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Le rôle de la stimulation cérébrale non invasive dans la médecine vasculaire. Recherche et réalité.

Alexander Thiel, MD

Neurology & Neurosurgery

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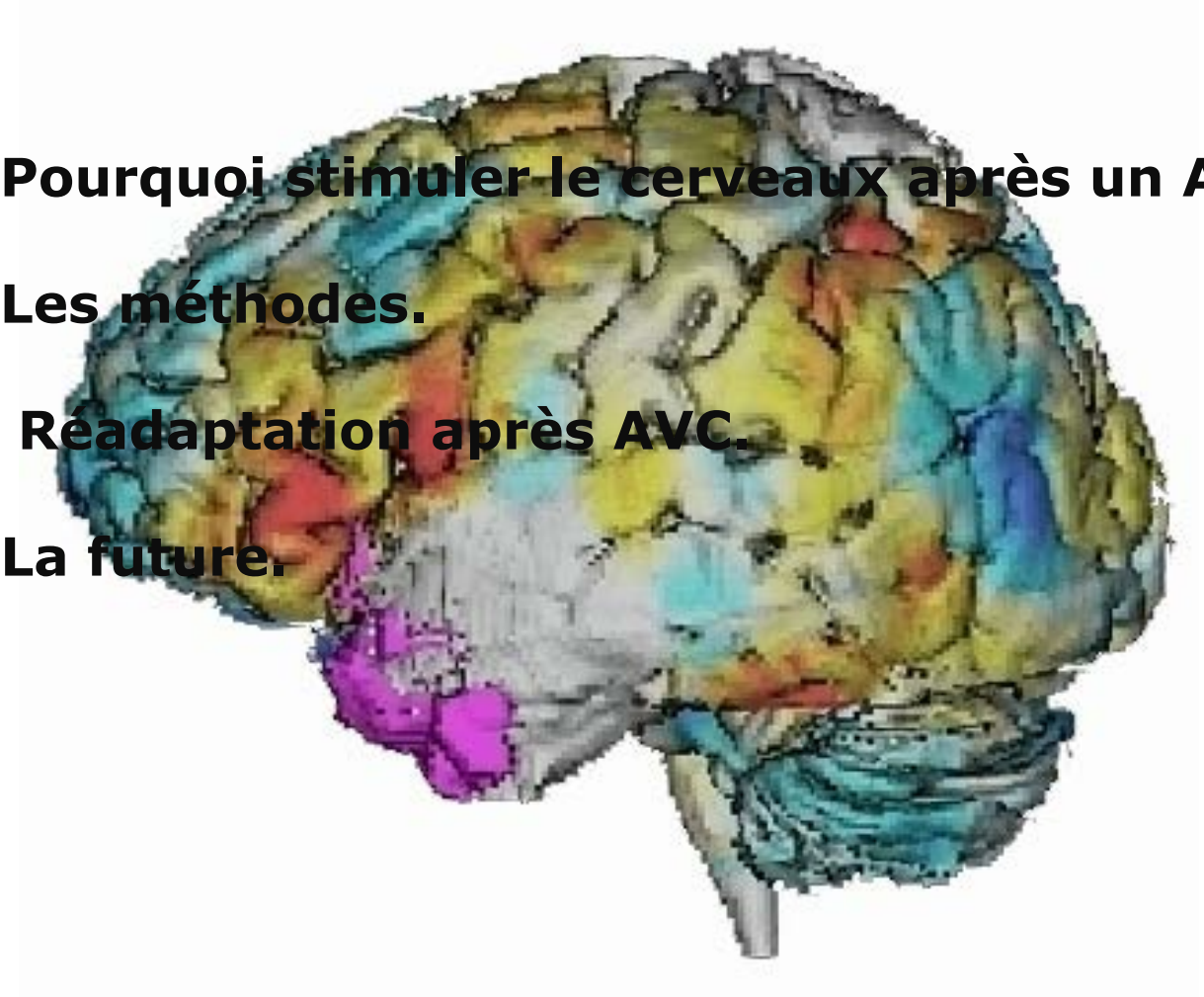

I. Pourquoi stimuler le cerveaux après un AVC ?

II. Les méthodes.

III. Réadaptation après AVC.

IV. La future.

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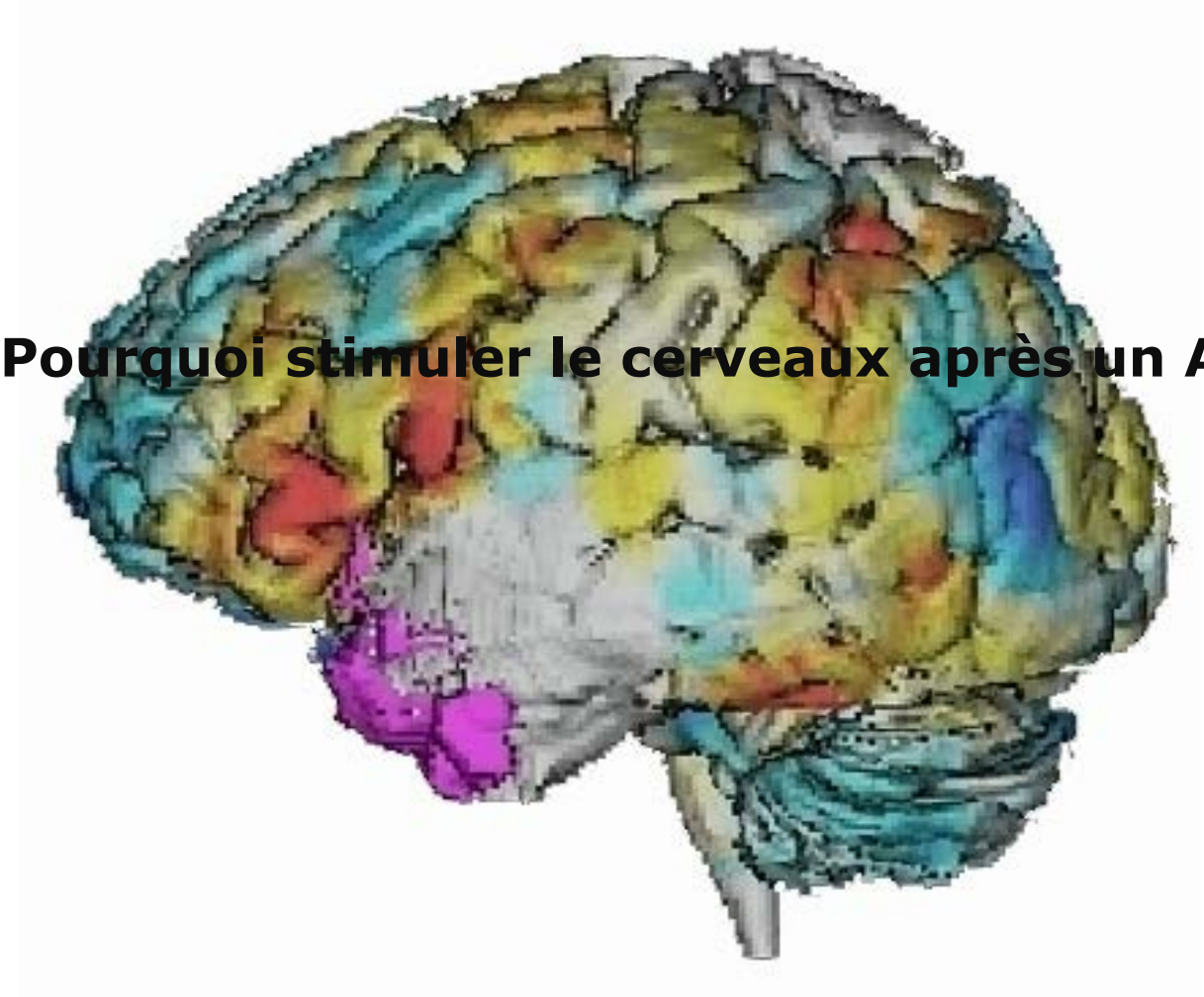

I. Pourquoi stimuler le cerveaux après un AVC ?

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Le principe

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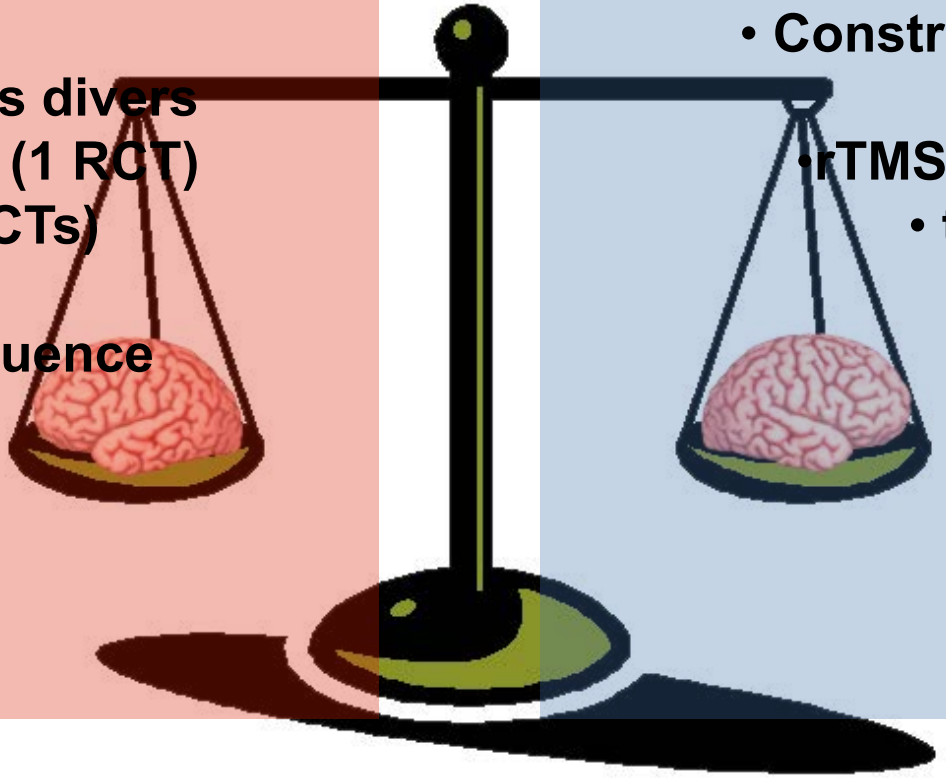
La Balance entre activation et inhibition

Activer l'hémisphère ipsi-lésionnelle

- Orthophonie
- Physiothérapies divers
- Amphétamines (1 RCT)
- Piracetam (4 RCTs)
- t-DCS anodal
- TMS haute fréquence

Inhiber l'hémisphère contra-lésionnelle

- Constrained-Induced-Therapy
- rTMS bas fréquence
- t-DCS cathodal
- médicaments



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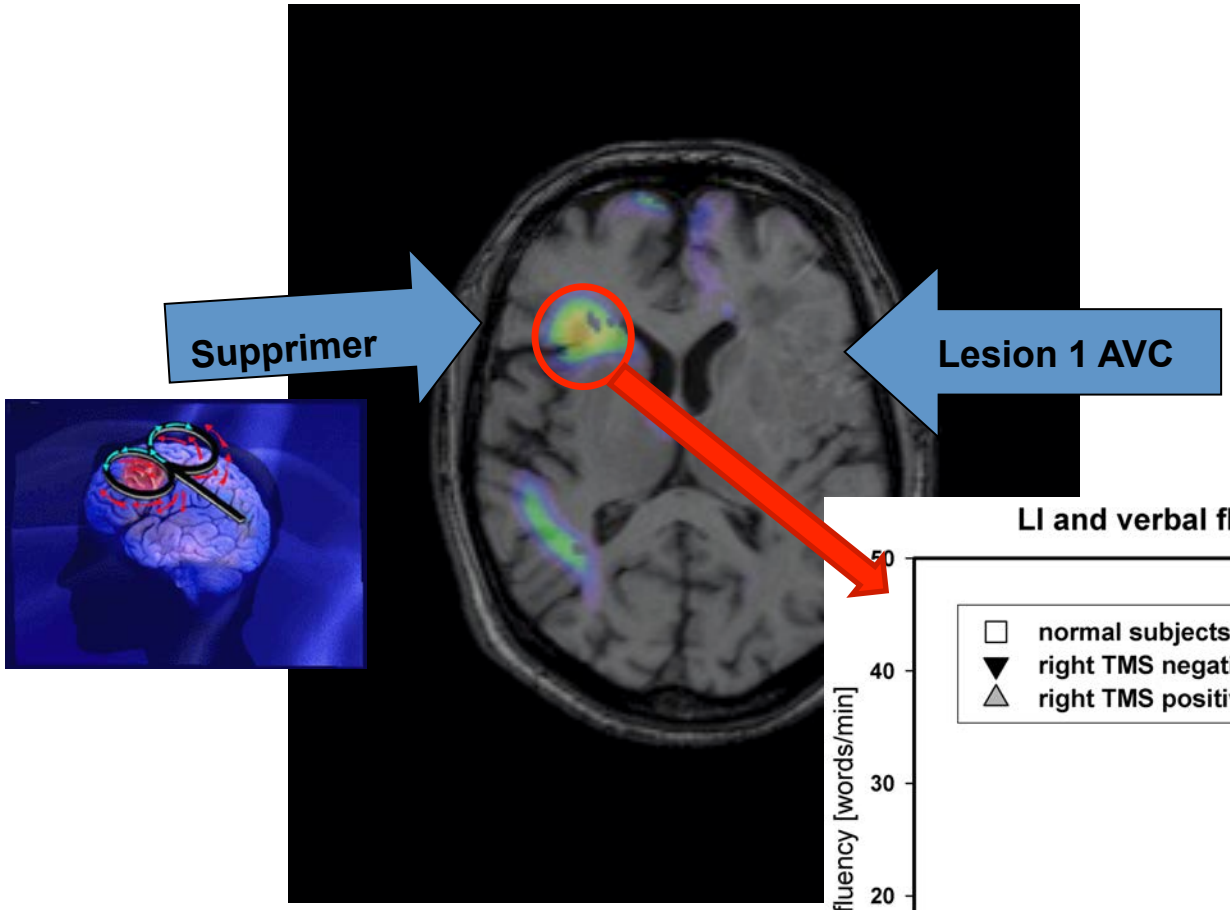
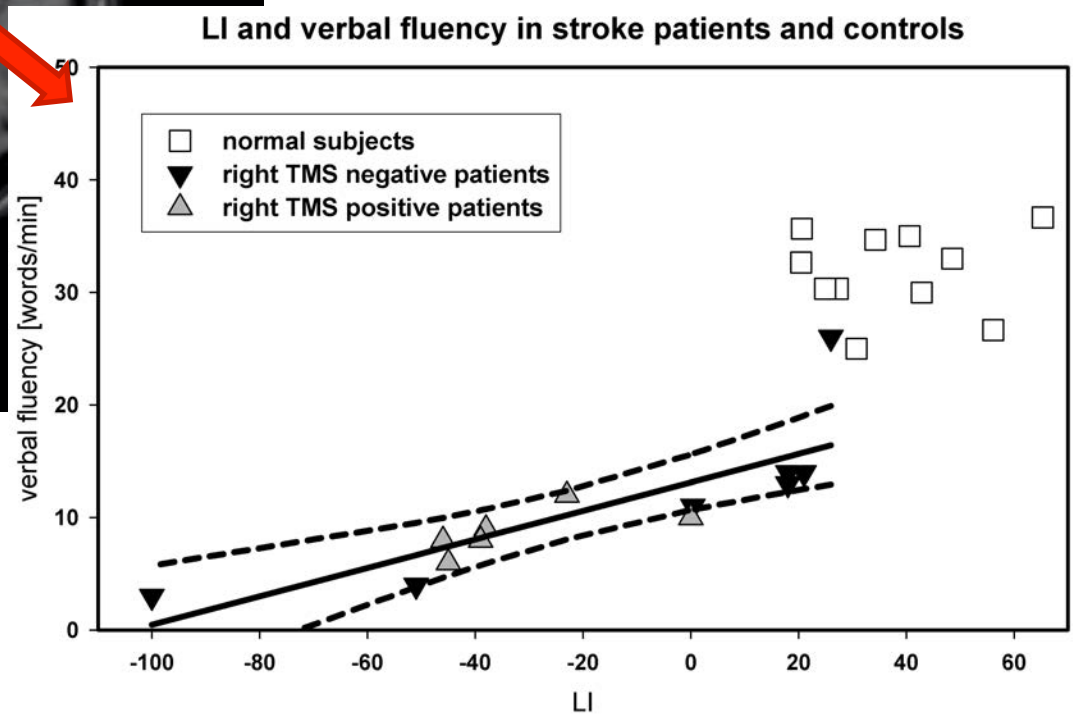
Relation entre latéralisation et fonction verbale





Winhuisen, Thiel et al., Stroke, 2005

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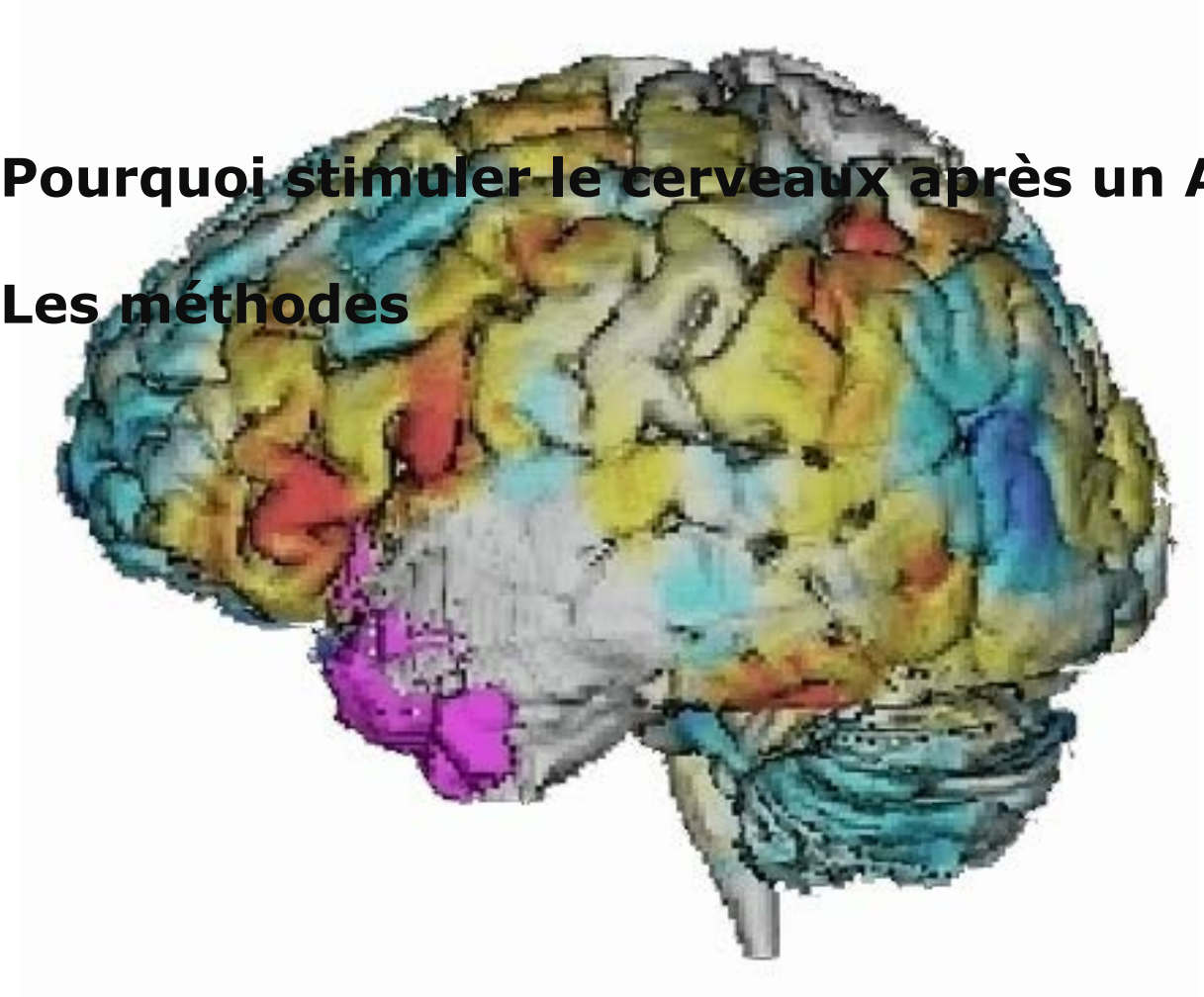

I. Pourquoi stimuler le cerveaux après un AVC

II. Les méthodes

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Le Principe du TMS

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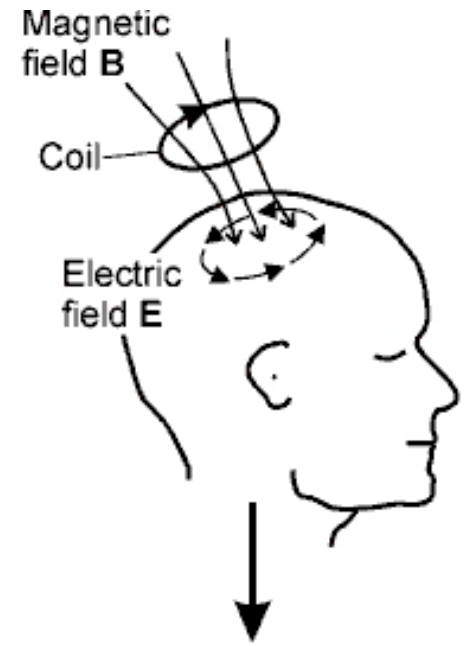
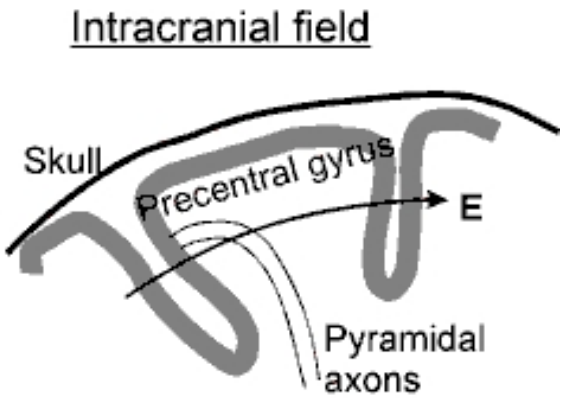
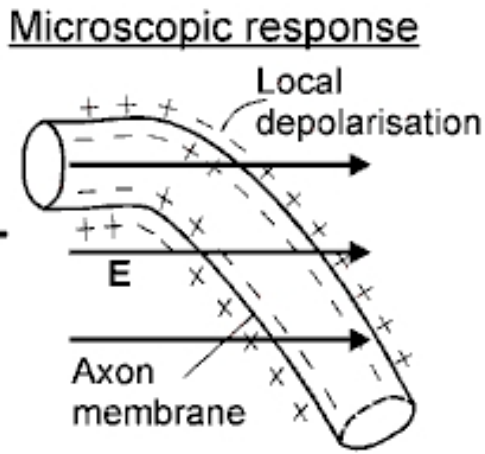




Macroscopic response

- evoked neuronal activity (EEG)
- changes in blood flow and metabolism (PET, fMRI, NIRS, SPECT)
- muscle twitches (EMG)
- changes in behaviour



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TMS repetitive

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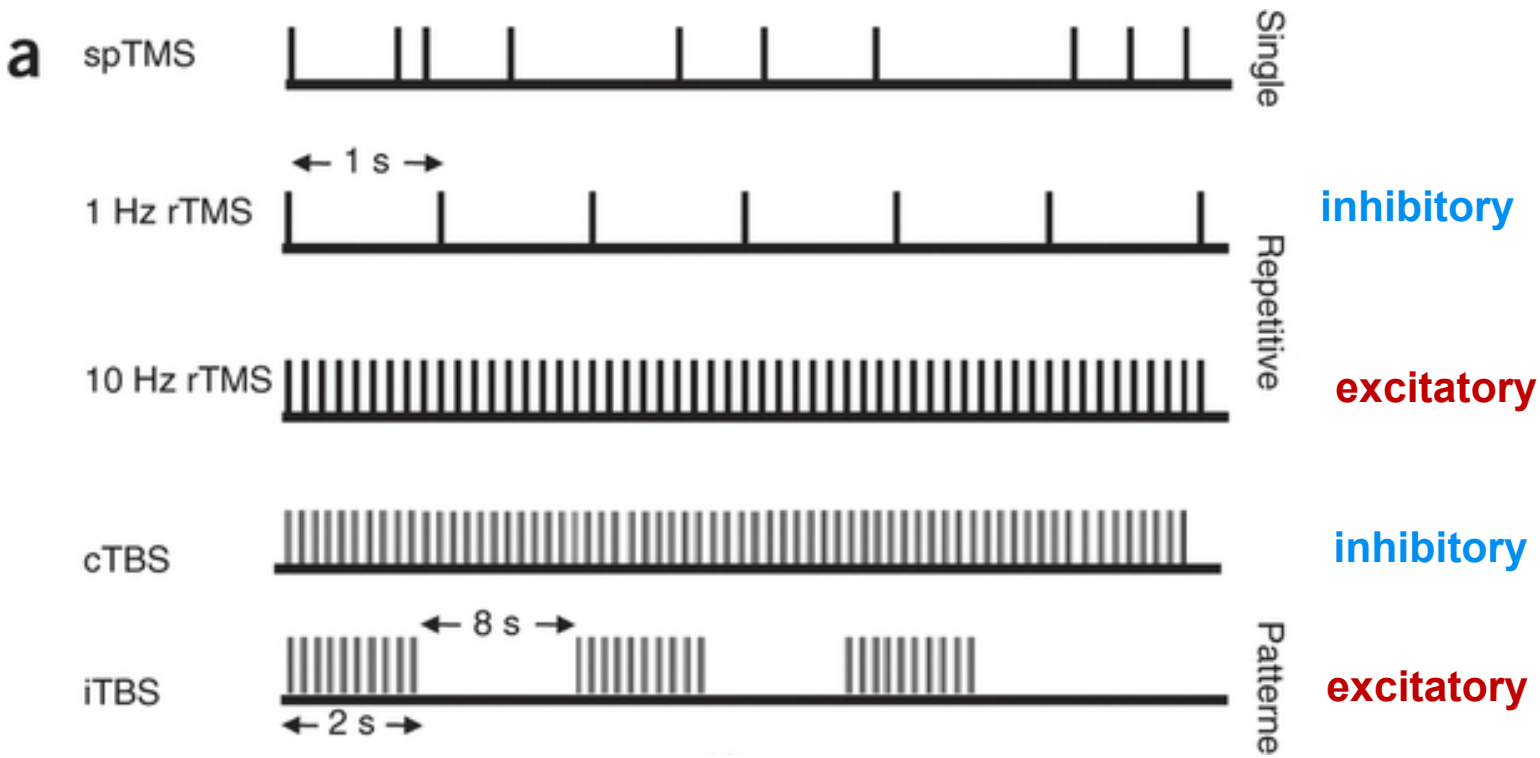

Dayan et al., Nature Neuroscience 16, 838–844 (2013)

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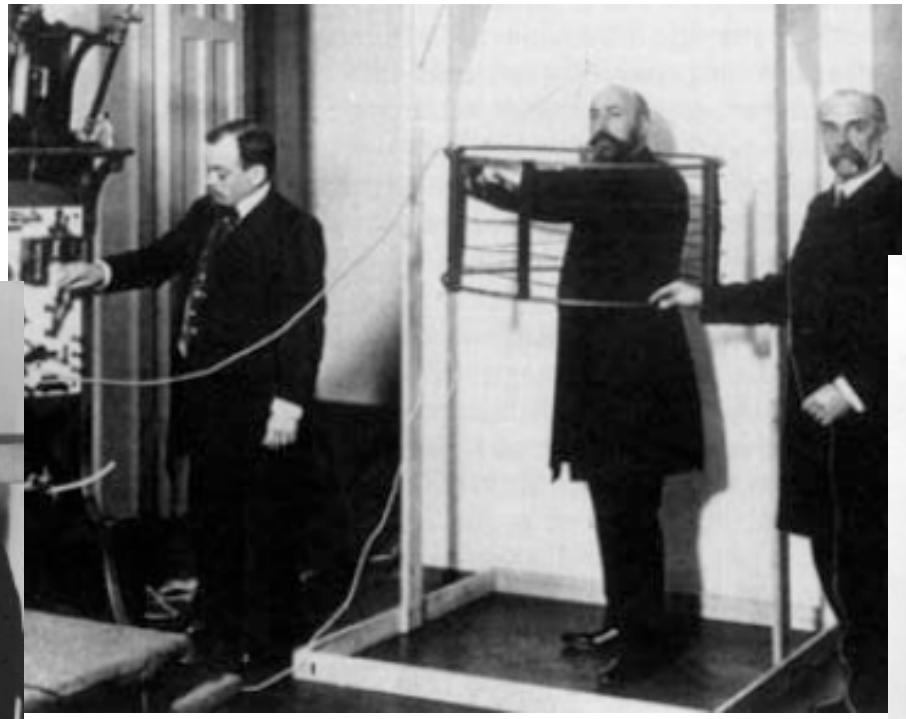
TMS n'est pas une idee nouvelle

Thompson (1896)



d'Arsonval (1896)

Magnussen & Stevens (1911)

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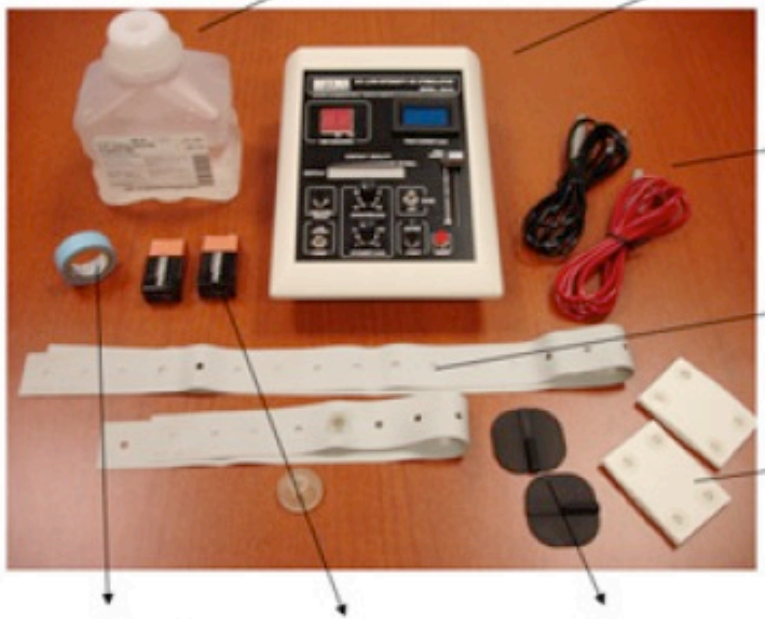
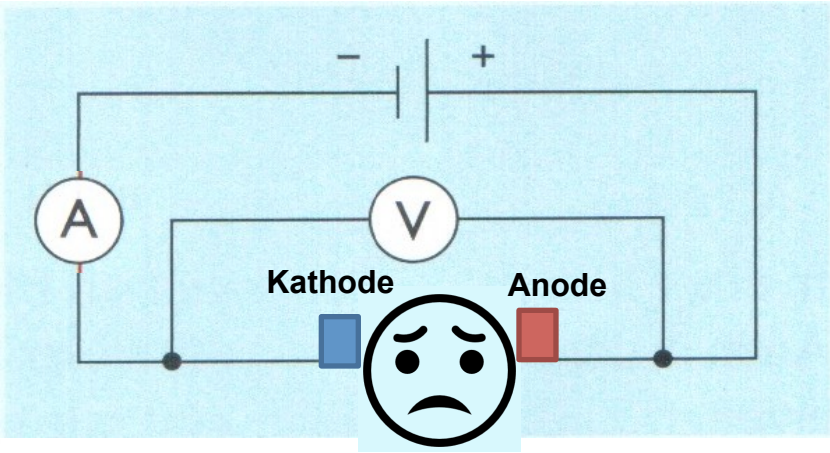
Le cerveaux en circuit aux courant continue (DC)

tDCS Toolkit





tDCS device:

- DC power source
- Ampère meter
- Volt meter

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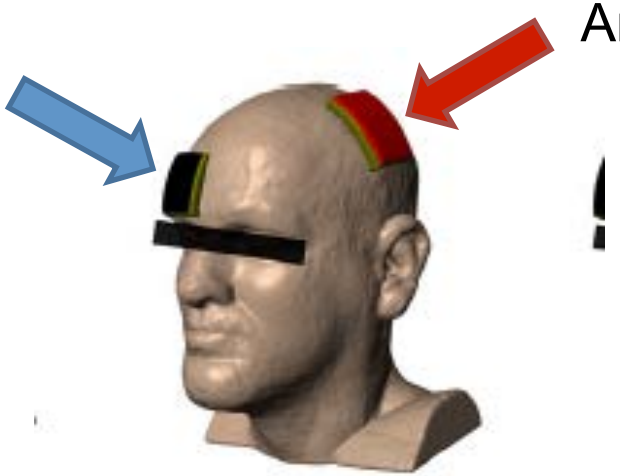
Stimulation au courant continue (tDCS)

Cathode (negative)

Anode (positive)



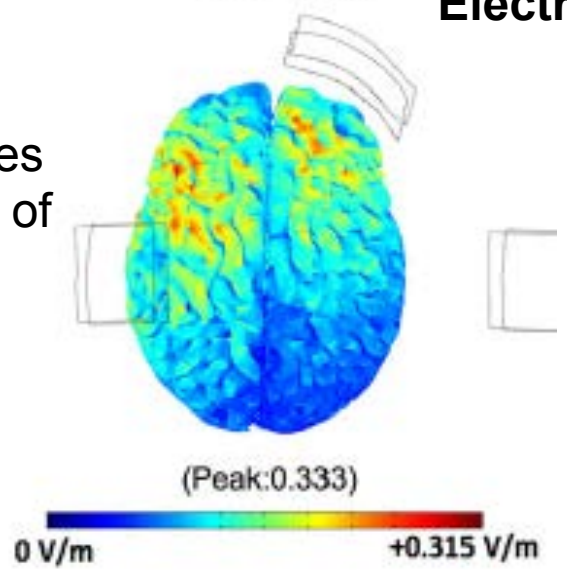
8.00 mm

Electrophysiological effects:

anodal tDCS ? excitatory

cathodal tDCS ? inhibitory

Static Electric field modulates resting membrane potential of neurons



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Visualiser les effects

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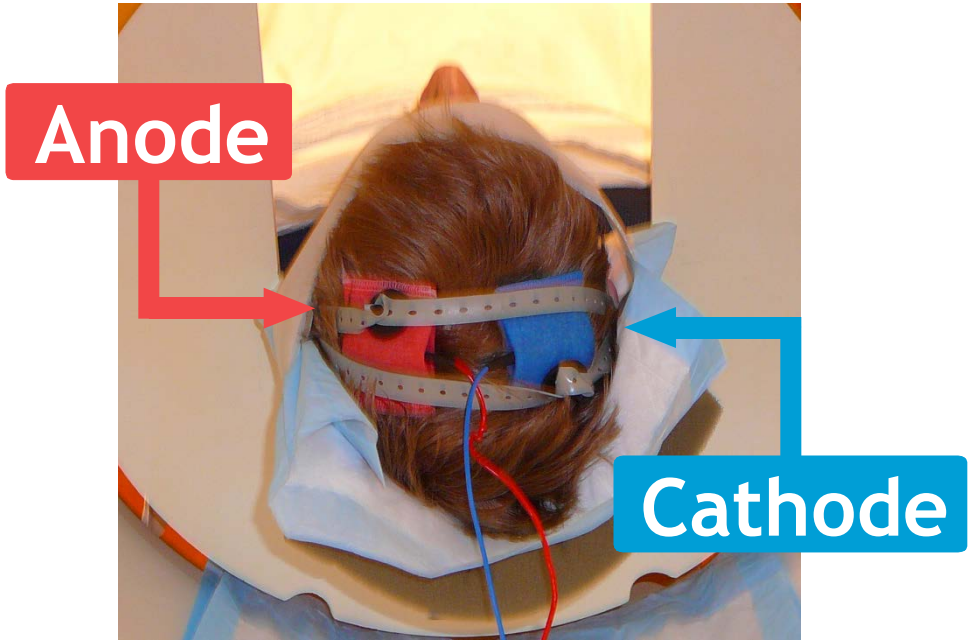


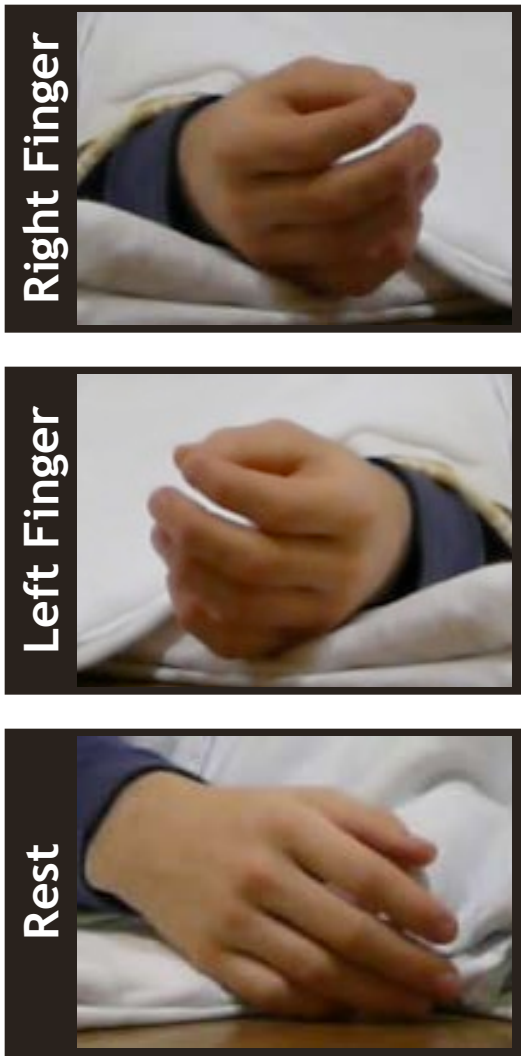
tDCS
stimulator

ON
(anodal + cathodal)

SHAM

Paquette et al 2011 JCBFM

Motor Task



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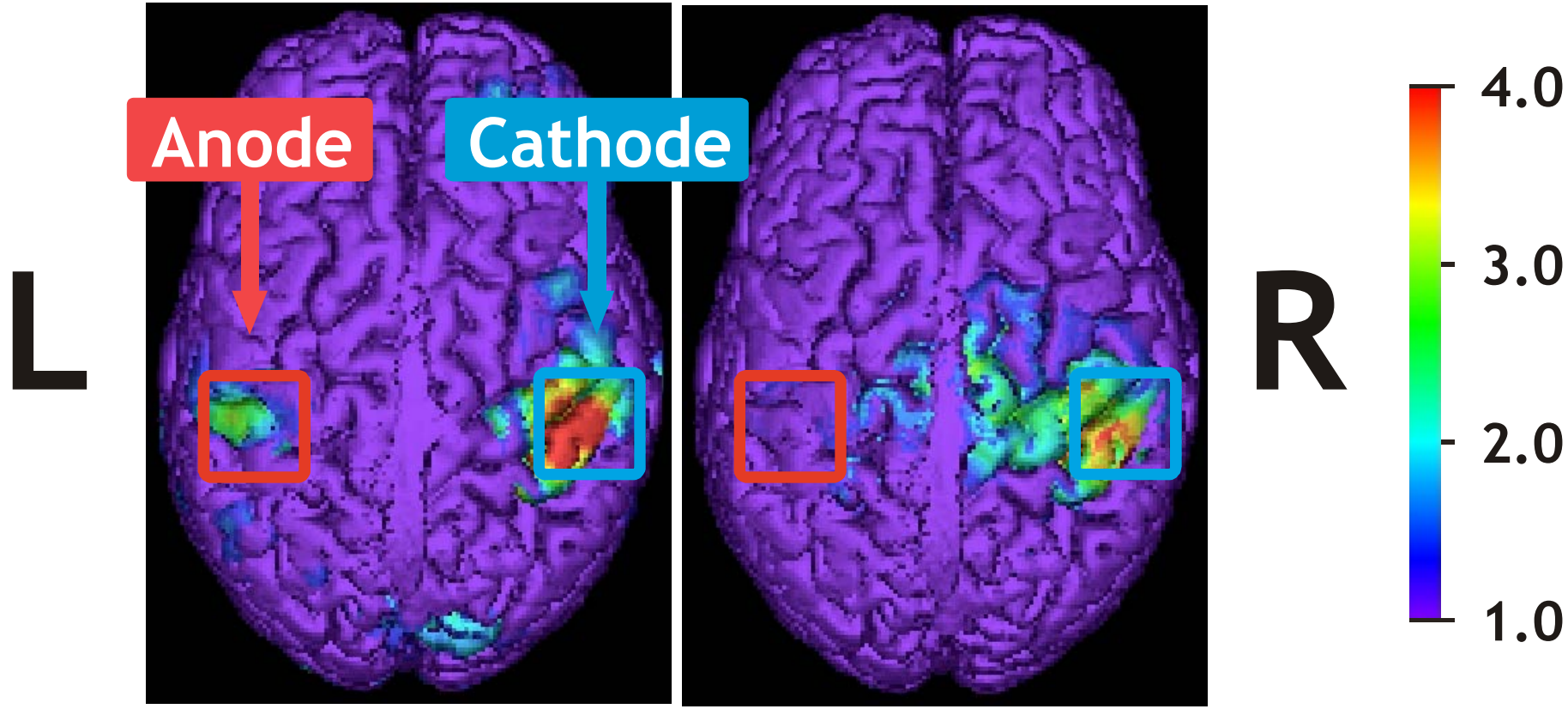
Cathodal tDCS stimulation decreases rCBF

LEFT Finger Movements

(RIGHT hemisphere activation)

Sham tDCS **tDCS**



Z-transformed difference image (vs. Rest Sham) in one typical subject

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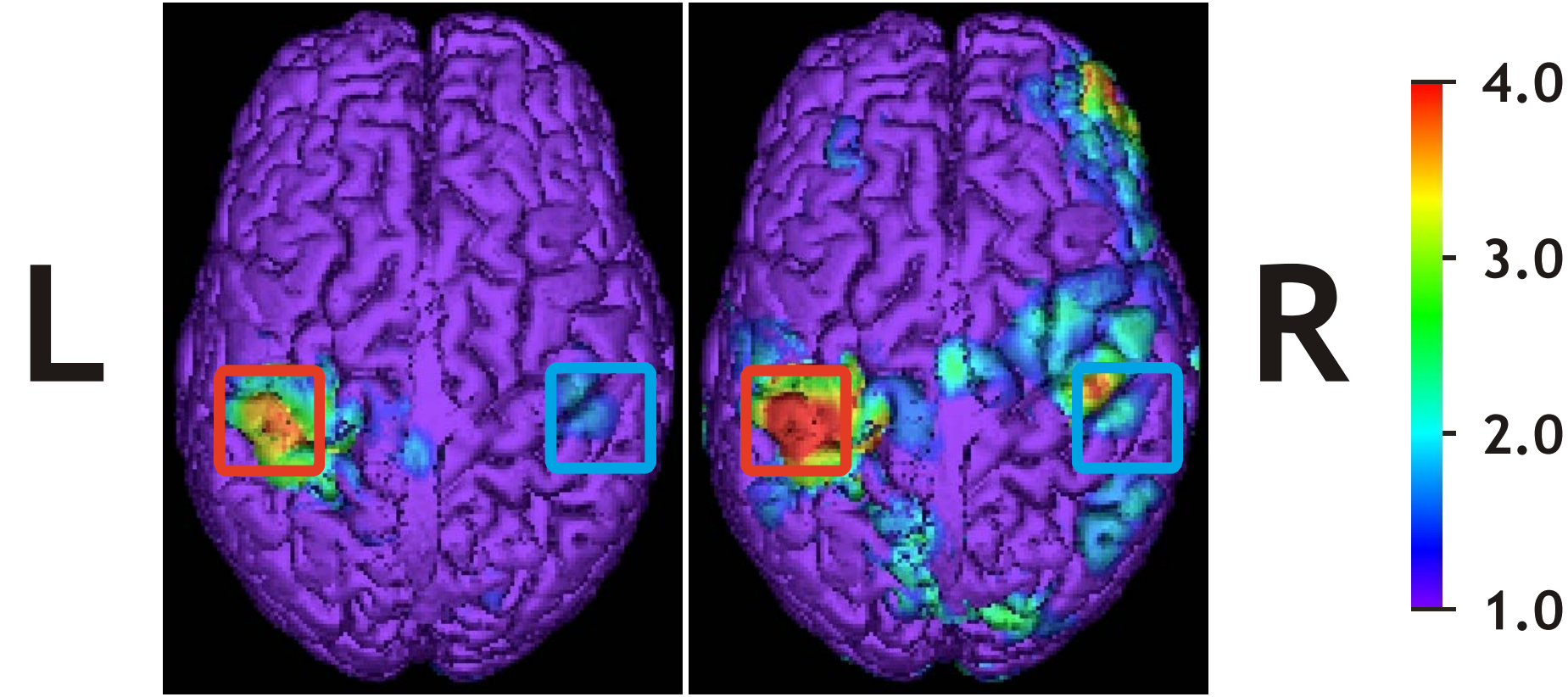
Anodal tDCS stimulation increases rCBF

RIGHT Finger Movements

(LEFT hemisphere activation)

Sham tDCS **tDCS**



Z-transformed difference image (vs. Rest Sham) in one typical subject

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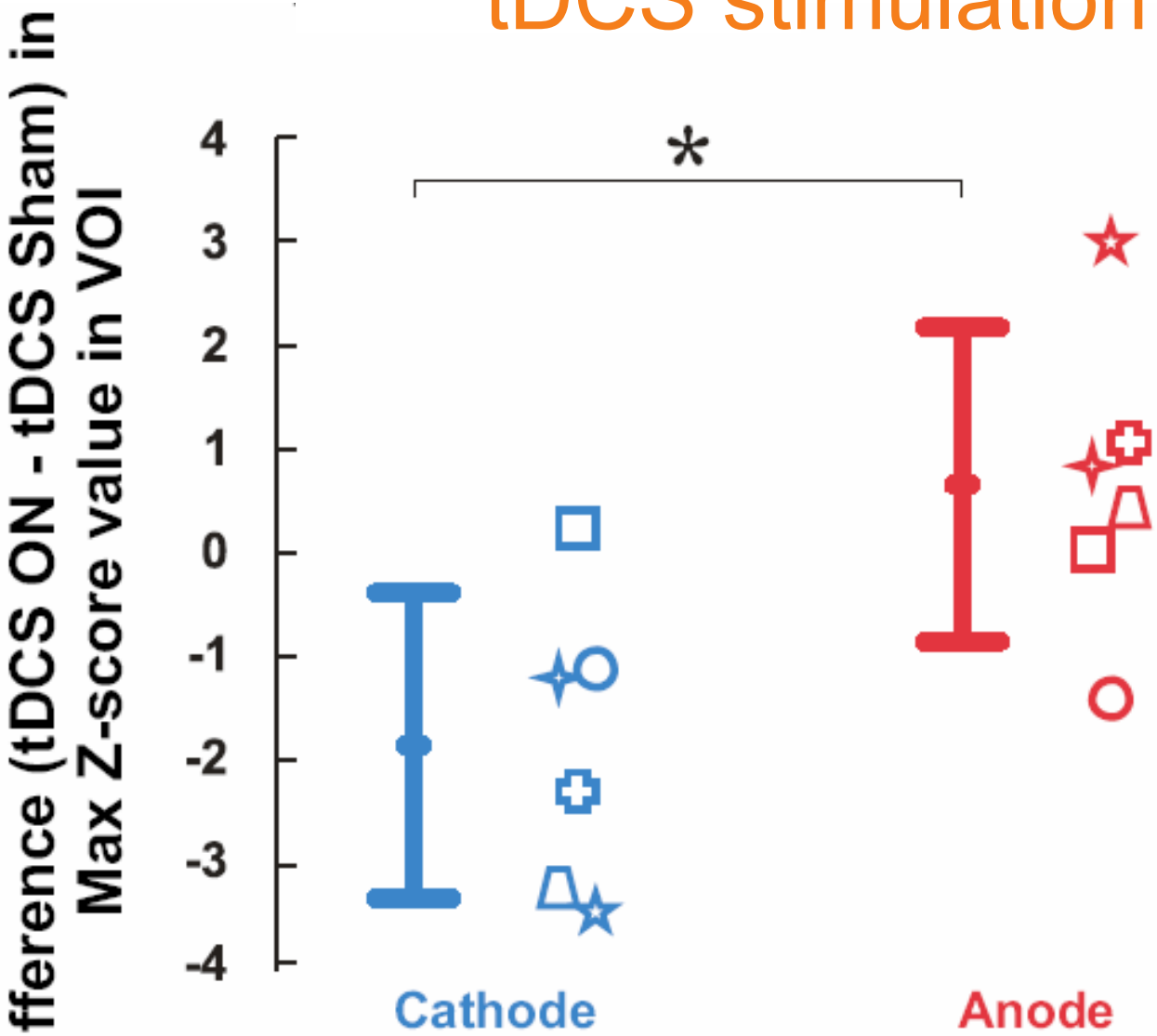
rCBF change during tDCS stimulation



* one-tailed paired T-test

- Decrease of 1.84 in Z-score with cathodal stimulation p=0.02
- Anodal stimulation did not reach significance

Mean +/- 1SD

Symbols represent individual subjects

Paquette et al 2011 JCBFM

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Les stimulateurs ….

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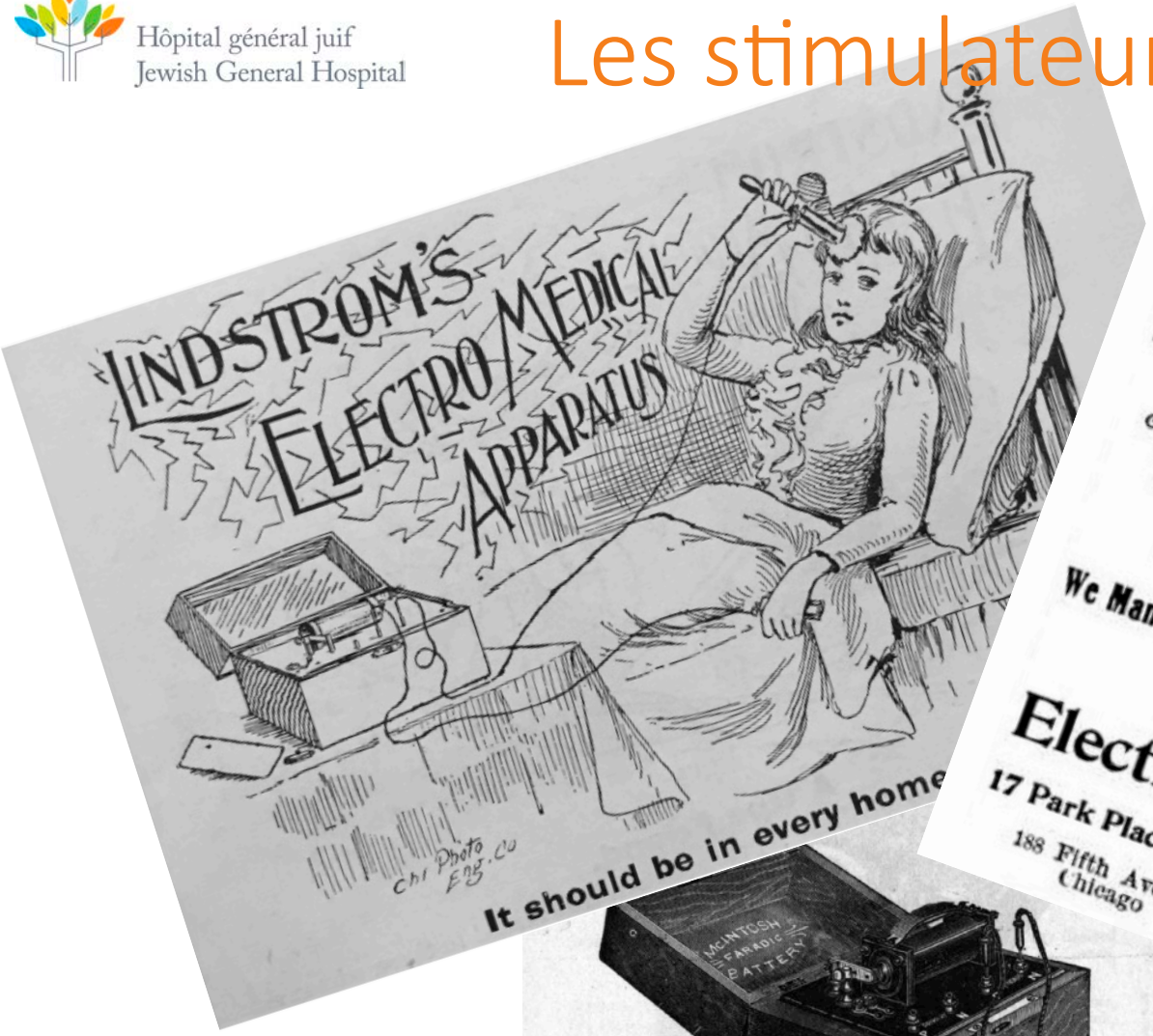

McINTOSH PHYSICIANS' FARADIC BATTERY.

Wexler, Brain Stimulation 10 (2017) 187e195

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… et accessoires

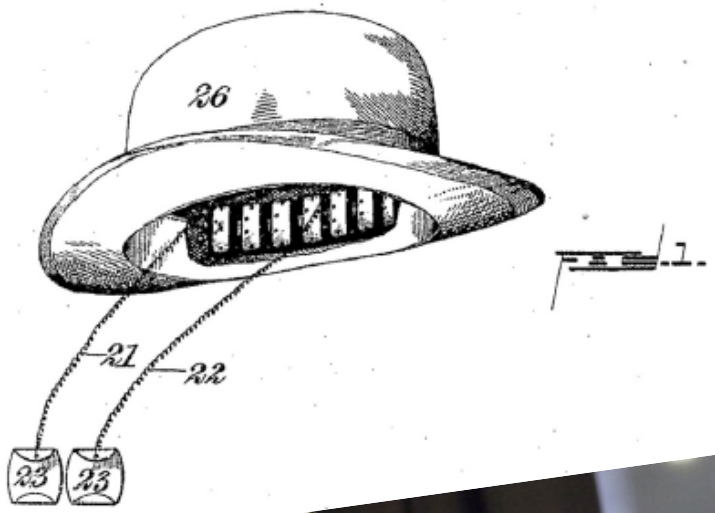
No. 765,530. PATENTED JULY 19, 1904.

G. F. WEBB.

MEDICAL BATTERY.

APPLICATION FILED MAY 3, 1904.

NO MODEL. 2 SHEETS—SHEET 1.



Wexler, Brain Stimulation 10 (2017) 187e195

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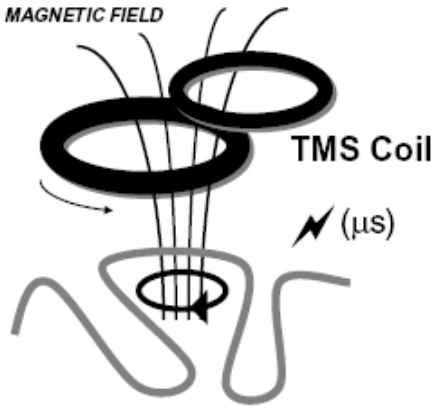
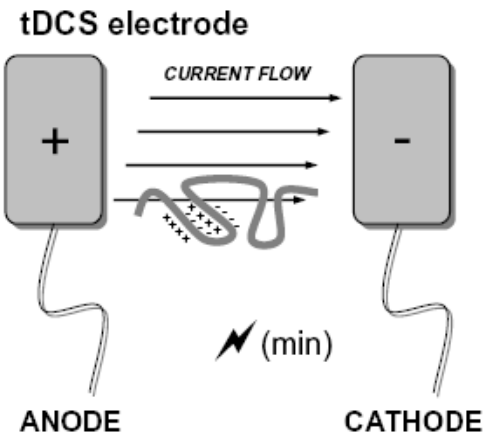
TMS vs. tDCS





Focal	Non-focal
Bobine (figure 8)	Grand electrodes (↓ densite de courrant)
Courrants hautes (~5 kA) et brefs (µs)	Courrant petit (1-2 mA) et longue duree (minutes)
Stimulation <u>avant</u> la therapie	Stimulation <u>pendant</u> la therapie
Possibilité des effets indésirables (convulsions)	Pas de effets indésirables

From Sparing & Mottaghy, Methods. (2008) 44:329-337.

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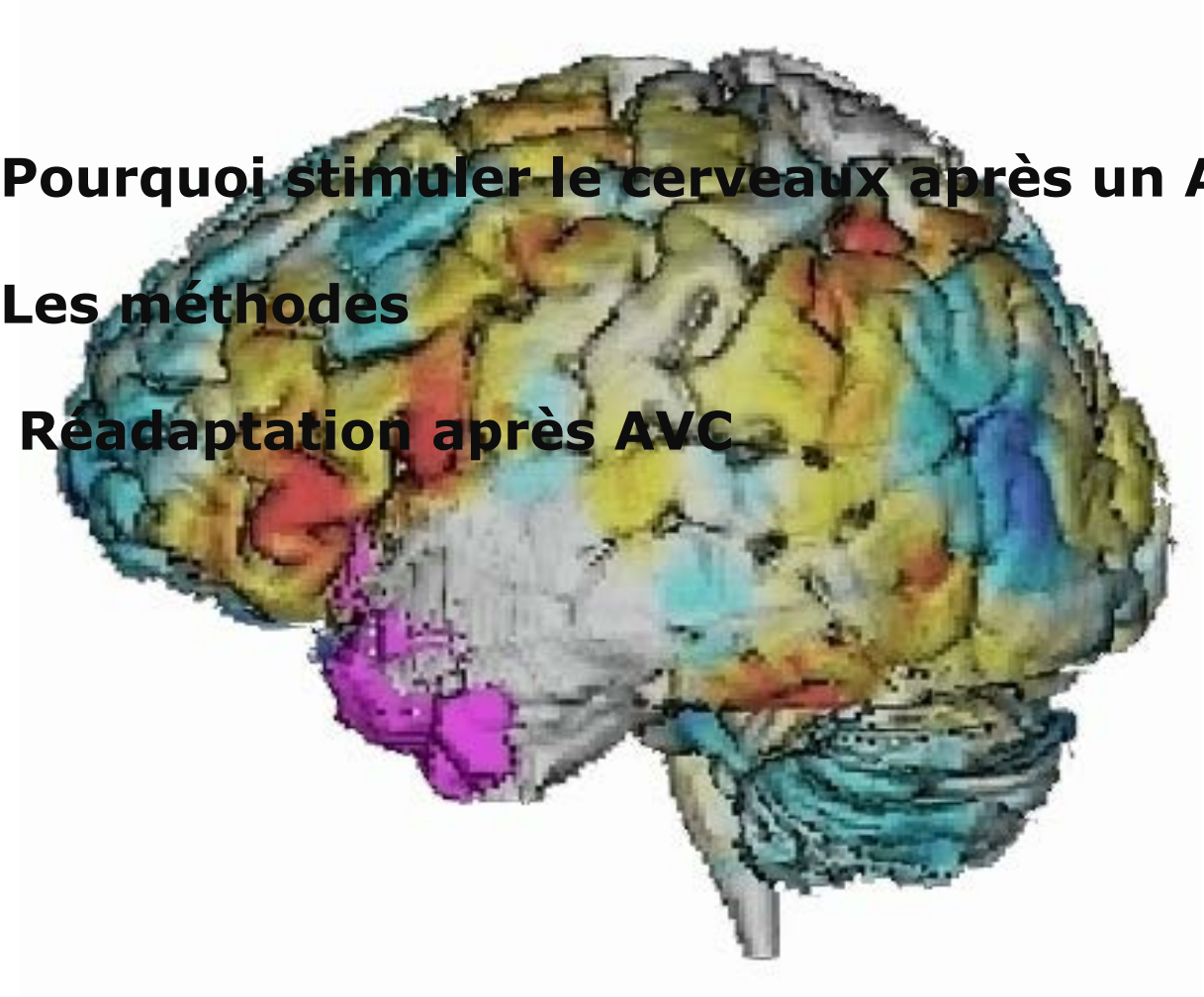

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Stimulation cérébrale pour déficits motrice

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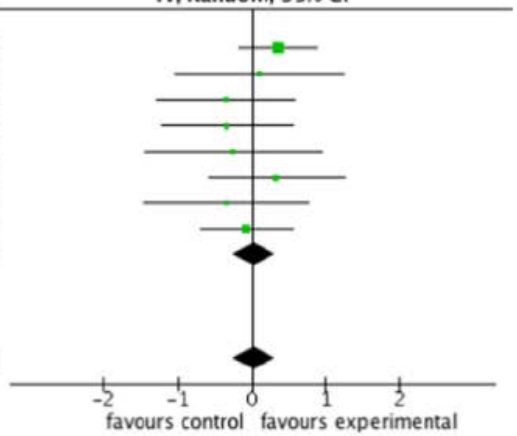
Essai d'une metaanlyse

Study or Subgroup	rTMS and exercise Mean	SD	Total	Sham rTMS and exercise Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.7.1 New Subgroup								
Abo et al., 2014	5.4	5.52	44	3.1	7.63	22	30.6%	0.36 [-0.15, 0.88]
Di Lazzaro et al., 2013	7.07	5.58	6	6.33	7.07	6	6.3%	0.11 [-1.03, 1.24]
Etoh et al., 2013	-0.5	10.59	9	3.5	11.37	9	9.3%	-0.35 [-1.28, 0.59]
Galvão et al., 2014	5.6	8.36	10	8.6	8.84	10	10.4%	-0.33 [-1.22, 0.55]
Higgins et al., 2013	5.5	16.74	6	10.2	19.36	5	5.7%	-0.24 [-1.43, 0.95]
Malcolm et al., 2007	4.8	5.76	9	1.9	9.87	10	9.8%	0.34 [-0.57, 1.25]
Pomeroy et al., 2007	5.2	11	6	10.25	15.9	7	6.7%	-0.34 [-1.44, 0.76]
Seniów et al., 2012	6.3	8.5	20	6.9	9.46	20	21.1%	-0.07 [-0.69, 0.55]
Subtotal (95% CI)			**110**			**89**	**100.0%**	**0.03 [-0.25, 0.32]**
Heterogeneity: Tau² = 0.00; Chi² = 4.04, df = 7 (P = 0.78); I² = 0%								
Test for overall effect: Z = 0.23 (P = 0.82)								
Total (95% CI)			**110**			**89**	**100.0%**	**0.03 [-0.25, 0.32]**
Heterogeneity: Tau² = 0.00; Chi² = 4.04, df = 7 (P = 0.78); I² = 0%								
Test for overall effect: Z = 0.23 (P = 0.82)								
Test for subgroup differences: Not applicable								



The standardized mean difference (SMD) and 95% confidence interval (CI)

études cliniques très hétérogène:

- aigue et chronique
- Paramètres de stimulation différents (240 – 1500 pulses)
- Mesures des résultats différents
- Physiothérapie différent

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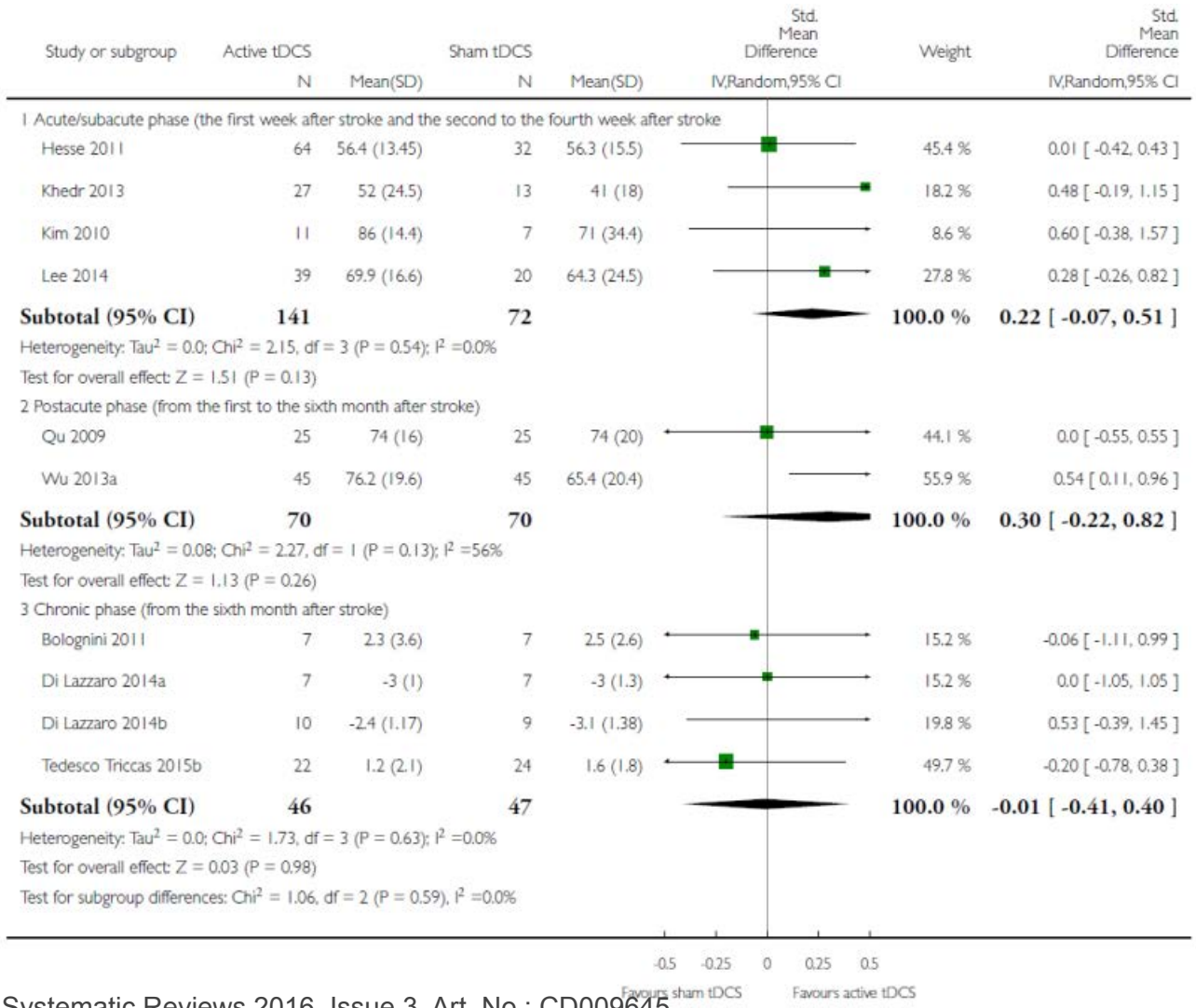
tDCS for motor rehabilitation

1-4 weeks

1-6 months

>6 months



Elsner, Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD009645.

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Ipsi- vs cotralateral

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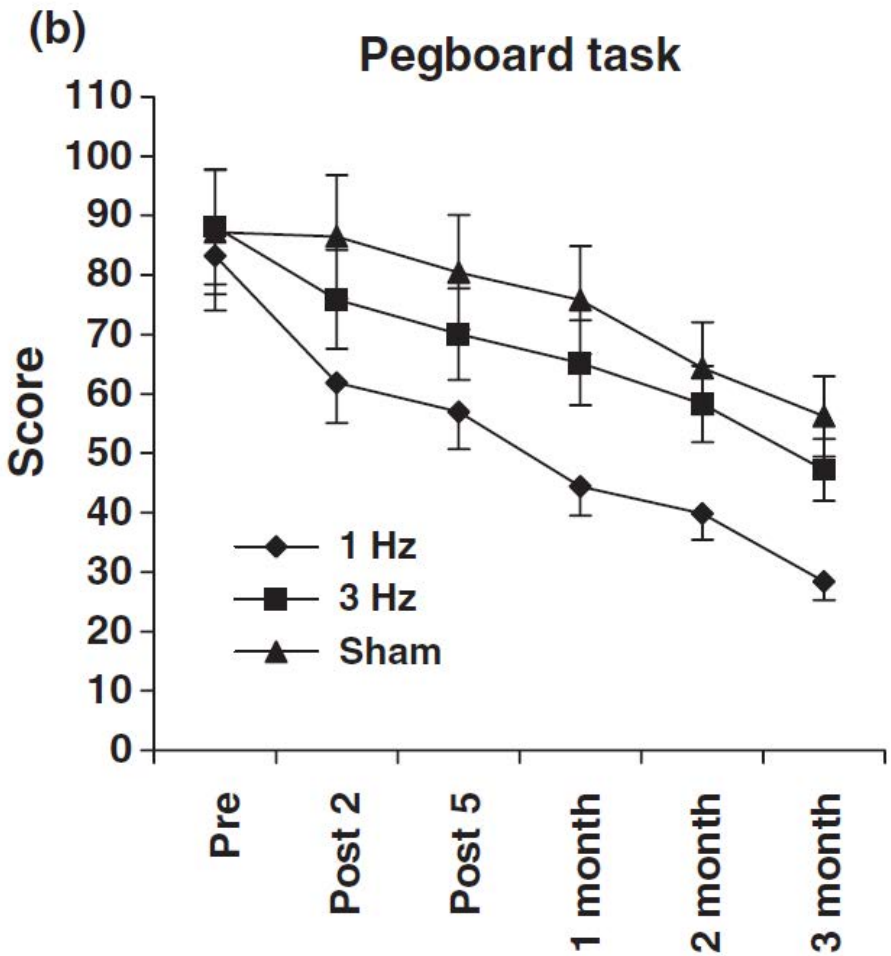

Acute stroke 7-20 days post onset

Kehder et al 2009 Eur. J. Neurol

In direct comparison, inhibitory TMS seems to be more effective. The early sessions seem to make a difference !

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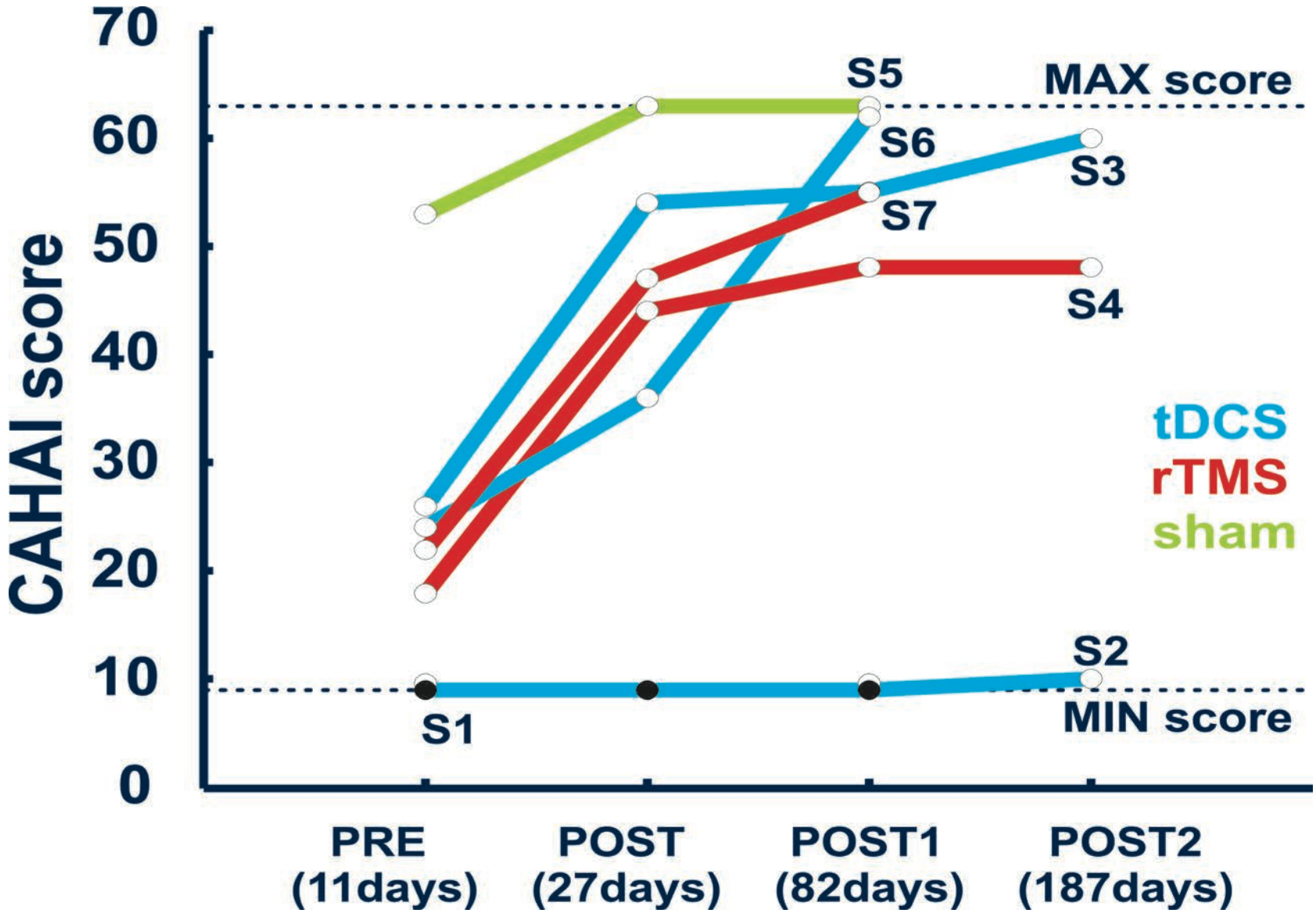

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rTMS pour traitement de l' aphasie

	Sham	TMS
N	14	15
Age (y)	69.0 (6.33)	68.5 (8.19)
Therapy onset (d)	50 .1 (23.96)	39.7 (18.43)
Therapy duration (d)	16.6 (2.06)	18.4 (5.32)
Infarct Volume (ccm)	21864 (22279)	23600 (17987)
Infarct location		
Anterior MCA	3	3
Posterior MCA	5	5
Subcortical	6	6
Aphasia Type		
Broca	4	2
Wernicke	4	8
Amnestic	4	3
Global	2	2

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Results (I)

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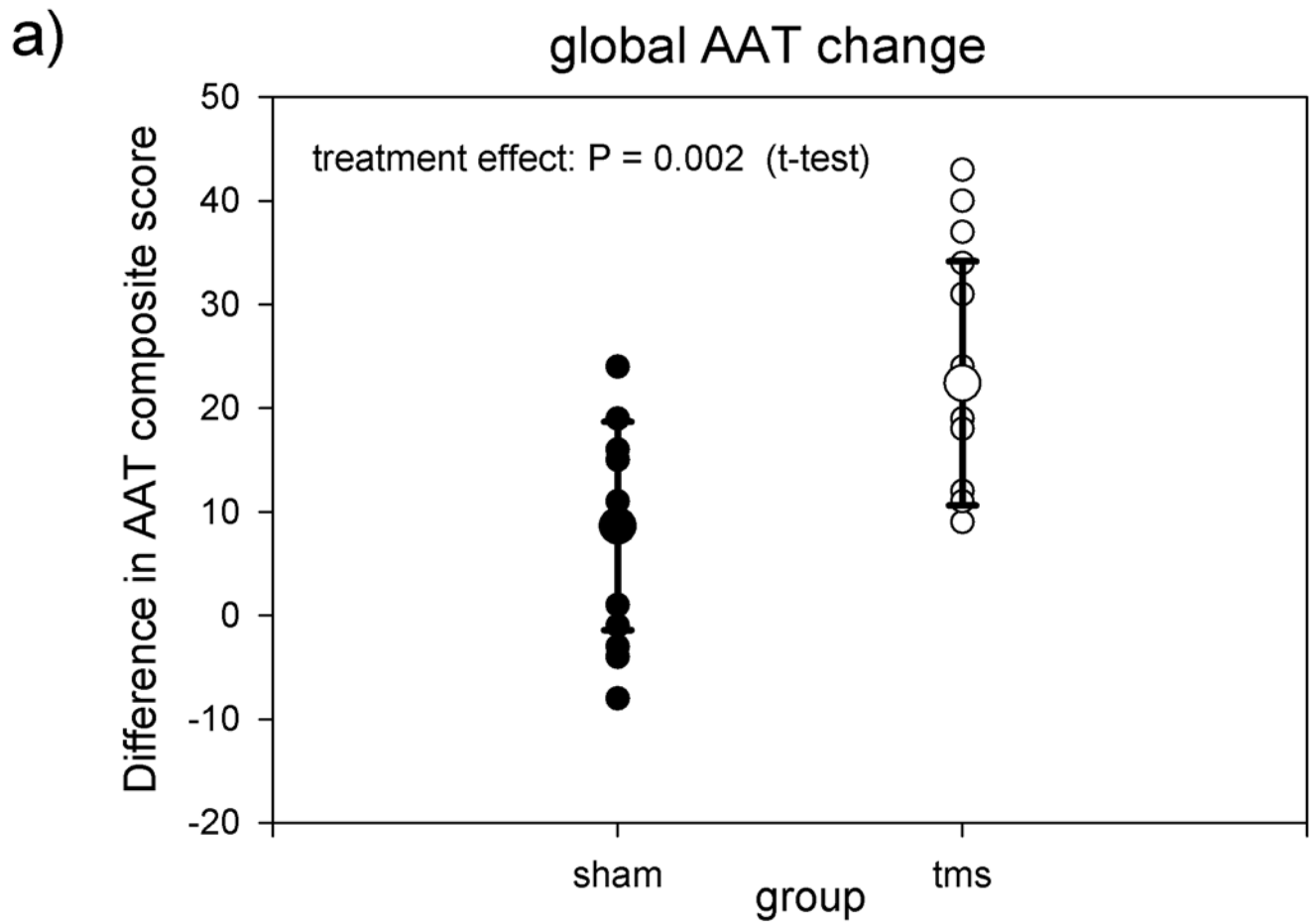
Overall treatment effect



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Results (II)

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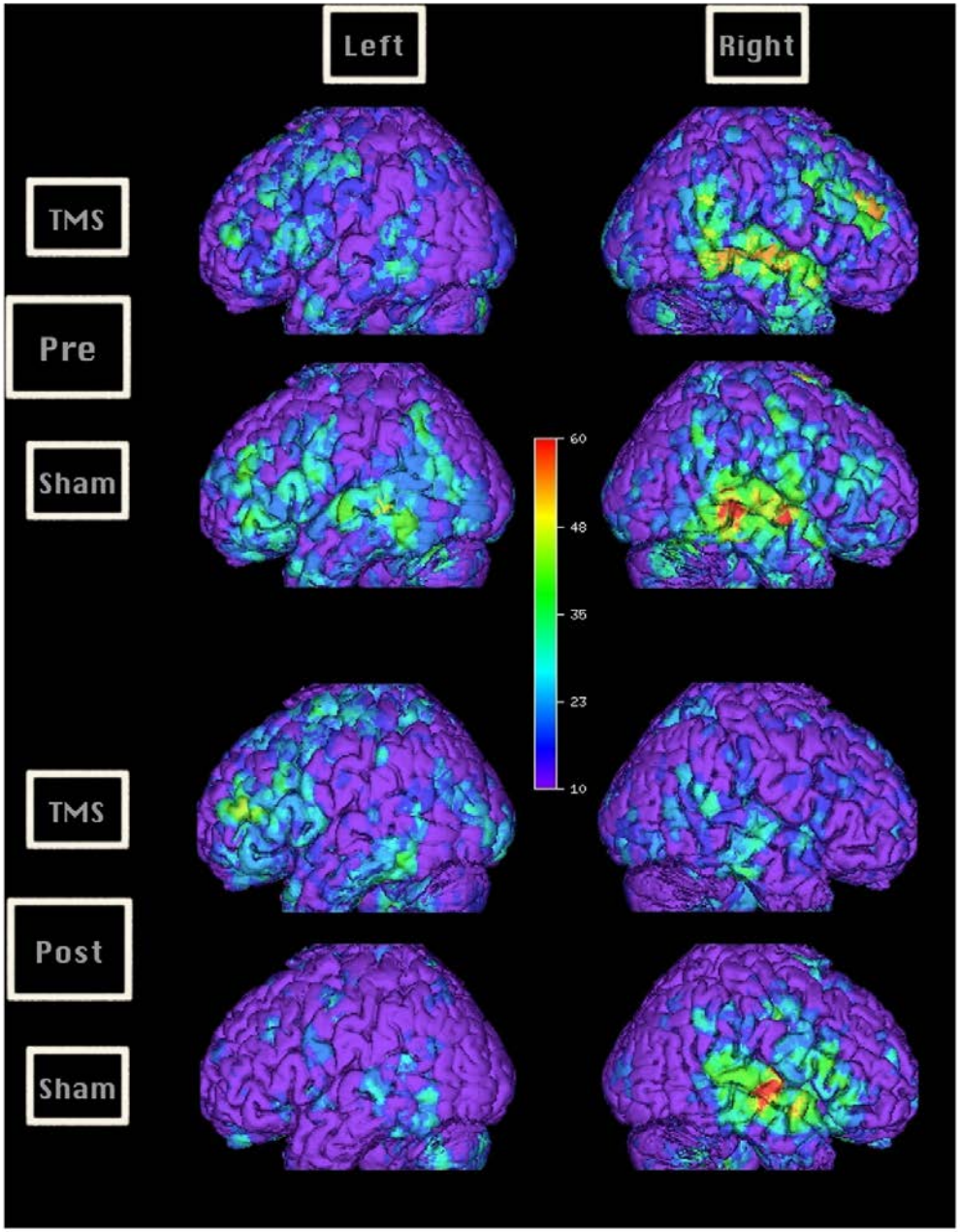

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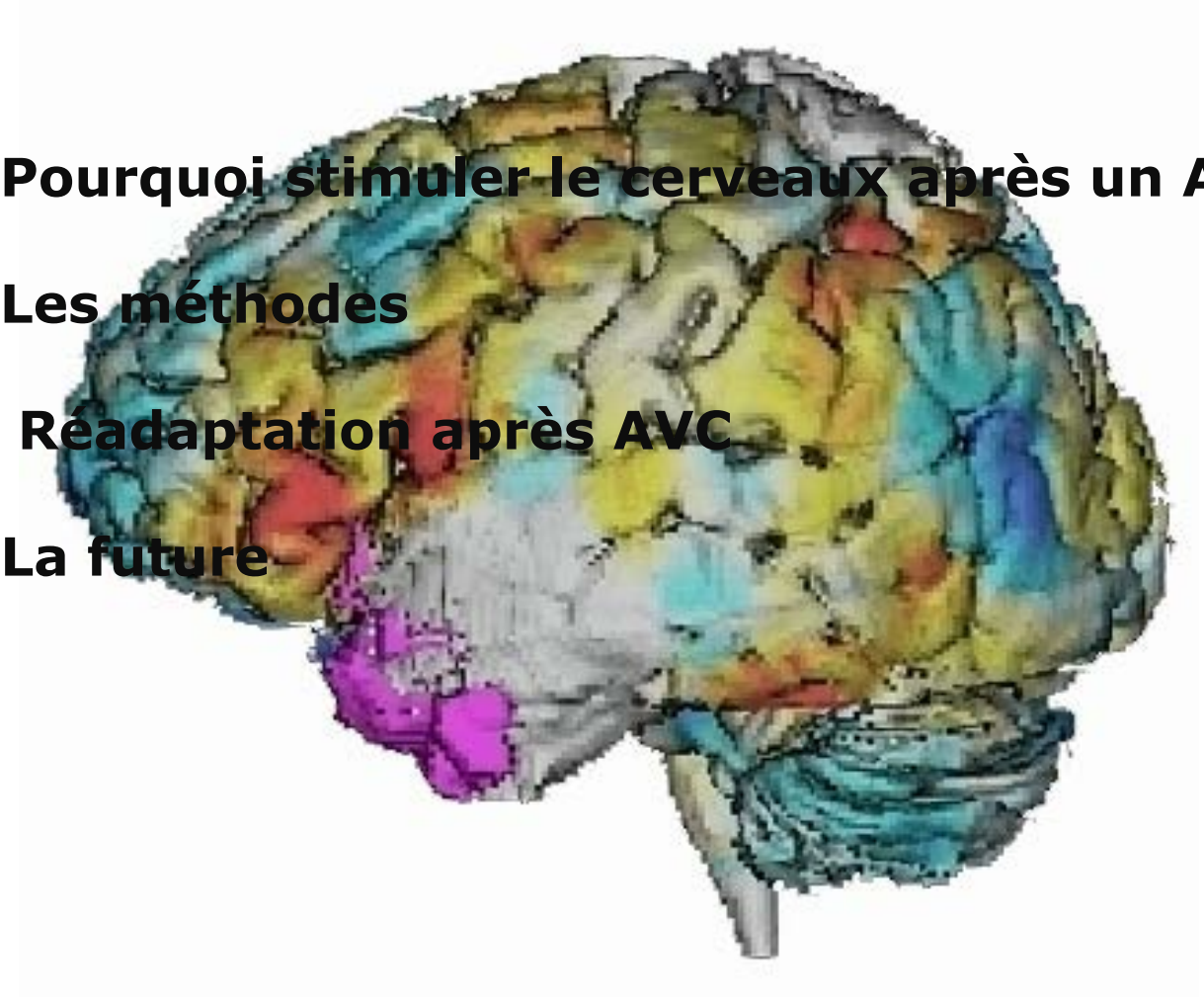

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La Future ? Les défis !

- **plus des essais en phase aigue**
- **standardiser les thérapies (phyiso, orthophonie)**
- **localisation de l' AVC**
- **plus de recherche systématique sur les paramètres de stimulation optimaux**
- **plus de recherche sur l'endroit de stimulation**
- **essais cliniques plus grands**

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CanStim

*Can*adian Platform for Trials in Non-Invasive Brain *Stim*ulation

Dr. Alexander Thiel & Dr. Jodi Edwards
For the CanStim Investigative Team

HEART & STROKE FOUNDATION
Canadian Partnership for Stroke Recovery

CSC CNC
Canadian Stroke Consortium
Consortium Neurovasculaire Canadien

CaSTOR Canadian Stroke Trials for Optimized Results