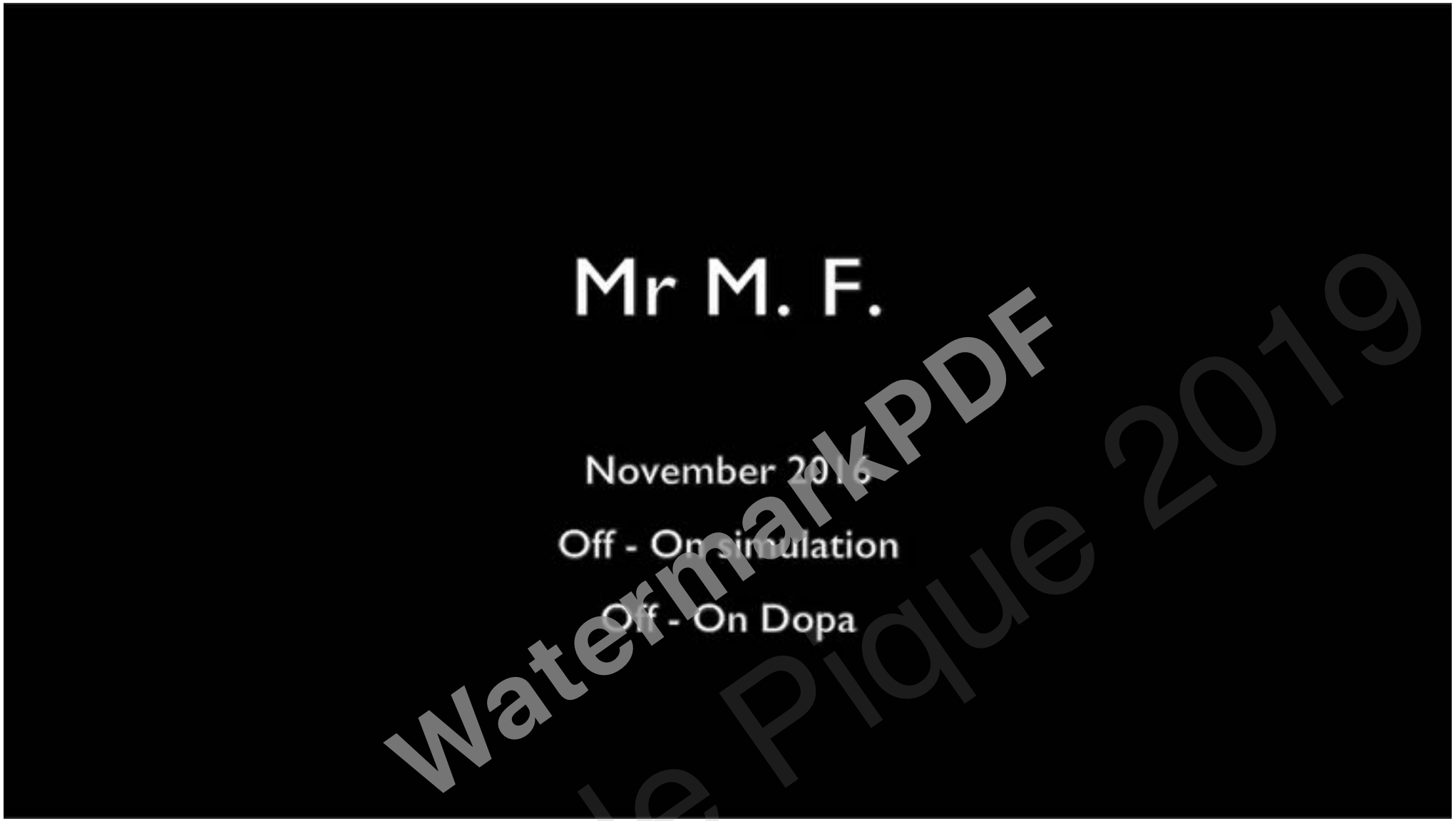
Progressive Freezing of Gait

Le plus ancien cas
bénéficiant d'une SCS
toujours efficace
après plus de 30 ans

La SCS rétablit une marche
volontaire quasi normale

Inhibition d'une
commande
parasite
au niveau
du CPG

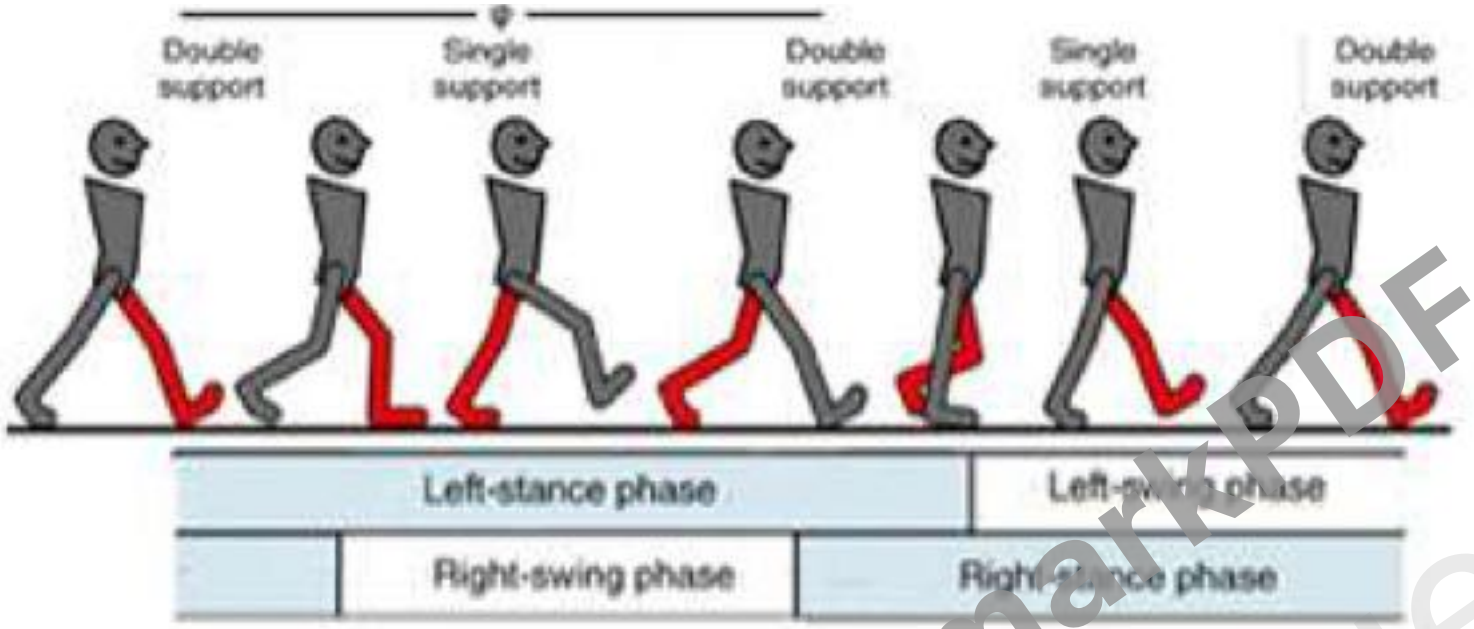


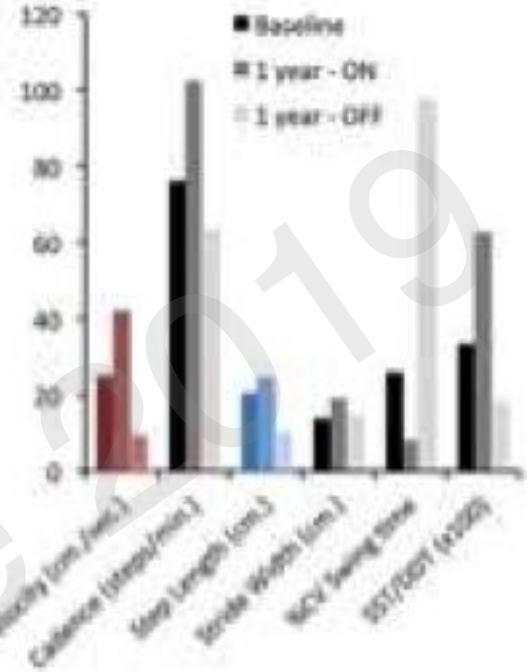


Maladie de Parkinson

Patient Dopa sensible ayant bénéficié d'une stimulation du noyau sous thalamique pour syndrome on-off. Persistance de troubles axiaux, en particulier de la marche avec Freezing. Implantation d'une stimulation médullaire. Amélioration de la vitesse, de la longueur du pas et très nette diminution du Freezing. Recul de plus de 2 ans.

Les troubles de la marche du Parkinson





Bradikinésie et FOG (freezing of gait)

Traitement des troubles axiaux : Dopa – STN – PPN…MLR – SCS – “cueing“

Etude de la marche 3D – Synergies musculaires

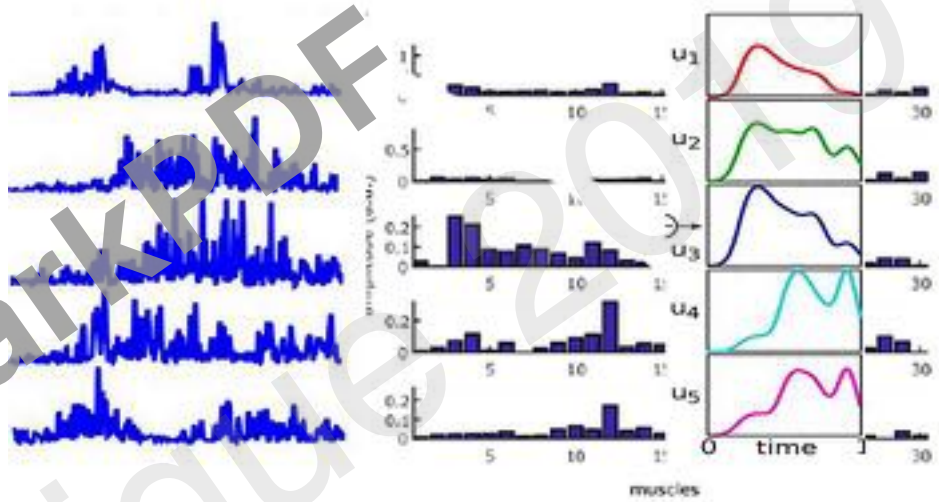
"Bernstein problem"

How does the CNS "choose" among the infinity of solutions of a given motor task

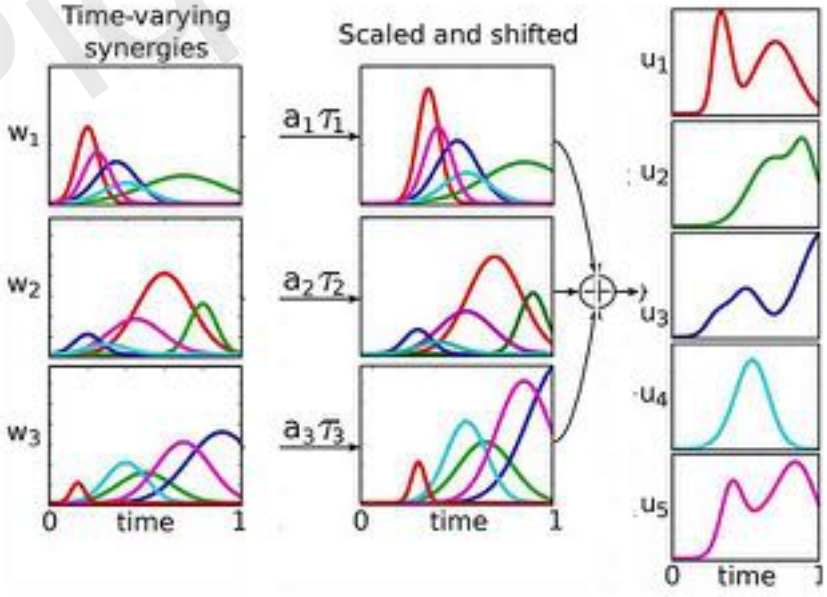
Ivanenko 2003 Temporal components of the motor patterns expressed by the human spinal cord reflect foot kinematics

Supiot 2017 Caractérisation des organisations locomotrices par la quantification des synergies musculaires chez le sujet asymptomatique et cérébrolésé

Delis 2018 Deciphering the functional role of spatial and temporal muscle synergies in whole-body movements



$$m^s(t) = \sum_{i=1}^{P}\sum_{j=1}^{N} wi(t)a_{ij}^s wj + \text{residu.}$$



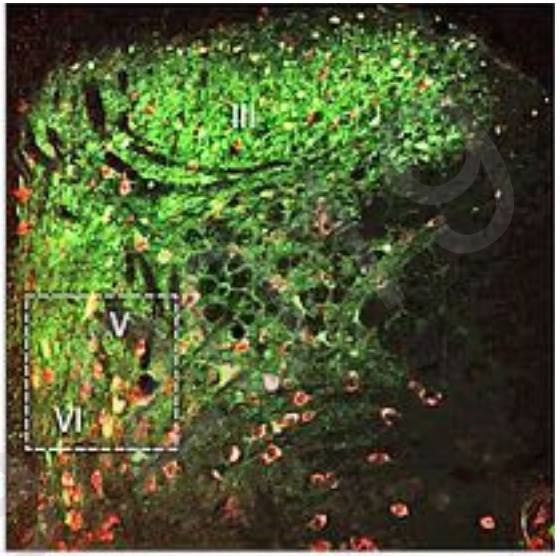
- *the non-negative matrix factorization (NNMF) VAF et R^2*

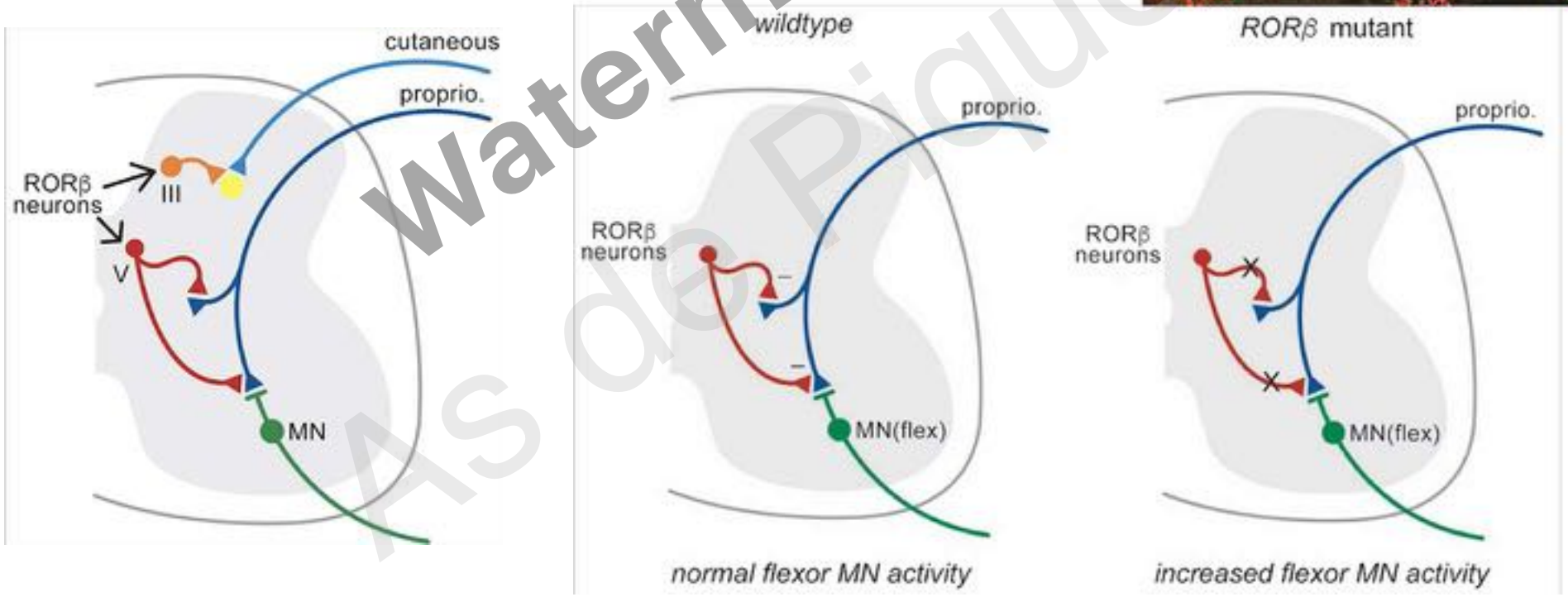
Koch 2017 RORbeta Spinal Interneurons Gate Sensory Transmission during Locomotion to Secure a Fluid Walking Gait

- Rythme de locomotion fluide :

nécessité d' interneurones inhibiteurs exprimant le récepteur nucléaire RORb pour un feedback afférent durant la marche

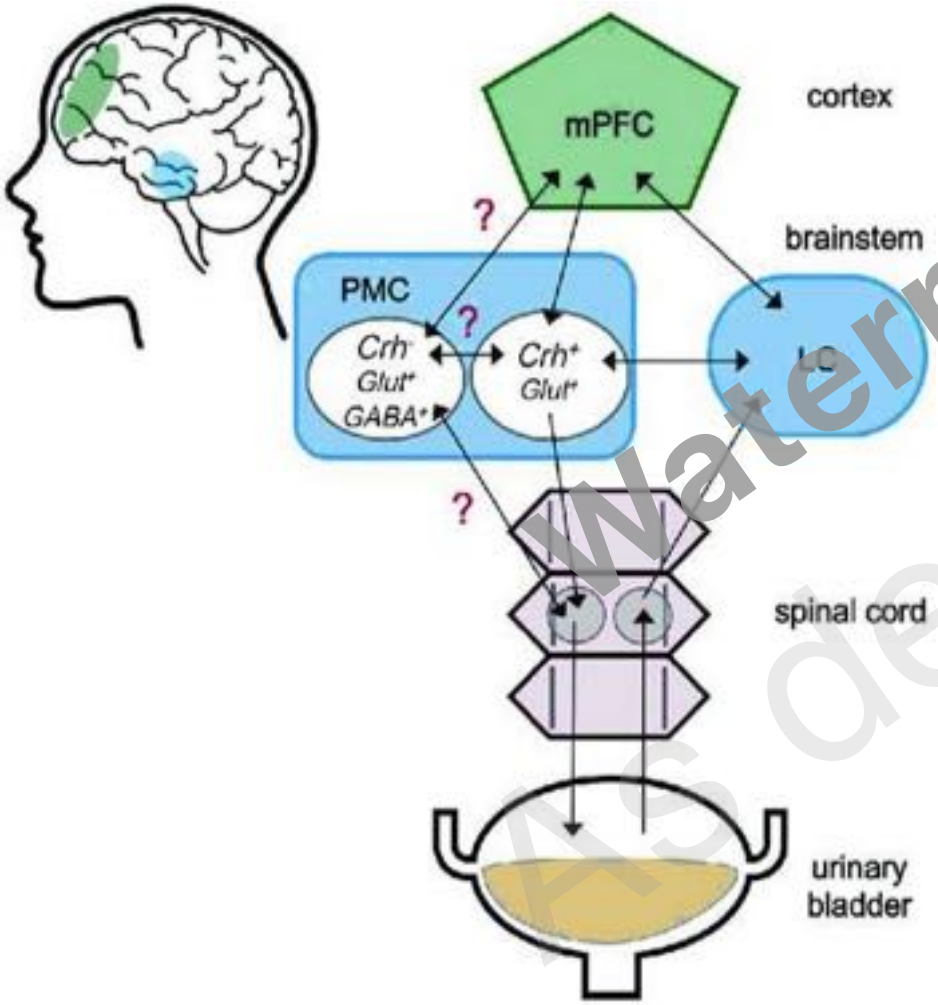
- Manipulation génétique supprimant la fonction inhibitrice entraîne une marche ataxique par exagération des mvts de flexion
- Inactivation de RORb leads diminue l' inhibition présynaptique

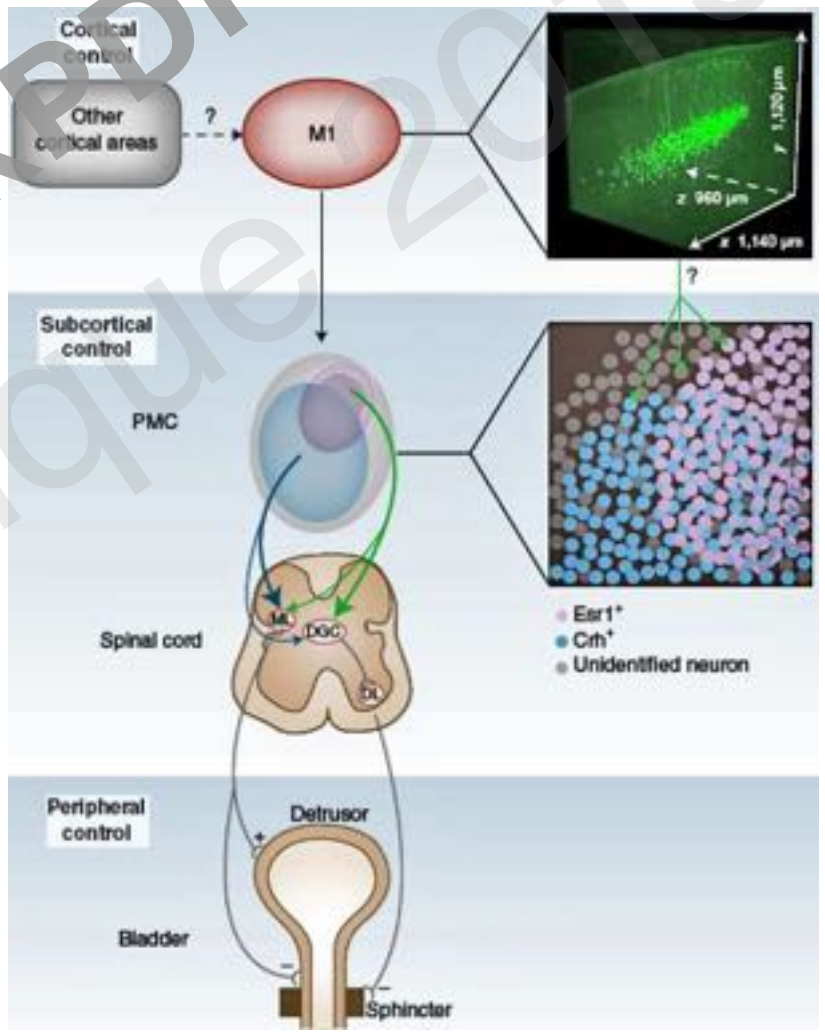




Troubles vésico sphinctériens - Commande mictionnelle

Hou	2016 Central control circuit for context-dependent micturition
Keller	2018 Voluntary urination control by brainstem neurons that relax the urethral sphincter
Malykhjna	2017 How the brain controls urination
Manohar	2017 Brainstem network dynamics underlying the encoding of bladder information
Ni	2018 Let it go: central neural control of urination
Yao	2018 A corticopontine circuit for initiation of urination

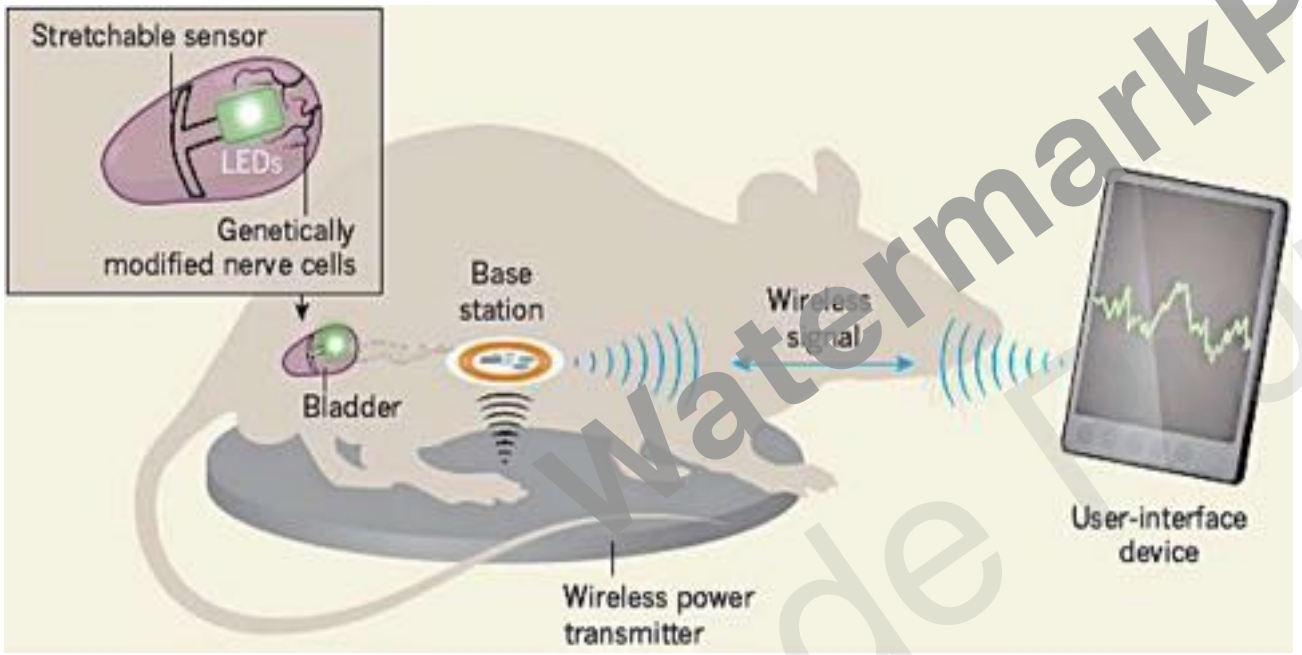


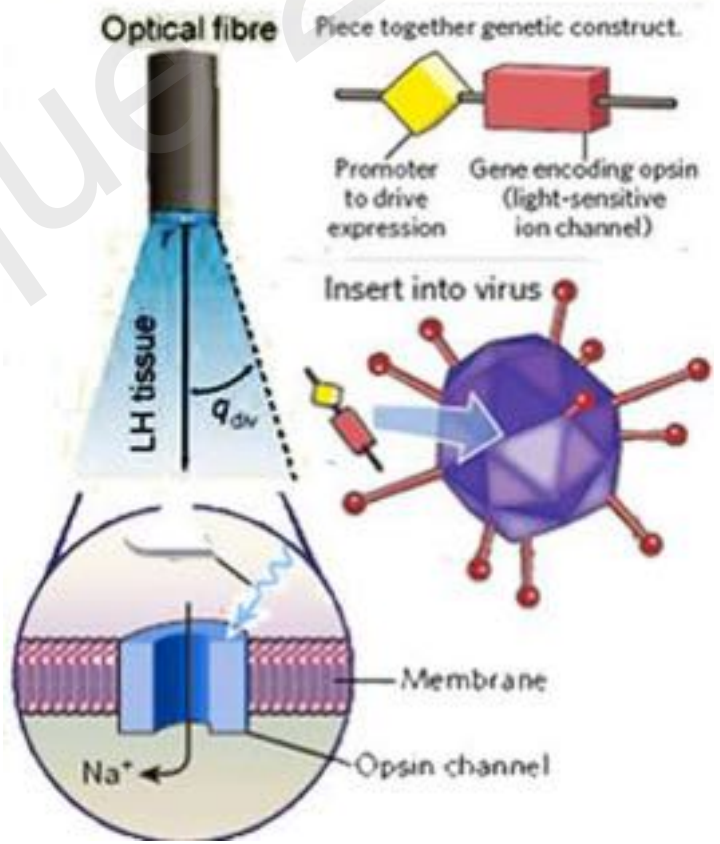


Optogenetics illuminating biology

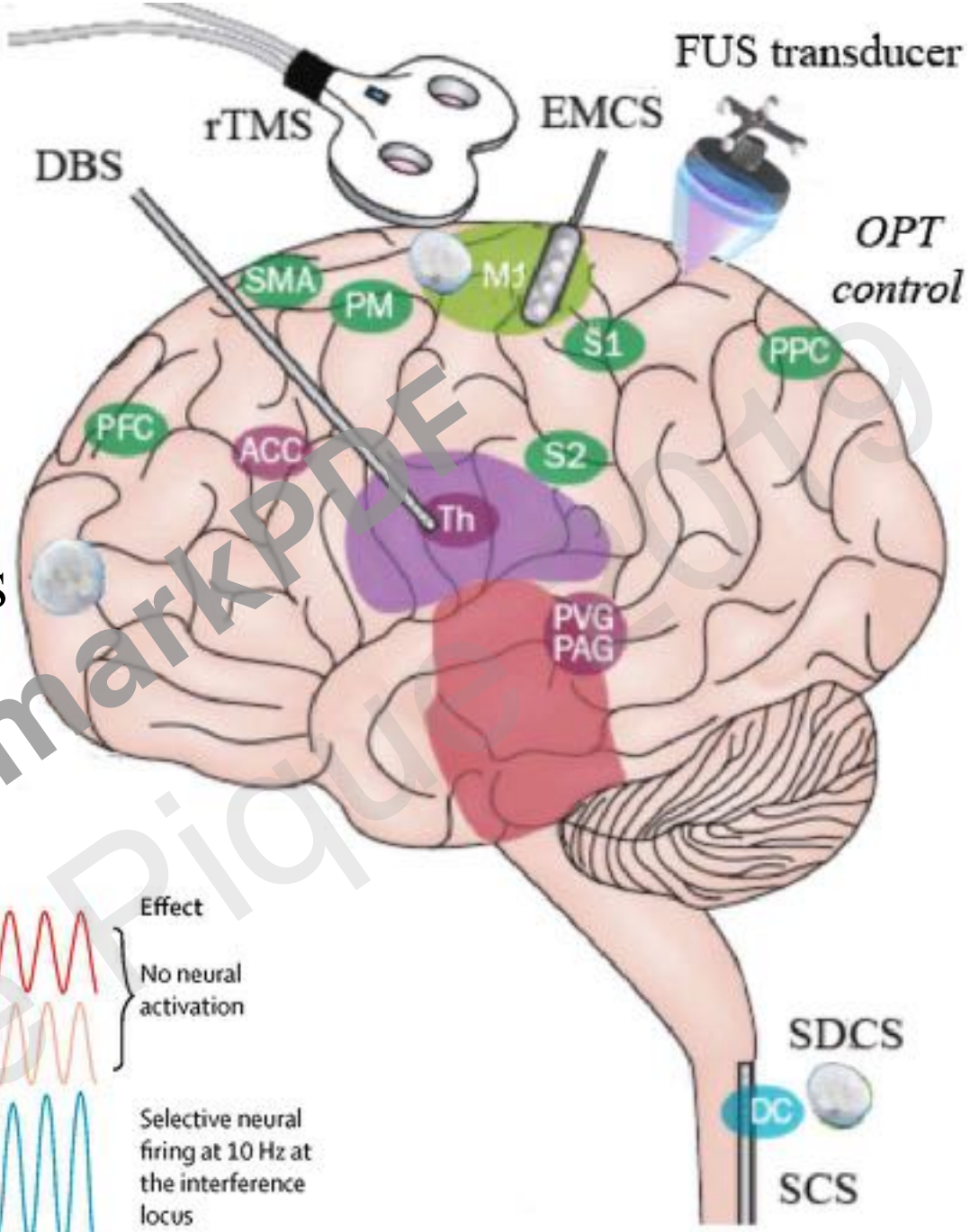
Deisseroth 2005

Mickle 2019 A wireless closed-loop system for optogenetic peripheral Neuromodulation

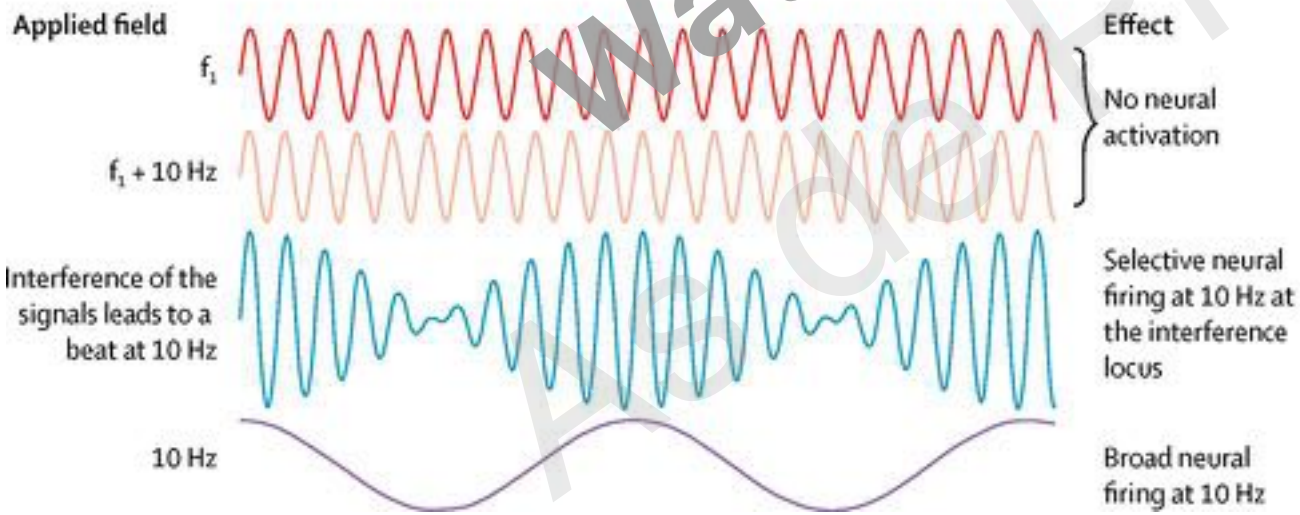




Modulation cérébrale



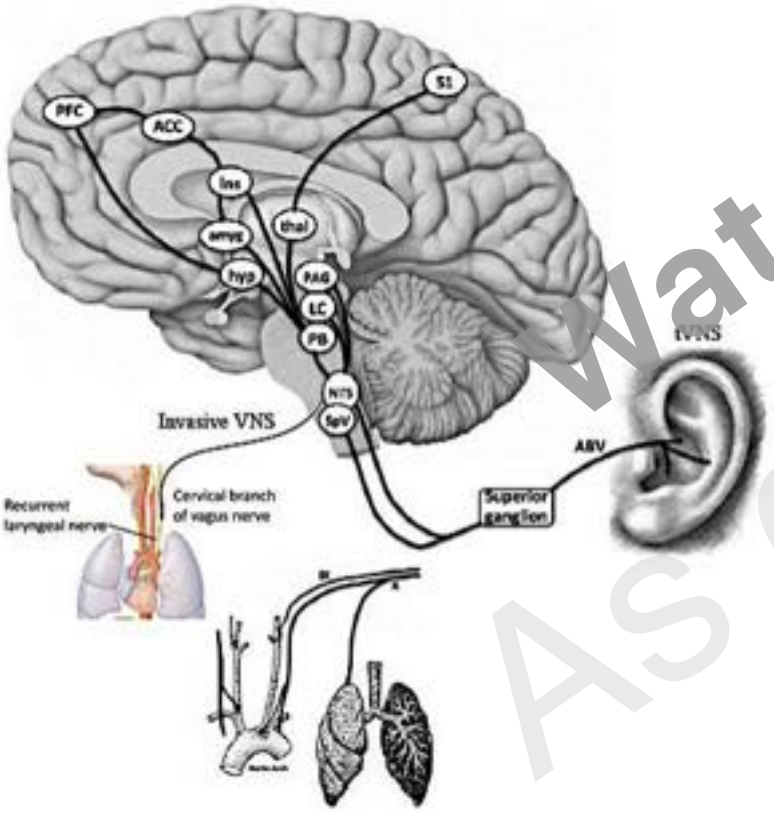
Gunduz 2017 *A new non-surgical approach for DBS*

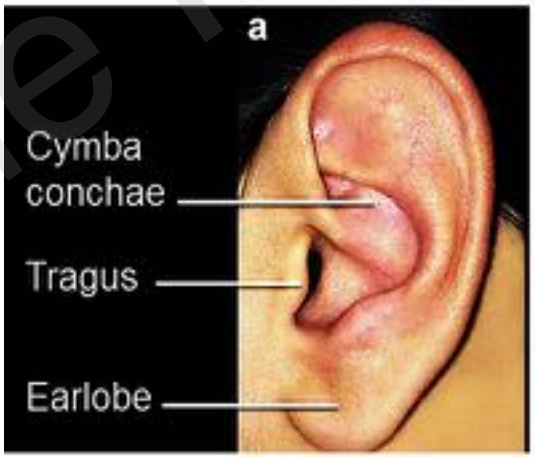


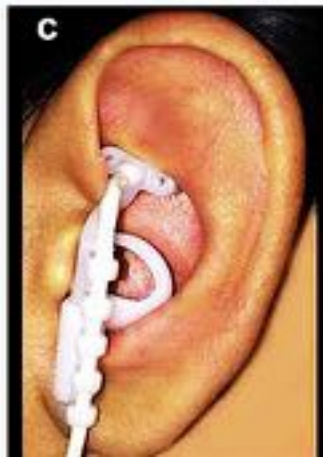
- Stimulation du Vague

Stimulation vagale transauriculaire

- Frangos 2014 Non-invasive Access to the Vagus Nerve Central Projections via Electrical Stimulation of the External Ear: fMRI Evidence in Humans
- Napadow 2012 Evoked Pain Analgesia in Chronic Pelvic Pain Patients Using Respiratory-Gated Auricular Vagal Afferent Nerve Stimulation
- Holle-Lee 2016 Noninvasive vagus nerve stimulation in the management of cluster headache: clinical evidence and practical experience
- Azabou PHRC 2018 Etude randomizee en crossover evaluant l'efficacite de la stimulation non invasive du nerf vague dans la spondyloarthrite axiale resistante aux biotherapies







NTBS - méthodes non invasives de stimulation cérébrale

- TMS à visée diagnostique
- rTMS (stimulation magnétique transcranienne répétitive) à titre prédictif en1996
- NTBS à visée thérapeutique : rTMS et tDCS

Transcranial Magnetic Stimulation: Applications in Neuromodulation, Perioperative Monitoring and Neurorestoration

By J. Rothwell, D. De Ridder, F. Vergani, S. Taylor and L. Oberman

Monday February 18, 2019

5:00 pm (Dublin, Edinburgh, Lisbon, London) - 6:00 pm CET (Amsterdam, Berlin, Bern, Paris, Rome, Stockholm, Vienna) - 12:00 am (Eastern time - New York, Canada) - 2:00 pm (Brasilia) - 2:00 am (Tokyo) - 9:00 am (Pacific time - Los Angeles) - 3:00 am (Brisbane)

The WSSFN is happy to announce its second webinar! We will continue hosting webinars every quarter which will focus on relevant topics pertaining to our subspecialty and will aim to engage a global audience.

tDCS - Points clé

Moduler les activités cérébrales par une méthode non invasive

de façon prolongée

ça marche ou ça ne marche pas

quid dans la douleur

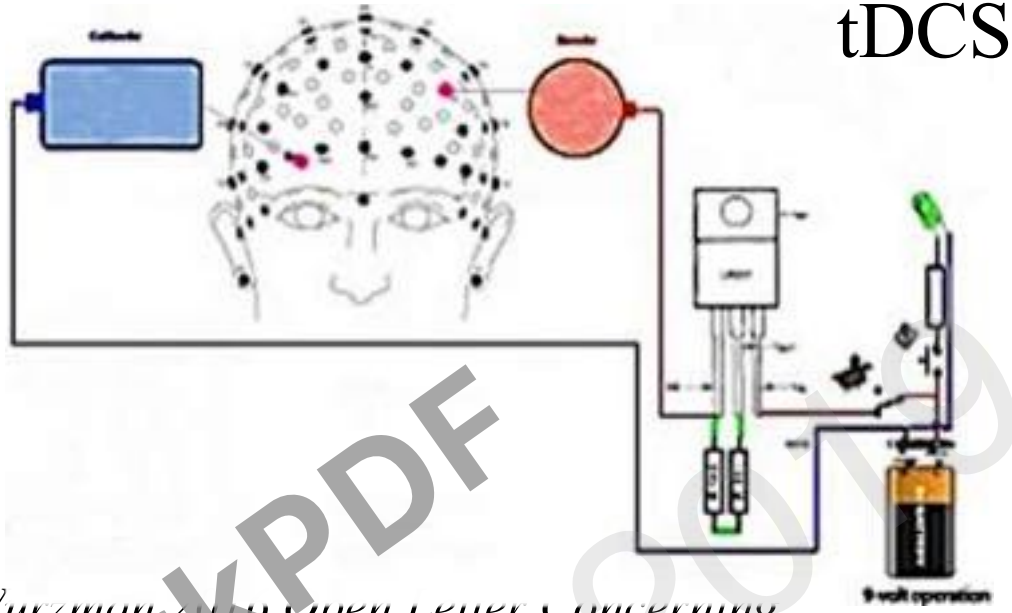
le cortex moteur dans le traitement de la douleur

cible improbable ou “ major breakthrough“

on a 2 hémisphères

le placebo “revisité“

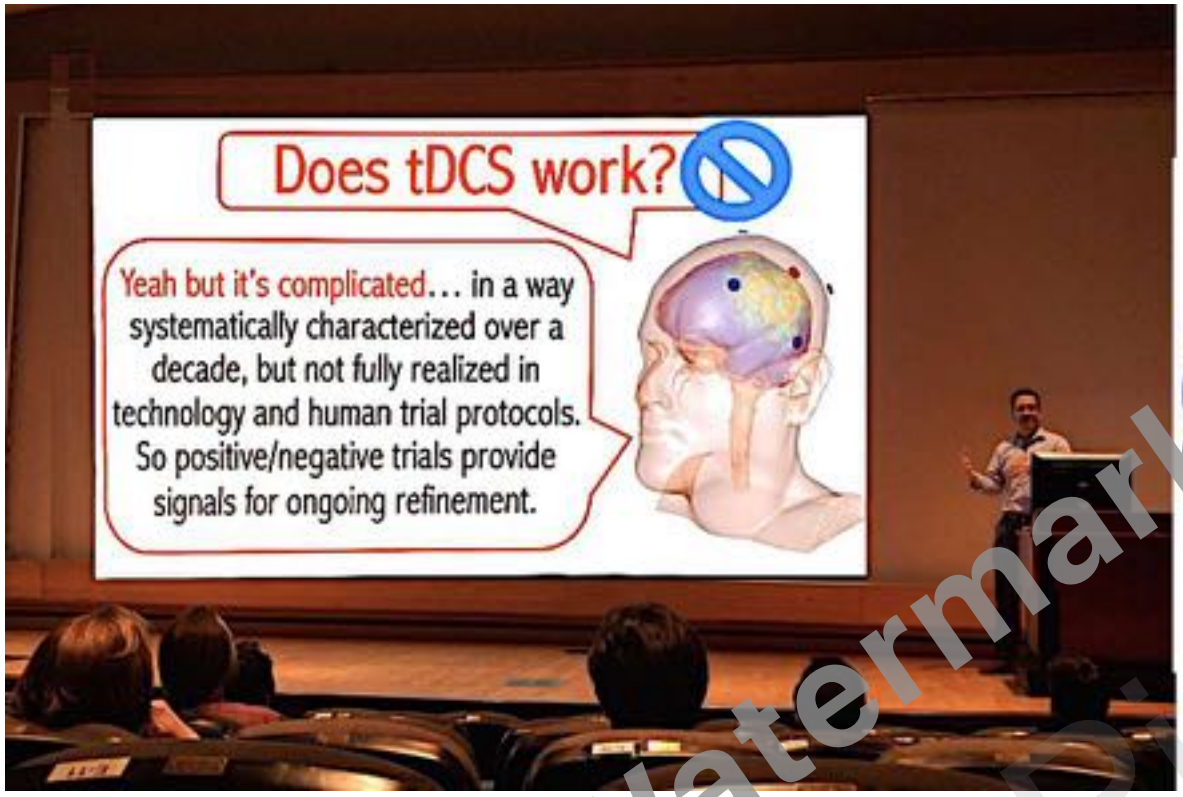
tDCS

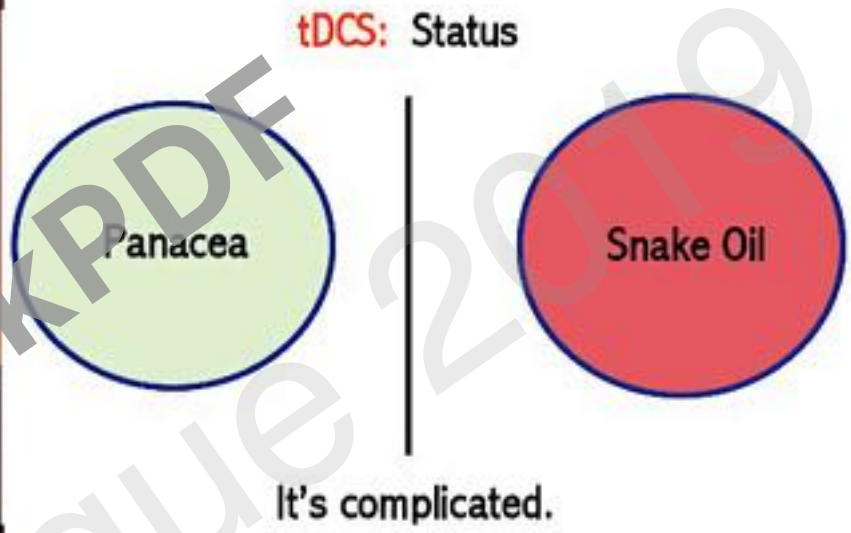


Wurzman 2013 Open Letter Concerning Do-It-Yourself Users of tDCS

Moduler les activités cérébrales par une méthode non invasive de façon prolongée

tDCS





Technologie simple ne veut pas dire mécanisme d'action simpliste ou trivial
ou absence de sophistication dans l'utilisation

La complexité résulte de la complexité du fonctionnement (ou du dysfonctionnement) cérébral

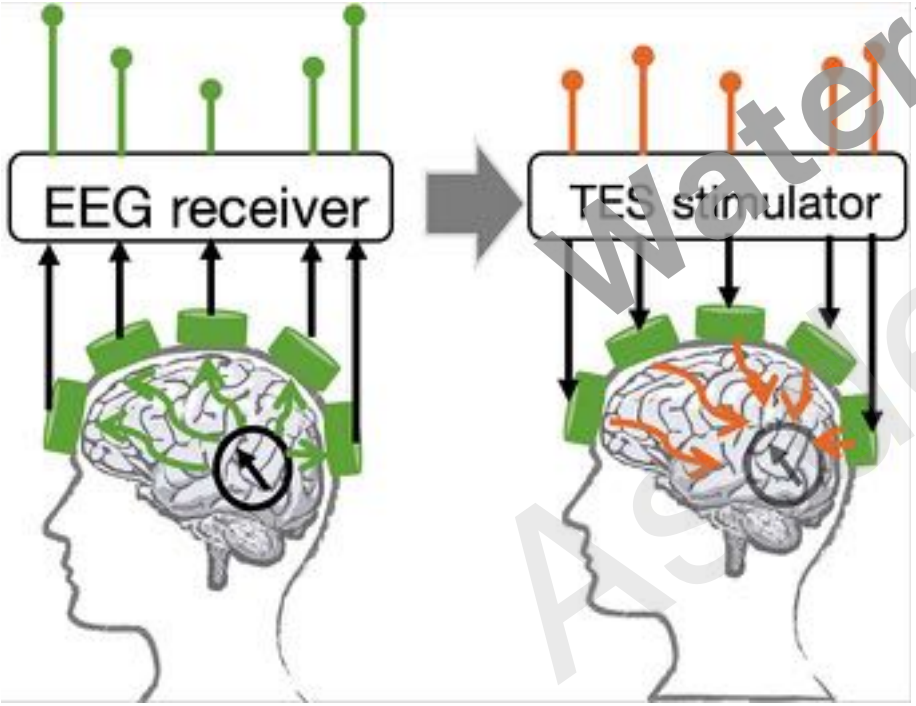
Santarnecchi 2017 The Illusion of the Perfect Brain Enhancer

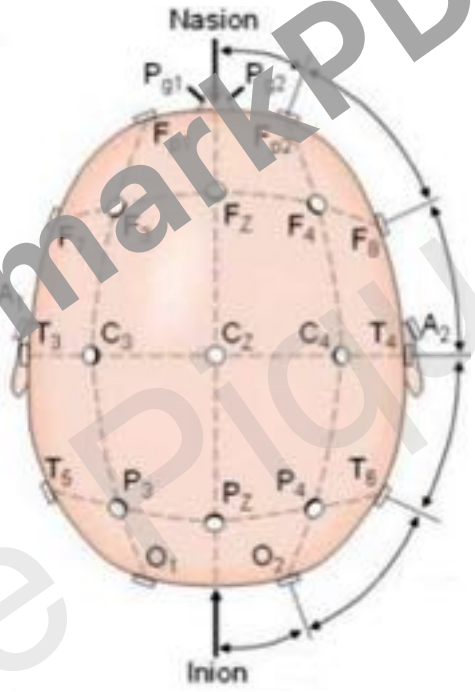
Les signaux électriques traversent le crâne

Kim 2018 Modulation of Electrophysiology by tDCS in Psychiatric Disorders
tDCS : Plasticité cérébrale et amélioration clinique

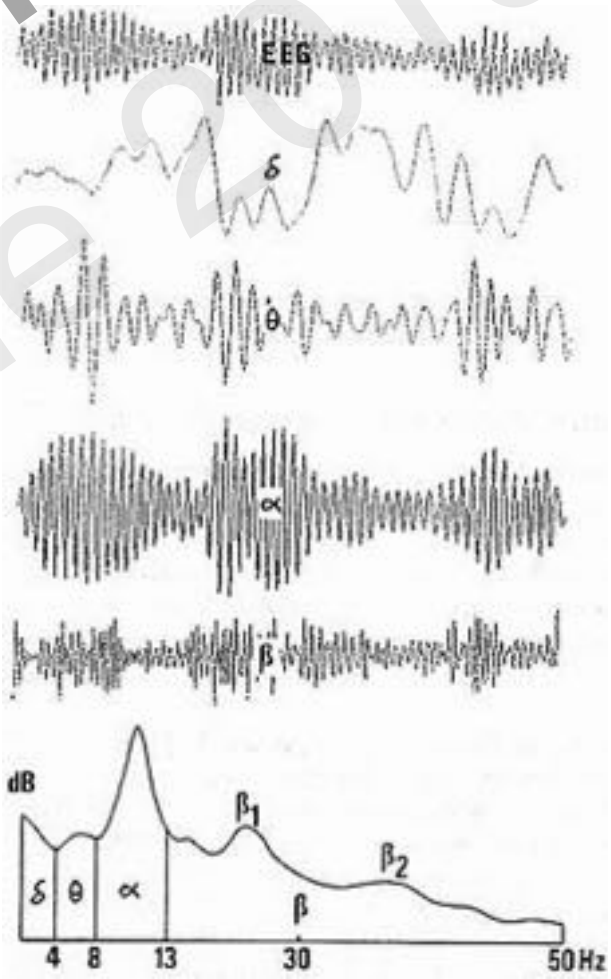
Enregistrments EEG
tDCS stimulation électrique transcranienne

Localisation EEG permet de focaliser tDCS





EEG – bandes d'oscillation
Marqueurs d'efficacité



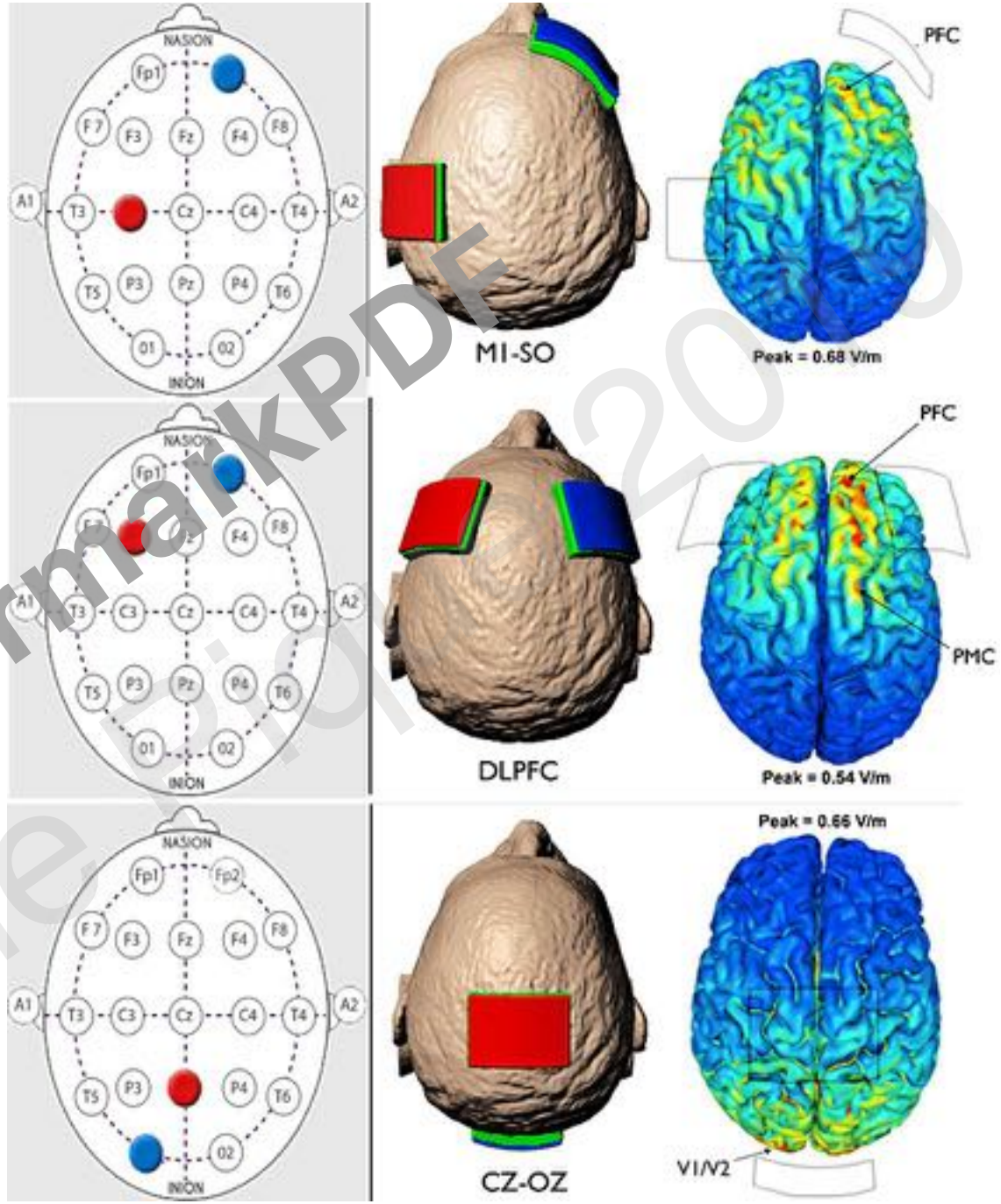
tDCS et douleur - cibles

système EEG International 10–20
anode sur l'hemisphère controlatéral /douleur
cathode en homolatéral

- M1
  C3/C4
  majorité des cas

- DLPFC gauche
  F3
  FM et migraine o

- cortex visuel
  primaire (V1)
  migraine



Les cibles – le cortex moteur M1

Stimulation du cortex moteur (M1) dans le traitement de la douleur

Migita 1995 Transcranial magnetic coil stimulation of motor cortex in patients with central pain

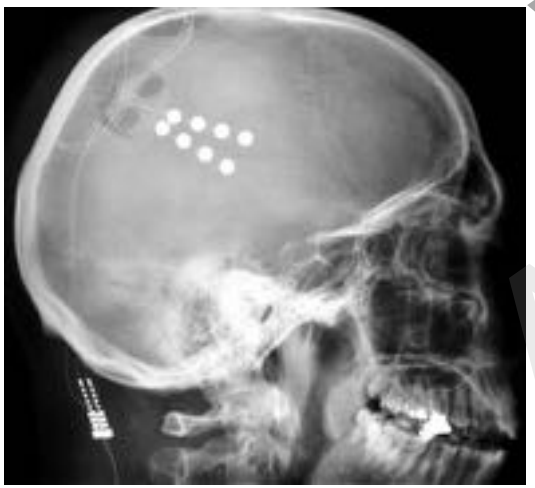
Lima and Fregni 2008 Effects of electrical stimulation of M1 with invasive or non-invasive methods

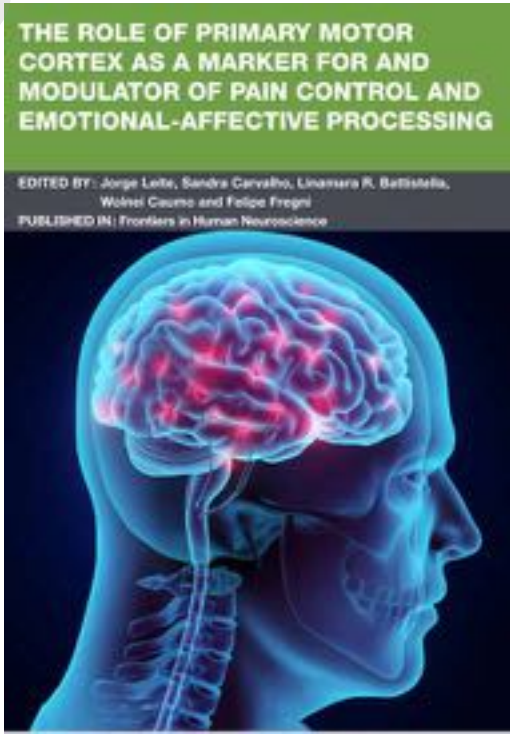
Lefaucheur 2006, Hosomi 2013-5

Kirimoto 2018 Transcranial Static Magnetic Field Stimulation over the Primary Motor Cortex Induces Plastic Changes in Cortical Nociceptive Processing

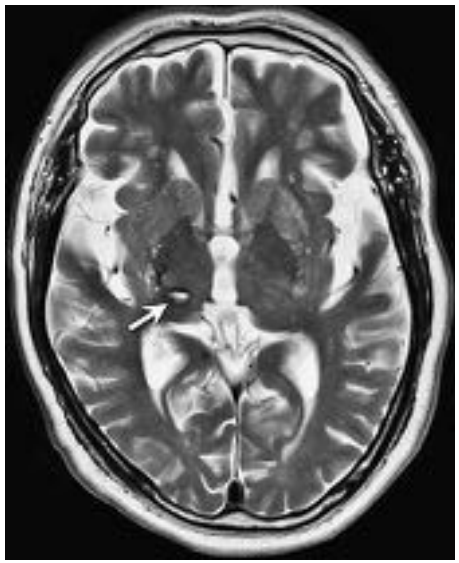
Goodwil 2018 Bihemispheric tDCS and Upper Limb Rehabilitation Improves Retention of Motor Function in Chronic Stroke

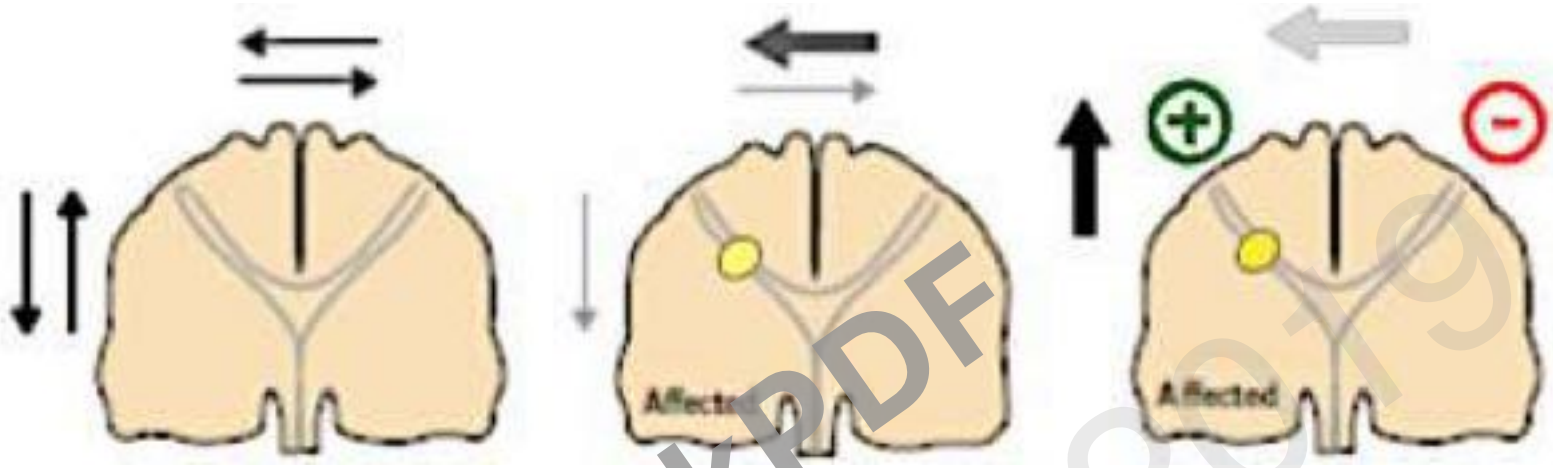
Fisher 2017 Multifocal tDCS targeting the resting state motor network increases cortical excitability beyond traditional tDCS targeting unilateral motor cortex





Morishita 2016 : 2 CPSP cases pain reduction was successfully achieved with tDCS therapy





Interhemispheric Neural Network Remodeling

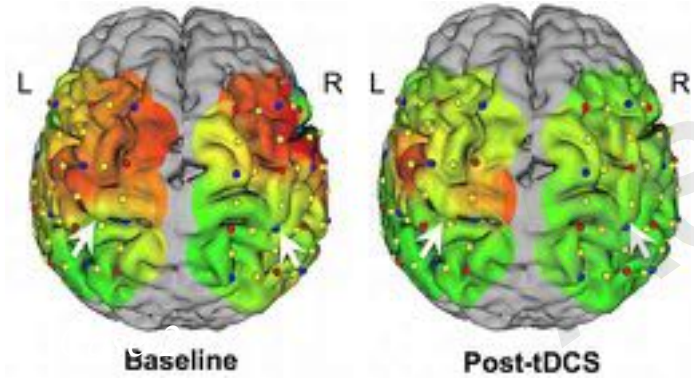
tDCS améliore CPSP et fonction motrice

modulation balance inter hemispherique en imagerie

Procedure Electrode aiming at the M1

anode and cathode enM1 côté lésionel et contro lésionel C3 and C4

Parameters continuous stimulation 2500 mA for 20 or 25min



Functional near infrared spectroscopy (fNIRS)

•tDCS

activité hémisphère droit réduite

aire motrice activée plus focalisée

amélioration de la balance interhémispherique

tDSC, un “booster“ des fonctions cérébrales le TENS du système nerveux central ?

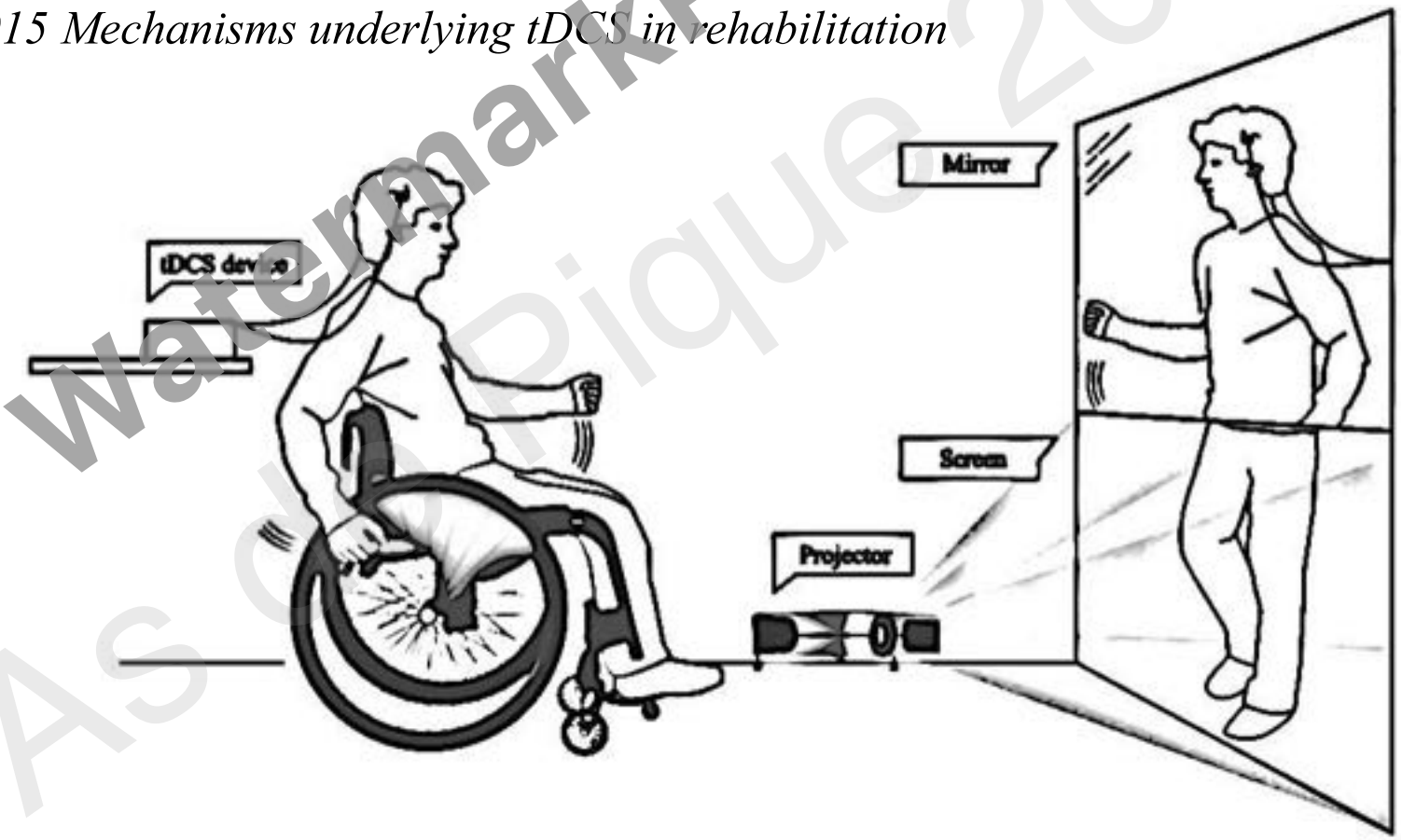
To 2018 Changing Brain Networks Through Non-invasive Neuromodulation

tDCS - “booster“ en pratique

tDCS associé à

- une tâche
- une réadaptation, un autre traitement
- une prise en charge psycho comportementale

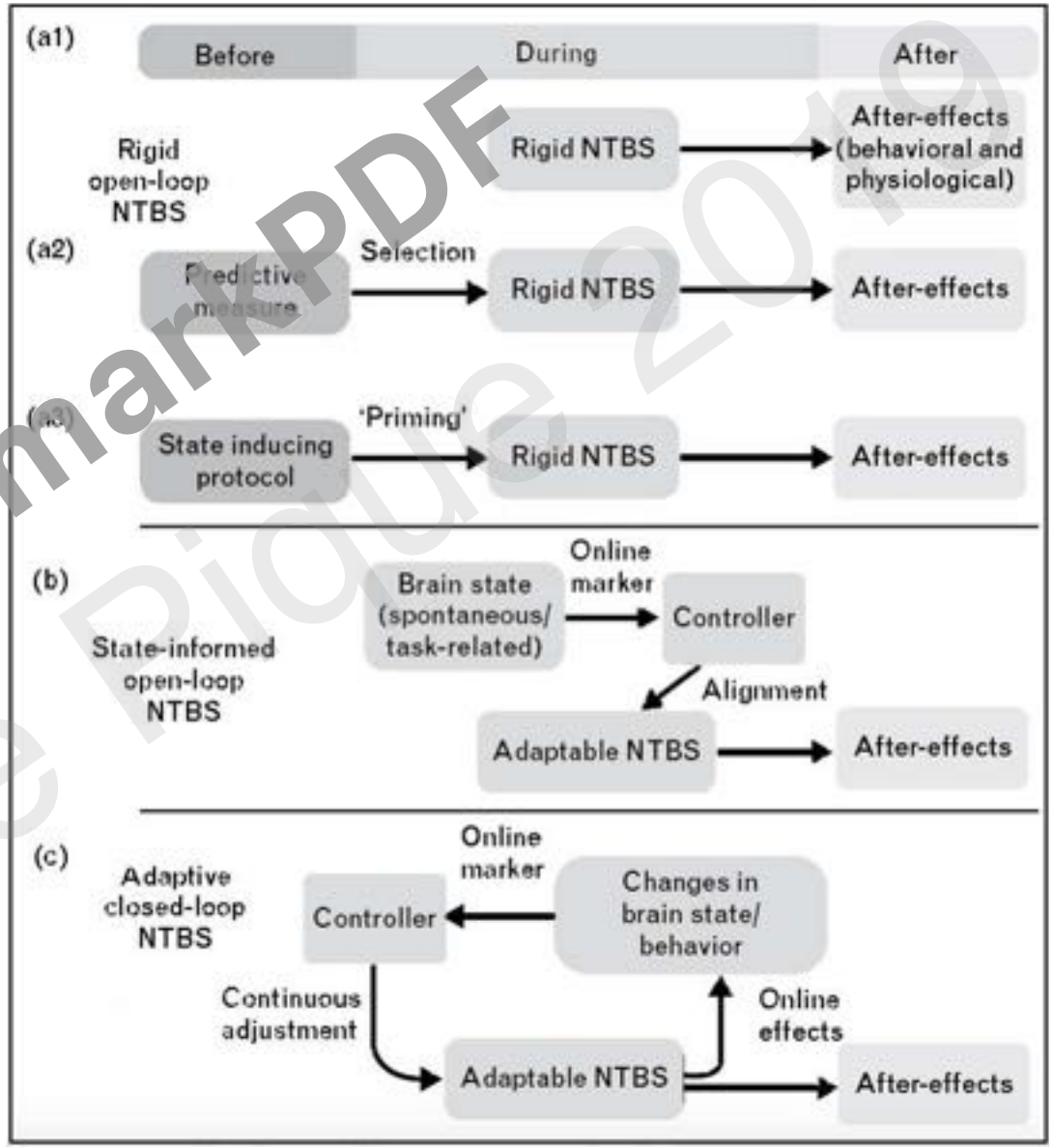
Soler 2010 Effectiveness of tDCS and visual illusion on neuropathic pain in spinal cord injury
Kaski 2014 Combining physical training with tDCS to improve gait in Parkinson's disease
Roche, Geiger, Bussel 2015 Mechanisms underlying tDCS in rehabilitation



Mais aussi : développer des systèmes de feed-back

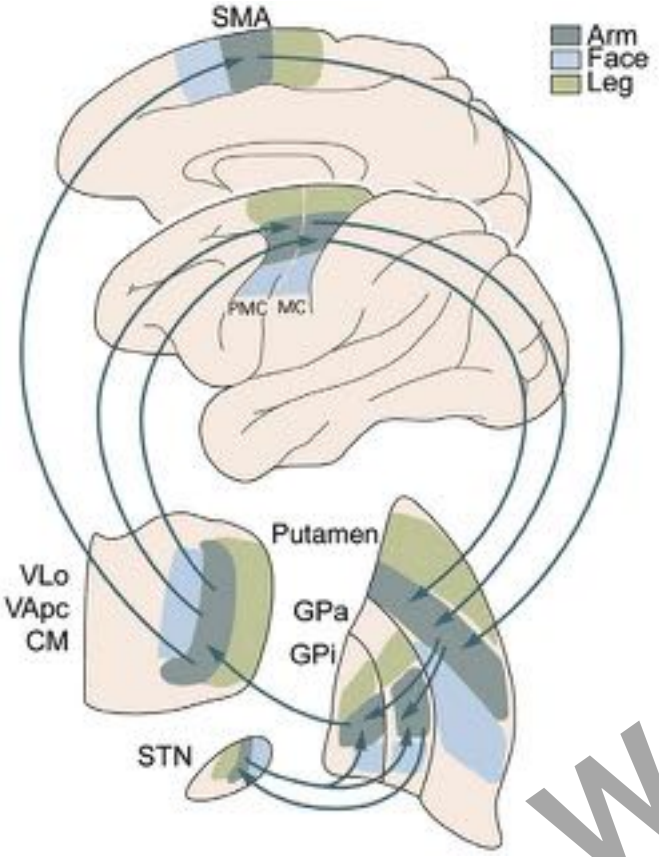
Karabanov 2016
tDCS : closing the loop between brain and stimulation

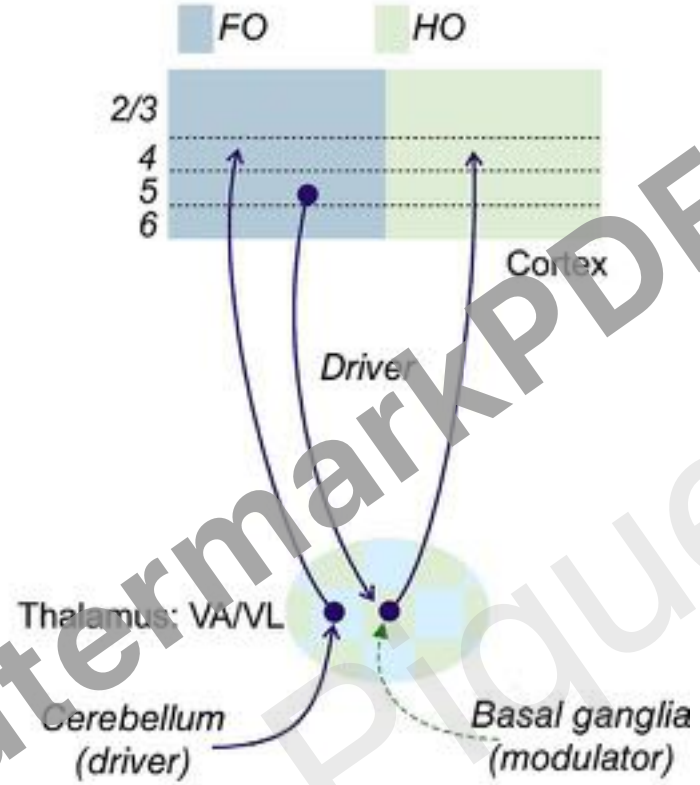
Bergmann 2016 Combining non-invasive tDCS with neuroimaging and electrophysiology

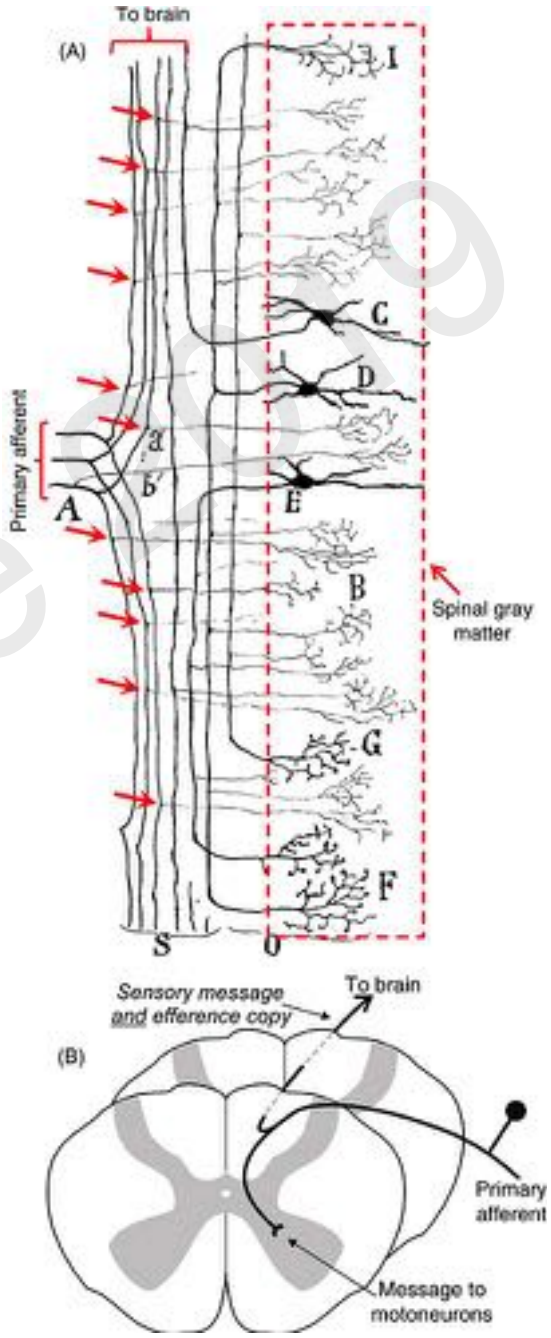


Boucles thalamo corticales - *Sherman 2016*

Schéma de Cajal





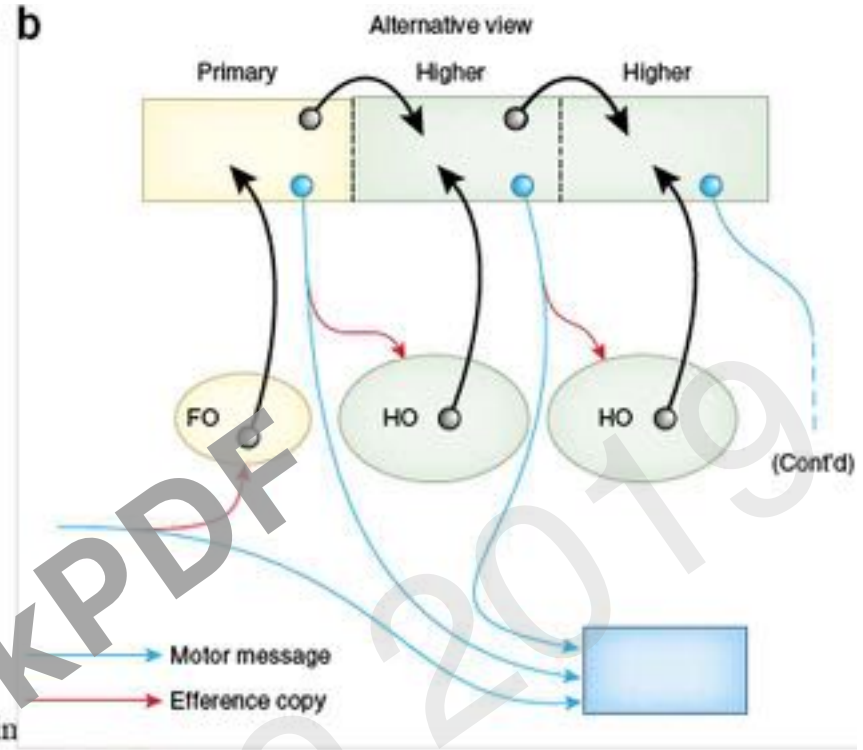


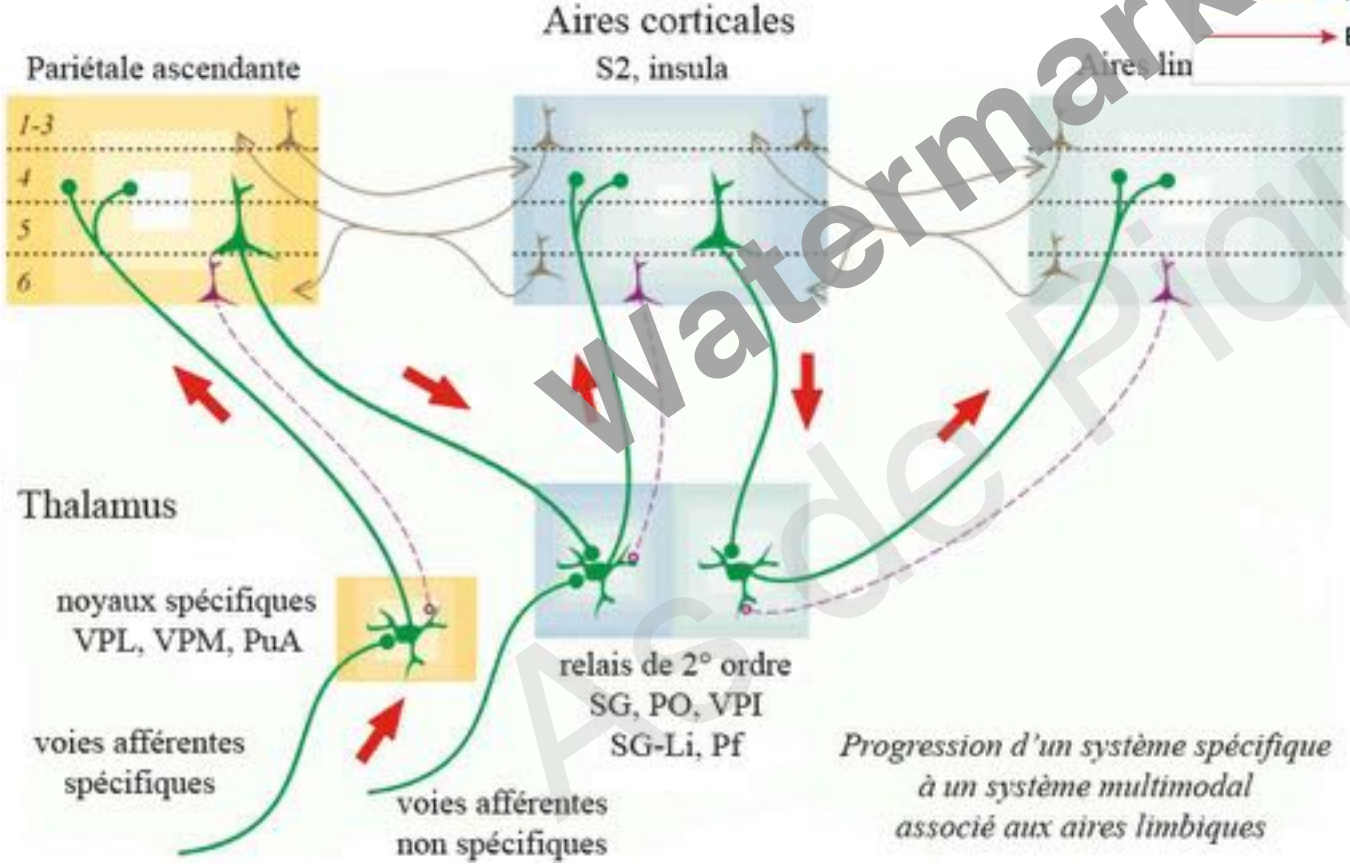
Ancien schéma

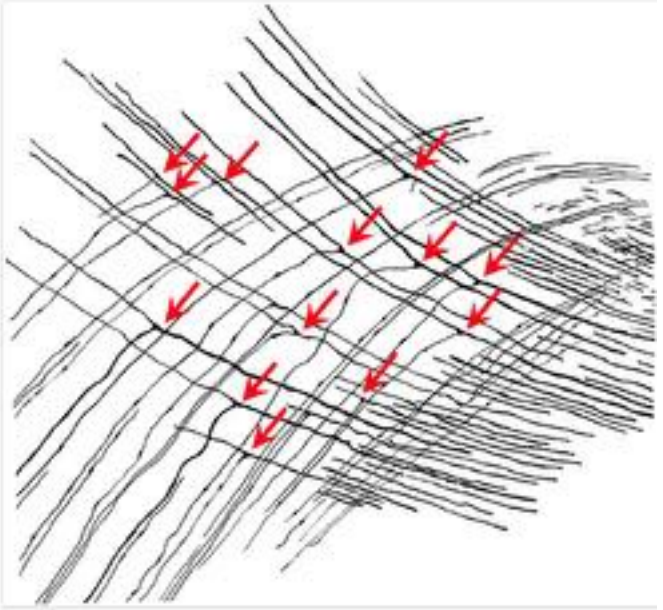
Modèle dynamique
Copie aux différents niveaux

Boucles thalamo corticales

Sherman 2016





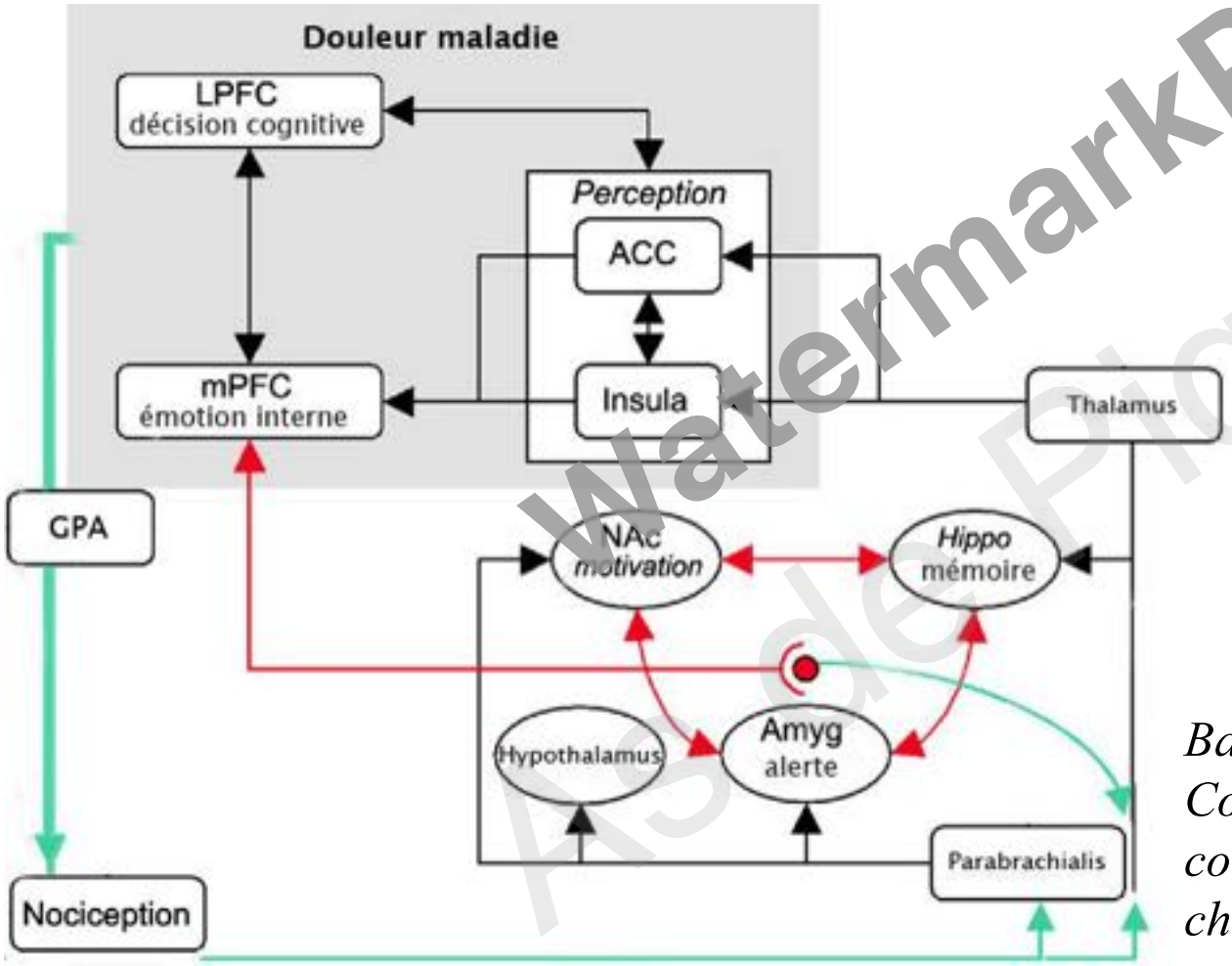


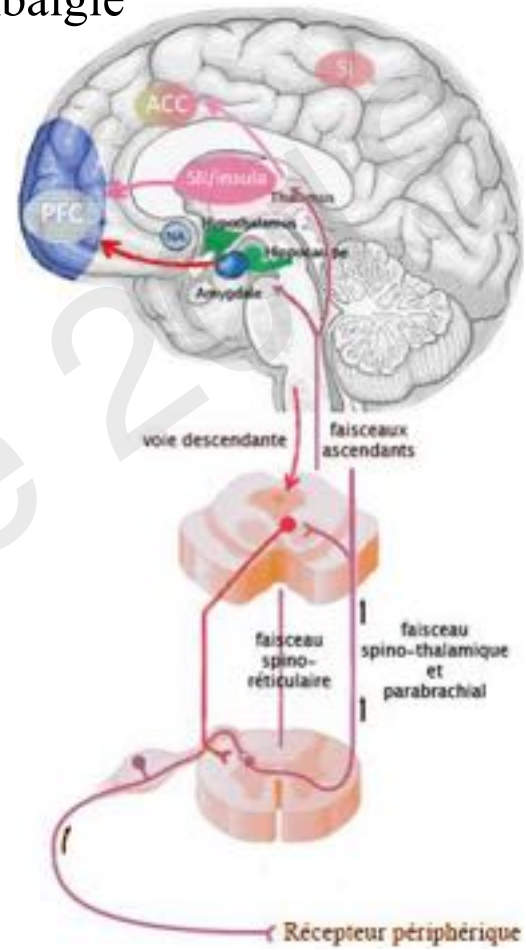
La douleur en boucle

De la douleur aigue à la douleur chronique dans la lombalgie

De la “pain matrix“ au aires limbiques

Conditionnement à la douleur





Baliki, Apkarian 2012
Corticostriatal functional connectivity predicts transition to chronic back pain

Traitement de la douleur chronique

- Traitements pharmacologiques

  40% à 60% des patients soulagés
  efficacité limitée à long terme
  effets secondaires

- Causes probables
  Action limitée au versant somatique
  Mécanismes mal controlés :
  état d'excitabilité centrale, plasticité inadaptée, conditionnement

- Approches alternatives :
  Méthodes cognitivo omportementales, réadaptation, neuromodulation

Deldar 2018 Enhancement of pain inhibition by working memory with anodal transcranial direct current stimulation of the left dorsolateral prefrontal cortex

It's All in Your Head: Reinforcing the Placebo Response With tDCS

Schambra 2014

Egorova 2015. Neuromodulation of conditioned placebo/nocebo in heat pain: anodal vs cathodal tDCS to the right dorsolateral prefrontal cortex

Brunoni 2012. tDCS for the treatment of major depressive disorder

Brunoni 2013 The sertraline vs. electrical currenttherapy for treating depression clinical study

tDCS seul a peu d'effets dans le traitement de la dépression

Par contre effet positif du placebo renforcé par tDCS

Donc

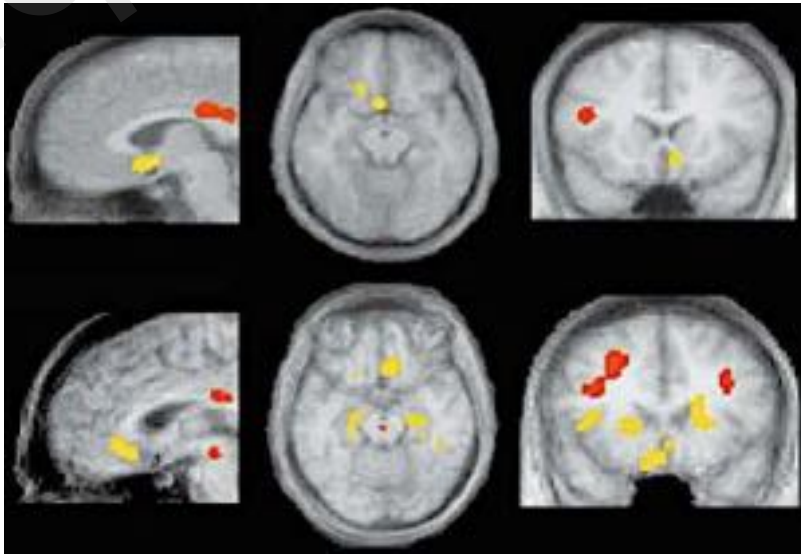
tDCS fortifie la réponse placebo à laquelle il peut contribuer

Placebo et tDCS activent les mêmes régions

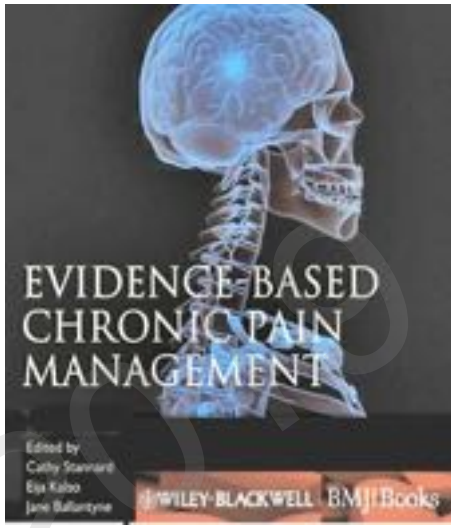
Mayberg 2002 The Functional Neuroanatomy of the Placebo Effect

Benedetti 2010 No prefrontal control, no placebo response

Benedetti 2011 How placebos change the patient's brain



Evidence based medicine

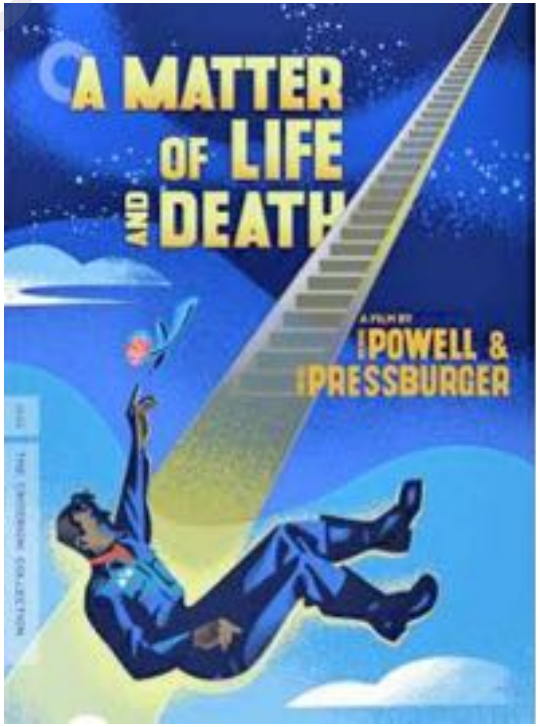


- *North 2018 Clinical study designs for neuromodulation*

- *Kunz 1998 The unpredictability paradox:*
  review of empirical comparisons of randomised and non-randomised clinical trials

- *Smith 2003 Parachute use to prevent death and major trauma related to gravitational challenge:*
  systematic review of randomised controlled trials

  No randomised controlled trials of parachute
  Basis for parachute purely observational



Studies of free fall do not show 100% mortality

Parachute use to prevent death and major trauma when jumping from aircraft randomized controlled trial - Ye 2018

- Weak evidence supporting the efficacy of parachutes
  Guideline recommendations based on expert opinion

- 1rst randomized clinical trial of the efficacy of parachutes in reducing death and major injury when jumping from an aircraft
- Primary efficacy analysis tested the hypothesis that parachute is superior to the control in preventing death and major traumatic injury
- Test for differences between the outcomes of the two trial arms
  9 patients in the parachute group and 11 in the control group
  Student's t test (continuous variables) and Fisher's exact test (categorical variables)

Conclusion

Parachute use did not reduce death or major traumatic injury when jumping from aircraft

- *Tez 2018 Reply*

9 patients in the parachute group and 11 in the control group
A parametric test (Student's t test) is not appropriate for statistical analyses
Authors should have used the non-parametric Mann-Whitney-U test
In brief, the results of the study must be re-interpreted with an appropriate statistical test

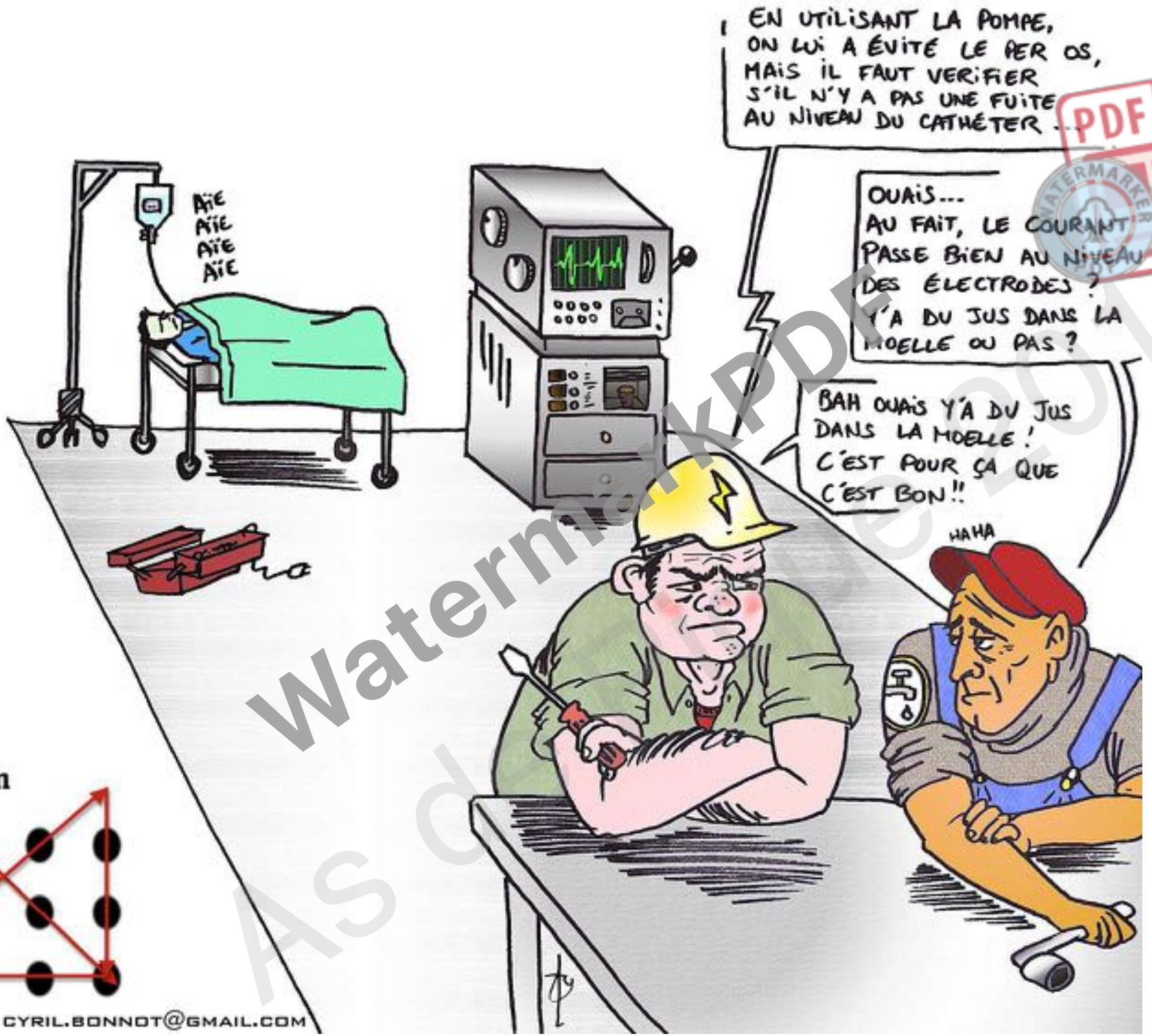
Parachute use to prevent death and major trauma when jumping from aircraft randomized controlled trial - Ye 2018

- Weak evidence supporting the efficacy of parachutes
  Guideline recommendations based on expert opinion

- 1rst randomized clinical trial of the efficacy of parachutes in reducing death and major injury when jumping from an aircraft
- Hypothesis : parachute is superior to the control in preventing death and major traumatic injury
- 2 trial arms
  9 patients in the parachute group and 11 in the control group
  Student's t test (continuous variables) and Fisher's exact test (categorical variables)

Conclusion

Parachute use did not reduce death or major traumatic injury when jumping from aircraft



Solution

CYRIL.BONNOT@GMAIL.COM