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# Mittwochsfortbildung

**"Strom, Magnet oder Ketamin:  
Was hilft?"**

**Ein Symposium der DGHP zur  
Behandlung von Patienten mit  
therapieresistenten Depressionen**

Mittwoch, 16. Juni 2021, 16:30 – 18:30 Uhr



Deutsche Gesellschaft für  
**Hirnstimulation** in der Psychiatrie e.V.

# **rTMS zur Behandlung der Depression**

## **Aktueller Konsensusartikel der DGHP**

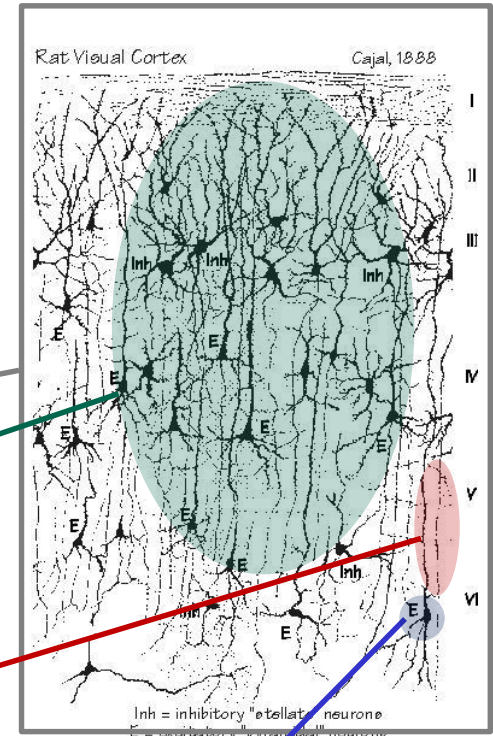
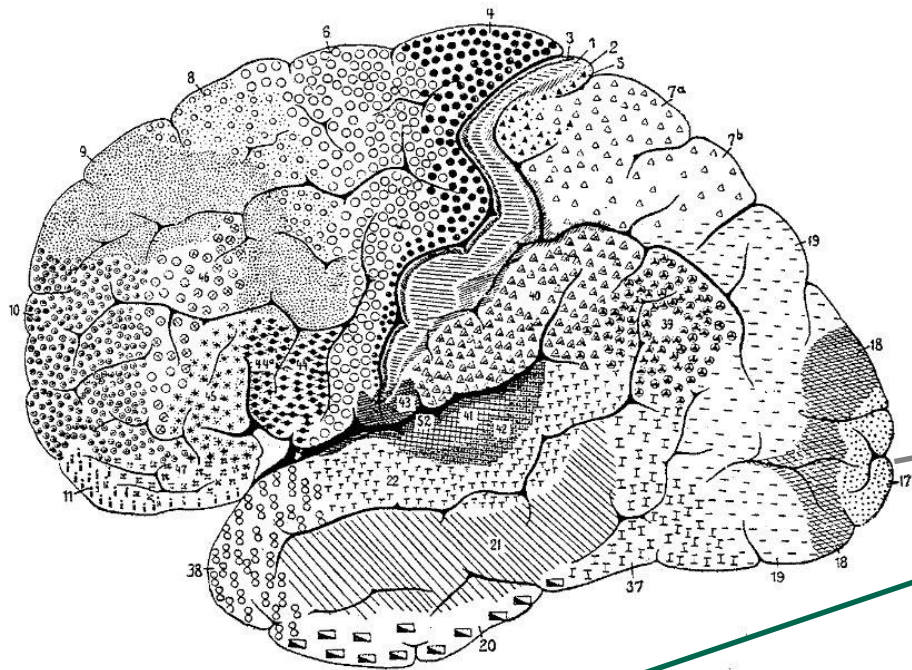
**Prof. Dr. Berthold Langguth**

**Dr. Tobias Hebel**

**Bezirksklinikum Regensburg**

**Klinik für Psychiatrie und Psychotherapie der Universität Regensburg**

# das Gehirn: ein bio-elektro-chemisches Organ



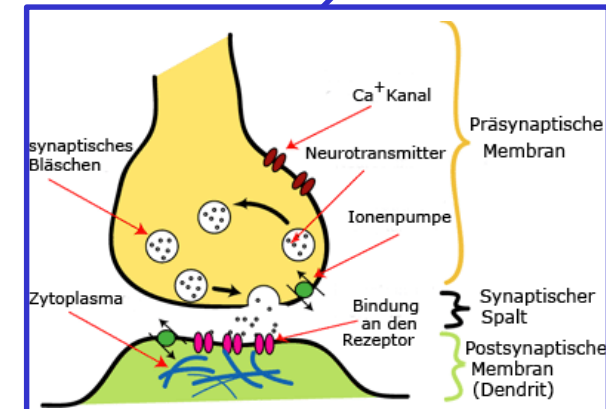
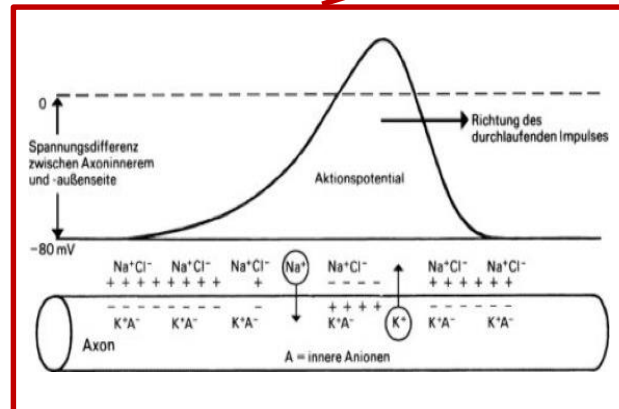
**White matter changes (DTI)**  
 Large scale axonal remodeling  
 - changes in anisotropy

Exercise

**Gray matter changes (e.g. VBM)**

- Synaptogenesis
- Angiogenesis
- Gliogenesis
- Neurogenesis
- Increase in cell size
- Increase of interstitial fluid or blood flow

TRENDS in Cognitive Sciences



Übung / Aktivität

elektrisch

Pharmakologisch

# Gehirnstimulation zur Depressionsbehandlung

- **Elektrokonvulsive Therapie (EKT)**
- **Transkranielle Magnetstimulation (TMS)**
- **Vagusnervstimulation (VNS)**
- **Magnetische Krampftherapie (MST)**
- **Tiefe Hirnstimulation (DBS / THS)**
- **Transkranielle Gleichstromstimulation (tDCS)**
- **Transkutane Vagusnervstimulation (tVNS)**
- .....

# Gehirnstimulation zur Depressionsbehandlung

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[www.dghp-online.de](http://www.dghp-online.de)



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**Hirnstimulation** in der Psychiatrie e.V.

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**1995: erste Nachweise für die antidepressive Wirkung der rTMS**

**1999: Gründung der AG TMS in Deutschland**

**2010: Gründung der DGHP**

**2010: Etablierung der Gehirnstimulationsreferate in der DGPPN**

**2014: German Center for Brain Stimulation (BMBF gefördert)**

**2021: Konsensusartikel zur rTMS bei Depression**

**(zusammen mit den DGPPN Referaten)**

### **Andere Aktivitäten der DGHP**

- **Multizentrische Studien zum Einsatz von rTMS und tDCS**
- **Jährliche Tagungen**
- **Zertifizierung**
- **Zusammenarbeit mit anderen nationalen Organisationen auf europäischer Ebene**



## Ziel des Konsensuspapers

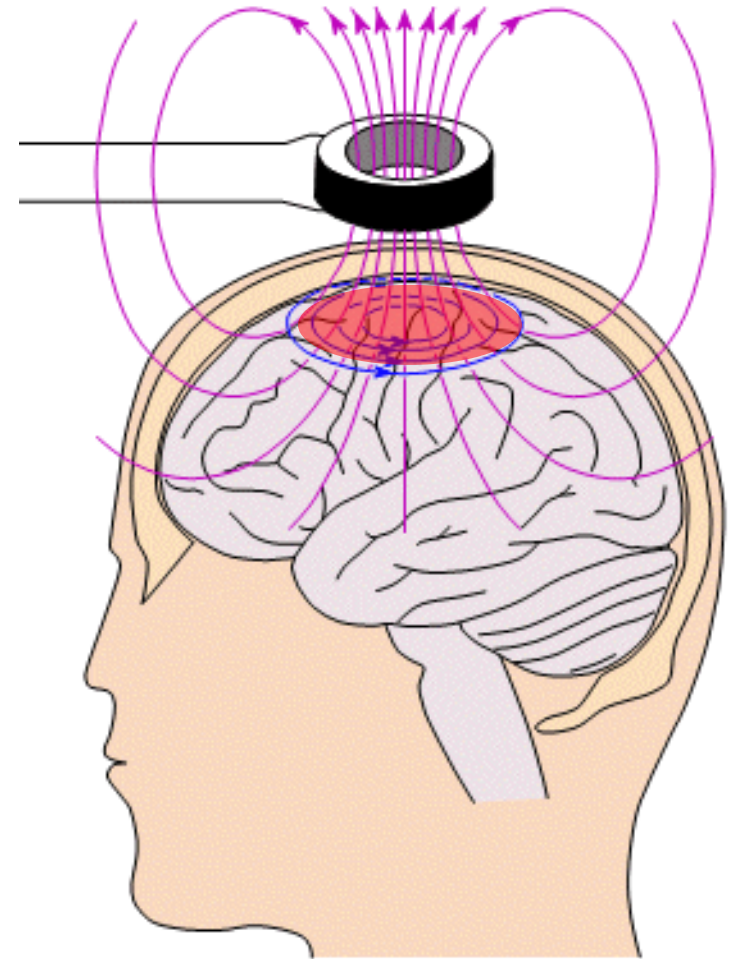
*This paper aims to present*

- *a practical guide to the application of rTMS in depression that is*
- *based on evidence from the literature*
- *as well as on the clinical experience of a group of leading German experts in the field.*

# Transkranielle Magnetstimulation

**Das magnetische Feld:**

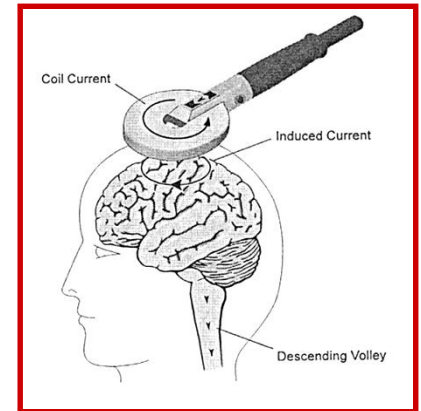
- **durchdringt den Schädel nahezu widerstandslos**
- **induziert neuronale Depolarisation in oberflächlichen Gehirnarealen**
- **„transportiert“ den elektrischen Stimulus durch den Schädel zum Kortex**





# Neurobiologie der rTMS

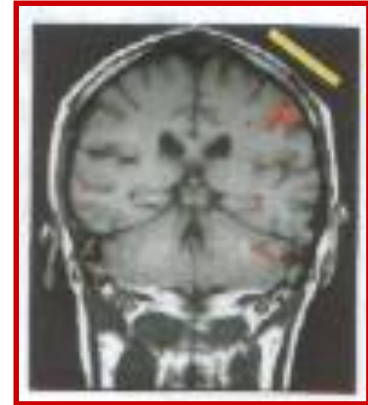
**Transkranielle Magnetstimulation  
depolarisiert kortikale Neurone**



# Neurobiologie der rTMS

Transkranielle Magnetstimulation  
depolarisiert kortikale Neurone

**repetitive TMS führt zu anhaltenden  
Veränderungen der kortikalen Erregbarkeit**

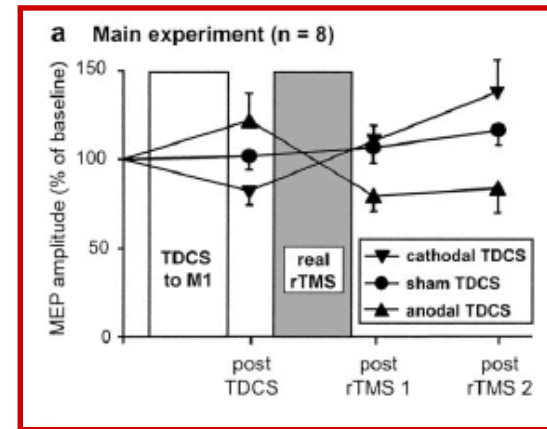


# Neurobiologie der rTMS

Transkranielle Magnetstimulation  
depolarisiert kortikale Neurone

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**Effekte der rTMS hängen ab von  
Stimulationsparametern und von der  
Aktivität des stimulierten Areals**



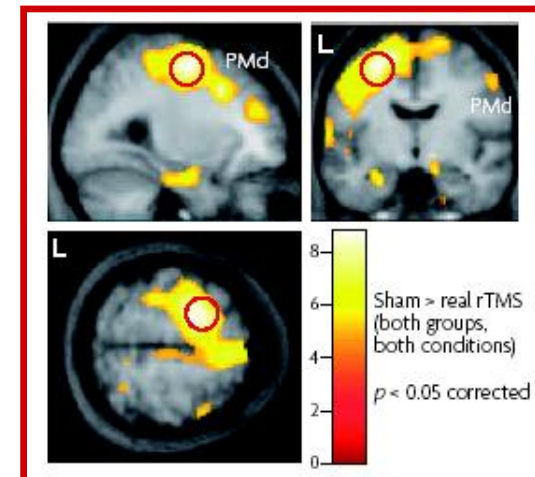
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Arealen**



# Neurobiologie der rTMS

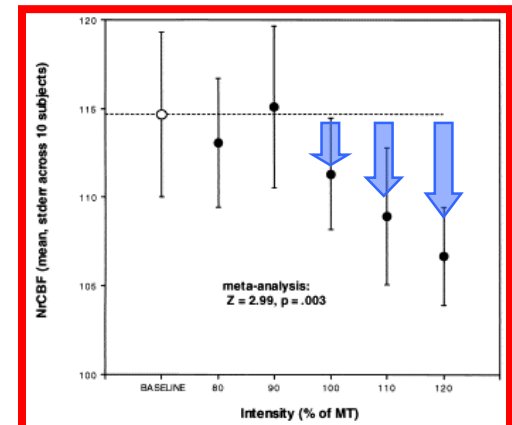
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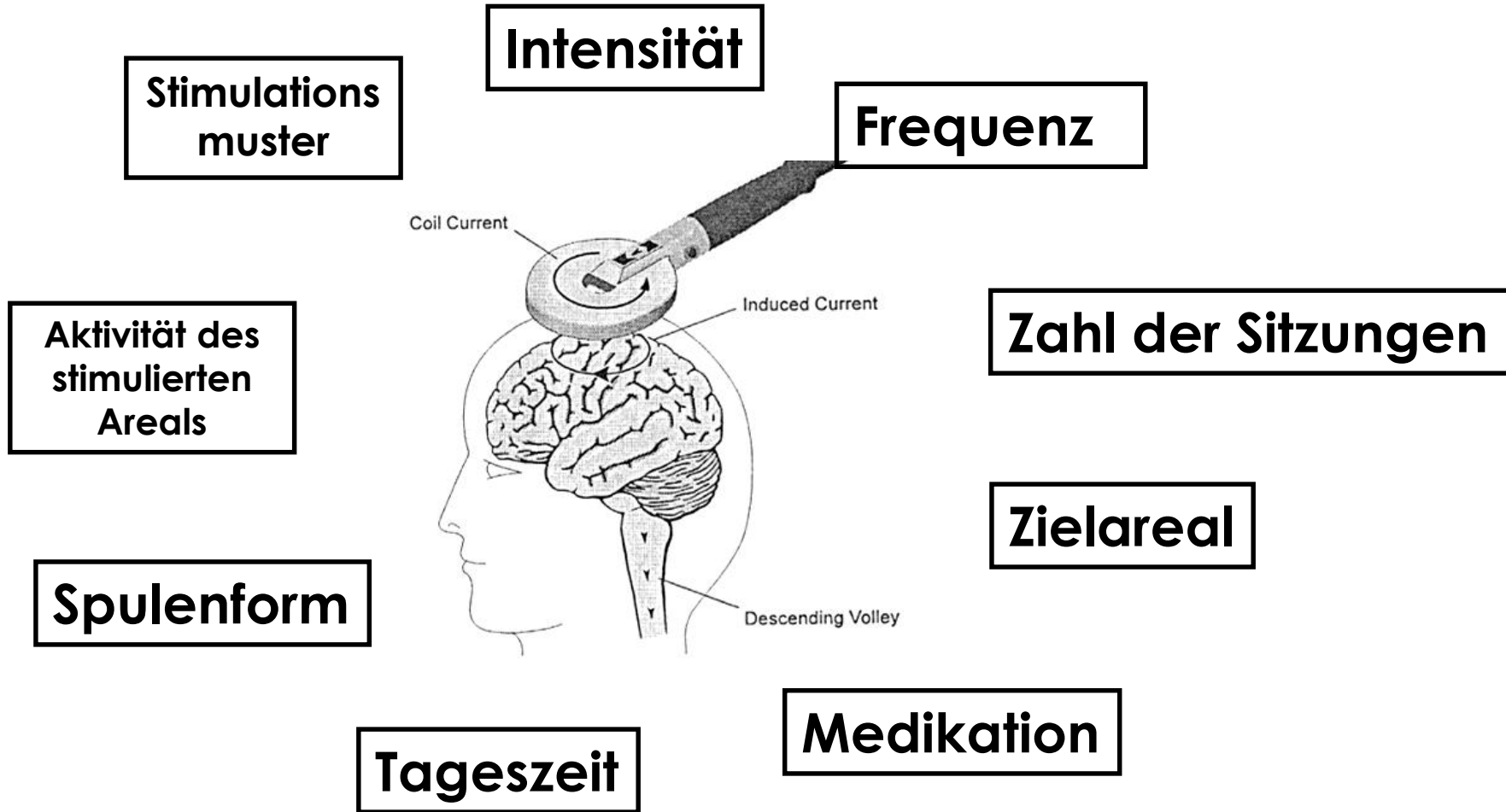
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**In der Regel führt hochfrequente rTMS zu  
einer Erhöhung und niedrigfrequente rTMS  
zu einer Verminderung kortikaler Aktivität**



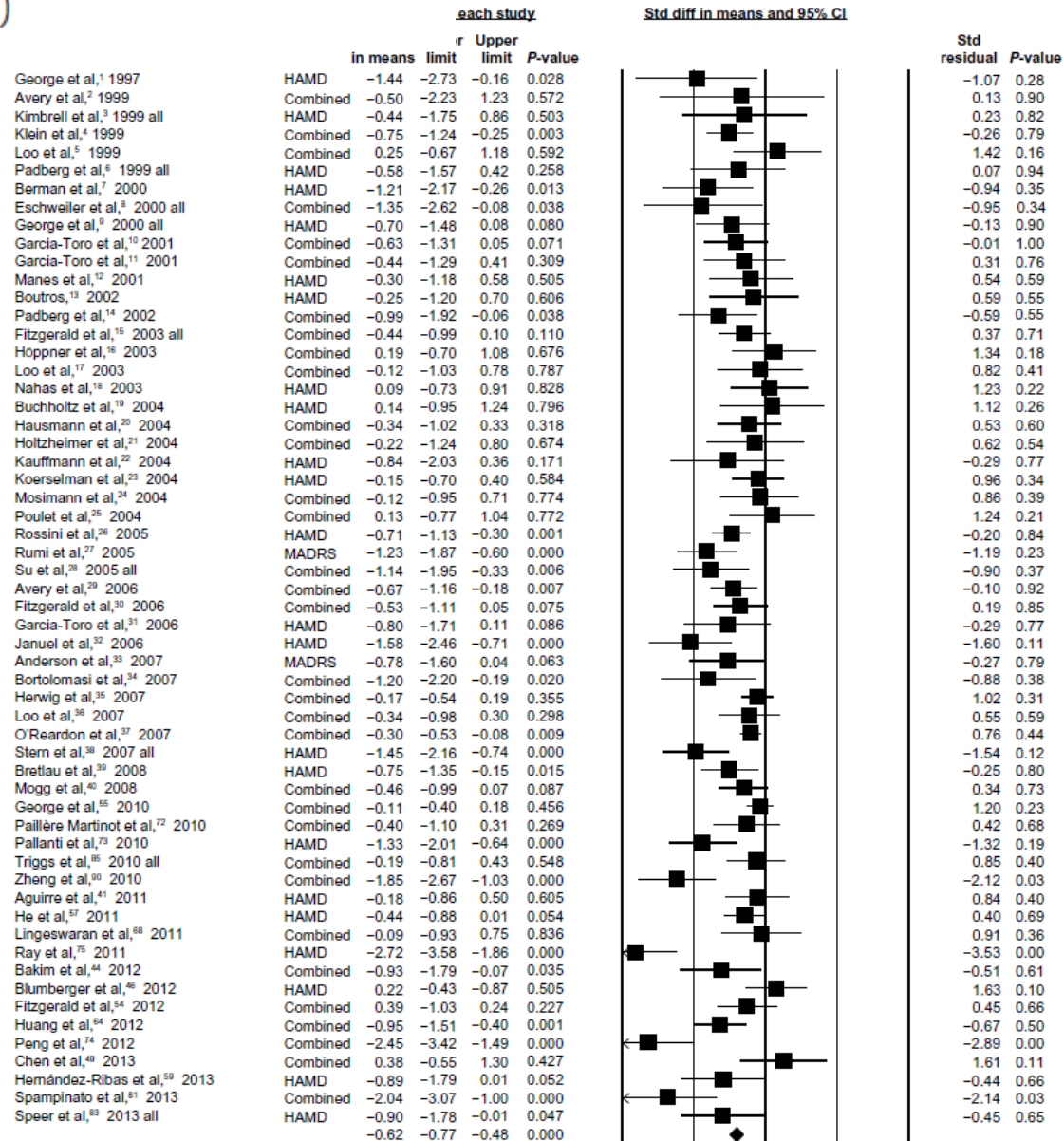
# Relevante Stimulationsparameter:



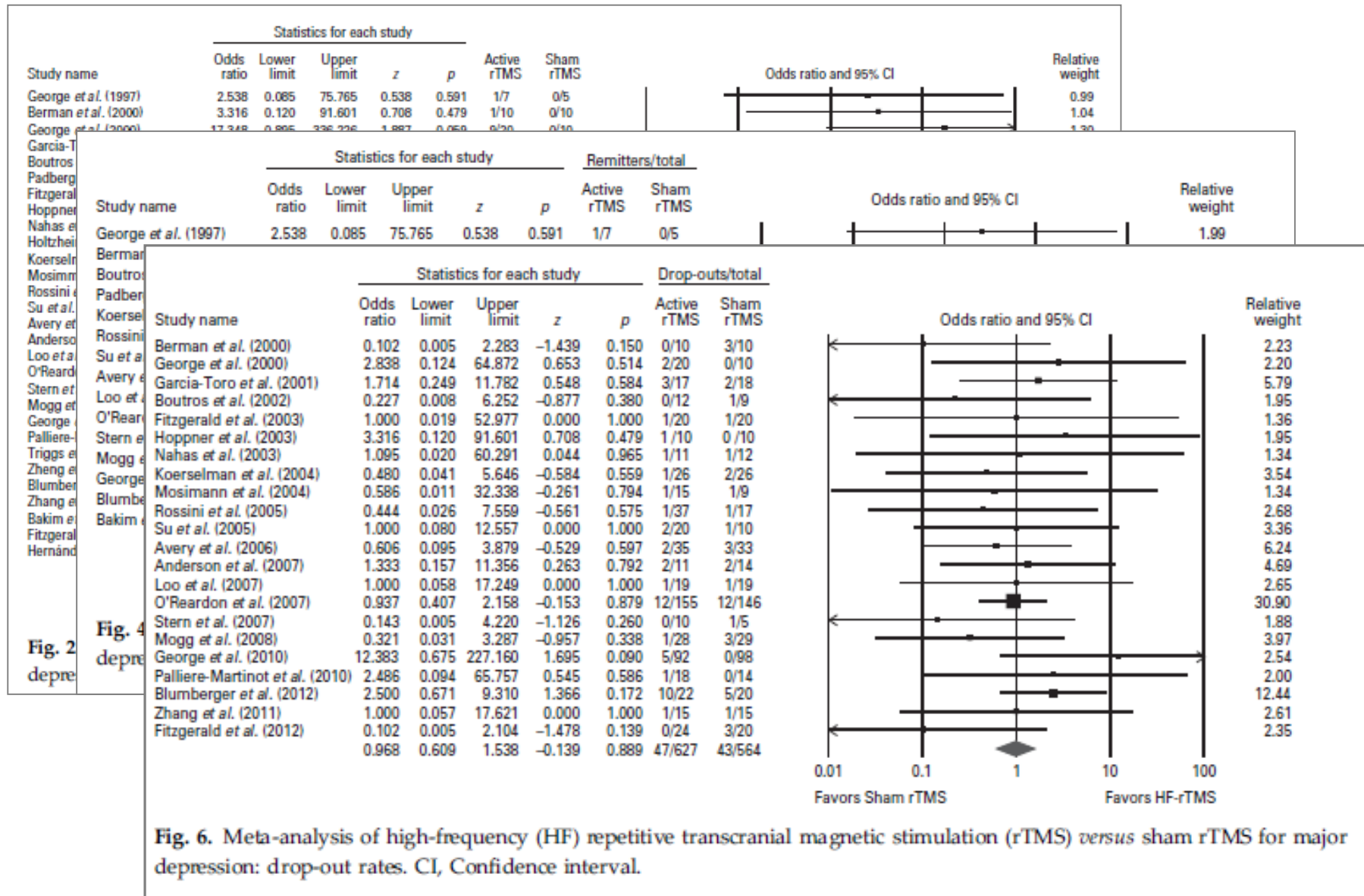
# Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS)

Jean-Pascal Lefaucheur<sup>a,b,\*</sup>, Nathalie André-Obadia<sup>c,d</sup>, Andrea Antal<sup>e</sup>, Samar S. Ayache<sup>a,b</sup>, Chris Baeken<sup>f,g</sup>, David H. Benninger<sup>h</sup>, Roberto M. Cantello<sup>i</sup>, Massimo Cincotta<sup>j</sup>, Mamede de Carvalho<sup>k</sup>, Dirk De Ridder<sup>l,m</sup>, Hervé Devanne<sup>n,o</sup>, Vincenzo Di Lazzaro<sup>p</sup>, Saša R. Filipović<sup>q</sup>, Friedhelm C. Hummel<sup>r</sup>, Satu K. Jääskeläinen<sup>s</sup>, Vasilios K. Kimiskidis<sup>t</sup>, Giacomo Koch<sup>u</sup>, Berthold Langguth<sup>v</sup>, Thomas Nyffeler<sup>w</sup>, Antonio Oliviero<sup>x</sup>, Frank Padberg<sup>y</sup>, Emmanuel Poulet<sup>z,aa</sup>, Simone Rossi<sup>ab</sup>, Paolo Maria Rossini<sup>ac,ad</sup>, John C. Rothwell<sup>ae</sup>, Carlos Schönfeldt-Lecuona<sup>af</sup>, Hartwig R. Siebner<sup>ag,ah</sup>, Christina W. Slotema<sup>ai</sup>, Charlotte J. Stagg<sup>aj</sup>, Josep Vallis-Sole<sup>ak</sup>, Ulf Ziemann<sup>al</sup>, Walter Paulus<sup>e1</sup>, Luis Garcia-Larrea<sup>d,am,1</sup>

## Definite antidepressive efficacy of HF rTMS over the left DLPFC

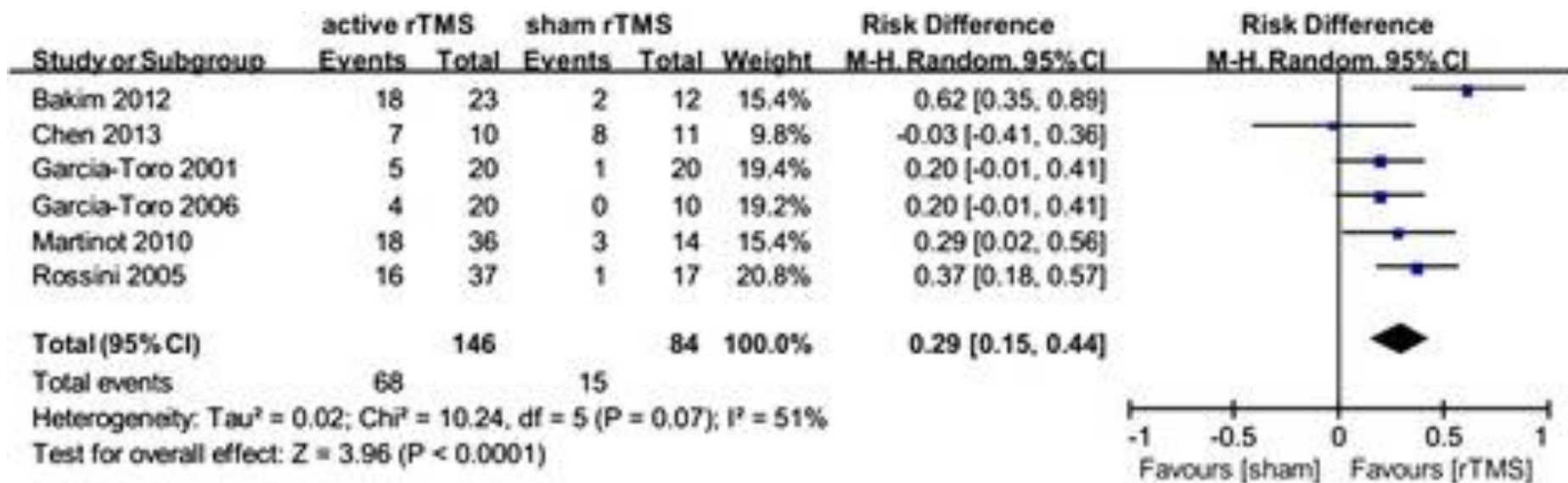


# Responders, remitters and Drop-out





# rTMS as an augmentative strategy add-on to medication in TRD





# Empfehlung 1

## Evidenz und Zielgruppe

***1.1 rTMS of the DLPFC is an effective treatment for depressive disorders.***

***1.2 The use of rTMS in depression should not be restricted to patients who have not responded to pharmacotherapy, as patients not fulfilling this criterion may benefit as well.***



## Empfehlung 2

# Rahmenbedingungen der Behandlung

**2.1 rTMS can be used as a treatment in both *in- and outpatient settings*, given the site fulfils specific criteria.**

**2.2 The initiation of a course of rTMS must be decided upon by a *physician with expertise in psychiatry and brain stimulation*, and he/she must obtain *informed consent from the patient* prior to the treatment.**

**2.3 rTMS can be administered by physicians, psychologists, nursing staff or medical technical assistants after specific training**



# Empfehlung 3

## Indikationen und Kontraindikationen

**3.1 rTMS can be used as treatment for *unipolar and bipolar depression*.**

**3.2 rTMS treatment of depressed patients with psychiatric co-morbidities remains understudied and can be used in individual cases.**

**3.3 In patients with *current alcohol or drug abuse*, rTMS should be applied with greater *caution*, weighing antidepressant and potential anti-craving effects against treatment risks and the necessity of other treatment modalities (e.g. psychotherapy).**

**3.4 There is *no upper age limit for rTMS* and geriatric patients can be treated with rTMS as well, if no formal contraindication exists**

**3.5 Treating patients with implanted devices, a history of seizures or epilepsy, of cerebral disease or trauma and pregnant or breastfeeding patients may be considered after weighing the individual risks and benefits. In the event that treatment with rTMS is preferred, all possible precautionary measures have to be taken to prevent complications**



## Empfehlung 4

# Wo steht TMS im Behandlungsalgorithmus

**4.1 rTMS can be used *at any step within a treatment algorithm for depression*, and we suggest it should not only be considered after failure of pharmacological or psychotherapeutic treatment.**

**4.2 rTMS can be applied concomitantly to antidepressant medication or psychotherapy, though additive or synergistic effects are not proven.**

**4.3 rTMS can be used prior to ECT, but also in patients who have already had ECT. *For severe depressed states with psychotic symptoms or suicidality* which is difficult to control otherwise, *ECT should be given preference.***

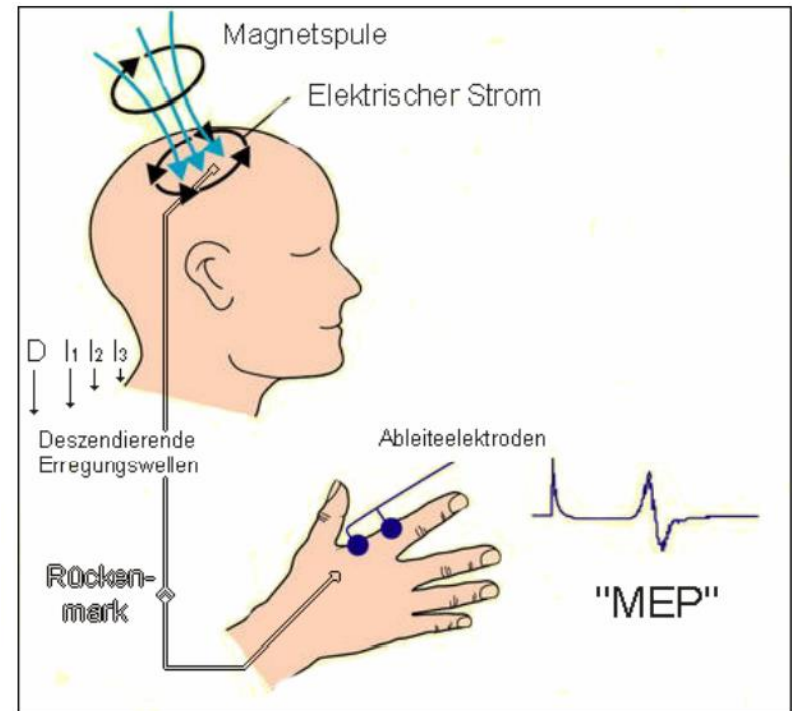


# Empfehlung 5

## Bestimmung der Behandlungsintensität

**5.1 The individual motor threshold should be determined at the beginning of an rTMS series.**

**MEP based measurement should be preferred, visual assessment is acceptable if no EMG is available.**





# Empfehlung 6a Stimulationsparameter

6.1 Operators outside of research should primarily opt to use **high-frequency stimulation (i.e. 10-20Hz) of the left DLPFC**.

6.2 Recommended treatment parameters are a stimulation intensity of **100-120% resting motor threshold, 1500-3000 pulses per sessions and 15-30 sessions per treatment course**.

6.3 **iTBS of the left DLPFC appears to be non-inferior to high-frequency stimulation and can be used, especially if shorter treatment sessions are preferable.**

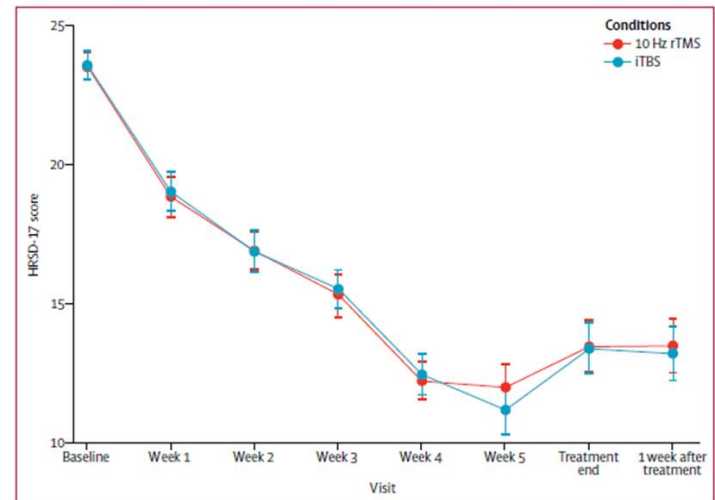


Figure 3: Change in HRSD-17 scores over time, comparing the 10 Hz rTMS and iTBS treatment groups. Data are mean scores with lower and upper 90% CIs.

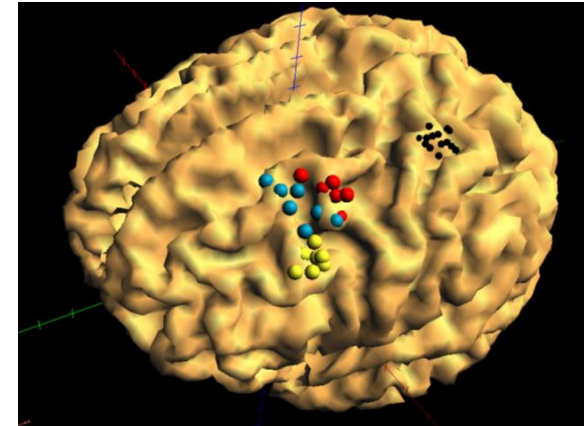


# Empfehlung 6b Stimulationsparameter

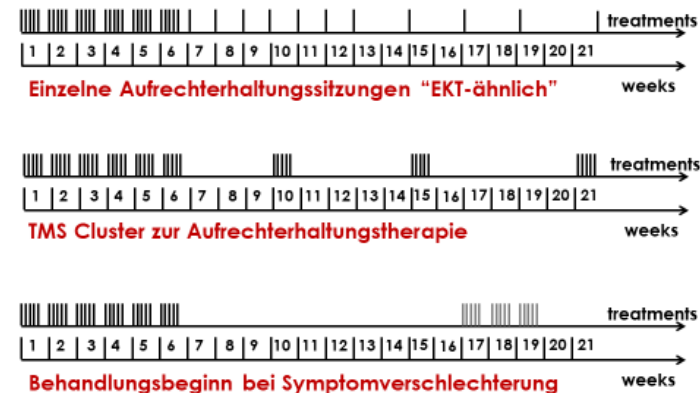
6.4 The individual **coil position over the left DLPFC** is usually defined using surface-based heuristics. Neuronavigation may be applied if accessible but is not mandatory

6.5 Clear evidence for a clinical equivalence or superiority of accelerated protocols is still lacking.

6.6 High-level evidence for **maintenance rTMS** sessions is also lacking. We suggest a pragmatic approach, offering maintenance sessions to patients with recurring episodes of depression who have responded well to an initial course of the treatment.



## Verschiedene Dauerbehandlungsstrategien







## Empfehlung 7 Begleitmedikation

**7.1 Initiating rTMS treatment does usually not require a discontinuation of medication.**

**However, *benzodiazepines seem to inhibit the treatment effect.***

**Therefore a reduction of benzodiazepine dosage seems preferable.**

***Antidepressants, antipsychotics, lithium and anticonvulsants (mood stabilizers) are currently not expected to exert clinically relevant adverse effects on treatment outcome.***



# Empfehlung 8

## Sicherheitsaspekte

**8.1 *Local discomfort and headache are common, but usually self-limiting side effects.***

**8.2 *Seizures are extremely rare side effects of rTMS. Nevertheless, patients should be assessed for a history of seizures, and rTMS operators have to be trained in managing an epileptic seizure. Emergency drugs should be readily available.***

**8.3 *Though there is no definite evidence on hearing damage by rTMS, patients should be encouraged to wear a hearing protection.***

**8.4 *Increased suicidal ideation or hypomanic switch are not to be expected to be caused by rTMS per se, but may occur accompanying the natural course of depression***

**8.5 *Patients should be specifically screened for suicidality and history of hypomanic or manic episodes as part of their psychiatric evaluation.***

**8.6 *There is no evidence, that rTMS exerts adverse effects on cognition and memory.***

**8.7 *Patients' subjective complaints should always been taken seriously and followed, as not all possible side effects may be represented in the scientific literature***



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# TMS: ein hoch dynamisches Forschungsfeld

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repetitive transcranial magnetic stimulation depression

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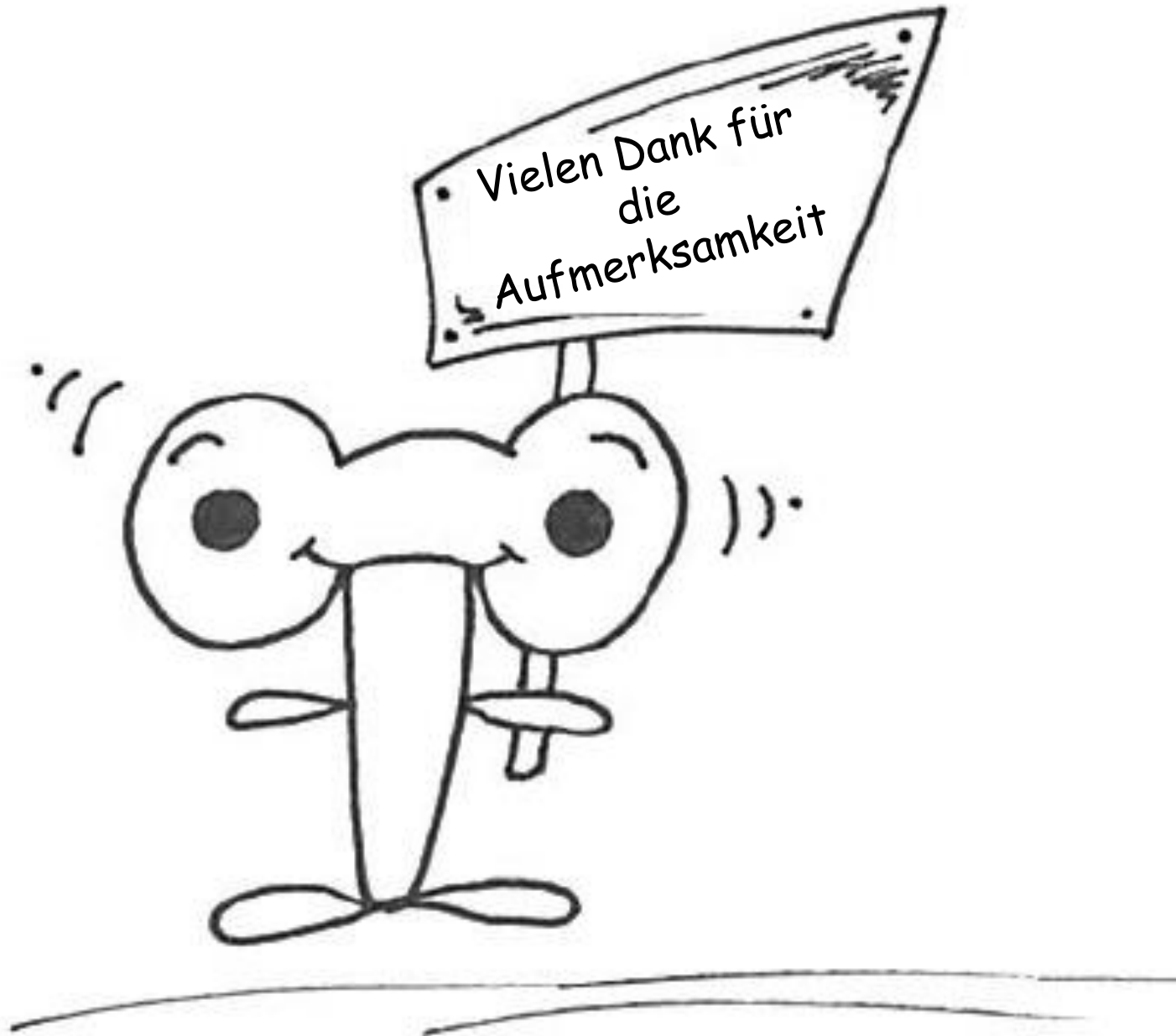
3,026 results

RESULTS BY YEAR



TEXT AVAILABILITY

- 1 **A case of treatment-resistant depression with psychogenic movement disorder during repetitive transcranial magnetic stimulation.**  
Cite Matsuda Y, Yamada K, Terada R, Yamazaki R, Nunomura A, Shigeta M, Kito S.  
Share Asian J Psychiatr. 2021 Jun 6;62:102737. doi: 10.1016/j.ajp.2021.102737. Online ahead of print. PMID: 34118561 No abstract available.
- 2 **Childhood trauma mediates repetitive transcranial magnetic stimulation efficacy in major depressive disorder.**  
Cite Hu YT, Hu XW, Han JF, Zhang JF, Wang YY, Wolff A, Tremblay S, Tan ZL, Northoff G.



Vielen Dank für  
die  
Aufmerksamkeit