RTMS INDICATIONS IN PSYCHIATRY

FOCUS ON DEPRESSION

HOW TO IMPROVE RESPONSE AND REMISSION RATES FOR DEPRESSED PATIENTS?

Chris Baeken MD, PhD

ICANN, Brussels 2023

GHENT UNIVERSITY: DEPARTMENT OF HEAD AND SKIN (UZGENT), GHENT EXPERIMENTAL PSYCHIATRY (GHEP) LAB, BELGIUM
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EINDHOVEN UNIVERSITY OF TECHNOLOGY, DEPARTMENT OF ELECTRICAL ENGINEERING, THE NETHERLANDS

Disclosure

Relevant Financial Relationship(s)

None

Off-Label Usage

None

OPEN DOOR

The chemical brain….

Major Depressive Disorder

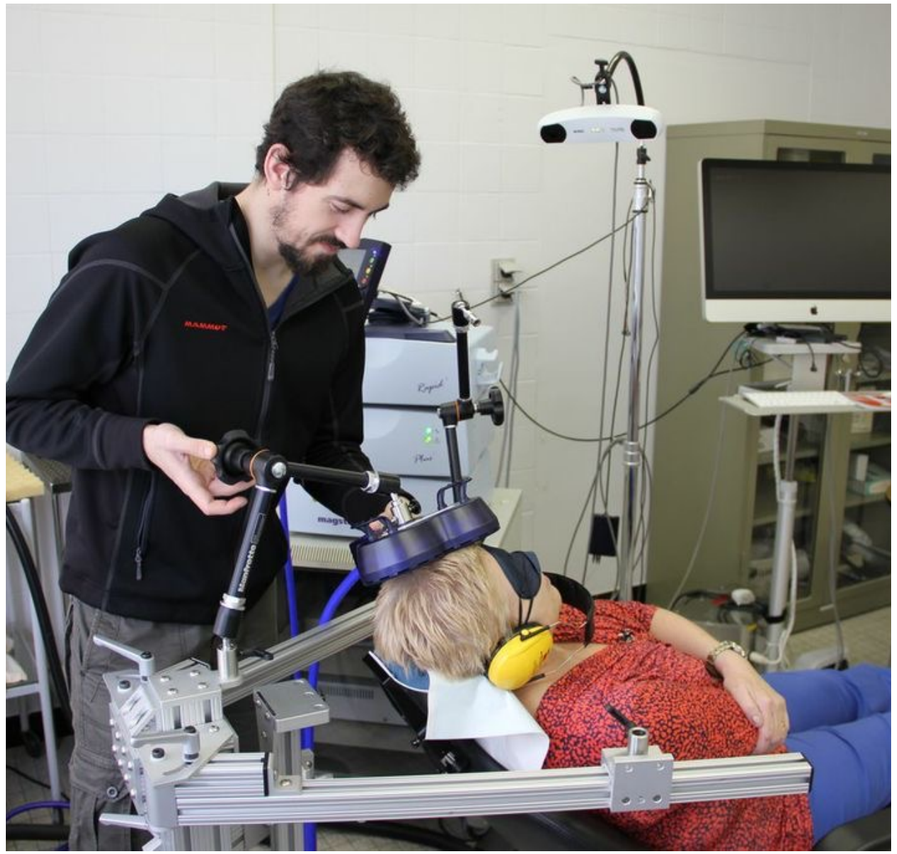
Severe psychiatric disorder

WHO common mental disorders

- Relapse
- Treatment-resistance
- Chronicity

The electrical brain….

(r)TMS procedure



Non-invasive, ‘painless, no anesthesia (ECT)

Conscious

Allows a non-invasive stimulation of well-defined **neocortical** regions

Allows to investigate **causal** relationships between brain activity and behaviour

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)

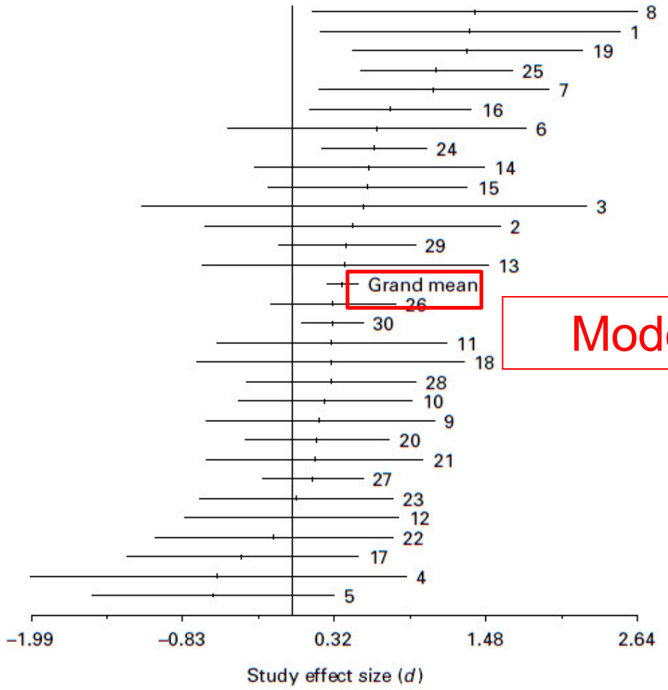
Jean-Pascal Lefaucheur [a,b,*], André Aleman [c], Chris Baeken [d,e,f], David H. Benninger [g], Jérôme Brunelin [h], Vincenzo Di Lazzaro [i], Saša R. Filipović [j], Christian Grefkes [k,l], Alkomiet Hasan [m], Friedhelm C. Hummel [n,o,p], Satu K. Jääskeläinen [q], Berthold Langguth [r], Letizia Leocani [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]

FDA approved treatment for depression

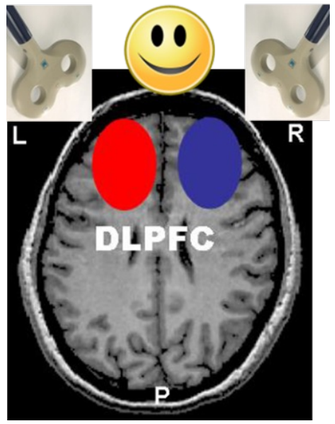
Level A evidence

Lefaucheur et al., 2014, 2020

Efficacy



Modest



Application

HF-rTMS /LF-rTMS/ bilateral/ (i)TBS

DLPFC/ DMPFC

Multiple sessions

Daily, spread over weeks

Cave: Treatment resistant depression

Schutter 2009, Psych Med

GHEPLab

REVIEW

Curr Opin Psychiatry 2019, 32:000–000
DOI:10.1097/YCO.0000000000000533

OPEN

CURRENT OPINION

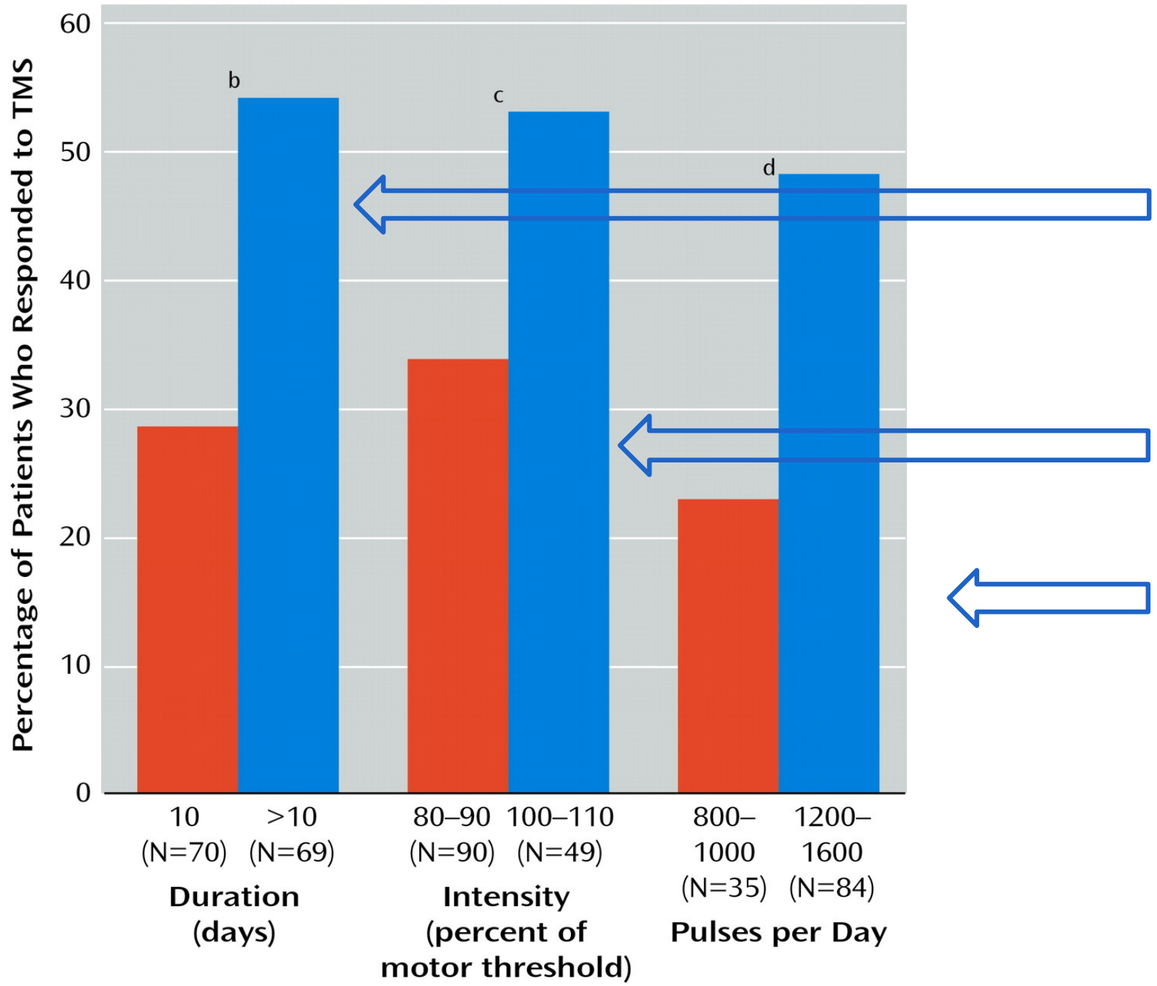
Repetitive transcranial magnetic stimulation treatment for depressive disorders: current knowledge and future directions

Chris Baeken[a,b,c], *Anna-Katharine Brem*[d,e], *Martijn Arns*[f,g], *Andre R. Brunoni*[h], *Igor Filipčič*[i,j], *Ana Ganho-Ávila*[k], *Berthold Langguth*[l], *Frank Padberg*[m], *Emmanuel Poulet*[n], *Fady Rachid*[o], *Alexander T. Sack*[p], *Marie-Anne Vanderhasselt*[q], *and Djamila Bennabi*[r]

How to improve response and remission rates for our depressed patients?

To increase response…

Parameters



1. **Longer treatment duration**
2. **Higher intensities**
3. **More pulses**

Gershon et al., 2003, Am J Psychiatry

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REVIEW

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OPEN

4. Accurate localization

CURRENT OPINION

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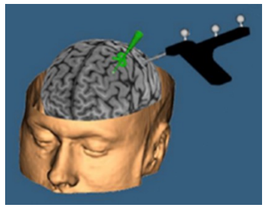
Chris Baeken[a,b,c], Anna-Katharine Brem[d,e], Martijn Arns[f,g], Andre R. Brunoni[h], Igor Filipčič[i,j], Ana Ganho-Ávila[k], Berthold Langguth[l], Frank Padberg[m], Emmanuel Poulet[n], Fady Rachid[o], Alexander T. Sack[p], Marie-Anne Vanderhasselt[q], and Djamila Bennabi[r]

PERSONALIZED AND STRATIFIED TREATMENT AS AN AVENUE TO PRECISION MEDICINE

TMS coil positioning

- 5-cm-rule
- Stimulation over F3
- Neuronavigated stimulation
- ….



The absence of a clear anatomical criterion to define the optimal brain target keeps the uncertainty around the clinical relevance of precision targeting

No large *a priori* clinical trials have clearly demonstrated superiority between neuronavigated and non-neuronavigated targeting

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5. Personalisation treatment

REVIEW

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PERSONALIZED AND STRATIFIED TREATMENT AS AN AVENUE TO PRECISION MEDICINE

NeuroImage xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

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Measuring and manipulating brain connectivity with resting state functional connectivity magnetic resonance imaging (fcMRI) and transcranial magnetic stimulation (TMS)

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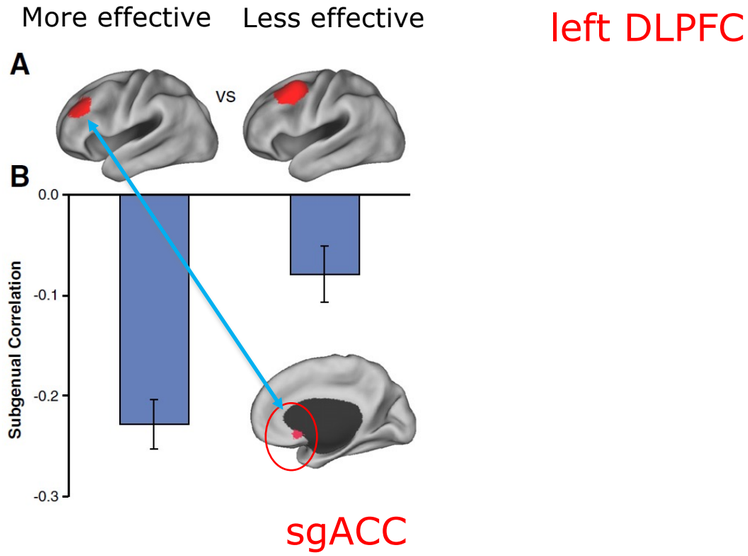

left DLPFC

sgACC

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REVIEW

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DOI:10.1097/YCO.0000000000000533

OPEN

6. Accelerated stimulation

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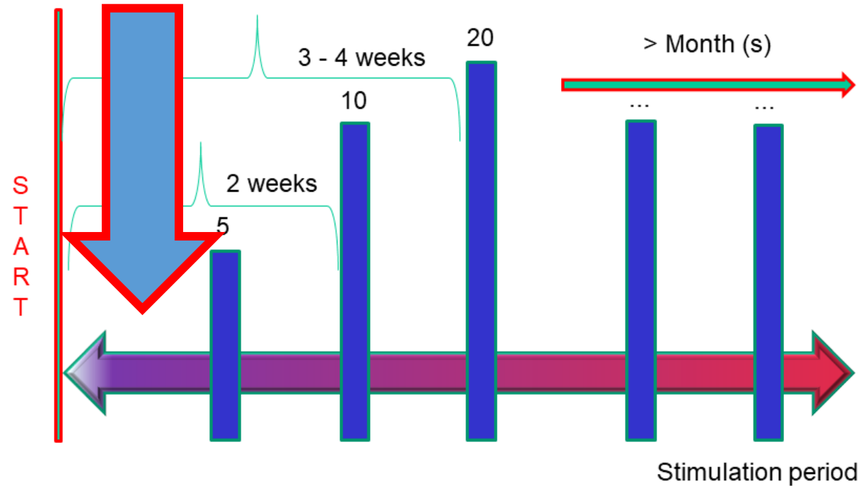
NOVEL STIMULATION PATTERNS, TARGETS, AND COILS

What about accelerated rTMS ?



Daily stimulation

Intensify rTMS paradigms?

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REVIEW

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6. Accelerated stimulation

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NOVEL STIMULATION PATTERNS, TARGETS, AND COILS

What about accelerated rTMS ?

N = 14

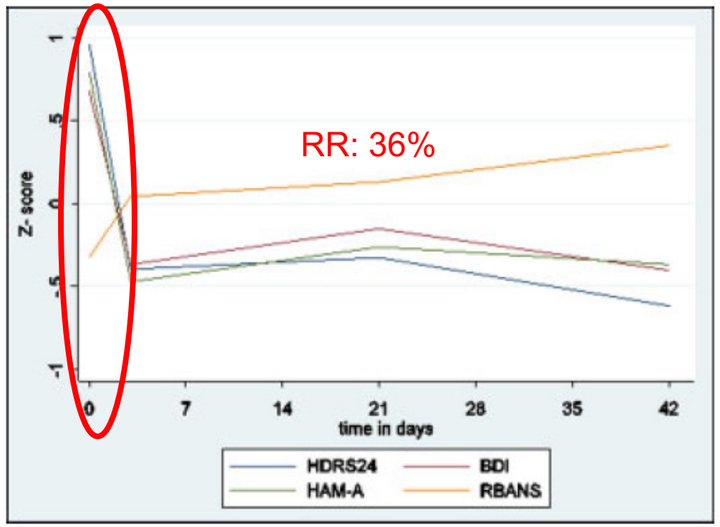
Open label study

Unipolar treatment resistant major depression

'add on' therapy'

15 HF-rTMS (10Hz) sessions/ 2 days (5-10)

100% MT



Holtzheimer et al., 2010, Depress Anxiety

Accelerated SHAM-controlled-crossover studies

Journal of Affective Disorders 151 (2013) 625–631

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research report

Intensive HF-rTMS treatment in refractory medication-resistant unipolar depressed patients

Chris Baeken [a,b,c,*], Marie-Anne Vanderhasselt [d], Jonathan Remue [d], Sarah Herremans [b], Nathalie Vanderbruggen [b], Dieter Zeeuws [b], Liesbeth Santermans [b], Rudi De Raedt [d]

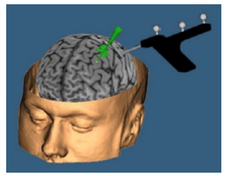
[a] Department of Psychiatry and Medical Psychology, Ghent University, De Pintelaan 185, 9000 Ghent, Belgium
[b] University Hospital (UZBrussel), Department of Psychiatry, Brussels, Belgium
[c] Ghent Experimental Psychiatry (GHEP) Lab, Ghent University, Ghent, Belgium
[d] Department of Experimental Clinical and Health Psychology, Ghent University, Ghent, Belgium

aHF-rTMS

n=21

35 % **Response**

35 % **Remission**



5 times/day, 4 days (20 sessions)

1620 pulses/session: total 32.400 pulses

110% rMT, 15 min intersession interval

Journal of Affective Disorders 200 (2016) 6–14

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research paper

Accelerated intermittent theta burst stimulation treatment in medication-resistant major depression: A fast road to remission?

Romain Duprat [a,b,1], Stefanie Desmyter [a], De Raedt Rudi [c], Kees van Heeringen [a], Dirk Van den Abbeele [a], Hannelore Tandt [a], Jasmina Bakic [c], Gilles Pourtois [c], Josefien Dedoncker [a,b], Myriam Vervaet [a], Sara Van Autreve [a], Gilbert M.D. Lemmens [a], Chris Baeken [a,b,d,*,1]

[a] Department of Psychiatry and Medical Psychology, Ghent University, Ghent, Belgium
[b] Ghent Experimental Psychiatry (GHEP) Lab, Ghent University, Ghent, Belgium
[c] Department of Experimental Clinical and Health Psychology, Ghent University, Ghent, Belgium
[d] Department of Psychiatry, Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Laarbeeklaan 101, 1090 Brussels, Belgium

aiTBS

n=47

28% **38%** **Response**

15% **30%** **Remission**

PRELIMINARY CONCLUSIONS 1

- **Safe procedure**, well-tolerated

- **Ca 35 % response ≈ remission after 4 days!**
  (delayed effects aiTBS)

- ***Neurobiological changes present after 4 days of accelerated stimulation***




Time gain…!

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REVIEW

Curr Opin Psychiatry 2019, 32:000–000
DOI:10.1097/YCO.0000000000000533

OPEN

Repetitive transcranial magnetic stimulation treatment for depressive disorders: current knowledge and future directions

Chris Baeken[a,b,c], Anna-Katharine Brem[d,e], Martijn Arns[f,g], Andre R. Brunoni[h], Igor Filipčič[i,j], Ana Ganho-Ávila[k], Berthold Langguth[l], Frank Padberg[m], Emmanuel Poulet[n], Fady Rachid[o], Alexander T. Sack[p], Marie-Anne Vanderhasselt[q], and Djamila Bennabi[r]

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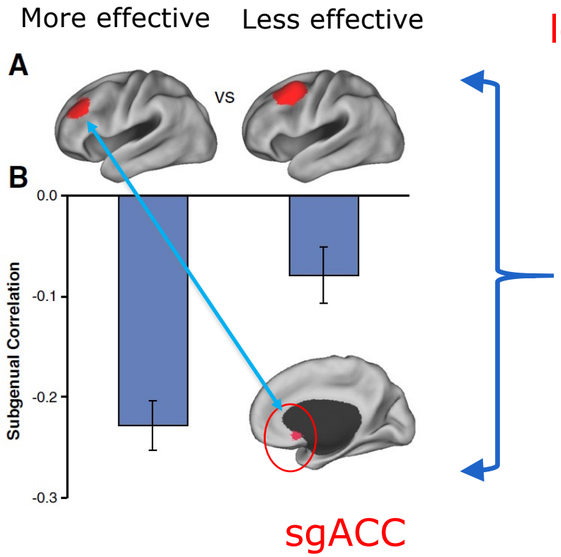


left DLPFC

Personalized sgACC-left DLPFC functional connectivity

sgACC

High-dose spaced theta-burst TMS as a rapid-acting antidepressant in highly refractory depression

N= 6 Open label

Nolan R. Williams,[1,*] Keith D. Sudheimer,[1,*] Brandon S. Bentzley,[1,#] Jaspreet Pannu,[1,#]
Katy H. Stimpson,[1,#] Dalton Duvio,[1] Kirsten Cherian,[1] Jessica Hawkins,[1]
Kristen H. Scherrer,[2] Benjamin Vyssoki,[1] Danielle DeSouza,[3] Kristin S. Raj,[1]
Jennifer Keller[1] and Alan F Schatzberg[1]

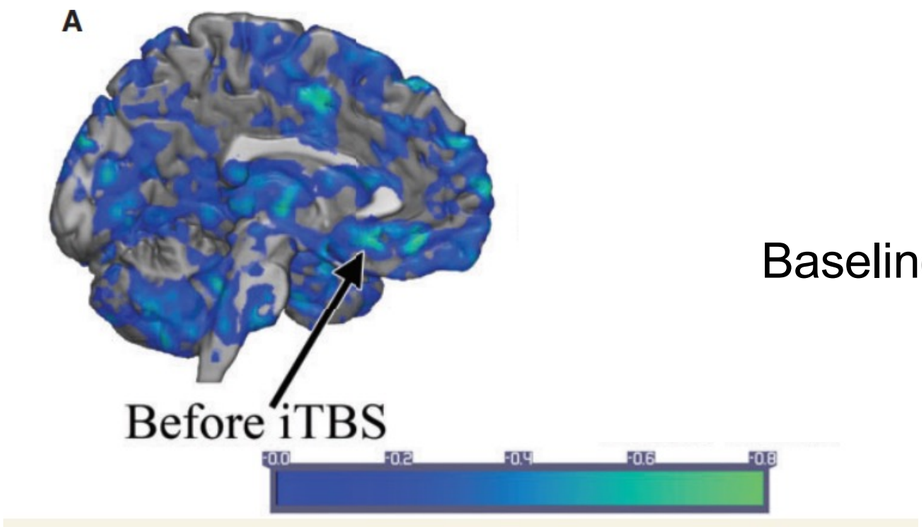
Ten sessions per day

50 min ISI

18 000 pulses/day

for five consecutive days

<u>90 000 total pulses</u>



Baseline

Personalized and targeted iTBS anti-correlations between Left DLPFC and sgACC

Five of six participants qualified as responders (>50% decrease in the HDRS17), and four participants were in full remission (HDRS17 < 7)

Williams et al., 2018, Brain

STANFORD NEUROMODULATION THERAPY (SNT):

2020

N=22

open

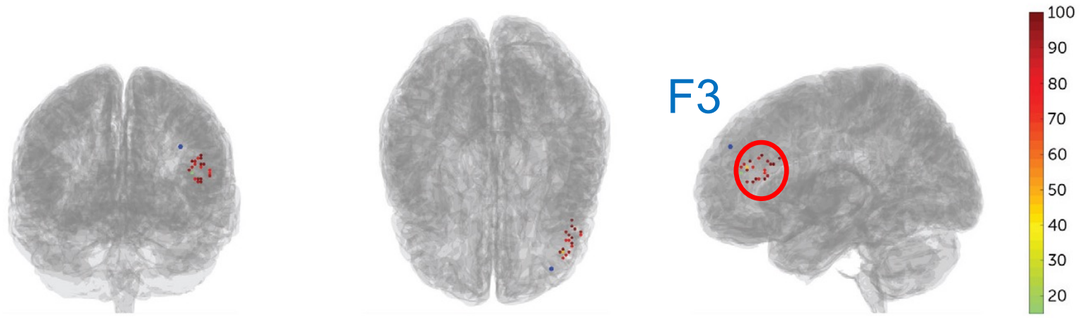
The American Journal of Psychiatry ARTICLES

Stanford Accelerated Intelligent Neuromodulation Therapy for Treatment-Resistant Depression

Eleanor J. Cole, Ph.D., Katy H. Stimpson, B.S., Brandon S. Bentzley, M.D., Ph.D., Merve Gulser, B.S., Kirsten Cherian, Ph.D., Claudia Tischler, B.S., Romina Nejad, M.S., Heather Pankow, B.S., Elizabeth Choi, B.S., Haley Aaron, B.S., Flint M. Espil, Ph.D., Jaspreet Pannu, B.S., Xiaoqian Xiao, Ph.D., Dalton Duvio, B.S., Hugh B. Solvason, M.D., Jessica Hawkins, B.A., Austin Guerra, B.A., Booil Jo, Ph.D., Kristin S. Raj, M.D., Angela L. Phillips, Ph.D., Fahim Barmak, M.D., James H. Bishop, Ph.D., John P. Coetzee, Ph.D., Charles DeBattista, M.D., Jennifer Keller, Ph.D., Alan F. Schatzberg, M.D., Keith D. Sudheimer, Ph.D., and Nolan R. Williams, M.D.

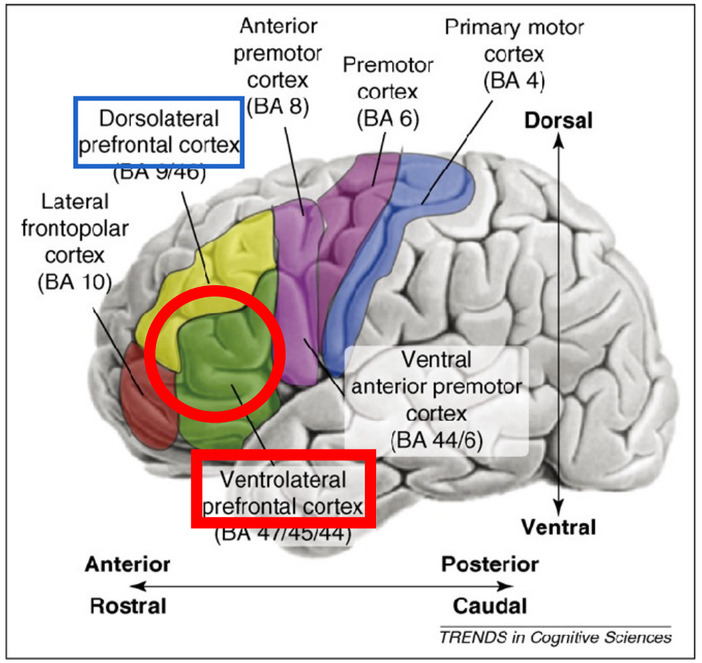
Nineteen of 21 participants (90.5%) met remission criteria

FIGURE 2. Individual target locations used in this study of Stanford Accelerated Intelligent Neuromodulation Therapy in comparison to the average coordinates for the F3 location in the 10-20 system[a]



[a] The average F3 location (at MNI coordinates −35.5, 49.4, 32.4) is shown in blue (78). The colors of the targets represent the percent change in Montgomery-Åsberg Depression Rating Scale score, with dark red indicating greater change. The mean distance from F3 was 25.18 mm (SD=6.15).

STANFORD NEUROMODULATION THERAPY (SNT):



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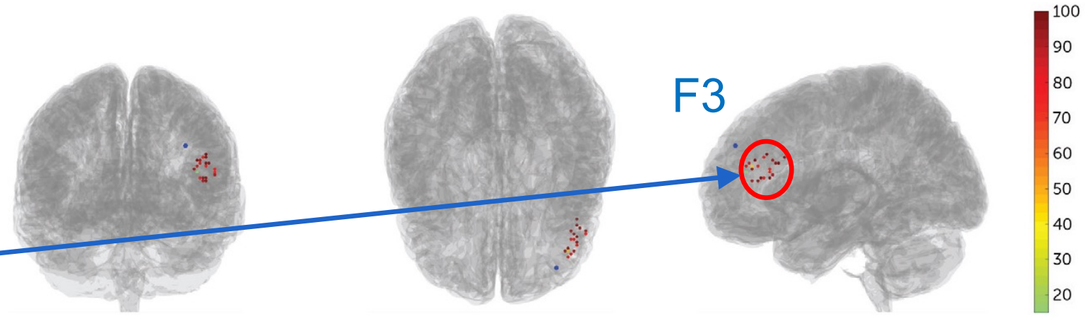

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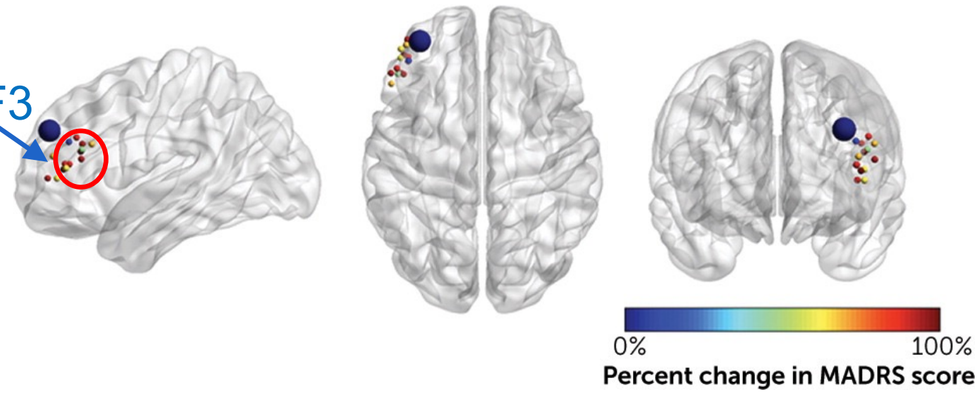
Randomized active (N=14) or sham (N=15)

Active 85.7% response, 78.6 % remission

Sham 26.7% response, 13.3 % remission



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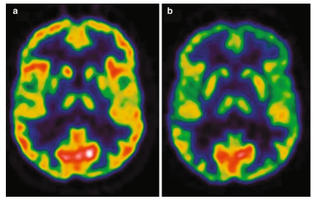


Brain Stimulation 16 (2023) 642–644

Contents lists available at ScienceDirect

Brain Stimulation

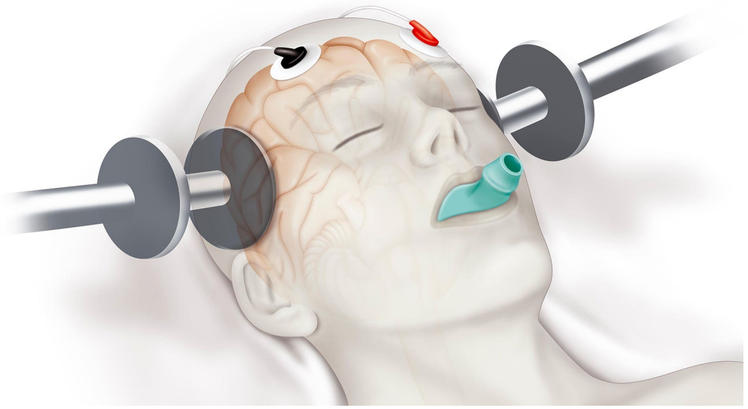
journal homepage: http://www.journals.elsevier.com/brain-stimulation

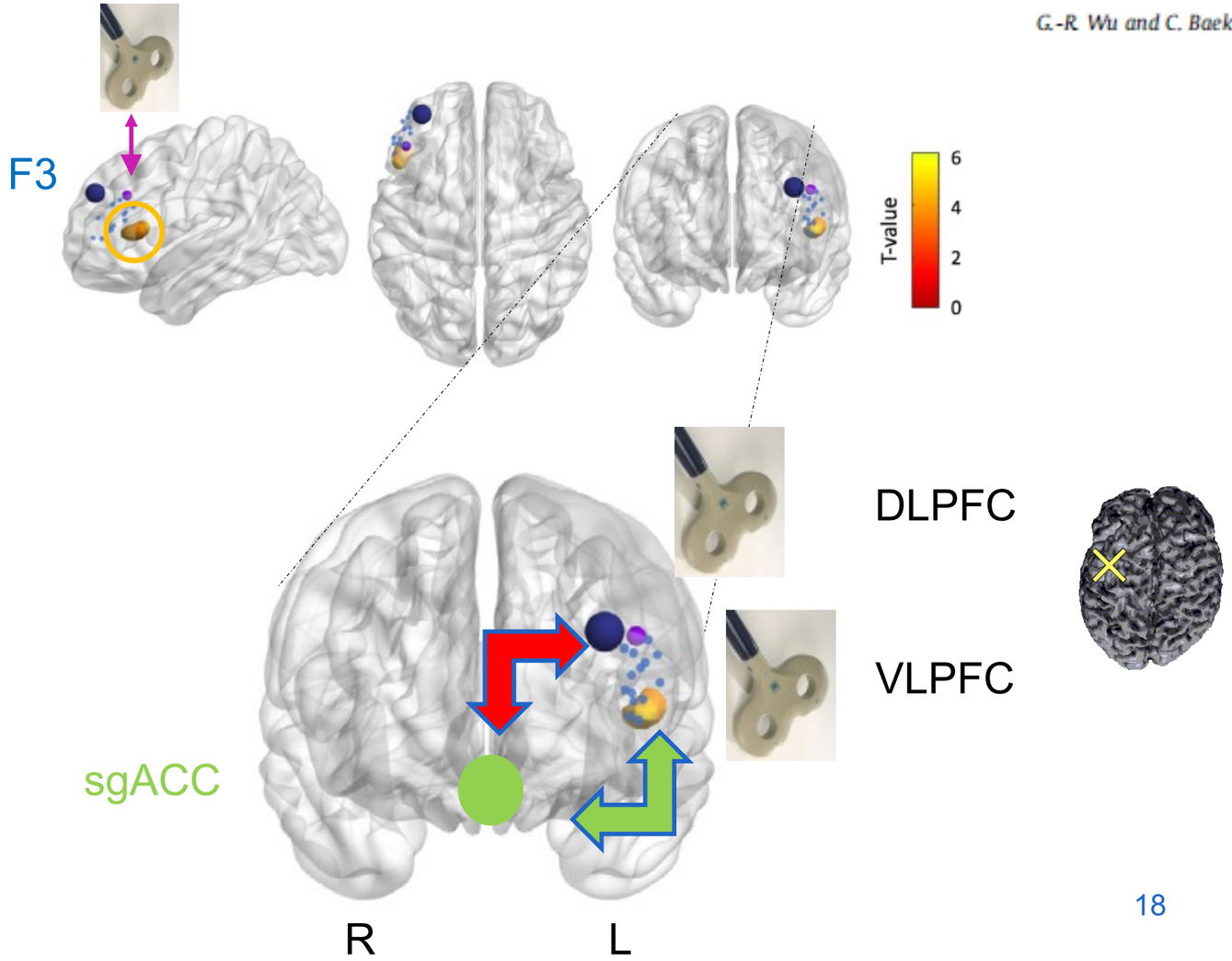
The left ventrolateral prefrontal cortex as a more optimal target for accelerated rTMS treatment protocols for depression?

G.-R. Wu and C. Baeken

PRELIMINARY CONCLUSIONS 2

The left VLPFC: a potentially more optimized stimulus target for accelerated rTMS ?





Future Directions

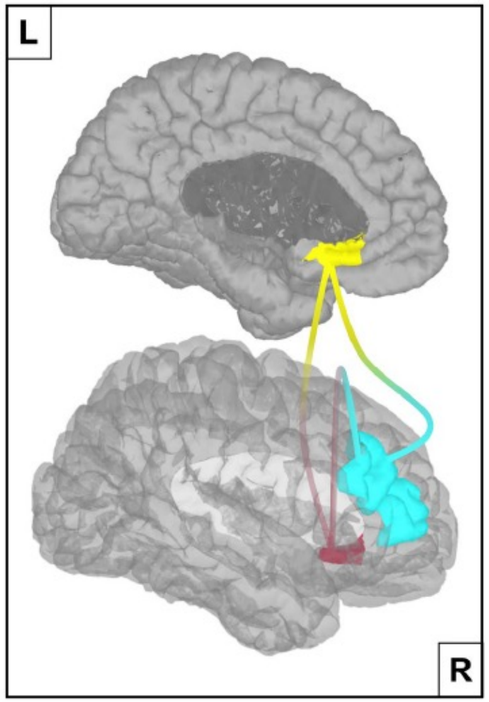
Accelerated rTMS may coming closer to higher response and remission rates in depression

Need for large prospective studies…!

Brain imaging and rTMS treatment as clinical guidance tool

Future Directions

MRI/EEG



scientific reports

Check for updates

OPEN

Reduced subgenual cingulate–dorsolateral prefrontal connectivity as an electrophysiological marker for depression

2022

Lars Benschop[1✉], Gert Vanhollebeke[1], Jian Li[2,3], Richard M. Leahy[4], Marie-Anne Vanderhasselt[1,5,8] & Chris Baeken[1,6,7,8]

- Acute treatment: ECT rTMS tDCS
  - Maintenance sessions?
- Long- term treatment: DBS VNS
- Relapse prevention: VNS

GHEPLab

Thank you for your attention

Ghent Experimental Psychiatry (GHEP) Lab

European Society for Brain Stimulation

https://www.brain-stimulation.eu/

europeansbs@brain-stimulation.eu

UZ GENT

Universitair Ziekenhuis Brussel

VUB VRIJE UNIVERSITEIT BRUSSEL

TU/e EINDHOVEN UNIVERSITY OF TECHNOLOGY

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