Les thérapeutiques physiques dans la dépression: Lesquelles et quand ?

Pr POULET Emmanuel
Psychiatrie des urgences HCL
Centre de prévention du suicide CH Le Vinatier
PsyR2 –INSERM, U1028; CNRS, UMR5292; Lyon Neuroscience Research Center
AFPBN French NIBS section (STEP)

Les méthodes de neuromodulation non invasive dans le traitement de la dépression ?

Resolution spatiale

TMS

MST

Considérer :

- L'efficacité
- La sécurité
- Les aspects pratiques
- Le cout

tDCS

ECT

Caractère invasif

Mr E. Lectroconvulsivo

- Patient de 72 ans
- **ATCD psychiatriques**
  - EDC en 2011 (rémission sous venlafaxine 150mg)
  - EDC en 2014 (rémission venlafaxine 150mg)

- **Histoires des troubles actuels**

  EDC depuis juillet 2017, d'intensité sévère, suite à opération chirurgicale
  - Échec venlafaxine 150 mg juillet aout
  - + mirtazapine 30 mg sept octobre puis hospitalisation
  - Clomipramine 125 mg novembre-janvier, + abilify 5 mg depuis fevrier, amélioration 20%

- **Examen clinique**
  - EDC d'intensité sévère avec caractéristiques mélancoliques (anhédonie ++, douleur morale); idées suicidaires scénarisées avec intentionnalité faible
  - Pas d'élements psychotiques
  - Sd parkinsonien iatrogene et dysurie

Traitement actuel

- Clomipramine 75mg 1,5 cp le soir
- Aripiprazole 5 mg le soir
- Temesta 2,5mg matin midi et soir

Quelles évaluations paracliniques et psychométriques?
Quelles indications de neuromodulation?

Mr E. Lectroconvulsivo

- **Evaluation psychométriques**
  - MADRS (37/60 , BDI (20)
  - MoCA 27/30

- **Examen paracliniques**
  - Dosages psychotropes (clomipramine)
  - Bilan dépression résistante : IRMc, bio

- **Technique de neuromodulation à envisager**
  - Indication ECT
  - Dépression sévère résistant à 3 antidépresseurs dont 1 tricyclique

Discuter arret abilify; switch antidép selon tolérance

Mme M. Ancolique

- Patiente de 32 ans
- **ATCD psychiatriques**
  - Trouble bipolaire type 1
  - 1 épisode maniaque à 22 ans
  - EDM à 26 ans (post-partum), virage maniaque sous escitalopram 10m
  - Stabilisée depuis sous lithium

Traitement actuel

- Teralithe 400 LP : 2 le soir
- Quetiapine : 800mg le soir
- Tercian 100 mg/ jour

- **Histoires des troubles actuels**
  - EDM mélancolique du post-partum depuis 3 mois, SPDT depuis 2 mois pour idées suicidaires et refus d'alimentation
  - Echec lithium + quetiapine (depuis 2 mois)

- **Examen clinique**
  - EDM d'intensité sévère avec caractéristiques mélancoliques et psychotiques
  - Idées délirantes de culpabilité, d'être possédée par le diable, doute sur hallucinations cenesthésiques
  - Idées de suicide scénarisées et d'infanticide
  - Refus d'alimentation et hydratation depuis 3 jours, discussion SNG

Quelles évaluations paracliniques et psychométriques?
Quelles indications de neuromodulation?

Mme M. Ancolique

- **Evaluation psychométriques**
  - MADRS : 48/60
  - MoCA : 23/30

- **Examen paracliniques**
  - Dosages psychotropes

- **Technique de neuromodulation à envisager**
  - Indication ECT en urgence
  - Dépression sévère mélancolique avec pronostic vital engagé
  - Bilan pré-anesthésie et pré ECT : imagerie cérébrale en urgence

Discuter switch APA

Mme D. Primé

- Patiente de 62 ans
- **ATCD psychiatriques**
  - Trouble dépressif récurrent
  - EDC à 45 ans : résolutif sans traitement médicamenteux
  - EDC à 53 ans : sertraline 50 mg non supporté, résolutif sous mianserine

Traitement actuel

- Mianserine 90 mg le soir
- Seresta 10 mg 3/jour

- **Histoires des troubles actuels**
  - EDM dans un contexte de conflits avec sa fille
  - Traité par fluoxetine 20 mg mal supporté, seroplex idem
  - Mianserine 60 mg peu efficace hormis sommeil, 90 mg mais plaintes de sédation)

- **Examen clinique**
  - EDM d'intensité modéré (anhédonie partielle, cognitions dépressogenes, aboulie modérée)
  - Risque suicidaire évalué comme faible

Quelle conduite à tenir?
Quelles évaluations paracliniques et psychométriques?

Mme D. Primé

- **Evaluation psychométriques**
  - MADRS : 23/60, BDI 16
  - MoCA : 30/30

- **Examen paracliniques et adaptations**
  - Dosages psychotropes
  - Discuter génotypage (métaboliseuse lente?)

- **Technique de neuromodulation à envisager**
  - rTMS
  - Dépression non résistante d'intensité modérée
  - HF CPFDL gauche ou BF CPFDL droit (20 à 30 séances)

HAUTE AUTORITÉ DE SANTÉ

ÉVALUER
LES TECHNOLOGIES DE SANTÉ

RAPPORT D'ÉVALUATION

Stimulation magnétique transcrânienne dans le traitement de la dépression résistante de l'adulte

SCIENCES • SANTÉ

La rTMS est une thérapeutique innovante de la dépression qui doit être reconnue

TRIBUNE

Un collectif de psychiatres dénonce l'absence de remboursement d'une technique de traitement de la dépression résistante par stimulation magnétique du cerveau. Selon eux, l'avis négatif de la HAS sur cette technique utilisée dans 150 centres en France est biaisé.

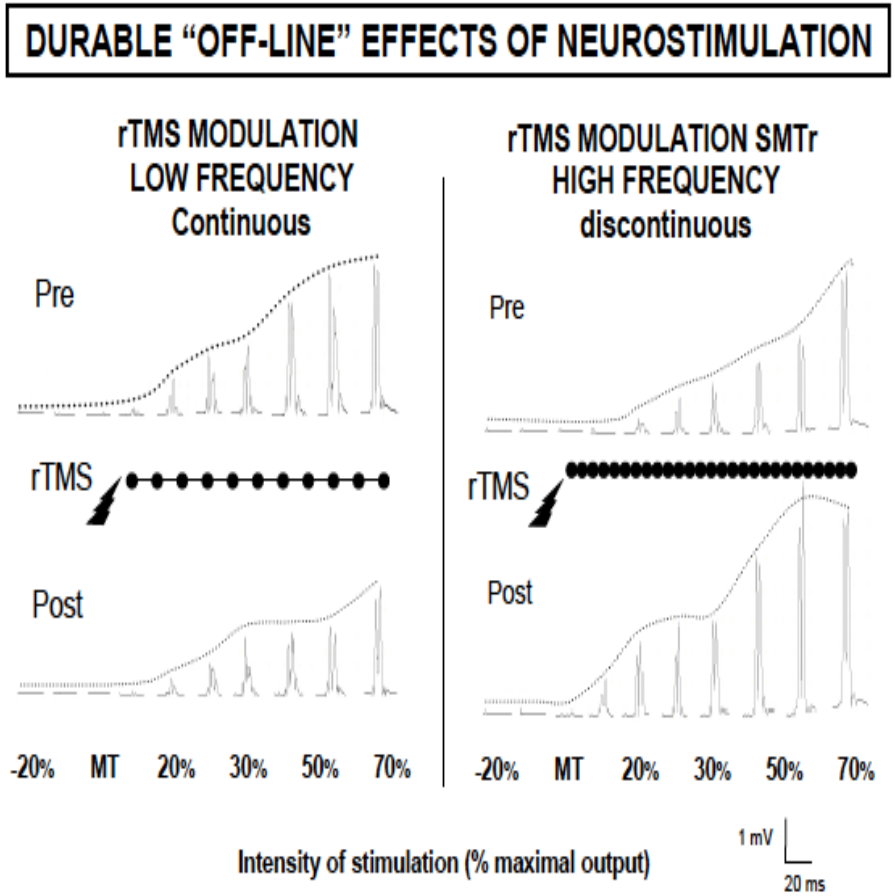
Publié le 24 novembre 2022 à 06h00, mis à jour le 29 novembre 2022 à 17h24 | Lecture 3 min.

Step
STIMULATION TRANSCRÂNIENNE EN PSYCHIATRIE

https://step-afpbn.org/accueil

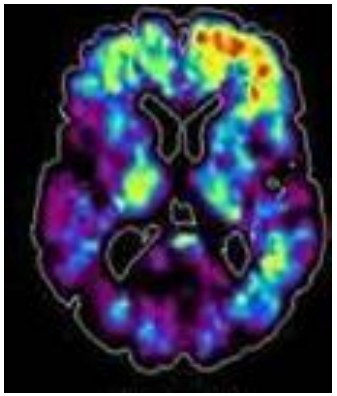
rTMS dans la DEPRESSION – Efficacité

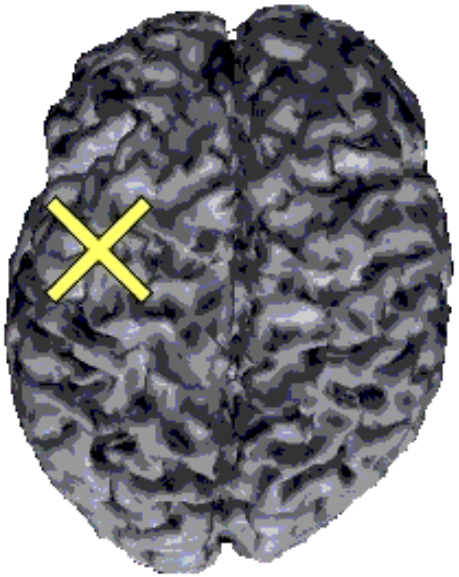
Impacte de la fréquence dans les effets de neuromodulation



« Considérer la dépression clinique comme une maladie impliquant un dysfonctionnement du cortex préfrontal et des régions cérébrales connectées »

M George, TA Ketter, RM Post (1994)





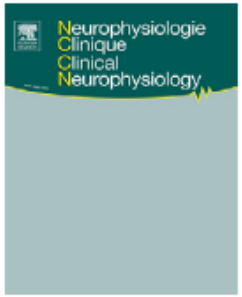
Un effet bilatéral

rTMS dans la DEPRESSION – Efficacité

Neurophysiologie Clinique/Clinical Neurophysiology (2011) 41, 221–295

Disponible en ligne sur
SciVerse ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en



French guidelines on the use of repetitive transcranial magnetic stimulation (rTMS): Safety and therapeutic indications

J.-P. Lefaucheur [a,*,b,1], N. André-Obadia [c,d,1], E. Poulet [e,f,1], H. Devanne [g,h,i,1],

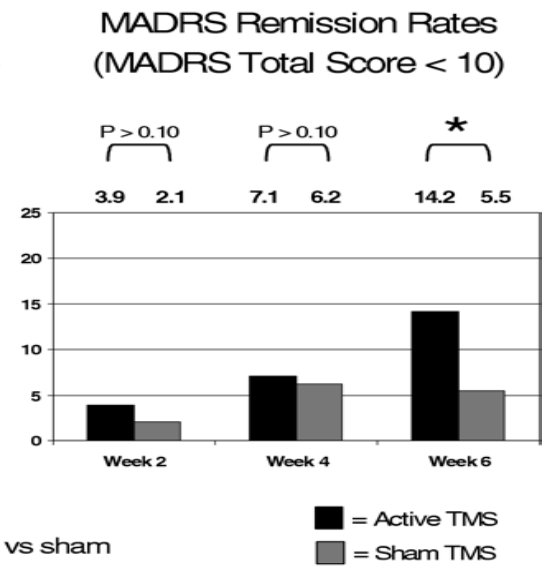
- We have convincing Class I evidence in monotherapy
  Left prefrontal rTMS for acute depression

(O'Reardon et al, 2007 – George et al , 2009)

"Certainly efficacy"

US FDA Approved 2008

•10 Hz, 4-second train duration, and 26-second intertrain interval) for **37.5 minutes (**3000 pulses per session)



rTMS for depression

Clinical Neurophysiology 125 (2014) 2150–2206

Contents lists available at ScienceDirect

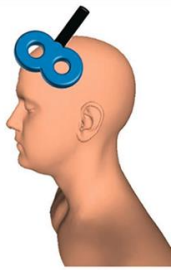
Clinical Neurophysiology

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

Guidelines

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

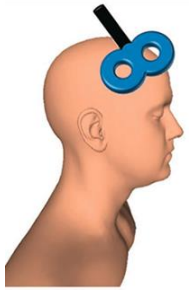
Jean-Pascal Lefaucheur [a,b,*], Nathalie André-Obadia [c,d], Andrea Antal [e], Samar S. Ayache [a,b], Chris Baeken [f,g], David H. Benninger [h], Roberto M. Cantello [i], Massimo Cincotta [j], Mamede de Carvalho [k], Dirk De Ridder [l,m], Hervé Devanne [n,o], Vincenzo Di Lazzaro [p], Saša R. Filipović [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]



- Definite antidepressant effect of HF rTMS of the left DLPFC **(Level A)**

  38 studies, **6 class I**

(RCT with n≥25 patients receiving active treatment)



- Probable antidepressant effect of LF rTMS of the right DLPFC **(Level B)**

  5 studies, 4 in favor of active rTMS, 3 class II

- **No recommendation** for the antidepressant effect of bilateral rTMS combining HF rTMS of the left DLPFC and LF rTMS of the right DLPFC

rTMS for DEPRESSION – Cost effectiveness ?

- Total number of stimulation globally smallest with LF
  - Medico economical impact ?

LF rTMS of the right DLPFC							
Klein et al., 1999b	70 (active: 36; control: 34)	Right DLPFC, F8c	Tilted coil	1Hz, 110% RMT	120 pulses, 10 sessions	Positive (49% responders, 47% improvement)	I I
Januel et al., 2006	27 (active: 11; control: 16)	Right DLPFC, F8c	Sham coil	1Hz, 90% RMT	120 pulses, 16 sessions	Positive (64% responders, 54% improvement)	I II
Fitzgerald et al., 2008b	60	Right DLPFC, F8c	Tilted coil	1Hz (6Hz priming), 110% RMT	900 pulses, 20 sessions	Positive (30% responders for 6Hz primed rTMS; 11% responders for non-primed rTMS)	I I
Bares et al., 2009	60 (active: 29; control: 31)	Right DLPFC, F8c	Tilted coil	1Hz, 100% RMT	600 pulses, 20 sessions	No difference of efficacy between rTMS (33% responders) and venlafaxine (39% responders)	I I
Aguirre et al., 2011	34 (active: 19; control: 15)	Right DLPFC, F8c	Tilted coil	1Hz, 110% RMT	1200 pulses, 20 sessions	No difference of efficacy between active and sham rTMS, except for patients younger than 45 years old	I II
Recommendation: probable antidepressant effect of LF rTMS of the right DLPFC (Level B)							

?

rTMS for DEPRESSION – interest of Low Frequency ?

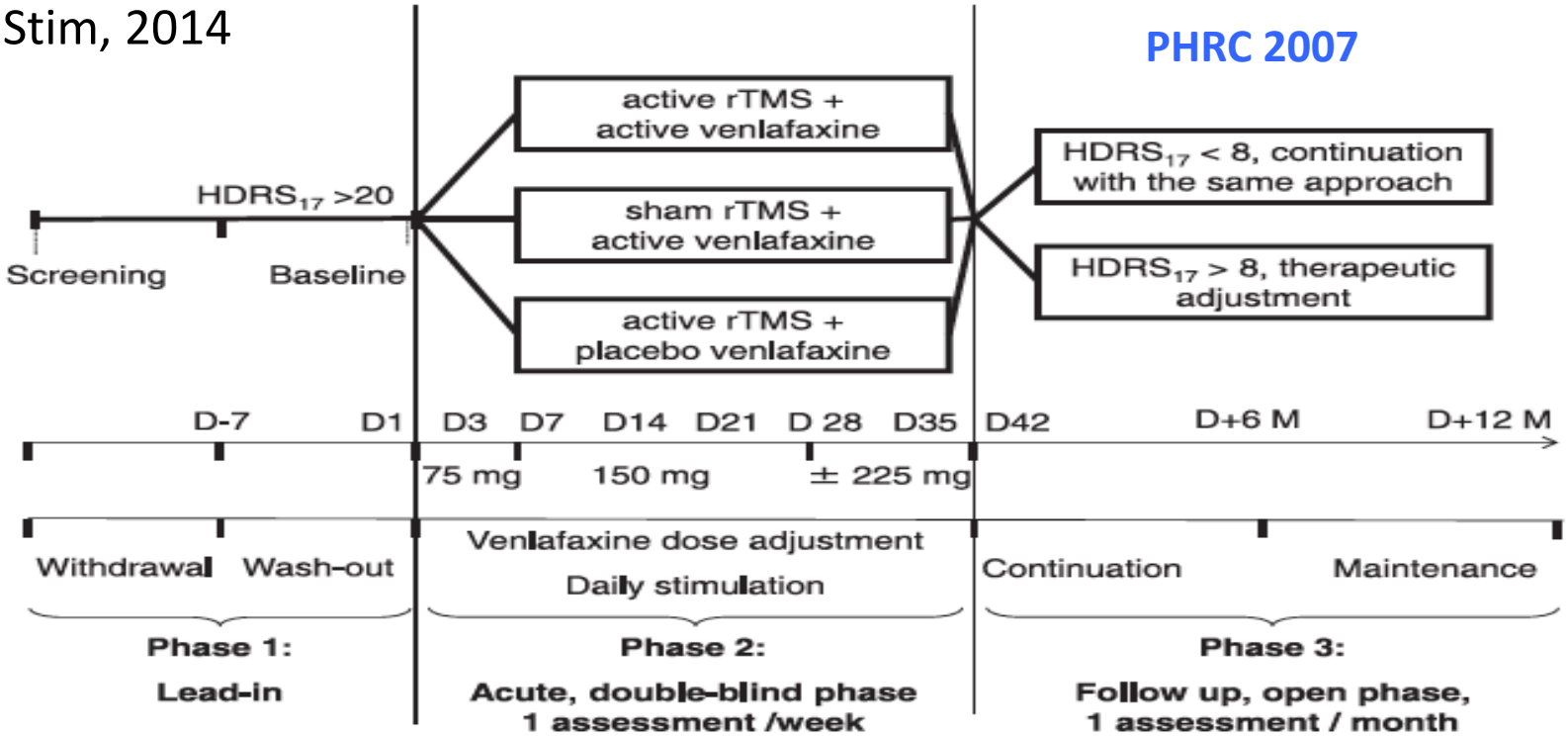
Original Research

The Efficacy and Safety of Low Frequency Repetitive Transcranial Magnetic Stimulation for Treatment-resistant Depression: The Results From a Large Multicenter French RCT

Jerome Brunelin [a,*], Isabelle Jalenques [b,c], Benoit Trojak [d], Jerome Attal [e], David Szekely [f,g,h], Aurélia Gay [i], Dominique Januel [j], Emmanuel Haffen [k], Anne-Marie Schott-Pethelaz [l], Coralie Brault [l], The STEP Group [1], Emmanuel Poulet [a,m]

Brain Stim, 2014

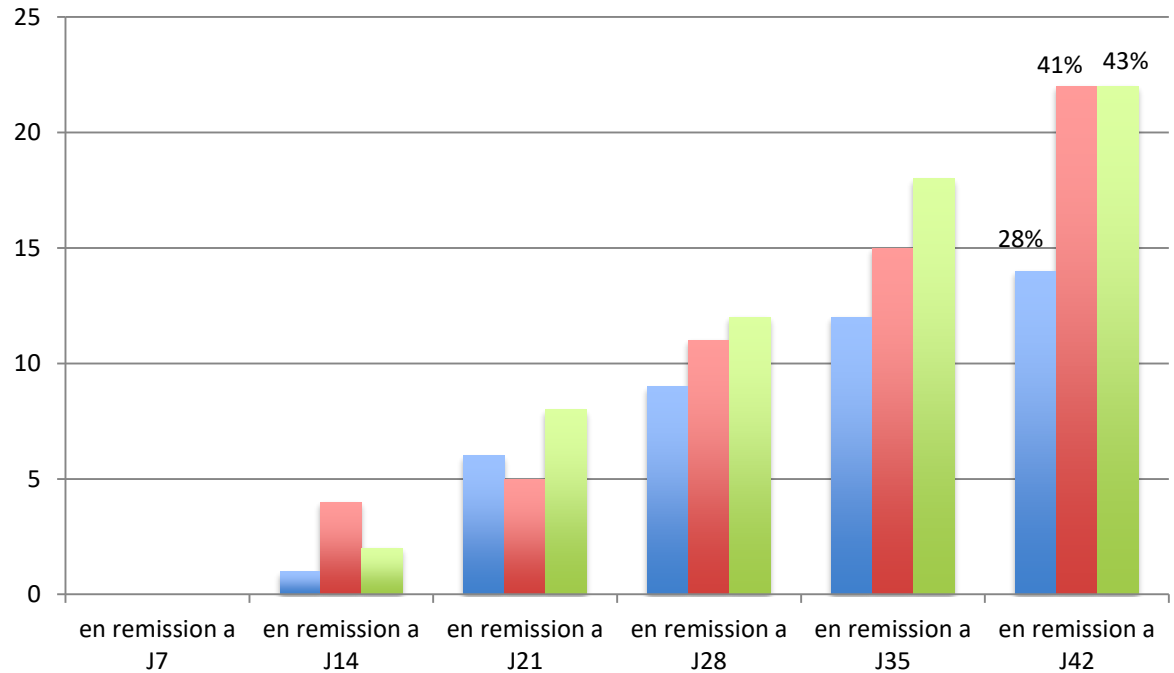
PHRC 2007



The Efficacy and Safety of Low Frequency Repetitive Transcranial Magnetic Stimulation for Treatment-resistant Depression: The Results From a Large Multicenter French RCT

Combination – TMS – Venlafaxine

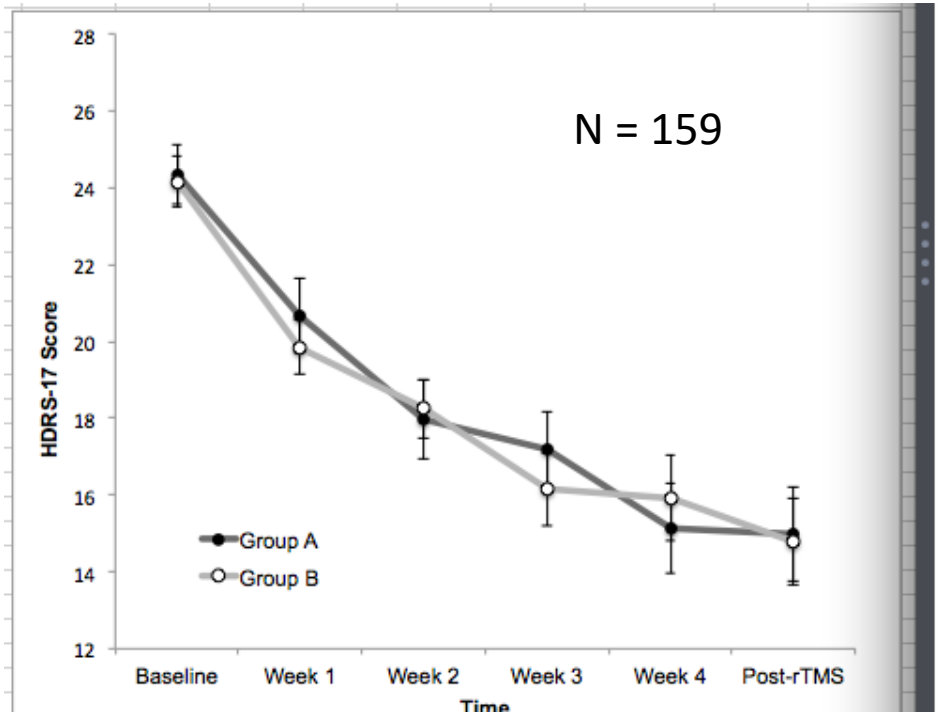
An efficiency method
A safety solution
A very good tolerance
A short time treatment

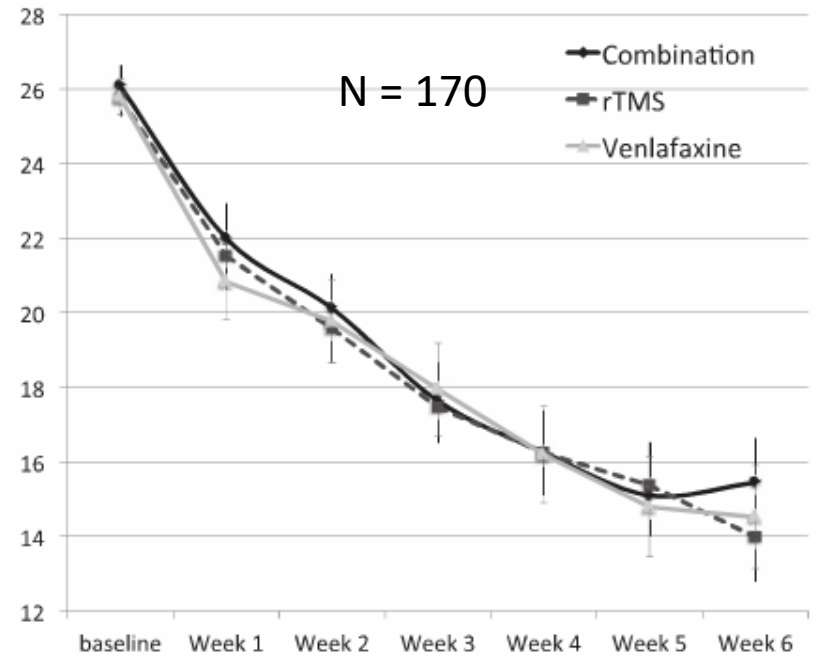


170 patients

Brunelin et al 2014

1 Hz, 10 Hz, iTBS : COMPARABLE EFFICACY ?





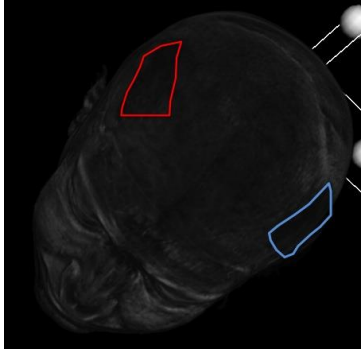
iTBS, 3 min, 600 pulses
10 Hz, 37.5 min, 3000 pulses

Downar et al, 2016

1 Hz, 8 min, 360 pulses
± venlafaxine pharmacotherapy

Brunelin et al., 2014

tDCS for DEPRESSION – Efficacy



Clinical Neurophysiology 131 (2020) 474–528

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

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]

Effects of repetitive transcranial magnetic stimulation of the left dorsolateral prefrontal cortex on symptom domains in neuropsychiatric disorders: a systematic review and cross-diagnostic meta-analysis

Rebecca L D Kan, Frank Padberg, Cristian G Giron, Tim T Z Lin, Bella B B Zhang, Andre R Brunoni, Georg S Kranz

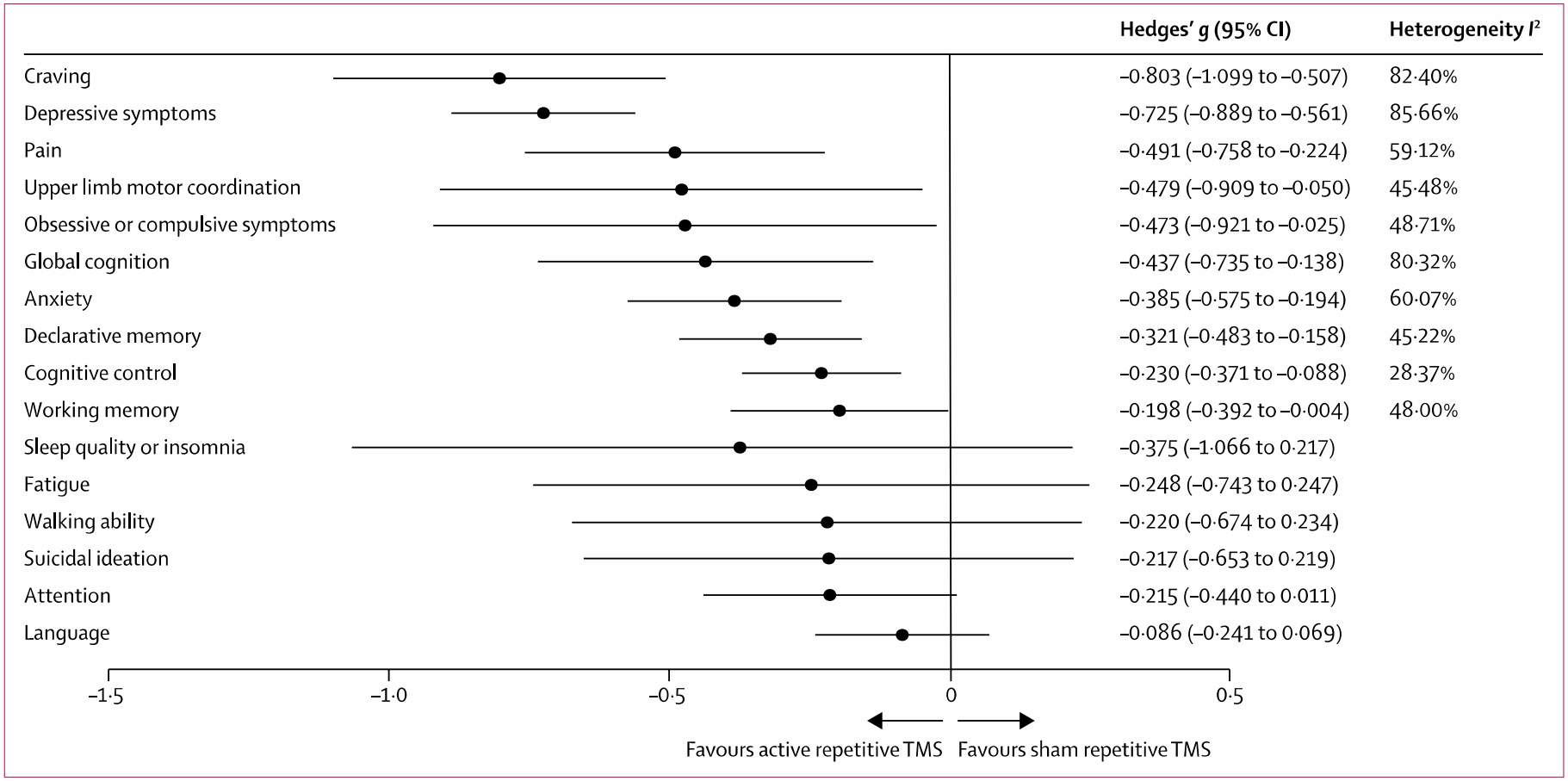
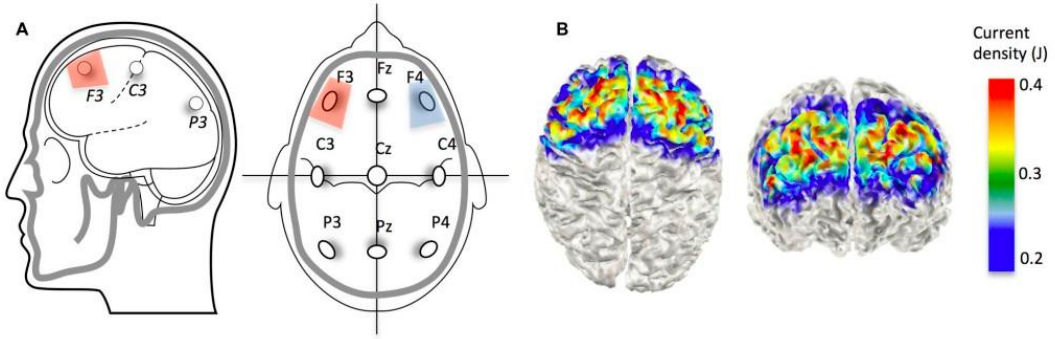
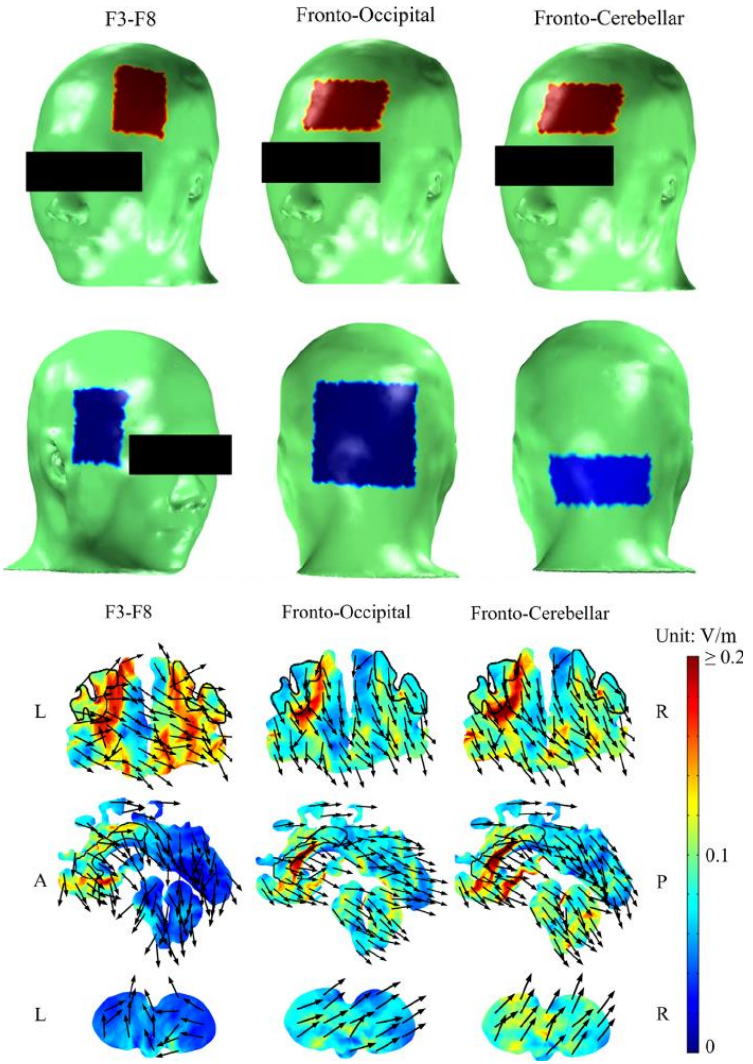


Figure 2: **Effect of active repetitive transcranial magnetic stimulation (TMS) and sham repetitive TMS of the left dorsolateral prefrontal cortex on various symptoms**

Several tDCS protocols

- F3/F4
- F3/FP2
- F3/ extra cephalic
- F3/ cerebellum …

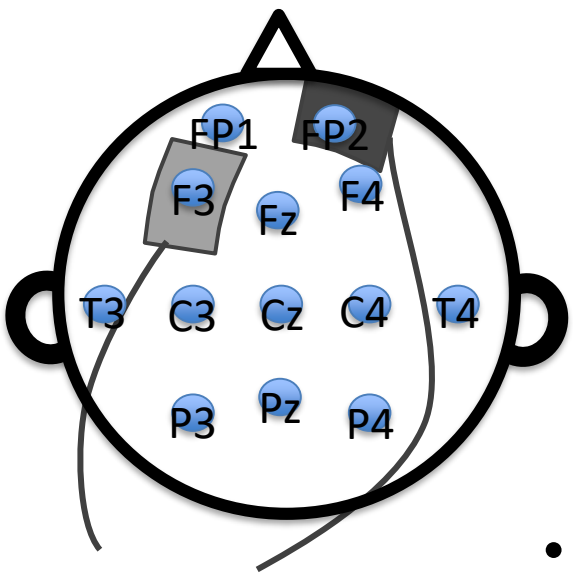




Guidelines

Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS)

Depression



- Anodal tDCS of the left DLPFC with right orbitofrontal cathode **is probably effective in patients with no drug-resistant major depressive episode (Level B)**

  and probably ineffective in patients with drug- resistant major depressive episode **(Level B)**

  5 studies, 1 class I, 4 class II

- **No recommandation** for other tDCS montage

A recent negative RCT with 130 patients

International randomized-controlled trial of transcranial Direct Current Stimulation in depression

Colleen K. Loo [a,*], Mustafa M. Husain [b,c], William M. McDonald [d], Scott Aaronson [e], John P. O'Reardon [f], Angelo Alonzo [a], Cynthia Shannon Weickert [g,h], Donel M. Martin [a], Shawn M. McClintock [b,c], Adith Mohan [g], Sarah H. Lisanby [c,i] on behalf of the International Consortium of Research in tDCS (ICRT)

ECT / rTMS ?

Meta-analysis	No. of studies/sample size	Mean age range	Summary of effect
Berlim *et al*[47] 2013	7/294	31.0-63.6	NNT = 6 favouring ECT for short-term response; at baseline, ECT samples had shorter illness duration and higher HAMD scores than rTMS samples. Age has no moderating effect on the differences
Ren *et al*[46] 2014	9/425	31.0-63.6	NNT = 7 for response; 6 for remission favouring ECT; No significant group difference when continuous change in HAMD scores is considered as outcome; In the absence of psychosis, rTMS as efficacious as ECT; Cognitive domains are better preserved after rTMS than ECT
Micallef-Trigona[49] 2014	9/384	34.0-63.6	Hedges'g = 1.28 for rTMS and 2.15 for ECT. rTMS produces a mean reduction of 9.3 points; ECT produces a mean reduction of 15.42 points on the HDRS
Xie *et al*[48] 2013	9/395	31.0-63.6	OR = 0.55 for response and 0.49 for remission in favour of ECT; rTMS is better tolerated than ECT (OR = 0.70); rTMS > 1200 stimuli/d is as efficacious as ECT

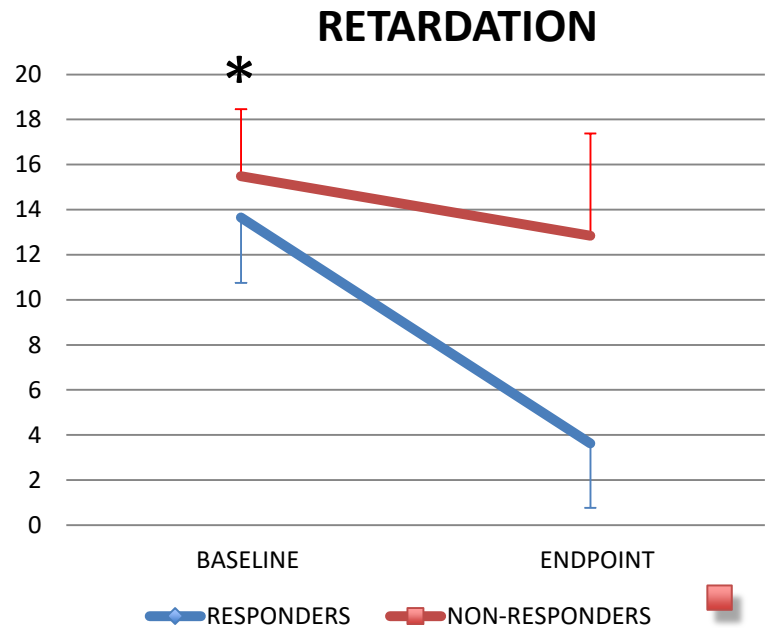
- **ECT seemed more effective** than rTMS in the short term (Ren 2014).
- Especially in the presence of **psychotic depression** (Grunhaus, Berlim, 2013; Ren, 2014)
- Less evidence suggested the short term benefits are maintained in the follow-up (Eranti 2007)
- rTMS as a maintenance treatment after ECT course ? (Cristancho 2013, Brunelin 2010)
- Cost-effective option ? Favor to ECT for resistant severe depression (Vallejo-Torres 2015; Knapp 2008)

rTMS : Predictive markers of response ?

Variable name	Variable definition	*p*-value (interaction of predictor variable and treatment group)	Direction of effect on outcome
Categorical			
Age	⩾55 years *vs* <55 years	0.590	—
Gender	Male *vs* female	0.936	—
Duration of current episode	**⩽2 years *vs* >2 years**	**0.069**	Greater effect for illness <2 years, ($P=0.015$, active arm only)
Comorbid anxiety disorder	Any anxiety disorder *vs* none	0.420	—
Course of illness	First episode *vs* recurrent illness	0.862	—
Treatment resistance (current episode)	**One adequate treatment in current episode *vs* more than one**	**0.021**	Superior outcome for one adequate treatment group, ($P=0.067$, active arm only)
Employment status	Employed full or part time *vs* unemployed	0.100	—
Atypical depression	Defined by IDS-SR criteria	0.159	—
Continuous			
Baseline symptom severity	MADRS total score at baseline	0.774	—
Baseline motor threshold	Motor threshold (% machine output) at baseline	0.108	—

Variables indicated in bold demonstrated a significant predictor variable × treatment arm interaction effect ($P<0.10$).
—, No statistically different benefit at the specified level in either treatment arm.
Please see text for further discussion of within treatment arm results and direction of effect on outcome.

Lisanby 2009



Poulet et al, 2016

ECT : better indications ?

CANMAT Guidelines

Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 4. Neurostimulation Treatments

Roumen V. Milev, MD, PhD[1], Peter Giacobbe, MD, MSc[2], Sidney H. Kennedy, MD[2], Daniel M. Blumberger, MD, MSc[2], Zafiris J. Daskalakis, MD, PhD[2], Jonathan Downar, MD, PhD[2], Mandana Modirrousta, MD, PhD[3], Simon Patry, MD[4], Fidel Vila-Rodriguez, MD, MSc[5], Raymond W. Lam, MD[5], Glenda M. MacQueen, MD, PhD[6], Sagar V. Parikh, MD[2,7], Arun V. Ravindran, MB, PhD[2], and the CANMAT Depression Work

Table 5. Clinical Indications for Electroconvulsive Therapy as a First-Line Treatment for Major Depressive Disorder.

- Acute suicidal ideation (Level 1)
- Psychotic features (Level 1)
- Treatment-resistant depression (Level 1)
- Repeated medication intolerance (Level 3)
- Catatonic features (Level 3)
- Prior favourable response to ECT (Level 3)
- Rapidly deteriorating physical status (Level 3)
- During pregnancy, for any of the above indications (Level 3)
- Patient preference (Level 4)

Treatment for depression - Choice criteria

	Medications	tDCS	rTMS	ECT
Efficacy	+++	? (++)	+++	++++
Tolerability / adverse effects	++/+++	+++	+++/++++	++
Cost	+++	+++/++++	++	++
Practicability	+++++	++++	+++	++

Curr Psychiatry Rep (2015) 17: 59
DOI 10.1007/s11920-015-0592-y

GERIATRIC DISORDERS (W MCDONALD, SECTION EDITOR)

Neuromodulation Therapies for Geriatric Depression

Verònica Gálvez[1,2] • Kerrie-Anne Ho[1,2] • Angelo Alonzo[1,2] • Donel Martin[1,2] • Duncan George[1,2] • Colleen K. Loo[1,2,3]

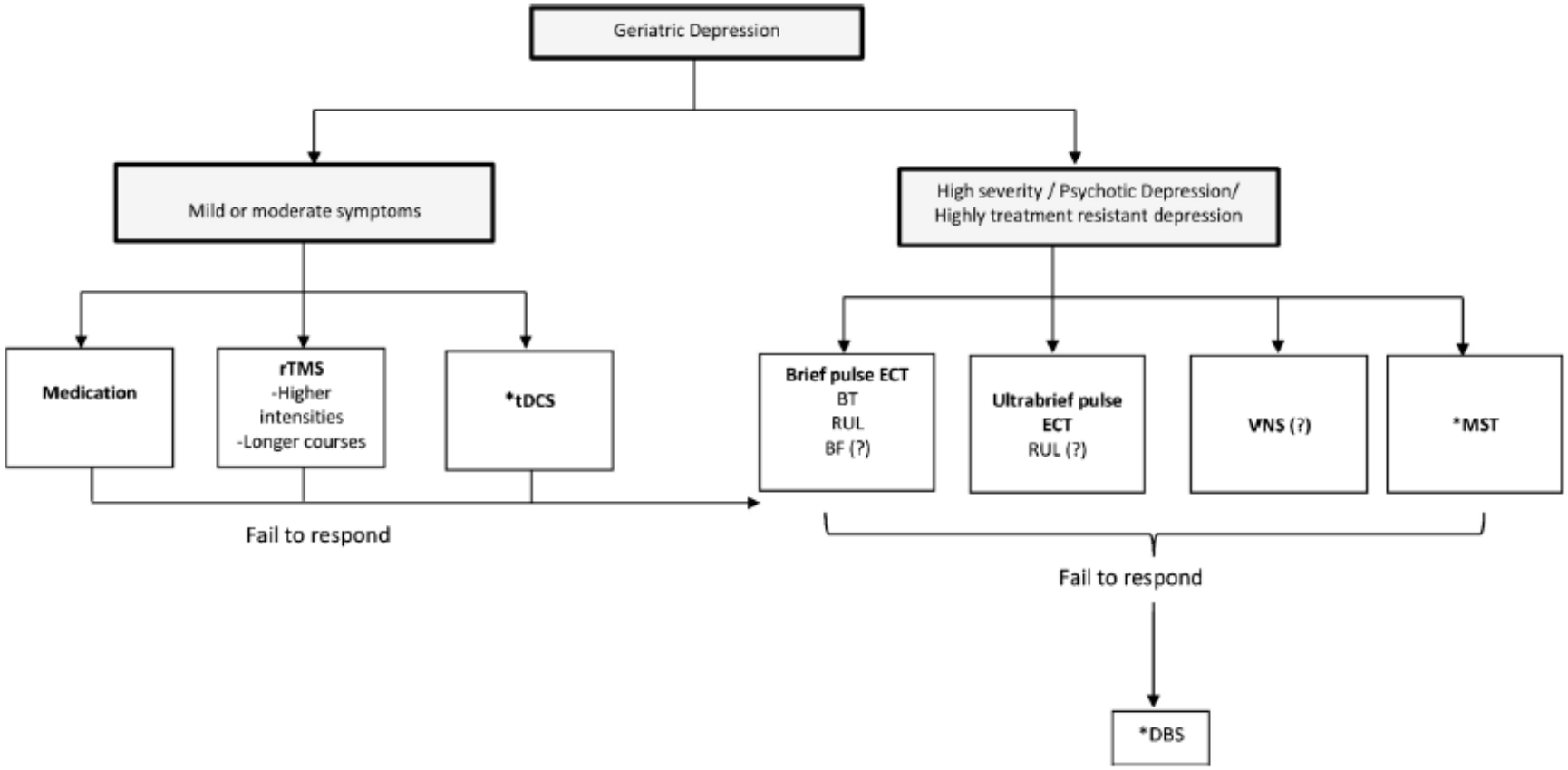


Fig. 1 Proposed algorithm for the treatment of geriatric depression with neuromodulation techniques. Treatment currently considered experimental for depression (*). Limited evidence specific to geriatric depression (?). *rTMS* repetitive transcranial magnetic stimulation, *tDCS* transcranial direct current stimulation, *ECT* electroconvulsive therapy, *BT* bitemporal, *RUL* right-unilateral, *BF* bifrontal, *VNS* vagus nerve stimulation, *MST* magnetic seizure therapy, *DBS* deep brain stimulation

Conclusion :

Neuromodulation methods for depression

CANMAT Guidelines

The Canadian Journal of Psychiatry / La Revue Canadienne de Psychiatrie
2014, Vol. 4.0(9) 561-575
© The Author(s) 2014
Reprints and permission:
sagepub.com/journalPermissions.nav
DOI: 10.1177/0706743714546033
TheCJP.ca | LaRCP.ca
SAGE

Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines for the Management of Adults with Major Depressive Disorder: Section 4. Neurostimulation Treatments

Roumen V. Milev, MD, PhD[1], Peter Giacobbe, MD, MSc[2], Sidney H. Kennedy, MD[2], Daniel M. Blumberger, MD, MSc[2], Zafiris J. Daskalakis, MD, PhD[2], Jonathan Downar, MD, PhD[2], Mandana Modirrousta, MD, PhD[3], Simon Patry, MD[4], Fidel Vila-Rodriguez, MD, MSc[5], Raymond W. Lam, MD[5], Glenda M. MacQueen, MD, PhD[6], Sagar V. Parikh, MD[2,7], Arun V. Ravindran, MB, PhD[2], and the CANMAT Depression Work Group[8]

Table 2. Summary of Neurostimulation Treatment Recommendations for Major Depressive Disorder.

mulation	Overall Recommendation	Acute Efficacy	Maintenance Efficacy	Safety and Tolerability
rTMS	First line (for patients who have failed at least 1 antidepressant)	Level 1	Level 3	Level 1
ECT	Second line	Level 1	Level 1	Level 1
	First line in some clinical situations (see Table 5)			
tDCS	Third line	Level 2	Level 3	Level 2
VNS	Third line	Level 3	Level 2	Level 2
DBS	Investigational	Level 3	Level 3	Level 3
MST	Investigational	Level 3	Not known	Level 3

DBS, deep brain stimulation; ECT, electroconvulsive therapy; MST, magnetic seizure therapy; rTMS, repetitive transcranial magnetic stimulation; tDCS, transcranial direct current stimulation; VNS, vagus nerve stimulation.

Sumarised :

- **tDCS – to be evaluate – eventually in first line if patient ask**
- **rTMS - After one line of treatment – alterative to ECT**
- **ECT - for resistant patients and emergency – psychotics features ++**

And other indications … ?

SAVE THE DATE

5rd European Conference
on Brain Stimulation in Psychiatry

http://www.afpbn.org/section/step

Zagreb june 2022

emmanuel.poulet@chu-lyon.fr