Erasmus MC
Universitair Medisch Centrum Rotterdam

Rijndam
Revalidatie

Hersenstimulatie na CVA: een stimulerende gedachte?

Kennisnetwerk CVA Nederland

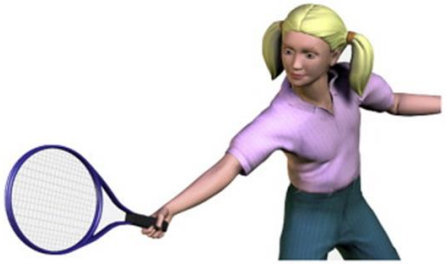
30 November 2018

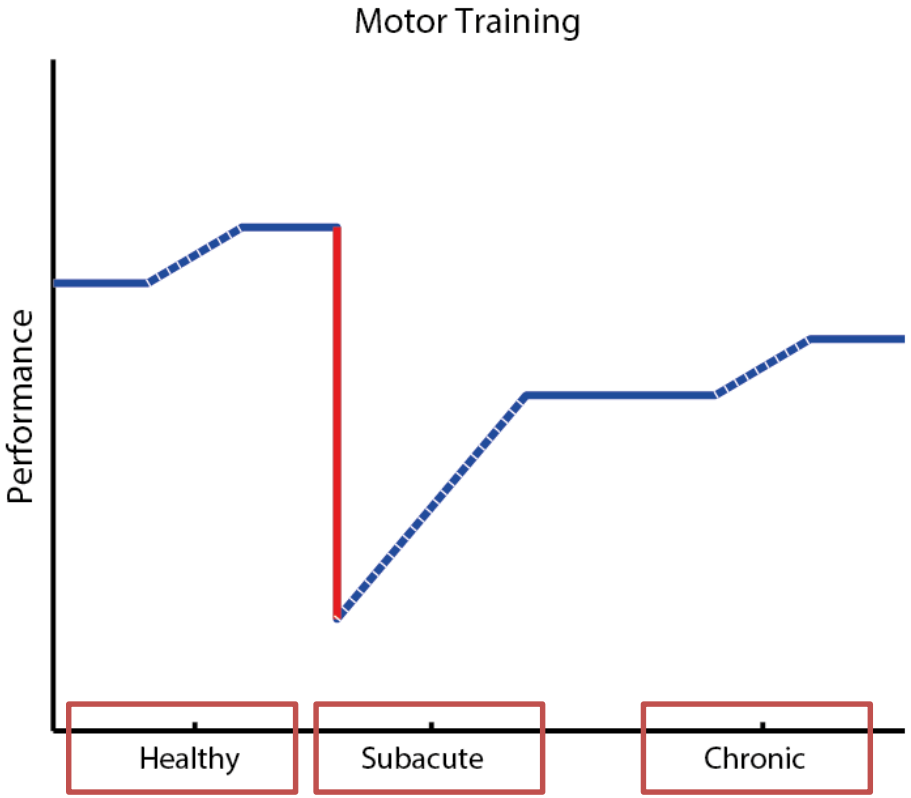
Drs. Z.D. Jonker

Motorisch leren

Natuurlijk herstel

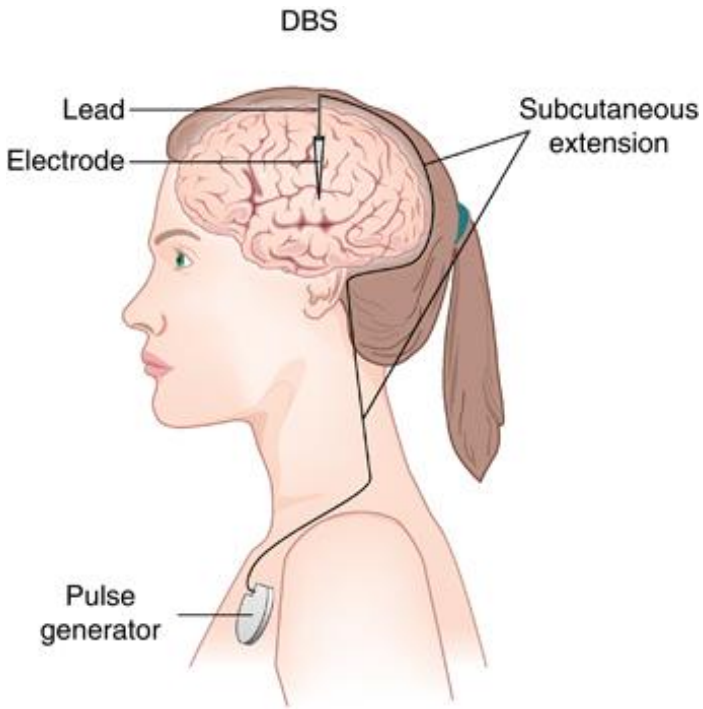
Motor training



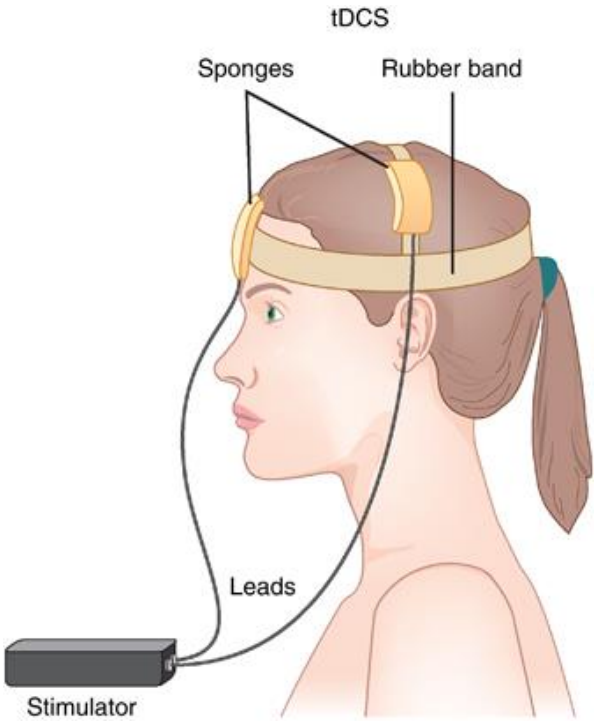


Hersenstimulatie

Deep Brain Stimulation (DBS)



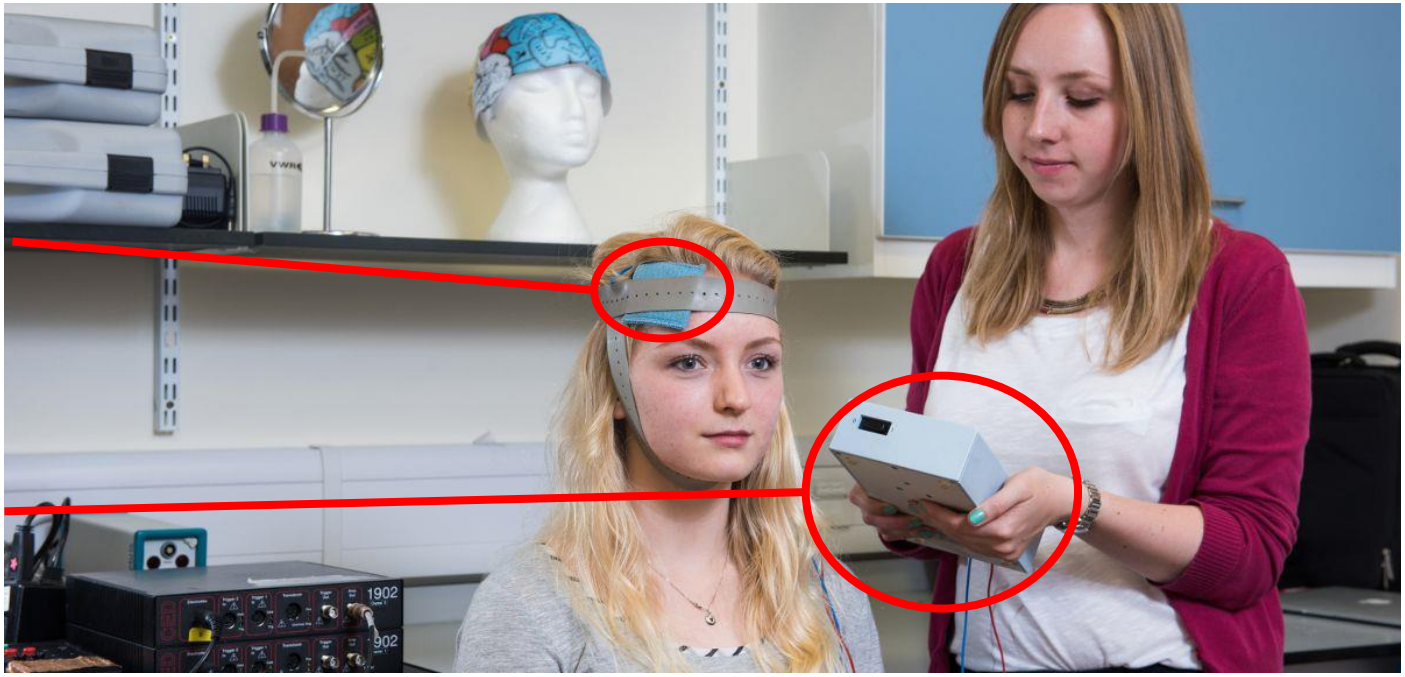
Transcranial Direct Current Stimulation (TDCS)



Transcranial Direct Current Stimulation

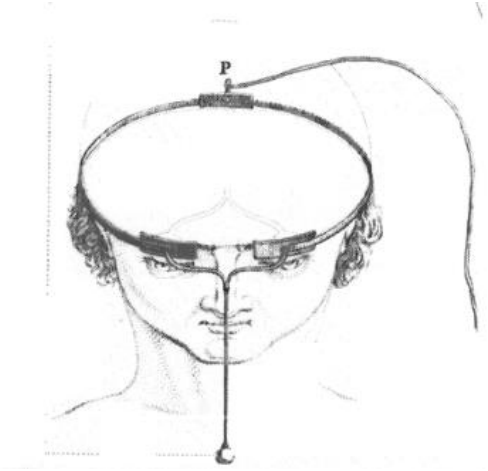
Electroden

Stimulator

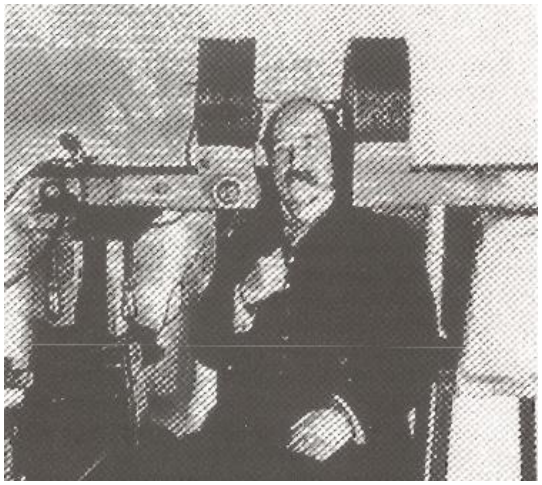


Tijdslijn

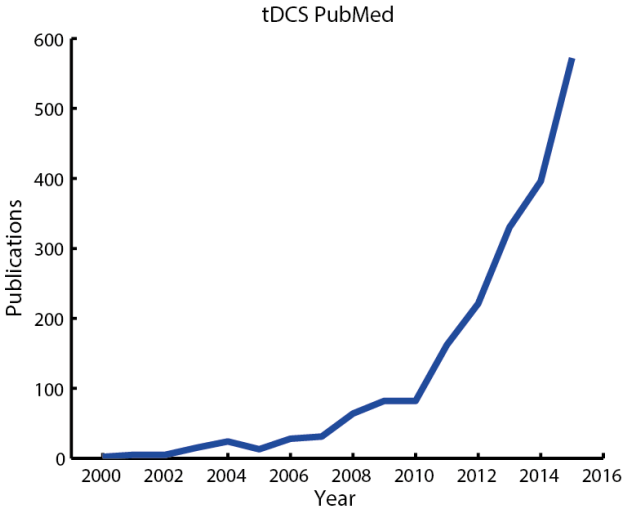
- 2000-2014: Ontdekkingen
- 2015-nu: Replicaties
- Nu →: Lopend onderzoek



18e Eeuw



19e Eeuw

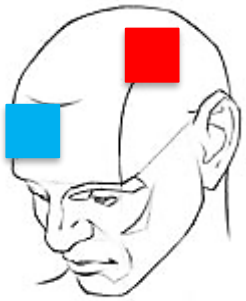


21e Eeuw

Exciteerbaarheid (2000)

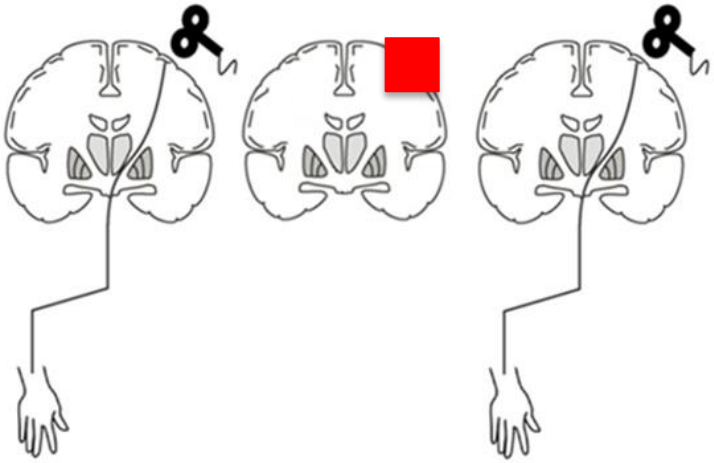
TDCS over de motorische schors kan de exciteerbaarheid beïnvloeden – *Nitsche (2000)*

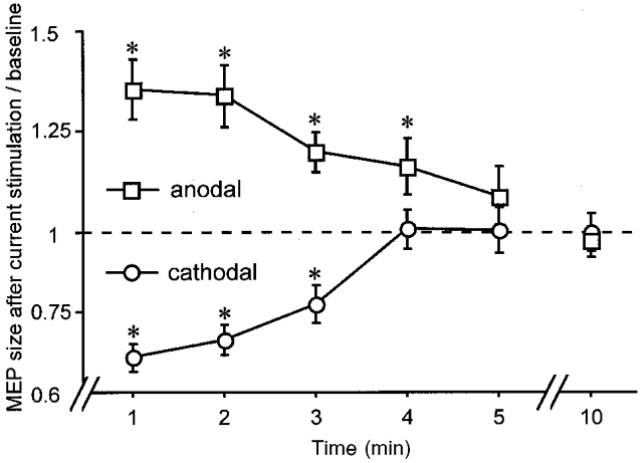
Motorische Schors



Gezonde Proefpersonen

Transcraniële magnetische stimulatie





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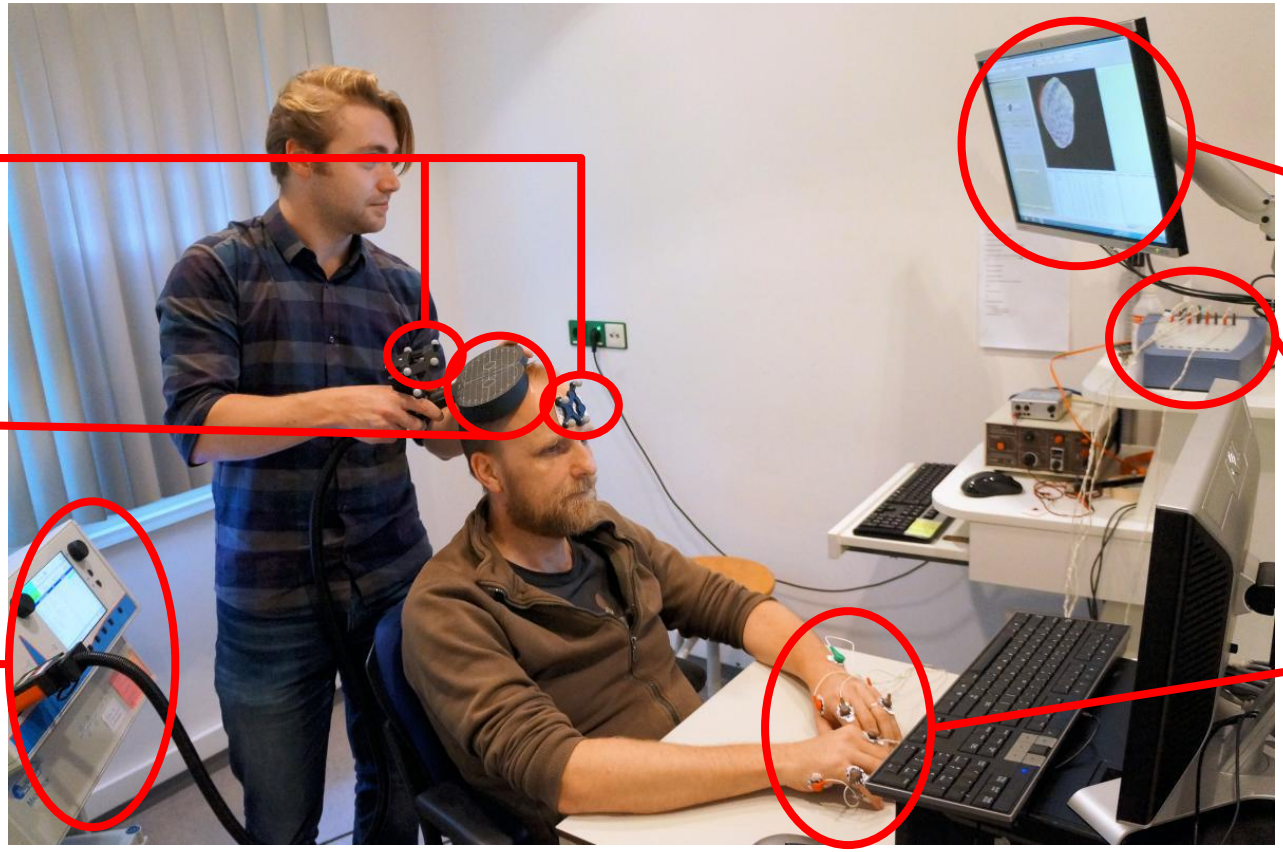
Transcranial magnetic stimulation

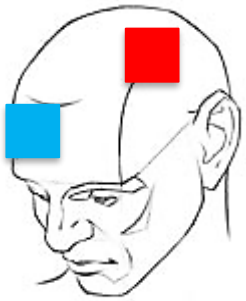


Werking: NMDA-receptor (2002)

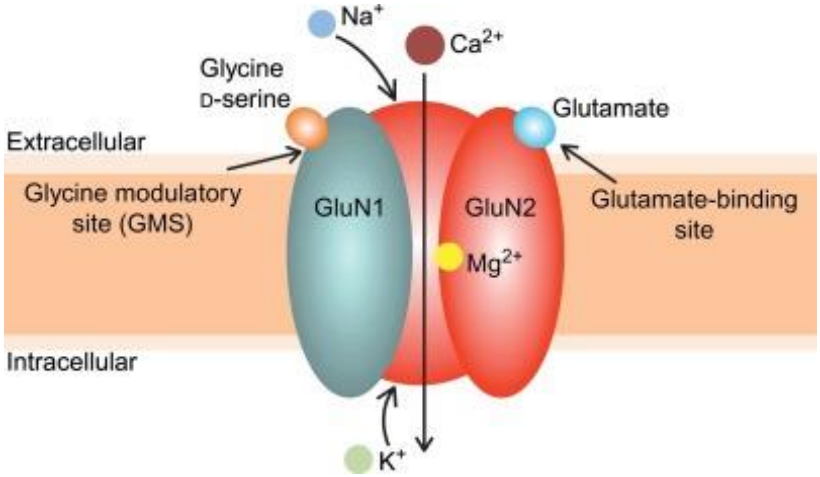
Blokkade van de NMDA-receptor verhindert het effect van TDCS

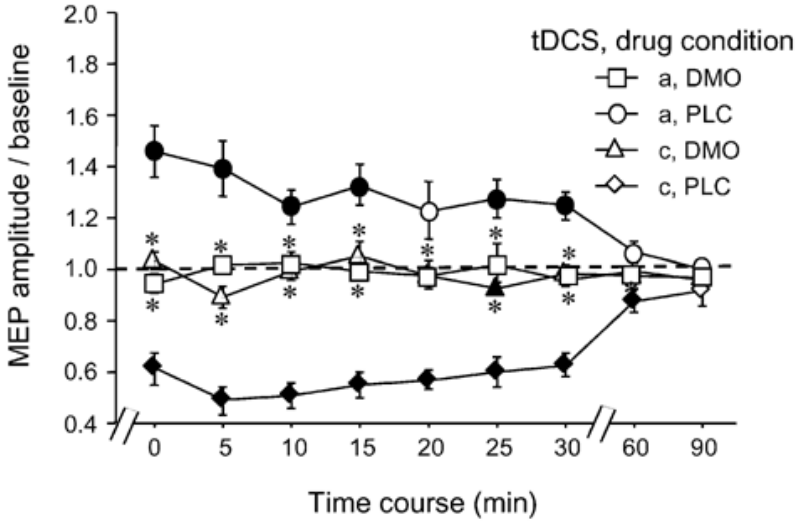
Nitsche (2003)

Motorische Schors



Gezonde Proefpersonen

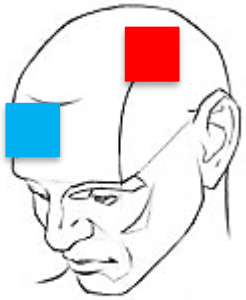




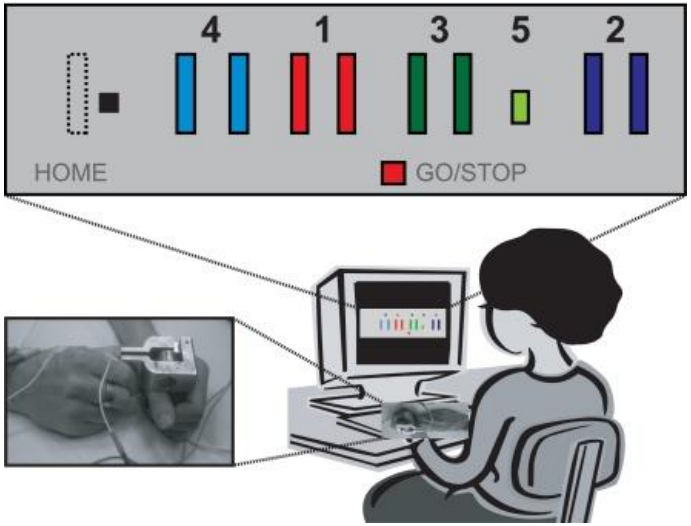
Toepassing: Motorisch leren (2003 – 2009)

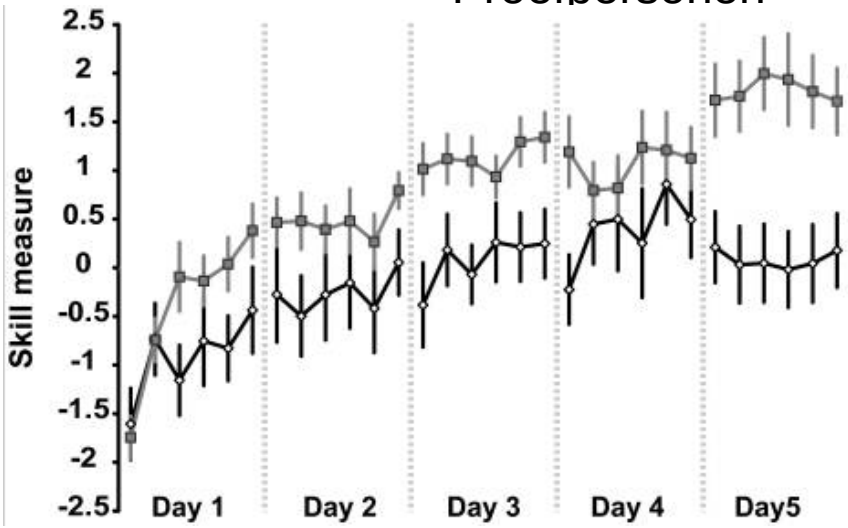
- Gezonde proefpersonen – *Nitsche (2003)*
- Chronische CVA patiënten – *Hummel (2005)*
- Meerdere sessies – *Reis (2009)*

Motorische Schors



Gezonde Proefpersonen

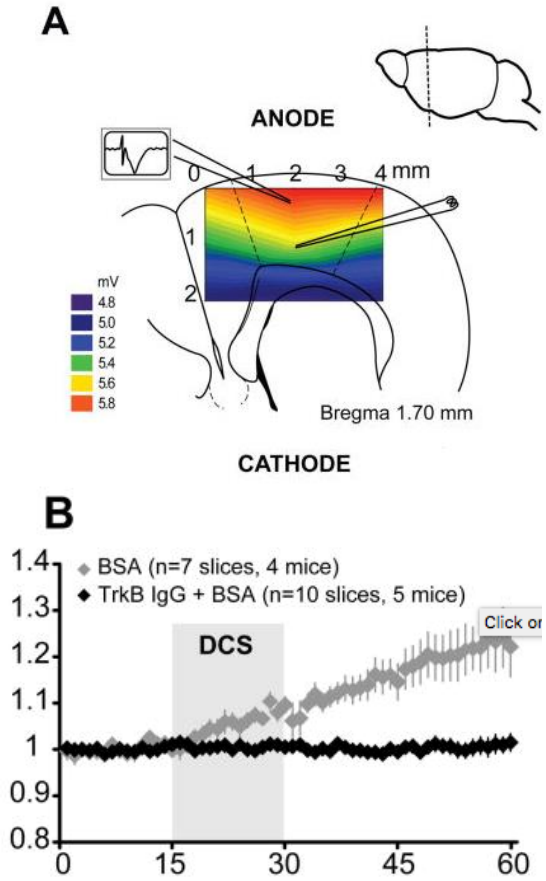




Werking: BDNF (2010)

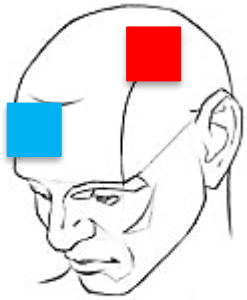
Brain Derived Neurotrophic Factor is een groeifactor

BDNF val66met komt voor in 33% van de populatie

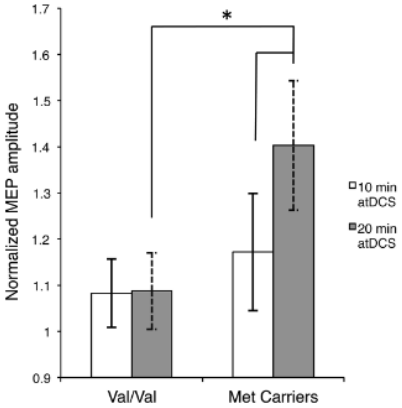


Fritsch (2010)

Motorische Schors



Gezonde Proefpersonen

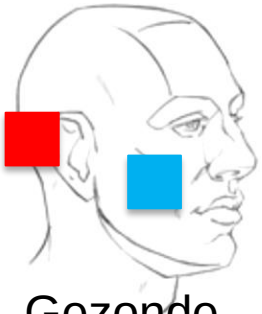


Antal (2010), Puri (2016)

Locatie: Cerebellum (2011)

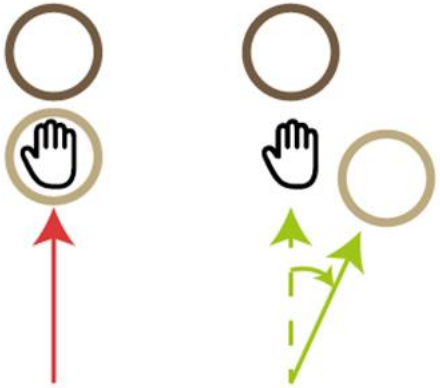
TDCS over het cerebellum kan motor adaptatie versnellen in gezonde proefpersonen – *Galea (2011)*

Cerebellum



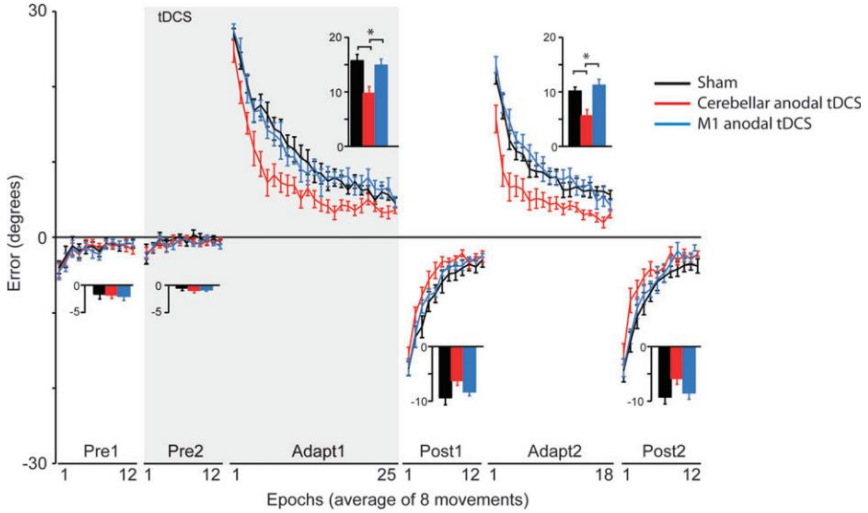
Gezonde Proefpersonen

Visuomotor Adaptation



Unperturbed Vision Perturbed Vision

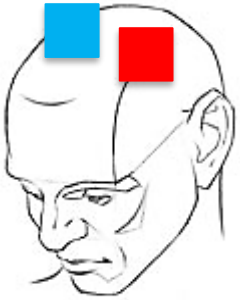
n = 10



Locatie: bi-hemisferisch (2013)

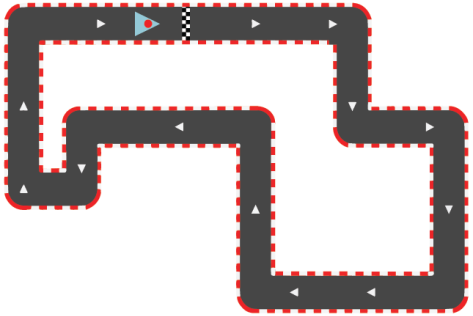
- Bi-hemisferische TDCS verbetert motorisch leren in chronische CVA patiënten – *Lefebvre (2013)*

Bi-hemisferisch

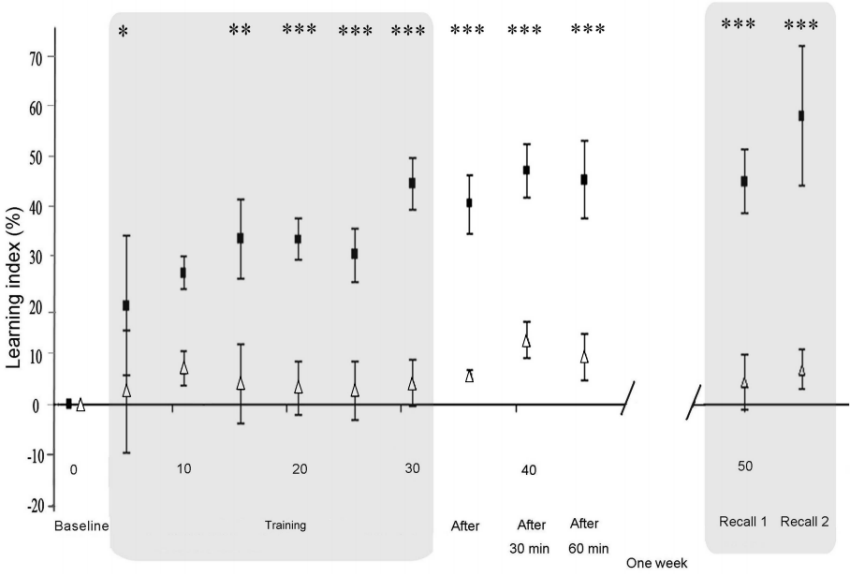


Chronische CVA-patienten

Motor Vaardigheid

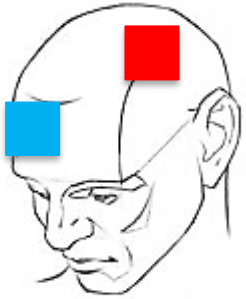


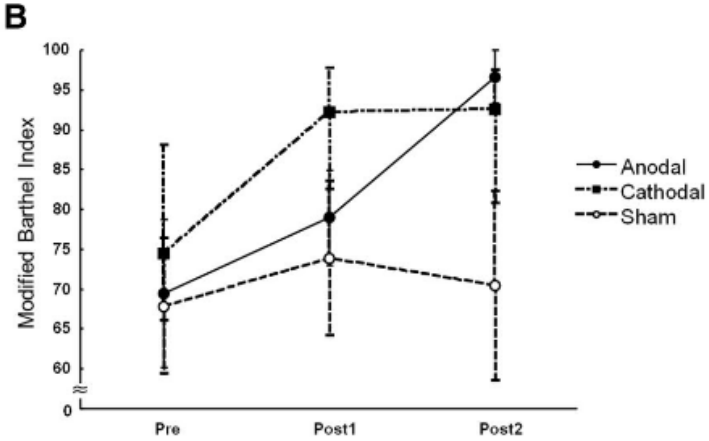
n = 18



Subacute CVA patiënten (2010-2014)

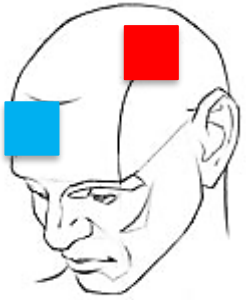
Motorische Schors
Anodaal

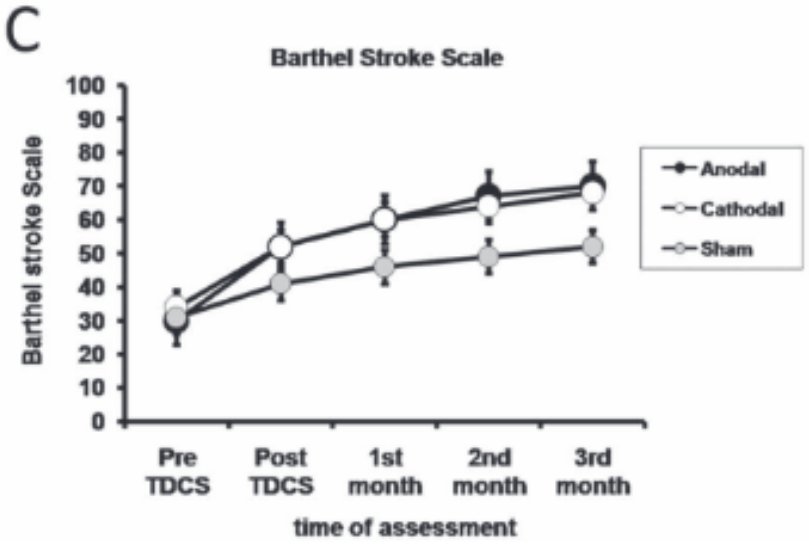




Kim (2010) n = 18

Motorische Schors
Cathodaal





Khedr (2014) n = 40

Samenvatting ontdekkingen 2000-2014

- TDCS kan de exciteerbaarheid van de hersenen beïnvloeden
  - Hierbij is de polariteit belangrijk
- TDCS kan het effect van motor training verbeteren
  - Hierbij is de locatie van de electroden belangrijk
- TDCS kan het herstel na een beroerte verbeteren
  - Hierbij werkt zowel anodale als cathodale stimulatie
- TDCS werkt via NMDA-receptoren en Brain Derived Neurotrophic Factor

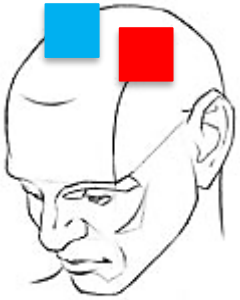
Replicatie 1. Locatie: Bi-hemisferisch

‘Geen van de TDCS protocollen had een effect op motor vaardigheidsleren.’

‘De toename in motorische vaardigheid was minder in BDNF met-carriers.’

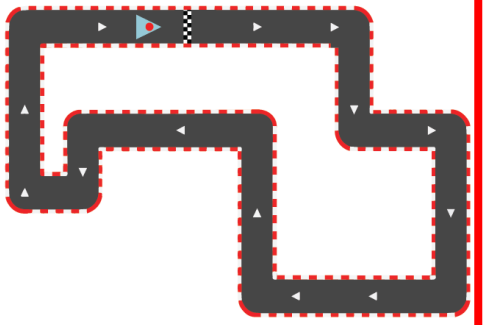
‘Een interactie effect tussen BDNF en TDCS kon niet worden onderzocht vanwege de verschillende TDCS protocollen.’

Bi-hemisferisch

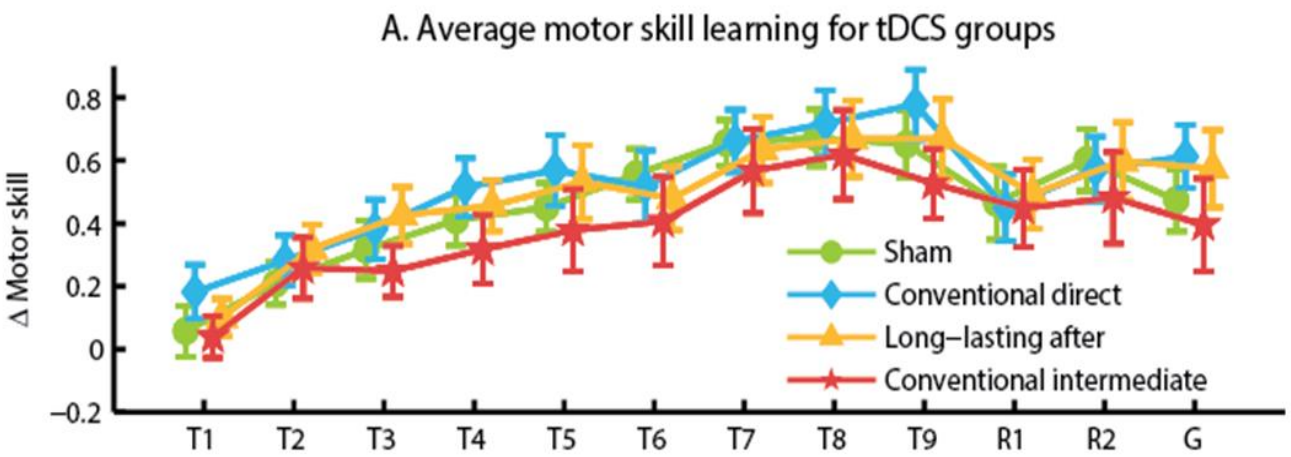


Chronische CVA patiënten

Motor Vaardigheid



n = 80



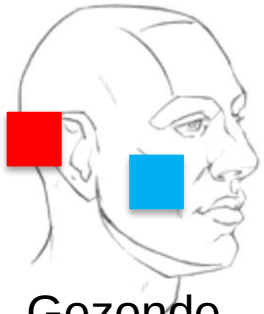
Van der Vliet (2017)

Replicatie 2. Locatie: Cerebellum

‘ Cerebellaire TDCS heeft geen consistent effect op visuomotor adaptatie’ - *Jalali (2017)*

‘ Deze studie laat niet het duidelijke effect zien van cerebellaire TDCS op eyeblink conditioning, zoals eerder beschreven’ - *Beyer (2017)*

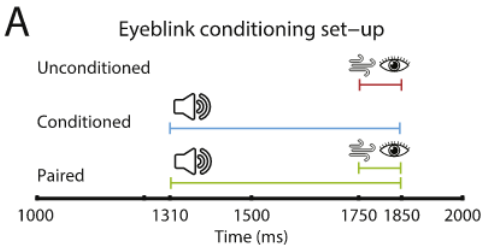
Cerebellum



Gezonde Proefpersonen

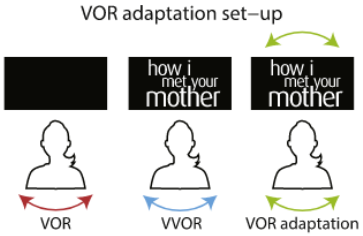
BDNF

Eyeblink Conditioning



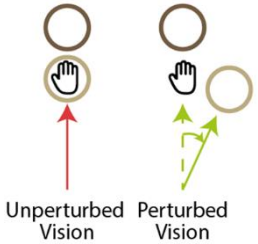
n = 120

Vestibular-Ocular Reflex Adaptation



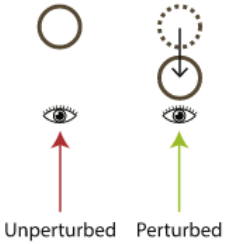
n = 55

Visuomotor Adaptation



n = 25

Saccade Adaptation



n = 25

Van der Vliet (2018)

Replicatie 3. Subacute CVA patiënten

Cochrane review: Elsner (2016)

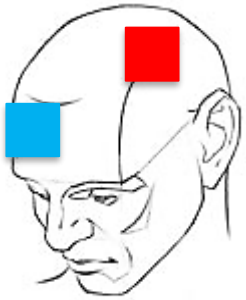
‘TDCS kan mogelijk activities of daily living verbeteren.’

‘Het is onduidelijk of TDCS arm- en beenfunctie kan verbeteren’

‘De kwaliteit van het bewijs is zeer laag tot matig’

‘Toekomstig onderzoek moet uitwijzen welke patiënten het meeste baat hebben van TDCS na een CVA’

Motorische Schors



Subacute CVA-patienten

Klinische Revalidatie

n = 48 (nu 33)

Jonker (in progress)

Samenvatting Replicaties 2015-nu

- De effecten van TDCS op motorisch leren zijn variabel
- De effecten van TDCS op het herstel na CVA zijn variabel

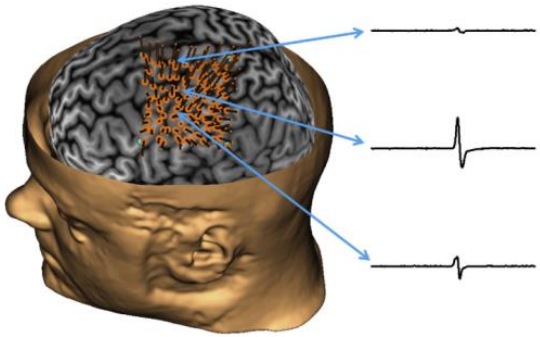
- Als oorzaak worden vaak <u>mogelijke</u> verschillen tussen proefpersonen genoemd:
  - Fysiologie
  - Genetica
  - Anatomie

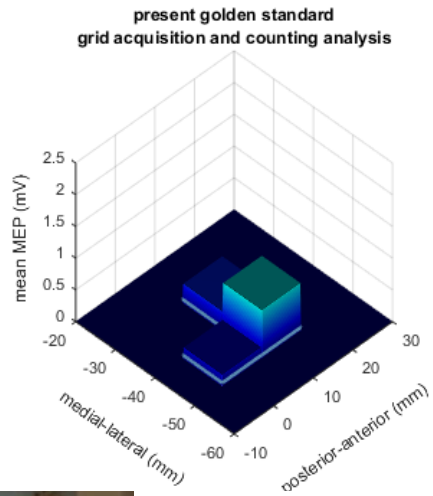
- Af en toe worden verschillen binnen proefpersonen genoemd als <u>mogelijke</u> oorzaak:
  - Fysiologie (attentie)

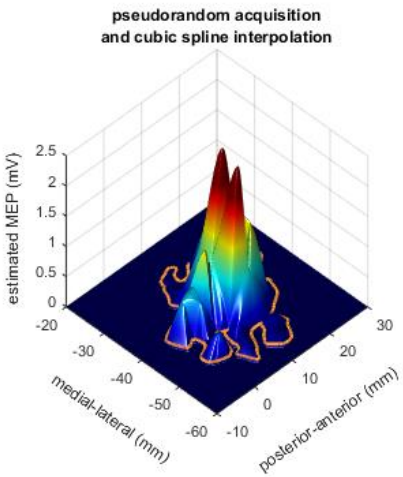
Exciteerbaarheid

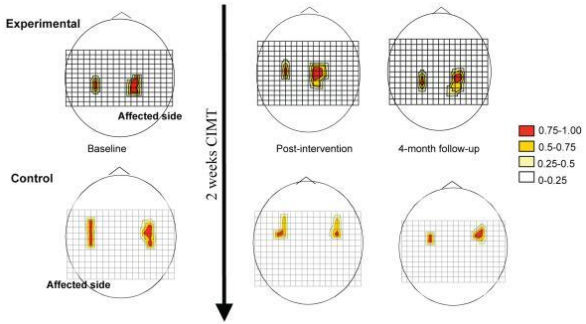
Hoe betrouwbaar is de uitkomstmaat?

- Optimale locatie: <5 minuten en <2mm afwijking
- Voor stabiele meting 30-50 pulsen op optimale locatie









Sawaki (2008), Van der Ruit (2015), Jonker, et al. (under review)

Fysiologie & genetica

Heeft TDCS een effect op de exciteerbaarheid van de hersenen?
Kunnen we individuen selecteren voor de huidige behandeling?

- Zit de variabiliteit inderdaad <u>tussen</u> proefpersonen?

Fysiologie
TMS - Latentietijden

Genetica
Speeksel – BDNF val66met

n = 80;
2x placebo 2x anodale TDCS
Inclusie gestart: Oktober 2018

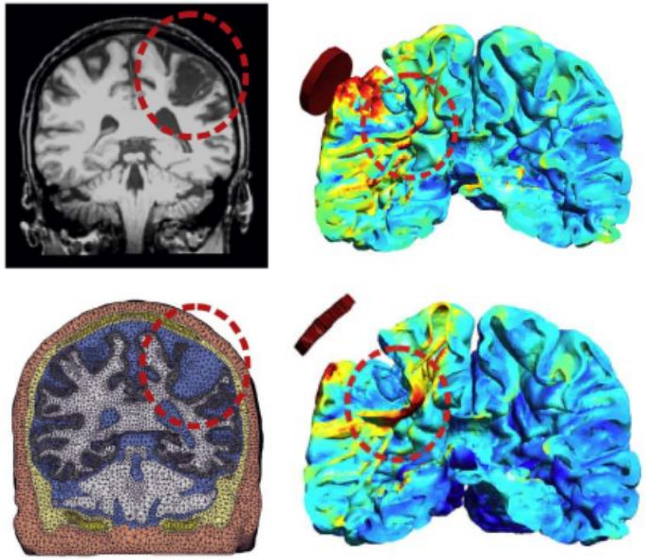
Jonker, et al. (in progress)

Anatomie & Fysiologie

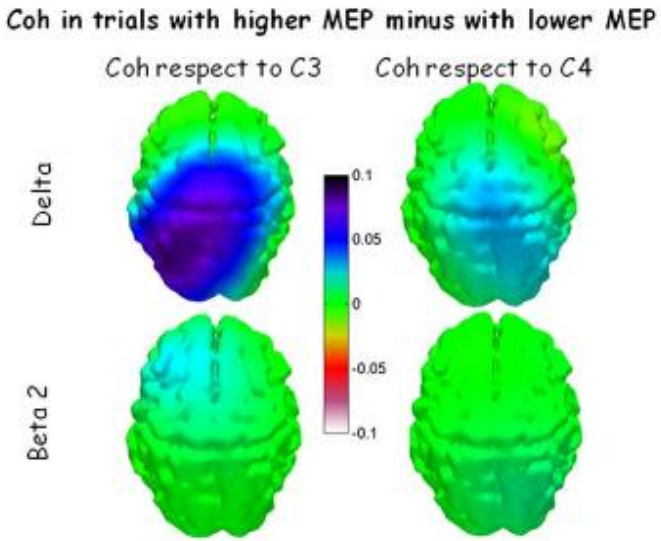
Kunnen we de behandeling aanpassen aan het individu?

- Waar en hoe sterk moet er gestimuleerd worden
- Wanneer en hoe lang moet er gestimuleerd worden?

Anatomie
MRI & SimNIBS



Fysiologie
EEG



Ferreri (2014), Manjoli (2018), Van der Cruijsen (in progress)

Take home messages

- TDCS kan mogelijk het herstel van CVA patiënten verbeteren
- Echter, in de huidige vorm is TDCS nog niet geschikt voor standaard klinische toepassing
- Mogelijk werkt het alleen in subgroepen en moet de behandeling afgestemd worden op het individu

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