



**NAH CONGRES**  
Niet-aangeboren hersenletsel  
in Vlaanderen vandaag

# Welkom

## Niet-invasieve hersenstimulatie

*C. Lafosse & S. De Witte*



Hersenletsel Liga  
Samen voor mensen met NAH



INCLUSIE IN ZICHT

1



**NAH CONGRES**  
Niet-aangeboren hersenletsel  
in Vlaanderen vandaag

# Tijd voor een getuigenis

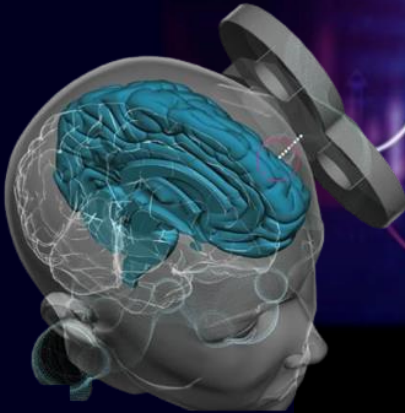


Hersenletsel Liga



2

C. Lafosse, *KULeuven, RZ RevArte*  
 S. De Witte, *VUB, UGent*



## Non Invasive Brain Stimulation (NIBS)

3

## Non-Invasive Brain Stimulation (NIBS) Publications



4

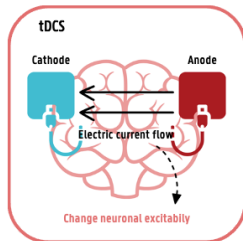
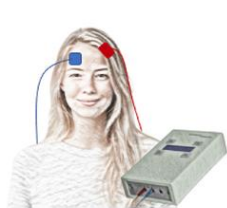
# Non-Invasive Brain Stimulation (NIBS) Societies



5

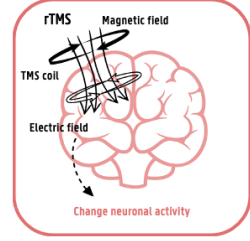
# Non-Invasive Brain Stimulation (NIBS) Overview

## Transcranial Electric Stimulation (TES)



- tDCS (Transcranial direct current stimulation)
- tACS (Transcranial alternating current stimulation)
- TRNS (Transcranial Random Noise Stimulation)
- TENS (Transcutaneous electrical nerve stimulation)

## Transcranial Magnetic Stimulation (TMS)



- rTMS (repetitive Transcranial Magnetic Stimulation)
- TBS (Theta Burst Stimulation)

6

# Non-Invasive Brain Stimulation (NIBS) Overview

	rTMS	TBS	tDCS	tACS
Stimulation method	Magnetic pulses applied to the brain	Magnetic pulses applied to the brain	Electrical current applied to the brain	Electrical current applied to the brain
Mechanism of action	Induces electrical currents in neural tissue	Induces electrical currents in neural tissue	Modulates neuronal resting membrane potential	Uses a rhythmic electrical current to synchronize the brain's natural activity patterns
Frequency of stimulation	Low-frequency (1 Hz or lower) High frequency (5 Hz or higher)	Burst patterns (three pulses at 50 Hz, given every 200ms)	Constant low current (typically 1-4 mA)	Constant low current (typically 1-4 mA)
Duration of session	Typically 20-30 minutes	Typically 3-5 minutes	Typically 20-30 minutes	Typically 20-30 minutes
Side effects	Scalp discomfort, headache, seizures (very rare)	Scalp discomfort, headache, seizures (very rare)	Mild tingling or itching, rare adverse effects	Mild tingling or itching, rare adverse effects
Costs	High	High	Low to moderate	Low to moderate

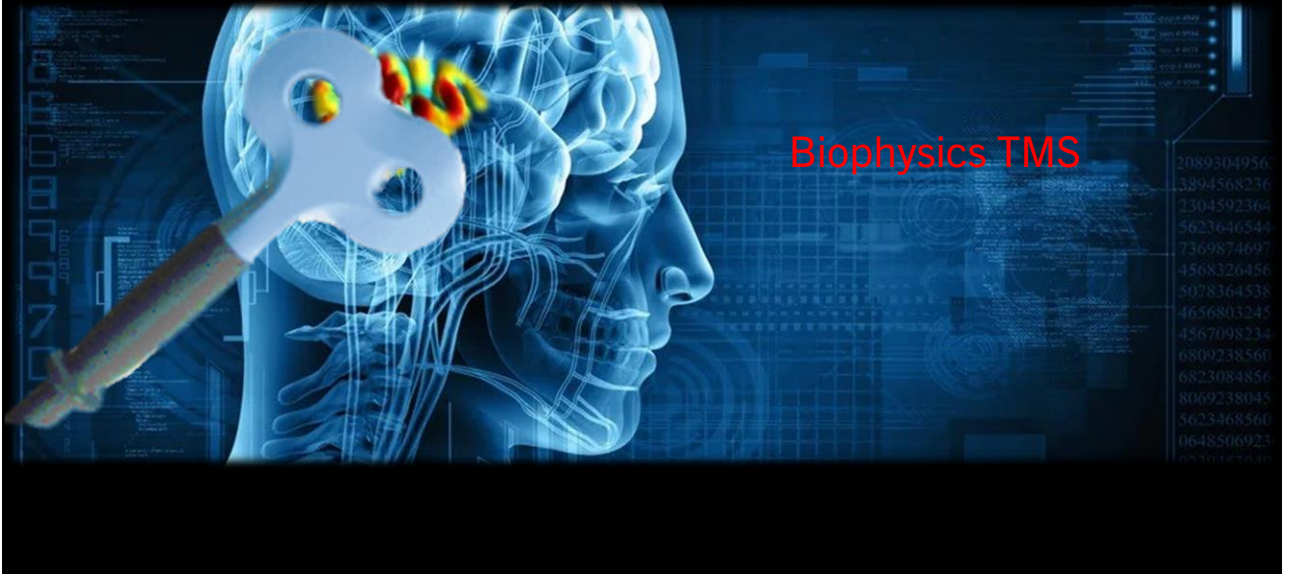
9

# Non-Invasive Brain Stimulation (NIBS) Overview

	rTMS	TBS	tDCS	tACS
Advantage	Most widely studied method Approved by FDA for the treatment of depression	Shorter sessions possible Approved by FDA for the treatment of depression	Easy use, low cost, possible home-based application, mobile	Easy use, low cost, possible home-based application, mobile
Disadvantage	Expensive, specialized medical staff is needed, treatment can only be given in hospital	Expensive, specialized medical staff is needed, treatment can only be given in hospital	Not specifically approved yet, often off-label use	Not specifically approved yet, often off-label use

10

# Non-Invasive Neuromodulation



11

## Transcranial Magnetic Stimulation (TMS)

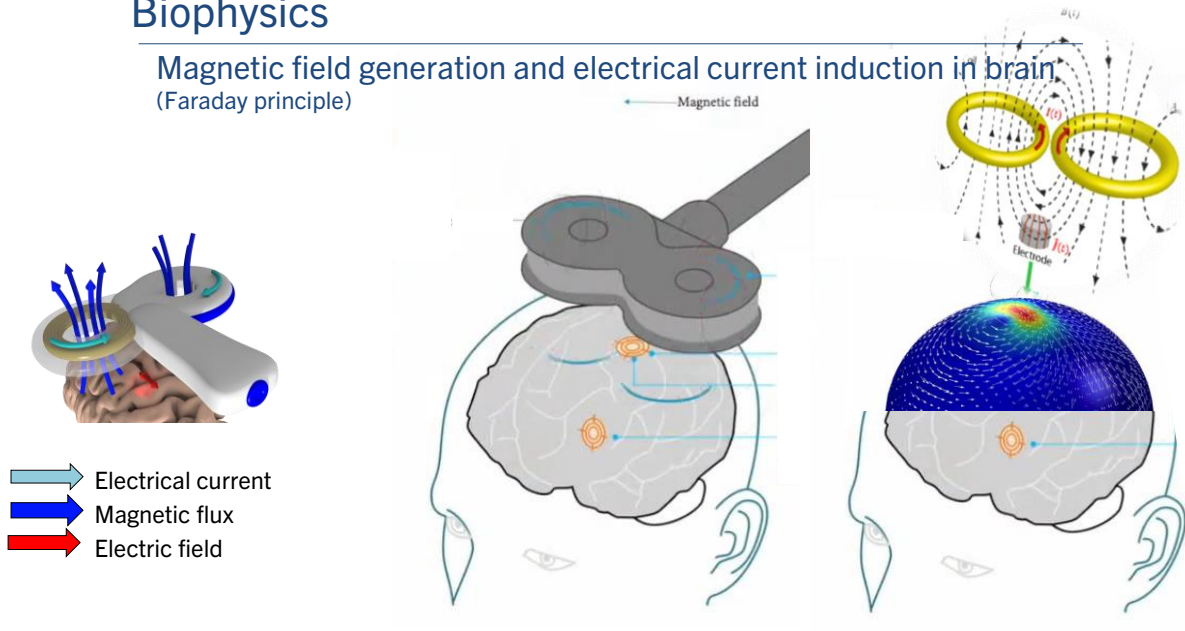


12

# Transcranial Magnetic Stimulation (TMS)

## Biophysics

Magnetic field generation and electrical current induction in brain  
(Faraday principle)



13

# Transcranial Magnetic Stimulation (TMS)

## Biophysics

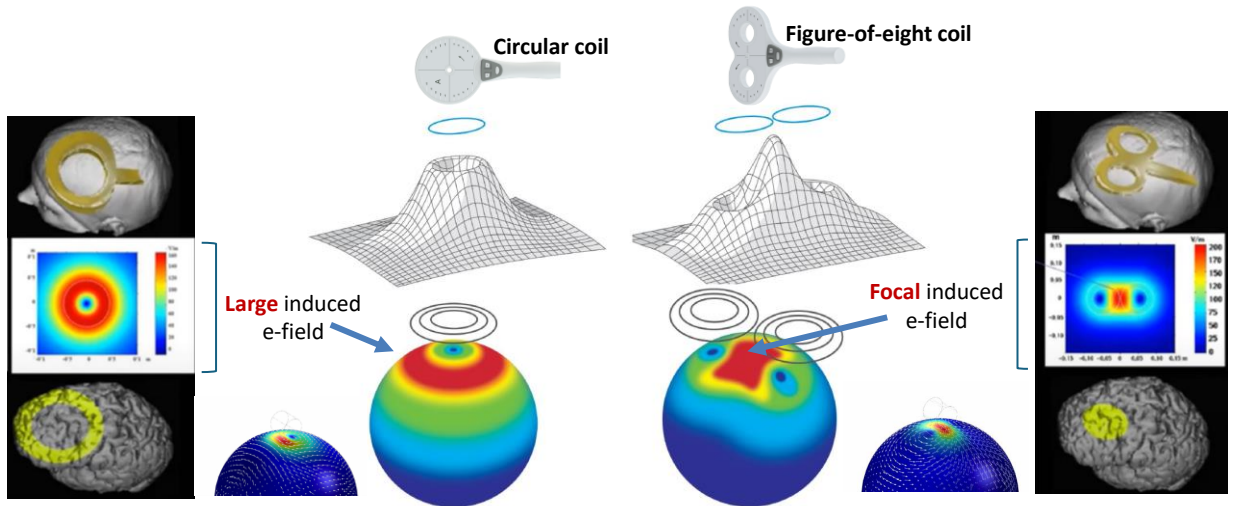
TMS coil designs



14

# Transcranial Magnetic Stimulation (TMS) Biophysics

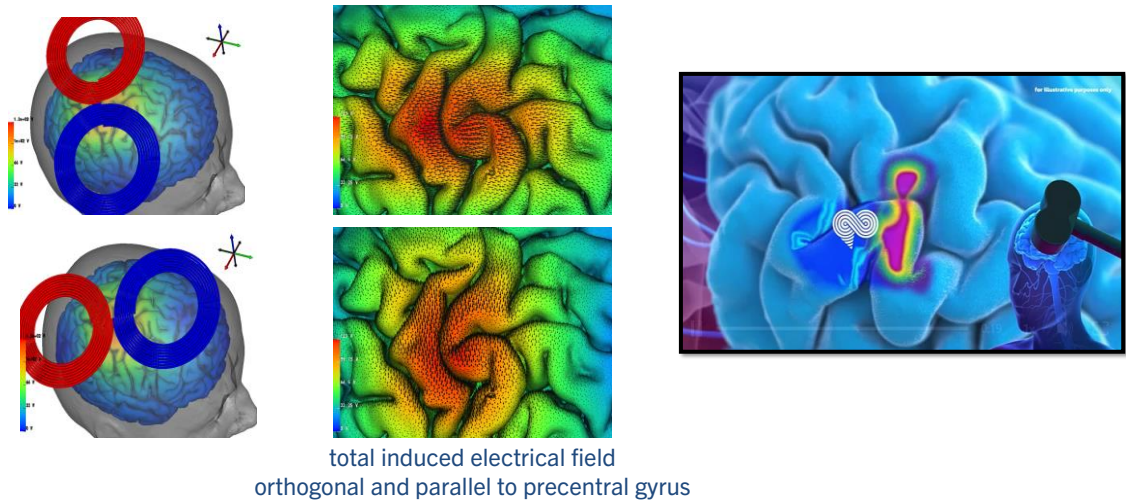
Effect of coil shape on induced electrical field



15

# Transcranial Magnetic Stimulation (TMS) Biophysics

Effect of coil orientation



16

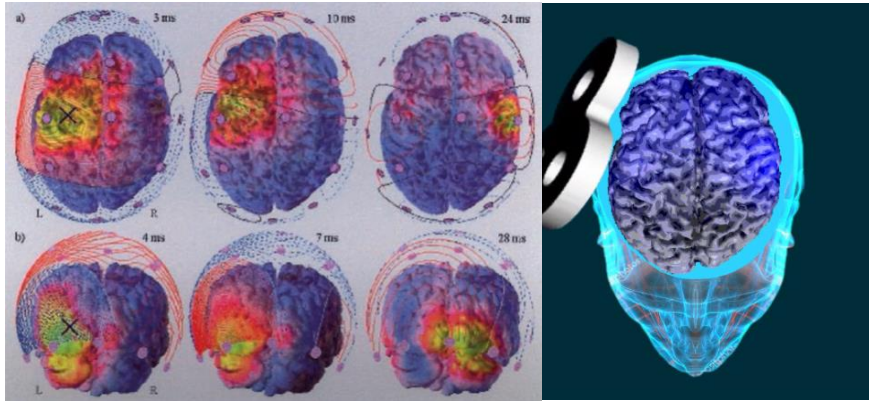




# Transcranial Magnetic Stimulation (TMS)

## Signal propagation

After local activation, induced neuronal activation propagates to distal areas

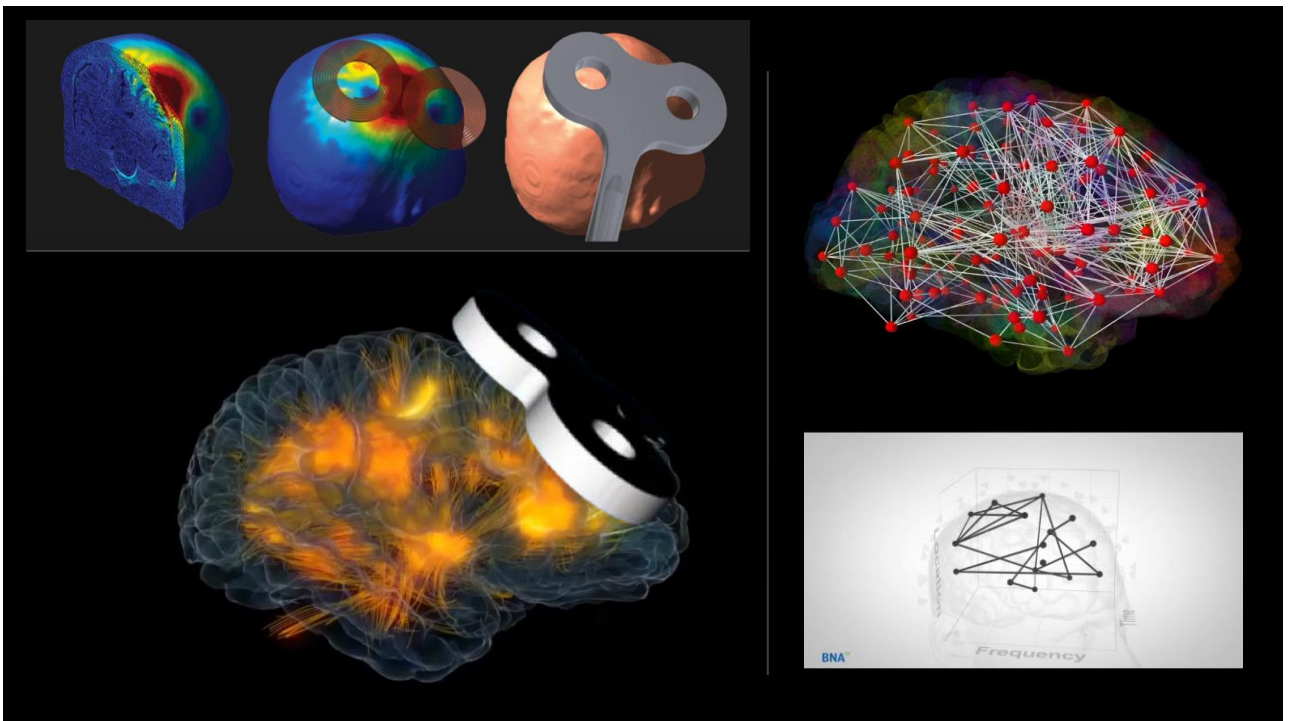


Ilmoniemi, et al. 1997



TMS-induced activity is not restricted to the target brain region but spreads to remote brain regions

21

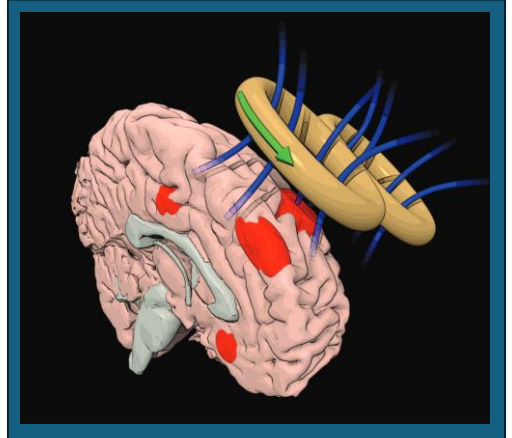
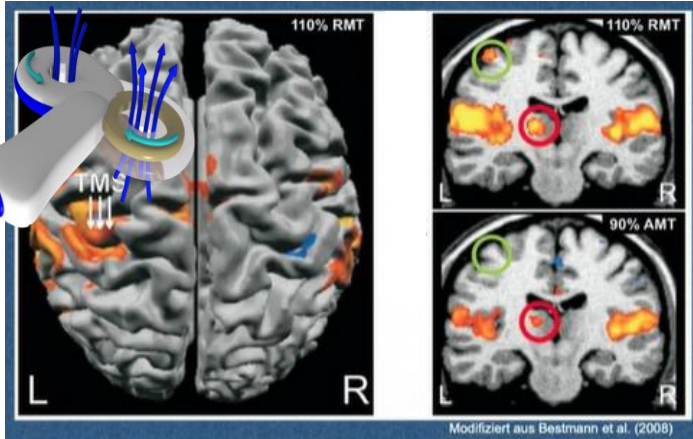


22

# Transcranial Magnetic Stimulation (TMS)

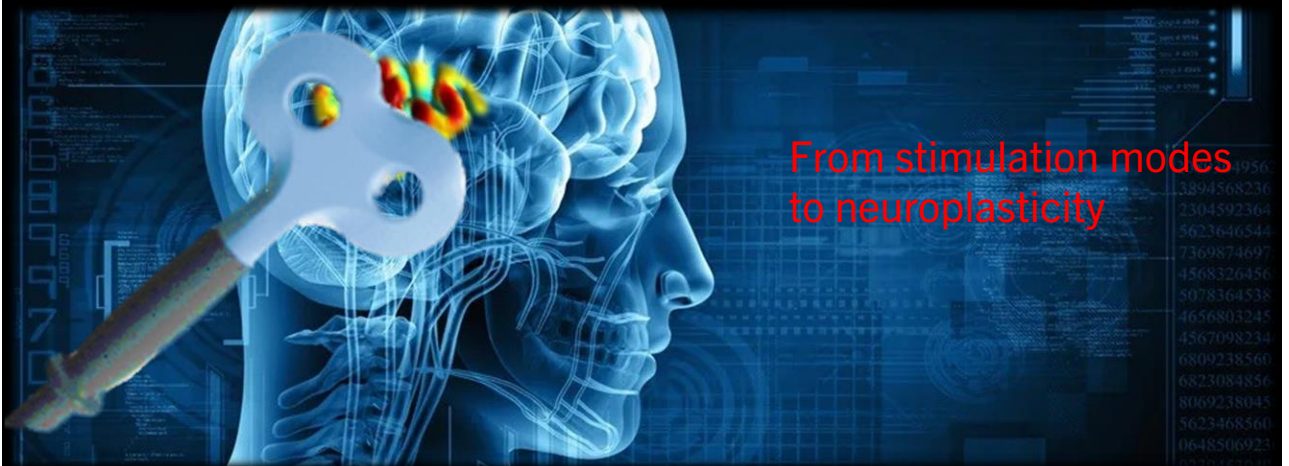
## Stroke

Full effect of TMS signal propagation can only be understood in terms of full **networks** of neuron activation



23

## Non-Invasive Neuromodulation



24

# Transcranial Magnetic Stimulation (TMS)

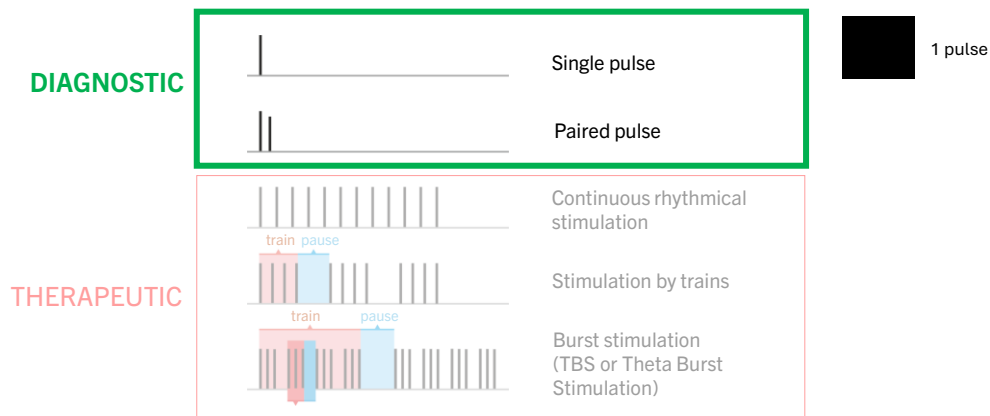
## Magnetic Stimulation Modes



25

# Transcranial Magnetic Stimulation (TMS)

## Magnetic Stimulation Modes



28

# Transcranial Magnetic Stimulation (TMS) Effects on neural systems

## Neuron level and neural signaling

Single-pulse TMS induced a highly (spatial) localized excitation of single neurons which interfere with normal task-related activity

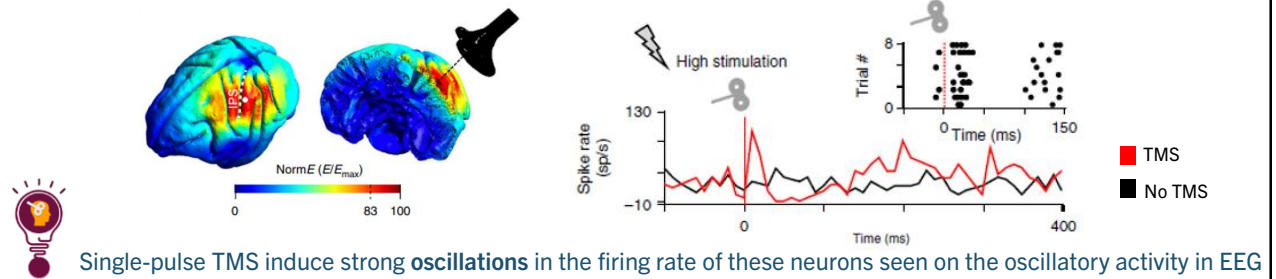
nature COMMUNICATIONS

ARTICLE

<https://doi.org/10.1038/s41467-019-10638-7>

Neural effects of transcranial magnetic stimulation at the single-cell level

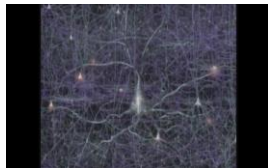
Maria C. Romero<sup>1,2,3,4</sup>, Marco Davare<sup>2,3,4</sup>, Marcelo Armendariz<sup>1,3</sup> & Peter Janssen<sup>1,3</sup>



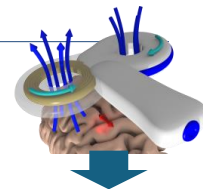
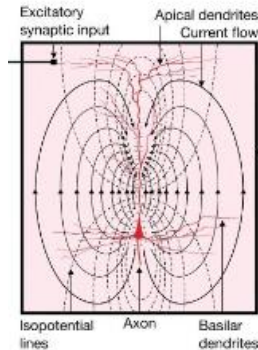
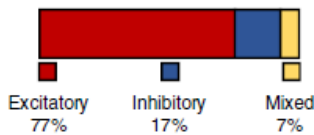
29

# Transcranial Magnetic Stimulation (TMS) Effects on neural systems

## Neuron level and neural signaling



**excitation and inhibition**  
Inhibition caused by the activation of neighboring inhibitory interneurons slightly later in time



The balance of these excitatory and inhibitory influences determines the overall "excitability" or activity level of a brain circuit or structure, or even of the whole brain

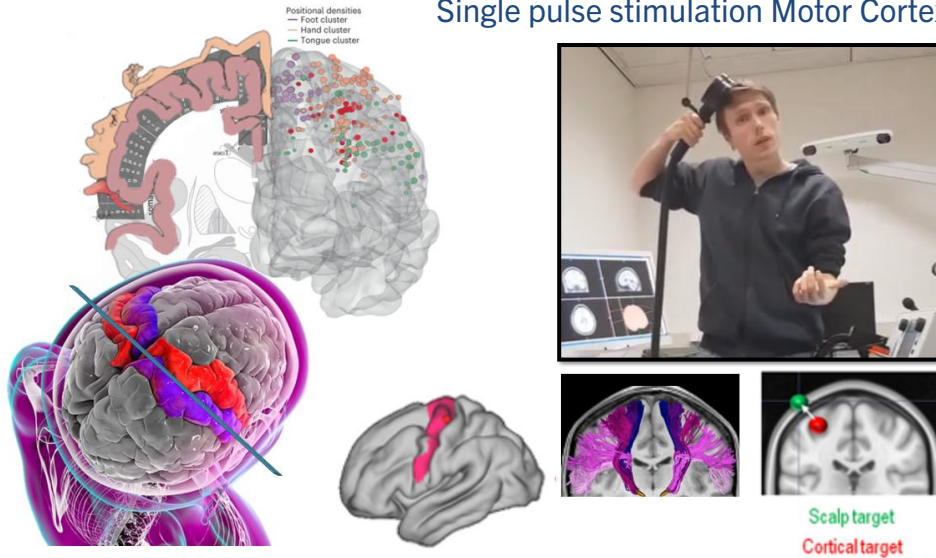
Single-pulse TMS induce strong oscillations in the firing rate of these neurons seen on the oscillatory activity in EEG

30

# Transcranial Magnetic Stimulation (TMS)

## Magnetic Stimulation Modes

### Single pulse stimulation Motor Cortex M1

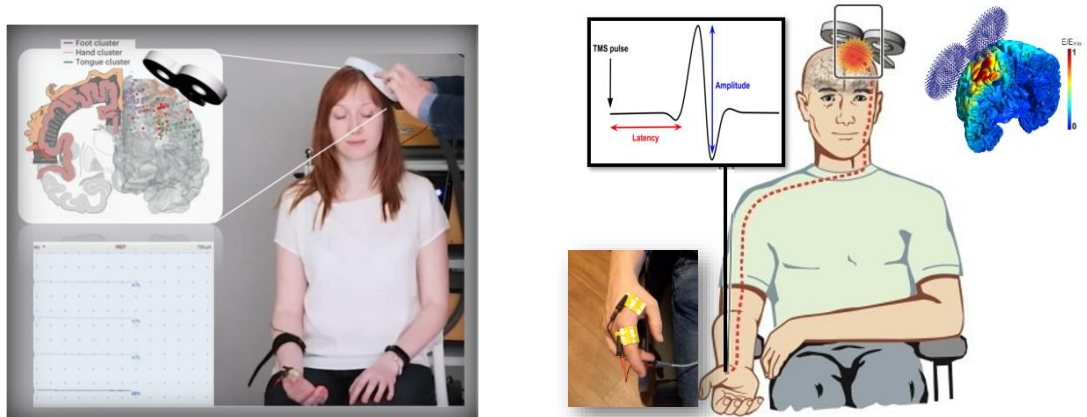


31

# Transcranial Magnetic Stimulation (TMS)

## Magnetic Stimulation Modes

### Single pulse stimulation Motor Cortex M1 and Motor Evoked Potential (MEP)



A single TMS pulse can evoke activity in the motor cortex resulting in a muscular motor response (MEP) that can be measured with EMG. TMS also activates different intracortical circuits within the M1 and connections from other cortical areas to the M1. These intracortical circuits interact with each other.

32

# Transcranial Magnetic Stimulation (TMS)

## Clinical applications

Single pulse TMS protocols can be used to:

- (a) assess the presence and severity of neurological impairments
- (b) investigate the pathophysiology of the disease
- (c) monitor disease progression
- (d) evaluate the mechanism of actions of various therapeutic approaches

36

# Transcranial Magnetic Stimulation (TMS)

## Guidelines Diagnostic TMS

**2012**

**2015**

**2023**

**2012**  
 A practical guide to diagnostic transcranial magnetic stimulation: Report of an IFCN committee  
 S. Groppa<sup>a</sup>, A. Oliviero<sup>b</sup>, A. Eisen<sup>c</sup>, A. Quartarone<sup>d</sup>, L.G. Cohen<sup>e</sup>, V. Mall<sup>f</sup>, A. Kaelin-Lang<sup>g</sup>, T. Miina<sup>h</sup>, S. Rossi<sup>i</sup>, G.W. Thickbroom<sup>j</sup>, P.M. Rossini<sup>k</sup>, U. Ziemann<sup>l</sup>, J. Valls-Solé<sup>m</sup>, H.R. Siebner<sup>n</sup>

**2015**  
 Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee  
 P.M. Rossini<sup>a</sup>, D. Burke<sup>b</sup>, R. Chen<sup>c</sup>, L.G. Cohen<sup>d</sup>, Z. Daskalakis<sup>e</sup>, R. Di Loro<sup>f</sup>, V. Di Lazzaro<sup>g</sup>, F. Ferreri<sup>h</sup>, P.R. Fitzgerald<sup>i</sup>, M.S. George<sup>j</sup>, M. Hallett<sup>k</sup>, J.P. Lefaucher<sup>l</sup>, R. Langguth<sup>m</sup>, H. Matsumoto<sup>n</sup>, C. Mitsuhashi<sup>o</sup>, M.A. Nitsche<sup>p</sup>, A. Pascual-Leone<sup>q</sup>, W. Paulus<sup>r</sup>, S. Rossi<sup>s</sup>, J.C. Rothwell<sup>t</sup>, H.R. Siebner<sup>u</sup>, Y. Ugawa<sup>v</sup>, V. Walsh<sup>w</sup>, U. Ziemann<sup>x</sup>

**2023**  
 Clinical diagnostic utility of transcranial magnetic stimulation in neurological disorders. Updated report of an IFCN committee  
 Steve Vucic<sup>a</sup>, Kai-Hsiang Stanley Chen<sup>b</sup>, Matthew C. Kiernan<sup>c</sup>, Mark Hallett<sup>d</sup>, David H. Benninger<sup>e</sup>, Vincenzo Di Lazzaro<sup>f</sup>, Paolo M. Rossini<sup>g</sup>, Alberto Benussi<sup>h</sup>, Alfredo Bardelli<sup>i</sup>, Antonio Curà<sup>j</sup>, Sandro M. Krieg<sup>k</sup>, Jean-Pascal Lefaucher<sup>l</sup>, Yew Long Lo<sup>m</sup>, Richard A Macdonell<sup>n</sup>, Marcello Massimini<sup>o</sup>, Mario Rosanova<sup>p</sup>, Thomas Picht<sup>q</sup>, Cathy M Steiner<sup>r</sup>, Walter Paulus<sup>s</sup>, Yoshikazu Ugawa<sup>t</sup>, Ulf Ziemann<sup>u</sup>, Robert Chen<sup>v</sup>

37

# Transcranial Magnetic Stimulation (TMS)

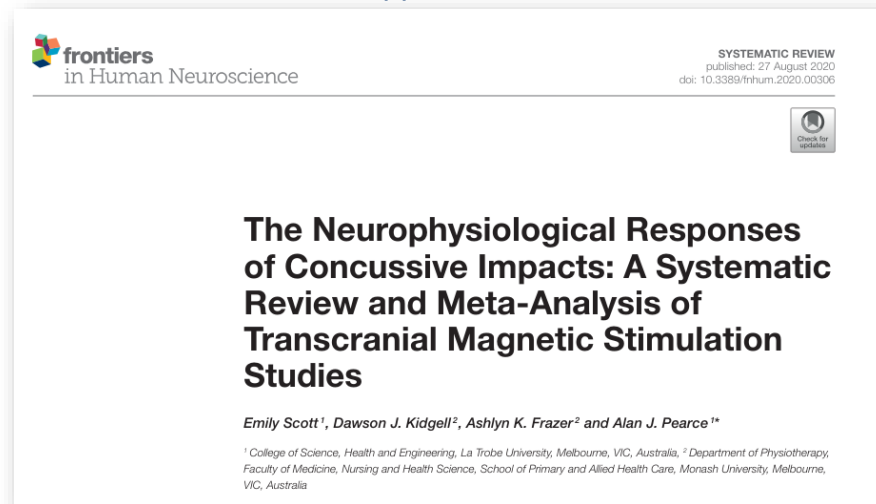
## Clinical applications



38

# Transcranial Magnetic Stimulation (TMS)

## Clinical applications



39

# Transcranial Magnetic Stimulation (TMS)

## Clinical applications

### Transcranial magnetic stimulation confirms hyperexcitability of occipital cortex in migraine

S.K. Aurora, MD; B.K. Ahmad, MD; K.M.A. Welch, MD; P. Bhardhwaj, MD; and N.M. Ramadan, MD

### TMS for Migraine (abortive)

#### Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham-controlled trial

Richard B Lipton, David W Dodick, Stephen D Silberstein, Joel R Saper, Sheena K Aurora, Starr H Pearlman, Robert E Fischell, Patricia L Ruppel, Peter J Goadsby

40

# Transcranial Magnetic Stimulation (TMS)

## Clinical applications

<https://doi.org/10.1093/brain/awad395>

BRAIN 2024; 147; 1423–1435 | 1423

**BRAIN**  
ORIGINAL ARTICLE



## The pathobiology of psychomotor slowing in psychosis: altered cortical excitability and connectivity

Stephanie Lefebvre,<sup>1,2</sup> Gwendolyn Gehrig,<sup>1</sup> Niluja Nadesalingam,<sup>1,2</sup>  
Melanie G. Nuoffer,<sup>1,2,3</sup> Alexandra Kyrou,<sup>1</sup> Florian Wüthrich,<sup>1,2</sup>  
and Sebastian Walther<sup>1,2</sup>

the TMS data suggest a specific inhibitory deficit in patients with schizophrenia and hypokinetic motor abnormalities, i.e. psychomotor slowing and catatonia

41



# Transcranial Magnetic Stimulation (TMS)

## Clinical applications



Contents lists available at ScienceDirect

### Clinical Parkinsonism & Related Disorders

journal homepage: [www.sciencedirect.com/journal/clinical-parkinsonism-and-related-disorders](http://www.sciencedirect.com/journal/clinical-parkinsonism-and-related-disorders)



Transcranial and muscular single-pulse magnetic stimulation is efficient on motor functional neurological disorders by the feedback of induced muscle contractions — A retrospective case series

Bonnan Mickael

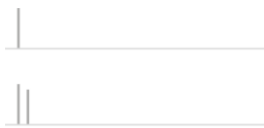
Service de Neurologie, Centre Hospitalier de Pau, 64000 PAU, France PRDOA 5 (2021)

42

# Transcranial Magnetic Stimulation (TMS)

## Magnetic Stimulation Modes

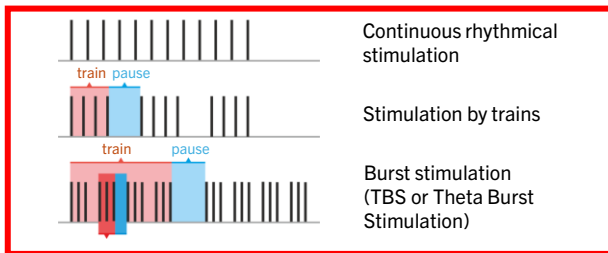
DIAGNOSTIC



Single pulse

Paired pulse

THERAPEUTIC



Continuous rhythmical stimulation

Stimulation by trains

Burst stimulation (TBS or Theta Burst Stimulation)



10 pulses / sec



9 pulses / train  
3 sec train  
2 sec pause



Burst van 3 pulses

repetitive TMS (rTMS)  
Theta Burst Stimulation

43

# Transcranial Magnetic Stimulation (TMS)

## Magnetic Stimulation Modes



44

# Transcranial Magnetic Stimulation (TMS)

## Magnetic Stimulation Modes



repetitive TMS protocols can either temporarily **increase** or **decrease** neuronal **excitability**

### Continuous rhythmical stimulation

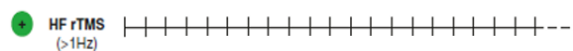
- Low frequency rTMS stimulation (< 3Hz)

– **Inhibitory** effect



- High frequency rTMS stimulation (> 3Hz)

– **Excitatory** effect



47

# Transcranial Magnetic Stimulation (TMS)

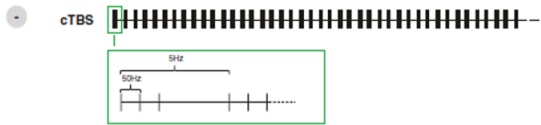
## Magnetic Stimulation Modes



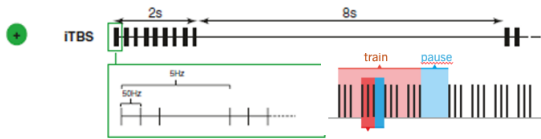
repetitive TMS protocols can either temporarily **increase** or **decrease** neuronal **excitability**

### Theta burst stimulation

- Continuous theta burst stimulation
  - **Inhibitory** effect



- Intermittent theta burst stimulation
  - **Excitatory** effect

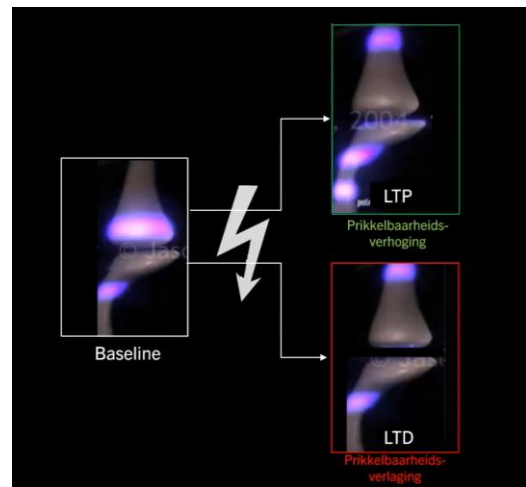
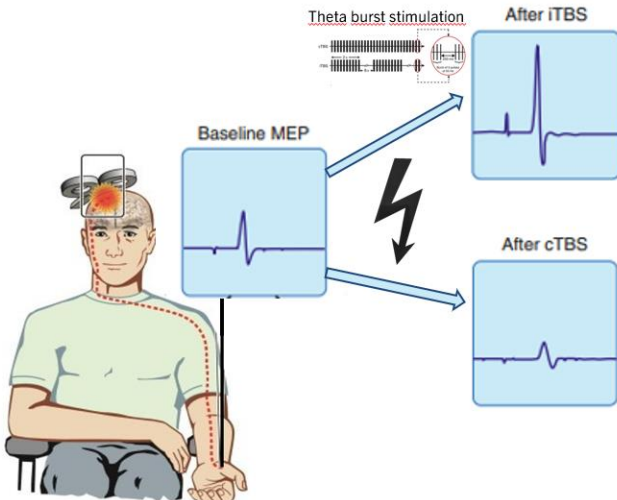


48

# Transcranial Magnetic Stimulation (TMS)

## Magnetic Stimulation Modes

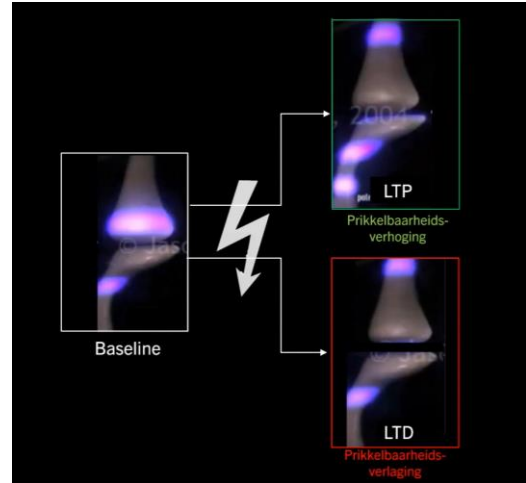
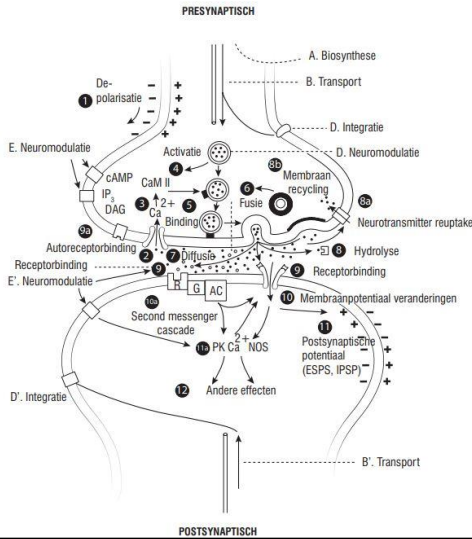
### Neuroplasticity (LTP and LTD)



50

# Transcranial Magnetic Stimulation (TMS) Magnetic Stimulation Modes

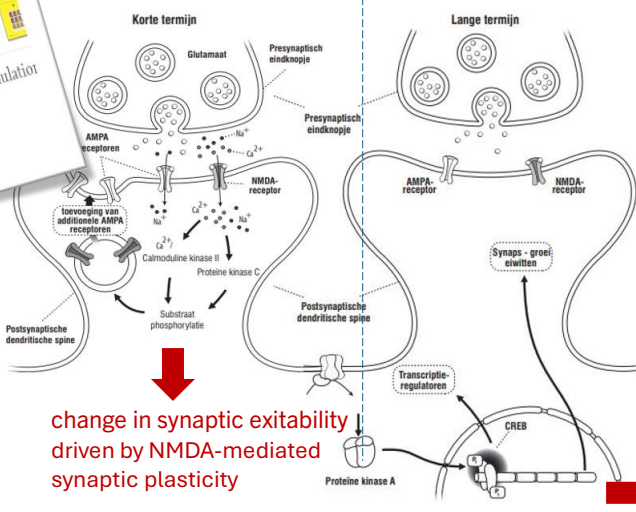
## Neuroplasticity (LTP and LTD)



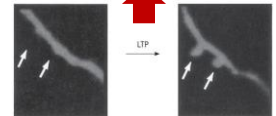
51

# Transcranial Magnetic Stimulation (TMS) Effects on neural systems

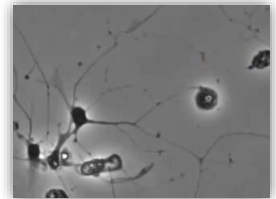
## Neuroplasticity (LTP)



synaptic changes



modification of dendritic spines

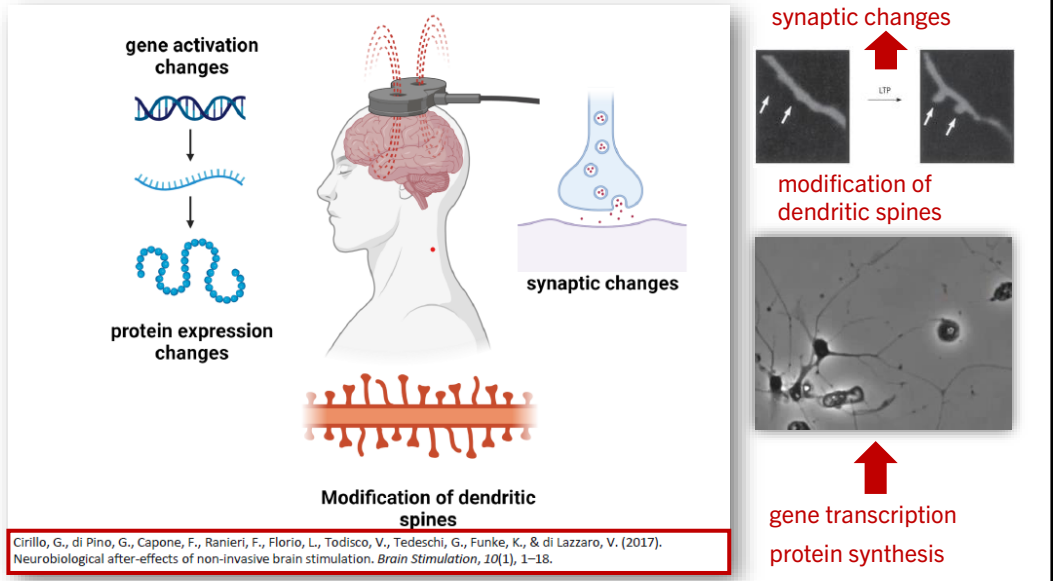


gene transcription  
protein synthesis

52

# Transcranial Magnetic Stimulation (TMS)

## Effects on neural systems



53

# Non-Invasive Brain Stimulation

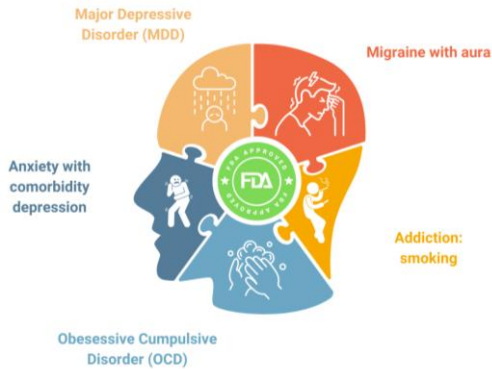


54

# Transcranial Magnetic Stimulation (TMS)

## What is it used for?

### FDA APPROVED



### POTENTIALLY EFFECTIVE



55

# Transcranial Magnetic Stimulation (TMS)

## Depression



56

# Transcranial Magnetic Stimulation (TMS) Depression



In Belgium, 1 in 3 people feels bad in their skin

9% of the population experiences depression



33% of those people do not respond to treatment

Belgium ranks 3rd in Europe in terms of the highest number of suicides per year



Deep TMS

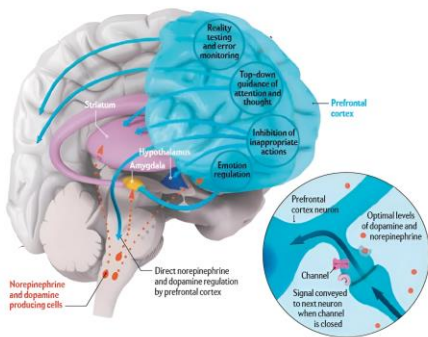


Conventional TMS

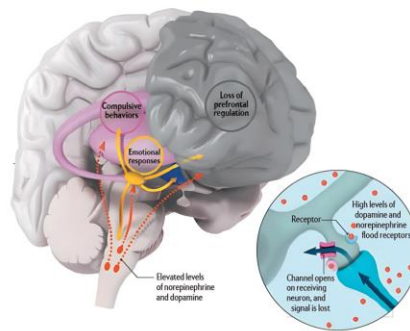
57

# Transcranial Magnetic Stimulation (TMS) Depression

NORMAL BRAIN



BRAIN UNDER STRESS

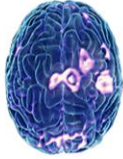


Arnstén, 2009

58

## Transcranial Magnetic Stimulation (TMS) Depression

Before rTMS



Prefrontal  
Hypoactivity

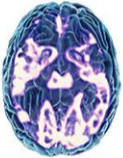


Unbalance



Amygdala  
Hyperactivity

After rTMS



Prefrontal  
rTMS



Balanced

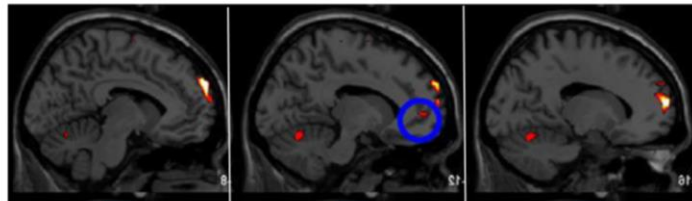


Amygdala  
Top down control

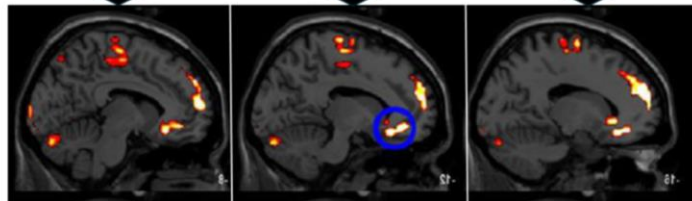
59

## Transcranial Magnetic Stimulation (TMS) Depression

BASELINE



AFTER rTMS

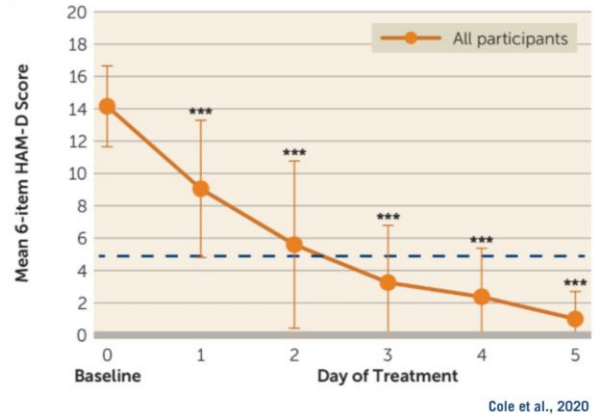
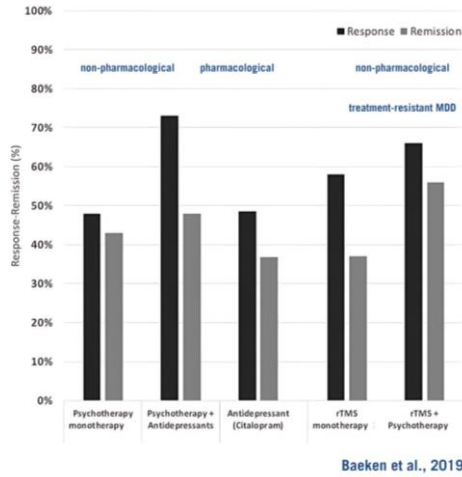


Vink et al. 2018

60

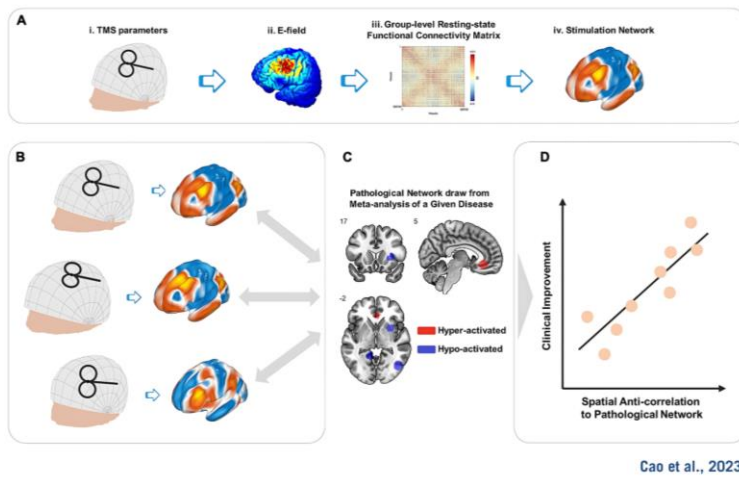


# Transcranial Magnetic Stimulation (TMS) Depression



61

# Transcranial Magnetic Stimulation (TMS) Depression



62

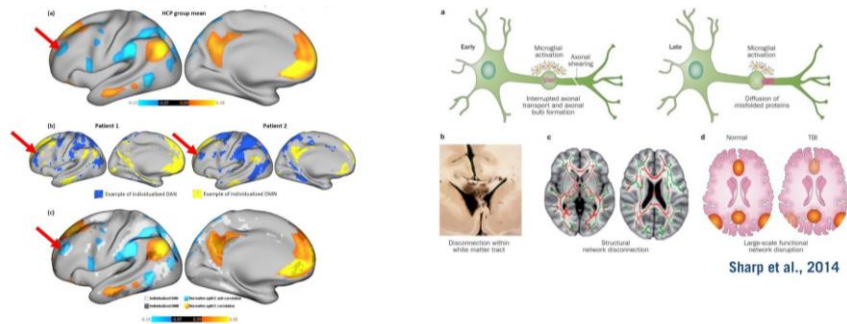
# Transcranial Magnetic Stimulation (TMS)

## Depression after a traumatic brain injury

Article | [Open access](#) | Published: 11 March 2023

### Individualized precision targeting of dorsal attention and default mode networks with rTMS in traumatic brain injury-associated depression

Shan H. Siddiqi , Sridhar Kandala, Carl D. Hacker, Nicholas T. Trapp, Eric C. Leuthardt, Alexandre R. Carter & David L. Brody



63

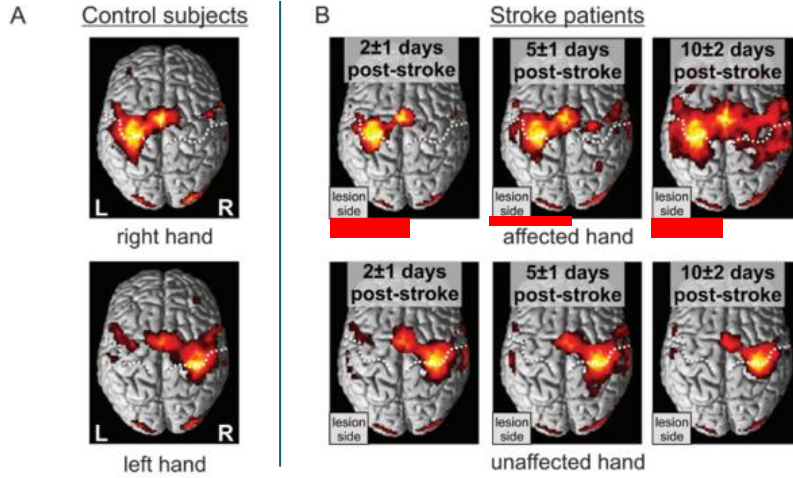
## Non-Invasive Neuromodulation



64

# Transcranial Magnetic Stimulation (TMS) Stroke

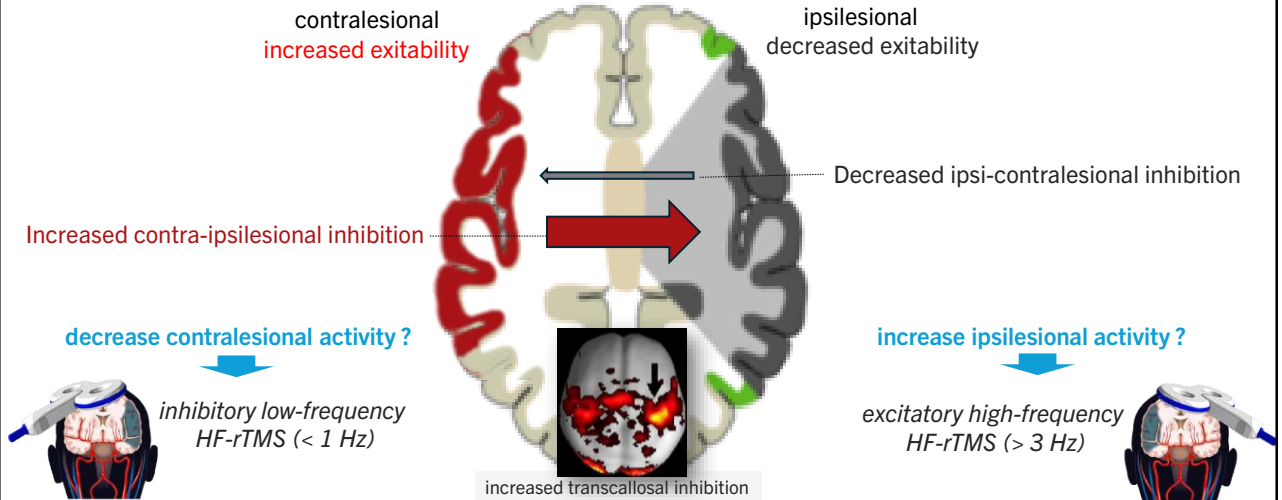
Imbalanced interhemispheric activity



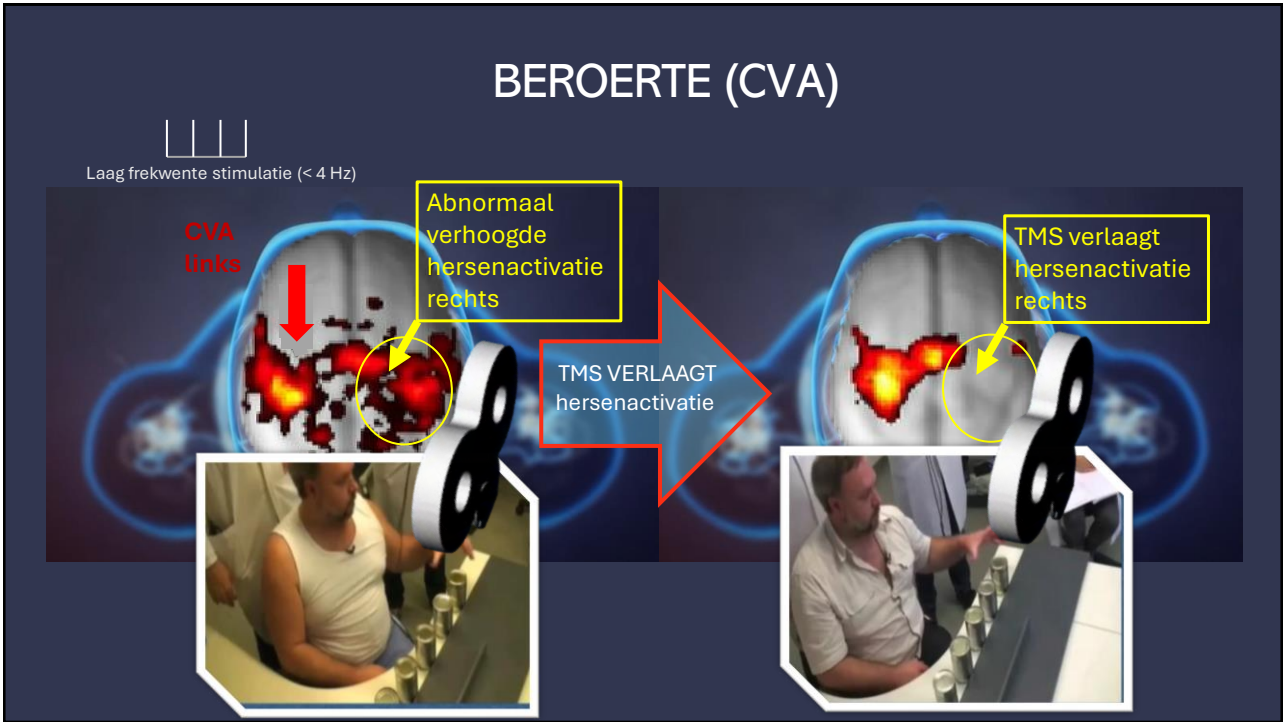
65

# Transcranial Magnetic Stimulation (TMS) Stroke

Paradoxical Functional Facilitation



66




67

# Transcranial Magnetic Stimulation (TMS) Stroke







Clinical study


**Stroke**  
Volume 54, Issue 8, August 2023; Pages 1962-1971  
<https://doi.org/10.1161/STROKEAHA.123.042924>

 American Heart Association.

**CLINICAL TRIALS**

**Continuous Theta-Burst Stimulation of the Contralesional Primary Motor Cortex for Promotion of Upper Limb Recovery After Stroke: A Randomized Controlled Trial**

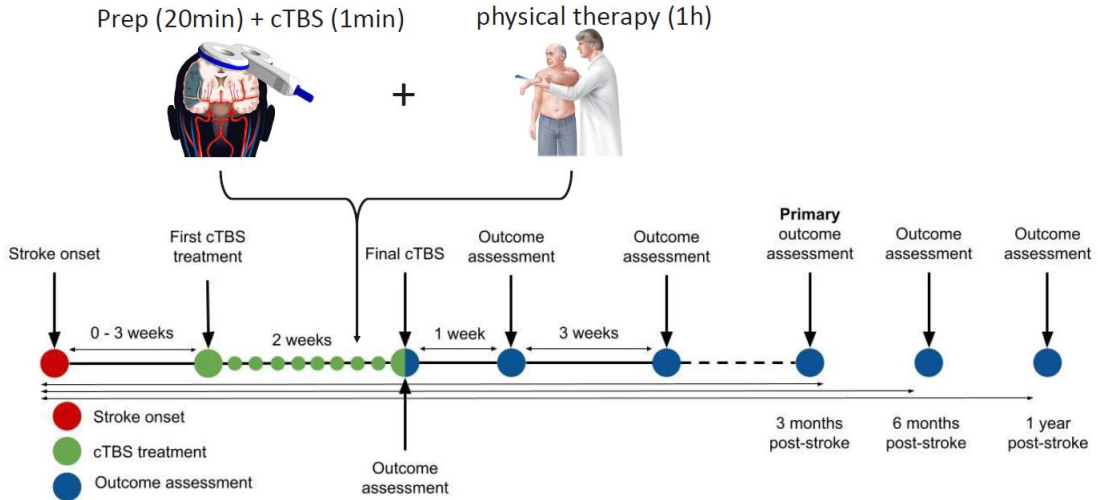
Jord J.T. Vink, MSc , Eline C.C. van Lieshout, PhD , Willem M. Otte, PhD, Ruben P.A. van Eijk, PhD , Mirjam Kouwenhoven, MD, Sebastiaan F.W. Neggers, PhD , H. Bart van der Worp, MD, PhD , Johanna M.A. Visser-Meily, MD, PhD, and Rick M. Dijkhuizen, PhD 



68

# Transcranial Magnetic Stimulation (TMS) Stroke

## Clinical study



69

# Transcranial Magnetic Stimulation (TMS) in neurorehabilitation

Over het KCRU Na

De Hoogstraat Revalidatie UMC Utrecht Partnerschap Producten

DCRM Dutch Congress of Rehabilitation Medicine VRA NEDERLANDSE VERENIGING VOOR REHABILITATIE

Nieuwe hersenstimulatiebehandeling verbetert motorisch herstel na een beroerte

Hersenstimulatie voor het verbeteren van uitkomsten van revalidatie

DCRM 09-11

B-STARS<sup>2</sup> Brain Stimulation for Arm Recovery after Stroke

70

# Transcranial Magnetic Stimulation (TMS) in neurorehabilitation



Federatie  
**Medisch  
Specialisten**

## Herseninfarct en hersenbloeding

### Non-invasieve hersenstimulatie met rTMS

Vooraf stimulatie van de contralaterale, gezonde hemisfeer met LF rTMS of iTBS binnen drie maanden na een herseninfarct of -bloeding is herhaaldelijk geassocieerd met een beter herstel van uiteenlopende functies.

71

# Transcranial Magnetic Stimulation (TMS) in neurorehabilitation

*Editorial*



## International Stroke Recovery and Rehabilitation Roundtable Consensus Statements Are Driving Growth and Progress in Our Field

**Kathryn S. Hayward, PhD<sup>1</sup>, Gert Kwakkel, PhD<sup>2</sup>,  
and Julie Bernhardt, PhD<sup>3</sup>**

Neurorehabilitation and  
Neural Repair  
2024, Vol. 38(1) 3–6  
© The Author(s) 2023  
Article reuse guidelines:  
[sagepub.com/journals-permissions](https://sagepub.com/journals-permissions)  
DOI: 10.1177/15459683231223648  
[journals.sagepub.com/home/nnr](https://journals.sagepub.com/home/nnr)

**S Sage**

72

# Transcranial Magnetic Stimulation (TMS) in neurorehabilitation

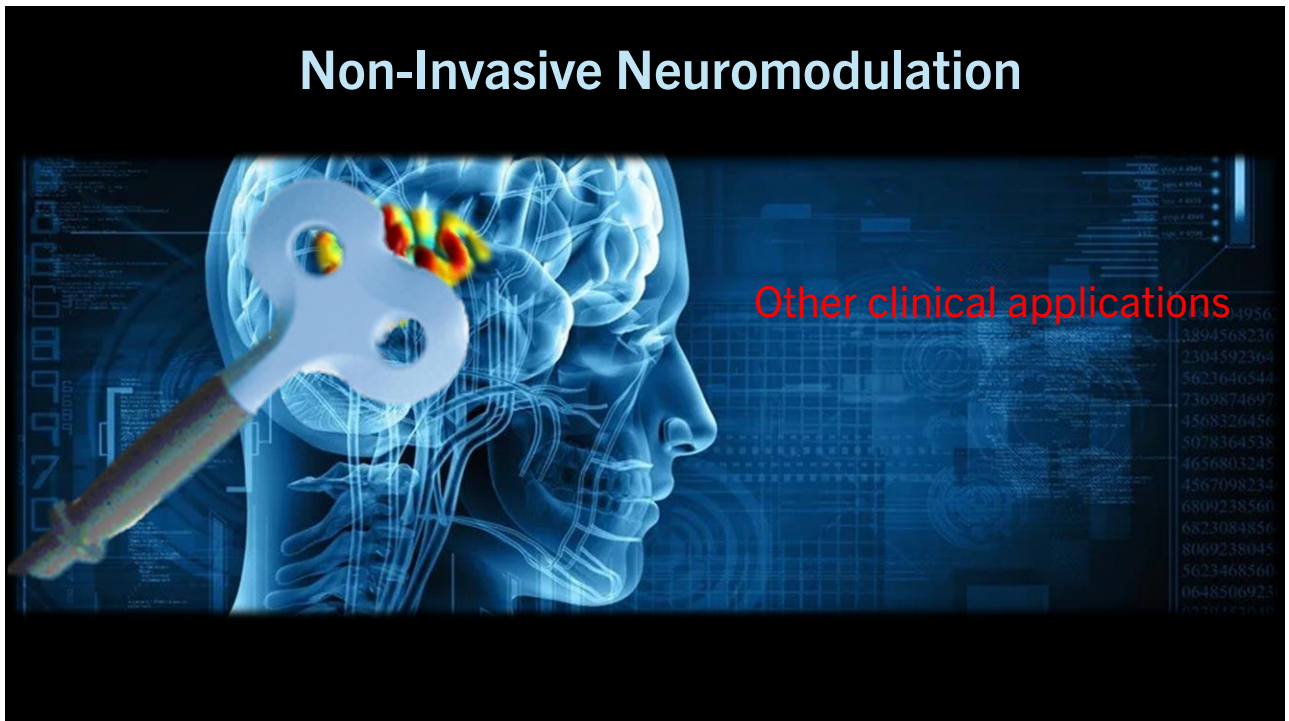
## International Stroke Recovery and Rehabilitation Roundtable Consensus Statements Are Driving Growth and Progress in Our Field

Kathryn S. Hayward, PhD<sup>1</sup>, Gert Kwakkel, PhD<sup>2</sup>, and Julie Bernhardt, PhD<sup>3</sup>

Table 1. Topics for Which Consensus Recommendations Were Established in the First, Second, and Third Stroke Recovery and Rehabilitation Roundtable efforts.

Taskforce topic	Provides consensus recommendations for
<b>SRRR1</b>	
Timeline definitions <sup>1</sup>	Common language and definitions for stroke recovery and rehabilitation field and an agreed vision for accelerating progress in stroke recovery research.
Biomarkers <sup>2</sup>	Biomarkers that were considered ready to be included in clinical trials, and others that were promising and represent a developmental priority.
Standardized measurement of sensorimotor recovery <sup>3</sup>	Core measurement standards and patient characteristics that should be collected in all future stroke recovery trials to help build our understanding of the trajectory of stroke recovery and aid discovery of new and more targeted treatments.
Preclinical and clinical alignment <sup>4</sup>	Appropriate preclinical stroke recovery research and to align preclinical to clinical stroke recovery studies to avoid past mistakes and maximize clinical translation.
Monitoring and reporting of stroke recovery research <sup>5</sup>	Issues identified as limiting stroke rehabilitation research in the areas of developing, monitoring, and reporting stroke rehabilitation interventions
<b>SRRR2</b>	
Preclinical and clinical trial development <sup>6</sup>	Key knowledge units to develop stroke recovery treatment trials that can be addressed within a framework that defines GO and NO-GO decision pathways to guide selection of the most appropriate trial (including phase) given current knowledge.
Cognition <sup>7</sup>	Cognitive assessments to be integrated into stroke recovery studies generally and defined priorities for ongoing and future research for stroke recovery and rehabilitation.
Translation into practice <sup>8</sup>	Research evidence to be prioritized for implementation into stroke rehabilitation practice to have maximal impact.
Standardized measurement of quality of movement <sup>11</sup>	Kinematic and kinetic movement quantification for standardized measurements of sensorimotor recovery in stroke trials.
<b>SRRR3</b>	
Control comparator trial design <sup>12</sup>	Challenges that impact control comparator design that can be addressed with a tool produced to guide control comparator selection, description, and reporting of preclinical and clinical trials in stroke recovery and rehabilitation.
Fatigue <sup>13</sup>	Definition, clinical screening tools, and outcome measurement for fatigue after stroke and provided a roadmap for future research.
Non-invasive brain stimulation <sup>4</sup>	Outstanding barriers for the translation of preclinical and clinical research using the non-invasive brain stimulation techniques, transcranial magnetic stimulation, and transcranial direct current stimulation and provided a roadmap for the integration of these techniques into clinical practice.
Standardized measurement of balance and mobility <sup>14</sup>	Standardized outcome instruments for measuring balance and mobility recovery after stroke to optimize the quality of stroke rehabilitation and recovery studies and to enable data synthesis across trials.

73



74

# Transcranial Magnetic Stimulation (TMS) in neurorehabilitation

**Table 20**

Summary of recommendations on rTMS efficacy according to clinical indication.

Neuropathic pain	Definite analgesic efficacy of HF-rTMS of M1 contralateral to pain side (Level A), while LF-rTMS is probably ineffective (Level B)
CRPS type I	Possible analgesic efficacy of HF-rTMS of M1 contralateral to pain side (Level C)
<b>Fibromyalgia</b>	<b>Possible efficacy of HF-rTMS of the left M1 in improving quality of life of patients with fibromyalgia (Level B)</b>
<b>Fibromyalgia</b>	<b>Probable analgesic efficacy of HF-rTMS of the left DLPFC in patients with fibromyalgia (Level B)</b>
Parkinson's disease	Probable efficacy of HF-rTMS of bilateral M1 regions in motor symptoms of PD patients (Level B)
Parkinson's disease	Probable antidepressant efficacy of HF-rTMS of the left DLPFC in PD patients (Level B)
<b>Motor stroke</b>	<b>Definite efficacy of LF-rTMS of contralesional M1 in hand motor recovery at the postacute stage (Level A)</b>
<b>Motor stroke</b>	<b>Probable efficacy of HF-rTMS of ipsilesional M1 in hand motor recovery at the postacute stage (Level B)</b>
<b>Motor stroke</b>	<b>Possible efficacy of LF-rTMS of contralesional M1 in hand motor recovery at the chronic stage (Level C)</b>
<b>Post-stroke aphasia</b>	<b>Probable efficacy of LF-rTMS of right IFG in nonfluent aphasia recovery at the chronic stage (Level B)</b>
Hemispatial neglect	Possible efficacy of cTBS of the contralesional left parietal in visuospatial hemineglect recovery at the post-acute stage of stroke (Level C)
<b>Multiple sclerosis</b>	<b>Probable efficacy of iTBS of the leg area of M1 contralateral to the most affected limb (or both M1) in lower limb spasticity (Level B)</b>
Epilepsy	Possible antiepileptic efficacy of LF-rTMS of the epileptic focus (Level C)
<b>Alzheimer's disease</b>	<b>Possible efficacy of multiset rTMS-COG to improve cognitive function, memory and language level of AD patients, especially at a mild/early stage of the disease (Level C)</b>
Tinnitus	Possible efficacy of LF rTMS of the auditory cortex of the left hemisphere (or contralateral to the affected ear) in chronic tinnitus (Level C)
Depression	Definite antidepressant efficacy of HF-rTMS of the left DLPFC in major depression using a figure-of-8 coil or a H1-coil (Level A)
Depression	<b>Definite antidepressant efficacy of deep HF-rTMS over the left DLPFC in major depression (Level A)</b>
Depression	Probable antidepressant efficacy of LF-rTMS of the right DLPFC in major depression (Level B)
Depression	<b>Probable antidepressant efficacy of bilateral right-sided LF-rTMS and left-sided HF-rTMS of the DLPFC in major depression (Level B)</b>
Depression	<b>Probable antidepressant efficacy of bilateral right-sided cTBS and left-sided iTBS of the DLPFC in major unipolar depression (Level B), while unilateral right-sided cTBS is possibly ineffective (Level C)</b>
Depression	<b>Possible no differential antidepressant efficacy between: right LF-rTMS vs. left HF-rTMS, bilateral vs. unilateral rTMS of the DLPFC, and rTMS performed alone vs. combined with antidepressants (Level C)</b>
Post-traumatic stress disorder	<b>Probable efficacy of HF-rTMS of the right DLPFC in PTSD (Level B)</b>
<b>Obsessive compulsive disorder</b>	<b>Possible efficacy of LF-rTMS of the right DLPFC in OCD (Level C)</b>
Schizophrenia:auditory hallucinations	Possible efficacy of LF-rTMS of the left TPC in auditory hallucinations in schizophrenia (Level C)
<b>Schizophrenia: negative symptoms</b>	<b>Possible efficacy of HF-rTMS of the left DLPFC on negative symptoms of schizophrenia (Level C)</b>
Addiction and craving	Possible efficacy of HF-rTMS of the left DLPFC on cigarette craving and consumption (Level C)

In all other conditions, there is "no recommendation", which means the absence of sufficient data to make a recommendation, but not the evidence for an absence of effect. Recommendations that change from our previous work (Lefaucheur et al., 2014) are shown in bold.

## Level of Evidence A

Data derived from multiple randomized clinical trials or meta-analyses.

## Level of Evidence B

Data derived from a single randomized clinical trial or large non-randomized studies.

## Level of Evidence C

Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

75

# Transcranial Magnetic Stimulation (TMS) Indications

Depression

OCD

Motor stroke: contralesional motor cortex

Motor stroke: ipsilesional motor cortex

Stroke: hemispatial neglect

Post-stroke non-fluent aphasia

Stroke: Dysphagia

Concussion

Neuropathic pain

Non-neuropathic pain

MS

Parkinson's disease: movement disorders

Parkinson's disease: levodopa-induced dyskinesia

Parkinson's disease: depression

Epilepsy

Dementia Alzheimer's disease

Pelvic floor stimulation

Fibromyalgia

Visceral pain

Post-traumatic stress disorder (PTSD)

Addictive disorders

Essential tremor (cerebellar stimulation)

Tinnitus

Addictive disorders

ASS

ADHD

Whiplash

76



# Transcranial Magnetic Stimulation (TMS) Indications

Brain Research Bulletin 148 (2019) 1-9

Contents lists available at ScienceDirect

Brain Research Bulletin

journal homepage: [www.elsevier.com/locate/brainresbull](http://www.elsevier.com/locate/brainresbull)

ELSEVIER

Brain Research Bulletin

Phantom limb pain Amputees without pain Healthy controls

Transcranial magnetic stimulation in subjects with phantom pain and non-painful phantom sensations: A systematic review

Raffaele Nardone<sup>a,b,c</sup>, Viviana Versace<sup>c</sup>, Luca Sebastianelli<sup>c</sup>, Francesco Brigo<sup>a,d</sup>, Monica Christova<sup>a,f</sup>, Giuditta Iliara Scarano<sup>e</sup>, Leopold Saltuari<sup>g,h</sup>, Eugen Trinka<sup>b,i,j</sup>, Larissa Hauer<sup>m</sup>, Johann Selner<sup>b,n</sup>



77

# Non-Invasive Neuromodulation



Safety

2089304956  
 3894568236  
 2304592364  
 5623646544  
 7369874697  
 4568326456  
 5078364538  
 4656803245  
 4567098234  
 6809238560  
 6823084856  
 8069238045  
 5623468560  
 0648506923  
 059010070111

78

# Transcranial Magnetic Stimulation (TMS) Safety

Expert Guidelines TMS **2021**



79

# Transcranial Magnetic Stimulation (TMS) Safety

## Safety guidelines recommendations for TMS

- Patient screening
  - Medical history
  - Family history
  - Use of medication
- Treatment dose/duration
  - Max train duration of 4.2s for 10Hz rTMS at 120% RMT
  - Inter-train intervals
- Training



INTERNATIONAL  
CLINICAL  
TMS CERTIFICATION  
COURSE

80

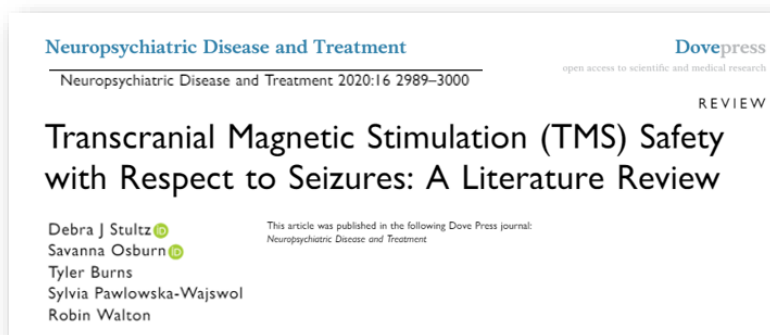
# Transcranial Magnetic Stimulation (TMS) Safety

## Contraindications

1. **The only absolute contraindication** to TMS/rTMS is the presence of metallic hardware in close contact to the discharging coil (such as cochlear implants, or Internal Pulse Generator or medication pumps).
2. **All the rest contraindications are relative** ones. In each individual case the benefit of the test should be weighed against possible adverse effects.
  - **Increased risk of inducing seizure:**
    - related to the protocol of stimulation;
    - related to the disease or patient's condition (epilepsy, lesion of the brain, administration of drugs that potentially lower seizure threshold, sleep deprivation, alcoholism).
  - **Increased risk of other events:**
    - related to patient's condition (implanted brain electrodes, pregnancy, severe or recent heart disease).

81

# Transcranial Magnetic Stimulation (TMS) Safety



- The risk of TMS-related seizures is < 1% overall.
- TMS has successfully been used in patients with epilepsy, traumatic brain injuries, and those with a prior TMS-related seizure.

82

# Transcranial Magnetic Stimulation (TMS) Safety



83

# Transcranial Magnetic Stimulation (TMS) Safety

Based on the vast amount of safety data collected over the past 30 years, several publications, meta-analyses, reviews, guidelines and consensus papers have provided peer-reviewed evidence-based assessments of the safety of TMS (see e.g., Rossi et al., 2020) as well as low output transcranial electric stimulation, TES (see e.g., Antal et al., 2017; 2022; Bikson et al., 2018a; b; Caulfield et al., 2022; Zewdie et al., 2020). **Based on these data, the current scientific and clinical evidence suggests both rTMS and low intensity TES are safe treatment and research interventions with few and mild adverse effects.**

The prominent mentioning of rTMS/TES-related seizure risks contradicts the most recent consensus statement in the field based on actual clinical data which demonstrated that **observed seizure rates are so much lower than previous guidelines advised, that the prior caution about seizure risk is no longer supported by scientific evidence** (Rossi et al., 2020).

To put this into perspective, the likelihood of a seizure from rTMS (**0.003%**) is lower than that associated with the use of antidepressants and antipsychotics (0.1-1, 5%), which are one of the most frequently prescribed treatments for depression (George et al., 2013).

84

# Transcranial Magnetic Stimulation (TMS) Safety



Uit het onderzoeksprotocol voor B-STARS2:

The most serious adverse effect is the occurrence of a seizure at a crude risk of approximately **0.02% per stimulation session, as reported in a systematic review of 67 studies with 1,040 subjects and >4,500 sessions. (1/4500 sessions)**

More common adverse events during and after TBS are transient headache and neck pain, reported by <3% of subjects.

CTBS treatment **did not lead to seizures** in our phase II trial (B-STARS). We only observed mild side effects, such as headache (<4%) and muscle pain (<1%) and the intervention was reported to be tolerable and comfortable.

Oberman, Lindsay, et al. "Safety of theta burst transcranial magnetic stimulation: a systematic review of the literature." *Journal of Clinical Neurophysiology* 28.1 (2011): 67.

85



# Transcranial Magnetic Stimulation (TMS) Training



86



87